European Union Risk Assessment Report

CADMIUM OXIDE

CAS No: 1306-19-0

EINECS No: 215-146-2

RISK ASSESSMENT

GENERAL NOTE

This document contains two different volumes:

- **Volume 72** cadmium oxide and cadmium metal, **Part I Environment** (publication EUR 22919 ENV)
- **Volume 75** cadmium oxide, **Part II Human Health** (publication EUR 22766 EN)

European Chemicals Bureau

Institute for Health and Consumer Protection

European Chemicals Bureau

Existing Substances

European Union Risk Assessment Report

cadmium metal and cadmium oxide

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European Union Risk Assessment Report

CAS No: 1306-06-19 7440-43-9	EINECS No: 215-146-2 231-152-8

cadmium oxide and cadmium metal
Part I - environment

Cd

CdO

3rd Priority List

Volume: 72

EUROPEAN COMMISSION

EUR 22919 EN

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CADMIUM OXIDE AND CADMIUM METAL

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RISK ASSESSMENT

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RISK ASSESSMENT

Final Report, 2007

Belgium

This document has been prepared by Belgium on behalf of the European Union. The work has been prepared by the Federal Public Service Health, Food Chain Safety and Environment.

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Risk assessment: update based on recent site-specific exposure data regards all scenarios (except disposal)

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Final report:	**2007**

Foreword

We are pleased to present this Risk Assessment Report which is the result of in-depth work carried out by experts in one Member State, working in co-operation with their counterparts in the other Member States, the Commission Services, Industry and public interest groups.

The Risk Assessment was carried out in accordance with Council Regulation (EEC) 793/93[1] on the evaluation and control of the risks of "existing" substances. "Existing" substances are chemical substances in use within the European Community before September 1981 and listed in the European Inventory of Existing Commercial Chemical Substances. Regulation 793/93 provides a systematic framework for the evaluation of the risks to human health and the environment of these substances if they are produced or imported into the Community in volumes above 10 tonnes per year.

There are four overall stages in the Regulation for reducing the risks: data collection, priority setting, risk assessment and risk reduction. Data provided by Industry are used by Member States and the Commission services to determine the priority of the substances which need to be assessed. For each substance on a priority list, a Member State volunteers to act as "Rapporteur", undertaking the in-depth Risk Assessment and recommending a strategy to limit the risks of exposure to the substance, if necessary.

The methods for carrying out an in-depth Risk Assessment at Community level are laid down in Commission Regulation (EC) 1488/94[2], which is supported by a technical guidance document[3]. Normally, the "Rapporteur" and individual companies producing, importing and/or using the chemicals work closely together to develop a draft Risk Assessment Report, which is then presented at a meeting of Member State technical experts for endorsement. The Risk Assessment Report is then peer-reviewed by the Scientific Committee on Health and Environmental Risks (SCHER) which gives its opinion to the European Commission on the quality of the risk assessment.

If a Risk Assessment Report concludes that measures to reduce the risks of exposure to the substances are needed, beyond any measures which may already be in place, the next step in the process is for the "Rapporteur" to develop a proposal for a strategy to limit those risks.

The Risk Assessment Report is also presented to the Organisation for Economic Co-operation and Development as a contribution to the Chapter 19, Agenda 21 goals for evaluating chemicals, agreed at the United Nations Conference on Environment and Development, held in Rio de Janeiro in 1992 and confirmed in the Johannesburg Declaration on Sustainable Development at the World Summit on Sustainable Development, held in Johannesburg, South Africa in 2002.

This Risk Assessment improves our knowledge about the risks to human health and the environment from exposure to chemicals. We hope you will agree that the results of this in-depth study and intensive co-operation will make a worthwhile contribution to the Community objective of reducing the overall risks from exposure to chemicals.

Roland Schenkel
Director General
DG Joint Research Centre

Mogens Peter Carl
Director General
DG Environment

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[1] O.J. No L 084, 05/04/199 p.0001 – 0075

[2] O.J. No L 161, 29/06/1994 p. 0003 – 0011

[3] Technical Guidance Document, Part I – V, ISBN 92-827-801 [1234]

0 OVERALL RESULTS OF THE RISK ASSESSMENT[4]

0.1 General remark on the scope, the approach and the limitations of the study

The present document contains the semi-integration of three study reports that were started at different years and conducted over different time lines i.e. the so-called overall or global RAR, the targeted risk assessment on batteries ('TRAR') and the update risk assessment. The first and main report was started in 1997 and based essentially on exposure data from around 1996. Few years later the study on batteries was initiated as a separate investigation and exposure data are mainly from 1999/2000. This report was previously presented as a separate document, the TRAR, in Annex to the first report. Finally, an update assessment for the local scenarios was started end 2004 and based on site specific exposure data for the reference year 2002.

The structure of the present document still reflects to some degree the scope and content of each of these three studies and reports (see **Table 0.1**). More in particular, Section 2 (production volumes, uses) and 3 (i.e. Section 3.1 environmental exposure and Section 3.3 risk chracterisation) present the following general structure: first the subsections related to all production and use scenarios are given with the exception of those related to batteries and their further life-cycle. Then the subsections follow dedicated to the batteries' related issues (inclusive their waste management). Finally the subsections reporting update site-specific informations on all production, processing and use scenarios are given (thus the scenarios of the overall RAR and of the TRAR). However no disposal scenarios are included in this update.

The regional exposure assessment (see Section 3.1.3.4 and further) and the effect assessment (see Section 3.2) are common to all three studies and thus do not present the aforementioned substructure.

Table 0.1 Overview of the structure of the present document as composed of the three studies and reports related to the risk assessment of cadmium metal and cadmium oxide for the environment

Section : Current document	Content	Source document identification and its section
1.	General substance information	Global/overall RAR (1.)
2.1.1.	Production process	Global/overall RAR (2.1.1)
2.1.2	Production volume	Global/overall RAR (2.1.2)
2.1.2.1	Data for the reference year 1996	Global/overall RAR (2.1.2)
2.1.2.2	Update data (for the reference year 2002)	Update document (2.1.2)
2.2	Uses	
2.2.1	General overview	Global/overall RAR (2.1.3)
2.2.2	Batteries	TRAR (on/in batteries) (2.)
2.2.3	Update data (for the reference year 2002)	Update document (2.2.1)
2.3	Legislative control measures	Global/overall RAR (2.2)

Table 0.1 continued overleaf

4 Conclusion (i) There is a need for further information and/or testing.
Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.
Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Table 0.1 continued Overview of the structure of the present document as composed of the three studies and reports related to the risk assessment of cadmium metal and cadmium oxide for the environment.

Section: Current document	Content	Source document identification and its section
2.4	Voluntary control measures	Global/overall RAR (2.3)
2.5	Other supranational instruments	Global/overall RAR (2.4)
3.1	Environmental exposure	Global/overall RAR (3.1)
3.1.1	Methods and definitions	Global/overall RAR (3.1.1)
3.1.2	Emissions	Global/overall RAR (3.1.2)
3.1.2.1	Source of data	Global/overall RAR (3.1.2.1)
3.1.2.2	Emissions during production and use	Global/overall RAR (3.1.2.2)
3.1.2.2	Releases due to batteries' related scenarios	TRAR (on/in batteries) (3.1.2)
	Life cycle stage 1	TRAR on/in batteries (3.1.2.1)
	Life cycle stage 2	TRAR on/in batteries (3.1.2.2)
	Life cycle stage 3	TRAR on/in batteries (3.1.2.3)
	Life cycle stage 4	TRAR on/in batteries (3.1.2.4)
	Life cycle stage 5	TRAR on/in batteries (3.1.2.5)
	Summary	TRAR on/in batteries (3.1.2.6)
3.1.2.3	Releases based on update site-specific exposure data (reference year 2002)	Update document (3.1.1.1)
	Cd metal and CdO production	Update document (3.1.1.1.1)
	Release during processing and use	Update document (3.1.1.1.2&3)
	Releases during the production of other non-ferrous metals	Update document (3.1.1.1.4)
3.1.3		
3.1.3.1	Local exposure assessment: production, processing and use scenarios excl. those related to batteries	Global/overall RAR (3.1.2.3)
	Aquatic compartment	Global/overall RAR (3.1.2.3.1)
	Sediment	Global/overall RAR (3.1.2.3.2)
	Atmospheric compartment	Global/overall RAR (3.1.2.3.3)
	Terrestrial compartment	Global/overall RAR (3.1.2.3.4)
3.1.3.2	Local exposure assessment: batteries related scenarios	TRAR on/in batteries (3.1.3.2)
	Aquatic compartment	TRAR on/in batteries (3.1.3.2.1)
	Sediment	TRAR on/in batteries (3.1.3.2.1)
	Atmospheric compartment	TRAR on/in batteries (3.1.3.2.1)
	Aquatic compartment	TRAR on/in batteries (3.1.3.2.4)

Table 0.1 continued overleaf

Table 0.1 continued Overview of the structure of the present document as composed of the three studies and reports related to the risk assessment of cadmium metal and cadmium oxide for the environment.

Section : Current document	Content	Source document identification and its section
3.1.3.3	Local exposure assessment: update data (reference year 2002)	Update document
	Aquatic compartment: calculated PECs	Update document (3.1.2.1 and 3.1.2.2)
	Terrestrial compartment	Update document (3.1.3)
	Atmospheric compartment	Update document (3.1.4)
	Non compartment specific effects relevant to the food chain	Update document (3.1.5)
3.1.3.4	Regional and continental exposure assessment	Global/overall RAR (3.1.2.4)
	Regional and continental concentrations calculated according to TGD	Global/overall RAR (3.1.2.4.1)
	An alternative model predicting regional and continental concentrations in soils	Global/overall RAR (3.1.2.4.2)
	Measured regional data in the environment	Global/overall RAR (3.1.2.4.3)
3.2	Effects assessment	Global/overall RAR (3.2)
3.3	Risk characterisation	
3.3.1	Introduction	Global/overall RAR (3.3.1)
3.3.2	Risk characterisation for production and use (excluding batteries)	Global/overall RAR (3.3.2 to 3.3.6)
3.3.3	Risk characterisation for battery related life cycle steps	TRAR in batteries (3.3.1 to 3.3.4)
3.3.4	Risk characterisation for all scenarios: update data (year 2002)	Update document (3.3.1 to 3.3.4)
4	Human health	In separate document/report
5	Results	
5.1	Introduction	
5.2	Local level: current situation (updated for 2002)	Update document (4.2), TRAR (5.1) and global/overall RAR (5.2)
5.3	Local level: disposal step: future situation and/or sensitivity analysis	TRAR (5.2)
5.4	Regional level	Global/overall RAR (5.2) [TRAR (5.3)]

Important All references to ‘Global or overall RAR’, ‘TRAR in/on batteries’ and ‘Update document’ are references to the previously stand-alone source documents.

0.1.1 The so-called ‘global’ or ‘overall’ risk assessment on cadmium (based on data from around 1996)

This study is focused on assessing the risks of the two priority substances cadmium metal and cadmium oxide as foreseen under the Regulation 793/93/EEC, and thus especially during the production and the intentional use of these two specific substances.

Several other studies on ‘cadmium’ (generic) are dealing with other fields and/or compounds (e.g. the studies and reports performed in the framework of the Fertiliser Directive (76/116/EEC), the Cadmium Directive (91/338/EEC), the Ambient Air Directive, etc).

The present study does not cover all fields and all compounds and it is advised to consult the aforementioned studies for detailed (risk) assessment of these compounds in these fields.
The current study essentially covers the production of cadmium metal and cadmium oxide, the use of these substances in the production of stabilisers, pigments, alloys and plated products. Further down-stream uses are not or only limitedly included.

However, major attention is attributed to the most important application, i.e. batteries with the whole life-cycle covered, thus including the main waste management options (recycling, incineration and landfill). For more details on the scope and limitations of the latter study i.e. the so-called targeted risk assessment of cadmium (oxide) as used in batteries, reference is made to the NiCd batteries’ related (sub)sections. In addition to the standard current scenarios an attempt was made to include some future scenarios.

For the environment, at regional level, the inventory of anthropogenic cadmium emissions has attempted to include all cadmium sources, thus including emissions from fertilisers, sludge, waste incineration, other industrial activities, etc. Sources and data were retrieved from open literature and unpublished reports available at the time this section was most importantly revised (reporting year 2000, based mainly on data from the 90’s). Stormwater and combined sewer overflows, being identified as a significant Cd-source to the surface water, have not been quantified in this assessment and may not be entirely covered.

The risk of cadmium (oxide) to the marine environment is not assessed (it is judged inappropriate to apply freshwater chemistry and ecotoxicity thresholds to the marine environment).

Cadmium in fertilisers (where cadmium is present as an impurity of the phosphate nutrient) and the potential risk linked with the use of sewage sludge on arable land, is covered to the extent needed for an appropriate assessment of the indirect exposure pathway (i.e. the use of fertilisers and sewage sludge is taken into account at the regional and continental scale). For more detailed in-depth examination of the fertilisers’ topic, reference is made to the studies of national authorities and the EC reports made in that framework (see Legislative control measures in Section 2.3). The emissions from the rest of the sewage sludge (applications other than on arable land) could not be quantified.

As to the general assessment’s approach, it was, for several reasons, preferred to adopt the ‘total risk approach’ in contrast with the ‘added’ approach in (some) other risk assessments on metals under the Existing Substances’ Regulation.

In the total risk approach, the risk characterisation is performed on the ‘total cadmium’ concentrations in the environment, i.e. including the natural background and past anthropogenic (diffuse) input. As mentioned above, the anthropogenic sources are limited here by the context of the Regulation. Cadmium emissions of historic origin are taken into account for the soil and sediment compartment given the (very) long retention time of the substance (generic) in these compartments. The regional and continental risk characterisation for the environment is mainly based on measured data because of the limited predictive power of the exposure models at that scale.

More specifically, the following observations are made related to the environmental part of the present study. It should be born in mind that these findings are of the utmost importance in the development of an adequate risk reduction strategy.

It is estimated in the actual assessment that the emissions by cadmium(oxide) producing and using companies contribute only 3.8% to the total emissions of cadmium in water and 3.8% to total emissions to air. For water, the total EU emission by the Cd(O) producing and using plants is estimated at 1.5 tonnes/year (see **Table 3.155**). Emissions of other sources at regional level are estimated at > 39.2 tonnes/year (see **Table 3.155**: Cd EU emission data to water). Hence, it is concluded that the cadmium emission from the cadmium(oxide) industry only amounts to 3.8% (1.5 tonnes versus a total of 1.5 + 39.2 tonnes) of the total cadmium emission to surface water.

The total European emissions to air from all other sectors is estimated at > 124 tonnes Cd per year while the total EU cadmium(oxide) industry emission is estimated at 4.7 tonnes/year (approximately 3.8% of the total 124 + 4.7 tonnes emitted).

Total Cd emissions to agricultural soils are mainly related to P fertiliser application and are about 230 tonnes Cd year^{-1} (see **Table 3.156**). Additional net Cd sources are imported animal feed, sewage sludge and atmospheric deposition. The Cd deposition onto agricultural land, derived from Cd(O) production, processing and recycling is estimated to be 1.2 tonnes Cd year^{-1} (i.e. 4.7 tonnes Cd year^{-1} multiplied by 0.27, the fraction surface area that is agricultural soil).

The actual assessment assumes good waste practices by all cadmium(oxide) producers and users.

Some *future* scenarios are included in the assessment.

Related to the *arable soil* compartment (within Section 4 of the human part of the present study, in separate document):

A number of scenarios were developed to represent agricultural practices in the EU. Besides other input and output factors these scenarios relate to distinct uses of fertilisers. The impact of the food-chain being more critical for human than for the ecosystem, the assessment is limited to the derivation via food-chain modelling of the so-called critical soil cadmium concentration and the comparison of the predicted future soil concentrations with this threshold.

0.1.2 The so-called Targeted Risk Assessment on cadmium as used in batteries

This study previously presented as stand-alone document and shortly called TRAR on batteries, is focused on assessing the risks for the environment of cadmium as used in NiCd batteries over different life cycle stages such as manufacturing, recycling and disposal. Guidance on how to estimate the emissions from the waste disposal stage is not provided within the Technical Guidance Document (TGD, 1996). The revised TGD includes some sections on waste disposal but no specific guidance is given on how to quantify these emissions. A full assessment of cadmium from NiCd batteries from the waste life cycle stage is thus not included. This section gives an overview of the concern areas that have been assessed in the present TRAR/batteries' related (sub)sections and which areas that have not been dealt with, either because of lack of methodology or because those areas are regarded as being outside the scope of the study.

Emissions of the disposal phase were quantified for Municipal Solid Waste (MSW) landfills and MSW incinerators only where the contribution of sealed portable NiCd batteries to the waste stream have been considered. Industrial NiCd batteries, representing 20% of the cadmium used in NiCd batteries, are recycled and/or disposed off in industrial landfills. The emissions related to the disposal of industrial NiCd batteries i.e. via industrial landfills and hazardous waste incinerators are not addressed in this report.

Quantifying the specific cadmium emissions caused by landfills or incineration of NiCd batteries is hampered by the fact that available data on landfill and incineration emissions always represent the total emissions of cadmium containing materials present in the waste stream. Therefore the total cadmium emissions were calculated first. By using a specific allocation key specific contribution of NiCd batteries to the overall cadmium emission/risk could be quantified. Since waste management strategies may differ considerably between the Member States, due consideration is given to these differences by means of including several scenarios (with the extremes: 100% land-filling and 100% incineration).

Main emissions of cadmium from incineration of waste are expected to occur through air[5] and the disposal and/or re-use of incineration residues (bottom ash and fly ash). The re-use and/or land-filling of incineration residues may result in a long-term diffuse emission potentially contaminating groundwater, surface water and soil. Neither the delayed cadmium emissions of the re-use of incineration residues nor the impact of future expected increase in cadmium content of bottom ash and fly ash on the re-usability of these incineration residues have been quantified. The major environmental concerns associated with metals in landfills are usually related to the generation and eventual discharge of leachate into the environment. The risks associated with the discharge of these leachates in surface water have been quantified. The contamination of the groundwater compartment due to fugitive emissions of landfills has been quantified in this report but no risk characterisation on this compartment has been performed

If NiCd batteries cannot be collected efficaciously, the future cadmium content in the MSW is predicted to increase. The impact of this potential increase on future emissions has been assessed for MSW incineration only. The impact of a future change in the MSW composition on the composition of the leachate of a landfill could not be judged based on the current lack of knowledge and methodology. The contribution of NiCd batteries on the overall cadmium content is calculated for a worst case scenario where only 10% of the NiCd batteries is being collected and a scenario in which 75% of the NiCd batteries is being collected.

Within the approach used in the TRAR/batteries' related (sub)sections to estimate the cadmium emissions associated with waste management strategies such as land-filling and incinerations different assumptions have been made that lack validation due to the limited availability of data on this subject. Although due to this paucity of data it is sometimes difficult to really judge if all assumptions taken are indeed worst case, as a general premise it was tried to use reasonable worst case conditions (based on expert judgment) to perform the calculations . In other cases average values were used instead of worst case estimates in order to conserve the environmental realisms of the estimates. **Table 3.253** in Section 3.3.3.1 provides an overview of the assumptions and default values taken in this report and the associated level of conservatism introduced with them.

[5] Although a quantitative risk characterisation for exposure of organisms to airborne cadmium has not been done due to lack of useful data on the effects of airborn cadmium in environmental organisms, the (calculated) cadmium air emissions and concentrations of MSW incinerators are used in the risk assessment of man indirectly exposed via the environment (see Section 4 of the RAR in a separate document).

However, by means of a rudimentary sensitivity analysis an attempt was made to determine the key parameters having an effect on the overall results.

An overview of the different scenarios for the disposal phase investigated in the TRAR/batteries' related (sub)sections of this report is given in Section 5, **Figure 5.1**. The risk assessment for the waste life cycle step was made in a comparative way meaning that the risks of the total cadmium was compared with the risks of the total cadmium without NiCd batteries' contribution.

0.1.3 Update assessment for site-specific exposure data (reference year 2002)

The update report provides a re-assessment of the risks of the two priority substances cadmium metal and cadmium oxide on the basis of new emission information collected from cadmium and cadmium oxide production and processing industries (i.e. cadmium metal production, cadmium oxide production, production and recycling of NiCd batteries, production of cadmium containing pigments, production of cadmium containing stabilisers) for the reference year 2002. Concerning the use of Cd/CdO in alloys, plating and other uses, no update information was submitted to the Rapporteur.

Since the finalisation of the final overall Cd/CdO ENV RA report (July 2003) for submission to CSTEE, a number of updates were made regarding the identity of the producing facilities and the produced amounts of each of the priority substances. The number of Cd metal and Cd oxide producing plants reduced from 14 in 1996 to 4 in 2002. The total number of processing plants participating in the update exercise by submitting new exposure data was 13 compared to 23 in 1996. Next to the closures of companies in this time period and the stopping of cadmium-related processes, improvements in air and water emission measures have been made by several companies, resulting in a reduction of the total site emissions.

In the update document, re-assessments have been made of PEClocals for different environmental compartments on the basis of update emission information for specific sites. The PECs regional and the PNEC values were extracted from the overall Cd/CdO RAR (July 2005). All these updated values are included in the same integrated report under Section 3.2.

Environment

As a general remark it is important to stress the general scope and limitations of the present report (see above). Within this RAR no assessment could be done for the atmosphere or for the marine environment.

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

This conclusion applies to the assessment of:

- the local surface water at 1 Cd metal production site (site 1), and 4 processing (pigments production sites (A and C), plating and alloy) sites/scenarios. Both latter are generic scenarios ('Cd plating' and 'Cd alloys'). Local concentrations are based on modeling using standard default values and could possibly have been refined if substantial monitoring data would have been provided. Monitoring data are available for the Cd metal production site 1: these data indicate risk at background level but do not allow a judgment regarding potential additional risk caused by the site's operations.

- the local surface water at one NiCd batteries recycling site where modeled freshwater Cd concentrations exceed the $PNEC_{water}$. This risk would be removed if no assessment factor (i.e. 2 and reflecting most of the uncertainty) is applied in deriving the PNEC. Monitoring data are available for this site: these data indicate risk at background level but do not allow a judgment regarding potential additional risk caused by the site's operations.
- the modeled regional PEC of surface water has a risk factor of 0.6 using a mean K_p value for EU while the risk factor is 1.7 using a K_p value that is distinctly smaller than average. This suggests potential regional risk. However, it is proposed to use measured values for the risk characterization because of the uncertainties in the choice of the natural background (which is combined with the added concentration to derive the regional PEC) and in the coverage of the surface water with small K_p values. Monitoring data were collected for 13 EU countries (of the EU-16 surveyed) but limitation in data quality (detection limit, geographical coverage etc.) reduced this information to 7 countries (as proxy for regions) for which conclusions can be derived. The regional averages of 90^{th} percentiles of measured Cd concentrations of European rivers and lakes in these regions range from 0.0395 to 0.31 $\mu g\ L^{-1}$). The majority of regional averaged 90^{th} percentiles have a risk factor < 1 whereas these values are > 1 in the UK (based on a limited dataset of 1996) and the Walloon region of Belgium. Outliers have a large impact on the risk factors as, for example, 20 sites of the 728 investigated in the largest database of UK (data of 2003) determine risk in UK. The PNEC for water was derived with an assessment factor of 2 reflecting most of the uncertainties in the effects assessment. The Conclusions about risk in the regions mentioned are not affected by either in- or excluding this assessment factor. During the development of the RRS, decision about (possible) reduction measures has to take into account the information on potential cadmium emission sources in these regions. In order to better characterize the regional risks to surface water in part of the EU which have not been covered in this assessment (i.e. eastern and southern Europe are underrepresented in the entire dataset, because detection limits are often too high and because fractionation is often not reported) it might be useful to obtain more information for these regions. It may be that the foreseen monitoring actions under for example the Water Framework Directive will provide this information in the future.
- the local terrestrial compartment: there are potential risks at cadmium plating and alloy production sites.
- the regional terrestrial ecosystem: the 90^{th} percentiles of measured Cd concentrations of European soils have risk factors 0.43-1.56 (mean: 0.86; data from 6 EU countries). Regional risk for the terrestrial ecosystem cannot be excluded in one region (UK). However, it should be noted that the 90^{th} percentile for the UK (1.4 mg Cd/kg_{dw}) falls within the range of the proposed $PNEC_{soil}$ (1.15 – 3.2 mg Cd/kg_{dw}) based on ecotoxicity to soil microbial processes. Hence risk cannot be excluded but will depend on the magnitude of the assessment factor chosen (either 1 or 2, see Section 3.2.3.6.2) in the derivation of the $PNEC_{soil}$.
- the secondary poisoning (regional level) as measured soil Cd concentrations of European soils have risk factors 0.43-1.56 for poisoning to mammals (mean: 0.86; data from 6 EU countries). Regional risk for the terrestrial ecosystem cannot be excluded in one region (UK). The uncertainty surrounding the effects assessment, however, suggests that this is a borderline situation: the available information shows that literature data on Cd uptake in mammals dwelling in acid soils sensitively influences the effects assessment. If data on acid soils (pH < 4.2) are excluded from the effects assessment, a larger PNEC is obtained and risk in the UK would be excluded. That conclusion would only remove concern provided that the P90 value in UK does not refer to acid soils, which is unknown. This analysis is,

morover, qualitatively because there is no validated model to estimate risk to mammals along the entire range of soil pH.

- the wastewater treatment plants: as risk is predicted for the micro-organisms of the STP for the NiCd battery recycling plant (site 2) discharging its effluent to an off-site STP. Risk to on-site and off-site STP cannot be excluded for Cd plating and alloy industry.

Conclusion (i) There is a need for further information and/or testing.

For the aquatic compartment, there is a need for better information regarding the toxic effects of cadmium to aquatic organisms under low water hardness conditions.

In particular, information is required on:

- Cd toxicity testing in very soft waters (H below about 10mg $CaCO_3$/L). There are no data for the very soft waters and these areas may be unprotected by the proposed $PNEC_{water}$ for soft water (0.08 µg Cd/L).

For sediment[6], there is a need for further information regarding the bioavailability of cadmium in order to possibly refine the assessment at regional and local level.

In particular:

- the AVS and Organic Carbon normalisation should be further validated (see outcome of **conclusion (i)** program, see separate document: 'RAR Stage II')

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

This conclusion applies to the assessment of:

- the local surface water and sediment compartment for the CdO production site, for some NiCd batteries production sites (6 and 7) and one NiCd recycling site (site 2) because there are no emissions to water at these sites.
- the local surface water compartment for the Cd metal production site 6, NiCd battery producing sites (3 and 4), Cd pigments producing site B and all (two) Cd stabilizer production sites (X, Y) emitting to the aquatic compartment.
- the local surface water compartment for a hypothetical landfill currently releasing a leachate with 5 µg L^{-1} of cadmium directly or indirectly in the aquatic environment, and for current hypothetical incinerator (equipped with an on-site WWTP) discharging total Cd emissions in a river with a dilution factor of 100 to 1,000. Removal of NiCd batteries in the MSW has a negligible influence on the calculated risk ratios.
- no risk is predicted for the micro-organisms in the off-site STP for Cd stabilizer production site (X) discharging its effluents to a municipal STP, for the hypothetical landfill site discharging a leachate with a cadmium concentration of 5µg L^{-1} to a STP and for the hypothetical incinerator plant (equipped with an on-site WWTP) discharging to a STP.
- modeled local soil Cd concentrations for Cd metal production, CdO production and processing/user i.e. stabilizers and pigments production plants, NiCd batteries producing and recycling plants and hypothetical MSW incineration plant (equipped with an on-site

[6] After the TMIV'02 last visit discussion on cadmium in sediment a number of MSs (UK, FR, DE) and Industry commented on the sediment assessment and the current conclusions drawn in line with the outcome of that last TM (for more details, see effects assessment and risk characterisation).

WWTP) (10 years aerial deposition) indicate no risks neither for the terrestrial compartment nor for secondary poisoning.

- modeled regional soil Cd concentrations that include natural soil, industrial soil and 8 different agricultural scenario's are all below the $PNEC_{soil}$. All these modeled values are total concentrations that are expected after 60 years (agricultural soils) or far beyond that (natural and industrial soils) with current regional emissions to soil. The starting concentrations are EU average values for the ambient concentrations. If 90th percentiles of measured concentrations would have been used in such calculations, then risk cannot be excluded.
- secondary poisoning as field data (body burden: kidney and liver Cd data) of birds (excluding pelagic birds[7]) do not indicate Cd poisoning, even in top predators. No risk to mammals is predicted from modeled regional soil Cd concentrations.

[7] no risk characterisation of marine environments was made in this report

CONTENTS

EUSES Calculations can be viewed as part of the report at the website of the European Chemicals Bureau: http://ecb.jrc.it

TABLES

1 GENERAL SUBSTANCE INFORMATION

As much of the (eco)toxicological information on Cadmium metal is derived from Cadmium oxide (and other cadmium compounds), and as a close relationship exists between both priority substances (see mass-balance) it was proposed that both RARs should be merged for the sections 1 to 4 with exception of the risk characterisation in the Human Health part where for each substance a separate section on risk characterisation and conclusions should be developed.

Primary source of information for this section and more particularly Sections 1.1, 1.2 and 1.3, was the 'IUCLID' document provided by Industry (Lead-company) in 1997 as a background document and complement to the HEDSETs.

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS-n°:	7440-43-9	1306-19-0
EINECS-n°:	231-152-8	215-146-2
IUPAC name:	Cadmium metal	Cadmium oxide
Synonyms:	Not applicable	Not applicable
Molecular formula:	Cd	CdO
Atomic/Molecular weight:	112.41 (several naturally-occurring isotopes ranging from 106-116 (Lexicon, 1972; WHO, 1992)	128.41
Colour	blue-white (Sax and Lewis, in: ATSDR, 1998)	varies from greenish-yellow through brown to nearly black, depending on the thermal history (due to lattice defects) and on the particle size

1.2 PURITY/IMPURITIES, ADDITIVES

	Cadmium metal	Cadmium oxide
Purity (powder):	Min. 99.9%	min. 99.999% (IUCLID, 1997)
Purity (massive):	Min. 99.99%	
Impurities (max.):	for 99.99% Cd metal: Fe: 10 ppm; Cu: 20 ppm; Ni: 10 ppm; Pb: 100 ppm; Zn: 30 ppm, Th: 35 ppm. Other levels are specified for other purity grades. (ASTM B440-00)	n.a. powder reagent grade: max. chloride 0,002%; nitrate 0,01%; sulphate 0,20%; copper 0,005%; iron 0,002%; lead 0,01% (JT Baker chemical Co, 1984)
Additives:	none	none

Remark: It is stated that the purity levels and chemical analyses indicated here are purely arbitrary as many grades of both cadmium metal and cadmium oxide exist. It is recommended that the ranges or specifications should be listed using the appropriate ISO or EN standards (ICdA, com. 2003). However, only the ASTM standard was provided for Cd metal grades 99.95, 99.99 and 99.995%.

1.3 PHYSICO-CHEMICAL PROPERTIES

Table 1.1 Summary of physico-chemical properties

Property	Cadmium metal	Cadmium oxide
Physical state:	solid (massive or powder)	solid (powder)
Crystal structure:	distorted hexagonal close-packed	cubic structure with each ion surrounded by six ions of opposite electric charge, octahedrally arranged. Also an amorphous form exists: stable at lower temperatures, forming crystals of the cubic type at red heat
Melting point:	320,9°C (Lexicon, 1972, Sax and Lewis: in ATSDR, 1998;CRC: in IUCLID, 1997)	Decomposes at 900-1000 °C (CRC, 1985; IUCLID, 1997)
Boiling point:	765°C (idem); 767°C (Sax and Lewis: in ATSDR, 1998)	CdO is non-fusible but volatilises at high temperature. Sublimation at 1559°C
Relative density:	8.64 g/cm^3 (Lexicon, 1972, Sax and Lewis: in ATSDR, 1998: analysis by WIAUX S.A., in LISEC, 1998e).	8.15 g/cm^3 (cubic form); 6.95 g/cm^3 (amorphous) (EPA 1985).
Vapour pressure:	1 mmHg at 394°C (Sax and Lewis: in ATSDR, 1998 133 hPa at 394°C (CRC, in: IUCLID, 1997)	1 mmHg at 1000°C (Sax, N.I., 1984)
Water solubility:	quoted as 'insoluble' (The Merck index; in: ATSDR, 1998; CRC, in: IUCLID, 1997). However it was mentioned: 0,05 mg/1 at pH 10,5 a curve in function of pH and hardness: at pH 7: solubility is 10 to 100 times higher than at pH 8.5 dependent on the total carbonate concentration (M. Farnsworth, 1980). Measured dissolved cadmium concentrations after 7 days transformation/dissolution test with cadmium metal powder at loading 1 – 100 mg/l, were in the range 0.192 – 0.135 mg/l (at pH +/- 8) (LISEC, 1998e).	quoted as 'insoluble' However measured dissolved cadmium concentrations after 7 days transformation/dissolution test with cadmium oxide powder at loading 1 – 100 mg/l were in the range 0.095 – 0.227 mg/l (at pH +/- 8) (LISEC, 1998f). Soluble in acids and solutions of ammonium salts (Farnsworth, 1980).
Partition coefficient:	No data	No data

Table 1.1 continued overleaf

Table 1.1 continued Summary of physico-chemical properties

Property	Cadmium metal	Cadmium oxide
n-octanol/water(log-value):	Not applicable	Not applicable
Flammability:	Slight fire hazard. The finely divided metal may be pyrophoric in air (MSDS, 1992; IUCLID, 1997)* GLP testing conform EC Testing methods A.10, A.12 and A.13 (BAM, 2002): Cadmium metal 'powder' [particle size distribution (in volume-%): d(0.1): 3.462µm; d(0.5): 7.154 µm; d(0.9): 14.117 µm; mean water content: 0.03] and cadmium 'fine billes' [particle size distribution (in volume-%): d(0.1): 2.485µm; d(0.5): 7.040µm; d(0.9): 15.753µm; mean water content: 0.05] are not flammable and do not have pyrophoric properties in sense of the EC-methods, Dir. 92/69/EEC.	Not flammable
Explosive properties:	Dust/air mixture may be explosive. Even as fine powder, cadmium is hardly explosive (MSDS, 1992; INRS, 1987)	
Self-ignition:	Not applicable	Not applicable
Oxidising properties:	Not applicable	Not applicable
Granulometry:	The average spherical diameter of cadmium powder prepared by distillation is about 18 µm +/- 13.3 µm (S.D.) (inhalable fraction) and the specific surface area : 580.4 cm2/g (analysis by WIAUX S.A., in: LISEC, 1998e). Particle size and surface area depend very much upon the specific process and specific application. For example, INMETCO produces a cadmium metal shot which is many times larger than the aforementioned cadmium metal powder (ICdA, com. 2003). See also remark related to flammability testing.	The average spherical diameter of CdO powder prepared by oxidation of Cd metal is about 0.55 µm (respirable fraction) (La Floridienne, 1997). Particle size and surface area depend very much upon the specific process and specific application (ICdA, com. 2003).

Table 1.1 continued overleaf

Table 1.1 continued Summary of physico-chemical properties

Property	Cadmium metal	Cadmium oxide
Odour threshold:	No data	No data
Ionisation potential:	E°Cd/Cd2+ = 0.4025 eV (= fairly reactive)	
Caloric value	0.16 Cal/g	

GLP testing on flammability and pyrophoric properties of the products, Cadmium metal powder and Cadmium 'fine billes' according to the EC Methods A.10, A.12 and A.13 was performed by Industry (ICdA) on a voluntary basis (final report of BAM, October 2002). The substances are not flammable and do not have pyrophoric properties in sense of the EC-methods, Dir. 92/69/EEC and are thus not to be classified (and labelled) related to these properties.
The grade Cadmium 'fines billes' is stated as being the finest grade of Cadmium 'powder' from current EU manufacturing that is put on the market (since 2001). However, other qualities may be manufactured elsewhere e.g. in Japan and China (ICdA, pers. com. 2003).
The physical, thermal, electrical, magnetic, optical, and nuclear properties of cadmium metal are summarised by Morrow (2001), however without indication of testing specifications or the primary source. Where available, this source confirms the aforementioned entries for physico-chemical properties.

1.4 CLASSIFICATION

According to Annex I of Directive 67/548/EEC (29th ATP) of 16/06/2004.

Cadmium metal and oxide

Classification

Carc. Cat. 2; R45	Category 2 Carcinogen; May cause cancer
Muta. Cat. 3; R68	Category 3 Mutagen; Possible risks of irreversible effects.
Repr. Cat. 3; R62-63	Category 3 Toxic to Reproduction; Possible risk of impaired fertility, and of harm to the unborn child
T; R48/23/25	Toxic: danger of serious damage to health by prolonged exposure through inhalation and if swallowed
T+; R26	Very toxic by inhalation
N; R50-53	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Labelling

T+; N

R: 45-26-48/23/25-62-63-68-50/53

S: 53-45-60-61

1.4.1.1 Note on environmental classification and labelling

A general introduction and description of the methodology on classification and labelling of insoluble and sparingly soluble metals, including the dissolution test and the criteria for classification is given in the RAR on zinc metal[8][9]. The results of Dissolution and Short-term toxicity tests will be discussed in detail in Section 3 (Environment) of the present Risk Assessment Report.

[8] http://ecb.jrc.it/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/zincmetalHHreport072.pdf

[9] It should be noted that the 'critical surface approach' as suggested in OECD context is not considered in the reports for neither cadmium metal nor cadmium oxide.

2 GENERAL INFORMATION ON EXPOSURE

2.1 PRODUCTION

Cadmium metal

Cadmium is a naturally occurring element with ubiquitous distribution. Although cadmium ores also exist (greenockite) these are not commercially important. Zinc (sulphide) ores are the primary source for cadmium production. Smaller amounts of cadmium are produced during the production of other non-ferrous metals such as lead. In the refining of these ores cadmium is obtained as a by-product (Technical notes on cadmium, 1991).

Whereas the extraction and refining of the primary non-ferrous metal from the ores can be obtained either by pyrometallurgical or electrolytic processes, the final step of cadmium production is done by fractional distillation or electrolysis.

Cadmium oxide

Although cadmium oxide is an important commercial compound it is not manufactured from the zinc or mixed non-ferrous metal ores, phosphate rock, coal or other rock forms, as cadmium oxide but indirectly from the cadmium produced as a by-product in the manufacture of zinc and lead. The substance is important commercially for itself and also because of its extensive use in the preparation of other cadmium compounds.

2.1.1 Production processes

Cadmium metal

The primary non-ferrous metal can be produced via two distinct types of production.

The formerly used pyrometallurgical processes. Here the residual sintered concentrate (calcine) containing oxidised zinc and cadmium materials is heated to about 1,100 to 1,350°C, reduced by carbonaceous material and the zinc and cadmium volatilised. The metal vapours are condensed and collected as metal dust. Most of the cadmium collects with the zinc metal and may be removed in the refining of zinc by fractional distillation (refluxing). In this process the boiling points of the metals present (cadmium 767°C, zinc 906°C and lead 1,750°C) are well separated and the cadmium can be concentrated in a cadmium-zinc alloy. Further repeating the distillation process under reducing conditions will result in cadmium metal with increasing purity.

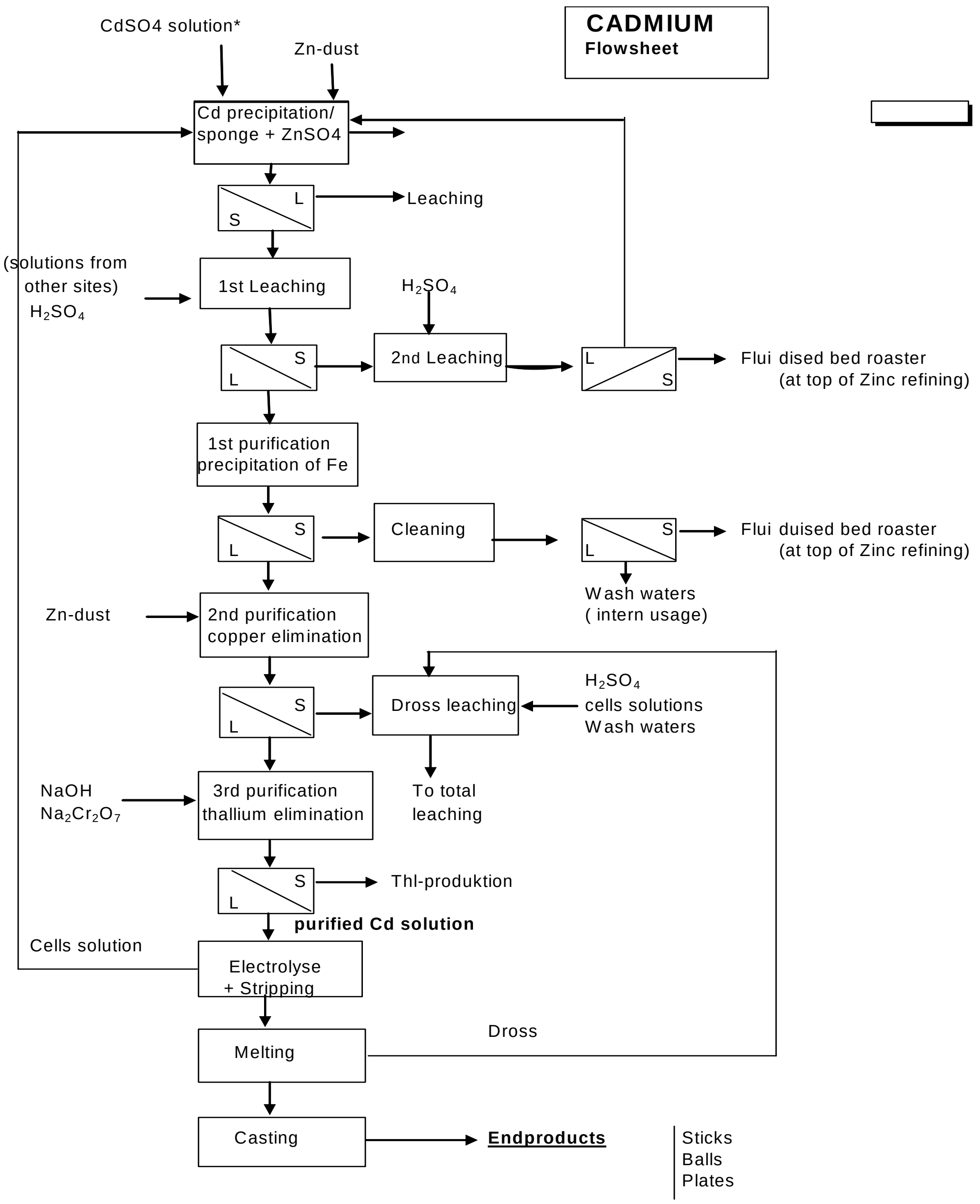
The present-day electrolytic process has the following main features. During the production of zinc, at the purification of the solutions of zinc sulphate, before the electrolysis, cadmium is present in dissolved impurities ($CdSO_4$). Cadmium is precipitated herein by adding zinc (as zinc powder or dust). The resulting impure cadmium residue (cadmium sponge) is purified and leached with aqueous sulphuric acid solution. A reasonably pure cadmium sponge is produced after two additional acid solution/zinc dust precipitation stages. The sponge is again dissolved in sulphuric acid and the solution, if sufficiently pure, is passed into electrolytic cells where the cadmium is deposited on cathodes (see **Figure 2.1**).

After deposition, the cathodes are stripped and the cadmium melted and cast into the required shapes (sticks and balls). The metal is typically either 99.95 or 99.99% pure. Higher purity grades for special purposes can be obtained by further vacuum distillation (Lexicon, 1971; Technical notes on cadmium, 1991).

Variations in the production flow-sheet exist from one production site to the other. These may be due to differences in the type of the ores (zinc, lead), origin, form and content, the purity of the end-product that is aimed at, legal environmental criteria and the extent of (auto) recycling activities (scraps, flue dust etc.).

In the EU cadmium metal is produced mainly as a by-product of zinc production via electrolytic processes (approximately 77.5% of the total volume). The rest is obtained in association with pyrometallurgical refining processes (Industry Questionnaire, 1997).

Figure 2.1 Cadmium production flow-sheet: an example of electrolytic process in a closed production system (Union Minière, 1998)



L\S : liquid solid separation (via filter)
* : CdSO4 solution is coming from repulping step of the residues after the purification step in the Zinc leaching section

Cadmium oxide

In the commercial production process, cadmium oxide is prepared by the reaction of cadmium metal vapour with air. For the production of cadmium as part of the refining of zinc ores, we refer to the aforementioned paragraph. Other production possibilities are thermal decomposition of the carbonate, nitrate, sulphate or hydroxide but these are stated not to be in use for current industrial production (IcdA, com., 2003).

Cadmium oxide is available on the market in powder form. Its average particle size (spherical diameter) is 0,5 to 0,55µm (IUCLID, 1997).

It is packaged in metal drums, big bags, flo bins or containers (IUCLID, 1997).

Figure 2.2 Cadmium oxide production: flow-sheet

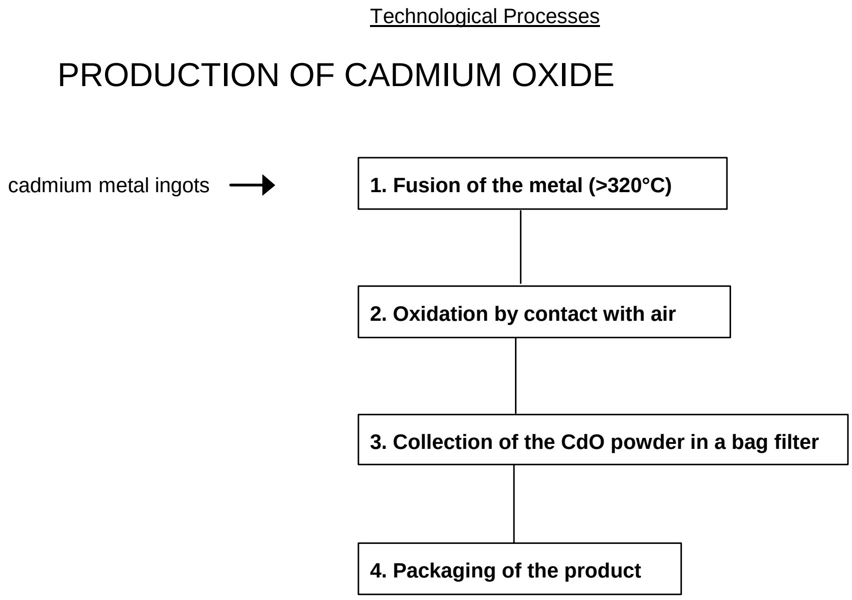
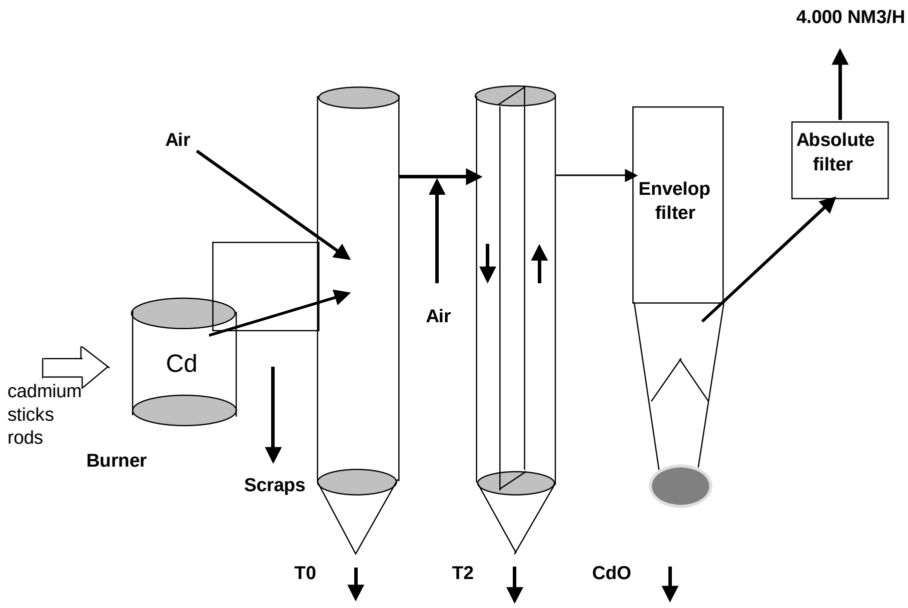


Figure 2.3 Production of cadmium oxide (PC WIAUX company information, 1998)



The manufacturing process for cadmium oxide is partly enclosed. Cadmium metal in ingots is manually placed in furnaces heated at 320°C. Emitted fumes are oxidised by contact with air in a closed system. The produced CdO powder is filtered and collected in bags, flo bins and metal drums or directly into silo. The packaging station has local exhaust ventilation at the discharge point. Workers have to place and adjust the bag or drum under the discharge and to set the process in motion (semi-automated process). Filled bags and drums are subsequently closed and carried to the storage area.

2.1.2 Production volumes

2.1.2.1 Data for the reference year 1996

Cadmium metal

The world primary cadmium production is estimated at 14,000 to 16,000 tonnes/year, the corresponding figure for Europe was approximately 5,000 tonnes/year (1994) – 5,800 tonnes/year (1996) (Industry, 1997), produced at 12 sites all over the EU territorial surface with, in these years, a major site localised in Belgium.

The amount imported in Europe in the same period is estimated at 1,500 tonnes/year – 960 tonnes/year (figure representative for January-July '96) (Eurostat, 1997; in: IUCLID, 1997). Export out of Europe is estimated at 2,200 tonnes/year (1996). This latter figure is obtained by subtracting the total EU consumption from the total EU production (IZA, personal comm., 1997).

Table 2.1 Cadmium production plant size distribution for 1996

Tonnes	Number of cooperating companies
< 300 tonnes	5
300-600 tonnes	4
> 600 tonnes	3

Table 2.2 Production sites of metallic Cadmium in the EU (in the range 10 to >1,000 tonnes/year, EUREX), IUCLID 1997

Company (and plant)	Country
Produits Chimiques Wiaux SA*	Belgium
Asturiana de Zinc	Spain
Britannia Zinc Limited	UK
Budel Zink BV	The Netherlands
Enirisorse	Italy
Espanola Del Zinc S.A.**	Spain
Metaleurop Nord S.A.S.	France
Metaleurop Weser Zink GmbH	Germany
Norzink	Norway

Table 2.2 continued overleaf

Table 2.2 continued Production sites of metallic Cadmium in the EU (in the range 10 to >1,000 tonnes/year, EUREX), IUCLID 1997

Company (and plant)	Country
Outokumpu Zinc OY	Finland
Ruhr-Zink GmbH	Germany
Union Miniere Balen***	Belgium

* Production/conversion stopped in 2001 (plant is closed down; Ind., pers. Comm., 2002)

** Last cadmium production in 1991; since: zinc refinery without cadmium production

*** Company's name became UMICORE (2001) and production stopped in 2002

Remark: one company identified by the EUREX CD ROM is not included in the risk assessment process (phase 3 company with a production/import volume between 10 and 1,000 tonnes/year). Apparently it concerns a German pigment manufacturer presumably importing/using cadmium metal for further processing only.

An update provided by Industry (IcdA, com., 2003) reveals that Asturiana de Zinc in Spain no longer produces cadmium. Britannia Zinc and Metaleurope (France) have both recently closed down. Española del Zinc and Ruhr-Zink have not produced for many years. Outokumpu and Umicore exited the cadmium production business more recently. The **Table 2.2** needs thus some serious revision. It gives the impression that there are 12 active cadmium production plants in Europe when in fact there are now only three, possibly four: Budel (now known as Pasminco Budel), Norzink (now known as Norzinc Outokumpu), Enirisorse (now known as Porto Vesme, owned by Glencore) and possibly Metaleurop Weser Zink (recently taken over by Glencore). No more details were submitted.

Table 2.3 Raw EU production, import, export and consumption data of cadmium metal in metric tonnes (Industry site specific questionnaire, 1997)

Year	EU production	EU import	EU export	EU consumption
1994	5,000	1,582	n.d.	n.d.
1995	5,648	2,822	4,953	3,517
1996	5,808	960 (until July)	2,200 (derived)	n.d.

n.d. No data

The available figure for 1996 has been derived from the production figure and the consumption figure of 1995 (assuming that this remained roughly the same in 1996); IZA, personal comm., 1997). The consumption figure for 1995 has been roughly derived from the information on production volumes used downstream in plating, pigments, stabilisers and batteries production facilities (IcdA, 1997).

Cadmium oxide

The world production of cadmium (metallic) is estimated at 14,000 to 16,000 tonnes/year. The production of cadmium oxide for Europe was approximately 3,070 tonnes/year (1994) – 2,536 tonnes/year (1996) (Industry Questionnaire, 1997), produced at 2 major sites in the EU (Belgium).

Table 2.4 Production sites of cadmium oxide in the EU (EUREX), IUCLID 1997.

Company (and plant)	Country
Floridienne Chimie S.A., Ath	Belgium
Produits Chimiques Wiaux SA*	Belgium

* Production was taken over by Floridienne in 2000, and was definitively stopped in 2001 (Ind., pers. Comm., 2002)

Remark: one company identified by the EUREX CD ROM is not included in the risk assessment process (the concerned company has a production volume in the range: 10 – 1,000 tonnes/year). It concerns a pigment manufacturer presumably importing/using cadmium metal for further processing – via an in-house production of cadmium oxide - to pigments only.

The amount of cadmium oxide imported in Europe is unknown with the exception of the first half of 1996 (January to July) for which 23 tonnes was reported (IUCLID, 1997). The latter document does not cite information on export. The site-specific information however mentions an important export activity taking place every year (approximately 1,000 tonnes/year leave the EU).

Table 2.5 Raw EU production, import, export and consumption data of cadmium oxide in metric tonnes (IUCLID, 1997; Industry site specific questionnaire, 1998)

Year	Production	Import	Export	Consumption
1994	3,069	n.d.	≥ 1,050	n.d.
1995	2,757	n.d.	≥ 1,350	n.d.
1996	2,536	23 (until July)	1,000	n.d.

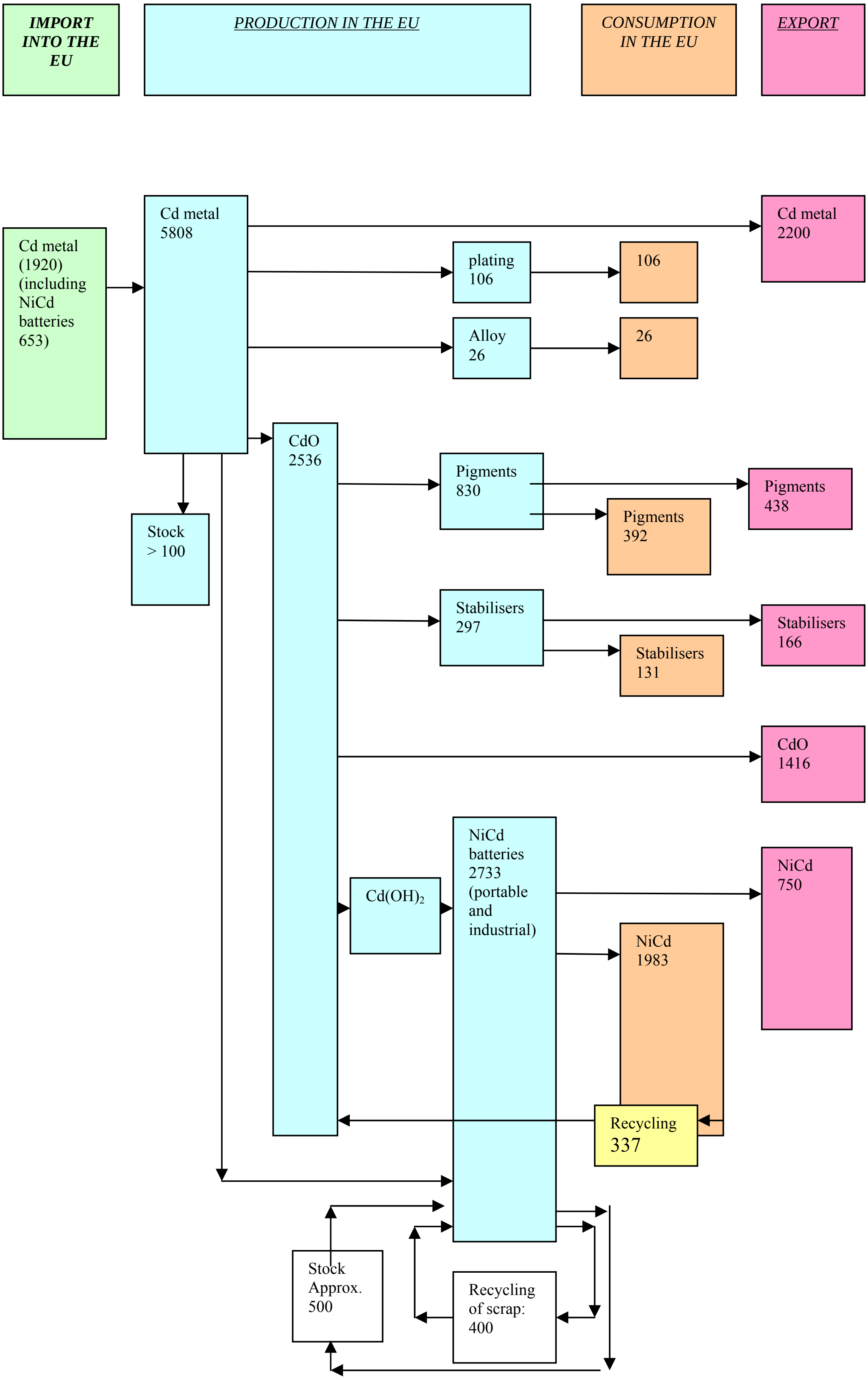
Production, import, export and consumption figures for both priority substances, cadmium metal and cadmium oxide, submitted by Industry are fragmentary.

In 2000, Industry provided a mass-balance for the reference year 1996, accompanied by an explanatory note (see **Figure 2.4** and further), reflecting the best possible estimate at the moment.

An update for the year 2000 was provided in the context of the batteries' targeted risk assessment (see **Figures 2.9** and **2.10** in Section 2.2.2.3.2) and estimates for the year 2002 in the context of the update site-specific assessment (see **Figure 2.11** in Section 2.2.3.1).

Two important confounding factors make it difficult to establish accurate cadmium consumption figures: 1) the conversion of cadmium metal into cadmium oxide and other cadmium compounds and 2) shipments of cadmium-containing residues to zinc smelters from recycling operations (Morrow, 2001).

Figure 2.4 Cadmium mass flow sheet (metric tonnes)- reference year 1996 (Source: IZA-Europe, IcdA, UM and CollectNiCd, 2000 and 2001)



Explanatory note to the mass-flow of cadmium (as provided by Industry)

The mass balance reveals that 5,808 tonnes of cadmium were produced in Europe in the reference year (1996). The imports were estimated to 1,920 tonnes including the contribution of the metal present in imported consumer/sealed portable nickel-cadmium batteries. Cd metal stocks exists in Rotterdam which may influence the trading balance but the data reported hereafter have been mainly obtained from use at the industrial level for the various applications.

It can be observed that a large industrial activity consists in the transformation of cadmium metal in the oxide: the equivalent of 2,536 tonnes of cadmium are used in the production of cadmium oxide.

The EU regional use of metal reaches the value of 2,638 tonnes, which are distributed for 75.2% to Ni-Cd batteries, 14.9% to pigments, 5% to stabilisers and 5% into alloys and plating.

Portable Nickel-Cadmium batteries are introduced on the market as a power source incorporated in Electrical and Electronic equipment in more than 90% of the cases. This is the origin of a significant export ratio for batteries. This ratio has been estimated between 33% to 50% (according to applications and countries) for the consumer/sealed portable batteries produced in Europe on the basis of the Import- Export balance.

Industrial Ni-Cd batteries are not imported in significant quantities (less than 5%). They are manufactured in European countries and are exported in a significant proportion, estimated to 35% for the global European market. The net export of cadmium from batteries reaches the estimated volume of 750 tonnes.

The largest export quantity is found in the cadmium metal produced by European companies in order to satisfy the demand in USA, Asia and South America. A significant fraction of the cadmium oxide produced in Europe is exported to non-European battery manufacturers which demonstrates the competitiveness of this European industry involved in the transformation of Cadmium into the oxide. When the battery is marketed, the cadmium content is present as cadmium hydroxide (discharged battery) or as cadmium metal (charged battery).

It has been estimated that cadmium from recycling operations reached approximately 337 tonnes from used batteries collected from the market and industrial sources. In addition, there are two types of stocks to be considered. First, the manufacturing rejects and secondly, a cadmium stock for the work in progress. Those have been presented in a closed loop independently of the total inlet and outlet of the primary cadmium. Indeed recycling operations leads to a 99% recovery of the cadmium content of the battery. The metal has a purity higher than 99.9% and is re-used in new battery manufacture. The battery manufacturing capacity will produce a new volume of waste equivalent to the treated one, which is re-introduced in the circuit. At the same time, the management of a stock required for the “work in progress” is considered.

Mass-balances are available for several EU countries, and years (e.g. Denmark for 1996 (Danish EPA, 1994 and 2000), Germany for 1990, 1991, 1992, 1993 and 1994 (UBA, 1996), the Netherlands for 1980 (VROM, 1991), France for 1995/1996 (l’Académie des Sciences Rapport N° 42, 1998) and Greece for 1993 and 1997 (EUPHEMET, 2000). From these documents, the overall consumption patterns and trends are roughly confirmed, with a largely predominant flow of cadmium in batteries that dramatically increased since the eigthies and continued during the nineties while most other uses have been declining.

2.1.2.2 Update date (reference year 2002)

In 1997, from the companies liable to the Regulation 793/93/EEC, there were 12 companies producing cadmium metal and 2 producers of cadmium oxide. Regards the import of the substances, one company for cadmium metal and one company for cadmium oxide were active in the field and were subject to the existing substances regulation.

In 2005, this picture has significantly changed. An overview is given here below.

<u>Cadmium metal</u>

The companies that stopped the production of cadmium metal/cadmium oxide and the approximate date are listed in **Table 2.6**.

Table 2.6 Production sites of metallic cadmium/CdO in the EU in the range 10 to > 1,000 t/y that stopped production

Company (and plant)	Country	Date/year of production stop
Asturiana de Zinc (now: Xstrata Zinc)	Spain	1998
Britannia Zinc Limited (in liquidation: 2003)	UK	2003
Espanola del Zinc S.A.	Spain	1991/1992
Metaleurop Nord S.A.S.	France	2003
Outokumpu Zinc OY (now: Boliden Kokkola)	Finland	2002
Ruhr-Zink GmbH	Germany	1998-1999
Union Minière Balen (now : Umicore)	Belgium	2002
Produits Chimiques Wiaux S.A.	Belgium	2000/2001

Former activities at Produits Chimiques Wiaux S.A.: limited to the conversion of massive cadmium metal into cadmium metal powder

The companies still manufacturing cadmium metal in 2005 are reported in **Table 2.7**. All companies produce the substance in massive form (e.g. plates, sticks, balls).

Table 2.7 Current producers of cadmium metal liable to the Regulation 793/93/EEC

Company (and site)	Country
Budel Zink (now: Zinifex Budel)	The Netherlands
Norzink (now: Boliden Odda A.S.)	Norway
Metal Europ Weser Zink (now: Xstrata Zinc GmbH)	Germany

Updated data on EU-16 production data are given in **Table 2.8**. No data are available on the situation in the EU-25.

Table 2.8 EU production, import, export and consumption data on primary cadmium metal in metric tonnes (Industry site specific questionnaire, 2004/2005)

Year	EU production	EU import	EU export	EU consumption
2002	1,114	n.d.	n.d.	n.d.
2003	1,207	n.d.	n.d.	n.d.

n.d. No data available

Based on the data of one producer 85% of the production volume is exported outside the EU-25. A second company mentions 100% export but it is not clear if this is meant as outside the EU or outside country where production is located.

The amount of secondary cadmium produced by recycling is given under Section 2.2.3.2.

The total volume of cadmium consumed within the old EU-16 (including Norway) and the new EU-25 territory is unknown.

Cadmium oxide

Update information regards the producers of cadmium oxide is given in the **Table 2.9** and **Table 2.10**.

Table 2.9 Production sites of metallic cadmium in the EU in the range 10 to > 1,000 t/y that stopped production

Company (and plant)	Country	Date/year of production stop
Produits Chimiques Wiaux S.A.	Belgium	2000/2001

Former activities at Produits Chimiques Wiaux S.A.: limited to the conversion of massive cadmium metal into cadmium oxide

Table 2.10 Production sites of cadmium oxide in the EU with volume > 1,000 tonnes/year (reference year: 2002)

Company (and site)	Country
La Floridienne	Belgium

Information on the total production of cadmium oxide by La Floridienne was submitted for the reference year 2002. Since 1996 there is an increase of the production volume.

2.2 USES

2.2.1 General overview

Cadmium metal

Metallic cadmium is mainly used in the production of batteries, cadmium compounds (cadmium oxide and to a lesser extent cadmium hydroxide). Further also in coatings, alloys and other miscellaneous uses (see **Table 2.11** showing the industrial and use categories of cadmium). The two types of ‘Main categories’ for cadmium are characterised as non-dispersive use and use resulting into or onto a matrix.

Metallic cadmium is commercialised in different forms: powder, balls (3-5 cm diameter), plates (10-200-200 to 1.000mm) or sticks (200 to 240-10 to12 mm) (IUCLID, 1997).

CdO production

An important proportion of the cadmium metal produced is subsequently used in the production of cadmium oxide powder. This substance has several applications and constitutes the (principal) raw material in the production of other cadmium compounds.

The CdO produced has a high purity (at least 99% CdO) resulting in a cadmium wt% of 87.25 to 87.5.

A short description of the uses of respectively cadmium metal and cadmium oxide and processes involved is given below (source: IcdA, 1997, unless specified otherwise).

<u>Cadmium metal</u>

Batteries

See the batteries' related sections (see Section 2.2.2).

Plating

By plating of metals or alloys a coating is provided that is resistant to corrosion by alkalis, salt water and atmosphere. Furthermore these coatings are highly ductile and easily soldered.

Cadmium coatings have low coefficients of friction and maintain high electrical conductivity, and hence are used mainly in applications where both corrosion resistance and lubricity or good electrical conductivity are required (IcdA, com., 2003). Cd-Ti and Cd-Sn electroplated coatings are used to resist hydrogen embrittlement in high strength steel fasteners.

The coating can be realised by electrochemical reaction: cadmium is the anode in the cell formed with an iron substrate in water. Other technologies for coating are vacuum deposition (mainly cyanide baths), dipping or spraying[10] , or mechanical plating[11] with cadmium powder, where glass shot is used. Cadmium ion vapour deposition is another technique also used. For further details on the processes see the human health part of this report in a separate document .

Electrodeposition of cadmium on a metal substrate accounts for 90% of the cadmium used in plating. The remaining 10% is applied by vacuum deposition, metal spraying[2] or mechanical[3] plating.

Cadmium plating by electrodeposition uses an alkaline cyanide solution of the metal as starting material. The plating solutions can be purchased direct from chemical manufactures; alternatively they can be prepared on-site from cadmium metal or oxide. The plating solution normally contains 18-22 g/l Cd. Baths usually have cadmium bars or ball anodes, placed in steel anode baskets with a surface area of cadmium equal to the plating load. Barrel plating usually uses and electrolytes with less cadmium (15 g/l). After electroplating, and heat treatment if required, a chromate conversion coating is usually applied on a subsequent bath (IcdA, 1997).

Plating contains 99,95% cadmium (IUCLID, 1997).

Alloys

Cadmium has been a common component of many alloys which uses are related to their melting temperatures, e.g. tin-lead-bismuth-cadmium alloy joining metal parts which may be heat sensitive; silver-cadmium-copper-zinc-nickel alloy for joining tungsten carbide to steel tools. The EU use of cadmium as a constituent of alloys (mainly Cu-Cd and Ag-CdO) has declined in importance in the recent years (4% of total use in 1985, about 0.6% in 1996) as these have been

[10] dipping and spraying are no longer used (ICdA, com., 2003)

[11] mechanical coating has declined significantly (ICdA, com., 2003)

substituted by cadmium free alloys with comparable characteristics of ductility and strength in the majority of uses.

Cu-Cd alloys are prepared by re-melting high conductivity copper in suitable furnaces and adding the necessary cadmium in the form of a copper-cadmium master alloy, or by 'side-casting' from holding furnaces fed by the large reverberatories of refineries.

During the manufacturing of the master alloys, drosses containing Cd are released. Usually, they are recycled internally or in other metal plants.

The normal form of the casting is a wire bar, which is hot rolled before drawing to wire. Normal practise is followed in drawing the rod to wire, using dies of suitable shape in the case of trolley wire. Limited quantities of sheet and strip are produced by rolling and of rod by extrusion and drawing (IcdA, 1997).

Cu-Cd alloys contain usually 0.2-0.8% cadmium. The production of these alloys occurs via pre-alloys (containing 49-51% cadmium) which are further processed by other industries to prepare the final Cu-Cd alloys (IUCLID, 1997).

Ag-CdO electrical contact alloys are produced by internally oxidising an Ag-Cd alloy. The percentage of Cd in Ag-CdO alloys is generally in the range of 5% to 15% (IcdA, pers. Com., 2003).

Other uses

Applications as reported by Farnsworth (1980): deoxidiser in nickel plating, in process engraving, in electrodes for cadmium vapour lamps, in photoelectric cells and in the photometry of ultraviolet sunlamps, in selenium rectifiers and Jones reductors and application of cadmium powder as an amalgam (1Cd:4Hg) in dentistry, are stated by Industry as no longer in use (IcdA, pers. Com., 2003).

Cadmium oxide

Cadmium oxide is used as starting material for a wide variety of other cadmium compounds (PVC heat stabilisers, pigments). Cadmium oxide has been used as a stabiliser for the cadmium sulphide and sulpho-selenide forms in glass[12]. In nitrile rubbers the substance improves heat resistance; in plastics, it improves high temperature properties.

Another field of (minor) applications is based on the catalytic properties of cadmium oxide. It catalyses reactions between inorganic compounds, as well as organic reactions such as oxidation-reduction, dehydrogenation, cleavage and polymerisation (use as vulcaniser). It sensitises photochemical reactions.

Other (former) uses included phosphors, semi-conductors, manufacture of silver alloys, and as nematocide-anthelmintic in swine and poultry.

A short description of the uses and processes involved is given below (source: IcdA, 1997, unless specified otherwise).

[12] This use is not known by Industry (ICdA, pers. com., 2003)

Batteries

Although cadmium metal is one of the principle raw materials, cadmium oxide is used in the manufacture of certain types of cadmium electrodes (IcdA, 1997). See the batteries' related sections (see Section 2.2.2).

Stabilisers

Barium cadmium stabilisers can be manufactured in a number of ways. The starting materials are usually the metals or the metal oxide. They are combined with various organic compounds. Three general processes can prepare the salts:

- Direct dissolution of finely divided metal oxides in heated organic acids
- Precipitation from aqueous solution of metal salts (chlorides or nitrates) and alkali soaps
- Fusion of metal oxides with organic acids.

For liquid barium/cadmium stabilisers the production starts from metal oxides which are dissolved directly in the heated organic acids in the presence of solvents. The reaction water is removed and the finished product filtered.

Solid stabilisers are prepared by the precipitation process through the method of preparing metal soaps of natural fatty acids to give for example, cadmium laurate. Following precipitation the resultant slurry is filtered and dried (IcdA, 1997).

Pigments

There is a number of proprietary manufacturing processes, which use either cadmium metal, or cadmium oxide as the essential raw material. In general the manufacturing process involves the preparation of a cadmium sulphate or nitrate solution; filtration to remove recoverable solids; addition of sodium sulphide and precipitation of cadmium sulphide, with simultaneous additions of other salts to alter colour characteristics; filtration to define precipitate and drying; calcination to convert crystal structure to more stable form; further rinsing, milling and blending followed by packaging (IcdA: compilation of Industry data, 1997).

Table 2.11 Industrial and use categories of cadmium in the EU (HEDSET, 1994)

Industrial category	EC No.	Use category	EC No.
Chemical industry: basic chemical	2		
Chemical industry: chemicals used in synthesis	3	Intermediates Laboratory chemicals	33 34
Electrical/electronic engineering industry	4	Conductive agents Batteries and cells...	12
Personal domestic	5	see Product Register	
Metal extraction, refining and processing industry	8	Electroplating agents Others: Alloys	17 55
Paint, lacquers and varnishes	14	Reprographic agents	45
Others: Basic metal used in metal industry	15	Corrosion inhibitors	14

Table 2.12 Industrial and use categories of cadmium oxide in the EU (HEDSET, 1995; Product Registers, 1997 and 1998)

Industrial category	EC No.	Use category	EC No.
Chemical industry: basic chemical	2		
Chemical industry: chemicals used in synthesis	3	Intermediates Laboratory chemicals Raw material for the production of other cadmium chemicals	33 34 55
Electrical/electronic engineering industry	4	Conductive agents Electroplating agent	12 17
Polymers industry	11	Stabilisers	49
Paints, lacquers and varnishes industry	14	Colouring agents Fillers Reprographic agents	10 20 45
Others: Industrial : other = colours/frits Other : Ceramic industry Other: Glass and related industry	- 15 15	- Colouring agents Colouring agents	- 10 10

This Table reflects the information as reported by Industry falling under the HEDSET obligation and was further completed by information contained in the Product Registers.

<u>Other data on uses of the substances: Product Registers</u>

Cadmium metal

The Danish Product Register (1997) reports under the CAS number of metallic cadmium, in descending order of involved amount: construction industry and chemical industry (private household insignificant). In the same way, product types are listed: paints, lacquers and varnishes, construction materials and laboratory chemicals. With 31 out of 49 products containing 0-1% cadmium and 3 products with 80-100% cadmium content the total quantity used in products in 1997 was lower than 1 tonne for Denmark.

The register of 1998 gives a similar picture. The additional information concerns the content in the different product types: paints, lacquers and varnishes: 12 of the 26 products contain lesser than 1% of the substance; construction materials: all products contain maximum 1% cadmium; laboratory chemicals: two of the three products have a content of 80-100% cadmium; colouring agents: eight products of the twelve contain maximum 1% cadmium. The quantity for each major product type is smaller than 10kg and the overall quantity is less than 1 tonne/year.

The Swedish product register (15/09/97) reflects the presence of the substance - albeit at low concentration (< or = 10%) – in a range of products and trades. The largest number of products and highest volume are used in dyestuffs (pigments) and in fillers plastic, paints etc. The total volume in products did not exceed 1 tonne in 1996 (More details of the industrial and use categories can be found in **Annex F**).

When over viewing the information contained in the product registers it could be questioned if the entry with CAS-N° of cadmium metal (i.e. 7440-43-9) is not used also to report on cadmium in a (more) generic way.

Cadmium oxide

The Danish Product Register (April 1997) reports 14 of the 25 products containing 1-10% cadmium oxide and two products with 80-100% of the substance. The major Industry implicated is the manufacturing of electronic equipment. Product types (in descending order of used substance's quantity): Laboratory chemicals and conductive agents. The total quantity in products is less than 1 tonne/year. For 1998 the Register is very similar. Nevertheless, here reprographic agents seem quantitatively most important, followed by conductive agents (11 products) and laboratory chemicals. The total quantity of the substance used in products is less than 1 tonne/year.

Details of the Swedish Register (1997: figures of 1996) are annexed (see **Annex G**).

The consumption pattern of cadmium (oxide and other cadmium compounds):

The world wide overall consumption pattern of cadmium (and its compounds) has been estimated by the International Cadmium Association (cited in Pearse, 1996) as follows: batteries (61%), pigments (20%), stabilisers (10%), plating (8%), alloys (3%) and other uses (4%).

For the Western World, Morrow came for the year 1996 to the following figures: batteries (69%), pigments (13%), stabilsers (8%), coatings (8%) and alloys and other (2%) (cited in: Morrow, 1998). In the context of the ESR Programme, Industry estimated the consumption pattern of cadmium (oxide) in Western Europe for the year 1996 as follows: batteries (60%), stabilisers (20%) and pigments (20%). Other uses are considered insignificant (IUCLID, 1997) and estimated to be less than 0.1% (IcdA, CollectNiCad, pers. Com., 2002). The figures were reviewed by Industry, refined and reported in the mass-balance (see **Figure 2.4**).

Use of Production, Consumption and Import/Export data

The data from the HEDSET/IUCLID, 1997 and the site specific Questionnaire (producers/importers of Cd (O)) provide the basis for the exposure assessment of these industrial sources.

The data from WS Atkins and underlying completed Questionnaires were used for the exposure assessment of pigments as well as stabiliser producers and users.

For plating an EU generic scenario is used (by lack of any site-specific exposure data) and based on the amount of cadmium estimated to be consumed in this application in the EU as a whole (estimation from IcdA, 1997).

Site-specific data (collated by the Questionnaires 1998, 2000 and 2001) are used for the exposure assessment of the batteries' producing and cadmium recycling companies.

Data on the cadmium flow related to batteries and recyclers (see the mass-balance updated for the year 2000) are used in the targeted risk assessment of cadmium (oxide) used in batteries, and in particular for estimating the emissions from waste disposal (see batteries' related Section 2.2.2).

Site-specific data collected via the Questionnaires (2004) are used to update the local assessment for all scenarios related to production and use of the priority substances for which new data were submitted (see Section 2.2.3). The reference year for the latter update was set at the year 2002.

2.2.2 Batteries

2.2.2.1 Used terminology on Nickel-Cadmium batteries

Electrochemical cells and batteries are identified as primary (non-rechargeable) or secondary (rechargeable), depending on their capability of being electrically recharged[13]. Within this classification different types of battery formats exist.

A battery can consist of only one cell or can be put together of several cells, which are connected among each other. There are cylindrical cells, button cells, prismatic batteries and battery packs available on the market (see **Table 2.13**) depending on application type, use, equipment.

Table 2.13 Overview of the different battery formats and chemistry

Product Group	Sub-groups		
	Rechargeability	Format	System
Batteries type and geometry	Primary[14] (non-rechargeable)	Button	Lithium: $LiMnO_2$, $Li(CF_x)_n$
			Others: AM, ZnO_2, ZnAgO, ZnHgO
		Cylindrical	Lithium: $LiMnO_2$, $Li(CF_x)_n$, $LiSOCl_2$, ZnO_2
			Others: ZN, AM
		Prismatics Packs	Lithium: $LiMnO_2$, $Li(CF_x)_n$
			Others: ZN (E-Block 9V, normal 4,5 V), AM (E-Block 9V)
	Secondary (rechargeable)	Buttons	NiCd, NiMH
		Cylindrical	NiCd, NiMH, AM, Pb-acid, Lithium: Li-ion
		Prismatics Packs	NiCd, NiMH
			Pb-acid
			Lithium: Li-ion

$LiMnO_2$	Lithium manganese dioxide	ZnO_2	Zinc-air
$Li(CF_x)_n$	Lithium polycarbonmonofluoride	ZnAgO	Zinc silver oxide
$LiSOCl_2$	Lithium thionyl chloride		
AM	Alkali-manganese	ZnHgO	Zinc mercury oxide
ZN	Zinc-carbon	NiCd	Nickel-cadmium
NiMH	Nickel-metal-hydride	Pb-acid	lead-acid

Source: IOW, 1997

[13] Rechargeable batteries can be charged many times. After a certain amount of charge cycles they are no more rechargeable and must also be disposed of.
For information: the definition as set by the EC Battery Directive reads: Battery: any source of electrical energy generated by direct conversion of chemical energy and consisting of one or more primary battery cells (non rechargeable). Accumulator: any secondary battery cell or set of secondary battery cells (rechargeable).

[14]Cadmium has been used in some primary batteries in the past. There is no current application of cadmium in primary batteries (ICdA, pers. comm., 2000)

Ni-Cd batteries are generally viewed as high performance battery chemistries with good energy density and power density, especially suitable for high drain rate applications. Included in their best performance characteristics are their long useful life, wide temperature operating range, resistance to electrical/mechanical abuse and rapid charge/discharge characteristics. Disadvantages are low energy density, the so-called 'memory effect' and higher costs than lead-acid batteries. Nickel-cadmium batteries may readily be formulated into many different types, shapes and sizes of batteries designed to meet the specific requirements of many different applications.

The pocket-plate battery is the oldest and most mature of the various designs of nickel-cadmium batteries available and is manufactured in a wide capacity range, 5 to more than 1200 Ah and is used in a number of applications. Developmental work has been conducted continuously since the introduction of the pocket-plate nickel-cadmium battery to improve the performance characteristics and reduce battery weight. These innovations have resulted in the sintered-plate, fiber-structured and plastic-bonded or pressed-plate technologies (Evjes and Catotti, 2002). The sintered plate battery consists of a perforated mechanical substrate (e.g. nickel-plated steel or nickel-clad steel wire) coated with a highly porous sintered nickel matrix which is impregnated with nickel hydroxide (positive electrode) or cadmium hydroxide (negative electrode). The fiber (foam) structure technology uses a three-dimensional nickel-plated fiber matrix, which is highly porous.

Within these technologies a further distinction can be made between vented (open) and sealed cells. A functional vented battery generates a stoichiometric mixture of hydrogen and oxygen gases during overcharge and expels them normally from the cell into the battery container. Most often vented batteries have been used in industrial applications.

Sealed nickel-cadmium batteries incorporate specific battery design features to prevent a build-up of pressure in the battery caused by gassing during overcharge. As a result, batteries can be sealed and require no servicing or maintenance other than recharging.

Since both the term sealed and portable can be applied to some industrial batteries the term consumer batteries was initially used in the questionnaire sent to the Member States to indicate batteries with mainly domestic application. However, in general sealed, portable batteries not exceeding a weight limit (e.g. < 3 kg) irrespective of some other uses are referred to under this terminology.[15] Furthermore since household applications represent to date less than 20% of the market by weight (see **Table 2.27**) it is deemed more appropriate to use the term portable batteries in order to indicate that the figures presented in this report may include professional applications next to household applications.

A battery is made of cells assembled in series. Roughly Ni-Cd batteries can be divided into the following weight categories. Sealed cells: cell weight between 10 and 150 grams (maximum 500 g), usually assembled by 3 to 10 to make packs for portable applications. The most common are 3 and 4 cell packs. Larger batteries do exist for stationary industrial applications. Vented cells: cell weight between 1 and 70 kg (typically 3 to 10), usually assembled by at least 10 cells but up to several hundred. (CollectNiCad, personal communication, October 2002). A compilation of some of the different subtypes of Ni-Cd batteries and their specific characteristics is given in **Table 2.14**.

[15] Definitions may differ within, between MSs, IND, OECD, etc; e.g. the weight limit by industry is/can be different from those applicable elsewhere e.g. by Member States

Table 2.14 Format, size and characteristics of Ni-Cd batteries

Product group	Subgroup					
	Format and size	IEC n° (US-Standard)	Weight (in g)	Nominal Voltage (in V)	Capacity (in Ah)	Cadmium content (in g per 100 g battery)
Portable batteries[16]	Button			1.2	up to 1 Ah	11-15 typical/average content = 13.8
	Cylindrical	R 20 (D)	145	1.2		
		R 14 (C)	75	1.2		
		R 6 (AA)	22	1.2		
		R 03 (AAA)	12	1.2		
		KR6	26	1.2	0.75	
	Prismatics	9 V E-block		9.6 V		
	Packs		20-450			
Industrial/ professional use[17]	Automotive vehicles		200 kg			8
	Safety and back-up systems		200 g to 1,000 kg			
	Aviation		20 kg (per battery) > 1 kg (per cell)			

Sources: Individual producers/recyclers (via Questionnaire 1998, 2000/2001)

2.2.2.2 Ni-Cd chemistry and composition

The nickel-cadmium (Ni-Cd) battery is a rechargeable battery system based on the reversible electrochemical reactions of nickel and cadmium in an alkaline potassium hydroxide electrolyte. The chemical compositions of Ni-Cd batteries can vary widely depending on the type and its specific application. For industrial batteries cadmium content may vary between 3 and 11%. For portable batteries values between 11 and 15% have been reported (battery questionnaire 2000). In addition, most Ni-Cd batteries contain significant amounts of nickel, iron, plastics and electrolytes and small amounts of metals such as cobalt and copper (Morrow and Keating, 1997).

Ni-Cd cells use a reversible electrochemical reaction between nickel and cadmium electrodes packed in an alkaline electrolyte (potassium hydroxide or sodium hydroxide and lithium hydroxide as an additive). The active materials are insoluble in the electrolyte, whose ions act only as a charge carrier and do not take part in the electrochemical charge/discharge reactions (Cornu, 1995). At the cadmium electrode during discharge, cadmium is oxidised by combining with two OH^- ions to form cadmium hydroxide [$Cd(OH)_2$] and releasing two electrons (US EPA, 1993, Gross, 1995). During charging the reverse happens. Hydrated nickel (III) oxide is reduced

[16] Since household applications represent to date less than 20% of the market by weight (see Table 2.27) it is deemed more appropriate to use the term portable batteries (instead of consumer batteries) in order to indicate that the figures presented in this TRAR may include professional applications next to household applications.

[17] For information: the definition as set by the draft EC Battery Directive ‘industrial and automotive batteries and accumulators’: any battery or accumulator use for industrial purposes, for instance as standby or traction power, emergency lighting, or for automotive starting power for vehicles. Remark: definitions may differ within and between MSs, IND, OECD, etc

to nickel (II) hydroxide at the other electrode (US EPA, 1993). The charge-discharge equation is as follows (Cornu, 1995):

$$2\ Ni(OH)_2 + Cd(OH)_2 + 2\ e \xRightarrow{\text{Charge}} 2\ NiOOH + Cd + 2H_20$$

$$2\ Ni(OH)_2 + Cd(OH)_2 \underset{\text{Discharge}}{\Leftarrow} 2\ NiOOH + Cd + 2H_20 – 2e$$

The principal difference between the various types of Ni-Cd cells is the nature of the cell electrodes. The three primary types of positive electrodes used are pocket plate, sintered plate, and fiber plate. The hydrated nickel oxide electrode is usually in powder form and is held in pocket plates or suspended in a gel or paste and placed in sintered (perforated mechanical support) or fiber electrodes (US EPA, 1993).

The negative electrodes use pocket plate, sintered plate, fiber plate, foam or plastic banded supports to hold the cadmium (hydroxide) in place. Graphite or iron oxide is commonly added to improve the conductivity of both the nickel and cadmium hydroxide. Since the individual cells are recycled before assembling into batteries, it is not important whether the negative electrodes are originally impregnated with $Cd(OH)_2$ (the product of discharge reactions) or Cd metal (the product of charging reactions) (US EPA, 1993).

A typical chemical composition for a Ni-Cd cell is given in **Table 2.15**.

Table 2.15 Average chemical composition for a Ni-Cd battery

Material	Weight %	
	Portable[a] Ni-Cd battery	Industrial[b] Ni-Cd battery
Iron	35	48
Nickel	22	8
Cadmium[c]	13.8[c]	8[c]
Plastic	10	10
$(OH)_2$	9	5
Water	5	16
Potassium hydroxide	2	5
Others	3.2	0
Total	100	100

Source of the figures: EPBA and EUROBAT product information (1997) in ERM (1997)

a) Portable Ni-Cd battery, are batteries weighing between 10 g and 3 kg. Since household applications represent to date less than 20% of the market by weight it is deemed more appropriate to use the term portable batteries in order to indicate that the figures presented in this report may include professional applications next to household applications.

b) Industrial Ni-Cd battery: large size batteries weighing over 3 kg in weight

c) Latest update of information from industry i.e. manufacturers/recyclers (CollectNiCad,,2000)

Large, industrial-size batteries contain on average approximately 8% cadmium. Small, portable-type batteries contain approximately 13.8% cadmium. These figures refer to actual manufacturing and production data and have been confirmed by the information collected from individual battery producers via the Battery Questionnaire 2000 and will be used in this report as representative for industrial batteries and portable batteries respectively.

2.2.2.3 Production, recycling and use

2.2.2.3.1 Ni-Cd batteries manufacturing processes

Nickel-Cadmium batteries are widely used in many different applications where an autonomous energy source is required. Each application demands a different battery design, adapted to its performance requirements. For industrial applications different battery technologies are available: pocket plate cells, sintered plate cells, nickel fiber plate cells, plastic bonded plate cells.

Pocket plate batteries represent the conventional battery technology. Pocket plate electrodes contain the active materials in perforated steel pockets. This type of plates is mechanically very strong and the steel strip retains the active material during cycling, minimising swelling. In each cell a number of positive and negative electrodes are paralleled to form the plate group. Nickel-plated steel is used for connecting the elements and the terminals. The electrodes and separators are immersed in the alkaline electrolyte and the cell has a vented design.

A process flow diagram for the pocket plate batteries process is shown in **Figure 2.5**.

The reported emission/waste data represent site specific data (local worst case) from a pocket plate Ni-Cd batteries manufacturing plant (Industry Questionnaire, 2000/2001). The emission factors for air and water were calculated using the used Cd amount for the manufacturing of Ni-Cd batteries and the emissions to air/water. The sludge factor for cadmium in the WWTP sludge was calculated from plant supplied data (Cd content of sludge, amount of sludge, Cd used during manufacturing).

The emissions/wastes from the production of this type of battery include the following:

a) Wastewaters containing cadmium. The sources of these wastewaters are the manufacturing of active materials, nickel strip manufacturing and the cell formation process. This wastewater is estimated to amount to 0.124 kg/tonne of Cd used in the battery manufacturing process ($F_{WW}=1.24 \cdot 10^{-4}$).

b) Air emissions occur during manufacturing of pocket plates and during assembling. For this specific plant no air emission data were reported. However for another pocket plate manufacturing plant, recycling its emissions to water, an air emission factor of 0.464 kg/tonne Cd used was reported.

c) Sludges recovered from treatment of wastewaters (manufacturing of active materials, nickel strip manufacturing, cell formation process). These are estimated to contain 17.7 kg cadmium per tonne of Cd used. The sludge from the wastewater treatment plant is sent to an external recycling plant.

d) Rejected battery cells from the test and package step: 118.8 tonnes/year. This waste is treated at a recycling plant.

e) Other waste: raw material bags, substituted filters, cleaning materials and tools: 1.15 tonnes/year.

Nickel fiber batteries are characterised by the use of a nickel fiber mat as electrode support. The active materials are impregnated by mechanical or electrochemical methods. Average diameter of the nickel fibers is around 20 µm. Porosity, pore size and electrode thickness can be adjusted as required for every application: lower porosity, smaller pores and thinner plates are adequate for high rate applications, while higher porosity, bigger pores and thicker plates are the choice for medium rate batteries. Thickness, porosity, pore size and the impregnation method are then adjusted to each specific application, in order to achieve the best electrical performance/battery cost ratio.

A process flow diagram for the nickel fiber plate process is shown in **Figure 2.6**.

The reported emission/waste data represent site specific data (local worst case) from a fiber plate Ni-Cd batteries manufacturing plant. The emission factors for air and water were calculated using the used Cd amount for the manufacturing of Ni-Cd batteries and the emissions to air/water. The emission factor for cadmium in the filter cake was calculated from plant supplied data (Cd content of filter cake, amount of filter cake, Cd used during manufacturing).

The emissions/wastes from the production of this type of battery include the following:

a) Wastewaters containing cadmium. The source of this waste is the impregnation step. This wastewater is estimated to amount to 0.769 kg/tonne of Cd used in the battery manufacturing process. This wastewater is collected and recycled in an external recycling plant.

b) Emissions to air occur during assembling are very small; 0.00027 g/tonne of Cd used.

c) Filter cake recovered from formation process. This is estimated to contain 10.5 kg Cd/tonne of Cd used. The filter cake is recycled.

d) Rejected batteries (no information)

Sintered plate batteries contain a cadmium anode, a potassium hydroxide electrolyte, and a nickel oxide cathode. For the electrodes, sintered plates containing the active materials are used. In one operation, the plates are made by impregnating sintered nickel substrates with nickel and cadmium nitrate salts. The nickel and cadmium nitrates are converted to hydroxides in sodium hydroxide solution. The plates are then washed thoroughly and dried in a hot oven. The impregnation cycle is repeated to deposit the desired amount of active material. The plates then go through a formation treatment, which removes impurities and brings the active materials to a condition similar to that existing in working electrodes. The cell is assembled into final form using an absorbent plastic separator and a nickel-plated steel case. With the addition of the alkaline electrolyte, they are ready for electrical testing, packing, and shipping.

There are currently three distinct manufacturing processes used for preparing the electrodes of the electrodes of the sintered plate batteries. The preceding paragraph described the worst case from an environmental standpoint of the three, due to the high concentration of cadmium and nickel compounds contained in the wash water. The other processes in use are:

- An electrolytic deposition process which deposits active materials directly on the sintered plates – this process produces wastewater containing nickel and cadmium compounds, though the amount is not as large as in the impregnation process described above; and
- A pressed powder process involving active materials mixed with binders in a dry powder form. The powder mix is pressed onto a wire mesh or expanded metal grid in a mold. This is a dry process and no wastewater is involved.

A process flow diagram for the impregnation-sintered plate process is shown in **Figure 2.7**.

The reported emission/waste data represent site specific data (local worst case) from a sintered-plate Ni-Cd batteries manufacturing plant. The emission factors for air and water were calculated using the used Cd amount for the manufacturing of Ni-Cd batteries and the emissions to air/water. The sludge factor for cadmium in the WWTP sludge was calculated from plant supplied data (Cd content of sludge, amount of sludge, Cd used during manufacturing).

The emissions/wastes from the production of this type of battery include the following:

a) Wastewaters containing cadmium and nickel salts together with sodium hydroxide. The source of this waste is the washing step. This wastewater is estimated to amount to 0.048 kg) per tonne of Cd used in the battery manufacturing process.

b) Atmospheric emissions are stated not to occur since the process is merely wet.

c) Sludges recovered from treatment of wastewater. These are estimated to contain cadmium (6.3 kg per tonne of Cd used) and nickel hydroxide. The WWTP sludges are land-filled (special landfill class I).

d) Rejected batteries from the test and package step, together with other scrap, are externally recycled for cadmium.

Figure 2.5 Flowsheet manufacturing process pocket plate Ni-Cd batteries

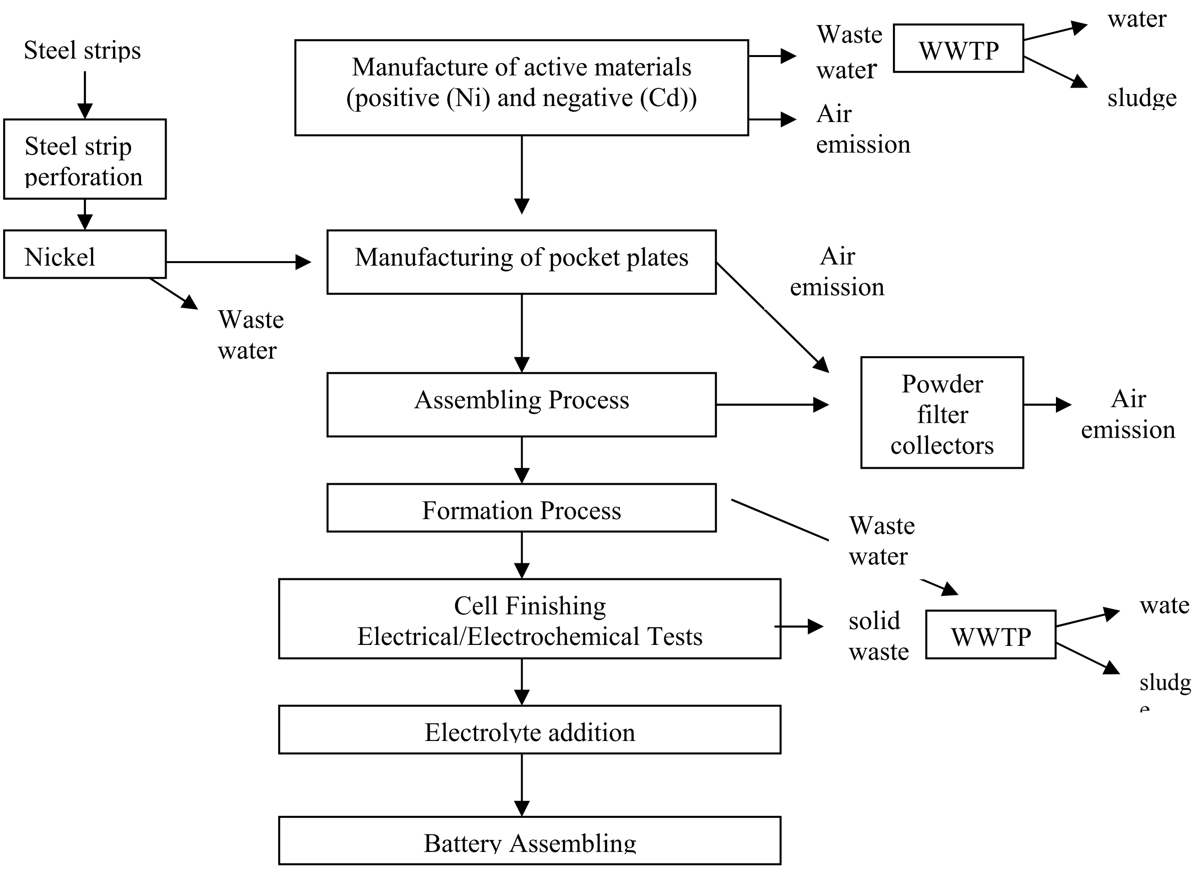


Figure 2.6 Flowsheet production process Nickel fiber plate Ni-Cd batteries

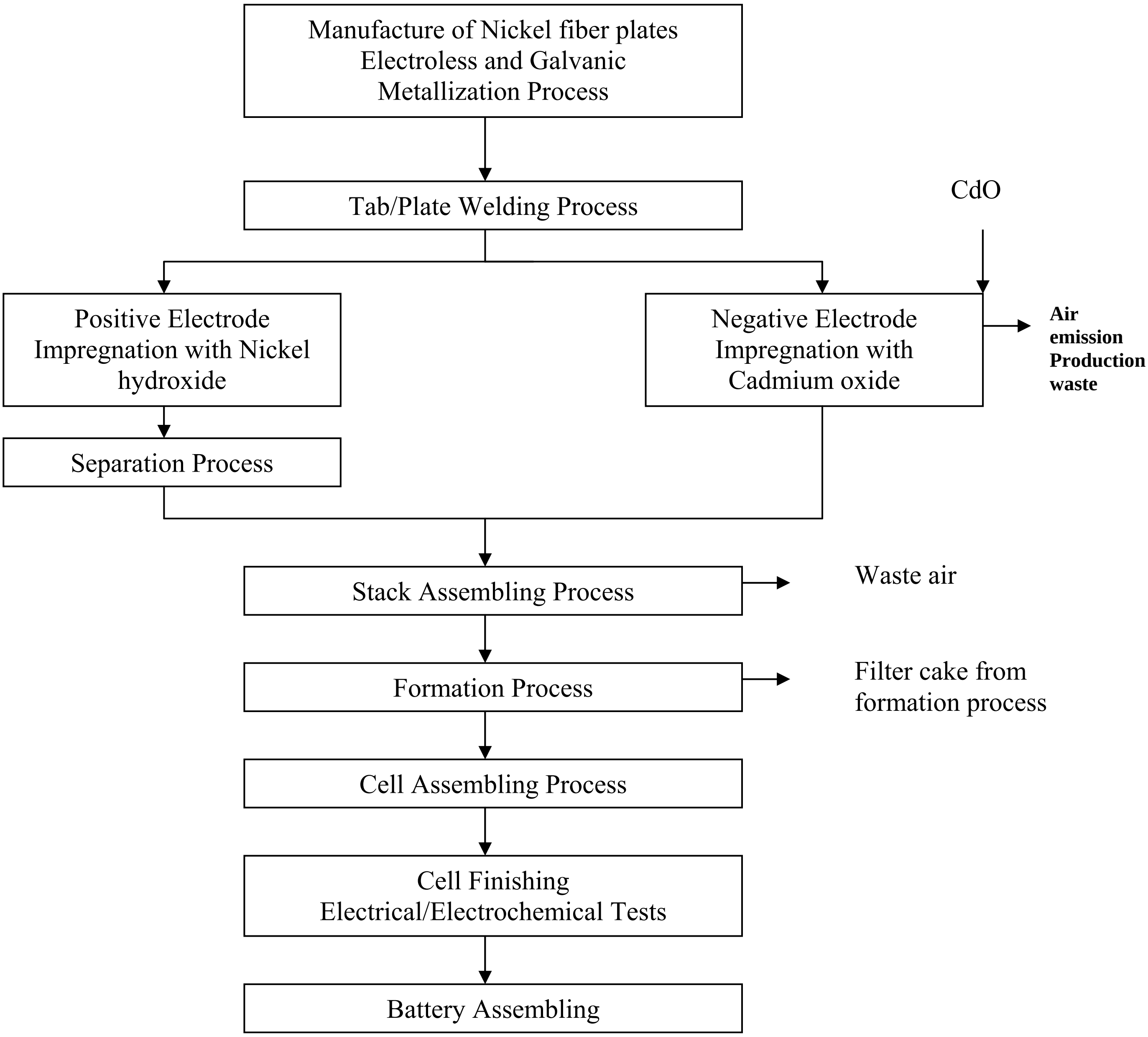
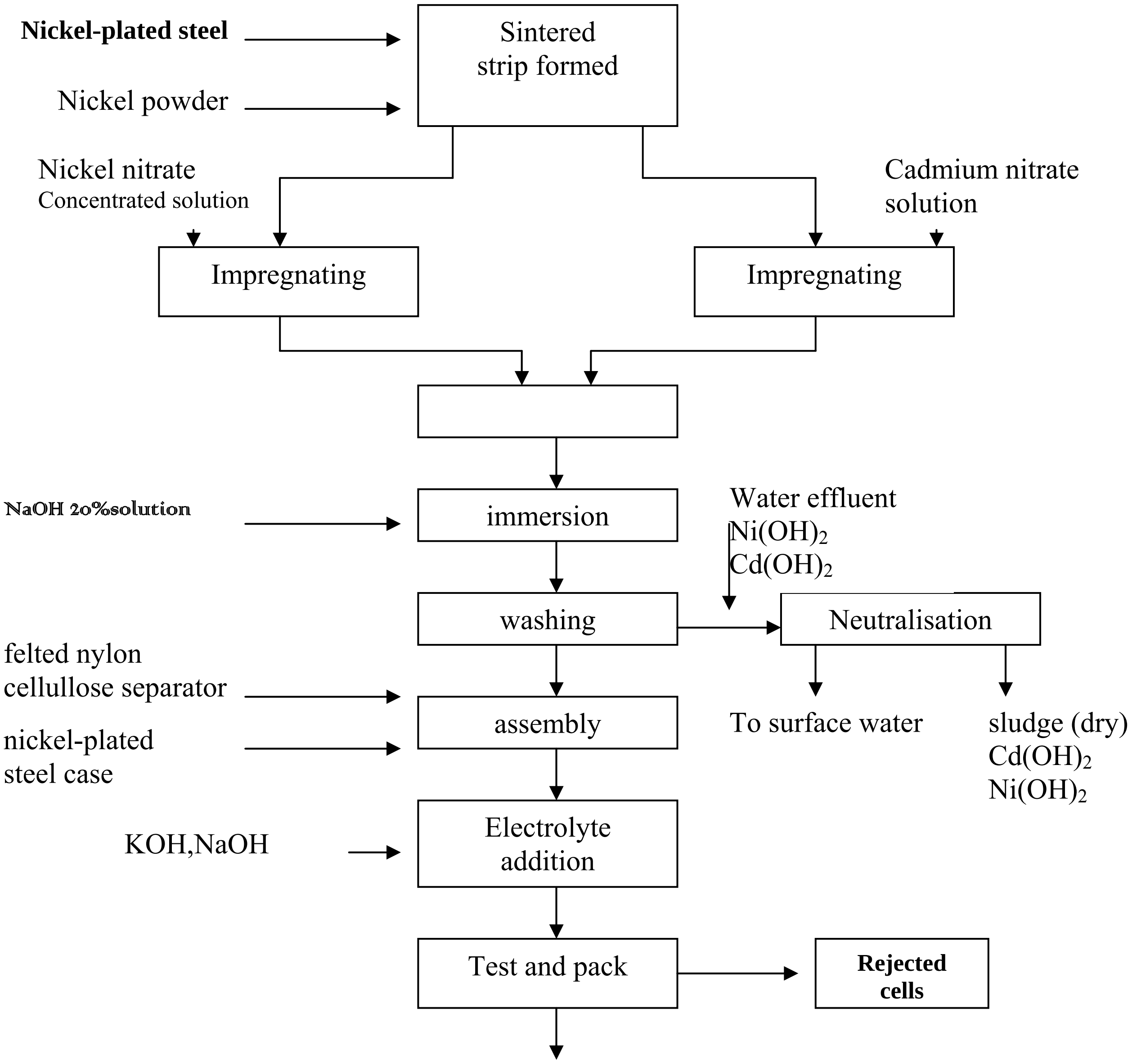


Figure 2.7 Flowsheet of major operations in sintered plate Ni-Cd batteries manufacture



Recycling processes

Ni-Cd batteries might be recycled either pyrometallurgical (high-temperature) or hydrometallurgical (wet chemical) processes. Today, commercial Ni-Cd battery and manufacturing scrap-recycling systems are usually based upon pyrometallurgical (high temperature) processes. Hydrometallurgical (wet chemical) systems have also been designed and have reached the pilot plant stage, but no purely hydrometallurgical systems are utilised today to recycle Ni-Cd batteries. Some recycling systems may have elements of both pyrometallurgical and hydrometallurgical processes in their overall system. (Morrow, 1997).

In pyrometallurgical recycling processes, cadmium-containing wastes or used batteries are heated at a low temperature to drive off moisture and organic compounds, and then heated to above 800°C to volatilise the cadmium. The vapour is then condensed, either as cadmium oxide or metal, and collected for final processing into high purity material (> 99.99%) suitable for any re-use in industrial applications. In hydrometallurgical processes the cadmium containing wastes are dissolved in a suitable reagent, usually a strong acid, and then subjected to a series of wet chemical reactions designed to successively remove impurities. The final cadmium product is normally a cadmium sulphate, chloride or nitrate solution from which high purity cadmium may be electrochemically obtained. Ion exchange techniques have been utilised in some hydrometallurgical recycling schemes, depending on the nature of other impurities present. (OECD, 1996).

A schematic presentation of the recycling processes for industrial and portable Ni-Cd batteries is supplied in **Figure 2.8**.

The reported emission/waste data represent site specific data from a Ni-Cd batteries recycling plant. The emission factors for air and water were calculated using the recycled Cd amount from Ni-Cd batteries only and the emissions to air/water. The emission factor for cadmium in waste was calculated from plant supplied data (Cd content of waste, amount of waste, Cd recycled (from batteries only).

The emissions/waste from the recycling of Ni-Cd batteries include the following:

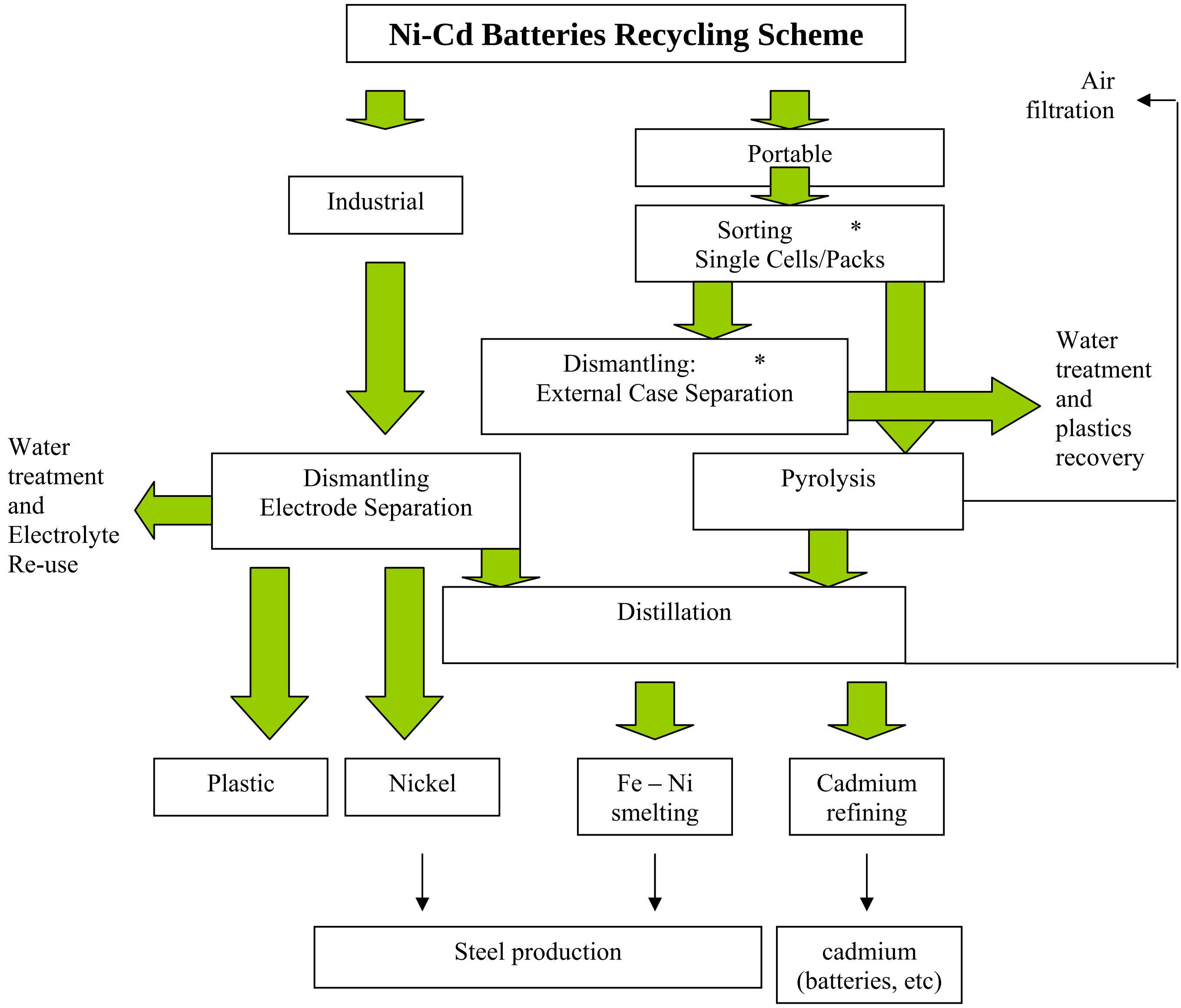
a) Wastewaters containing cadmium. The source of this waste is the dismantling step. This wastewater is estimated to amount to 0.32 g/tonne of Cd recycled (from batteries only).

b) Emissions to air occur during pyrolysis and distillation; 4.7 g/tonne of Cd recycled (from batteries only).

c) Waste:

- plastic boxes from batteries: 0.0011 kg/tonne Cd recycled (batteries) (landfilled)
- metallic boxes from batteries: 1.23 kg/tonne Cd recycled (batteries) (externally recycled)
- Fe/Cd electrodes after treatment: 1,2 kg/tonne Cd recycled (batteries) (ext. recycled)
- Conc. electrolytes: 5,7 kg/tonne Cd recycled (batteries) (ext. scrap treatment)
- Process slag: 154 kg CdO/tonne Cd recycled (batteries) (internal treatment)
- Air treatment dust: 61kg CdO/tonne Cd recycled (batteries) (internal treatment)
- Used filters: 0.138 kg/tonne Cd recycled (batteries) (internal treatment)
- Rainwater sludges: 0.0016 kg/tonne Cd recycled (batteries) (internal treatment)

Figure 2.8 Ni-Cd Battery Recycling (CollectNiCad, 2000b adapted)



* Facultative step(s)

In **Table 2.16** a summary is given of the Cd processing facilities in the world along with their location, type and estimated processing capacity (Morrow, 1999).

Table 2.16 Worldwide Cd processing facilities

Company	Location	Type	Capacity (tonnes of Ni-Cd/year)
Accurec Gmbh	Germany	NiCd Recycler	1,000
INMETCO	USA	Stainless steel	3,000
Japan Recycle Center	Japan/Korea	NiCd recycler	3,000
Kansai Catalist	Japan	Zinc refinery	500
Mitsui Mining and Smelting	Japan	Zinc Refinery	1,800
SAFT AB	Sweden	NiCd Recycler	1,500
SNAM	France	NiCd Recycler	5,400*
Toho Zinc Co, Ltd	Japan	Zinc Refinery	1,700

* SNAM St. Quentin stopped its recycling activities (2001), it has now become a battery sorting plant, all recycling capacity is transferred to the Viviez site.

The present capacities of the world's Ni-Cd battery recycling plants vary from 500 tonnes to 5,400 tonnes with a present total effective capacity of approximately 15,000 tonnes (Morrow and Keating, 1999). The total EU capacity is estimated at 7,900 tonnes.

The facilities located in the EU i.e. SAFT AB (Sweden), SNAM (France), and ACCUREC (Germany) are being considered in this report.

2.2.2.3.2 Mass balance

A complete overview of the mass balance for cadmium in the EU for the reference year 1996 is given in **Figure 2.4** (see Section 2.1.2.1). The production volume of cadmium in the EU in 1996 is estimated to be 5,808 tonnes/year. Corrected for import/export 5,528 tonnes/year is available for different applications. Approximately 2,733 tonnes/year is used for battery manufacturing which equals approximately 47% of the cadmium being produced in Europe. The EU regional consumption of cadmium reaches the value of 2,638 tonnes, which are distributed for 75.2% to Ni-Cd batteries, 14.9% to pigments, 5% to stabilisers and 5% into alloys and plating.

Table 2.17 Cadmium consumption in the Western World (1990 and 1994) or EU (1996) by application

Application	% of total consumption		
	1990[a]	1994[a]	1996[b]
Ni-Cd batteries	55	60	75.2
Cadmium pigments	20	16	14.9
Stabilisers for PVC	10	12	5
Protective coatings	8	7	4
Cadmium containing alloys	3	2	0.9

Table 2.17 continued overleaf

Table 2.17 continued Cadmium consumption in the Western World (1990 and 1994) or EU (1996) by application

Application	% of total consumption		
	1990[a]	1994[a]	1996[b]
Miscellaneous	4	3	< 0.1
Total	100	100	100
Total production in the Western world (in tonnes)	15,900[c]	16,500[c]	13, 840[c]

a) Source: Cadmium Association, OECD Risk Reduction Monograph N° 5 (1994);
b) Source: mass balance (see Section: 2.1.2.1), EU consumption only;
c) Source: World Bureau of Metal Statistics (2000), production in the Western world (does not include Central and Eastern European countries)

Updated (year 2000) and detailed mass balances for industrial and sealed/portable Ni-Cd batteries (Cd content) are presented in **Figure 2.9** and **Figure 2.10**.

Figure 2.9 Industrial Ni-Cd batteries mass balance (EU-16 + Switzerland, Year 2000) (Cadmium content) (CollectNiCad, 2002a, revised July 2002)

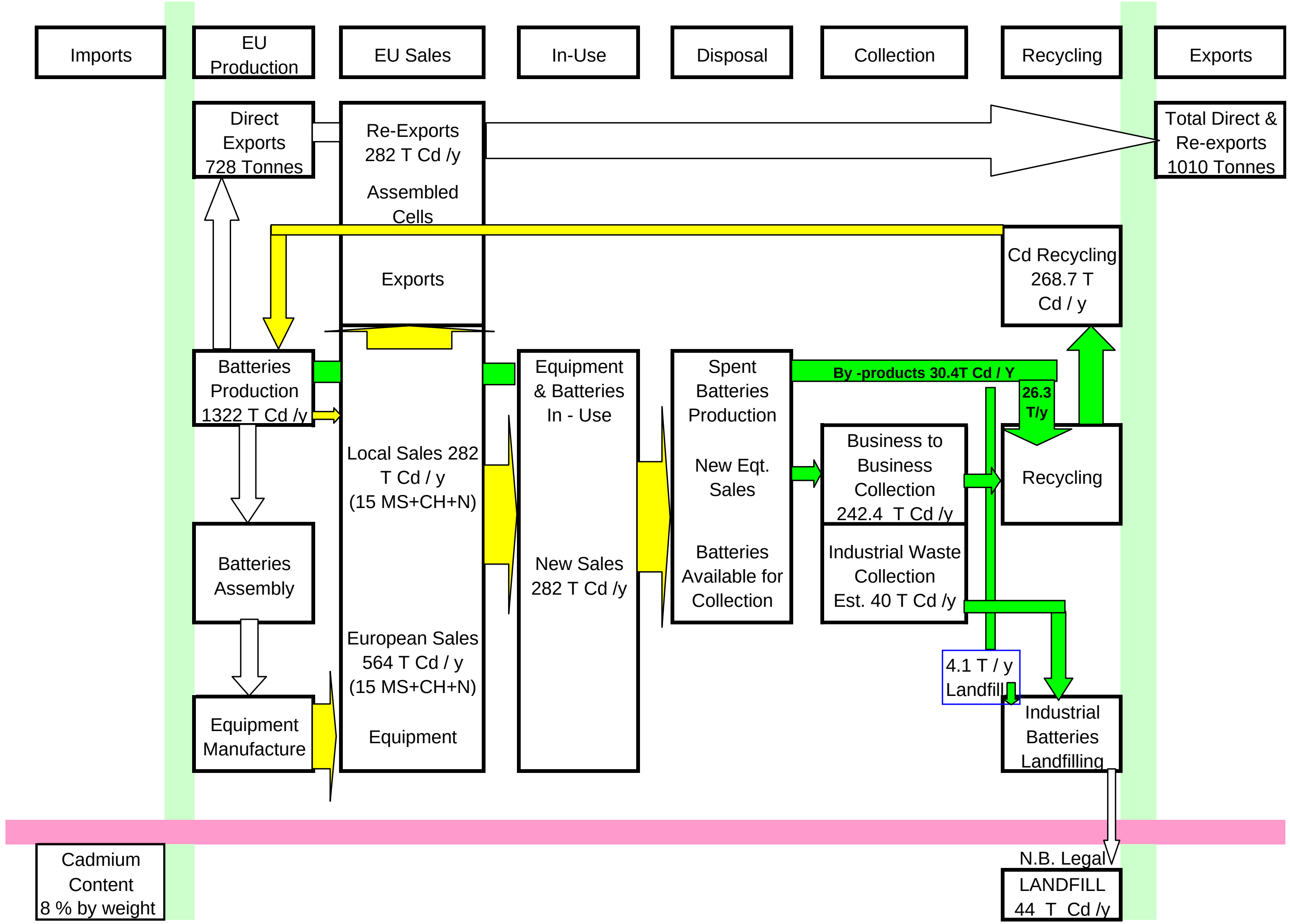
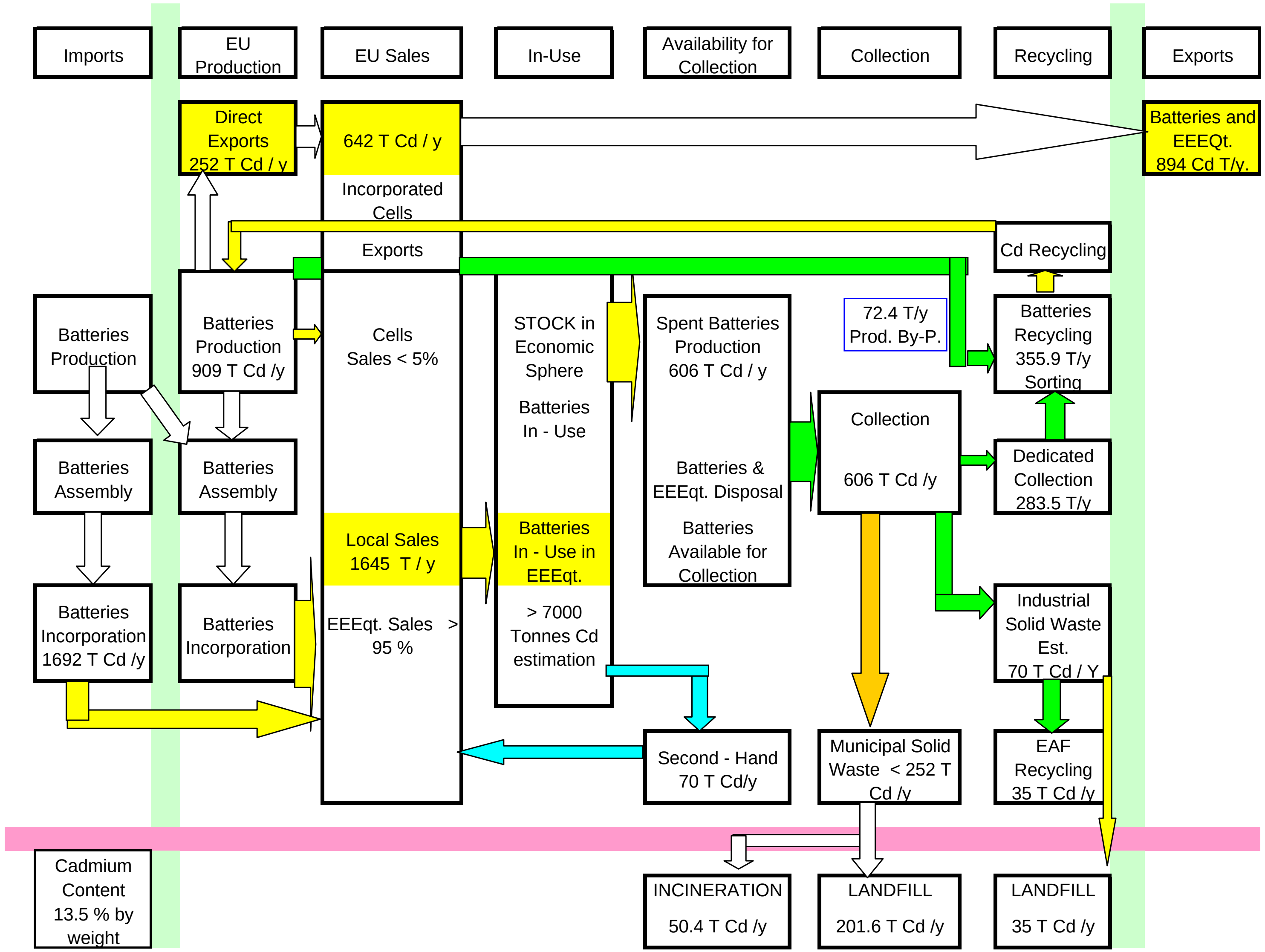


Figure 2.10 Portable Ni-Cd batteries mass balance (EU-16 + Switzerland, Year 2000) (Cadmium content) (CollectNiCad, 2002a, revised July 2002)



2.2.2.3.3 Ni-Cd batteries producing/recycling companies

In the current Risk Assessment Report the exposure data were generated by a number of companies that collaborated voluntarily in the data collection (Industry Questionnaire, 1998 and update questionnaire 2000/2001). The list of companies given in **Table 2.18** is considered as giving a complete overview of the Ni-Cd batteries producing/recycling companies.

Table 2.18 Companies producing/recycling Ni-Cd batteries in EU

Ni-Cd producers		
Country	Location	Company
France	Roullet St. Estephe	SAFT Nersac
	Bordeaux	SAFT Bordeaux
Germany	Duisburg	Friwo (EXIDE-group)[c]
	Brilon	Hoppecke
	Zwickau	GAZ (Zwickau)
Spain	Torrejon De Ardoz/ Madrid	EMISA (EXIDE- group)[b]
Sweden	Oskarhamn	SAFT-AB[a]
Ni-Cd recyclers		
Country	Location	Company
France	Viviez	SNAM
Germany	Mülheim	ACCUREC
Sweden	Oskarhamn	SAFT-AB[a]

a) Production and recycling at the same site
b) EMISA stopped the manufacturing of Ni-Cd batteries in 2003, SAFT, May 2003.
c) FRIWO, production stopped (year?), ICdA, pers.com. 2005.
SNAM St. Quentin stopped recycling (2001) with transfer of recycling capacity to the site of Viviez; VARTA stopped production (end 2000); SANYO: no production of battery cells in the EU, only assembly of imported constituents, therefore not included under manufacturers (pers. comm. 2001); PHILIPS stopped manufacturing cells and shifted to assembly (of non-EU manufactured cells into packs) only since June 2001, Panasonic (former Philips), letter 30.09.02.

At world scale other major manufacturers are Sanyo, Panasonic, GP Batteries, BYD and many of them are importers of batteries incorporated in OEMs equipment[18].

2.2.2.4 Market and sales data

2.2.2.4.1 General

Portable rechargeable batteries are utilised for a wide variety of products and applications. The most important application fields are Cordless Power Tools (CPT), Emergency Lighting Units (ELU) and applications in various Electrical and Electronic Equipment (EEE). Industrial

[18] OEM= Original Equipment Manufacturer

applications of rechargeable batteries include military and space applications, transportation applications, power systems such as reserve power supply for industrial processes.

The nickel-cadmium portable battery market has been analysed in several different ways, in some cases according to geography, in others according to millions of cells sold, and yet in others in terms of the total sales value. In compiling these data, in particular those related to the historical market, EURAS has relied heavily on work done by Industry (e.g. CollectNiCad, 2000c).

2.2.2.4.2 Portable Nickel-Cadmium batteries[19]

<u>General</u>

A compilation of the available data from different data sources on Ni-Cd battery sales in the EU is given in **Table 2.19**.

Table 2.19 Summary of the market data (million units) available on portable Ni-Cd batteries in the EU

Year	Market study						
	ERM[a]	EPBA[b]	Nomura[c]	SANYO[d]	SAFT[e]	CollectNiCad1[f]	CollectNiCd2[f]
1970					12.5		
1975					21		
1980					42		
1985	66	66					
1986							
1987					143		
1988					177		
1989			201				
1990	203	203	226.5				
1991		286	276				
1992			287				
1993			315	310			
1994		244	343	350			
1995	620	564	356	360			
1996		213	334	290			

Table 2.19 continued

[19] Since household applications represent to date less than 20% of the market by weight it is deemed more appropriate to use the term portable batteries (instead of consumer batteries) in order to indicate that the figures presented in this RAR may include professional applications next to household applications.

Table 2.19 **continued** Summary of the market data (million units) available on portable Ni-Cd batteries in the EU

Year	Market study						
	ERM[a]	EPBA[b]	Nomura[c]	SANYO[d]	SAFT[e]	CollectNiCad1[f]	CollectNiCd2[f]
1997		233	356	260			
1998		236	353	250			
1999			352	250		338	343

a) ERM (1997)
b) EPBA production sheets
c) Nomura (1994) in CollectNiCad (2000c)
d) Carcone (1998) in CollectNiCad (2000c)
e) Eloy in CollectNiCad (2000c)
f) CollectNiCad (2000c)

The results of the ERM study have been based on data provided by EPBA (European Portable Battery Association). While the presented results for the years 1985 and 1990 are in concordance with the results of the other studies the figure of 1995 is clearly out of scope. The main reason for this discrepancy is the assumption taken in the other market studies in deducing the EU share from the world market data. The EU market share in the ERM study mounts up to 40% of the world market in 1995, while the EU world market share in the other studies have been assumed to be respectively 25% in the Nomura and SANYO study and 20% for the SAFT study. The latest survey conducted by CollectNiCad (CollectNiCad, 2000c) supports these latter suppositions and will be discussed in more detail here below.

The European sales volume for the year 1999 for portable Ni-Cd batteries has been established) on the basis of data obtained from battery manufacturers and original equipment manufacturers O'EM's. Two different and independent methodologies have been used.

The first method (CollectNiCad. 1) calculates the total sales of Ni-Cd batteries from the number of cells used in the three major application areas: cordless power tools, emergency lighting, household equipment (shavers, dust busters, dental care etc.), telecommunications and the sales of single cells. In order to translate the number of cells into a weight estimate an average weight of 38.0 g of one cell has been assumed, calculated from the total number of cells introduced on the EU Countries market.

The second method (CollectNiCad 2) is based on production data (in number of cells and in tonnes of batteries) of all Ni-Cd battery manufacturers active in Europe and corrected for import/export ratios of cells and packs as well as of batteries incorporated in electrical and electronic equipment.

Data for portable Ni-Cd Batteries by market segments/applications (CollectNiCad. 1)

For the breakdown of the market data by application an in depth analysis was performed of the European sales of portable Ni-Cd batteries in the three major applications areas: cordless power tools, emergency lighting and household and 'electrical and electronic equipment' (EEE).

Table 2.20 provides a summary of the market data by application. Those data show a total annual market of 12,700 tonnes in 1999.

Table 2.20 Portable Ni-Cd batteries EU market, sales by application (million cells/year) reference year 1999

Electrical and Electronic Equipment (EEE)		
Application	Average weight/cell (g)	Sales (million cells/year)
Household equipment	22	28
Dust buster	48	12
Toys	55	5
Audio-Video	26	10
Single cells and others	22	54
Cordless phones	14	50
Emergency lighting		
Application	Average weight/cell (g)	Sales (million cells/year)
Emergency light	120	26
Power tools		
Application	Average weight/cell (g)	Sales (million cells/year)
Cordless tool	41	138
Others		
Application	Average weight/cell (g)	Sales (million cells/year)
Medical	20	10
Military	40	5
Average weight/unit	37.8	
Total sales		338

Source: CollectNiCad (2000d)

The average weight of approximately 38 g for a portable Ni-Cd battery is used in the further calculations

Data for portable Ni-Cd Batteries based on production data (CollectNiCad 2)

The data obtained by the second method are presented in **Table 2.21**.

Table 2.21 Overview EU market corrected for import and export in 1999

	Local annual sales (millions of cells)	Domestic sales (%)	Export sales (%)	Import Europe (%)	Net EU market (millions of cells)
Japan	158	n.d.	50	30	23.7
Europe	324	65	35		210.6
North America	457	n.d.	15	50	34.3
Asia	530	n.d.	70	20	74.2
Total	1,469	n.d.	n.d.	n.d.	342.8

n.d. No data available

Those data indicate that a total market of approximately 1,4 billion of Ni-Cd cells have been reached in 1998 and 1999. To evaluate the market in the E.U. countries the import-export of Ni-Cd cells assembled into packs and of packs incorporated in EEE were taken into account (see

Table 2.21). The net EU market contribution for each country/continent was calculated with the following formula:

Net EU market contribution = Local annual sales X export (%) X import Europe (%)

According to **Table 2.21**, 342.8 millions of cells have been sold in 1999 within the 15 EU. Member States corresponding to approximately 23.3% of the world market. The assumption of the EU market share of 20-25% is therefore confirmed and will be used to select data to build a historical market curve. In this respect the high ERM figure for 1995 is being rejected.

Historical market development

In order to make any predictions on the amounts of batteries available for collection and/or disposal it is imperative to have a good picture of the historical market development. In **Table 2.22** the selected data for the portable consumer/sealed portable market are summarised. To express these market figures in tonnes/year these values have been multiplied with the estimated average unit weight of 38 grams. Missing values were extracted by interpolation.

Table 2.22 Overview of the historical reference data for portable Ni-Cd batteries

Year	Millions/cells	Tonnes/year	Year	Millions/cells	Tonnes/year
1980	42	1,596	1991	276	10,488
1981	n.d	*1,778*	1992	287	10,906
1982	n.d	*1,960*	1993	315	11,970
1983	n.d	*2,142*	1994	343	13,034
1984	n.d	*2,324*	1995	356	13,528
1985	66	2,508	1996	334	12,692
1986	n.d	*3,971*	1997	356	13,528
1987	143	5,434	1998	353	13,414
1988	177	6,726	1999	352	13,376
1989	201	7,638	2000	314	11,930
1990	226.5	8,607	2001	275	10,995

n.d. No data available
Figures denoted in italics are interpolated

2.2.2.4.3 Industrial Ni-Cd batteries (CollectNiCad 2000c)

The European market for industrial batteries can be split into a number of well-defined sectors as follows:

- Standby, or stationary, applications - safety, and back-up systems at airports, hospitals, power stations, offshore installations etc.
- Transportation - railways, metro cars, etc.
- Aviation - starting of engines, oil board safety systems, etc.
- Electric vehicles (EV)

The batteries within the two largest segments - standby and transportation - are used within a country's infrastructure. The need for batteries for new installations is the largest during this infrastructure development phase. Batteries for standby applications are often purchased by equipment manufacturer (OEM) and delivered together with the equipment to the user. Many of these OEM's are situated in Western Europe while the users are situated in e.g. the Middle East and Far East. Thus, the batteries are purchased by and invoiced to a European customer, but they are very often re-exported to other parts of the world. In some of the Member states with important OEM'S, the re-export factor of standby batteries can be as high as 50%.

Batteries for transportation and aviation purposes are to a higher extent delivered directly to the end user and the re-export factor is lower (15%). The EV (Electric Vehicles) market is still at a low level. Main part of the EV nickel-cadmium is produced in EU and is used within EU.

The volumes of the different industrial Ni-Cd batteries for use within the EU market has been estimated from data of the three major suppliers (representing more than 95% of the market supply) with addition for an estimated volume of imported batteries and are listed in **Table 2.23**.

Table 2.23 Industrial Ni-Cd batteries EU market sales (tonnes/year)

Year	Industrial Ni-Cd battery (tonnes/year)
1995	3,242
1996	3,608
1997	3,625
1998	3,964
1999	3,697
2000	3,566

Sources Original references Saft, Exide and Hoppecke in CollectNiCad (2000c,2002)

From this table it is clear that the industrial batteries' market has reached a stable level of 3,500 to 4,000 tonnes/year. Cross-validation with the ERM study shows the same magnitude (4,000 tonnes in 1995).

2.2.2.4.4 Country by country data

The data presented in this section are obtained mainly by two ways. The first was through the Questionnaire on Batteries sent out in 2000 by the MSR to the national authorities of the EU and Norway, the collector organisations as well as the EU associations of manufacturers (i.e. EPBA). The second series of data was compiled via the efforts run in parallel by Industry (CollectNiCad 2000d).

It needs to be mentioned that to date the information in this document is rather limited and no attempt was made to verify the correctness of each figure. Another remark concerns the fact that figures obtained via different sources are not necessarily independently generated (e.g. the data provided by the national collector organisations may be the only data available at the authority level). Finally the data obtained via different ways may in some case be 'complementary' to each other (e.g. the data on collection as provided by the collection organisation versus Industry's data obtained from the recyclers) and thus allowing for at least some approximate direct check by comparison.

Data sources

Responders to the Questionnaire are indicated by a figure between brackets in the last column of the Tables and accompanied by details in a footnote, if needed. The figure (1) is used when data were obtained from the MS (national authority). The indication (1C) is used when Collection organisation(s) replied. The main primary generators of data in so far as these are known, are indicated under the corresponding subsections. Data compiled and submitted by CollectNiCad are indicated by the figure (2).

Data errors and deviations

Besides the well known sources of errors e.g. reporting, (de)coding, transcription, etc deviation of data generated by different types of sources may be due to (a different degree of taking into account) stockpiling, as well as import and/or export of new, spent or recycled material or appliances containing batteries. On the other hand, differences in used definitions of e.g. 'portable', 'consumer' and 'industrial' but also 'marketing' and the specific sorting or not of Ni-Cds may cause divergences between figures generated by different MS, collector organisations and Industry. Finally, difficulties may arise due to the different units in which marketing figures versus collection amounts are expressed. The former are generally in units (or mAh) while the latter are reported in weight units. Together with the variation in battery weight, this may cause deviations.

Portable Ni-Cd batteries

A summary of the available data is given in **Table 2.24** for consumer/sealed portable Ni-Cd batteries.

Table 2.24 Portable Ni-Cd battery market data (tonnes/year) for EU countries

Country	1994	1995	1996	1997	1998	1999	2000	2001	Reference
Austria				62	98	97			(1C)*
						309	286	247	(2)
Belgium			381	388	368				(1)
						327	302	261	(2)
Denmark	214[b]	233[b]	218-328[b]	291	242	210			(1C)
						137	127	110	(2)
Finland[a]			250						(1)
						134	124	107	(2)
France						130			(1)*
						2,212	2,046	1,768	(2)
Germany	3,095	2,642	2,334	2,214	2,050	3,210		2,880	(1C)
						2,261	2,091	1,808	(2)
Greece						404	374	323	(2)
Ireland						233	216	186	(2)

Table 2.24 continued overleaf

Table 2.24 continued Portable Ni-Cd battery market data (tonnes/year) for EU countries

Country	1994	1995	1996	1997	1998	1999	2000	2001	Reference
Italy						1,567	1,449	1,253	(2)
Luxembourg						25	23	20	(2)
The Netherlands						652	603	521	(2)
Portugal						241	223	193	(2)
Spain						1,168	1,080	934	(2)
Sweden	486	338	333	328	190	175 249	 230	 199	(1) (2)
UK[a]	2,001	1,766	1,958	2,167	2,652	2,983 2,706	 2,503	 2,163	(1) (2)
Norway		199	187	124	175	215 125	 116	 100	(1) (2)
Total EU-16[a]						14,005	11,793	11,265	
Switzerland						274	253		(2)
Total[a]						14,279	12,046		

1) Questionnaire Member States (2000). Primary sources: (B): BEBAT, (F): only SCRA members, (UK): ERM, (S): based on information from importers and manufacturers, updated '02: Ni-Cd batteries that have been put on the Swedish market, as reported to the Swedish EPA, (NO): sealed cells, separate or in appliances, in this table: with the assumption that all cells in appliances are totally attributed to consumer application.
1C) Questionnaire (2000) Collection organisations. (A) : only data via UFB (Incl. some industrial uses, DK: Danish Battery Association, (DE): Data provided by ARGE Batterien, data for 2001 submitted by UBA, 2002.
* Incomplete data-set(2): Industry Country by country data (CollectNiCad 2000d)
a) Upper limit used and assuming average battery cadmium content of 13.8% see Table 2.2.5
b) Miljoprojekt (2000)

For the data submitted by the authorities, the way the data are obtained/generated and the surrounding uncertainties are in general not explicitly specified. Industry (CollectNiCad) compiled data mainly through the information given by manufacturers and their commercial network (no primary data are available).

Six Member States have submitted their figures on the sales of portable[20] Ni-Cd batteries. Additional data for 17 countries were provided by CollectNiCad (2000f) for the year 1999. In general the latter figures are in concordance with the figures reported by the Member States. However, the market figures provided for France collated from the Member State Questionnaire are incomplete (130 versus. 2,212 tonnes/year). In comparison with countries of a similar population size (UK, Italy) the industry's estimate seems a more realistic one. The industry's estimates for Denmark, Norway and Germany are approximately 30-40% lower than the figures provided by these countries. According to Industry the differences in the market data for Germany are mainly related to exports. A considerable amount is claimed to represent exported batteries, amount which is said by Industry to be neglected as such in the German data provided by the DE MS (neither primary data nor details from Arge Batterien were submitted to the Rapporteur).

Overall it can be concluded that approximately a maximum of 14,000 tonnes of portable Ni-Cd batteries is put on the EU-16 market (including Norway) for the reference year 1999.

[20] Those MSs replied to the Questionnaire under the section 'Consumer batteries'. Some MSs gave details related to the types and applications of batteries while others did not.

Recent data given by industry indicate a decrease in the weight volume introduced on the market with respectively 11,930 and 10,995 tonnes/year for the years 2000 and 2001.

Industrial batteries

Very few countries replied on the Questionnaire 2000. The primary data sources for Industry's submitted data are in the first place the manufacturers. An overview of the present available data is given in **Table 2.25** for industrial Ni-Cd batteries.

Table 2.25 Industrial Ni-Cd battery market data (tonnes/year) for the EU Member States

Country	1994	1995	1996	1997	1998	1999	Reference
Austria						144	(2)
Belgium						97	(2)
Denmark				48-54[c]		20	(2)
Finland[a]			23	121	104	68 87	(1) (2)
France						1,097	(2)
Germany						213? 251	(1*) (2)
Greece						230	(2)
Ireland							
Italy						243	(2)
Luxembourg						1	(2)
The Netherlands						80	(2)
Portugal						13	(2)
Spain						758	(2)
Sweden	250	200	200	200	150	150 142	(1) (2)
UK[a]	853	858	862	907	958	1,008 404[b]	(1) (2)
Norway		95	104	119	84	57 1	(1) (2)
Total EU-16[a]						3,632	
Switzerland						93	(2)
Total[a]						3,725	

1) Questionnaire Member States (2000) Primary sources: (B): BEBAT, (F): only SCRA members, (UK): ERM, (S): SAFT
1C) Questionnaire (2000) Collection organisations (DE) : only data from VfW-REBAT (consumer/sealed portable + industrial): data from ZVEI not available
2) Industry Country by country data (CollectNiCad, 2000f)
* Incomplete data-set on country basis
a) Upper limit used except for UK figure(s) that were corrected cfr text
b) UK + Ireland
c) Miljoproject (2000)

Four Member States have submitted market data on industrial Ni-Cd batteries. Additional data for 17 countries were provided for the year 1999 by industry. For the few cases where comparison is possible, the figures are in concordance with the figures provided by the Member States. Industry's estimate for the UK is much lower then the figure submitted by the UK-MS (DTI). ERM (on behalf of UK) provided this estimate based on sales information from SAFT and Exide ranging from 600-1000 tonnes. It was acknowledged by ERM that they did not correct for export that is estimated to be 50% (ERM, Pers. com., 2000). Applying the export rate gives an estimated figure for the UK market ranging from 400 to 670 tonnes (the figure '404' is used for calculating the totals for the year 1999).

Overall approximately 3,700 tonnes of industrial Ni-Cd batteries is put on the EU-16 market (EU including Norway) for the reference year 1999.

Market trends

Most of the data related to market evolution come from Industry. The data submitted by CollectNiCad relate to the past and to semi-quantitative information on the application's market shares (see paragraph below). No precise information is (made) available on how the Ni-Cd battery market is likely to evolve in the future.

Ni-Cd batteries can be classified into four lines of products according to their market applications: industrial batteries, Emergency Lighting units (ELU), Cordless Power Tools (CPT) and applications in numerous Electrical and Electronic Equipment (EEE).

The largest application field for Ni-Cd batteries and a growing market have become the CPT applications (separated between the Professionals and Consumer market). The ELU market is under a slight growth rate with higher market shares in countries like France, United Kingdom, Italy and Spain, by opposition to Germany where centralised units powered by lead-acid batteries are used. The EEE market, which has been the largest market segment for Ni-Cd batteries during the first half of the nineties, is declining. From 1995, Ni-Cd batteries have gradually being replaced on the market by other types of batteries like the Nickel-Metal Hydride, the Lithium-Ion and the Lithium-Polymer batteries. Industrial Ni-Cd batteries are continuously in competition with lead-acid batteries but forms a stable market. A summary of the market shares for the different applications for the years 1999 and 2000 is given in **Table 2.26** and **Table 2.27**.

Table 2.26 Weight distribution in percent of the market share of Ni-Cd batteries by applications- reference year 1999

Industrial	Portable CPT
22% (Stable)	35% (growing)
Portable ELU	Portable EEE
18% (Stable)	25% (Declining)

Source CollectNiCad (2000e)

Table 2.27 Weight distribution in percent of the market share of Ni-Cd batteries by applications (reference year 2000)

Industrial	Portable CPT
24% (Stable)	35% (growing)
Portable ELU	Portable EEE
19% (Stable)	16% (Declining)
Specialities (Aviation, Industrial Comm. and Computing)	
6% and growing	

Source CollectNiCad (2002b)

From the information available it can be concluded that the Ni-Cd market has increased significantly in the 80's to reach a more or less stable level in the late 1990's of around 13,500 tonnes/year for consumer/sealed portable nickel-cadmium batteries and 3,500 to 4,000 tonnes/year for the industrial nickel-cadmium battery market.

To date, no market projections are available for the amount of portable Ni-Cd batteries, which will be put on the market in the future. A study by ERM (2000) employed a positive common growth rate for all types of portable secondary batteries. However, since the market evolution is stated to be mainly technology driven and, as there is confidential business implication, it is difficult to get any good specific estimate for the growth rate of Ni-Cd chemistry applications.

Between 1996 and 1999 the portable Ni-Cd battery market in the EU seems to be oscillating around 13,000 -14,000 tonnes[21]. Although recent figures for 2000 and 2001 indicate a decrease in sales, the figure of 13,500 tonnes has been chosen as a worst case scenario to forecast future battery waste arising. The industrial batteries remain at the level of 3,600 tonnes.

2.2.2.5 Collection/recycling data

2.2.2.5.1 Country by country data

Portable Nickel-cadmium batteries

Data on the Ni-Cd battery collection/recycling efforts for individual EU countries were collated from the Questionnaire 2000. In addition Industry (CollectNiCad) provided a second series of data for the year 1999 and 2000. The latter represent the amount collected and processed for recycling. An overview of the available data is given in **Table 2.28** for portable Ni-Cd batteries.

[21] The reference year 1999 has been chosen because this was the most recent year for which cross validation of the data provided by industry with those provided by the Member States was possible.

Table 2.28 Total weight (tonnes/year) of collected/recycled portable Ni-Cd batteries for the individual EU countries

Country	1994	1995	1996	1997	1998	1999	2000	2001	Reference
Austria	22.5	26.7	42.5	61.8	97	97	53	84	(2) (A)
Belgium				37	79	59	177		(1)
	9	10	10	50	66	59	115	70	(2) (B)
Denmark	34	54	9	94	80				(1C)
	34	54	--	103	78	66	59	108	(2) (Dk)
Finland					91	113			(1)
		1	6		12	5	10	1	(2)
France	33	50	65	95	100				(1)
	60	35	70	105	92	140	140	182	(2)
Germany	220	206	303	440	403	596	1,001		(1)
							950	921	(2) (GRS)
Greece							1	1	(2)
Ireland						9	11	5	(2)
Italy	1			2	1	25	33	36	(2)
Luxembourg					5	5	5	5	(2)
The Netherlands	10	29	35	75	119	150	210	160	(2) (NL)
Portugal							1	1	(2)
Spain		4				38	30	66	(2)
Sweden	111	112	113	141	144	170	142	167	(1)
		108	110	142	143	169	147	167	(2)
UK					50	106			(1)
	18	63	72	94	46	75	78	93	(2)
Norway				66	63	53			(1)
		2	10			12	10	43	(2)
Total EU-16[a]	459	539	663	1,106	1,125	1,446	1,852	1,943	
Switzerland	34	96	46	21	114	48	194	198	(2)
Total[a]						1,494	2,046	2,141	(2)

1) Questionnaire (2000) Member States. Sources: (B):data from BEBAT figure of 2000 is still provisional: lower figure: amount of sorted batteries, upper figure: amount of recycled batteries during the year 2000, (F): Ministere de l'amenagement du territoire et de l'environment, (UK): data as from SNAM, (S):data as from SAFT, (DE): data from UBA, comments 2002.

1C) Questionnaire (2000) Collection organisation. DK: Danish Battery Association: figure of '95 includes collection till 31 March'96

2) Industry Country by country data (CollectNiCad, 2000f and 2001a) (A) Rumpold AG, (B) BEBAT, (Dk) Battery Association Denmark, (GRS) Gemeinsames Rücknamesystem Batterien, (NL) STIBAT

a) Lower limit used

The primary data source for Member States is data on collection as obtained via governmental or private collection organisations. Additional verification procedures by external independent organisms may enhance the confidence in these figures. Industry (CollectNiCad) compiled its series of figures through information obtained via the recycling companies and/or collection organisations (primary data are not available to the Member States Rapporteur). The transboundary movement of spent Ni-Cd batteries is liable to the Basel Convention administrative rules and offers a means to trace back collected amounts on national basis.

For the few cases where comparison is possible, no large differences are observed between the data provided by industry and the Member States. Overall approximately 1,852 tonnes of portable Ni-Cd batteries has been collected in the EU-16 for the year 2000 and 1,943 tonnes for the reference year 2001. Countries for which no (or poor) data are available have most often not yet a dedicated Ni-Cd collection system in place. A short overview of the situation in the EU is given by CollectNiCad in **Table 2.29**. The information on existing Ni-Cd collection schemes and programs present in Europe gathered by the Questionnaire is limited (only DK, S, UK, F, FIN and NO) and mostly does not provide many further details than those already reported in other publications (ERM, 1997; EUPHEMET, 2000 and CollectNiCad, 2000f). More details are available in Annex I.

Table 2.29 Overview of Ni-Cd Collection programs running in various European countries

Country	Collection Ni-Cd	Collection all type (primary and rechargeables)	Start	NCRA[a]	Sorting	Financial system (€/kg)
Austria	Yes	Yes	1990	UFB	Yes	2
Belgium	Yes	Yes	1993	BEBAT	Yes	3
Denmark	Yes*		1996**	Ministry**	No*	16
Finland	Yes			Municipalities/ importers/retailers	Some	
France	Yes		1999	SCRA	Yes	2
Germany	Yes	Yes	1998	GRS	Yes	2
Greece						
Italy						
Luxembourg						
Portugal						
Spain	Yes-local	Yes-local	1999			
Sweden	Yes	Yes	1998	Municipalities	Yes	34
The Netherlands	Yes	Yes	1995	STIBAT	Yes	2
UK + Ireland	Partial		1994	REBAT		
Norway	Yes		1997	Batteriretur		
Switzerland	Yes	Yes	1990	BESO	Yes	3-5

Source CollectNiCad (2000g), adapted.
* Will change in future: all batteries (primary and rechargeable will have to be collected);
** Before that date: other in place e.g. Danish Battery Association
a) NCRA = National Collection and Recycling Association

Industrial Nickel-Cadmium batteries

Data on the Ni-Cd battery collection/recycling efforts for individual EU countries were collated from the questionnaire 2000. In addition CollectNiCad provided data for the year 1999. An overview of the available data for industrial Ni-Cd batteries is given in **Table 2.30**.

Table 2.30 Total weight (tonnes/year) of collected/recycled industrial Ni-Cd batteries for the individual EU countries[22]

Country	1994	1995	1996	1997	1998	1999	2000	2001	Reference
Austria		91	115	173		148	304	134	(2)
Belgium	14	105	71	140	112	65	91	104	(2)
Denmark		3	5 14[b]	3	1	7	11	34	(2)
Finland		 41	 47	 70	70 98	160 131	 82	 188	(1) (2)
France	158 528	153 560	251 1,100	383 560	400 618	 529	 817	 780	(1) (2)
Germany	935	1,074	987	1,124	1,295	998	799	826	(2)
Greece			3						
Ireland						20	8	8	(2)
Italy	31	103	131	151	41	125	194	190	(2)
Luxembourg				4	3		10	5	(2)
The Netherlands	83	127	261	185	172	150	146	124	(2)
Portugal									
Spain		12		41	181	160	94	154	(2)
Sweden	136	157 147	254 254	204 204	189 189	 200	 216	 295	(1) (2)
UK	 29	 21	 24	 80	52 51	112 112	 136	 112	(1) (2)
Norway		 53	 53	 57	20 34	32 67	 55	 84	(1) (2)
Total EU-16[a]						2,677	2,963	3,038	
Switzerland	39	19	18	20	23	21	160	42	(2)

1) Questionnaire Member States (2000) Primary sources: (B): BEBAT, (F): Ministere de l'amenagement du territoire et de l'environment, (UK): SNAM, (S):SAFT
2) Industry Country by country data (CollectNiCad, 2000), updated for the years 2000 and 2001 (CollectNiCad, 2002)
a) Lower limit used
b) Miljoprojekt (2000)

In the few cases where two sets of data are available, no large differences are observed between the data provided by industry and the Member States. Overall approximately 2,677 tonnes of industrial Ni-Cd batteries have been collected in 1999.

2.2.2.5.2 Collection rate/Collection efficiency

Data on the absolute amounts of Ni-Cd batteries being collected was obtained from a questionnaire submitted in 2000 to the EU Member States. In addition CollectNiCad provided country by country data for the year 1999. Collection percentages mentioned in the questionnaires are not given in the **Table 2.28** and **Table 2.30**. Any comparison of these numbers should be performed with caution since most often the rationale behind the calculation

[22] With update for 2000 and 2001, via CollectNiCad, 2002.

of collection rates are not the same for the various EU Member States. Typically, collection rates are being calculated as the percentage collected batteries of a base year sale. In that case the collected amount corresponds to only a small percentage of same years' sales of portable Ni-Cd batteries (e.g. UK). However, this kind of approach is difficult to apply for long life articles[23] such as Ni-Cd batteries for which no correlation can be found between the base year sales data and the collected quantities for that same year.

So, Industry as well as Member States developed a number of alternative calculation formulas. One of the most recent is the so-called 'collection efficiency' being defined by STIBAT as the ratio between the amount of Ni-Cd batteries collected over the maximally available amount for collection (STIBAT, Deauville, 1999) with the latter equalling the sum of the collected Ni-Cd batteries and the quantity of Ni-Cd batteries disposed in the municipal waste stream.

Calculating the collection efficiency

$$\text{Collection efficiency} = Q._{Ni-CdColl} = \frac{Q._{Ni-CdColl}}{Q_{Ni-CdColl} + Q_{Ni-CdMSW}}$$

$Q._{Ni\text{-}Cd\ Coll}$ = Quantities of batteries collected separately
$Q._{Ni\text{-}Cd\ MSW}$ = Quantities of batteries eliminated with Municipal Solid Waste

Although this equation may have advantages (i.e. independent of present market volume and battery's lifetime) it needs to be mentioned that detailed studies dealing with the analysis of MSW are complex and for the moment limited to a few countries. Furthermore the amount of Ni-Cd batteries found in MSW might not be completely representative for all Ni-Cd batteries going into the waste stream. For example, replacement of batteries in emergency lighting units is not common. Therefore, the majority of end-of-life Ni-Cd batteries in emergency lighting become waste during building refurbishment and are generally disposed of as mixed industrial and some as municipal waste (ERM, 2000). For pure conceptual and mathematical reasons the use of a collection ratio, defined as a simple percentage of the total amount of used Ni-Cd batteries coming available for collection and that will effectively be collected for recycling, is preferred. By subtraction, the remaining amount of batteries arriving into the waste stream is obtained.

Since not all European countries have a (Ni-Cd) battery collection system in place two collection ratio's are considered further in this report:

- 10% collection of the Ni-Cd batteries coming available for collection: representative for a country with a collection system with low efficiency;
- 75% collection of the Ni-Cd batteries coming available for collection: considered by Industry as representing an EU-wide realistic target (CollectNiCad, Pers. com., July 2002) and chosen to be representative for a country with a collection system with a high efficiency.

The span of 10-75% is believed to cover all possible combinations in the EU (limited to waste management options). Hence, in this regard the development of country specific scenarios are not deemed necessary.

[23] Long life articles are defined in the revised TGD as articles having a service life longer than one year

2.2.3 Updated data (reference year 2002)

2.2.3.1 Introduction

Quantitative update information regards the use of the substances in the different applications is fragmentary.

Consumption volumes are updated for the uses in batteries, in pigments and in stabilisers for those companies that participated in the updating exercise (see **Table 2.31**).

Furthermore some producers provided tentative data regards the break-down of the quantities cadmium metal and cadmium oxide: the uses of cadmium oxide expressed as percentages of the production in 2002 are estimated as follows: batteries: 83.5%, stabilisers: approximately 27% pigments: 1.5% and others: 4%. This latter information is substantially different from the data provided by the processors/users of the substances.

No update consumption data are available for Cd plating, alloys and others.

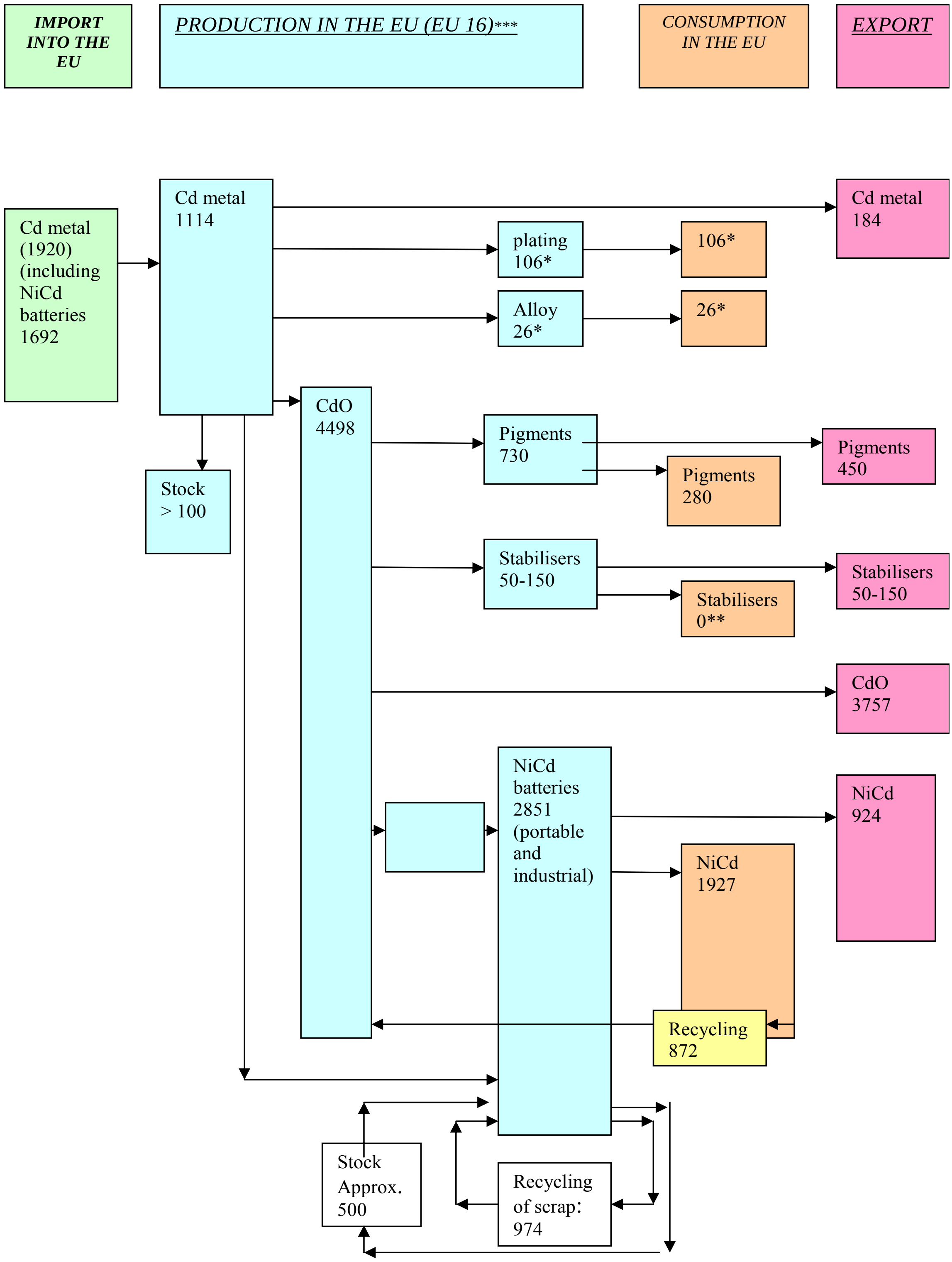
Table 2.31 Consumption data on cadmium metal and cadmium oxide for the major use applications (amounts in metric tonnes and expressed as elemental cadmium)

Year	Batteries	Pigments	Stabilisers
2002	1634.6*	n.d.	in the range 50 to 150
2003	1725*	299	in the range 50 to 120

n.d. No data available;
* Figures based on the information provided by 3 companies

Recently, an update of the mass-balance of cadmium in the EU (year 2000-2002) was provided by industry (see **Figure 2.11**). The production volume of cadmium in the EU in 2000-2002 is estimated to be 1,114 tonnes/year. Corrected for import/export 2,850 tonnes/year is available for different applications.

Figure 2.11 Cadmium mass balance flow in the EU for the reference year 2000-2002 (mass balance drawn up by ICdA, IZA-Europe and Recharge)



* Data refers to 1996. No update in figures was received

** Due to the Vinyl 2010 Commitment

*** Not included is cadmium contained in imported raw materials (zinc, copper and lead ores). For zinc ores the estimated amount of cadmium in the EU-16 is 5,000 tonnes/year. Most of this cadmium is stated to be separated in the production processes, stabilised and disposed of in authorised hazardous waste disposal sites.
Estimated amount is 5,000 tonnes for EU zinc industry.

2.2.3.2 Ni-Cd Batteries

Since the previous update of information in 2002/2003, the number of companies producing Ni-Cd batteries has further decreased. **Table 2.32** mentions those companies that ceased the production of these batteries. Current producers are given in **Table 2.33**.

Table 2.32 Companies formerly producing Ni-Cd batteries and date/year of ceasing production

Company (and plant)	Country	Date/year of production stop
Friwo (EXIDE-group)	Germany	p.m. date to specify
EMISA (EXIDE- group)	Spain	2003

Table 2.33 Current producers of Ni-Cd batteries in EU*-16

Company (and location)	Country
SAFT Nersac	France
SAFT Bordeaux	France
Hoppecke	Germany
GAZ (Zwickau)	Germany
SAFT-AB	Sweden

Table 2.34 Current recyclers of Ni-Cd batteries in EU*-16

Company (and site)	Country
SNAM	France
ACCUREC	Germany
SAFT-AB	Sweden

The amount of cadmium (metal and oxide) used by three out of seven (for the year 2002) and five (for the year 2003) companies is approximately 1,635 metric tonnes for the year 2002. A slightly higher amount is reported for the year 2003 (see **Table 2.31**).

The volume of secondary cadmium produced in the EU-16 by the recycling of batteries, production scrap and other sources, was about 974 tonnes for the year (of which 56% batteries) 2002 and 10,23 tonnes for the year 2003 (of which 52% batteries). These figures are based on the information provided by 2 out of the 3 recycling companies (data of the company with highest capacity are included).

2.2.3.3 Cd containing Pigments

Compiled update information from the producers of cadmium containing pigments was submitted to the Rapporteur. Currently only three companies are producing these pigments in the EU-16. General Chimica and Degussa ceased production respectively in 2003.

Compiled data on the mass-balance of cadmium in pigments for the year 2003 was provided by the pigment producing companies and is given in **Table 2.35**.

Table 2.35 Mass-flow of cadmium within pigments for the year 2003 (in metric tonnes)

	Cd in pigments	Cd content
Production	1,216	730
Exports outside EU-16	750	450
EU-16 sales	466	280
Imports outside EU-16	33	20
EU-16 consumption	499	299

Note The calculation of the consumption figures assumes that the volumes of export and import of coloured articles are the same

2.2.3.4 Cd containing stabilisers

The production of stabilisers containing cadmium (compounds) decreased significantly since the end nineties in view of the Vinyl 2010 commitment. It should be noticed that any production of stabilisers by the companies adhering to this agreement, is destined solely for export and cannot be sold in the EU-15. The number of producers in the EU-16 dropped to only a few. Currently only 2 companies (three sites) acknowledged to the Rapporteur that some production still took place at their sites in Italy and Germany.

Only two of these use the priority substances as starting material in their process.

The consumption data of cadmium metal and cadmium oxide for this use are given as a range: between 50 and 150 tonnes in 2002. Somewhat lower values are given for the year 2003 (see **Table 2.31**).

Any EU production of stabilisers is for export and cannot be sold in the 15 original EU countries that are part of the Vinyl 2010 commitment.

2.2.3.5 Alloys, plating and other uses

No update information was submitted to the Rapporteur for these uses.

2.3 LEGISLATIVE CONTROL MEASURES

2.3.1 EU legislation

Cadmium (and its compounds) is a multi-regulated substance: in the EEC several directives have been adopted spread over the whole spectrum of risk reduction legislative instruments actually in use in the EU i.e. limitations in the marketing and use, environmental quality standards (emission and immission standards, protection of natural resources (groundwater, drinking water)), workplace (OEL's, etc) and consumer.

The directives, regulating at the source, are the Council Directive 76/769 (10th amendment; 91/338/EEC) relating to the restrictions on the marketing and use (see **Table 2.36**), and the Council Directive 91/157/EEC on batteries and accumulators. The latter directive establishes a marketing ban on batteries and accumulators with high mercury content as well as an obligation for Member States to undertake steps to ensure the separate collection of batteries with a view to their recovery or separate disposal. The latter obligation concerns spent batteries and accumulators containing certain amounts of cadmium, lead or mercury.

Table 2.36 Limitations and prohibitions on the marketing and use of Cadmium and its compounds (Directive 76/769/EEC, amendment Dir. 91/338 and Dir. 99/51/CE)

Cd and its compounds 91/ 338/EEC	1. May not be used to give colour to finished products 1.1.Manufactured from the substances and preparations listed below: ▪ polyvinyl chloride (PVC) [3904 10] [3904 21] [3904 22] ▪ polyurethane (PUR) [3909 50] ▪ low-density polyethylene (LDPE), [with the exception of low-density polyethylene used for the production of coloured master batch] [3901 10] ▪ cellulose acetate (CA) [3912 11] [3912 12] ▪ cellulose acetate butyrate (CAB) [3912 11] [3912 12] ▪ epoxy resins [3907 30] ▪ melamine-formaldehyde (MF) resins [3909 20] ▪ urea-formaldehyde (UF) resins [3909 10] ▪ unsaturated polyesters (UP) [3907 91] ▪ polyethylene terephtalate (PET) [3907 60] ▪ polybutylene terephthalate (PBT) ▪ transparent/general purpose polystyrene [3903 11] [3903 19] ▪ acrylonitrile methylmethacrylate (AMMA) ▪ cross-linked polyethylene (VPE) ▪ high-impact polystyrene ▪ polypropylene (PP) [3902 10] In any case, whatever their use or intended final purpose, finished products or components of products manufactured from the substances and preparations listed coloured with cadmium may not be placed on the market if their cadmium content (expressed as cadmium metal) exceeds 0.01% by mass of the plastic material. EXCEPTED for products to be coloured for safety reasons 1.2. May not be used in paints. However if the paints have a high zinc content, their residual concentration of cadmium must be as low as possible and at all events not exceed 0.1% by mass.

Table 2.36 continued overleaf

Table 2.36 continued Limitations and prohibitions on the marketing and use of Cadmium and its compounds (Directive 76/769/EEC, amendment Dir. 91/338 and Dir. 99/51/CE)

Cd and its compounds
 	
91/ 338/EEC
	2. May not be used to stabilise:
	
	2.1. The finished products listed below manufactured from polymers or copolymers of vinylchloride:
	▪ packaging materials (bags, containers, bottles, lids)
	▪ office or school supplies
	▪ fittings for furniture, coachwork or the like
	▪ articles of apparel and clothing accessories (including gloves)
	▪ floor and wall coverings
	▪ impregnated, coated, covered or laminated textile fabrics
	▪ imitation leather
	▪ gramophone records
	▪ tubes and pipes and their fittings
	▪ swing doors
	▪ vehicles for road transport (interior, exterior, underbody)
	▪ coating of steel sheet used in construction or in industry
	▪ insulation for electrical wiring
	
	In any case, whatever their use or intended final purpose the placing on the market of the above finished (components of) products is prohibited if their cadmium content (expressed as Cd metal) exceeds 0,01% by mass of the polymer.
	
	EXCEPTED for products using cadmium based stabilisers for safety reasons.
	
	3. May not be used for cadmium plating metallic products or components of the products used in the sectors/applications listed below:
	▪ Equipment and machinery for:
	    ▪ food production
	    ▪ agriculture
	    ▪ cooling and freezing
	    ▪ printing and book-binding
	▪ Equipment and machinery for the production of:
	    ▪ household goods
	    ▪ furniture
	    ▪ sanitary ware
	    ▪ central heating and air conditioning plant
	
	and the manufactured products as listed in this subsection

Table 2.36 continued overleaf

Table 2.36 continued Limitations and prohibitions on the marketing and use of Cadmium and its compounds (Directive 76/769/EEC, amendment Dir. 91/338 and Dir. 99/51/CE)

Cd and its compounds 91/ 338/EEC	In any case, whatever their use or intended final purpose the placing on the market of cadmium plated products or components of such products used in the sectors/applications listed and of the products manufactured in the sectors listed is prohibited. EXCEPTED sectors: aeronautical, aerospace, mining, off shore and nuclear whose applications require high safety standards and in safety devices in road and agricultural vehicles, rolling stock and vessels. EXCEPTED electrical contacts, in any sector of use, on account of the reliability required of the apparatus on which they are installed.
99/ 51 /EC	Exemptions for Austria and Sweden, already applying stricter provisions than the aforementioned, are granted until 31 December 2002, time by which the European regulations will be reconsidered and adapted to technical progress. See in this context the study reports by WS Atkins (1999a, b) and RPA Ltd (2000), on the risks to health and the environment by cadmium contained in certain products (i.e. used as a colouring agent or as stabiliser in polymers and for metal plating), as commissioned by the EC (DG Enterprise).

In addition to Dir. 91/338/EEC, toys should also comply to Directive 88/378/EEC (‘Safety of Toys Directive’) thus fulfilling the daily limit value for cadmium for the bioavailability resulting from the use of toys i.e. 0.6 µg per day (EC, 2003). Consumer protection is further also aimed at through the establishment of regulatory standards (e.g. European Standard EN 71 part 3) in circumstances where prevention from exposure is of particular importance, i.e. in toys and articles which come into contact with food (ICdA, 1997).

Commission Regulation EC 466/2001 sets maximum levels for certain contaminants in foodstuffs.

Table 2.37 Commission Regulation (EC) 466/2001: Maximum levels of Cd in food from aquatic sources (Official Journal L 077 , 16/03/2001)

Product	Maximum level (mg/kg wet weight)
Muscle meat of fish, excluding fish species listed below	0.05
Muscle meat of *Dicologoglossa cunneata, Anguilla anguilla, Engraulis encrasicholus, Luvarus imperialis, Trachurus trachurus, Mugil labrosus labrosus, Diplodus vulgaris, Sardina pilchardus*	0.1
Crustaceans, excluding brown meat of crab	0.5
Bivalve molluscs	1.0
Cephalopods (without viscera)	1.0

(information extracted from EC Working document EQS for cadmium, 2003)

End of pipe EEC directives concern putting limits to discharges/emissions of cadmium in the different environmental compartments (air, water, sewage sludge for agricultural use).

Quality objectives have been adopted for the workplace as well as for different environmental compartments.

Water

Standards for surface freshwater intended for the abstraction of drinking water, and for water intended for human consumption have been fixed through the Council Directives 75/440/EEC (will be repealed in December 2007 by Dir 2000/60/EC; the Water Framework Directive) and 80/778/EEC.

Table 2.38 Directive 75/440/EEC concerning the quality required of surface water intended for the abstraction of drinking water in the Member States

Standard in mg/l	Details	Source
0.005 mg/l	Permissible level; ≥ 95% of samples Guidance levels for several water parameters pH, zinc, max. Susp. matter etc.	O.J. L 194 , 1975
Standards adopted in Member States		
n.d.	n.d.	n.d.

Table 2.39 Directive 80/778/EEC and Directive 98/83/EC on water for human consumption

Standard in µg/l	Details	Source
5µg/l	MAC; min. total hardness 60mg/l Ca (or analogous cations	O.J. N° L 229, 1981 O.J. N° L 330, 1998
Standards adopted in Member States		
n.d.	n.d.	n.d.

(MAC: max. admissible concentration, GL: Guide Levels, MRC minimum required concentration). The reference detection method in this medium is given: i.e. atomic absorption.

Council Directive 80/68/EEC for groundwater comprises cadmium compounds in List I for which MS must prohibit the direct and avoid the indirect introduction to the groundwater. The directive shall be repealed in 2013 due to 2000/60/EC. Specific measures to prevent and control groundwater pollution will be adopted within the implementation of Art. 17 of 2000/60/EC.

In Council Directive 78/659/EEC on the quality of fresh water for fish and Council Directive 79/923 on shellfish waters, no specific cadmium concentration is given. The latter Directive only stipulates that no harmful effects on shellfish and larvae should occur and aim good quality of shellfish products. Atomic absorption spectrometry preceded if needed by concentration and/or extraction, is indicated as the reference detection method.

Council Directive 76/160/EEC concerning the quality of bathing water specifies cadmium but has yet not specified a 'Guide value' or 'Mandatory value'.

Council Directive 76/464/EEC on pollution by certain dangerous substances, and its daughter directive, Council Directive 83/513/EEC on the limit values and quality objectives for cadmium discharges, require Member States to set up an (prior) authorisation system for discharges of cadmium.

For most industrial discharges, with the exception of industrial plants manufacturing phosphoric acid and/or fertilisers, emission limit values are laid down. By way of alternative, Member States may base their authorisations on the quality objectives laid down for different types of waters.

Reference methods of measurement and monitoring procedures for cadmium in water, sediments and shellfish (i.e. AAS preceded by appropriate conservation and treatment of the sample) are laid down in Annexe III, of the directive including details on accuracy, precision and flow of the effluent.

Table 2.40 Directive 76/464/EEC: on pollution caused by certain dangerous substances discharged into the aquatic environment of the Community (Directive 83/513/EEC, the so-called Cadmium Discharges Directive)

Limit values* for zinc mining, refining lead and zinc and production of non-ferrous metals and metallic cadmium	Details	Source
0.2mg cadmium/l effluent	monthly mean measurements (limits for mean of daily measurements = 2-fold)	O.J. N° L 129, 1976
Limit values for the production of cadmium (compounds)	Details	
0.2mg cadmium/l effluent	mean of one month; total cadmium concentration	
0.5g cadmium/kg processed cadmium		
Minimum standards for the protection of aquatic life		
≤ 5 µg/l	in surface water; total cadmium conc	
≤ 5 µg/l	estuaries; dissolved cadmium	
≤ 2.5 µg/l	in marine territorial waters, coastal waters; dissolved cadmium	
Quality objective (target value)**		
≤ 1 µg/l	in surface water; total cadmium conc	
≤ 1 µg/l	estuaries; dissolved cadmium	
≤ 0.5 µg/l	in marine territorial waters, coastal waters; dissolved cadmium	
and no significant increase of concentration of cadmium in sediments or in shellfish and mollusca (e.g. Mytillus edulis)		
Standards adopted by Member States		
0.06	Nl; max. permissible conc.; dissolved	van Hout, 1994; in Pearse, 1996
0.01	Nl; target value; dissolved	van Hout, 1994; in Pearse, 1996

* To be considered as 'emission limit value' under the Dir. 2000/60/EC

** To be considered as 'environmental quality standards' under Dir. 2000/60/EC

The Water Framework Directive 2000/60/EC (O.J. L 327, 22.12.2000, p.1-73) aims at the establishing of a framework for the protection of surface, transitional, coastal waters and groundwater which prevents further deterioration and protects and enhances the status of the aquatic ecosystems and depending terrestrial ecosystems and wetlands; promotes sustainable water use; aims at enhanced protection and improvement of aquatic environment through specific measures for the progressive reduction of discharges, emissions and losses of priority substances and the cessation of phasing-out of discharges, emissions and losses of priority hazardous substances, pollution; contributes to mitigating the effects of floods and droughts. Herewith the objectives of relevant international agreements including those which aim to prevent and eliminate pollution of the marine environment with the ultimate aim of achieving concentrations of priority hazardous substances near the background values for naturally occurring substances (e.g cadmium) and close to zero for man-made synthetic substances.

The list of priority substances (Annex X of Directive 2000/60/EC) has been established by Decision N° 2455/2001/EC, as has specified cadmium as a Priority Hazardous Substance.

This implies (art. 16 of 2000/60/EC) that the European Commission has to submit proposals for progressive reduction of discharges, emissions and losses, but also, as cadmium is listed as Priority Hazardous Substance, cessation or phasing-out of discharges, emissions and losses within 20 years after adoption of the proposals.

The proposals must at least cover quality standards, for water, sediment or biota, and emission controls for point sources, and also review the Cadmium Discharges Directive (83/513/EEC). If no agreement on the proposals is reached at Community level by 2006, Member States have to establish themselves quality standards and controls on the principal sources.

As the quality standards are part of the surface water status, these would have to be reached at the latest by 2015.

Air

Waste Incineration Directives: 89/369 and 89/429 set emission limit values to air based on BAT for new and existing municipal waste incineration plants (new = exploitation permit delivered after December 1, 1990). For new installations (with a nominal capacity of at least 1 tonne waste/hour) the emission value for cadmium and mercury is fixed at 0.2 mg/Nm^3 off-gas. Old installation with minimal 6 tonnes/hour nominal capacity must apply to this value at the latest by December 1, 1996.

The hazardous waste incineration Directive (94/67) controls emissions of heavy metals by prior authorisation procedure of plants. Emission limits in flue gas for existing installations (before December 31, 1996): the sum of cadmium (compounds), expressed as cadmium and thallium(compounds) must be lower than 0.1 mg/m^3. For new installations, the corresponding limit is fixed at 0.05 mg/m^3.

In addition to Directive 75/442/EEC, Directive 2000/76/EC on the incineration of waste sets stricter emission limit values, in particular for cadmium to air (the total emission limit value of ‘Cd + Tl’ = 0.05 mg/(N)m^3 as daily average value suitably standardised depending on the type of combustion; air emission limit value for cadmium and its compounds: all average values over sampling period of a minimum of 30 minutes and a maximum of 8 hours: expressed as cadmium: total: 0.05 mg/m^3; exemption until January 1, 2007 for existing plants and certain conditions, hazardous waste incinerators only), water (the emission limit value for the discharges of waste water from the cleaning of exhaust gases, mentions for cadmium and its compounds, expressed as cadmium and in mass concentration for unfiltered samples: 0.05 mg/l). These emission limit values should be met by means of stringent operational conditions and technical requirements of the installations (existing plants as from December 28, 2005; for new plants as from December 28, 2002).

Council Directive 96/62/EC of 27 September 1996 on ambient air quality assessment and management (O.J. L 296, November 11, 1996, p. 5-63) aims to define the basic principles of a common strategy to define and establish objectives for ambient air quality (AAQ i.e. related to outdoor air excluding workplaces) in the Community designed to avoid, prevent or reduce harmful effects on human health and the environment as a whole; assess the ambient air quality in the MSs on the basis of common methods and obtain adequate information on the issue and ensure its public accessibility (e.g. by means of alert thresholds) maintain AAQ where it is good and improve it in other cases. Cadmium is mentioned in the list of atmospheric pollutants to be taken into account in the assessment and management of AAQ (for cadmium, an air quality standard of 5 ng/m^3 has been proposed).

Soil

Council Directive 86/278/EEC concerns the protection of the environment and in particular of the soil when sewage sludge is used in agriculture. Limit values concentrations have been set of the substance in soil, in sludge for the agricultural use and for the maximum amounts of cadmium which may be add annually to the agricultural land.

Table 2.41 Directive 86/278/EEC: on the protection of the environment and in particular of the soil, when sewage sludge is used in agriculture (Annex IA)

Annex IA		
Limit values in soils in mg/kg	Details	Source
1 up to 3		O.J. N° 181, 1986
Standards adopted by Member States (COM(97) 23 final)		
1 up to 3	BE; Flanders: sandy soil: 1 clay soil: 3; Wallonia: 1	
1 up to 3	ES: pH < 7: 1; pH > 7: 3	
2	FR	
1 up to 4	PT: pH < 5.5: 1; pH 5.5 <7: 3; pH > 7: 4	
3	UK	

Remark: for DE: limit values: 1.5 mg/kg (or 1 mg/kg dry weight) at pH > 5 and < 6 (UBA, comments 2000).

Table 2.42 Directive 86/278/EEC: on the protection of the environment and in particular of the soil, when sewage sludge is used in agriculture (Annex IB)

Annex IB		
Limite values in sludge (mg/kg)	Details	Source
20 to 40		O.J.
Standards adopted in Member States (COM(97) 23 final)		
10 and 12	BE; Flanders: 12; Wallonia: 10	
20 up to 40	ES: pH < 7: 20; pH > 7: 40	
20 and 40	FR: reference value: 20; limit value: 40	
20	PT	

Remark: here there are no data for UK; for SE: A charge of 30 SEK per gram of cadmium exceeding 50 g/tonne P (changed to 5 g Cd/tonne P) was introduced in Sweden in 1994 and was changed to a tax in July 1995 (KEMI, comments 2000); for DE: limit value: 10 mg/kg (or 5 mg/kg dry weight) at pH > 5 and < 6 (UBA, comments 2000).

Table 2.43 Directive 86/278/EEC: on the protection of the environment and in particular of the soil, when sewage sludge is used in agriculture (Annex IC)

Annex IC		
Limit values for the introduction of metals in arable soils in kg/ha/year		
0.15		
Standards adopted by Members States (representative for the p'riod '91 – '94) (COM(97) 23 final)		
0.012 and 0.024	BE: Flanders: grassland: 0.012; culture land: 0.024	
0.15	ES	
0.06	FR	
0.15	PT	
0.15	UK	

Remark: for DE: limit value: maximum 0.017 kg Cd/ha/annum (based on the limit value in sludge and the max. sludge application), maximum sludge application of 5 tonnes/ha/3 years (UBA, comments 2000).

The Fertiliser Directive (76/116/EEC) is currently under revision. In that framework, extensive work has been done by Member States in performing national risk assessment reports and by the EC (see ERM, final reports of January 2000 and June 2001, commissioned by DG Enterprise). The aim of the exercise is to review the data on the exposure of risk groups and on environmental conditions in the Member States to judge whether or not cadmium in fertlisers presents an unacceptable risk and thus to harmonise the situation within the EU (Austria, Finland and Sweden have a derogation[24] from Article 7 of the Directive in so far it concerns cadmium i.e. these MS may prohibit the marketing of fertilisers containing cadmium at concentrations in excess of those which were fixed nationally at the date of Accession) and to adopt EU-wide risk management measures related to the cadmium (content) in fertilisers, if needed so. In that context several Member States have implemented national regulations limiting the maximum cadmium concentration in fertilisers, the cadmium input in and/or the cadmium concentration in agricultural soil. A non-exhaustive overview of these figures is given in the environmental part of the Risk Assessment Report (see separate document).

Waste

Council Directive 78/319/EEC on toxic and dangerous waste determined cadmium and its compounds as requiring priority consideration in the control, prevention, recovery and recycling of any waste containing or contaminated by the substance.

The packaging and packaging waste Directive (i.e. Dir. 94/62/EC of 20 December 1994; Commission Decisions 1999/177/EC and 2001/171/EC) aims to reduce the impact of these materials (and waste arisings) by limiting the total quantity that may be put on the market, by enhancing re-use and recycling and by setting limits to hazardous substances. The sum of the concentrations of four heavy metals (lead, cadmium, mercyury and hexavalent chromium) in packaging which are not to be exceeded at different points in time, are: 600 ppm (July 1998); 250 ppm (July, 1999) and 100 ppm (July 2001). Exemptions are included in the Directive (e.g. packaging made entirely of lead crystal glass) and following COM decisions (for recycled

[24] Council Common Position (EC) No 62/98 adopted on 13 October 1998, O.J. of 14.12.98, C 388, p. 1 – 3.

material used in closed product loops and controlled chain i.e. plastic crates and pallets, and for glass packaging).

The Directive on 'End of Life Vehicles' (Dir. 2000/53/EC) aims at the prevention of waste from vehicles and at re-use, recycling and other forms of recovery of end-of life vehicles and their components so as to reduce the disposal of waste as well as at the improvement in the environmental performance of all economic operators involved and especially those directly involved in the treatment of end-of- life vehicles. Limitations of the use of hazardous substances in vehicles are encouraged and the use of heavy metals (lead, mercury, cadmium and hexavalent chromium) in materials and components of vehicles put on the market after July 2003 are prohibited, with exemptions (e.g. cadmium in batteries for electrical vehicles) foreseen in Annex II under the specified conditions (at least until 1 January 2003).

Directive 2002/95/EC on the restriction of the use of certain hazardous substances in electrical and electronic equipment (EEE) requires the substitution of various heavy metals (incl. Cadmium) and other chemicals in new EEE put on the market from 1 July 2006. Exempted is Cd plating except for applications banned by Directive 76/769/EEC. The Directive 2002/95/EC should apply without prejudice to other Community legislation in particular the Batteries Directive (91/157). Directive 2002/96/EC on waste electrical and electronic equipment aims at the prevention of the waste of EEE (EEE: including large and small household appliances, IT and telecommunications equipment, tools, toys, medical devices, etc) by promoting re-use, recycling and other forms of recovery. The list of materials and components of WEEE that should be selectively treated (i.e. removed) mentions 'batteries'.

2.3.2 National legislation

Nordic countries have been even more comprehensive in regulating cadmium and its compounds resulting in a stricter legislation than that on community level (Nordiske Seminar- og Arbejdsrapporter, 1992). Since the early eighties the use of the substance in pigments, in stabilisers (and in plating) has been banned in Denmark (since 1983) and Sweden (since 1982). All Nordic countries have strictly regulated the content of the substance in fertilisers and in sewage sludge since 1992 at the latest. Regulations on batteries did exist years before the adoption at EEC level of a directive with similar objectives.

A non-exhaustive overview of the Danish legislation focusing in particular to issues related to the environment, is given as to exemplify the extent of regulation in Nordic countries (DEPA, Pers. comm.. 2001).

Table 2.44 Danish environmental legislation on cadmium (Danish EPA, Pers. com., 2001).

Regulation	Content
No. 223 of April 5, 1989 Statutory order from the Ministry of the Environment on the content of cadmium in phosphorus-containing fertilisers	The phosphorous fertilisers are regulated on the content in phosphorous containing fertilisers sets the maximum content of cadmium relative to phosphorus in fertilisers containing ≥1% phosphorus be weight. The order does not cover manure, compost, sludge or other waste products they are added phosphorous manufactured from raw phosphate. After 01.07.1998 the maximum content of cadmium in phosphorous fertilisers are 100 mg Cd/kg P.

Table 2.44 continued overleaf

Table 2.44 continued Danish environmental legislation on cadmium (Danish EPA, Pers. com., 2001)

Regulation	Content
No. 1199 of December 23, 1992 Statutory order from the Ministry of Environment and Energy on the prohibition of sale, import and manufacture of cadmium-containing products	Importation, sale and manufacture of cadmium-containing products are prohibited. For the purpose of this Order cadmium-containing products means products in which cadmium is used either as surface treatment agent (cadmium plating), colour pigment or plastic stabiliser with more than 75 ppm in the homogeneous components of the product. Irrespective of the prohibition in subsection 1 above, manufacture, importation and sale of cadmium-containing products are permitted for the purposes specified in the Annex to this Order, within the stated deadlines.
No. 93 of February 22, 1996 Statutory order from the Ministry of Environment and Energy on collection of hermetically sealed nickel-cadmium accumulators (closed nickel-cadmium batteries) and remuneration for collection and disposal for recycling	Remuneration may be paid for environmentally sound collection and disposal for recycling of hermetically sealed nickel-cadmium accumulators (closed nickel-cadmium batteries). Remuneration may be paid to private persons and public enterprises, associations, municipalities etc. collecting and delivering or being in charge of delivery of closed nickel-cadmium batteries for recycling. In this Statutory Order recycling means recovery of the cadmium and possibly the nickel content of closed nickel-cadmium batteries.
No. 130 of February 10, 1997 Statutory order from the Ministry of Environment and Energy on provision of information by export of certain used production plants	This Order lays down rules on the duty to provide information on export of used production plants from heavily polluting enterprises (listed activ–ties - including wastewater containing cadmium), including non-complete plants, located in Denmark. The rules apply to categories of production plants which have been installed in the types of enterprises listed in Annex IA, and which meet one or more of the criteria listed in Annex IB. The duty to provide information applies no matter whether the used plant is exported for the purpose of final mounting and operation in the receiving country, or with a view to resale only. The disposer of a plant listed in Annexes IA and B of this Order shall notify the supervision authority of agreements made for export of the plant. Notification may take place before the final agreement is concluded, when the question of importing country and receiving party is decided.

Table 2.44 continued overleaf

Table 2.44 continued Danish environmental legislation on cadmium (Danish EPA, Pers. com., 2001)

Regulation	Content
No. 298 of April 30, 1997 Statutory order from the Ministry of Environment and Energy on certain requirements for packaging	This Statutory Order lays down provisions for essential requirements for the manufacture, composition, and utilisation of packaging, as well as limit values for the content of heavy metals (including cadmium) in packaging. The provisions of the Statutory Order apply to all packaging, including packaging containing products. Roads, railways, ships, and airfreight containers are outside the scope of this Statutory Order. This Statutory Order shall apply without prejudice to existing quality requirements for packaging, including requirements for health, protection of health and hygiene for the packed products, or existing requirements for the transport of hazardous goods. Between 30 June 1999 and 30 June 2001, packaging and packaging components may only be placed on the market in Denmark provided the sum of concentration levels of lead, cadmium, mercury, and hexavalent chromium does not exceed 250 ppm by weight. After 30 June 2001 packaging and packaging components may only be placed on the market in Denmark provided the sum of concentration levels of lead, cadmium, mercury, and hexavalent chromium does not exceed 100 ppm by weight.
Statutory order no. 1065 of November 30, 2000 Statutory order from the Ministry of Environment and Energy on classification, packaging, labelling, sale and storage of chemical substances and products.	This Order applies to chemical substances and products. Chemical substances means chemical elements and their compounds in the natural state or obtained by any production process, including any additive necessary to preserve the stability of the substance and any impurity deriving from the process used, but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition. Dangerous chemical substances and products shall be classified in one or more of the following danger categories: explosive, oxidising, extremely flammable, highly flammable, flammable, very toxic, toxic, harmful, corrosive, irritant, sensitising, carcinogenic, mutagenic and toxic to reproduction as well as (for substances only) dangerous for the environment. Dangerous chemical substances and products shall be assigned danger symbols and indications of danger risk indications (R-phrases),and safety advices (S-phrases).
No. 594 of June 6, 2000 Statutory order from the Ministry of Environment and Energy on cosmetic products	This Order shall apply to cosmetic products, which are marketed and to substances used in such products. According to this order cadmium and its substances may not be uses in cosmetic products.
No. 1044 of December 16, 1999 Statutory order from the Ministry of Environment and Energy on certain batteries and accumulators containing dangerous substances	Import and sale of batteries and accumulators containing: more than 0.025% cadmium by weight, shall not take place unless the battery or accumulator is marked with one of the symbols indicated in Annex I to this Order, with a view to separate collection and subsequent recovery or disposal.

Table 2.44 continued overleaf

Table 2.44 continued Danish environmental legislation on cadmium (Danish EPA, Pers. com., 2001)

Regulation	Content
No. 1042 of December 17, 1997 Statutory order from the Ministry of Environment and Energy on regulation of sale and usage of some dangerous chemicals and products to some specific purposes	Use of cadmium in paints and varnishes is forbidden. Use of cadmium in foodstuffs and stimulants is not allowed The cadmium content in glazing and decorative paintings is not allowed to be more than 0,002 percent.
No. 733 of July 31, 2000 Statutory order from the Ministry of Environment and Energy on the list of dangerous substances.	Classification of dangerous substances including cadmium compounds.

2.4 VOLUNTARY CONTROL MEASURES

On the Swedish food market, voluntary cadmium-limits are already imposed on products through initiatives taken by producer associations as well as retailing companies. These limits, which are stricter than the legally imposed criteria, have been set as a response to the perceived consumer demands. Also the tax on cadmium reduces the profitable level of cadmium in phosphorus fertiliser substantially below the allowed limit.

As an example, the co-operatives supplying the farmer with fertilisers, the Swedish Farmers Regional Selling and Purchaser Associations (sw: Lantmännen) have introduced its own limit value for soil, 0.30 mg/kg, for its most important trademark. If the top soil of a single field contains more Cd, the farmer may proceed to the second step, which consists of an analysis of the cadmium content in the wheat grains. If this level is below 0,100 mg Cd/kg, the crop can be sold under the trademark, otherwise not (KEMI, 2000, as derived from Drake and Hellstrand, 1998, The economics of the Swedish Policy to Reduce cadmium in Fertilisers, KemI PM 2/98).

The voluntary commitment of the European PVC Industry aimed – amongst other targets – to phase out the use of cadmium in all stabilisers systems placed on the EU market (i.e. by ESPA members). This target was achieved in March 2002 (Vinyl 2010, The Voluntary Commitment of the PVC Industry, Progress Report 2002).

2.5 OTHER SUPRANATIONAL INSTRUMENTS

Cadmium is included in several international declarations and programmes on reduction of micropollutants.

The OECD started in 1990 a Risk Management Programme on five chemicals, one of them cadmium, for which Risk Reduction Monographs were published. The OECD programme on Cadmium actually recommends collection and recycling of Ni-Cd batteries as a means of reducing risk.

Cadmium falls under the UN-ECE-LRTAP Protocol for Heavy Metals, the aim of which is the reduction of heavy metal emissions due to human activity (at stationary sources) and with the potential of causing harmful affects at long distance from the source via transport trough the atmosphere.

The WHO air quality guideline value for cadmium is 5 ng/m^3 (this value was established to prevent any further increase of cadmium in agricultural soils that could increase the dietary intake of future generation, given that no reliable unit risk could be derived to estimate the excess lifetime risk for lung cancer in the general population).

In 1998, the Ministerial Meeting of the OSPAR Commission in Sintra identified Cadmium (among other substances) as a substance for priority action under its Hazardous Substances Strategy. A Background document on Cadmium was prepared and adopted in 2002.

Several PARCOM Recommendations have been adopted related to the substance i.e. Rec. 92/3 concerning New secondary steel production and rolling mills, and Rec. 92/4 relating Electroplating industry. Cadmium is one of the substances that should be substituted in the latter field of uses.

The Rhine Commission has adopted a Ministerial declaration on heavy metals (with cadmium included) that have to be banned.

In 1998, the Helsinki Commission (HELCOM) Recommendation 19/5 was adopted including cadmium on the list of substances for priority action.

Cadmium also appears on the list of candidate-substances to include in the next extension of the monitoring programme of the International Commission for Protection of the river Scheldt.

The substance is also identified within the North Sea Conference framework (1990), and is one of the substances that ‘cause a major threat to the marine environment’ for which ‘reductions between 1985 and 1995 of all inputs of the order of 70% or more - provided that the use of BAT or other low waste technology measures enable such reductions’ - should be achieved. Atmospheric emissions by 1995, or by 1999 at the latest, should be significantly reduced (by 50% or more). Within that framework, harmonised quantification and reporting procedures for chemicals were developed. One of these procedures concerns Cadmium.

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

3.1.1 Methods and definitions: added Cd, natural background and ambient concentrations

The environmental exposure to Cd is calculated based on all known current anthropogenic emissions of Cd, i.e. Cd that is emitted by the Cd/CdO producers and processors and Cd in diffuse sources such as fertilisers, steel production, traffic, waste incineration, landfills etc. Local exposure assessment is based on emissions from Cd/CdO producers and processors. Regional and continental exposure assessment is based on all anthropogenic Cd emissions, including diffuse emissions. Actual Cd concentrations in the environment (ambient concentrations) are furthermore determined by the natural background of Cd (from geological origin or from natural processes) and Cd that was added to the environment in the past by man (historical pollution).

The natural Cd and Cd from historical pollution determine the background Cd concentrations in the environment. The predicted environmental concentrations (PEC's) are based on predicted added (anthropogenic) concentrations plus the background concentrations. The background Cd in surface water and air is assumed to be the natural background. The residence time of Cd in these two compartments is less than one year (see Section 3.1.3.4.1) and historical pollution should, therefore, not affect actual Cd concentrations. Background Cd in air originates from natural processes such as volcanic eruptions, bush fires etc. and, therefore, these diffuse Cd sources are not included in the anthropogenic emission inventory. Background Cd in surface water originates from runoff, leaching and atmospheric deposition of Cd from natural origin. Again, none of these processes are included in the anthropogenic emission inventory. Runoff and leaching of Cd added by man are, however, included in the anthropogenic emissions to water. The natural background in surface water and air is estimated in Section 3.1.3.4.3 and is added to the continental anthropogenic Cd concentrations, yielding the PECcontinental. This PECcontinental is then used in the PECregional and PEClocal according to standard procedures of the TGD. The approach is different for soils and sediments where the residence time of Cd is at least several decades (see Section 3.1.3.4.1). The historical Cd emissions by man affect ambient Cd concentrations in soils and sediments, even far away from point sources such as smelters (see Section 3.1.3.4.3 and the human health part of this Risk Assessment Report, in separate document). Therefore, the actual background of Cd in soils and sediments exceeds the natural background. Background Cd concentrations in soils and sediments are estimated from the ambient Cd concentrations in areas away from point sources (see Section 3.1.3.4.3). That background Cd is added to the predicted added anthropogenic Cd concentration, yielding the PECcontinental which, in turn, is used for the PECregional and PEClocal.

The standard TGD procedure to calculate the PECregional in soil appears not adequate for various reasons (see Section 3.1.3.4.1 and 3.1.3.4.2). Because soil Cd is an important compartment in Cd risk assessment, an alternative model for the TGD protocol was developed (see Section 3.1.3.4.2). This model predicts future trends in soil Cd based with a more detailed Cd input/output balance than the TGD model.

The metallic Cd and the CdO powder are less harmful in the environment than soluble Cd^{2+}. However, the metallic Cd and the CdO powder transform in the environment to the toxic Cd^{2+}. Details on the extent of transformation in water and in soil are given in Section 3.1.3, 3.2.1.1.2

and 3.2.2.1.2 of this report. The source of Cd (from the Cd/CdO producers and processors, from the diffuse sources or from the background) is not taken into account in the environmental risk assessment. Releases to the aquatic compartment by the producers and processors are often based on measurements in effluents after the sewage treatment plant (STP). Most Cd/CdO particles are retained in the STP and the Cd in the effluent is mainly present as dissolved Cd. Atmospheric losses are deposited onto soil where the metal or metal-oxide readily transforms to a species with the same fate as soluble Cd^{2+} (see Section 3.2.2.1.2). Arguments for similar bioavailability of soil background Cd and recently added Cd are given in human health part of this Risk Assessment Report (see separate document) where soil-plant transfer of Cd is discussed.

No attempt was made to express environmental Cd concentrations as bioavailable concentrations, with the exception of Cd concentrations in water where only the dissolved fraction is considered. The bioavailability of Cd is known to vary with properties of the compartment (see Section 3.2). Unfortunately, there are no standard procedures to correct for that variance. This variance is however accounted for in the effect assessment where PNEC values are calculated as a function of properties of the compartment. Predicted total concentrations are then compared with the properties specific PNEC's for risk characterisation.

3.1.2 Environmental releases

3.1.2.1 Releases during production and use (excluding batteries' related scenarios)

3.1.2.1.1 Source of data

In this section, input of cadmium into the environment of the EU is calculated. Major anthropogenic sources of cadmium into the environment are associated with Cd-production and -processing, with iron and steel production, with cement manufacturing, with combustion of fossil fuels, with the use and disposal of Cd containing products and with the use of Cd containing fertilisers.

Emissions from the Cd and CdO producing industry are based on plant information submitted by the Cd-producing industries of the EU and Norway (further denoted as EU-16). These emissions are annual averages. This information was collated from a questionnaire submitted in 1997 to all Cd and CdO producing plants in EU-16. Data of two plants that are dedicated Cd recycling plants also provided emission data. Information on Cd losses associated with processing of Cd in pigments and in stabilisers is based on detailed data reported by WS Atkins (1998). The data are those for 1996. In Corden et al. (2001) some more recent data are available. Information on Cd losses at EU-level from plating processes is also based on the WS Atkins report. More general information is provided by the IPPC report on the surface treatment of metals (2004). This reports indicates that in this sector process waters are often treated on-site and then discharged usually to municipal (urban) waste water (sewage) treatment plants, or if the effluent is treated to a suitable standard (i.e. in compliance with the national/regional limit values for the discharge of waste water: for the metal treatment sector: in general the regulatory limit value (in total Cd) varies between 0.2 mg $L^{-1}$and 0.6 mg L^{-1}although lower limits are provided by law for some areas), directly to surface waters.

No accurate information on Cd emissions during processing of Cd in alloys was found. Estimated total EU emission data from processing of Cd in alloys reported by ERL (1990) and ICdA (1998) were used for the atmospheric compartment. Calculation of local PEC's from processing of Cd in plating and alloys was done by treating the emission at EU-level as point sources and by using standard values (see Section 3.1.2.3). No emission data to the aquatic compartment were available for Cd alloy processing sites. The default emission factor to water (A-table) is 0.5 and which is a large value compared to all other emission factors (see **Table 3.1**). Therefore, emission factor for alloy production was selected based on data obtained for the Cd plating sites (2360 g t^{-1} processed). This value is 30-fold larger than the worst-case scenario proposed for Zn alloy processing sites (80 g Zn t^{-1}) in the Zn RAR (2004).

The Cd emission during use and disposal of Cd containing products and from other sources such as iron and steel production, cement manufacturing, municipal waste incineration, fuel combustion and use of Cd containing fertilisers are calculated in two ways. The first way is based on calculations according to the TGD (1996) with Cd emission data at the EU-level (including Norway) (see Section 3.1.3.4.1). The second approach consists of alternative calculations, only made for agricultural soils for which measured (or estimated) emissions are collated for different European countries (see Section 3.1.3.4.2). Sewage sludge application as a source of Cd is included in the diffuse source inventory described in that section. Country average fluxes are used in this assessment and not the fluxes in the restricted number of soils where sludge is applied. Sewage sludge is a minor source of Cd for soils on an average basis; however it is a major source of Cd in soils where sludge is applied. This RAR does not assess the risks of Cd on theses soils where sludge is applied. Sludge borne Cd has a different fate and effect than Cd added through fertiliser or atmospheric emissions. The lower bioavailability of sludge born metals soil is conserved on the long-term, even if most of the sludge organic carbon has decayed (Brown et al., 1998 and references therein). Therefore, the assessment of effects and the transfer to the food-chain are different between sewage sludge treated soils and soils enriched by inorganic Cd sources. The Cd fluxes through sludge vary widely and depend on local restrictions on the use of sludge in agriculture. Legislation in EU-16 countries is either based on maximal Cd concentrations in sludge (i.e. 1.2-10 mg Cd/kg) or maximum Cd fluxes (e.g. 3-15 g $ha^{-1}y^{-1}$). Some countries restrict a cumulative load (OECD, 1994). Total Cd input from sludge in the EU-16 is estimated to be at least 11.6 tonnes y^{-1} (see **Table 3.156**).

There are no specific use scenarios described in this RAR. The main use of Cd/CdO is in NiCd batteries and emissions during the whole life-cycle (incl. disposal) are described in the TRAR/batteries' related (sub)sections. Current worst case Cd disposal scenarios are predicted to increase Cd emission to the environment in the future and the effect of the predicted future emissions on the PEC's are described in Section 3.1.3.4 as an illustration. In the present document, the risk characterisation is made using actual Cd emission.

The Cd emission, from Cd/CdO production and processing industry are presented in **Table 3.1** and **Table 3.2**. The total EU-16-emission to the aquatic environment from Cd/CdO -producing and -processing plants in 1996 is 1,504 kg y^{-1} with 81% originating from the Cd producing industry. In general, industrial effluents are treated in a sewage treatment plant (STP) before being discharged into surface waters. Unless mentioned in the table, all data refer to concentrations measured after the STP. Five of the Cd producing plants emit their effluents to the sea or a bay. These plants (which are indicated in italics in the corresponding tables) emit 497 kg Cd y^{-1} or 33% of the total amount emitted to the aquatic environment. Plant number 9 produces only minor amounts of Cd. Its Cd-emission is mainly due to the production of Zn.

The total EU-16-emission to the atmospheric compartment in 1996 from Cd-producing and processing plants is 4,646 kg y^{-1} with 83% originating from Cd producing plants.

There are no direct local emissions to the soil compartment (i.e. local disposal) originating from Cd- and CdO-producing plants. Wastes from production are recycled or disposed off to controlled industrial landfill sites (IZA-Europe, pers. communication). No such information is available for the Cd processors. However, much of the waste produced (e.g. sludge) from process activities is likely to be classified as hazardous (for the surface treatment of metals, see IPPC, 2004; EU legislation in: EC, 1991; EC, 2000) and therefore excluded from the use in agricultural soil practices.

Emissions during the conversion of Cd to CdO are very low. According to the emission data from two CdO-producing plants in Belgium, there are no emissions to water as the production of CdO from Cd is a dry process. Water -mainly cleaning water- containing Cd and CdO is recycled. Emissions to air are very low -2.16 kg y^{-1}- due to installation of air filters. Cadmium and CdO retained in the filters are recycled as is the waste containing Cd and CdO. During a monitoring program of a CdO-producing plant, Cd concentrations were measured in the ambient air at 150 to 200 m from the emission point. An average value of 7.6 ng Cd m^{-3} was recorded (Industry Questionnaire, 1997). However, at the same site, Zn-chemicals are produced, another emission source of Cd to the environment. The emission data represent losses from both production processes together and it is not possible to distinguish which part is due to the production of CdO. The same comments apply to the other CdO-producing plant where besides CdO also Cd-powder is produced.

It needs to be mentioned that during the last years (in particular since 2001) a significant number of Cd metal producers stopped the cadmium production (some with, others without stopping the refining of the primary metal zinc/copper/lead). The same occurred in the area of CdO production (see Section 2.1.2.1 and see Section 2.1.2.2).

A very recent update provided by Industry (ICdA, com., 2003) reveals that from the initial list of cadmium production plants in Europe (drawn in 1997 on the basis of data from 1996) to date only three, possibly four remained active in the field of cadmium production. However, further details (i.e. on current production, import, export and exposure data) were not submitted for more recent years.

Table 3.1 Aquatic emissions from Cd-producing and -processing plants in the EU-16

Use-Category	Plant N°	Production/ consumption volume	Production emission¶	Processing emission¶	Emission factor	Conc. in effluent[(c)]	Number of production days	Concentration in effluent[(a)]	Effluent flow[(a)]	Flow receiving water[(a)]	Year
		tonnes y^{-1}	kg y^{-1}	kg y^{-1}	g $tonnes^{-1}$			mg l^{-1}	m^3 d^{-1}	m^3 d^{-1}	
Cd-producers[(e)]	1	683	23.9[(g)]		35	M (T)	365	0.045	1,440	16,000	1996
	2	510	614		1,204	M (T)	365	0.44	3,823	1,204,245	1996
	*3**	596	15.7		91	M (D)	70	0.01	7,476	-*	1996
	*4**	14.7	21.6[(g)]		1,469	M (D)	15	0.12	4,000	-*	1996
	5	208	77.8[(f)]		374	M (D)	243	0.16	2,000[(b)]	18,000[(d)]	1996
	6	262	0.18[(g)]		0.69	M (T)	105	0.00068	1,320	39 10^6 [(h)]	1996
	7£*	274	70		255	M (T)	365	0.06	3,196	-*	1998
	8	378	11		19	M (T)	151	0.03	1821	1,700,000 [(h)]	1996
	*9**	0.696	29.4[(g)]		42,241	M (T)	365	0.0058	13,820	-*	1999
	10	1,579	0		0	(1)	316	(1)	(1)	(1)	1996
	11	32	0		0	(2)	32	(2)	(2)	(2)	1996
	*13**	307	372		1,212	M (D)	123	0.17	17,790	-*	1996
CdO-producers	11	1,256		0	0	(2)	251	(2)	(2)	(2)	1996
	12	1,280		0	0	(2)	256	(2)	(2)	(2)	1993
Cd-stabilisers	F			0.03		M(T)	20	0.001	1,490	725,760	1996
	G			0.5		M(T)	48	0.013	749	18,000[(d)]	1996
	H			0.78		M(T)	60	0.008	2571	259,200	1996
	I			0.1		E(T)	13	0.0004[(3)]	2,000[(b)]	18,000[(d)]	1996

Table 3.1 continued overleaf

Table 3.1 continued Aquatic emissions from Cd-producing and -processing plants in the EU-16

Use-Category	Plant N°	Production/ consumption volume	Production emission¶	Processing emission¶	Emission factor	Conc. in effluent	Number of production days	Concentration in effluent[(a)]	Effluent flow[(a)]	Flow receiving water[(a)]	Year
		tonnes y^{-1}	kg y^{-1}	kg y^{-1}	g $tonnes^{-1}$			mg l^{-1}	m^3 d^{-1}	m^3 d^{-1}	
Cd-stabilisers	J			0		M(T)	13	0	0	0	1996
	K			4.1		E(T)	12	0.017[(3)]	2,000[(b)]	18,000[(d)]	1996
	L			0		M(T)	155	0	0	0	1996
	M			0		M(T)	155	0	0	0	1996
	window manufacturer			0		M(T)	350	0	0	0	1996
Cd-pigments	A	237		0.6	3	M(T)	230	0.02	131	6,000	1996
	B	82.5		4.02	49	M(T)	231	0.002	5,112	504,5760	1996
	C	186		5.9	32	M(T)	276	0.08	200	135,000	1996
	D	283		0.9	3	M(T)	230	0.022	130	32,739	1996
	E	66		13.4	203	M(T)	85	0.044	3,618	89,856,000[(h)]	1996
Cd-plating	EU	106		250	2360	E (T)	155	0.081	2,000[(b)]	18,000[(d)]	1996
Cd-alloys	EU	26		61.3	2360	E (T)	62	0.05	2,000[(b)]	18,000[(d)]	1996

n.a. Not available;
* Emission to the sea;
¶ Annual averages;
(1) No water emissions: waste waters are recycled;
(2) No water emission: dry process;
(3) Value based on 90% elimination in sewer;
(a) Mean annual; (b) default value: 2,000 m^3 d^{-1};
M Measured value,
E Estimated value,
D Dissolved concentration,
T Total concentration;
(d) Default value: 18,000 m^3 d^{-1};
(e) Emissions included these from Cd recycling;
(f) Emission of Cd from Pb and Zn production; no waste water related to Cd-production;
(g) Emission of Cd from Zn or Zn and Pb production;
(h) Emission to big river;
£ Emission data are reported to have decreased in more recent years to average concentration of 0.038 mgCd/L in effluent water for the year 2003 (Industry/company information, 2004)

Table 3.2 Atmospheric emission from Cd-producing and -processing plants in the EU-16

Use-Category	Plant N°	Production/consumption Volume	Production Emission amount¶	Processing Emission amount¶	Emission Factor	Year
		tonnes y^{-1}	kg y^{-1}	kg y^{-1}	g $tonnes^{-1}$	
Cd-production	1	683	54(b)		80	1996
	2	510	1,683(b) (e)		3,300	1996
	3	596	800(b)		4,598	1996
	4	14.7(d)	3.03		206	1996
	5	208	946(b)		4,548	1996
	6	262	6.24(b)		23.8	1996
	7	274	200(b)		730	1996
	8	378	28.6		76	1996
	9	648	110		170	1996
	10	1579	3.32		2.1	1996
	11	32.2	1.61		50	1996
	13	307	24.6(a)		80	1996
CdO-producers	11	1,256		0.30	0.24	1996
	12	1,280		0.31(c)	0.24	1996
Cd-stabilisers	F			0.09	n.a.	1996
	G			0.8	n.a.	1996
	H			0.5	n.a.	1996
	I			0.1	n.a.	1996
	J			0.7	n.a.	1996
	K			0.04	n.a.	1996
	L			n.a.	n.a.	1996
	M			0	n.a.	1996
	Window manufacturer			n.a.	n.a.	1996
Cd-pigments	A	237		1.15	4.9	1996
	B	82.5		2.37	29	1996
	C	186		3.6	19	1996
	D	283		5.8	21	1996
	E	66		0.2	3.0	1996

Table 3.2 continued overleaf

Table 3.2 continued Atmospheric emission from Cd-producing and -processing plants in the EU-16

Use-Category	Plant N°	Production/consumption Volume	Production Emission amount¶	Processing Emission amount¶	Emission Factor	Year
		tonnes y-1	kg y-1	kg y-1	g tonnes-1	
Cd-plating	EU			0	n.a.	1996
Cd-alloys	EU			770	n.a.	1996

n.a Not available
¶ Annual averages
(a) Estimated from a typical emission factor
(b) Cd emission from whole plant (including Zn and/or Pb production)
(c) 1996 value extrapolated from 1993 emission factor
(d) Production volume in 1991
(e) Pyrometallurgical processes

Previous estimates of total Cd inputs to the EU environment from Cd producing- and processing plants (Hutton, 1982; Jensen and Bro-Rasmussen, 1992; OECD, 1994 and EUPHEMET, 2000) are much higher than those given in the current RAR (see **Table 3.3**).

Table 3.3 Total, direct emissions in the EU (tonnes y^{-1}). A comparison of different studies

	To Air (tonnes y^{-1}tonnes y^{-1})		To Water (tonnes y^{-1}tonnes y^{-1})	
	Cd-producing plants	Cd-processing plants	Cd-producing plants	Cd-processing plants
Hutton, 1982	19.5	8.8	50	107
Jensen and Bro-Rasmussen, 1992	22.8	12.2	17.3	45
OECD, 1994	/	4.05	/	1.6
EUPHEMET, 2000	< 15	~ 15	~ 15	< 3
RAR-Cd, 2002(1)	3.9	0.8	1.2	0.3

(1) Data from the EU and Norway

Data in the Hutton report are based on estimated emission data and emission factors of the end of 1970's. Data in the report of Jensen and Bro-Rasmussen (1992) are based on the ERL-study (1990) which, in turn, is based on estimated emission data and emission factors of the end of 1980s. The emission results reported in the OECD report (1994) are based on the same production data but emission factors were adapted with some more recent estimates. The assessments of EUPHEMET (2000) are based on previous generic calculations and reported results based on production data, as well as on the conclusions of a previous version of this report (RAR CdO, 1999). The RAR Cd/CdO (2002) data are based on actual production and measured emission data of the mid 1990’s, and therefore, at the moment, closer to reality than the EUPHEMET (2000) report.

The comparison in **Table 3.3** indicates a general decrease in the Cd emission from the Cd-producing and processing industry. Since the end of the 1970’s emissions to air decreased more than 80%, while emission to water decreased more than 97%. This trend, based on measured data, confirms earlier performed estimates. Elgersma et al. (1992) studied the change in the industrial Cd discharge to the River Rhine basin from 1970 to 1988. Emissions from primary Zn winning decreased from 2 tonnes y^{-1} in 1970 to 0.05 tonnes y^{-1} in 1988. The trend was the consequence of increasing regulatory pressure on Cd emitting industry and the consequent implementation of wastewater treatment plants in the seventies. The North Sea Conference report (1995) mentions a decrease in the Cd emission to water of about 50% over the period 1985-1995.

In Belgium a small decrease in Cd emission to water from non-ferrous-metal industry from 0.5 tonnes y^{-1} in 1980 to 0.4 tonnes y^{-1} in 1995 was recorded and further estimated to 0.2 tonnes in 2000 (BMM, 1997 and 2001). In Germany a decrease was calculated from 0.5 tonne/y^{-1} in 1990 to 0.2 tonnes y^{-1} in 1994 for the same sector (Barbier, 1996). Pacyna et al. (1991) estimated a 60% decrease of Cd emission to air in Europe between 1975 and 1982. The North Sea Conference report (1995) mentions a decrease in the Cd emission to air in EU between 50% and 70% over the period 1985-1995. In Belgium, Cd emission to air from non-ferrous-metal industry decreased from 6.9 tonnes y^{-1} in 1980 to 2.1 tonnes y^{-1} in 1995 and a further reduction to 0.36 tonnes y^{-1} for 2000 is estimated (VMM, 1997; BMM, 2001). Cadmium emission to air from the German non-ferrous-metal industry decreased from 1.1 tonnes y^{-1} in 1990 to 0.9 tonnes y^{-1} in 1994 (Barbier, 1996).

This general decreasing trend is also reflected in the measured Cd-levels in air and water (see Section 3.1.3.4 and the human health part of this Risk Assessment Report (in separate document). Recent trends of Cd in air, water and sediments are given in **Annex J**. The reductions are most likely the result from increasing environmental regulations in the EU, which prompted the implementation of technologies abating Cd losses.

3.1.2.1.2 Emission reduction during production and use

Various types of measures and initiatives on national and international level are being taken to reduce Cd emissions from the Cd producing- and processing industries to the environment.

<u>Emission reduction during production</u>

Water

Wastewater treatment at Cd-producing and -processing plants involves filtration and precipitation. Liquid effluents from the different stages during production and processing of Cd are collected and treated with sodium carbonate at alkaline pH to precipitate Cd. Filtration aids and flocculating agents are added. The sludge is then filtered from the solution. The filtrate is neutralised prior to discharge to the environment. At industrial non-ferrous metal producing sites and waste water treatment plants (WWTP) a cadmium removal efficiency of at least 90% is reported based on physico-chemical techniques only, to achieve total cadmium concentrations within the range 1 – 0.1 mg L^{-1}(IPPC report, 2000). EUSES calculations give a corroborating removal rate (WS Atkins, 1998 and RPA, 2001): the Simple Treat model run with the Kp value of 130,000 l/kg yields the following distribution in the waste water treatment plant: 90% in sludge and 10% in water.

However, for municipal STP in practice, the average removal efficiency can vary widely from > 80% (based on measurements of influent and effluent cadmium concentrations and the water flows; VMM, pers. com. 2002) to 60% (CUWVO, 1986; in: CBS/Milieucompendium, 2000). The latter, lower figure will be used in this RAR.

Air

The major categories of available control techniques for Cd emission abatement to air are primary measures such as raw material substitution and low-emission process technologies, and secondary measures such as fugitive emission control and off-gas cleaning. In the case of particle-bound emission of Cd, dust-cleaning devices are used such as fabric filters, dry and wet electrostatic precipitators and scrubbers. In the pyrometallurgical production process, furnaces can be provided with a double bell furnace top. The dust collected in the filters is recycled within the production process. When scrubbing is applied, Cd is removed as slurry after sedimentation in a settling tank. These slurries can be further processed or land-filled.

To reduce fugitive emissions from discharging, handling, and stockpiling of raw materials or by-products, these activities are removed to completely enclosed buildings, which may be equipped with ventilation and dust filters or spray systems.

Land

Slugs and ashes formed during the melting process can be recycled when it contains sufficiently high Cd content. If the material meets the requirements of regulatory leaching tests, it may be used for road construction. All solid wastes from the production of NiCd batteries are recycled to recover the Cd and other metals.

Emissions of leachates of modern landfills are reduced to a minimum through the installation of containment, collection and attenuation practices. Basins are lined with plastic or impervious clay. Leachates are controlled and neutralised or recirculated. In order to minimise the quantities of residues to be land-filled, recycling and prevention campaigns of wastes are promoted by regulations.

Emission reduction during use and end-of-life

Since the 1980’s restrictions exists in several OECD-countries on the use of Cd in pigments, stabilisers and plating. This has led to a significant decrease of Cd consumption in these products.

3.1.2.2 Releases due to batteries’ related scenarios

Releases to the environment have been estimated for different life cycles stages of Nickel-Cadmium batteries (see **Table 3.4**).

Table 3.4 Overview of the main life cycle stages of NiCd batteries[25]

Life cycle stages	Phase

[25] The cadmium emissions during the production of battery raw materials have been covered by the Section 3.1.2.1 issuing from the previously separate overall RAR on Cd/CdO and are not repeated here.

1. Production/manufacturing of NiCd Batteries and/or Battery Packs	Production
2. Incorporation into Battery-Powered Devices and Applications (EEE)[a b]	
3. Use, Recharging and Maintenance by End Users[a]	Use/Useful life
4. Recycling Collection Sorting Processing Recovery	Waste-Management
5. Disposal Incineration Land-filling	

a) Life cycle stage 2 and 3 are not deemed relevant for the RA of the substance under study
b) Life cycle stage 2 is a facultative step not relevant for individual cells or batteries put on the market

3.1.2.2.1 Life cycle stage 1: Manufacturing of NiCd batteries and/or battery packs

The emissions to air and water from the NiCd battery manufacturers are presented in **Table 3.5** and **Table 3.6**. Site specific information on the local Waste Water Treatment Plant (i.e. quantity of sludge produced, Cd content, destination of sludge) is presented in **Table 3.7**. Information on waste -other than sludge- is given in **Table 3.8**. The data for 1999/2000 were obtained from Industry Questionnaire, 2000/2001.

It must be noted that plant 2 is a producer and recycler; since no distinction could be made between emissions from production/recycling, the company is listed with NiCd producing companies.

All plants except 1 (i.e. plant 2) release Cd to freshwater (surface water). Plant 2 emits to the marine environment. The total EU-emission to the aquatic environment from NiCd batteries producing plants in 1999/2000 is 62 kg year^{-1}. Emission factors to surface water varying between 1.1 and 48 g tonne^{-1} Cd used (average: 18.7 g tonne^{-1} Cd used) are calculated. In comparison with emission data from 1996 (presented in Annex IV), very similar emission factors are obtained for water (1.6-145 g tonne^{-1} Cd used and on average: 29.5 g tonne^{-1} Cd used respectively). The large variation in emission factors cannot be explained by distinguishing between consumer/sealed portable batteries (plant 4 (partly)) and industrial batteries producers (other plants). On the basis of the information available on electrode production processes for the sites no conclusions can be formulated with regard to differences in emission factors due to different production processes (see **Table 3.5**).

The processing emission of plant 1 decreased substantially from 9.6 kg year^{-1} (in 1996) to 2.1 kg year^{-1} in 2000. In 1999 still 4.9 kg year^{-1} was emitted. The reduction in cadmium emission is due to the implementation of a new treatment plant (fully operational mid 2001) and the changing in the production process (since January 2000, no further details available) and cleaning method (from wet to mainly dry cleaning).

In general industrial effluents from the plants are treated in an on-site Waste Water Treatment Plant (WWTP) before being discharged into surface waters unless mentioned otherwise. All data refer to concentrations measured after the WWTP. Plant 1 and plant 5 discharge after on-site treatment into the public sewer system. These discharges will undergo an extra dilution before entering the surface water. Plant 6 and 7 reports that the wastewater is collected separately and treated off-site (external recycling). Since no additional information concerning the Cd content of influents of the local treatment plant was provided by industry, the emissions to wastewater and sludge could not be specified. However, in the questionnaires, specific information was requested with regard to quantity, Cd content and destination of waste generated (including WWTP sludge). This information reveals that the total amount of sludge produced by the companies is 730 tonnes y^{-1} with an average Cd content varying between 1.7 and 12.5%. The total quantity of generated WWTP sludges is sent to recycling plants (see **Table 3.7**).

The total EU emission to the atmospheric compartment in 1999/2000 from NiCd batteries producing plants is 51 kg $year^{-1}$. The calculated emission factors to air for the different plants are situated between 0.27 and 464 g $tonne^{-1}$ Cd used (on average: 23 g $tonne^{-1}$ Cd used). Data from 1996 (Annex II) showed higher emission factors between 1.16 and 901 g $tonne^{-1}$ Cd used (average: 31.45 g $tonne^{-1}$ Cd used). Reductions in air emissions can be explained by improvements in air treatment systems. On the basis of the information available no conclusions can be drawn with regard to differences in emission factors between industrial/ portable battery producing sites and different electrode production processes (see **Table 3.6**). No data regarding emissions to air could be provided for company 1 and 3. However, plant 3 stated that since it concerns wet processes, the Cd emissions are mainly through effluents. It should be noted that plant 7 -processing less than 5% of total Cd amount- emits 28.99 kg $year^{-1}$ to air, that corresponds with 57% of the total air emissions of all NiCd batteries manufacturing plants.

The total amount of waste –apart from on-site WWTP sludge- generated by the NiCd batteries producing industry is 2,353 tonne/year. It should be noted that this waste includes packaging material, NiCd batteries material (plates, cells, electrolytes), cakes and filters from off-siteoff-site wastewater treatment. The majority (91.7%) of this waste is recycled; the other fraction (8.3%) is disposed in a landfill. 2,091 tonnes of this waste is sent to an external recycling plant, 66 tonnes is internally recycled.

In analogy with the Cd/CdO producing plants the receiving environmental compartments for the emissions of the NiCd batteries plants are water and air. The total amount of cadmium released to the environment during manufacturing of NiCd batteries in 1999/2000 is 116 kg $year^{-1}$. The total use of cadmium for the production of batteries is 2,166 tonnes (based on individual plant data for 1999/2000).

Table 3.5 Aquatic emissions from NiCd batteries producing plants in the EU (UC 12: Conductive agents)

Plant N°	Battery type	Electrode production process	Consumption volume	Processing emission	Emission factor	Conc. in effluent[b]	Number of production days	Concentration in effluent	Effluent flow	Flow receiving water[a]	Year
			tonnes y^{-1}	kg y^{-1}	g $tonne^{-1}$			mg L^{-1}	m^3 day^{-1}	m^3 day^{-1}	
1	Industrial	Pocket plate	39.5	4.9	124	M (T)	225	0.43 (P90)	127 (P90)	External to municipal STP	1999
2[b]	Industrial	Pocket plate - vented	395 (production only) (507) (total, inclusive recycling) (Cd from batteries: 85)	7.3	18.5	M (T)	330	0.12 (P90)	367[c] (P90)	432,000	2000
3	Industrial	Sintered and PBE	635	30.5	48	M (T)	315	0.12 (P90)	960	$13\ 10^6$	2000
4	Portable	Sealed cylindrical shaped/ sintered and PBE	842	21.9	26	M (T)	330	0.13 (P90)	771 (P90)	$5.4\ 10^5$	2000
5	Industrial	Fiber and (Pocket plate: imported)	59.7	<0.07	<1.1	M (T)	230	< 0.03	5	External to municipal STP	2000
6[f]	Industrial	Fiber plate	132.7	0[d]	0[d]	N/A	250	N/A	N/A	N/A	1999

Table 3.5 continued overleaf

Table 3.5 continued Aquatic emissions from NiCd batteries producing plants in the EU (UC 12: Conductive agents)

Plant N°	Battery type	Electrode production process	Consumption volume	Processing emission	Emission factor	Conc. in effluentb	Number of production days	Concentration in effluent	Effluent flow	Flow receiving water[a]	Year
			tonnes y^{-1}	kg y^{-1}	g $tonne^{-1}$			mg L^{-1}	m^3 day^{-1}	m^3 day^{-1}	
7[g]	Industrial	Pocket plate - vented	62.5	0[e]	0[e]	N/A	300	N/A	N/A	N/A	1999
			Total amount of Cd used during production of batteries (tonnes y^{-1})	Total Cd emission to water (kg y^{-1})	Emission factor (g/ on Cd used)						
			2,166	65	31.1						

N/A Not applicable;
M Measured value;
T Total concentration;
a Minimum flow rate;
b Company 2 emits to the marine environment;
c If cadmium emissions via storm water are included the effluent flow increases to 424 m^3;
fd All process wastewater is collected and sent to recycling company, no emissions to water;
g Emissions to water from cleaning operations are disposed in alkaline solution and externally recycled, no emissions to water; PBE: Plastic Bonded Electrode.

Table 3.6 Atmospheric emissions from NiCd batteries producing plants in the EU (UC 12: Conductive agents)

Plant N°	Battery type	Electrode production process	Production/consumption volume	Processing emission amount	Emission factor	Year
			tonnes y^{-1}	kg $year^{-1}$	g $tonne^{-1}$	
1	Industrial	Pocket plate	39.5	n.d.[a]	n.d.[a]	1999
2	Industrial	Pocket plate -vented	395 (production only) (507) (total, inclusive recycling) (Cd from batteries: 85)	1.6	4.1	2000
3	Industrial	Sintered and PBE	635	n.d.[a]	n.d.[a]	2000
4	Portable (emergency lighting)	Sealed cylindrical shaped/ sintered and PBE	842	13.5	16	2000
5	Industrial	(Pocket plate: imported) and fiber	59	7	119	1999
6	Industrial	Fiber plate	132.7	0.036	0.27	1999
7[a]	Industrial	Pocket plate -vented	62.5	28.99	464	1999
			Total amount of Cd used during production of batteries (tonnes y^{-1})	Total Cd emission to air (kg $year^{-1}$)	Emission factor (g $tonne^{-1}$ Cd used)	
			2,166	51	23	

a No data. However, it is noted that it concerns a wet process, so the emissions of Cd are mainly through effluents;
PBE Plastic Bonded Electrode;
It should be noted that plant 7 -processing less than 5% of total Cd amount- emits 28.99 kg $year^{-1}$ to air, that corresponds with 57% of the total air emissions of all NiCd batteries manufacturing plants.

Table 3.7 On-site Waste Water Treatment Plant (WWTP) and sludge information (UC 12: Conductive agents)

Plant N°	Type of WWTP	Efficiency (% removal)	Amount of sludge produced (t/y)	Cd Content (%)	Destination sludge	Year
1	Physico-chemical treatment	n.d.	17.5	2-4 (<30% water)	External recycling plant	1999
2[a]	Flocculation and filtration facility	99.7%	128.7	2 (water content: 55%)	(On-site) recycling plant	2000
3	Flocculation, flottation, filtration	99.2%	244	1.7 (water content: 57%)	Landfilled	2000
4	Flocculation and filtration facility	99.9%	330	9.7 (water content: 50%)	External recycling plant	2000
5	Filtration	n.d.	10	n.d.	External recycling plant	1999
6[b]	No emissions to water (recycled)	/	/	/	/	1999

Table 3.7 continued overleaf

Table 3.7 continued On-site Waste Water Treatment Plant (WWTP) and sludge information (UC 12: Conductive agents)

Plant N°	Type of WWTP	Efficiency (% removal)	Amount of sludge produced (t/y)	Cd Content (%)	Destination sludge	Year
7[c]	No emissions to water (disposed of)	/	/	/	/	1999
			730.2/y			

a Producer and recycler;
b All process wastewater is collected and sent to recycling company;
c Emissions to water from cleaning operations are disposed in alkaline solution and externally recycled;
n.d. No data available.

Table 3.8 Waste information (UC 12: Conductive agents)

Plant N°	Type of waste produced	Quantity of waste (tonnes y^{-1})	Cd content	Waste disposal type	Year
1	Industrial battery cells	118.8	< 3% (overall average content)	External recycling plant (98 %) Landfill (2 %)	1999
	Raw material bags	0.4			
	Substituted filters	0.25			
	Cleaning materials and tools	0.5			
2[a]	Barium sulphate	194	< 0.001%	Land-filled	2000
	Used filters[b]	66	< 0.1%	External recycling plant	
3	Scraps	380	17.4%	External recycling plant	2000
4	Plates (neg.)	46	50%	External recycling plant	2000
	Cells	181	11%		
5	Pocket plate	6.2	30-40%	External recycling plant	1999
	Dust	3.3	45%		
	Batteries	8.1	3-10%		
	Electrolyte	126.4	0.2%		
6	Used KOH from formation process	852	Trace conc	External recycling plant	1999
				External recycling plant	
	Wastewater from impregnation	102	1 g/L	External recycling plant	
	Filter cake from wastewater formation process	7	20%		
7	Electrode overlefts	52.66	n.d.	External recycling plant	1999
	Old alk. Sol.	208			

a Producer and recycler;
b After Cd and Ni dust removal (dust is on-site recycled);
n.d. No data available.

Since the manufacturing activities of NiCd batteries are restricted to a small number of sites in a limited number of EU countries (i.e. Sweden, France, Germany, Spain and Belgium[26]), and

[26] Belgian manufacturer has stopped manufacturing cells and shifted to assembly (of non-EU manufactured cells into packs) only since June 2001, Panasonic (former Philips), letter 30.09.02.

hence are not equally distributed over the EU territory, it is not possible to apply the 10% rule for estimation of the regional emissions. In that case it is recommended to use the EU volume as input for the region and to apply another percentage or to use specific values as input for the regional model (e.g. emissions from the largest emitter). In this case the emissions from the largest emitter to air and water were allocated to the region. (EC, 1998).

Table 3.9 Summary emissions from production of NiCd batteries (life cycle stage 1)

Compartment	Total	Regional	Continental
	kg year^{-1}	kg year^{-1}	kg year^{-1}
Air	51	28.99	22.01
Wastewater	4.97	4.9	0.07
Surface water	60	30.5	29.5
Soil, urban/ind	0	0	0
Total	116	64.4	51.6

3.1.2.2.2 Life cycle stage 2: Incorporation into battery-powered devices and applications

No emissions of the substance under study are expected.

3.1.2.2.3 Life cycle stage 3: Use, recharging and maintenance by end user

No direct emissions of cadmium of the substances under study are expected from the use of batteries, except possibly in the cases of battery corrosion or destruction of the battery. The number of batteries affected in these ways is expected to be small. The indirect cadmium emissions (generation of electric power, e.g. combustion of coal) associated with recharging of batteries have not been considered in this report. Lankey (1998) estimated an average total energy consumption of 286 ± 222 MJ/kg for the use phase (1,000 charge cycles over the life of the battery). These figures are deemed negligible in comparison with the overall energy consumption and related indirect cadmium emissions.

3.1.2.2.4 Life cycle stage 4: Recycling

The emissions to air and water during the recycling of batteries are presented in **Table 3.10** and **Table 3.11** (Industry Questionnaire, 2000/2001). From the questionnaires it is also clear that information concerning on-site wastewater treatment is lacking (plant 1). Information on waste quantities generated – other than on-site WWTP sludge-is presented in **Table 3.12**.

Plant 2 stated that there are no “open treatment steps” at their site. As a consequence they do not emit Cd to either compartment. The wastewater produced is collected and treated off-site. The sludge produced during this process is land-filled. One company that is both producer and recycler is reported as a NiCd producer (see Section 3.1.2.2.1), since a split up of emissions was not feasible.

The total Cd emission to the aquatic compartment from Cd recyclers in the EU is based on information from 1 plant only and is 0.126 kg year^{-1}. The accompanying emission factor for that plant is 0.16 g tonne^{-1} Cd recycled. In comparison with emission data from 1996 (presented in

Annex IV), a very similar emission factor of 0.19 g $tonne^{-1}$ Cd recycled is obtained. No emission factor was calculated for recycling plant 2 since the on-site operating processes are zero emission processes. In general industrial effluents from the plants are treated in an on-site Waste Water Treatment Plant (WWTP) before being discharged into surface waters. However, plant 2 collects its wastewater for off-site treatment. Since no additional information concerning the Cd content of influents of the local treatment plant was provided by industry, the emissions to wastewater and sludge could not be specified.

The total EU emission to the atmospheric compartment in 1999/2000 from Cd recyclers producing plants is 1.77 kg $year^{-1}$ (based on plant 1 only). The calculated emission factor to air for plant 1 is 2.21 g $tonne^{-1}$ Cd recycled. Data from 1996 (Annex IV) showed a higher emission factor of 9.7 g $tonne^{-1}$ Cd recycled. Reductions in air emissions can be explained by improvements in air treatment systems. No emission factor was calculated for recycling plant 2 since the operating processes are zero emission processes.

The total amount of waste –including the off-site treated wastewater from plant 2- generated by the Cd recycling industry is 1,045 tonnes y^{-1}. It should be noted that this waste solely includes Cd containing material. The majority of this waste is sent to an external recycling plant (66.3%) internally treated (8%) or sent to a specialised landfill (25.6%). Taking into account the Cd content of this waste, it can be concluded that in total < 907 kg Cd is externally recycled, 134 kg Cd is internally treated and 0.4 kg Cd is land-filled.

The overall Cd emission to the environment is only 1.9 kg $year^{-1}$. 93% of this emission is directed to air. Since 842,300 kg $year^{-1}$ is produced by the Cd recycling plants a very low total emission factor of 0.0002% can be calculated.

Table 3.10 Aquatic emissions from Cd recycling plants in the EU (Cd recycled from batteries, production scrap and other sources)

Plant N°	Production/ Consumption volume	Processing emission	Emission factor	Conc. in effluent[b]	Number of production days	Concentration in effluent	Effluent flow	Flow receiving water	Year
	tonnes y^{-1}	kg $year^{-1}$	g $tonne^{-1}$			mg L^{-1}	m^3 day^{-1}	m^3 day^{-1}	
1[a]	800.5 (376 .8 batteries: 47.1%	0.126	0.16	M(T)	350	0.45 (P90) Average: 0.17	6.1 (P90) Average: 3.8	11,500	2000
2	41.8 (37.6 batteries :89.9%)	0[c]	0	N/A	240	N/A	N/A	N/A	1999
TOTAL	842.3[b] (414.4 from batteries)	0.126							

a) Only two recyclers (instead of three) have been listed under Cd-recyclers. The reason is that one company is both recycler and producer. A further breakdown of the submitted figures between the producing process and the recycling process was not feasible. For this reason this company has been listed with the other producers;

b) This total amount represents not only the cadmium recycled from NiCd batteries (414.4 t (256.3 tonnes portable batteries; 158.1 tonnes industrial batteries)) but includes also other Cd containing waste (production scrap: 286.4 t/y, other sources (not specified): 141.5 t/y). On average 81% of the batteries recycled are EU batteries; 19% is imported (Industry Questionnaires, 2000/2001; information from SNAM & SAFT). On the other hand, the recycled amount of Cd produced by the third recycler (115 t (battery fraction: 85t)) is not included in the given figure;

c) No "open" treatment steps; no emissions. Wastewater is collected and treated off-site. No further information is provided. Sludge is land-filled;

M (T) Measured total concentration after WWTP i.e. Cd concentration virtually equal to dissolved Cd concentration;

N/A Not applicable.

Table 3.11 Atmospheric emissions from Cd recycling plants in the EU (Cd recycled from batteries, production scrap and other sources)

Plant	Production/consumption	Processing	Emission	Year
N°	Volume	Emission amount	Factor	
	tonne/year	kg $year^{-1}$	g $tonne^{-1}$	
1[a]	800.5 (376.8 batteries: 47.1%)	1.77	2.21	2000
2	41.8 (37.6 batteries: 89.9%)	0[c]	0	1999
TOTAL	842.3[b] (414.4 from batteries)	1.77		

a) Only two recyclers (instead of three) have been listed under Cd-recyclers. The reason is that one company is both recycler and producer. A further breakdown of the submitted figures between the producing process and the recycling process was not feasible. For this reason this company has been listed with the other producers;

b) This total amount represents not only the cadmium recycled from NiCd batteries (414.4 t (256.3 tonnes portable batteries; 158.1 tonnes industrial batteries)) but includes also other Cd containing waste (production scrap: 286.4 t/y, other sources (not specified): 141.5 t/y). On average 81% of the batteries recycled are EU batteries; 19% is imported. (Industry Questionnaires, 2000/2001; information from SNAM & SAFT). On the other hand, the recycled amount of Cd produced by the third recycler (115 t (battery fraction: 85t)) is not included in the given figure;

c) No “open” treatment steps; no emissions. Wastewater is collected and treated off-site. No further information is provided. Sludge is land-filled.

Table 3.12 Waste information for Cd recyclers in the EU

Plant N°	Type of waste produced	Quantity of waste(tonnes y^{-1})	Cd content	Waste disposal type	Year
			mg kg^{-1}		
1[a]	Batteries plastic boxes	268	1.5	Special landfill	2000
	Batteries metallic boxes	231	< 2,000	External recycling	
	Fe/Cd electrodes after treatment	221	< 2,000	External recycling	
	Concentrated electrolytes	216	10,000	External scrap treatment	
	Process slag	58	Pure CdO	Internal treatment	
	Air treatment dust	23	Pure CdO	Internal treatment	
	Used filters	2.6	20,000	Internal treatment	
	Rainwater sludges	0.2	3,000	Internal treatment	
2	Plastic waste	Small	< 0.005% Cd	n.d.	1999
	Wastewater condensed with vacuum treatment furnace	25	n.d.	External treatment, Sludges are land-filled	

a) Only two recyclers (instead of three) have been listed under Cd-recyclers. The reason is that one company is both recycler and producer. A further breakdown in the submitted figures between the producing process and the recycling process was not feasible. For this reason this company has been listed with the other producers;

n.d. No data available.

Since the recycling activities of NiCd batteries are restricted to a small number of sites in a limited number of EU countries (i.e. Sweden, France and Germany), and hence are not equally distributed over the EU territory, it is not possible to apply the 10% rule for estimation of the regional emissions. In that case it is recommended to use the EU volume as input for the region and to apply another percentage or to use specific values as input for the regional model (e.g. emissions from the largest emitter). In this case the emissions from the largest (and only) emitter to air and water were allocated to the region. (EC, 1998).

Table 3.13 Summary emission from recycling of NiCd batteries (life cycle stage 4)

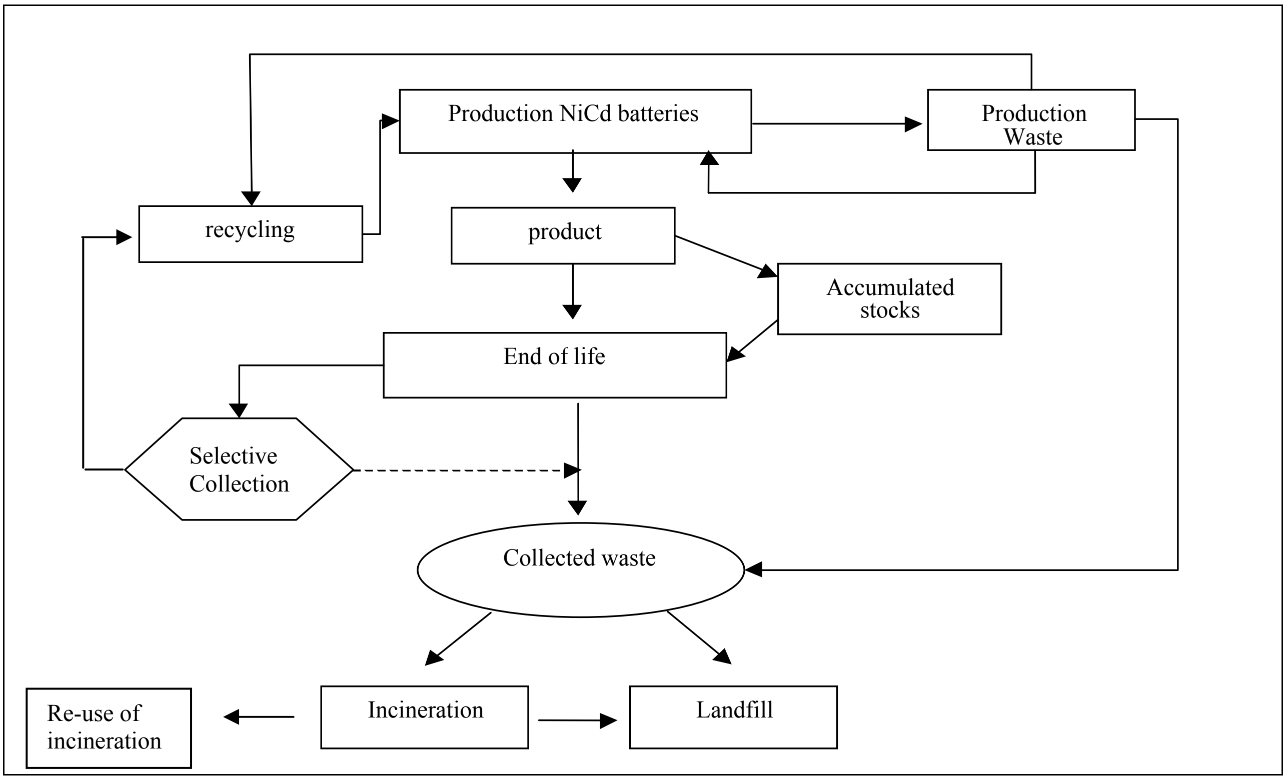
Compartment	Total	Regional
	kg year^{-1}	kg year^{-1}
Air	1.77	1.77
Wastewater	0	0
Surface water	0.13	0.13
Soil, urban/ind	0	0
Total	1.9	1.9

3.1.2.2.5 Life cycle stage 5: Disposal

Scope definition

At the end of their technical lifetime batteries or equipment containing NiCd batteries may end up in the waste stream or in private or municipal collection points. The end of life management of batteries consists of collection, recycling, landfills and incineration. A schematic overview of the cadmium flows related to the life cycle of NiCd batteries is given in **Figure 3.1**.

Figure 3.1 The life cycle of NiCd batteries



The size of the battery waste stream is related to the amount of batteries sold/used in previous years. In the case of NiCd batteries there is a considerable time lapse between the end of service life for the product and the occurrence of emissions from the waste treatment processing. The delay between marketing and emissions is mainly governed by (1) the service life-span (2) possible intermediate storage (stockpiling/hoarding) and (3) the transformation/transportation processes in landfills or incineration residues. As a result, current emissions probably may not be representative for the potential future emissions that are expected to take place several decades after production and processing of a substance have ceased.

In this regard this report addresses both the instantaneous cadmium emissions because of waste treatment (e.g. incineration) and the cumulative cadmium emissions of landfills. Guidance on how to estimate the emissions from the waste disposal stage is not provided within the Technical Guidance Document (TGD, 1996). The revised TGD includes some sections on waste disposal and has been taken as the starting point for the proposed approach as outlined here below.

Both the current and future cadmium emissions will be assessed albeit in a semi-quantitative way. Current emissions will initially be estimated based on an overall European situation. However, since waste management strategies may differ considerably between the Member States, due consideration will be given to these differences by means of including several scenarios (with the extremes: 100% land-filling and 100% incineration). Main emissions of cadmium from incineration of waste are expected to occur through air if no adequate flue gas treatment is in place and the disposal and/or re-use of incineration residues. However, neither the delayed cadmium emissions of the re-use of incineration residues nor the impact of future expected increase in cadmium content of bottom ash and fly ash on the re-usability of these incineration residues have been quantified. The major environmental concerns associated with metals in landfills are usually related to the generation and eventual discharge of leachate into the environment. Therefore the aforementioned emissions will be the focal point of this report. However, the impact of a future change in the MSW composition on the composition of the leachate of a landfill could not be judged based on the current lack of knowledge and methodology. Emissions of recycling are taken into account in this report at the manufacturing phase in Section 3.1.2.2.4.

<u>Contribution of NiCd batteries to the cadmium content of Municipal Solid Waste: current situation</u>

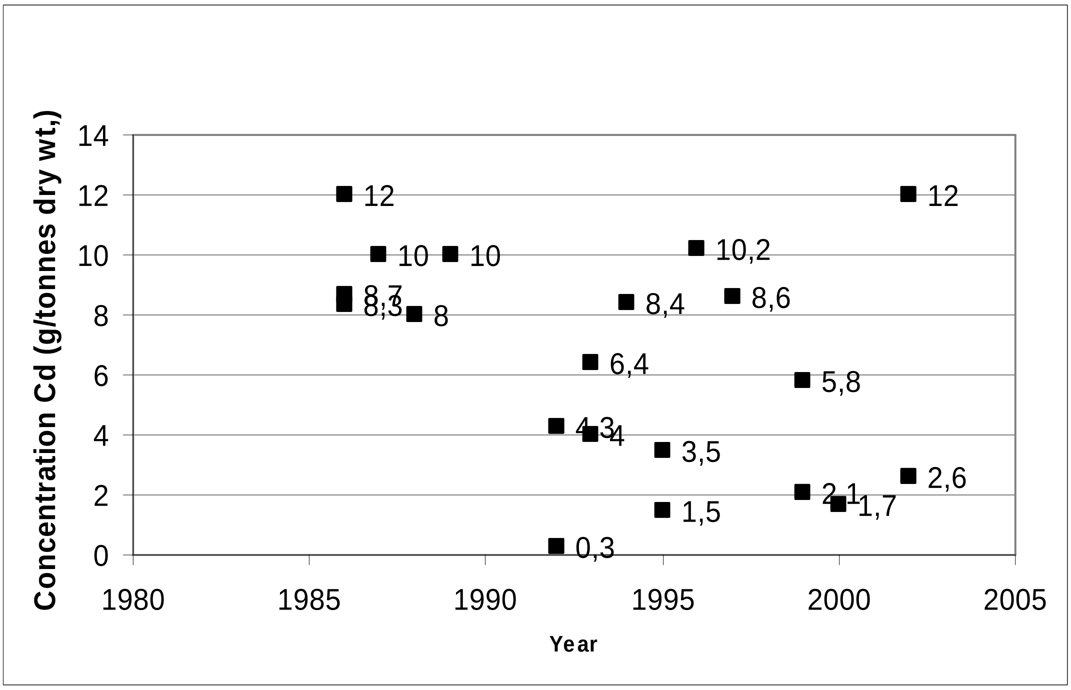
MSW consists of vast array of materials discarded after their useful life and is very heterogeneous of nature. Reported total concentrations of cadmium in MSW are summarised in **Table 3.14** and visualised in **Figure 3.2** and range between 0.3-12 g Cd/tonne $_{dry\ wt.}$ The observed differences are due to the heterogeneity of the Municipal Solid Waste stream, the methodology used to estimate the total cadmium concentration and possible pre-treatment steps For example the study of Maystre (1994) calculated the total flow of cadmium as a result of the individual cadmium content in a given type of material and the fraction of this material in the total amount of MSW. The obtained total cadmium concentration of 6 g $tonne^{-1}_{dry\ wt.}$ does not include the contribution of NiCd batteries. Brunner and Mönch (1986) and Brunner and Ernst (1986) reported total Cd values of 8.7-12 g $tonne^{-1}_{dry\ wt.}$ These values were calculated from the analysis of the composition of the incineration products. Direct waste analysis (Otte, 1995; ADEME, 1988 and 1993) revealed similar figures.

Table 3.14 Total cadmium concentrations (g $tonne^{-1}$ $_{dry\ wt.}$) in MSW

Country	g $tonne^{-1}$	Methodology used	Reference
Finland	0.3-4.3	Direct Waste Analysis	Assmuth (1992)
Switzerland	8.7 12	Analysis incineration products	Brunner and Mönch, (1986) and Brunner and Ernst (1986)
Switzerland	8.6		Titalyse (1997)
Germany	10	Not specified	Horch (1987) cited in Reimann (1989)
Germany	10	Not specified	Reimann (1989)
Germany	12	Not specified	Reimann (2002)
The Netherlands	3.5	Direct Waste Analysis	Otte (1995)
The Netherlands	6.4	Not specified	Rijpkema (1993b) cited in Bernard et al. (2000)
The Netherlands	2.6	Direct waste analysis after sorting	Wiaux (2002)
The Netherlands	10.2	Not specified	Rijpkema (1996) cited in Mersiowsky (2002)
The Netherlands	8.4	Analysis incineration products	Krajenbrink and Eggels (1997) (MSW of 1994)
UK	1.7	Direct Waste Analysis	(Ross et al., 2000)
UK	Average 0.8 P50: 0.7 P90: 1.5	Direct Waste Analysis (data 1992-1993)	NETC (1995)
Sweden	2.1-5.8	Direct Waste Analysis	Flyhammer and Hakansson (1999)
Sweden	8.3	Not specified	Statens Energiverk (1986) (cited in Flyhammer et al., 1998)
France	6[a]	Mass Flow	Maystre (1994)
France	8	Direct Waste Analysis	ADEME (1988) in SFSP (1999)
France	4	Direct Waste Analysis	ADEME (1993)

a) Batteries were not included

Figure 3.2 Evolution of Cd concentration (g tonne^{-1} $_{dw}$) in MSW



In general there seems to be a slight tendency that higher cadmium concentrations in the MSW have been found in the past (8-12 g tonne^{-1} $_{dry\ wt.}$) than at present (0.3-8 g tonne^{-1} dry wt) (see **Figure 3.2**: Since data are scarce and a large uncertainty surrounds the reported figures all data were, however, pooled together. Based on the pooled data the average Cd content of MSW is 6.2 mg kg^{-1} $_{dry\ wt.}$ (median = P50 = 6.4 mg kg^{-1} $_{dry\ wt.}$). In the EU-16, 160,058 ktonnes of MSW is generated (see subsection "Waste management strategies in Europe" under Section 3.1.2.2.5). The moisture content of MSW is typically on average 30% (Van der Poel, 1999, Mersiowsky, 2001; DTU, 2001) yielding 112,041 ktonnes of MSW (dry weight). The reasonable worst case total cadmium content of MSW on a dry weight basis is derived as the 90th percentile and equals 10 g Cd/tonne $_{dry\ wt.}$ This value is taken forward in the calculations of the emissions (see Section 3) and equals a cadmium load of 1.1 ktonnes.

Only a fraction of this total cadmium content originates from NiCd batteries. **Table 3.15** illustrates the typical average metal concentrations of MSW constituents.

Table 3.15 Average concentration (mg kg^{-1} $_{dry\ wt.}$) of metals in MSW components (Maystre et al., 1994 adapted)

Types of Materials	Cu	Zn	Cd	Hg	Pb
Plants and Food	28	74	3	< 1	235
Meat waste	24	96	4	< 1	82
Natural Fibers	58	104	< 2	< 1	24
Synthetic Fibers	9	43	2	< 1	19
Leather	75	437	5	< 1	372
Aluminium	2	17	53	< 1	84
Non Ferrous	1,792	46,827	10	< 1	30,010
Electronic Equipment	30,333	17,689	509	< 1	29,805

Table 3.15 continued overleaf

Table 3.15 continued Average concentration (mg kg^{-1} $_{dry\ wt.}$) of metals in MSW components (Maystre et al., 1994 adapted)

Types of Materials	Cu	Zn	Cd	Hg	Pb
Plastic foam	155	283	8	< 1	288
Rubber	28	7,028	8	< 1	197
Moulded Plastic Bodies	19	39	138	< 1	259
Primary Batteries Zn-C	2,725	95,305	5	72	102
Paper	280	35	8	< 1	399
Cardboard	84	60	2	< 1	43
Dust Bin Bags	200	363	6	86	470
Paper and Paraffine	210	77	4	< 1	263
Nickel-Cadmium Batteries[a]	-	< 100	130,000	< 1	1.0

a) In the study of Maystre (1994) Nickel-Cadmium batteries were not reported as a specifically identified type of material entering the composition of Municipal Solid Waste but for the purpose of Comparison. They have been added in Table 3.15.

It is obvious that NiCd batteries have the highest concentration of cadmium when compared to other types of materials. The final contribution, however, to the overall cadmium content is of course dependent on the weight distribution of the different waste components**.**

Different studies attempted to estimate the specific contribution of NiCd batteries to the overall cadmium load in MSW. Reported estimates of the amount of cadmium in the MSW originating from NiCd batteries vary widely from 10-85% (EPA, 1989, Walker, 1995, Chandler, 1995, STIBAT 1998 and 2000, SCRELEC, 1999, Lemann, 1995). The reason for this large variation is among other things related to the relative small sample volumes, the heterogeneity of the municipal waste stream and the method that is used to quantify the amount of NiCd batteries in MSW.

Roughly two approaches can be distinguished. The first approach tries to predict the MSW composition indirectly through a material flow analysis. In the second approach MSW is being sorted and the cadmium concentration of the constituents are directly analysed. Typically, a material flow analysis is based on the collection of product historical data on the quantity of cadmium consumed in the production of a product. Finally, after correction for import and export the time it takes for the cadmium to reach the waste stream is projected by estimating the life time of the product and assuming that the product will be discarded at the end of this period. These estimates of gross discards are adjusted for materials recovery (recycling) and the remaining portion is the estimate of the net discard in MSW. In the available mass flow studies on NiCd batteries hoarding has not been taken into account resulting in an overestimation of the contribution of NiCd batteries to the overall cadmium emissions in MSW in Europe. The Lemann study (1995) indicating the highest contribution (85%) of NiCd batteries was considered unreliable after a critical evaluation of the data presented. In this study an element and material balance of the Municipal Solid Waste incinerator Hagenholz was conducted in 1995 in parallel with a detailed slag analysis. The results revealed that only 3.64 tonnes NiCd scrap/year could be recovered. This figure was approximately 4 times lower than the estimated mass flow of NiCd batteries reaching the incineration plant, based on FOEFL statistics on the use of batteries in 1992 (11.5 tonnes y^{-1} on average). The authors of the study explained these conflicting results by the simple fact that more than three-quarters of the batteries decompose completely during the incineration process and are therefore unrecognisable in the crude slag. Based on the latter assumption the FOEFL statistics of 1992 were still used (the data from 1992 were compared with the analysis from March 1995 because the average life time for NiCd batteries were estimated to be between 1-3 years). Since the total cadmium load for 1994 was estimated to be 2,437 tonnes y^{-1} it was concluded that NiCd accumulators caused 85% of the cadmium input in the Hagenholz incinerator. However, if the measured discard of 3.64 tonnes of NiCd is used only 20% is attributable to NiCd batteries (assuming an average Cd content of 13.8%).

Another method of estimating cadmium in MSW is to examine actual concentrations of cadmium found in municipal refuse samples and to scale these concentrations to the overall waste stream. The analysis of the cadmium content of MSW offers the advantage of being a direct approach circumventing the above mentioned constraints. However, waste composition data are uncertain, and the proportions of individual components typically vary considerably from sample to sample. Sample numbers and waste quantity analysed should be sufficient high to develop a statistically reliable picture of composition. At present, while some data are available from various countries in waste quantities and component distribution, data that consider the chemical composition of the various components in the waste stream is limited. Three major campaigns for sorting portable batteries from M.S.W. streams have been realised in the Netherlands and France, during the last years[27]. The results of those campaigns are presented in **Table 3.16**. They indicate that the fraction of primary battery is found in the weight fraction range of 150 to 170 ppm. The rechargeable batteries' fraction, composed mainly of consumer/sealed portable NiCd batteries, are in the range of 4 to 9 ppm (on a wet weight basis). As such it can be concluded that NiCd batteries as a percentage of all battery types found in MSW is in the range of 2.6-6.6% (see **Table 3.16**). Similar figures have been reported by the Witzenhausen Institut (Witzenhauzen, 2001) with NiCd contributions ranging from 3.5-8.4%. A weighted average of 6% has been reported by Witzenhausen Institut (2004). Taken into account that on average a portable sealed NiCd battery contains 13.8% of Cd and contains 5% water (see **Table 2.15)** a lower limit of 0.5 g Cd/tonne $_{\text{wet wt.}}$ $(4 \cdot 0.138 \cdot 0.95 = 0.52)$ and an upper limit of 1.2 g Cd/tonne $_{\text{wet wt.}}$ can be calculated $(9 \cdot 0.138 \cdot 0.95 = 1.17)$. The moisture content of MSW is typically on average 30% (Mersiowsky, 2001; DTU, 2001). Based on this the above figures can be converted to a dry weight basis and a lower and upper limit of 0.7 and 1.7 g Cd/tonne $_{\text{dry wt}}$ is obtained.

Table 3.16 Fraction of Batteries found in MSW: Primary and sealed portable NiCd batteries in various European countries

Country	Year	Primary Battery Weight Ratio In M.S.W.(ppm)	NiCd Battery In M.S.W (mg kg^{-1} $_{\text{wet wt.}}$)	Quantity of M.S.W. studied In tonnes	Source
The Netherlands	1998	170	8	10,000(continuous)	STIBAT
The Netherlands	2000	160	9	10,000 (continuous)	STIBAT
Austria	2000	230	11	377 (sampling methodology)	U.B.F.
Belgium	1998 and 1999	100	5[a]	4.5 (sampling methodology)	I.B.G.E
Germany	2000	370	23[b]	400 (sampling methodology)	GRS
Sweden	1996	100-200	6-6-13.2[c]	(sampling methodology)	RVF

Table 3.16 continued overleaf

[27] More information on the applied methodology is given in Annex III (as submitted by CollectNiCad, 2002)

Table 3.16 continued Fraction of Batteries found in MSW: Primary and sealed portable NiCd batteries in various European countries

Country	Year	Primary Battery Weight Ratio In M.S.W.(ppm)	NiCd Battery In M.S.W (mg kg^{-1} wet wt.)	Quantity of M.S.W. studied in tonnes	Source
France	1999	150	4	8,900 (one month campaign)	SCRELEC & ADEME

a) Calculated on the basis of the estimate that the amount of NiCd is 5% of total consumer/sealed portable batteries;
b) Based on 82 millions inhabitants and 25.5 millions of tonnes MSW per year (1999);
c) Data supplied by Renova (2000).

Similar campaigns have been conducted in Austria, Belgium and Germany but on a much smaller scale (4.5-400 tonnes of MSW). These studies report values between 5 and 23 mg kg^{-1} $_{wet\ wt.}$ resulting in a maximum NiCd battery contribution of 3.01 g Cd/tonne $_{wet\ wt.}$ (23 · 0.138 · 0.95) or 4.3 g Cd/tonne $_{dry\ wt.}$

As a reasonable worst case it is assumed in this report that the total cadmium content of MSW equals 10 g Cd/tonne $_{dry\ wt.}$ The influence of this parameter to the overall assessment is explored in the sensitivity analysis (see subsection "Sensitivity analysis" under Section 3.1.2.2.5). Most of the prevailing evidence coming from MSW sorting studies supports a contribution of NiCd batteries to the overall cadmium load between 0.7 and 1.7 g $tonne^{-1}$ $_{dry\ wt.}$, i.e. a NiCd contribution of 10-20%. Based on the maximum obtained NiCd contribution of 4.3 g Cd/tonne $_{dry\ wt.}$ an allocation of 43% can be calculated. Taken into account the uncertainty surrounding the proposition of one figure, an allocation range of 10-50% is maintained in this report for the assessment of the current emissions due to NiCd batteries. For the current scenarios the 10% is representative of the typical situation. The 50% is representative of the worst case contribution. However, in modelling towards the future, the assumption of 10% will result in a worst case estimate.

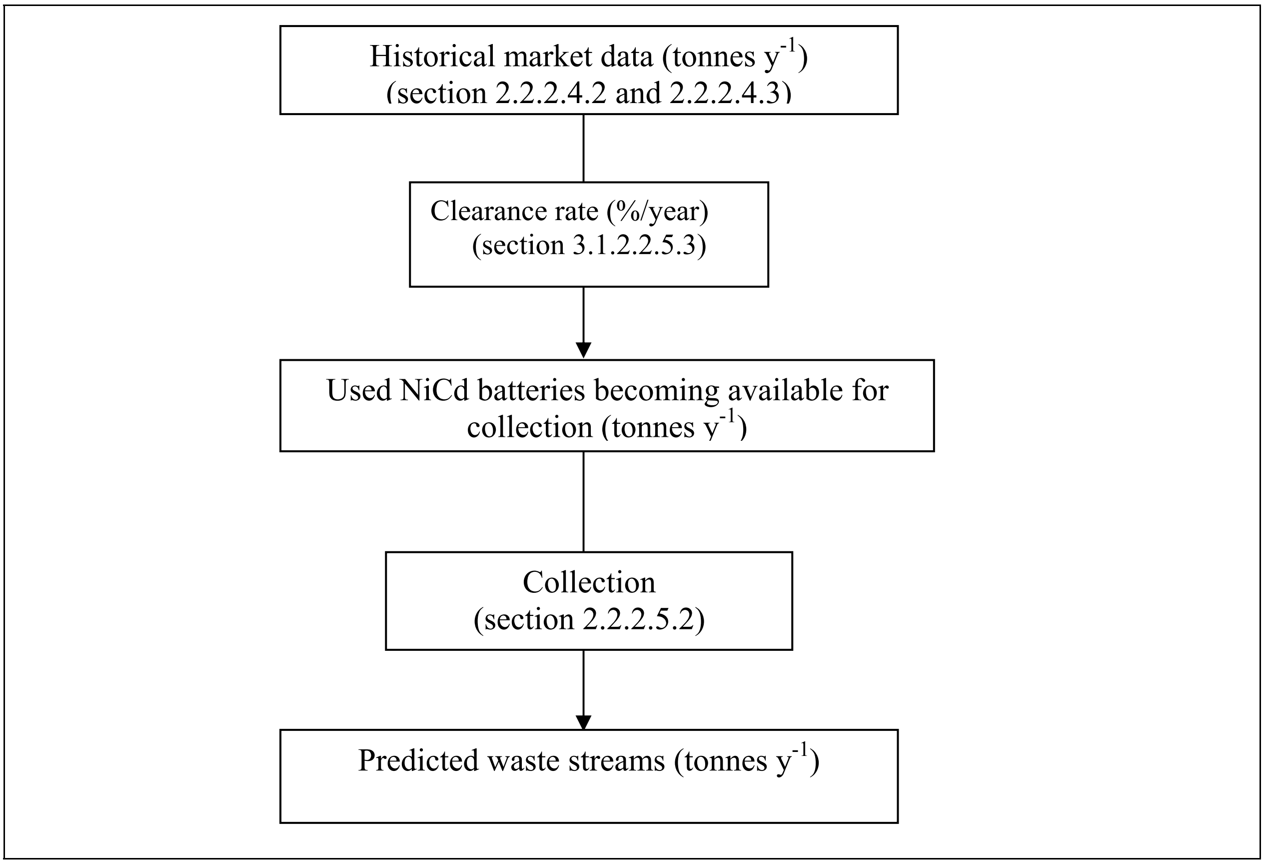
Forecasts of future battery waste streams

In order to calculate future emissions due to the presence of NiCd batteries in waste it is imperative that realistic forecasts of battery waste streams can be made. For the Municipal Solid Waste stream only the contribution of sealed portable NiCd batteries have been considered[28].

The predictions of future battery waste streams are hampered by the fact that the length of time between sale/first use and disposal of a battery by the user varies largely according to the type of the battery and its application. The amount of NiCd batteries ending up for the majority of cases in the MSW waste stream is function of the efficiency of collection and the amounts available for collection. The latter is again subject to the battery lifetime and the "hoarding" process. A schematic overview of the different phases in the calculation of the future waste streams is given in **Figure 3.3**.

[28] Industrial NiCd batteries, representing 20% of the cadmium used in NiCd batteries, are recycled at a high rate. In 1999 2,677 tonnes of industrial NiCd batteries were recycled (see Section 2.2.2.5.1). This represents 72% of the total sales for the same year. If it is assumed that there is no time delay between the sales and the occurrence in the waste stream, 82 tonnes ((3,700 – 2,677) · 0.08) of cadmium is disposed in industrial landfills each year. The emissions of industrial landfills are not addressed here.

Figure 3.3 Rationale used for calculating waste arising from NiCd batteries



The different steps are explained more in detail hereafter.

Calculation of the amount of used NiCd batteries coming available for collection

Future battery waste streams are calculated based on the amount of batteries coming available for collection in a certain year.

The amount of used NiCd batteries available for collection varies with the lifetime of the batteries and the hoarding behaviour of the end user. Since both battery lifetime and hoarding behaviour are difficult to assess, calculating the amount available for collection will thus be subject to an error proportional to the uncertainty over these parameters.

An alternative method, not sensitive to the above uncertainties, is the use of a battery half-life instead of a battery lifetime. The battery half-life is defined as the time needed to collect 50% of the quantity introduced to the market in a given year. This battery half-life can be derived from measurements of the quantity of batteries present in MSW wastes, mixed wastes and industrial wastes in conjunction with battery Date Coding campaigns.

In absence of more data on the subject the amount available for collection will be calculated based on the historical market base line (see Section 2.2.2.4.2 for consumer/sealed portable NiCd batteries) following two models. The first model is a simplified worst case model just taking into account that the batteries will come available for collection/disposal within the average battery lifetime and ignoring the effect of hoarding. In the second model hoarding (especially important for portable sealed NiCd batteries) is incorporated. Inclusion of a hoarding period will have the effect of delaying the reporting of a battery to the waste stream over the assumed hoarding period.

The actual lifetime of a NiCd battery may be five years to twenty-five years depending upon the specific battery design and its application. Reported values for consumer/sealed portable batteries typically range between 3-10 years (Cloke, 1999, Fujimoto, 1999). Similar values (4-8 years) are reported in a Danish study on the mass balance on cadmium (Miljostyrelsen, 2000). In this report the concept of an average battery lifetime for batteries will be used and is defined as the average lifetime until the battery is being collected. For portable batteries an average battery lifetime of 5 years will be used. Industrial batteries are assumed to have an average battery lifetime of 10 years. Results of hoarding studies indicate that the overall hoarded supply on consumer/sealed portable NiCd batteries 15 years after the useful lifetime is 65% (Fujimoto, 1999). Recent information obtained from a similar hoarding study in Europe revealed an average hoarding rate for replacement batteries of 62%. For batteries in large appliances that are disposed of without prior removal of the batteries the hoarding rate can be as high as 95% (TMO-CSA, 2001).

Projections of future battery waste streams

The amount of NiCd batteries that will end up in the waste stream in a certain reference year is calculated by summing up the respective fractions coming available for collection in that reference year and correcting this amount with the collection ratio. Since some countries have not yet started with collecting NiCd batteries a range of collection ratios covering both the lower as upper ranges is recommended (see Section 2.2.2.5.2) as input in the model to predict future battery waste streams.

Future battery waste streams for (sealed) portable NiCd batteries

An overview of the models for the (sealed) portable NiCd batteries is given in **Table 3.17**. Further details related to the models' calculations are available in Annex III.

Table 3.17 Overview of the clearance rates (% initial market volume/year) used in the models for predicting waste arising due to (sealed) portable NiCd batteries

MODEL 1: Based on average lifetime of 5 year			
Period (year)	Description	Clearance rate (%/year)	% marketed volume left at the end of the period concerned
1-5	No hoarding (worst case)	20	0
MODEL 2 : Gradual			
Period (year)	Description	Clearance rate (%/year)	% marketed volume left at the end of the period concerned
1 – 5	Useful life-time	1	95
6 – 20	Home storage/hoarding	2.2	62
21 – 30	Destock	6.2	0

In Model 1 no hoarding is considered. It is assumed that the purchased (sealed) portable NiCd batteries will come available for collection/disposal over a period of 5 years. In Model 2 a more gradual approach is being assumed taking into account the hoarding behaviour of the end user. Within the presumed maximum technical lifetime of 30 years the following clearance rates can be distinguished. Five years after market introduction, due to defects or malfunctions, 5% will be available for collection or disposal. Another 33% will be disposed of over the next 15 years. Finally the remaining volume (62% of the initial market volume) will be destocked within 10 years.

It should be clear that neither the choice of the model nor the battery lifetime will alter the predictions of the future risks associated with landfills due to the fact that the gradual model will only result in a time shift when compared to the model without hoarding. The model without hoarding is not realistic but is given in this report to illustrate the statement above.

For each model only those scenarios were considered which are most likely to occur:

- Scenario 1: Production of portable NiCd batteries will continue at a rate of 13,500 tonnes per year until the hypothetical cadmium ban in 2008 is imposed.
- Scenario 2: Production of portable NiCd batteries will continue at a rate of 13,500 tonnes per year.

For both scenarios collection/recycling was taken into account. Until 2001 the reported collection/recycling weights were used. Before 1994 no collection/recycling was assumed. After the year 2001 the scenarios have been run for the assumption of respectively 10 and 75% collection of NiCd batteries.

The evolution of the cadmium content of MSW solely due to NiCd batteries is summarised in the **Tables 3.18** and **Table 3.19**. These figures were obtained by dividing the weight of the disposed NiCd batteries with the average yearly amount of MSW (expressed as dry weight). Between 1995 and 2001 160,058 ktonnes (wet weight.) of MSW was generated. With a content of 70% dry matter this can be converted to 112,041 ktonnes (dry weight). Probably the amount of MSW will increase in the future (EEA, 2000) but this has not been taken into account.

Table 3.18 Cadmium content (g Cd/tonne waste $_{\text{dry wt.}}$) in MSW due to sealed portable NiCd batteries. Scenario 1: ban imposed

	Cd due to other sources[29]	Contribution (sealed) portable NiCd batteries			
		MODEL 1: ACCELERATED		MODEL 2: GRADUAL	
Year		10% collection	75% collection	10% collection	75% collection
1981	9	0.4	0.4	0.01	0.01
1985	9	2.4	2.4	0.1	0.1
1990	9	6.5	6.5	0.6	0.6
1995	9	12.9	12.9	1.0	1.0
2000	9	14.1	14.1	1.0	1.0
2005	9	15	4.2	4.9	1.4
2010	9	9	2.5	7.5	2.1
2015	9	0	0	9.8	2.7
2020	9	0	0	11.0	3.0
2025	9	0	0	10.2	2.8
2030	9	0	0	7.4	2.1
2035	9	0	0	2.8	0.8
2040	9	0	0		

[29] The current overall cadmium content of MSW is estimated to be 10 g tonne^{-1} $_{\text{dry wt.}}$ If it is assumed that at present only 10% of this content can be allocated to the presence of NiCd batteries, resulting in a worst case assumption for the future Cd content in MSW (see Table 3.20). A current contribution of all other cadmium sources of 9 g tonne^{-1}s dry wt can be calculated.

If a ban is imposed the maximum cadmium content in the MSW due to NiCd batteries is 10.8 g Cd/tonne $_{dry\ wt.}$ for the gradual model and 15 g Cd/tonne $_{dry\ wt.}$ for the accelerated model. In both cases no more NiCd batteries are expected to occur in the waste by the year 2040[30].

Table 3.19 Cadmium content (g tonne^{-1} $_{dry\ wt.}$ waste) in MSW due to portable sealed NiCd batteries. Scenario 2: no ban

	Cd due to other sources	Contribution (sealed) portable NiCd batteries			
		MODEL 1: ACCELERATED		MODEL 2: GRADUAL	
Year		10% collection	75% collection	10% collection	75% collection
1981	9	0.4	0.4	0.0	0.0
1985	9	2.4	2.4	0.1	0.1
1990	9	6.5	6.5	0.6	0.6
1995	9	12.9	12.9	1.0	1.0
2000	9	14.1	14.1	1.0	1.0
2005	9	15.0	4.2	4.9	1.4
2010	9	15.0	4.2	7.8	2.2
2015	9	15.0	4.2	11.2	3.1
2020	9	15.0	4.2	14.0	3.9
2025	9	15.0	4.2	14.9	4.1
2030	9	15.0	4.2	15.0	4.2
2035	9	15.0	4.2	15.0	4.2
2040	9	15.0	4.2	15.0	4.2

If no ban is imposed the cadmium concentration in the MSW due to NiCd batteries will increase until a steady state is reached. The steady state cadmium concentration in the MSW obtained is ranging between 4.2 and 15.0 g Cd/tonne $_{dry\ wt.}$ irrespective of the model used. The NiCd contribution for the year 2000 is estimated with the gradual model to be 1.0 g Cd/tonne $_{dry\ wt.}$ Note that the lower range of the currently presumed NiCd contribution is 0.7 g Cd/tonne $_{dry\ wt.}$ (upper range = 1.71. g Cd/tonne $_{dry\ wt.}$).

Future cadmium content in MSW

From the previous paragraph a steady state cadmium concentration solely due to the presence of NiCd batteries in MSW is estimated between 4.2 and 15 g tonne^{-1} $_{dry\ wt.}$).

The current overall cadmium content of MSW is estimated to be 10 g tonne$^{-1}{}_{dry\ wt.}$ If it is assumed that at present only 10% of this content can be allocated to the presence of NiCd batteries a current contribution of all other cadmium sources of 9 g tonne$^{-1}{}_{dry\ wt.}$ can be calculated (resulting in a worst case assumption for the future Cd content in MSW). If it is further assumed that this contribution will not change in the future this figure can be taken as the starting figure for the calculation of the future cadmium content in the MSW (see **Table 3.20**).

[30]However, it is clear that even when the production of NiCd batteries has ceased the non-refined cadmium cements obtained as a by-product of zinc refining will obviously still have to be landfilled. This TRAR will not address this issue as it is out of the scope of the study. Moreover, it is obvious that after the year 2040, Cd from other sources will still be present (if no legislative action is taken to prevent these).

Table 3.20 Future cadmium content of MSW

Collection (%)	Cd contribution due to NiCd batteries (g Cd/tonne $_{dry\ wt.}$)	Cd contribution due to other sources (g Cd/tonne $_{dry\ wt.}$)	Total future Cd content in MSW (g Cd/tonne $_{dry\ wt.}$)
10	15	9	24
75	4.2	9	13.2

In the worst case scenario, where the collection rate is only 10%, the cadmium contribution from NiCd batteries may rise to 15 ppm with a batteries' contribution of 63% of the total cadmium content in MSW. When collection is at a 75% rate, the cadmium contribution from NiCd batteries may rise to 13.2 ppm with a batteries contribution of 32% of the total cadmium content in MSW.

Waste management Strategies in Europe

Waste management practices[31] vary considerably among different countries and regions in the EU. The current status of waste management strategies for the different EU countries is presented in **Table 3.21** and **Table 3.22**. Most data were extracted from the databank provided by ETWC (ETWC, 2002) which on its turn is a compilation of the results of a joint Eurostat/OECD Questionnaire (2000) or based on national reports (France, Norway, Belgium, Sweden, Finland, Austria, Luxembourg and the Netherlands) and OECD statistics (Greece, Italy, Ireland, Spain and Portugal). The data for Germany (landfill and incineration), Spain (incineration) and Portugal (incineration and landfill) were updated with the latest information made available by the Member State.

Table 3.21 Land-filling and incineration of MSW (in ktonnes WW) in Europe for the period 1995-2001

Country	Year	MSW land-filled (ktonnes $_{wet\ wt.}$)	MSW incinerated (ktonnes $_{wet\ wt.}$)
Austria[a]	1999	1,099	479
Belgium[a]	1998	1,473	1,369
Denmark[c]	1999	361	1,730
Finland[a]	1997	1,610	80
France[a]	1998	23,352	10,781
Germany[b]	2001	16,000	12,000
Greece[d]	1997	3,561	0
Ireland[d]	1995	1,432	0
Italy[a]	1998	20,768	1,949
Luxembourg[a]	1998	62	123
The Netherlands[a]	1999	1,136	3,859

Table 3.21 continued overleaf

31 Only incineration and landfill practices are being considered in this TRAR. Other treatment methods as composting and recycling of MSW are either not applicable for NiCd batteries (presorting) or irrelevant in view of the quantities.

Table 3.21 continued Land-filling and incineration of MSW (in ktonnes WW) in Europe for the period 1995-2001

Country	Year	MSW land-filled (ktonnes $_{wet\ wt.}$)	MSW incinerated (ktonnes $_{wet\ wt.}$)
Norway[a]	1998	1,843	374
Portugal[a,e]	1999-2002	2,603	1,060
Spain[a]	1999	17,477	1,327
Sweden[a]	1998	1,300	1,400
UK[a]	1999	26,860	2,590
Total EU-16	160,058	120,937	39,121

a) Wastebase (ETWC, 2002)
b) Umweltsbundesamt (UBA, 2001)
c) Waste Statistics, 1999 (Danish EPA, 2001)
d) OECD compendium 1999
e) Lipor II, Calheiros JM and Almeida A., pers. com., 2002

The calculation of the share (%) of MSW waste being land-filled or incinerated is calculated using only the ratio between incineration and land-filling in the different Member States.

Table 3.22 Land-filling and incineration practices (in %) in Europe for the period 1995-2001

Country	Year	% of MSW land-filled	% of MSW incinerated
Austria	1999	69.6	30.4
Belgium	1998	51.8	48.2
Denmark	1999	17.3	82.7
Finland	1997	95.3	4.7
France	1998	68.4	31.6
Germany	2001	57.1	42.9
Greece	1997	100	0
Ireland	1995	100	0
Italy	1998	91.4	8.6
Luxembourg	1998	33.5	66.5
The Netherlands	1999	22.7	77.3
Norway	1998	83.1	16.9
Portugal	1999	71.1	28.9
Spain	1999	92.9	7.1
Sweden	1998	48.1	51.9
UK	1999	91.2	8.8
Total EU-16		75.6	24.4

Overall it can be concluded that land-filling remains the predominant disposal route for waste while there is a growing trend towards increased incineration (EEA, 2000). The overall ratio between incineration and land-filling of MSW within the European Union is 24.4 to 75.6 (situation 1995-2001).

Quantifying the cadmium emissions caused by landfills or incineration of NiCd batteries is hampered by the fact that available data on landfill and incineration emissions always represent the total emissions of cadmium containing materials present in the waste stream. Therefore the overall cadmium emissions are calculated first. By using a specific allocation key the specific contribution of NiCd batteries to the overall cadmium emission can be quantified.

The overall cadmium emissions may vary considerably depending on the used Flue Gas Cleaning System or the presence of a leachate treating system/protective lining in the case of landfills.

In this report the scenario based on the European average situation (24.4% incineration and 75.6% landfill) will be completed by two scenarios (100% land-filling and 100% incineration) to perform a rudimentary sensitivity analysis in order to reflect the extremes in waste management option.

Overall cadmium emissions from incineration MSW

Current emissions

Cadmium entering into standard MSW incineration will be distributed among various output fractions such as stack emissions (flue gas), wastewater, fly ash, bottom ash and slag. The distribution pattern of cadmium over these incineration residues is depending on the physical-chemical properties, the gas cleaning technology and the operation and maintenance conditions. While the flue gas and wastewater emissions are immediate, emissions of the incineration residues (via disposal and/or re-use) are delayed.

Flue gas emissions

Approximately 5,000-6,000 Nm^3 flue gas is generated per tonne $_{\text{wet wt.}}$ waste incinerated (Van De Wijdeven, 1991). Today, almost all incineration plants have some kind of flue gas cleaning system (FGCS) in place. The amounts of household waste incinerated per flue gas cleaning system in use by the different Member States are presented in **Table 3.23** and were extracted from the national data collected by ISWA (2002). It should be noted that not all countries or incinerators present in a country has been covered. The distribution of the FGCS in percent (based on a weight basis) is presented in **Table 3.24**.

Table 3.23 Amounts of household waste (ktonnes $_{\text{wet wt.}}$) treated per Flue Gas Cleaning System (reference year 1999) (ISWA, 2002)

Country	Dry	SD	WET	Dry + WET	SD +WET	ESP	FF	O	Total
Austria	0	0	437	0	0	0	0	0	437
Belgium[a]	38	304	208	0	203	0	0	0	753
Denmark	170	367	718	0	0	5	21	0	1,280
France	803	0	6,465	0	0	706	0	351	8,326
Germany	155	1,117	5,024	272	1,656	0	0	0	8,225
UK	150	488	0	0	0	0	0	0	639
The Netherlands	0	20	1,876	0	917	0	0	0	2,813
Norway	0	11	305	0	0	0	0	0	316

Table 3.23 continued overleaf

Table 3.23 continued Amounts of household waste (ktonnes $_{wet\ wt.}$) treated per Flue Gas Cleaning System (reference year 1999) (ISWA, 2002)

Country	Dry	SD	WET	Dry + WET	SD +WET	ESP	FF	O	Total
Portugal[c]	0	1,060	0	0	0	0	0	0	1,060
Spain[b]	21	991	320	0	0	0	0	0	963
Sweden	322	0	645	283	0	0	53	0	1,303
Total	1,660	4,358	15,997	555	2,776	712	74	351	26,483

Source ISWA, 2002;
Dry Dry scrubbing;
SD Semi dry scrubbing;
WET Wet scrubbing;
FF Fabric Filter;
ESP Electrostatic precipitator;
O Other;
a) Updated figures for Flanders (OVAM, P. Loncke, pers. com., 2002);
b) Updated figures for Spain (MMA, 2002);
c) Updated figures for Portugal (LIPOR II, Calheiros JM and Almeida A., pers. com., 2002).

Table 3.24 Distribution (%) of Flue Gas Cleaning Systems for different Member States

Country	Dry	SD	WET	Dry + WET	SD +WET	ESP	FF	O	Total
Austria	0	0	100	0	0	0	0	0	100
Belgium	5	40.4	27.6	0	27	0	0	0	100
Denmark	13.3	28.6	56.1	0	0	0.4	1.6	0	100
France	9.7	0	77.6	0	0	8.5	0	4.2	100
Germany	1.9	13.6	61.1	3.3	20.1	0	0	0	100
UK	23.5	76.5	0	0	0	0	0	0	100
The Netherlands	0	0.7	66.7	0	32.6	0	0	0	100
Norway	0	3.4	96.6	0	0	0	0	0	100
Portugal	0	100	0	0	0	0	0	0	100
Spain	1.6	74.4	24.0	0	0	0	0	0	100
Sweden	24.7	0	49.5	21.7	0	0	4.1	0	100
Total	6.3	16.5	60.4	2.1	10.5	2.7	0.3	1.3	100

Source ISWA, 2002;
Dry Dry scrubbing;
SD Semi dry scrubbing;
WET Wet scrubbing;
FF Fabric Filter;
ESP Electrostatic precipitator;
O Other.

From **Table 3.24** it can be concluded that approximately 22% of all the household waste incinerated in Europe is followed by dry and semi-dry flue gas cleaning. Wet flue gas cleaning accounts for 63%. Three percent of the household waste incinerated is followed by ESP or FF only.

Actual measured air emissions of cadmium by Municipal Solid Waste incinerators were available for a number of Member States and when available preference was given to these measured data (indicated in bold/italic). For some Member States (UK, France and Portugal) actual measured emission data (figures in bold/italic) were available. For other Member States a mix of measured and calculated data were available as best estimates. For example in Germany the cadmium emissions due to MSW incineration is estimated to be 0.3 tonnes in the year 1995 (Rentz et al., 1997; Jockel and Hartje, 1995) and was calculated by multiplying the average cadmium concentration measured in the flue gas of 20 incinerators with the amount of gas formed by the total amount of municipal waste incinerated in Germany. A similar approach has been followed for Spain and Belgium.

In the case no measured data were available the emission to air was estimated by applying the highest emission factor (based on measured data) to the amount of MSW incinerated (see **Table 3.21**).

The modelled/measured annual releases of cadmium to air for the different countries through the incineration of MSW are presented in **Table 3.25** for the scenario: 24.4% incineration.

Table 3.25 Overall cadmium emissions to air (in kg year^{-1}) in Europe due to incineration of MSW. Scenario current incineration 24.4%

Country	MSW incinerated (ktonnes wet wt.)	Measured/modelled emissions (kg year^{-1})[a,b]	Emission factor (g tonne^{-1} wet wt.)[c]
Austria	479	86[d]	0.18
Belgium	1,369	63	0.046
Denmark	1,730	300	0.17
Finland	80	14	0.18
France	10,781	1,922	0.18
Germany	12,000	300	0.025
Greece	0	0	0
Ireland	0	0	0
Italy	1,949	351	0.18
Luxembourg	123	22	0.18
The Netherlands	3,859	53	0.014
Norway	374	41	0.110
Portugal	1,060	3.2	0.003
Spain	1,327	54	0.041
Sweden	1,400	5	0.004
UK	2,590	17	0.007
Total EU-16	39,121	3,231	

a) Measured data Belgium (FEA, OVAM 2001, MMUM, 2001); Measured data France: ADEME, 1999; Measured data Norway and the Netherlands HARP-HAZ 2002, Measured data Spain:MMA 2002, Measured data Portugal: Lipor, 2002, Measured data Denmark (Miljostyrelsen, 2000), Measured data 'weden, (RVF's Faktarapport 2001 om Avfallsförbränning, cited in 'com_302+303_env_S9_annex_I provided by KEMI). Measured data UK: Environment Agency inventory 2001;
b) Measured data indicated in bold/italic are most of the time best estimates based on a combination of modelled and measured data;
c) In case no measured data were available the highest measured emission factor (i.e. France: 0.18 g tonne^{-1}) has been applied. This was the case for Austria, Finland, Italy and Luxembourg;
d) Please note that recently measured data came available for Austrian incinerators which show emissions that are much lower, i.e. 4.2 kg year^{-1} (Stubenvoll et al., 2002). Since the current air emissions for the EU 16 already have a negligible contribution to the overall cadmium air emission from all sources (see Table 3.61) in the EU, the regional calculations were not recalculated (the modelled data were kept as such). Only the local emissions were changed.

The total amount of MSW being incinerated in 1995-2001 for the EU-16 was 39,121 ktonnes corresponding with an overall EU incineration share of 24.4%. Based on the calculations above the cadmium emission to the air compartment due to this incineration activity is 3.2 tonnes Cd on a yearly basis.

The observed differences reflect the current technological improvements that have been made in the abatement of air emissions. For example Spain reported that in 2000 almost all incinerators included an active carbon step (Lipor II, personal communication, 2002). The large difference between the UK and France could also be explained by less stringent maximum emission levels in France. The figure of 3,231 kg Cd/year is taken forward for the calculations.

Based on the emission factor (g $tonne^{-1}$) calculated for each country, the cadmium emission to air has been calculated for the 100% scenario (see **Table 3.26**).

Table 3.26 Cadmium emissions to air (in kg $year^{-1}$) in Europe due to incineration of MSW. Scenario 100% incineration

Country	MSW incinerated (ktonnes $_{wet\ wt.}$)	Emissions (kg $year^{-1}$) Scenario 100%
Austria	1,578	283
Belgium	2,842	131
Denmark	2,091	363
Finland	1,690	296
France	34,133	6,085
Germany	28,000	525
Greece	3,561	641
Ireland	1,432	258
Italy	22,717	4,091
Luxembourg	185	33
The Netherlands	4,995	69
Norway	2,217	243
Portugal	3,663	11
Spain	18,804	764
Sweden	2,700	10
UK	29,450	216
Total EU-16	160,058	14,018

Based on the calculations above the cadmium emission to air in a 100% incineration scenario would result in an emission of 14 tonnes Cd/year.

Emissions from wastewater

Emissions to water results essentially from the discharge of wastewater from incineration plants with wet flue gas cleaning systems. The wastewater has been shown to be contaminated with metals and inorganic salts and have high acidity's or alkalinity's (Reimann, 1987). The main sources of wastewater from incinerators are from flue gas treatment as flue gas scrubber water, e.g. alkaline scrubbing of the gases to remove acid gases, and the quenching of incinerator ash. Water pollution from incinerators is generally not regarded as an important problem, because the limited amount of wastewater generated is of the order of 0.5-2.5 m^3 per tonne of municipal waste incinerated (Williams, 1998). Reimann (2002) reported a water consumption of 1.1 m^3/tonnes for the FGCS and 0.25 m^3/tonne as boiler water. Stubenvoll et al. (2002) reported amounts of waste water between 0.3-0.4 m^3/tonne. In the BREF document on waste incineration (BREF, 2005) volumes between 0.15-0.3 m^3 has been reported. As a worst case assumption the highest volume of wastewater generated (i.e. 2.5 m^3) is used to calculate the regional contributions. For the local assessment both a lower limit (i.e. ± 0.5 m^3) as the higher limit is used to calculate the dilution factors (see **Table 3.93**).

Reported wastewater cadmium concentrations (before treatment) are given in **Table 3.27**.

Table 3.27 Average cadmium concentrations in incinerator wastewater (mg L^{-1}) (influent) before treatment

	Cd concentration (mg L^{-1})	Reference
Flue gas scrubber water	0.46	Ozvacic et al. (1985)
	0.5	Reiman (1989)
	0.17	Novem/RIVM (1992) cited in Anthonissen and Meyer (1993)
	0.303 (incinerator 1) (average concentration 3 samples)	Aminal (1994)
	0.117 (incinerator 2) (average concentration 3 samples)	Aminal (1994)
	0.45 (stage 1 acid scrubber phase) (average concentration 104 measurements) min-max = < 0.01-0.76 0.37 (stage 2 alkaline scrubber phase) (average concentration 104 measurements) min-max = 0.1-0.62	Reimann (2002)
P50 (of average values)	0.3	Selected for regional calculations
P90 (of average values)	0.47	Selected for local calculations

Reduction of metal concentrations and mercury/cadmium concentration is usually through neutralisation via precipitation with calcium hydroxide in the presence of organic sulphides (e.g. the additive TMT_{15} (trimercaptotriazine) (Reimann, 1987, BREF, 2005). Treatment of an effluent with an average cadmium concentration (104 measurements) of 0.45 mg $L^{-1}$with TMT resulted in a cadmium concentration of < 0.01 mg L^{-1}indicating a removal efficiency of at least 98.8%[32] (Reimann, 2002). For the calculations in this report it will be assumed that 98.8% of the cadmium is removed to sludge going to a hazardous landfill and that 1.2% remains in the wastewater. This results in effluent concentration of approximately 0.004 mg L^{-1}(for the median value) and 0.0056 mg L^{-1}(for the P90 value)[33]. Reported Cd concentrations in the effluents of three Austrian MSW incinerator plants (reference year 2000) are 4 to 5.6 times lower and were respectively < 0.001 mg L^{-1}, 0.001 mg $L^{-1}$and < 0.05 mg L^{-1}(Stubenvoll et al., 2002). Measured effluent concentrations for two incinerators in Norway (Brobekk and Klemterud) in the Oslo region are a factor 2.5 lower and were 0.00159 mg $L^{-1}$and 0.00158 mg L^{-1}, respectively (Personal communication Jon-Ivar Andersen, Email 03-03-2003).

32 For the calculation the detection limit value was divided by two.

33 This value is also well below the emission limit of 0.05 mg L^{-1}(EC, 2000).

The annual releases of cadmium to water for the different countries through the incineration of MSW are presented in **Table 3.28** and **Table 3.29** for two scenarios: 24.4% incineration and 100% incineration. Since 89% of the incinerated MSW is followed by some kind of semi dry or wet FGCS it was assumed that for all countries the total incinerator process produced wastewater.

As indicated above for the regional emissions it has been assumed as a worst case estimate that 2.5 m^3 waste water per tonne $_{wet\ wt.}$ of MSW is generated. For the regional calculations the median influent concentration of 0.3 mg L^{-1}has been used (i.e. effluent concentration of 0.004 mg L^{-1}). For the local calculations (see Section 3.1.3.2) the 90^{th} percentile influent concentration of 0.47 mg L^{-1}has been used (i.e. 0.0056 mg L^{-1}effluent concentration). However, since information on measured effluent concentration are limited an additional scenario have been developed as sensitivity analysis with the maximum measured influent concentration of 0.76 mg L^{-1}(i.e. 0.009 mg L^{-1}in the effluent)

Table 3.28 Overall cadmium emissions to water and sludge (in kg $year^{-1}$) in Europe due to incineration of MSW. Scenario current incineration 24.4%

Country	MSW incinerated ((ktonnes $_{wet\ wt.}$)	Influent WWTP (kg $year^{-1}$)	Emissions to water (kg $year^{-1}$) Scenario 24.4%	Emissions to sludge (kg $year^{-1}$) Scenario 24.4%
			1.2 %	98.8%
Austria	479	359	4	355
Belgium	1,369	1,027	12	1,014
Denmark	1,730	1,298	16	1,282
Finland	80	60	1	59
France	10,781	8,086	97	7,989
Germany	12,000	9,000	108	8,892
Greece	0	0	0	0
Ireland	0	0	0	0
Italy	1,949	1,462	18	1,444
Luxembourg	123	92	1	91
The Netherlands	3,859	2,894	35	2,860
Norway	374	281	3	277
Portugal	1,060	795	10	785
Spain	1,327	995	12	983
Sweden	1,400	1,050	13	1,037
UK	2,590	1,943	23	1,919
Total EU-16	39,121	29,341	352	28,989

Based on the calculations above the cadmium emission due to this incineration of MSW is approximately 0.35 tonnes Cd/year to water and 28.9 tonnes Cd/year to sludge.

Table 3.29 Overall cadmium emissions to water and sludge (in kg $year^{-1}$) in Europe due to incineration of MSW. Scenario 100% incineration

Country	MSW incinerated (ktonnes $_{wet\ wt.}$)	Influent WWTP (kg $year^{-1}$)	Emissions to water (kg $year^{-1}$) Scenario 100%	Emissions to sludge (kg $year^{-1}$) Scenario 100%
			1.2 %	98.8%
Austria	1,578	1,184	14	1,169
Belgium	2,842	2,132	26	2,106
Denmark	2,091	1,568	19	1,549
Finland	1,690	1,268	15	1,252
France	34,133	25,600	307	25,293
Germany	28,000	21,000	252	20,748
Greece	3,561	2,671	32	2,639
Ireland	1,432	1,074	13	1,061
Italy	22,717	17,038	204	16,833
Luxembourg	185	139	2	137
The Netherlands	4,995	3,746	45	3,701
Norway	2,217	1,663	20	1,643
Portugal	3,663	2,747	33	2,714
Spain	18,804	14,103	169	13,934
Sweden	2,700	2,025	24	2,001
UK	29,450	22,088	265	21,822
Total EU-16	160,058	120,044	1,441	118,603

Based on the calculations above the cadmium emission to water in a 100% incineration scenario would result in an emission of approximately 1.4 tonnes Cd/year to water and 118.6 tonnes Cd/year to sludge.

Delayed emissions from incinerator residues

While the emissions with flue gas are immediate, emissions from the residual fractions will be delayed and may result in a diffuse emission of cadmium to the environment. In this study a distinction is only made between bottom ash and fly ash. Other flue gas cleaning products generated in the process of removing acid gases are not specifically addressed.

A number of studies have been carried out concerning the fate and distribution of cadmium in municipal solid waste incineration plants. The distribution of cadmium as a mass balance for incinerators equipped with different FGCs is given in **Table 3.30**.

Table 3.30 Partitioning of cadmium (%) in the various output fractions of a MSW incinerator

Flue gas (%)	Bottom- and boiler ash (%)	Fly ash (%)	Waste water (%)	Sludge and salt (%)	FGCS	Reference
12.1	10.8	77.1	/	/	ESP	Zimmerman (1996)
12	12	76	/	/	ESP	Brunner and Monch (1986)
< 2.5	15	80	N.A.	3	/	IAWG (1995)
0.1	21.5	78.5	< 0.1	N.A.	ESP/WET /AC	Morf et al. (2000)
0.02	15	72	< 0.001	13	ESP/WET	VROM (1997)
2.6	5.5	69.9	0	21.4	ESP/WET	Wiaux (1997)
0	7	89	0	4	ESP/WET	Lemann et al. (1995)

/ Not applicable;
N.A. Not available;
ESP Electrostatic precipitator;
WET Wet scrubbing;
AC Active carbon.

In general the largest fraction of cadmium can be found in FGCS residues such as fly ash (77-89%), i.e. the particulate material collected by electrostatic precipitators also called ESP dust. On average 78% of the cadmium can be found in the fly ash and 12% in the bottom ash. If only the solid residues are considered this ratio becomes 87% fly ash and 13% bottom ash.

Data on amounts of bottom ash and fly ash generated in the different Member States (ISWA, 2002) are presented in **Table 3.31**.

Table 3.31 Distribution of bottom ash and fly ash for different Member States (reference year 1999) based on ISWA (2002)

Country	Total waste incinerated (ktonnes $_{\text{wet wt.}}$)[a]	Bottom ash (ktonnes $_{\text{dry wt.}}$)	Fly ash (ktonnes $_{\text{dry wt.}}$)	Bottom ash (%)	Fly ash (%)
Austria	450	107	8	23.9	1.8
Belgium	191	25	5	13.1	2.6
Denmark	2,359	473	63	20.1	2.7
France	10,852	1,840	210	17.0	1.9
Germany	12,853	3,200	366	24.9	2.8
UK	1,074	289	31	26.9	2.9
The Netherlands	2,379	590	84	24.8	3.5
Norway	144	25	4	17.0	2.6
Portugal	322	59	27	18.4	8.5
Spain	996	188	59	18.8	5.9
Sweden	1,968	371	87	18.9	4.4
Total	33,589	7,167	944	21.3	2.8

a) Household waste and industrial waste

In general it can be concluded from **Table 3.31** that on average bottom ash constitutes 21.3% by weight of the waste input and fly ash 2.8% by weight of the waste input. Van der Poel (1999) reports similar figures.

These figures were used to calculate the amount of bottom- and fly ash produced by incineration MSW (see **Table 3.32**).

Table 3.32 Distribution of bottom ash and fly ash for different Member States Scenario under current incineration scenario of 24.4%

Country	MSW incinerated (ktonnes $_{wet\ wt.}$)	Bottom ash (ktonnes $_{dry\ wt.}$)	Fly ash (ktonnes $_{dry\ wt.}$)
Austria	479	102	13
Belgium	1,369	292	38
Denmark	1,730	368	48
Finland	80	17	2
France	10,781	2,296	302
Germany	12,000	2,556	336
Greece	0	0	0
Ireland	0	0	0
Italy	1,949	415	55
Luxembourg	123	26	3
The Netherlands	3,859	822	108
Norway	374	80	10
Portugal	1,060	226	30
Spain	1,327	283	37
Sweden	1,400	298	39
UK	2,590	552	73
Total EU-16	39,121	8,333	1,095

From **Table 3.32** it can be concluded that at present 8,333 ktonnes of bottom ash and 1,095 ktonnes of fly ash have to be disposed of on a yearly basis. The cadmium concentrations in the fly ash and bottom ash are calculated based on the cadmium balances for scenario 1 (24.4% incineration) presented in **Figure 3.3**. For bottom ash a concentration of 3.8 mg Cd/kg $_{dry\ wt.}$ can be calculated (31,366 kg Cd/8,333 ktonnes bottom ash). For fly ash a concentration of 192 mg Cd/kg $_{dry\ wt.}$ is obtained (209,908 kg Cd/1,095 ktonnes).

These figures are in concordance with data reported in the literature. Reported cadmium concentrations in fly ash range from 50 to 1,000 mg kg^{-1} $_{dry\ wt.}$ (EEA, 2000) but can be substantially higher (EPA, 1991). Cadmium concentrations in bottom ash are in general lower. Ranges reported in the Netherlands are 0.1-25 mg kg^{-1} $_{dry\ wt.}$ for bottom ash and 8-337 mg kg^{-1} $_{dry\ wt.}$ for fly ashes (Anthonissen and Meijer, 1993; Verhagen and Meijer, 2000). Typical cadmium concentrations in bottom ash and fly ash as reported by the International Ash Working Group are 0.3-70.5 mg kg^{-1} $_{dry\ wt.}$ for bottom ash and 50-450 mg kg^{-1} $_{dry\ wt.}$ for fly ash (IAWG, 1997). The calculated concentrations (3.8 mg kg^{-1} $_{dry\ wt.}$ for bottom ash and 192 mg kg^{-1} $_{dry\ wt.}$ for fly ash) are well in the range of these literature values.

Most of the fly ash generated by incinerators in the EC is land-filled with or without prior treatment. For fly ash it is general practice that they are placed in hazardous waste landfills or used for reclamation of old mine shafts or quarries. If treated the most common treatment form in the EC Member States is probably solidification/stabilisation with hydraulic binders (cement or cement-like substances) often supplemented with the mixing of various additives (Argus, 2000). However, in some countries fly ash are (still) re-used. The Netherlands produced in 1999 90 ktonnes of fly-ash from which 41 ktonnes (= 45%) was re-used with the largest application being as fill material in asphalt (25-30%) (VVAV, 2000, Anthonissen and Meijer, 1993). Belgium and the UK also indicate a re-use of fly ash (Jacobs et al., 2001; EA 2002). In the framework of the upcoming legislation it is, however, unlikely that the use of fly ashes in asphalt will be a viable option for the future.

The use of processed bottom ash in engineering applications just started in some countries like the UK whereas its use in the Netherlands in civil engineering started since the 1980's. The ashes are used unbounded as a bulk fill, for example, to construct embankments, as a substitute aggregate or for bound uses through incorporation into road paving (tarmac, asphalt) or construction blocs.

In the UK bottom ash processing in the year 2000 reached 270 ktonnes or 42% of the bottom ash production for that year (EA 2002). The percentage of bottom ash recycled in other countries such as the Netherlands, Denmark and France is respectively 100%, 70% and 50% (EA, 2002). In Germany approximately 80% of bottom ash is being re-used mainly in road and street construction and 20% of the bottom ash is presently deposited into landfills (personal communication with Bernt Johnke, Umweltbundesamt, Germany, July 31, 2002).

The re-use and/or land-filling of incineration residues may result in a long-term diffuse emission potentially contaminating groundwater, surface water and soil. A field study examining the leaching from two road construction sites showed that substantial leaching of metals from the road construction occurred but, transport through the underlying soil layer was limited due to soil-metal binding processes (Wesselink, 1995). In general two approaches can be used to determine the composition – and thus the potential future emissions -of residual leachates: (1) the generation of simulated leachates, and (2) the study of field-generated leachates. Most often laboratory leachability simulation studies are being used to understand the potential leachability of cadmium in MSW ash. But because a number of such leaching procedures exist, the data generated from these leachate tests have been criticised for the variability in experimental conditions, and for their inability to predict long-term leaching behaviour for all type of disposal options (EPA, 1991). Whether or not the results of these laboratory tests underestimate or overestimate the potential release of contaminants is still under discussion. But most often, the re-use of incineration residues is dependent on the outcome of these leaching tests. If the results of the leaching test are exceeding an imposed limit the bottom- or fly ash is classified as hazardous waste and should be land-filled in a hazardous landfill. For example some countries such as Belgium and the Netherlands provide guidance on acceptable contaminant levels in construction materials in terms of potential impacts on health and the environment. Both the Netherlands and Belgium rely for their conclusion, on whether the material can be used as construction material or not, on the outcome of the column test NEN 7343 (VLAREA, 1998, Aalbers et al., 1996). For non-prefabricated construction materials (unbounded use) maximal allowable cadmium emissions of 0.03 -0.07 mg kg^{-1} have been reported. For prefabricated construction materials 1.1 mg/m^2 is reported. Furthermore the total cadmium concentration should preferentially below the target value of 10 mg kg^{-1} $_{dry\ wt.}$ In Germany similar legislation is in place. For cadmium the target value for re-use is 20 mg kg^{-1} $_{dry\ wt.}$ and the cadmium concentration in the eluate should not exceed 5 µg L^{-1}(LAGA 1994 cited in Förstner and Hirschmann, 1997).

It can be concluded that at present 8,333 ktonnes of bottom ash and 1,095 ktonnes of fly ash have to be disposed of on a yearly basis. The cadmium concentrations in the bottom ash and fly ash are respectively 3.8 mg Cd/kg dry wt and 192 mg Cd/kg $_{dry\ wt.}$ The re-use and/or land-filling of incineration residues may result in a long-term diffuse emission potentially contaminating groundwater, surface water and soil.

The use of incineration residues is only allowed if the results of leaching tests are favourable. How limit values can be established in relation to the results of leaching tests have also not been addressed. The impact of the expected increase in cadmium content of bottom ash and fly ash (see subsection "Future emissions" under Section 3.1.2.2.5) on the re-usability of these incineration residues has also not been quantified because it is believed that this issue represents a general waste management problem rather than belonging to a substance specific risk assessment. For example most often the classification as hazardous waste or the re-use of incinerator residues is governed by the leachability of other metals as well such as copper, lead or zinc (OVAM, 2001; RIVM/LAE, 1998). The emissions associated with land-filling of incineration products have not been assessed.

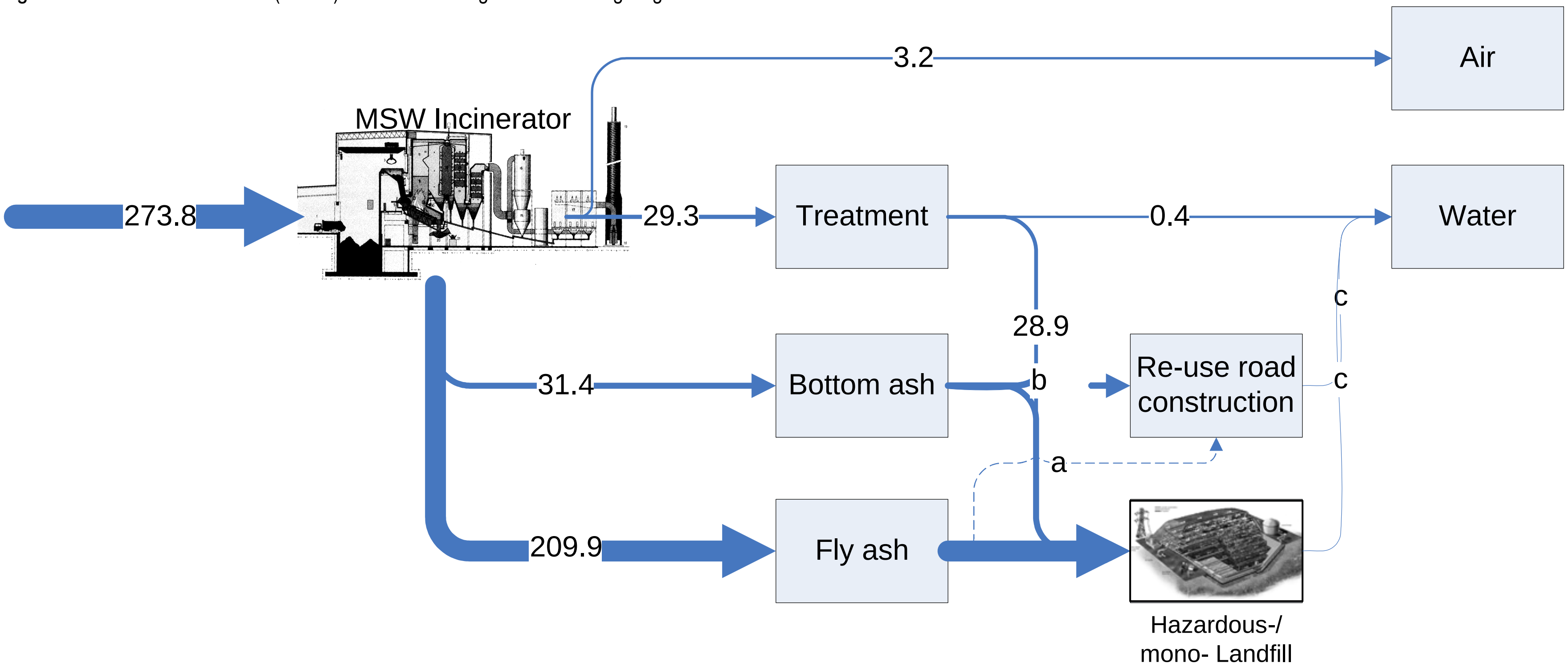
Summary of overall cadmium emissions due to incineration of MSW

An overview of the overall cadmium releases to the different compartments due to incineration of MSW containing 10g/Cd tonne $_{\text{dry wt}}$ is summarised for the different scenarios in **Figures 3.4-3.5**.

An example calculation is given hereunder for the current incineration practice (24.4%):

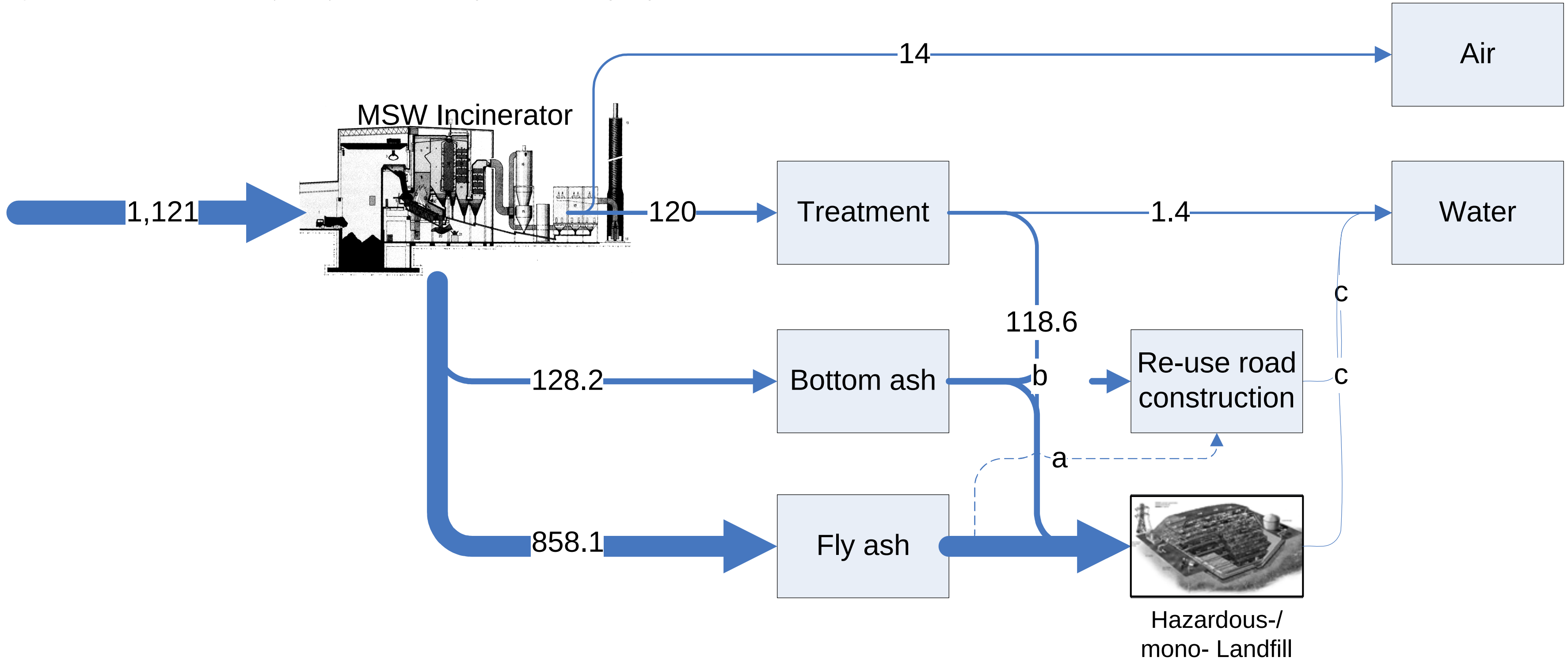
- Cd-content MSW = 10 g tonne$^{-1}_{\text{dry wt.}}$;
- Total volume of waste incinerated = 39,121,000 tonnes wet weight = 27,384,700 tonnes $_{\text{dry wt.}}$;
- Cadmium load present in MSW: 10 g tonne^{-1} dry wt · 27,384,700 tonnes dry wt = 273.8 tonnes Cd;
- Direct cadmium emissions to air = 3,231 kg (see **Table 3.25**) = 3.2 tonnes;
- Direct cadmium emissions to water = 352 kg (see **Table 3.28**) = 0.4 tonnes;
- Cadmium load to hazardous sludge = 28,989 kg (see **Table 3.28**) = 28.9 tonnes;
- Cadmium flow to incinerator residues = 273.8 tonnes Cd – 3.2 tonnes – 0.4 tonnes – 28.9 tonnes = 241.3 tonnes;
- Cadmium load to bottom ash = 241.3 tonnes · 0.13 = 31.4 tonnes;
- Cadmium load to fly ash = 241.3 · 0.87 = 209.9 tonnes.

Figure 3.4 Overall cadmium flow (tonnes) due to incinerating MSW containing 10 g Cd/tonne - Scenario 24.4 % incineration.



a) Most often fly ash is land-filled but some countries (The Netherlands, UK, and Belgium) still re-use a part of their fly ash;
b) Depending on the leaching results bottom ash can either be land-filled or re-used in road construction;
c) The delayed water emissions of re-use in road constructions and hazardous landfills have not been quantified.

Figure 3.5 Overall cadmium flow (tonnes) due to incinerating MSW containing 10 g Cd/tonne $_{dry\ wt}$ -100% incineration.



a) Most often fly ash is land-filled but some countries (The Netherlands, UK and Belgium) still re-use a part of their fly ash;
b) Depending on the leaching results bottom ash can either be land-filled or re-used in road construction;
c) The delayed water emissions of re-use in road constructions and hazardous landfills have not been quantified (c).

Allocation of current air emissions to a regional/local scale

The allocation of the total EU air emission amount to the regional and the local scale has been performed by dividing the regional emissions with the number of incinerators per country (see **Table 3.33**). Measured data are indicated in bold/italic. For those countries where no measured data were available an emission factor of 0.18 g Cd/tonne MSW $_{\text{wet wt.}}$ has been used.

Table 3.33 Allocation of air emissions to regional/local scale. Scenario current incineration 24.4%

Country	No. incineration plants[a]	Air emissions/country (kg year^{-1}) scenario 24.4% (see Table 3.22)	Air emissions/ plant (kg year^{-1}.plant)
Austria[b]	3	86 h	28.6 h
Belgium	18	63	3.5
Denmark[f]	31	300	9.7
Finland[c]	1	14	14
France	117	1,922	16.4
Germany	60	300	5
Italy	62	351	5.7
Luxembourg[c]	1	22	22
The Netherlands	11	53	4.8
Norway[d]	8	41	5.1
Portugal	2	3.2	1.6
Spain	8	54	6.8
Sweden[e]	22	5	0.2
UK[g]	11	17	1.5
Total	355	3,231	
Average	25 plants/country (=355/14)	231 kg year^{-1}/country (= 3,231/14) 10% rule = 323	9.1 kg year^{-1}/plant = (3,231/355)

a) Based on ISWA 2002;
b) Schuster, 1999;
c) Juniper 1997;
d) SFT, 2002;
e) RVF, 2002;
f) Waste Statistics 1999, Danish EPA (2001);
g) Environment Agency 2002;
h) Actual measured data have come available recently (Stubenvoll et al., 2002). These values indicate a cadmium emission of 4.2 kg year^{-1} or, on average, 1.4 kg year^{-1} plant.

Since emissions incineration plants are not (yet) considered in the TGD emission tables, the following approach is proposed to allocate incineration plant emissions to the regional/local scale. On the basis of country specific information, for 14 EU countries, a country average number of incineration plants of 25 can be calculated. In these 25 plants a hypothetical amount of 2,794 ktonnes of MSW (see **Table 3.25**: "MSW incinerated" divided by 14 countires = 39,121/14) can be incinerated, thereby emitting a Cd amount to air of 231 kg year^{-1} (Scenario 24.4%). Comparing these data to the emitted Cd amounts for individual countries, it seems that 9 out of 14 countries are covered, except for Denmark, France, Italy and Germany. Measured/estimated data in Belgium are between 1-12 kg/plant. For the UK typically concentration between 0.5 and 5 kg/plant are reported. Although France is accounting for 59% of the total EU air emission it is proposed to use the 10% rule to derive a reasonable worst case emission estimate of the regional emission since incineration activities (large number of site) are reasonably spread over the EU territory. Applying the TGD 10% rule to the total EU air emission amount gives a regional air emission amount of 323 kg $year^{-1}$ which is comparable with the calculated 231 kg $year^{-1}$ per region**.** On the basis of country specific information for incineration plants (air emission and number of incineration plants) an EU weighted average emitted Cd amount per plant of 9.1 kg $year^{-1}$ can be calculated. In comparison with the average emission per plant in each country it seems that Luxembourg, France, Denmark and Finland are the countries not completely covered. Individual measured data were available for France. The 90^{th} percentile of these measurements is 36.7 kg $year^{-1}$/plant. Measured data in Austria (Stubenvoll et al., 2002) indicate an emission of 1.4 kg $year^{-1}$. This value has been used for the local PEC calculations for Austrian incinerators.

The country specific local air emission estimates ranging between 0.2-16.4 kg $year^{-1}$/plant have been used in the local PEC calculations (see Section 3.1.3.2.3). These values have been taken forward in the risk characterisation together with the generic scenario based on the 10% rule and average emission of 9.1 kg Cd/year.plant. Since France contributes for 59% of the total emission to air and individual measured data were available an additional scenario for France based on these measured data was also taken forward into the risk characterisation (i.e. 36.7 kg)

In the 100% incineration scenario the allocation from the EU scale to the regional scale is performed applying the 10% rule to the EU emission amount. A regional emission amount of 1,402 kg $year^{-1}$ is calculated. Comparing this value to the country specific emission amounts shows that 14 out of 16 countries are covered. Larger air emissions have been obtained for France and Italy. In the 100% incineration scenario it is assumed that the number of incineration plants is proportionally increased to the amount of MSW to incinerate. Hence, on a local scale the exposure scenario will be similar to that from the 24.4% incineration scenario.

Measured cadmium loads to the surface water was lacking for most incinerators. Therefore the calculated water emissions (see **Table 3.28**) based on a generic median effluent concentration of 0.004 mg L^{-1}. have been used to calculate the EU emissions to surface water using the 10% rule in analogy to the air emission estimate. For the local scenario (PEC calculation and risk characterisation) the 90^{th} percentile Cd effluent concentration (0.005 mg L^{-1}= (1.2 · 0.42)/100) has been used.

A summary of all continental and regional emissions to air and surface water is given in **Table 3.34**.

Table 3.34 Total annual amount of Cd emissions to air and water within the EU from incineration plants

Scenario	Released amount Cadmium (kg/y)	Continental (90%) (kg/y)	Regional (10%) (kg/y)
	Air		
24.4% incineration	3,231	2,908	323
100% incineration	14,018	12,616	1,402
	Water		
24.4% incineration	352	317	35
100% incineration	1,441	1,297	144

Table 3.34 continued overleaf

Table 3.34 continued Total annual amount of Cd emissions to air and water within the EU from incineration plants

Scenario	Released amount Cadmium (kg/y)	Continental (90%) (kg/y)	Regional (10%) (kg/y)
	Landfill		
24.4% incineration	240,465	216,419	24,047
100% incineration	1,104,947	994,452	110,495

Contribution of NiCd batteries to the overall cadmium emissions

With the assumption that NiCd batteries account for 10-50% of the total MSW cadmium content, the contribution of NiCd batteries can be calculated by multiplying the overall cadmium emissions as presented in **Figures 3.3** to **3.6** by 0.1 and 0.5 (**Tables 3.35** and **Table 3.36**).

Table 3.35 Contribution of NiCd batteries to the overall cadmium emissions due to incineration- Scenario 10 mg kg^{-1} $_{dry\ wt.}$ total cadmium in MSW

Scenario	24.4% incineration		100% incineration	
Allocation key	10%	50%	10%	50%
Compartment	Direct emissions (kg $year^{-1}$)			
Air	323	1,617	1,402	7,009
Water	35	176	144	721
Compartment	(kg)			
Cadmium going to landfill	24,047	120,233	110,495	552,473

Table 3.36 Contribution of NiCd batteries to the continental and regional cadmium emissions due to incineration. Scenario 10 mg kg^{-1} $_{dry\ wt.}$ total cadmium in MSW

Scenario		Released amount Cadmium (kg/y)	Continental (90%) (kg/y)	Regional (10%) (kg/y)
		Air		
24.4% incineration	0.1	323	291	32
	0.5	1,617	1,455	162
100% incineration	0.1	1,402	1,262	140
	0.5	7,009	6,308	701
		Water		
24.4% incineration	0.1	35	31.5	4
	0.5	176	158	18
100% incineration	0.1	144	130	14
	0.5	721	649	72
		Landfill		
24.4% incineration	0.1	24,047	21,642	2,405
	0.5	149,113	134,202	14,911
100% incineration	0.1	110,495	99,456	11,050
	0.5	552,473	497,226	55,247

Future emissions

The future total cadmium concentration in MSW is expected to range between 13.2 and 24 g $tonne^{-1}$ dry wt (see **Table 3.20**) with an estimated specific contribution of NiCd batteries of respectively 4.2 g $tonne^{-1}{}_{dry\ wt.}$ (= 4.2/13.2 =32%) and 15 g $tonne^{-1}$ DW (= 15/24 = 63%).

As a worst case exercise the future emissions due to the expected increase of cadmium in the MSW for a 100% incineration scenario are presented.

Future cadmium emissions to air

There is no evidence for increased cadmium air emission due to an increase in cadmium load in the MSW unless the gas cleaning system fails (van der Poel, 1999). Therefore these emissions can be dealt with irrespective of the cadmium concentration in the MSW (an increase in cadmium concentration will of course be translated into higher cadmium concentrations in the solid residues). Higher overall cadmium air emissions are expected to occur related to an increase in the incineration practice and the higher amount of MSW that is likely to be generated in the future (EEA, 2000). However, the latter has not been taken into account. It is assumed that each year the same amount of MSW is being incinerated (i.e. 160,058 ktonnes $_{wet\ wt.}$) resulting in an overall emission of 14 tonnes Cd/year (see **Table 3.26**).

Future cadmium emissions from wastewater

Due to an increased cadmium load it can be expected that the washing water from the scrubber system will contain a higher cadmium concentration. If a linear relationship between the effluent concentration and the cadmium content in the MSW is assumed the cadmium concentration in the untreated effluent can then be adjusted for an altered waste composition, based on the ratio of the cadmium concentration in the influent for the current reference situation (10 g $tonne^{-1}{}_{dry\ wt.}$ cadmium). The equation hereunder demonstrates how future changes in cadmium wastewater concentration (before treatment) due to changing cadmium content of the MSW can be calculated with the assumption of a linear relationship (see **Table 3.37**).

$$CdConc_{Future,wastewater} = \frac{CdConc_{Present,wastewater}}{CdConc_{Present,MSW}} \times CdConc_{Future,MSW}$$

$CdConc_{Future,\ Wastewater}$: Future cadmium concentration in the wastewater (mg L^{-1})
$CdConc_{Present,\ wastewater}$: Present cadmium concentration in the wastewater (mg L^{-1}) = 0.3 mg L^{-1}(see Table 3.24)
$CdConc_{Future,\ MSW}$: Future cadmium concentration in MSW (g)[34]
$CdConc_{Present,\ MSW}$: Present cadmium concentration in MSW (g) = 10 g $tonne^{-1}$

Table 3.37 Future cadmium content of wastewater produced by the incineration process (influent of on-site treatment plant)

Collection (%)	Total future Cd content in MSW (g $tonne^{-1}$)	Cd concentration in wastewater[a] (mg L^{-1})
10	24	0.72
75	13.2	0.4

a) Before treatment

[34] Obtained via the modelling of future NiCd waste arisings (see subsection “Forecasts of future battery waste analysis” under Section 3.1.2.2.5). Remark: note that the total amount of the MSW will probably also further increase (EEA, 2000) but this has not been taken into account.

After treatment 98.8% of the cadmium will be removed resulting in effluent concentrations of 0.005-0.009 mg L^{-1}.[35]. These effluent concentrations have been used for the regional scenario. For the local scenarios future effluent concentrations have been calculated based on the current 90th percentile influent concentration of 0.47 mg L^{-1}resulting in future influent concentrations of 0.62 and 1.13 mg L^{-1}(i.e. 0.007- 0.0135 mg L^{-1}effluent concentration).

Future cadmium content of residues

The increase of the cadmium content in the MSW will be translated into an increase in the cadmium concentration of the incineration residues such as bottom ash and fly ash. In **Table 3.38** the expected bottom ash and fly ash concentrations have been calculated based on the assumption that bottom ash constitutes 21.3% by weight of the waste input and fly ash 2.8% by weight of the waste input.

Table 3.38 Future cadmium content (mg kg^{-1} $_{dry\ wt.}$) of bottom ash and fly ash: current and future scenarios

Total Cd content in MSW (g $tonne^{-1}$)	Scenario	Cd content in bottom ash (mg kg^{-1} $_{dry\ wt.}$)	Cd content in fly ash (mg kg^{-1} $_{dry\ wt.}$)
10	24.4% incineration	3.8	192
13.2	100% incineration	5.0	253
24	100% incineration	9.1	463

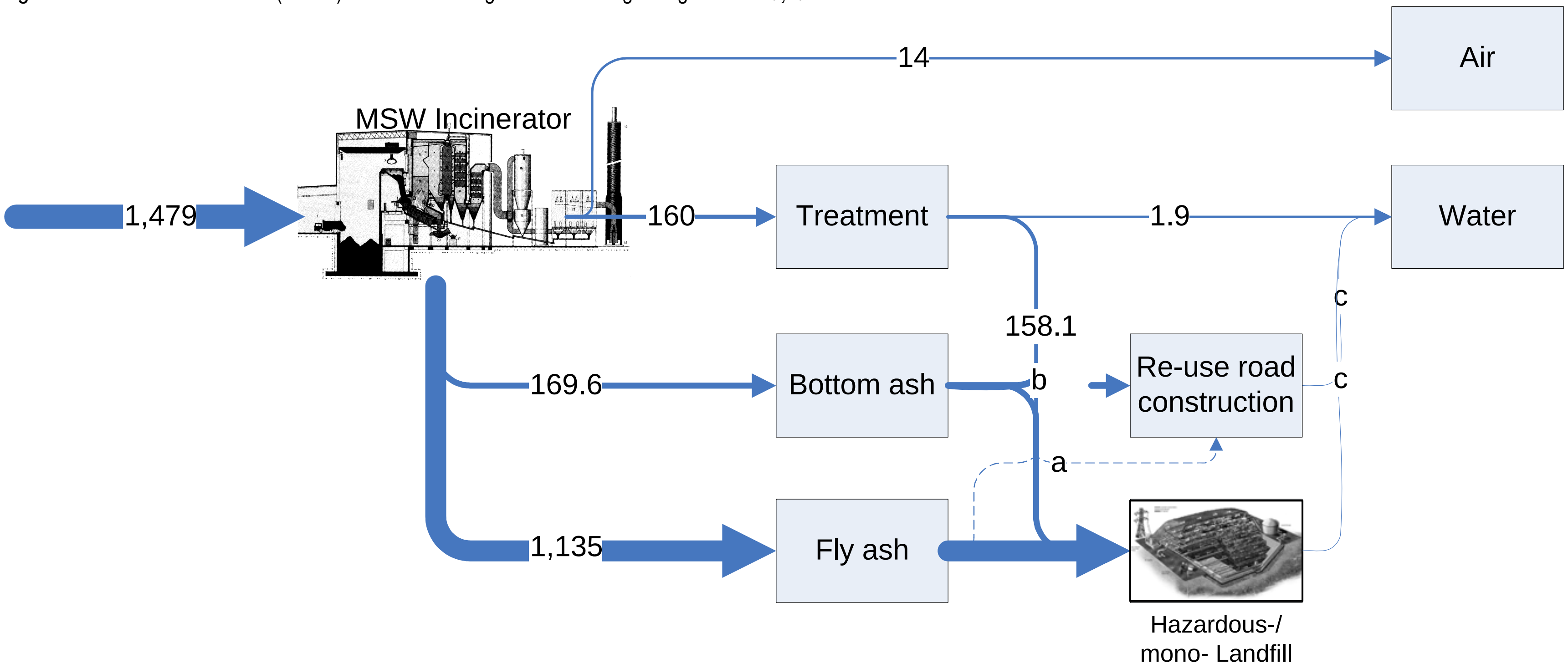
N.B. Shaded cells represent the current scenario.

From these results it can be concluded that the future cadmium content in fly ash and bottom ash is likely to double in the future under the 10% collection scenario (total Cd content in MSW: 24 g $tonne^{-1}$). In case the collection efficiency is 75% (total Cd content in MSW: 13.2 g $tonne^{-1}$) the cadmium content is expected to increase with 25%.

An overview of the future overall cadmium releases for a 100% incineration scenario to the different compartments due to incineration of MSW is summarised for the different scenarios in **Figures 3.6-3.7**.

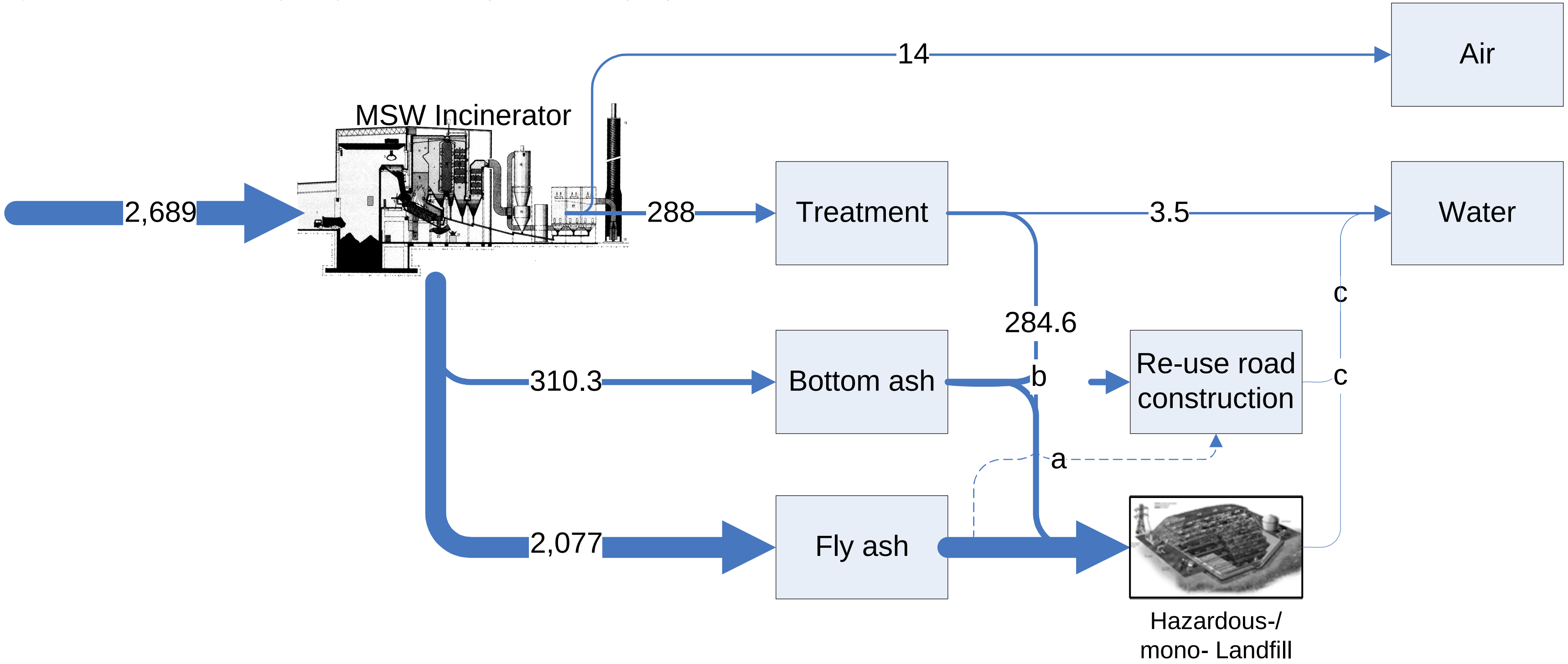
[35] These values are below the current EC limit of 0.05 mg L^{-1}(EC, 2000).

Figure 3.6 Overall cadmium flow (tonnes) due to incinerating MSW containing 13.2 g Cd/tonne $_{dry\ wt}$ -100% incineration with a 75% collection scenario



a) Most often fly ash is land-filled but some countries (The Netherlands, UK and Belgium) still re-use a part of their fly ash;
b) Depending on the leaching results bottom ash can either be land-filled or re-used in road construction;
c) The delayed water emissions of re-use in road constructions and hazardous landfills have not been quantified (c).

Figure 3.7 Overall cadmium flow (tonnes) due to incinerating MSW containing 24 g Cd/tonne $_{dry\ wt}$ -100% incineration with a 75% collection scenario



a) Most often fly ash is land-filled but some countries (The Netherlands, UK and Belgium) still re-use a part of their fly ash;
b) Depending on the leaching results bottom ash can either be land-filled or re-used in road construction;
c) The delayed water emissions of re-use in road constructions and hazardous landfills have not been quantified (c).

Allocation of future EU air and water emissions to the continental and regional scale

For the 100% incineration scenario the allocation from the EU scale to the regional scale is performed applying the 10% rule to the EU emission amount. A regional emission amount of 4,199 kg year^{-1} is calculated. Analogous to the air emission estimation, the EU emissions to surface water are allocated to the region using the 10% rule.

Table 3.39 Total annual amount of overall Cd emissions to air and surface water within the EU from incineration plants- Future scenarios

Scenario	Cd content MSW (g tonne^{-1})	Released amount Cadmium (kg year^{-1})	Continental (90%) (kg year^{-1})	Regional (10%)(kg year^{-1})
		Air		
100% inc. 75% coll.	13.2	14,018	12,616	1,402
100% inc. 10% coll.	24	14,018	12,616	1,402
		Surface water		
100% inc. 75% coll.	13.2	1,921	1,729	192
100% inc. 10% coll.	24	3,457	3,111	346
		Landfill		
100% inc. 75% coll.	13.2	1,462,997	1,316,697	146,300
100% inc. 10% coll.	24	2,671,499	2,404,349	240,435

The specific contribution of NiCd batteries for all waste streams of MSW incineration is given in **Table 3.40** and **Table 3.41**.

Table 3.40 Future contribution of NiCd batteries to the overall cadmium emissions due to incineration

Scenario	100% inc. (75% collection, 13.2 g cadmium/tonne MSW dry wt)	100% inc. (10% collection, 24 g Cd/tonne MSW dry wt.)
Allocation key (%)	32	63
Compartment	Direct emissions (kg year^{-1})	
Air	4,486	8,831
Water	615	2,178
Compartment	(kg)	
Cadmium going to landfill	468,159	1,683,044

Table 3.41 Contribution of NiCd batteries to the continental and regional cadmium emissions due to incineration

Scenario	Allocation key (%)	Released amount Cadmium (kg year^{-1})	Continental (90%) (kg year^{-1})	Regional (10%) (kg year^{-1})
		Air		
100% inc. 75% coll.	32	4,486	4,037	449
100% inc. 10% coll.	63	8,831	7,948	883
		Surface water		
100% inc. 75% coll.	32	615	554	62
100% inc. 10% coll.	63	2,178	1,960	218
		Landfill		
100% inc. 75% coll.	32	468,159	421,343	46,816
100% inc. 10% coll.	63	1,683,044	1,514,734	168,304

Overall cadmium emissions from land-filling MSW

Release of pollutants from a landfill can occur over an indefinite period. Hence, the daily or annual release may result in a very small PEC and does not reflect the long-term emissions of a landfill. For the moment no specific guidance is provided by the TGD on how to quantify the current and future landfill emissions**.** Due to the large uncertainties associated with this subject, the analysis that is performed in this report should merely be considered as a semi-quantitative approach.

Both regional and local emissions of land-filling have been addressed. Only for the local scenario the issue of dilution in time (long term emissions) has been analysed. The local emissions associated with land-filling MSW are given in this report for three separate time horizons beginning from waste placement:

- Short term time frame (20 years) corresponding roughly to the landfill's period of active decomposition.
- Intermediate term time frame (100 years) corresponding roughly to the life span of a given generation.
- Long term time frame (500 years) corresponding to an indefinite time reference where emissions of any given environmental flow have reached or nearly reached their theoretical yield.

Leachate generation

Emissions of landfills can occur primarily by generation of landfill gasses and leaching of contaminants. In the case of metals, emissions by generation of landfill gas are negligible in all cases except for Hg and possibly Cd (Baccini et al., 1987, Finnveden, 1996). However, in this document the pollution via leachate release is being considered as the most important long term flux impacting the environment since production of landfill gas lasts about one to two decades.

Leachate is generated as a result of the expulsion of liquid from the waste due to its own weight or compaction loading (termed primary leachate) and the percolation of water through a landfill (termed secondary leachate). The source of percolating water could be precipitation, irrigation, groundwater or leachate recirculated through the landfill.

Leachate quality

Current situation

In general, metals (specifically chromium, nickel, copper, zinc, cadmium, lead and mercury) are currently not present in high amounts in leachates from municipal landfills. Typical contaminant concentrations (µg L^{-1}) found in the interstitial water (leachate) of municipal solid waste landfills as collected by Assmuth (1992) are given in **Table 3.42**.

Table 3.42 Typical contaminant concentrations (µg L^{-1}) of municipal solid waste leachates

Substance	Mean	Maximum
Cd	< 0.5-3.4	5
Cr	4.9-14	39
Cu	1.5-30	90
Pb	4.9-19	800
Zn	23-60	90
Toluene	< 0.1-200	200
Dichloromethane	1.1-55	84
PCB compounds	< 0.05-0.71	0.71
Pentachlorophenol	0.05-5.3	13

An overview of reported cadmium concentrations in MSW leachates is given in **Table 3.43**.

Table 3.43 Overview of total cadmium concentrations (µg L^{-1}) in leachates of MSW landfills

N° of landfills	Type/origin	Min	Max	Mean	Percentiles	Reference
180	Germany: mainly old landfills with unknown solid content closed 15-20 years ago		1,330/173/136		P90 < 5	Eggenberger and Waber (2000)
71	Switzerland: closed within 10 years are still in use		100 µg L^{-1} (1 site)		P80 < 5	
	France, Italy and Japan				P75 < 3	
13	Finland: MSW and industrial landfills		5	0.5-3.4		Assmuth (1992)
21	UK: landfills with primarily domestic waste inputs	< 10	20	< 10		Robinson (1995)
Not reported	Sweden: active municipal landfills	< 0.5	2,700		P50 = 5	Seman (1986) cited in Flyhammer (1995)

Table 3.43 continued overleaf

Table 3.43 continued Overview of total cadmium concentrations (µg L^{-1}) in leachates of MSW landfills

N° of landfills	Type/origin	Min	Max	Mean	Percentiles	Reference
Not reported	Sweden: active municipal landfills	< 3	14		P50 < 3	Björklund (1989) cited in Flyhammer (1995)
Not reported	MSW and co-disposal landfills:					Hjelmar et al. (1994)
	France			< 10		
	Germany			6		
	The Netherlands			4		
	UK		up to 30 with co-disposal	< 10		
Not reported	MSW landfills	0.5	1,400	6		Ehrig (1990) cited in Dahm et al. (1994)
		0.7	525	37.5		Kruse et al. (1993) cited in Dahm et al. (1994)
1	Sweden:					Flyhammar et al. (1998)
	95 % MSW, 5 % sewage sludge					
	1 years			40		
	2 years			15		
	20-22 years			6		
71	Landfills (USA/France) with more than 75 % MSW. Recent sites (< 1 year) and older sites more than 20 years.				P50: 2.5-7	EREF (1999)
51 landfill total	Germany					Krümpelbeck (1999)
10 landf/30 measurement points	1-5 years	0.2	50	11		
16/55	6-10 years	0.2	192	5.8		
19/110	11-20 years	0.1	70	3.9		
6/21	21-30 years	0.2	18	2.8		

The data compiled by Eggenberger and Waber (2000) from 71 investigated landfills in Switzerland, Italy, Japan and France indicate that about 80% of the leachates have Cd concentrations below 5 µg $L^{-1}$and 75% below 3 µg L^{-1}. A similar distribution of Cd-concentrations in landfill leachates and contaminated ground water is obtained for old landfills (closed 15-25 years ago) in Germany. The results of 1,422 analyses from leachates of mainly old landfills (180) in Germany and more recent landfills (closed 10 years or still in use) in Switzerland and some data from France, Italy and Japan, revealed that roughly 90% of the investigated leachates Cd-concentrations is below 5 µg L^{-1}. It has to be mentioned that the Cd background concentrations as measured in uncontaminated shallow groundwater are very low, being generally below 1 µg L^{-1}. Flyhammer (1995) reported different cadmium concentrations in leachates from landfills in different countries and suggested to use 5 µg Cd/L as an average concentration in leachate from landfills (active and closed landfills) in Nordic countries. Similar values were reported in the Netherlands, Finland, US and France (see **Table 3.40**). Overall there seems to be a decreasing trend of the cadmium concentration in the leachate with the age of the landfill (Krümpelbeck, 1999, Flyhammar et al., 1998).

The measured concentration value represents the cadmium leached out from all cadmium sources present in the MSW. Since data on leachability of cadmium in MSW compounds is limited it is very difficult to assess the contribution of the NiCd batteries to this value. Only a few leaching tests have been conducted with NiCd batteries. These tests conducted under both aerobic and anaerobic conditions at a temperature of 50°C for 100 days showed corrosion around the positive terminal. Analysis of the leachate revealed total concentrations less than 0.01 mg L^{-1}. Field studies where NiCd batteries were deposited in a municipal landfill for seven months showed similar signs of corrosion at the positive terminal but less than had been produced in the anaerobic leachate test (Bromley et al., 1983). Similar observations were obtained in another study on the degradation of NiCd batteries under domestic waste landfill conditions (Jones et al., 1977). Long-term burial tests (not under landfill simulating conditions) with NiCd batteries have shown that after 13 years no exposure of the battery interior components had yet occurred. Only the exterior of the battery did show signs of corrosion (Oda, 1993). From the studies indicated above it is not possible to draw a general conclusion on when the interior of a NiCd battery will be exposed. According to Bromley et al. (1983) this is not expected to occur between 1 and 5 years after deposition. Data on the leaching after exposure of the interior have not been found.

In this report the current overall cadmium concentration, most representatives for the average situation, in an MSW landfill leachate is considered to be 5 µg $L^{-1}$and this value was used to perform the regional calculation. In the risk characterisation next to a local scenario with a leachate concentration of 5 µg L^{-1}an additional scenario have been developed based on an assumed cadmium leachate concentration of 50 µg L^{-1}(see future changes in leachate quality).

Furthermore it is assumed in this report that each waste component has the same likelihood of leaching out one gram of cadmium (e.g. one gram of cadmium in a certain amount of paper was assumed to have the same likelihood of leaching out as one gram of cadmium in NiCd batteries).

As a result the emissions due to NiCd batteries can be estimated to be 0.5-2.5 µg L^{-1}(based on the finding that 10-50% of the overall cadmium content in MSW is due to NiCd batteries).

Future changes in leachate quality

The impact of increasing cadmium content in the MSW on the composition of the leachate cannot be predicted on the basis of current knowledge since there is no direct relationship between the total content of Cd and the leachability of Cd. A 10% increase in total content of Cd in the MSW land-filled will not necessarily lead to a 10% increase in the leached amount of Cd. The leachability will depend on the chemical nature of the cadmium and the leaching conditions.

In this report the cadmium concentration in the leachate originating from a fixed amount of cadmium being land-filled is assumed to be constant over time**.** The question arises whether or not it is reasonable to assume one constant leachate concentration since the conditions in landfills are changing during the different degradation phases in a landfill. For metals the critical phase in the short term of a landfill is the acid anaerobic phase where the pH will drop due to the decomposition of the easily degradable material. Few studies have attempted to characterise leachates as being acetogenic or methanogenic (Ehrig, 1983 and Robinson and Gronnow, 1993 in Finnveden 1996). From these studies it can be concluded that the constant concentration assumption for the time period surveyed is reasonable for the metal cadmium. However, it is acknowledged that landfills have not yet reached their final development stage and as a result it is unclear what may happen after 100 year. Considering the geochemical evolution of waste deposits towards more oxidising and more acidic conditions with time, at first higher emissions could be expected in the future (Eggenberger and Waber, 2000). However, according to simulation work by Belevi and Baccini (1989), it is more plausible that alkaline conditions will be maintained for 2,000 years and that hence higher remobilisation rate of some metals due to lower pH is not expected at least for many centuries (Bozkurt et al., 2000). The effect of varying redox potentials and the effect of acid rain on the chemical equilibrium of a waste body were investigated by Gade et al. (1998). The results showed that severe mobilisation is not expected and a long term entrance of acid rain is not expected to exhaust the carbonate buffer before 400,000 years. And even if the carbonate buffer would be exhausted there will be still another buffer (silicates) effective.

Overall the cadmium concentration in the leachate seems to decrease with the age of the landfill (Krümpelbeck, 1999, Flyhammar et al., 1998). According to Gade et al. (1997, 1998, 1999, 2000), who investigated the behaviour of two Bavarian hazardous waste landfills with regard to their mineralogy, secondarily newly formed minerals (carbonates, phosphates, sulfates) reduced the mobility of the metals present in the waste. Under anaerobic conditions metals that form sulfides (e.g. cadmium, copper, zinc, nickel and lead) will tend to be immobilised as sulfides. In the long run when landfills develop aerobic conditions additional solubility limiting phases including carbonates and hydroxides will retard metal mobility in the future.

Johnson et al. (1999) suggested that $CdCO_3$ (otavite) precipitation is important for cadmium. Recent modelling work (Ross et al., 2000) on the retention and speciation of heavy metals (cadmium, chromium and zinc) in both immature and mature post methanogenic leachates indeed indicated that carbonate precipitation is likely the solubility limiting phase for cadmium. According to the performed geochemical modelling on mature waste, carbonate precipitation is likely to prevent cadmium concentrations rising from 60 to 90 µg L^{-1}. The laboratory results indicated, however, that for the aerobic columns, cadmium concentrations generally remained below 10 µg L^{-1} suggesting that the retention mechanism is probably not precipitation alone. Similar observations were observed by Gade et al. (1999) who predict a maximum cadmium concentration of 81 µg L^{-1}but observed a measured concentration of one order of magnitude lower i.e. 7.8 µg L^{-1}suggesting that other mechanisms such as adsorption phenomena are also limiting cadmium release.

In order to assess possible impact on the environment from possible higher cadmium concentrations in the future the risks will be quantified in the sensitivity analysis (see subsection “Sensitivity analysis” under Section 3.1.2.2.5) for an arbitrary chosen leachate concentration (i.e. 50 µg L^{-1}which is close to the solubility limit for cadmium carbonate). The leachate concentration of 50 µg L^{-1}can be considered as a conservative/worst case leachate concentration because in this case we are assuming that aerobic precipitation is the only metal retention mechanisms.

Leachate quantity

Leachate production is highly dependent on the landfill design and local climatic conditions. Precipitation represents the largest single contribution to the production of leachate. There is some variation in the potential generation of leachate within the EU because precipitation and evapotranspiration depends on geographical location. In Mediterranean areas (Greece, Spain and Italy) leachate generation is the smallest during summer season and leachate generation occurs principally during the colder, wet season (i.e. from October to April). For example an annual leachate production, expressed as height of water of 40-80 mm/year has been calculated for a landfill site near Athens (Greece, rainfall: 387 mm/y, Kouzeli-Katsiri et al., 1993). In a landfill site near Madrid (Gössele, 1993) the leachate production was calculated to be 7 mm/year and in a landfill near Pavia (Italy, Baldi et al., 1993) it was 82 mm/year. Leachate quantities tend to be higher in the North of the EU than the South. In Sweden an average leachate volume of 250-300 mm/year is reported during operation (Nilsson, 1993). In Denmark similar figures have been reported: 320-400 mm during operation and 56-89 mm/year (Hjelmar, 1988-1989). But equally large variations can be found from East to West and over relatively short distances within Member States (Hjelmar et al., 1994). Reported leachate volumes vary from 25 m^3 to 3,000 m^3 per hectare (Flyhammer, 1995, Qiang et al., 2002).

The results of various empirical studies are indicating that the average percentage of precipitation that results in leachate production depends on the age of the landfill and is largely controlled by the presence and type of cover. In general it has been noted that the amount of leachate produced is between 15 and 50% of the respective rainfall, depending mainly on the final landfill cover type and the manner of waste compaction (Canziani and Cossu, 1989). As an average to realistic worst-case scenario in this report the water balances has been calculated for a relatively high precipitation rate (800 mm/year) for different scenarios representative for common nowadays (or modern) landfill practices.

Scenario development

The EU directive on the landfill of waste (1999/31/EC) indicates that appropriate measures shall be taken, with respect to the characteristics of the landfill and the meteorological condition in order to:

- control water from precipitation to enter the landfill;
- to collect contaminated water and leachate
- and to treat contaminated water and leachate collected from the landfill to the appropriate standard required for their discharge.

It is further stated that protection of groundwater has to be achieved by the combination of a geological barrier and a bottom liner during the operational/active phase and by the combination of a geological barrier and a top liner during the passive post closure phase. For non hazardous landfills it is therefore required to have a leachate collection and bottom sealing (consisting of an artificial sealing liner and drainage liner > 0.5 m in addition to a geological barrier (> 0.5 m). If the prevention of leachate formation is necessary a surface sealing can be applied. The requirements for a top cover are at least a topsoil cover (> 1m) and a drainage layer (> 0.5m).

Although in the future all landfills will have to meet the requirements of the new EU landfill directive it is acknowledged that at the moment different landfill practices exist. Therefore the leachate generation simulations have been conducted in this report for 4 different sets of conditions representative for different landfill practices and the consecutive life stages of a landfill.

Set 1: corresponds with a landfill with no top cover

Set 2: corresponds with a landfill with daily top cover

Set 3: corresponds with a landfill with an intermediate top cover

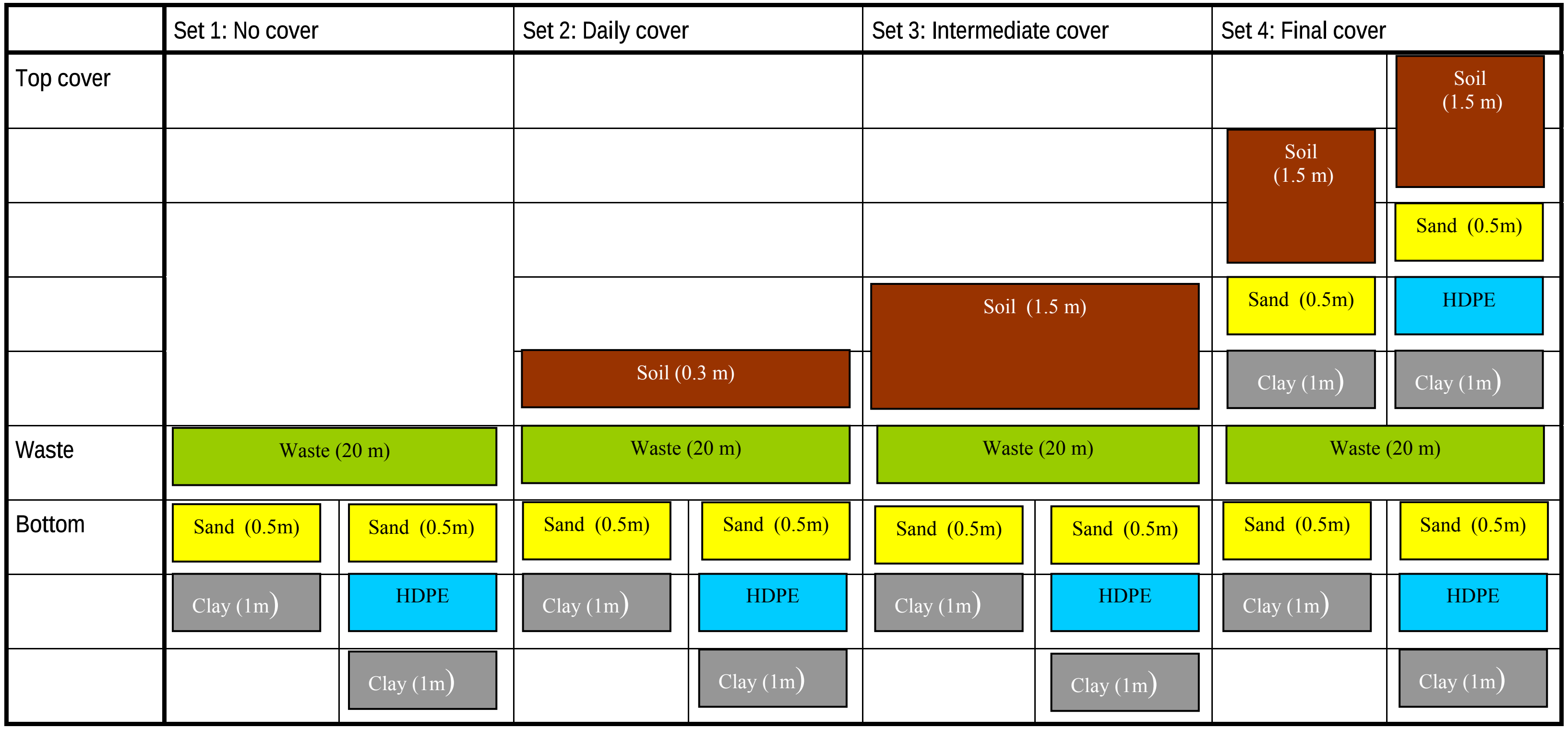
Set 4: corresponds with a landfill with a final top cover

In addition two sub-scenarios have been added in which the composition of the bottom liner or top liner has been changed:

- In this report both a single compacted clay liner as a single composite liner system are considered as a bottom liner. Proper functioning of a bottom liner system is critical to the containment effectiveness of a landfill. During the past few decades the trend has been to use composite liner systems comprising both clay and synthetic geomembranes together with interspersed drainage layers.
- For a final cap or cover system the following systems are considered in this report: 1) a cover system consisting of a top soil, drainage layer and a single compacted clay liner, 2) a cover system consisting of a top soil, drainage layer and a single composite clay line. The main purpose of a landfill final cover is to minimise water infiltration into the landfill to reduce the amount of leachate generated after closure.

An overview of the different landfill profiles considered in this report is given in **Figure 3.8**. The thickness of the layers and final cover materials are in agreement with the new landfill directive and are representative for common landfill practice.

Figure 3.8 Landfill profile structure for different landfill designs



Water balance

The most common way to calculate the amount of leachate is a simple water balance. In a water balance the amount of leachate is calculated as being the amount of precipitation minus the surface run-off, evapotranspiration, change in soil cover and waste moisture content.

$$L = P - R/O - ET - \Delta ST - \Delta SWST$$

L = Leachate quantity
P = Precipitation
R/O = run off
ΔST = change in soil moisture content
ET = Evapotranspiration
ΔSWST = change in solid waste moisture content

In this report the leachate production has been addressed with the theoretical landfill leachate model HELP (Hydrologic Evaluation of Landfill Production, US-EPA, Schroeder et al., 1994a and b). The HELP model is a sophisticated version of the water balance method and is used all over the world to predict leachate generation. The configuration of the model allows handling any type of cover, liner and can even address leakage.

In order to perform the model calculations a generic landfill has been defined. At the moment an average representative European standard landfill is hard to define. Since future landfills are assumed to be reasonably large a landfill of 20 hectares have been chosen for the generic reasonable worst case (large surface area hence more leachate production) local scenario. An overview of the main input data used in the modelling is given in **Table 3.44**. Default values chosen were based on values most commonly cited in literature (Kjeldsen and Christensen, 2001; Nielsen and Hausschild, 1998; Nielsen et al., 1998; EREF, 1999; Schroeder et al., 1994; Hjelmar et al., 1994; etc.).

Table 3.44 Default values used for the generic landfill

Parameter	Unit	Value
Surface of the landfill	m^2	200,000
Total depth of MSW land-filled	m	10-20
Bulk density of MSW		0.6
Volumetric water content in MSW		0.3
Field capacity MSW	%	29.2
Wilting point MSW	%	7.7
Duration of operation phase	Year	15
Duration of post closure phase	Year	30
Moderately compacted clay cover	m	1
Drainage layer (sand)	m	0.5
Slope drainage layer	%	1
Top cover (sandy loam)	m	0.3 (daily cover) 1.5 (final cover)
Slope top cover	%	1[a]

Table 3.44 continued overleaf

Table 3.44 continued Default values used for the generic landfill

Parameter	Unit	Value
HDPE liner	m	0.01
Precipitation	m/year	0.8 (i.e. 0.799)[b]

a) The choice was made to represent a reasonable worst case situation (OVAM, pers. com., 2002);
b) Calculated default value.

The HELP model was run for the 4 different sets of data and for one landfill location. As location for the landfill the Netherlands was chosen. The HELP model generated the weather and climatic data over a simulation period of 100 years. This resulted in an average annual precipitation of 0.799 m/year for the Netherlands and is used as a default average to realistic worst case scenario with regard to the amount of leachate generated for the different landfill scenarios. Mediterranean countries will have lower leachate volumes. Scandinavian countries will have similar leachate volumes as in the Netherlands.

During the operation phase the landfill cells are relatively flat. Therefore the area subjected to runoff was set to zero. Runoff was only taken into account when the final top cover was in place. In the cases where runoff is ignored any precipitation will result in more leachate resulting in a maximum leachate generation during landfill operations.

Tables 3.45-48 show the average annual results of the HELP model for a generic landfill taking into account the different landfill stages.

Table 3.45 Annual leachate generation for a landfill with no top cover and a bottom liner consisting of a single compacted clay liner or a single composite liner

	Scenario 1 : No top cover			
	Bottom liner: single compacted clay		Bottom liner: composite liner	
Parameter	m^3/ha/year	%	m^3/ha/year	%
Precipitation	7,999	100	7,999	100
Run-off	0	0	0	0
Evapotranspiration	5,645	70.6	5,645	70.6
Change in water storage	- 3.9	0.05	262	3.3
Leachate collected from drainage layer	119	1,5	2,024	25
Fugitive leachate	2,239	28	68	0.8

Table 3.46 Annual leachate generation for a landfill with a daily cover and a bottom liner consisting of a single compacted clay liner or a single composite liner

	Scenario 2: Daily cover			
	Bottom liner: single compacted clay		Bottom liner: composite liner	
Parameter	m^3/ha/year	%	m^3/ha/year	%
Precipitation	7,999	100	7,999	100
Run-off	0	0	0	0
Evapotranspiration	5,454	68.2	5,454	68.2
Change in water storage	- 3	0.03	300	3.5
Leachate collected from drainage layer	143	1.8	2,193	27.4
Fugitive leachate	2,406	30.1	73	0.9

Table 3.47 Annual leachate generation for a landfill with an intermediate cover and a bottom liner consisting of a single compacted clay liner or a single composite liner

	Scenario 3: Intermediate cover			
	Bottom liner: single compacted clay		Bottom liner: composite liner	
Parameter	m^3/ha/year	%	m^3/ha/year	%
Precipitation	7,999	100	7,999	100
Run-off	0	0	0	0
Evapotranspiration	5,454	68.2	5,454	68.2
Change in water storage	2	0.03	284	3.5
Leachate collected from drainage layer	136	1.7	2,189	27.4
Fugitive leachate	2,412	30.1	73	0.9

Table 3.48 Annual leachate generation for a landfill with a final cover (with or without a composite liner) and a bottom liner consisting of a single compacted clay liner or a single composite liner

	Scenario 4: Final cover			
	Final top cover: top soil , sand, composite liner			
	Bottom liner: single compacted clay		Bottom liner: composite liner	
Parameter	m^3/ha.y	%	m^3/ha.y	%
Precipitation	7,999	100	7,999	100
Run-off	1,850	23.1	1,850	23.1
Evapotranspiration	6,101	76.3	6,101	76.3
Change in water storage	31	0.4	32	0.4
Leachate collected from drainage layer	0.4	0.005	15.3	0.2
Fugitive leachate	16	0.2	0.25	0.003

Table 3.48 continued overleaf

Table 3.48 continued Annual leachate generation for a landfill with a final cover (with or without a composite liner) and a bottom liner consisting of a single compacted clay liner or a single composite liner

	Scenario 4: Final cover			
	Final top cover: top soil, sand, single compacted clay liner			
	Bottom liner: single compacted clay		Bottom liner: composite liner	
Parameter	m^3/ha.y	%	m^3/ha.y	%
Precipitation	7,999	100	7,999	100
Run-off	39	0.5	39	0.5
Evapotranspiration	5,454	68.2	5,454	68.2
Change in water storage	3.5	0.04	288	3.6
Leachate collected from drainage layer	105	1,3	2,148	26.8
Fugitive leachate	2,398	30	71	0.9

The amount of leachate generated is the highest during the filling/operational phase (no cover, daily cover and intermediate cover) of the landfill and mounts up to 31.8% (= 2,545 m^3/ha/year = precipitation - evapotranspiration - run-off from **Table 3.46** and **Table 3.47**) of the initial precipitation (7,999 m^3/ha/year). The use of a final cover with composite liner reduces the total amount of leachate significantly to 0.2% (= 16 m^3/ha/year). In the absence of a composite liner in either the top or bottom barrier the amount of leachate produced is still substantial (2,506 m^3/ha/year see **Table 3.48** = 7,999 -39 - 5,454). From the results presented above it is clear that the net release of leachate into the environment (i.e. fugitive leachate) is dependent on the presence and efficiency of a leachate collection system and subsequent treatment. In case the final cover and the bottom layer only consists of a single compacted clay liner 2,398 m^3/ha/year of fugitive leachate is produced (96% of the total volume leachate = 2,506 m^3 produced). In case only the final top cover consists of a composite liner only approximately 0.6% (16 m^3/ha) of the total volume leachate generated results in fugitive leachate. In the ideal case where both the bottom barrier and the top cover are comprised of a composite liner only 0.25 m^3/ha/year of fugitive leachate is produced which is negligible.

In order to cover all landfill types two landfill profiles are further considered in the local assessment:

- Landfill profile 1: landfill with bottom liner and final top layer consisting of a single compacted clay liner;
- Landfill profile 2: landfill with bottom liner and final top liner consisting of a single composite liner.

For the latter Scenario, the ageing of the geomembrane have been taken into account. It is assumed that the geomembrane will remain effective during the operational and post closure phase (= 45 years in total). While the top cover can be renewed, the renewal of the bottom liner is less feasible. Therefore it is assumed that after 45 years the bottom liner will only consist of a single compacted clay liner.

Taking into account the leachate volumes of the consecutive life stages of a landfill (see Section on leachate generation), the cumulated leachate volume expressed as m^3 per ha for the different time horizons (20, 100 and 500 years) can be calculated (see **Table 3.49**). For the time period of 0-2 years after waste placement, the landfill cells are assumed to have no cover or to be covered with a daily top cover. From years 2-5 years after waste placement cells are covered with an intermediate top cover. From years 5-15 after waste placement the cells are for 40% covered with a final top cover. After year 15 the landfill is assumed to be completely covered with a final top cover.

Table 3.49 Amount of leachate generated per ha of landfill over time

Time since waste placement (years)	Cumulative leachate generation (m^3/ha)			
	Landfill profile 1		Landfill profile 2	
Leachate	Collected	Fugitive	Collected	Fugitive
20	2,426	47,747	23,900	791
100	4,001	239,607	24,129	1,697
500	/	1,198,907	/	8,263

The collection of the landfill leachate is assumed to proceed throughout the active period of the landfill's operating life and is extended after the closure of a landfill for another 30 years (if a significant quantity of leachate is still being produced that contains high concentrations of contaminants).

The highest volume of leachate collected is in the operational phases of the landfill and decreases with time. For a generic landfill of 20 ha with a composite bottom liner and no top cover (see **Table 3.45**) 111 m^3/day (= (2,024 m^3/ha/year · 20 ha)/365 day.) is collected and has to be treated. If the leachate collection volume is averaged over 20 year and taking into account the different life stages of a landfill approximately 65 m^3/day is collected.

For this report the value of 100 m^3/day is taken forward in the local exposure calculations (see Section 3.1.3.2) as being representative for the amount of leachate collected per day for a generic landfill of 20 hectare. This figure is in the min-max range from the figures in literature: 5-650 m^3/day (Robinson et al., 1995) for landfills of different landfill surface areas.

The cadmium emissions (see **Table 3.50**), before treatment, were then calculated for the generic local landfill with a surface area of 20 hectares and assuming a current leachate concentration of 5 µg L^{-1}.

Table 3.50 Local cadmium emissions to water (in kg) for the generic local landfill (surface area of 20 ha)

	Leachate concentration = 5 µg L^{-1}			
Time since waste placement (years)	Cumulative cadmium emission (kg)			
	Landfill profile 1		Landfill profile 2	
Leachate	Collected[a]	Fugitive	Collected[a]	Fugitive
20	0.2	4.8	2.4	0.1
100	0.4	24.0	2.4	0.2
500	/	120	/	0.8

a) Before treatment.

From **Table 3.50** it is clear that the amount of cadmium released in the future[36] from a landfill is limited. The current generic landfill will contain at the end 1,200-2,400 ktonnes ($_{\text{wet wt.}}$) of MSW

[36] up to 500 year and under the assumption that the leachate concentration keeps constant during this time frame

(= 840-1,680 ktonnes $_{dry\ wt.}$) over and if we assume a 15 year filling period (80-160 ktonnes MSW/year). With a total cadmium content of 10 g tonne^{-1} $_{dry\ wt.}$ and emission factors (kg Cd emitted/kg Cd land-filled) between 1.5 10^{-3} (24.4 kg/16,800 kg) and 1.5 10^{-4} (2.6 kg/16,800 kg) can be calculated in case the landfill contains 2,400 ktonnes MSW. In comparison Finnveden (1996) reported an emission factor of 5.0 10^{-4} for a time survey period of 100 years. This indicates that the largest part of the land-filled cadmium (99.85-99.98%) remains in the landfill. If 24.4 kg Cd is released over a period of 100 year this means that on average 0.24 kg is released yearly which is a release rate of 0.001% per year. If only a landfill height of 10 m. is assumed (1,200 ktonnes MSW) the release factor is 0.0028%. Ehrig (1989) suggested a similar release rate of 0.002% per year.

Baccini et al. (1987) reported that more than 99.9% of the metals are still found in the residual solids at the end of the intensive reactor phase. It has, however, been suggested that metal concentrations in landfill leachate may rise again (Eggenberger and Waber, 2000). The environmental impact after a hypothetical infinite time period has not been addressed in this report since our knowledge on this issue is insufficient.

Regional emissions of land-filling MSW

The regional emissions of cadmium per year from MSW landfills in the EU can be calculated with the following formula.

Cadmium flux (kg year^{-1}) = Landfill surface (ha) · leachate generation (m^3/ha/year) · cadmium concentration in the leachate (5.10^{-6} kg/L)

In this report a concentration of 5 µg Cd/L is taken as a representative value for the average situation in MSW landfill leachate. In the previous section (local emissions landfill) a maximum leachate volume of 2,500m^3/ha/year was calculated for an average rainfall of 7,999 m^3/ha/year. The only unknown in the equation is the total surface area of the landfills. Reported landfill areas range between < 1 ha to > 10 ha while new established landfills are assumed to be reasonably large (average 20 ha, Hjelmar et al., 1994). However, almost no reliable data on the total number of MSW landfills or their landfill surface were found for most of the Member States. The values that have been reported for operational landfills for some countries are listed in **Table 3.51**. The cadmium flux has been calculated with the equation described above.

Table 3.51 Cadmium fluxes (kg year^{-1}) of operational MSW landfills for some countries

Country[a]	MSW land-filled (ktonnes)	Number of land-fills	ktonne MSW.y per landfill	Average surface area /landfill (ha)	Total surface area (ha)	Calculated cadmium flux (kg/y)	Reference
Finland	1,610	/	/	9.3	/	/	Assmuth (1992)
Sweden	1,300	270-280	4.8	10	2,800	42	Flyhammar (1995) and RVF (2002)
UK	26,860	764 + 796	17.2	18.9 9.1	14,482 + 7,300	181 + 91	Mc. Mellin (2002)
Germany	16,000	376	42.5	10[a]	3,760	235	UBA (2001)
The Netherlands	1,136	39	29	30.7	1,198	14.9	VVAV (2000)
Average			23.4	14.7			

a) Very rough approximation on the average landfill area.

The calculated cadmium fluxes range between 14.9 (The Netherlands) and 272 kg $year^{-1}$ (UK sum). As stated in the previous sections these fluxes are directly related to the landfill surface area and the yearly precipitation. Since the total landfill surface area for most of the Member States is unknown an indirect approach had to be developed in order to assess the overall cadmium emissions for these countries. Based on the information in **Table 3.51** an average landfill surface of 14.7 ha can be calculated. Furthermore approximately 23.4 ktonnes MSW ($_{\text{wet wt.}}$) is land-filled per landfill each year[37] based on an average of the data from Sweden, UK, Germany and the Netherlands. The latter information can be used to translate the amount of MSW land-filled (ktonnes) in each year per country (presented in **Table 3.21**) into a number of landfills. Assuming that each landfill has a surface area of 14.7 ha the total landfill surface can be calculated. Finally the cadmium flux is calculated with the equation mentioned above.

As an example the emission for France is calculated as follows:

Amount land-filled each year = 23,352 ktonnes $_{\text{wet wt.}}$
Number of landfills = 23,352/23.4 = 998
Total landfill surface = 998 · 14.7 ha = 14,671 ha

Total cadmium flux (kg $year^{-1}$) = 14,671 ha · 2,500 m^3/ha.y · 5.10^{-6}.kg/L = 183 kg $year^{-1}$

The generated flux (leachate) may either be discharged to an off-site municipal sewage plant, discharged directly to surface water or enter into the groundwater compartment. Collection and discharge to a Sewage Treatment Plant (STP) is by far the most common discharge route for leachates from municipal waste landfills. A smaller proportion of leachate is discharged directly to surface waters. The latter is only allowed if the leachate quality fulfils certain requirements (sometimes pre-treatment, e.g. aerated lagoons, is needed). Most often this quality is governed by the presence of increased levels of BOD, COD and ammonium (see **Table 3.52**).

Table 3.52 Detailed analysis of leachate sample taken at Chapel Farm landfill, Swindon, Wiltshire, 1990-1991 (Robinson, 1995)

Parameter	Concentration (mg L^{-1})
COD	850-10,600
BOD_5	239-4,100
Ammoniacal-N	283-531
Chloride	834-4,670
Cd	< 0.01-0.02

Metals have been regarded only as a minor problem in the waste management of leachates and only rarely posed a significant problem in leachates from domestic waste landfills (Robinson, 1995). Discharge criteria to surface water vary from one Member State to another. Landfill effluent requirements for cadmium as prescribed in the legislation of different European countries and reported by Doedens and Theilen (1992) vary between 2-5 µg L^{-1} (The Netherlands) to 100 µg L^{-1} (Germany, Austria, Switzerland). The highest proportion of

[37] This value is much smaller than the calculated amount of MSW landfille each year for the local generic landfill scenario, i.e. 80-160 ktonne $_{\text{wet wt.}}$ MSW/year). However, the driving parameter is the surface area. For the generic local landfill a surface area of 20 ha has been assumed which is in within the same order of magnitude as the average landfill surface area of 14.7 hectare based on reported values.

landfills discharging directly to surface water is 23% (Germany) with less than 10% in other Member States (Hjelmar et al., 1994).

Permitted discharge to groundwater is uncommon for modern MSW landfills but may occur by old landfills or in the framework of an engineered leachate attenuation-site (Robinson, 1995).

Since the number of sites designed with bottom liners and on-site leachate treatment plants is currently increasing it is proposed to use the following regional allocation key for assessing the current emissions of landfills operational to date:

- 10% direct discharge to groundwater (attenuation/dilution-sites)
- 10% direct discharge to surface water (sometimes an on-site pre-treatment step is included)
- 80% collected and discharged via public sewer systems or transported via tankers to a STP. In a STP an overall cadmium removal efficiency of 60% is assumed (CBS, 2002)[38].

It should be clear that a direct discharge to groundwater or surface water is only possible when the leachate quality is considered suitable. Since for our regional assessment we are working with a cadmium leachate concentration of 5 µg L^{-1} this is of suitable quality since according to some legislation we can discharge from 2-5 up to 100 µg L^{-1}. Therefore the scenario of direct discharge to surface water is included. If the quality is insufficient a form of pre-treatment is needed

The above regional scenario was validated with the data presented in the extensive report of Robinson (1995). The semi-quantitative and qualitative information on leachate management in the EU reported on a country by country basis also gives support to the aforementioned allocation key (EC Report, 1994). Some further more recent information was received from MSs during the risk assessment process (UBA, 2002; UK, 2002).

An overview of the overall cadmium emissions to groundwater/surface water and sludge (in kg $year^{-1}$) in Europe due to land-filling of MSW is presented in **Table 3.53** and **Table 3.54**. The overall cadmium flux was calculated with the methodology described in previous paragraphs.

[38] Although it could be questioned that the removal rate of 60% is also applicable to effluents with low cadmium concentrations (µg L^{-1}range) the removal percentage of 60% is deemed appropriate since the landfill leachate is not the only cadmium source in the STP resulting in overall higher cadmium concentrations in the final STP influent. At local scale, the landfill on-site STP needs in general further tertiary 'polishing' water treatment techniques to reduce cadmium concentrations below 5 µg L^{-1}(see Baeyens, pers. com., 2003; Verstraete, pers. com., 2003) and this does not seem (yet) a standard practice in landfill management to date (EC Report, 1994; UK, com. 2002; RDCHW, 2002).

Table 3.53 Overall cadmium emissions to groundwater/surface water and sludge (in kg year^{-1}) in Europe due to land-filling of MSW (operational landfills only). Current scenario: 75.6% land-filling

Country	MSW land-filled (ktonnes $_{wet\ wt.}$)	Total cadmium flux (kg/y)	Fugitive emissions to surface water (kg year^{-1})	Fugitive emissions to groundwater (kg year^{-1})	Collected leachate	
Allocation key			10%	10%	80%	
					Emissions to surface water (kg year^{-1}) after treatment	Sludge (kg/y)
					40%	60%
Austria	1,099	9	1	1	3	4
Belgium	1,473	12	1	1	4	6
Denmark	361	3	0.3	0.3	1	1
Finland	1,610	13	1	1	4	6
France	23,352	183	18	18	59	88
Germany	16,000	*235*	24	24	75	113
Greece	3,561	28	3	3	9	13
Ireland	1,432	11	1	1	4	5
Italy	20,768	163	16	16	52	78
Luxembourg	62	0.5	0.05	0.05	0.2	0.2
The Netherlands	1,136	*15*	1	1	5	7
Norway	1,843	14	1	1	5	7
Portugal	2,603	20	2	2	7	10
Spain	17,477	137	14	14	44	66
Sweden	1,300	*42*	4	4	13	20
UK	26,860	*272*	27	27	87	131
Total EU-16	120,937	1,158	116	116	371	556

The total amount of MSW being land-filled in 1995-2001 for the EU-16 was 120,937 ktonnes $_{wet\ wt.}$ (84,656 ktonnes $_{dry\ wt.}$) on yearly basis corresponding with an overall EU land-filling share of 75.6% (see subsection "Waste management strategies in Europe" under Section 3.1.2.2.5). A total yearly cadmium flux of 1,158 kg has been calculated. Based on the calculations above the cadmium emission to the groundwater compartment due to land-filling MSW is 116 kg Cd/year. An additional 487 kg is emitted to surface water and 556 kg of cadmium can be found in the sludge.

Similar to the section on local emissions of land-filling the release rate (%) per year can be calculated. If it is assumed that the landfills have a 15-year filling period then 1,269,838 ktonnes MSW ($_{dry\ wt.}$) have been land-filled. With a total cadmium content of 10 g tonne^{-1} $_{dry\ wt.}$ a total of 12,698,380 kg of cadmium is present. If 1,158 kg Cd is released per year a release rate of approximately 0.01% per year is calculated.

Table 3.54 Overall cadmium emissions to groundwater/surface water and sludge (in kg year^{-1}) in Europe due to land-filling of MSW (operational landfills only). Scenario: 100% land-filling

Country	MSW land-filled (ktonnes $_{wet\ wt.}$)	Total cadmium flux (kg/y)	Fugitive emissions to surface water (kg year^{-1})	Fugitive emissions to groundwater (kg year^{-1})	Collected leachate	
Allocation key			10%	10%	80%	
					Emissions to surface water (kg year^{-1}) after treatment	Sludge (kg/y)
					40%	60%
Austria	1,578	12	1	1	4	6
Belgium	2,842	22	2	2	7	11
Denmark	2,091	16	2	2	5	8
Finland	1,690	13	1	1	4	6
France	34,133	268	27	27	86	129
Germany	28,000	220	22	22	70	106
Greece	3,561	28	3	3	9	13
Ireland	1,432	11	1	1	4	5
Italy	22,717	178	18	18	57	86
Luxembourg	185	1	0.1	0.1	0.5	1
The Netherlands	4,995	39	4	4	13	19
Norway	2,217	17	2	2	6	8
Portugal	3,663	29	3	3	9	14
Spain	18,804	148	15	15	47	71
Sweden	2,700	21	2	2	7	10
UK	29,450	231	23	23	74	111
Total EU-16	160,058	1,257	126	126	402	603

Based on the calculations above the cadmium emission in a 100% land-filling scenario would result in an emission to the groundwater compartment of 126 kg Cd/year. An additional 528 kg is emitted to surface water and 603 kg of cadmium can be found in the sludge.

The allocation of the total EU landfill emissions to the regional scale has been performed with the 10% rule (see **Table 3.55**).

Table 3.55 Total annual amount of Cd emissions to groundwater/surface water and sludge within the EU from land-filling MSW

Scenario	Released amount Cadmium (kg year^{-1})	Continental (90%) (kg year^{-1})	Regional (10%) (kg year^{-1})
	Surface water		
75.6% land-filling	487	438	49
100% land-filling	528	475	53

Table 3.55 continued overleaf

Table 3.55 continued Total annual amount of Cd emissions to groundwater/surface water and sludge within the EU from land-filling MSW

Scenario	Released amount Cadmium (kg year^{-1})	Continental (90%) (kg year^{-1})	Regional (10%) (kg year^{-1})
	Surface water		
	Groundwater		
75.6% land-filling	116	104	12
100% land-filling	126	113	13
	Sludge		
75.6% land-filling	556	500	56
100% land-filling	603	543	60

Contribution of NiCd batteries to the overall cadmium emissions of land-filling MSW

With the assumption that NiCd batteries account for 10-50% of the total MSW cadmium content, the contribution of NiCd batteries can be calculated by multiplying the overall cadmium emissions as presented in **Table 3.52** by 0.1 and 0.5 (see **Table 3.56** and **Table 3.57**).

Table 3.56 Contribution of NiCd batteries to the overall cadmium emissions due to land-filling of MSW

Scenario	75.6% land-filling		100% land-filling	
Allocation key	10%	50%	10%	50%
Compartment	Direct emissions (kg year^{-1})			
Surface water	49	244	56	264
Groundwater	12	58	13	63
Sludge	56	278	60	302

Table 3.57 Contribution of NiCd batteries to the continental and regional cadmium emissions due to land-filling of MSW

Scenario		Released amount Cadmium (kg year^{-1})	Continental (90%) (kg year^{-1})	Regional (10%) (kg year^{-1})
		Surface water		
75.6% land-filling	0.1	49	44	5
	0.5	244	220	24
100% land-filling	0.1	56	50	7
	0.5	264	238	26

Table 3.57 continued overleaf

Table 3.57 continued Contribution of NiCd batteries to the continental and regional cadmium emissions due to land-filling of MSW

Scenario		Released amount Cadmium (kg year^{-1})	Continental (90%) (kg year^{-1})	Regional (10%) (kg year^{-1})
		Groundwater		
75.6% land-filling	0.1	12	11	1
	0.5	58	52	6
100% land-filling	0.1	13	12	1
	0.5	63	57	6
		Sludge		
75.6% land-filling	0.1	56	50	6
	0.5	278	250	28
100% land-filling	0.1	60	54	6
	0.5	302	272	30

Sensitivity analysis

The values used in the previous sections to produce the emissions of MSW incinerators and MSW landfills represent average or estimated values. Therefore, a large amount of uncertainty is associated with these numbers. This uncertainty is difficult to take into account explicitly. However, a sensitivity analysis was performed on some of the input parameters used to determine the effect that varying the parameters had on the overall results. The following parameters and ranges were used:

Table 3.58 Variation of model parameters used in the sensitivity analysis

Model parameter	Unit	Minimum value	Default value	Maximum value	Affected parameter
Incinerator					
Total Cd content in MSW	g tonne^{-1} dry wt.	5	10	15	bottom ash and fly ash concentrations Cadmium land-filled
Amount of wastewater	m^3/tonne	0.6	2.5	5	Emissions to water
Effluent concentration	mg L^{-1}	0.1	0.3	1	Emissions to water
Treatment efficiency	%	90	98.8	99.9	Emissions to water
Landfill					
Leachate concentration landfill	µg L^{-1}	0.5	5	50	Emissions to water
Percolation flux	%	1	10	20	Emissions to water
Treatment efficiency STP	%	40	60	80	Emissions to water
Allocation key					
Contribution NiCd batteries	%	10		50	Emissions to water

Ranges were chosen in such a way that they covered at least the figures reported in literature. The upper limit for the leachate concentration (50 µg L^{-1}that is close to the solubility limit for cadmium carbonate, Ross et al. (2000)[39]) in landfill leachates is added to represent a worst case

[39] Via laboratory experiments and modelling techniques it was concluded that levels close to 5 µg L^{-1}and an order of magnitude higher could be expected from moderately mature and mature wastes.

future leachate concentration as a result of an increasing cadmium content in the MSW. It should be stressed that this seems indeed a worst case since under aerobic conditions predicted solubility limits are around an order higher than measured leachate concentrations suggesting that other mechanisms such as adsorption phenomena are limiting cadmium release.

However, as it has already been indicated in subsection "Overall cadmium emissions from landfilling MSW" under Section 3.1.2.2.5 the composition of the future leachate cannot be predicted based on current knowledge since there is no direct relationship between the total content of Cd and the leachability of Cd. If the simplified assumption is taken that there would exist a simple direct linear relationship between the cadmium leachate concentration and the cadmium content in the solid mass as has been assumed in other studies (e.g. Leenaars and Steketee, 1997 (in: van der Poel, 1999) and Camobreco et al. (1999)) this could be calculated as followed:

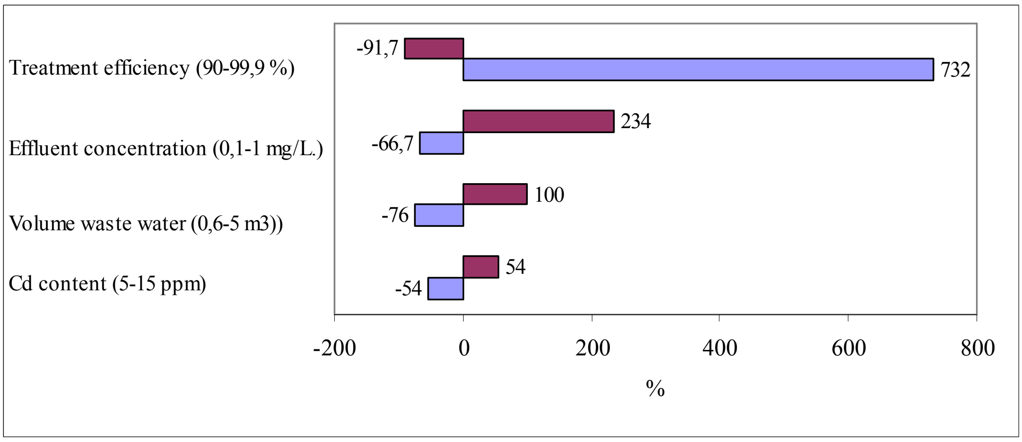
$$CdConc_{Future,leachate} = \frac{CdConc_{present,leachate}}{CdConc_{present,MSW}} \text{ x } CdConc_{Future,MSW}$$

$CdConc_{Future,\ leachate}$ = future cadmium concentration in the leachate (μg L^{-1})
$CdConc_{Present,\ leachate}$ = present cadmium concentration in the leachate (μg L^{-1}) =5 μg L^{-1}
$CdConc_{Future,\ MSW}$ = future cadmium concentration MSW (g)[40] = 24 g
$CdConc_{Present,\ MSW}$ = present cadmium concentration in MSW (g) = 10 g

The maximum leachate concentration is calculated based on the ratio of the current cadmium concentration in the leachate for one average tonne of waste to the total cadmium present in the average tonne of waste. The future cadmium concentration in the MSW has been calculated in Section 3.1.3.2.1. The results showed that a maximum steady state concentration in the MSW corresponds to 24 g $tonne^{-1}$ $_{dry\ wt.}$ From these assumptions and using the formula above a worst-case future leachate concentration of 12 μg L^{-1}can be calculated which is well within the range (0.5-50 μg L^{-1}) used in the sensitivity analysis.

The effects of varying the different input parameters (by the values shown in **Table 3.58**) on the overall results are shown in **Figures 3.9-3.10**. On the figures, the dark bar shows the effect of the maximum value and the grey bar shows the effects of the minimum values.

Figure 3.9 Effects of varying input parameters on MSW incinerator emissions

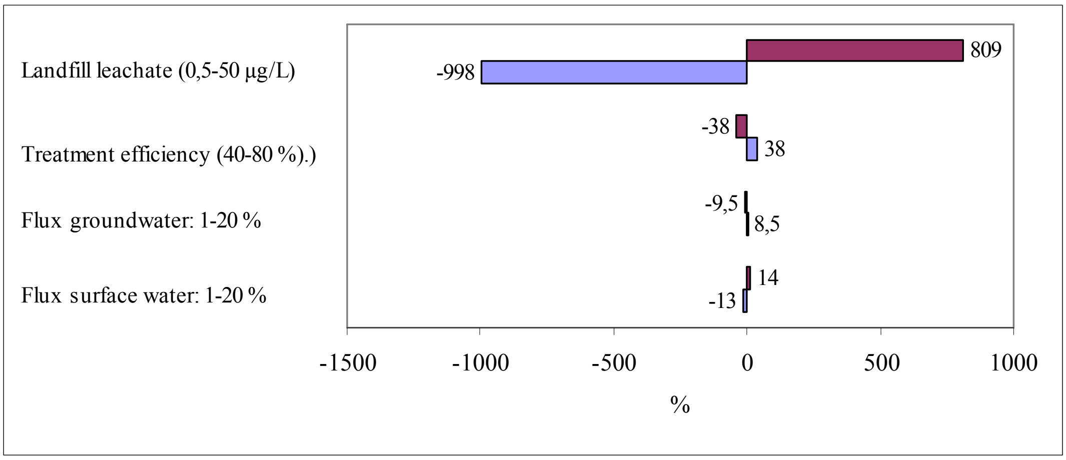


[40] Obtained via the modelling of future NiCd waste arisings (see subsection "Forecasts of future battery waste arisings" under Section 3.1.2.2.5). Remark: note that the total amount of the MSW will probably also further increase (EEA, 2000) but this has not been taken into account in this TRAR.

From **Figure 3.9**, varying the different parameters has a significant effect on the overall results:

- Cadmium concentrations in bottom ash and fly ash vary with 50%: 1.6-25.9 g tonne^{-1} $_{dry\ wt.}$ (bottom ash); 82.9-300 g tonne^{-1} $_{dry\ wt.}$ (fly ash);
- Emissions to surface water and sludge are the most influenced by the choice of treatment efficiency. A lower treatment efficiency (90%) will result in a higher emission to water (+ 732%).

Figure 3.10 Effects of varying input parameters on MSW landfill water emissions



From **Figure 3.10**, varying the different parameters has a significant effect on the overall results:

- The choice of the flux to groundwater or surface water has only a minor influence (± 8.5-14%);
- The choice of the treatment efficiency in the STP has a moderate influence (± 38%);
- The choice of leachate concentration has the highest impact and varies between – 998% to 809%.

Based on the results above it can be concluded that modifying certain default parameters can have a large effect on the overall emissions of the disposal phase. Where possible the effect of changing these parameters has been taken into account in this report. First of all the emissions to the different compartments have been quantified based on the European average situation (24.4% incineration and 75.6% landfill) and completed by two scenarios (100% land-filling and 100% incineration). The effect of increased total cadmium content in MSW is covered in the future scenarios (10 and 75% collection) for MSW incinerators with a cadmium content of respectively 13.2 and 24 g tonne^{-1} $_{dry\ wt.}$ The effect of a hypothetical higher landfill leachate concentration of 50 µg L^{-1}has also been taken forward as a scenario. Furthermore for landfills the assessment was performed with and without the presence of a STP.

3.1.2.2.6 Summary: releases to the environment due to battery related life cycle steps

The overall cadmium emission of the disposal phase originating from all products containing cadmium in MSW can be found in **Table 3.35** (incineration current situation), **Table 3.39** (incineration future situation) and **Table 3.55** (landfills). In **Tables 3.59-63** only a summary of the cadmium EU emissions from different parts of the life cycle of NiCd batteries taken forward in the analysis is given. It is important to note that a large uncertainty surrounds the figures of the disposal phase (see subsection "Sensitivity analysis" under Section 3.1.2.2.5).

Table 3.59 Summary of the distributions in kg (total in EU) of Cd emissions to different environmental compartments during the total life cycle of NiCd batteries (realistic scenario: 24.4% incineration and 75.6% land-filling). Scenario 10 mg kg^{-1} $_{dry\ wt.}$ cadmium

Life cycle stages	Emission distribution in kg $year^{-1}$				
	Air	Water	Urban/ind. soil/agr. soil	Ground-water	Total release
1 Manufacturing of NiCd batteries and/or battery packs	51	65	0	0	116
2 Incorporation into battery powered devices and applications	0	0	0	0	0
3 Use, recharging and maintenance by end users	/	/	/	/	/
4 Recycling • Collection • Processing • Recovery	1.8	0.1	0	0	1.9
5 Disposal (10-50% NiCd batteries contribution)					
• Incineration (24.4%)	323-1,617	35-176	N/A	N/A	358-1,793
• Land-filling (75.6%)	N/A	49-244	56-278	12-58	117-580
Total	376-1,670	149-485	56-278	12-58	593-2,491

/ No direct emissions. Indirect cadmium emissions associated with the energy consumption used to recharge the batteries are deemed negligible;
N/A Not applicable.

Table 3.60 Summary of the distributions in kg (total in EU) of Cd emissions to different environmental compartments during the total life cycle of NiCd batteries (worst case scenario: 100% incineration). Scenario 10 mg kg^{-1} $_{dry\ wt.}$ cadmium

Life cycle stages	Emission distribution in kg $year^{-1}$			
	Air	Water	Urban/ind. soil/agr. soil	Total release
1 Manufacturing of NiCd batteries and/or battery packs	51	65	0	116
2 Incorporation into battery powered devices and applications	0	0	0	0
3 Use, recharging and maintenance by end users	/	/	/	/
4 Recycling • Collection • Processing • Recovery	1.8	0.1	0	1.9

Table 3.60 continued overleaf

Table 3.60 continued Summary of the distributions in kg (total in EU) of Cd emissions to different environmental compartments during the total life cycle of NiCd batteries (worst case scenario: 100% incineration). Scenario 10 mg kg^{-1} $_{dry\ wt.}$ cadmium

Life cycle stages	Emission distribution in kg $year^{-1}$			
	Air	Water	Urban/ind. soil/agr. soil	Total release
5 Disposal (10-50% NiCd contribution)				
• Incineration (100%)	1,402-7,009	144-721	N/A	1,546-7,730
• Land-filling (0%)	N/A	N/A	N/A	N/A
Total	1,455-7,062	209-786	0	1,664-7,848

/ No direct emissions. Indirect cadmium emissions associated with the energy consumption used to recharge the batteries are deemed negligible;
N/A Not applicable.

Table 3.61 Summary of the distributions in kg (total in EU) of Cd emissions to different environmental compartments during the total life cycle of NiCd batteries (worst case scenario: 100% land-filling). Scenario 10 mg kg^{-1} $_{dry\ wt.}$ cadmium

Life cycle stages	Emission distribution in kg $year^{-1}$				
	Air	Water	Urban/ind. soil/agr. soil	Ground-water	Total release
1 Manufacturing of NiCd batteries and/or battery packs	51	65	0	0	116
2 Incorporation into battery powered devices and applications	0	0	0	0	0
3 Use, recharging and maintenance by end users	/	/	/	/	/
4 Recycling • Collection • Processing • Recovery	1.8	0.1	0	0	1.9
5 Disposal (10-50% NiCd contribution)					
• Incineration (0%)	0	0	N/A	0	0
• Land-filling (100%)	N/A	56-264	60-302	13-63	129-629
Total	53	121-329	60-302	13-63	247-747

/ No direct emissions. Indirect cadmium emissions associated with the energy consumption used to recharge the batteries are deemed negligible;
N/A Not applicable.

Table 3.62 Summary of the distributions in kg (total in EU) of Cd emissions to different environmental compartments during the total life cycle of a NiCd battery (Future scenario: 100% incineration. Scenario 13.2 mg kg^{-1} $_{dry\ wt.}$)

Life cycle stages	Emission distribution in kg $year^{-1}$			
	Air	Water	Urban/ind. soil/agr. soil	Total release
1 Manufacturing of NiCd batteries and/or battery packs	51	65	0	116
2 Incorporation into battery powered devices and applications	0	0	0	0
3 Use, recharging and maintenance by end users	/	/	/	/
4 Recycling • Collection • Processing • Recovery	1.8	0.1	0	1.9
5. Disposal (32% NiCd batteries contribution)				
• Incineration (100%)	4,486	615	N/A	5,101
• Land-filling (0%)	N/A	N/A	N/A	N/A
Total	4,539	680	0	5,219

/ No direct emissions. Indirect cadmium emissions associated with the energy consumption used to recharge the batteries are deemed negligible;
N/A Not applicable.

Table 3.63 Summary of the distributions in kg (total in EU) of Cd emissions to different environmental compartments during the total life cycle of a NiCd battery (Future scenario: 100% incineration. Scenario 24 mg kg^{-1} $_{dry\ wt.}$)

Life cycle stages	Regional releases in kg $year^{-1}$			
	Air	Water	Urban/ind. soil/agr. soil	Total release
1 Manufacturing of NiCd batteries and/or battery packs	51	65	0	116
2 Incorporation into battery powered devices and applications	0	0	0	0
3 Use, recharging and maintenance by end users	/	/	/	/
4 Recycling • Collection • Processing • Recovery	1.8	0.1	0	1.9

Table 3.63 continued overleaf

Table 3.63 continued Summary of the distributions in kg (total in EU) of Cd emissions to different environmental compartments during the total life cycle of a NiCd battery (Future scenario: 100% incineration. Scenario 24 mg kg^{-1} $_{dry\ wt.}$)

Life cycle stages	Regional releases in kg $year^{-1}$			
	Air	Water	Urban/ind. soil/agr. soil	Total release
5. Disposal (63% NiCd batteries contribution)				
• Incineration (100%)	8,831	2,178	N/A	11,009
• Land-filling (0%)	N/A	N/A	N/A	N/A
Total	8,882	2,243	0	11,125

/ No direct emissions. Indirect cadmium emissions associated with the energy consumption used to recharge the batteries are deemed negligible;
N/A Not applicable.

3.1.2.3 Releases based on update site-specific exposure data (reference year 2002)

3.1.2.3.1 Cadmium metal and cadmium oxide production

As described in Section 2.1.2, the number of companies still manufacturing cadmium metal is reduced to three. Only one plant is still producing cadmium oxide.

An overview of Cd emissions to water and air from Cd metal and CdO production is presented in **Table 3.64**, **Table 3.65**, **Table 3.66** and **Table 3.67** (reference year 2002). Information on waste for these sectors is presented in **Table 3.68** and **Table 3.69**. These data are extracted from plant information recently submitted by the remaining Cd metal/CdO producing plants in the EU-16 (Industry Questionnaire 2004).

Cadmium metal production

- The three remaining cadmium metal producing plants all reported information on emissions to water (emission factors varying between 1.10 and 277 g $tonne^{-1}$). The total Cd emission to the aquatic environment from the three existing Cd metal producing plants (plant 1, 6, 7) in 2002 is 70.5 kg $year^{-1}$. Water emission data for the year 2004 are reported for Cd metal production plant 7. The total yearly Cd emission to water is reduced by a factor of 1.6; the emission factor is reduced with 16% (i.e. 232 g $tonne^{-1}$ versus 277 g $tonne^{-1}$). As mentioned in the section below, on changes in emission reduction measures, substantial changes have taken place at this site in the collection and treatment of waste water in the period 2002-2004, resulting in a reduction of water emissions.
- All companies presented information on air emissions (stack emissions) (emission factors varying between 23.8 and 259 g $tonne^{-1}$). The total EU emission to the air compartment from cadmium metal producers is 94.6 kg Cd/year.
- For all sites fugitive emissions are included in the reported stack emissions. One site reports that fugitive emissions amount to 60-70% of total air emissions.
- Number of emission days to water and air is 365 days for all sites.

- Measured effluent concentrations (annual mean), effluent discharge rates and type of receiving surface water (ditch, tide influenced river, sea) are reported for all companies.
- For two out of three companies, detailed information with respect to on-site treatment of waste water in a WWTP is submitted. There are two physico-chemical treatment plants in use on-site 7; one central water treatment plant and one weak acid treatment plant. In the central water treatment plant; lime (CaO) and sodium sulphide (Na_2S) are used as the main precipitation agents. The main reaction is precipitation of the metals as hydroxides in the pH range of 8.3-8.5. In order to control the Cd concentration in the effluent, some sodium sulphide is added before the water enters a thickener in which the hydroxides/sulfides are settled. The effluent/overflow from the thickener is polished in sand filters. The water treatment plant is continuously controlled (24 hours a day: pH, flow and other parameters). The waste water from Cd metal production-site 1 is purified in an on-site waste water treatment plant using a bacteriological process in which metal sulphates are converted into metal sulphides. In the first step of this process –Biological DeSulfurisation (BDS) stage- process water containing a high sulphate concentration is treated. The BDS-process consists of an initial chemical pre-purification step (separation of metals (solids) and fluoride from the waste water) followed by a bacteriological purification stage (conversion of sulphate to sulphides). The sludges (metal-sulphates, solids) arising from previous treatment steps are recycled to the main production process. The effluent from the BDS water purification step is further purified in the next step, the SRB (Sulphate Reducing Bacteria) water purification process (capacity of 400 m^3/hour). The SRB water purification plant is fed with waste water containing low concentrations of metals and sulphate, i.e. the effluent from the BDS process and water from the geohydrological control system. In an UASB (‘upflow anaerobic sludge blanket’) reactor bacteria –fed by ethanol- convert sulphates to sulphides. The excess of formed sulphide is converted by bacteria to sulphur in a fixed film reactor. The sludge of metal sulphides is recycled to the main zinc production process. This technique is known as BAT. The purified water is discharged to a ditch. The effluent from the water purification plant of site 1 is controlled 52 times a year by taking flow proportional samples; the analytical method is according to national standard 6426; the detection limit is 0.3 µg L^{-1}. Site 6 mentions that the waste water is treated in an on-site water treatment plant; the effluents from this site are treated together with discharges from another metal producing site (distribution 50:50). There are no details on the treatment steps available.
- Waste is not generated during Cd metal production (dross, sludge, solid waste is recycled in the production).
- The flow of the receiving surface water –necessary to calculate a site specific dilution factor- is available for 2 companies (site 1, 6). Site 7 discharges its waste water to a sea environment for which a default dilution factor of 100 is applied.

Significant changes in production/emission reduction measures since 1996 are reported as follows:

- Site 1: in 2000, change of raw material (Century concentrate). Due to new national regulation entering into force, and the fact that Century concentrate was dustier than the concentrates worked up before, a lot of actions were taken: closed conveyor system, closed storage bins with under pressure and baghouse, house keeping etc. Cadmium concentration in Century concentrate is lower as in the concentrates used till 2000. So several Cd emissions (related to diffuse concentrate/calcine emissions) are proportional lower. Former concentrate until 2000: 0.19% Cd, after 2001: 0.12% Cd. Cd production in 1997: 745 tonnes, 2004: 549 tonnes. Cd emission is only for a small part related to the Cd plant, most of the Cd emissions are related to the zinc production. Since 2002 further remediation actions took place: formerly untreated historically contaminated water from the plant area is now also treated in the WWTP (see also the footnote of **Table 3.64**).

- Site 6: none reported.
- Site 7: 2001-2003. Collecting and treating/reuse of approximately 90% diffuse emissions and storm/runoff waters from the industrial site. A containment basin was built under the industrial site to collect surface and storm water. 2003. Modernising the central water treatment plant. 2003-2004. Construction of a new quay to reduce pollution/runoff due to spill during unloading of raw materials. 1995-to date: installation of abatement systems in stacks in the leaching plant.

Cadmium oxide production

- The only remaining Cd oxide production plant reports that no waste water discharges from the site occur since the production of cadmium oxide is a totally dry process.
- Very recently an update of the air emission data is provided. Total Cd emission to the atmosphere amounts to 6.6 kg $year^{-1}$ (in-house methods; predicted; year 2005 stack measurements: 53-55 µg Cd/m^3, average flow rate: 10,000 m^3/hour; number of emission hours: 6,000 hours/year , 2 stacks). Please note that for the year 2004 the total Cd emission to the air is reported as 11.7 kg $year^{-1}$ (independent laboratory) (based on an average Cd concentration of 97 µg/m^3 (two stacks), average flow rate: 10,000 m^3/hour; number of emission hours: 6,000 hours/year). Both emission values will be taken forward to the exposure assessment and risk characterisation.
- Number of emission days to air is 256 days.
- Information on waste is not available.

Release to water

Table 3.64 Aquatic emissions from Cd metal producing plants in the EU-16

Plant N°	Production volume	Production emission¶	Emission factor	Conc.l effluent[c]	Number of emission days	Concentration in effluent[a]	Effluent flow[a]	Low flow receiving water[b]	Year
	tonne y^{-1}	kg y^{-1}	g $tonne^{-1}$			mg l^{-1}	m^3 d^{-1}	m^3 d^{-1}	
1	485	12.0[d] [f]	25	M (T)	365	0.004 [g]	9,060	12,000	2002
6	420	0.50[d]	1.10	M (T)	365	0.0007[h]	1,169	13 10^6	2002
7*	209	58[e]	277	M (T)	365	0.05	3,200	-*	2002
7*	155	36[e]	232	M (T)	365	0.030	3,200	-*	2004

a) Mean annual;
b) 10^{th} percentile of flow rate or 1/3 of annual mean flow rate (TGD - EC, 2003);
c) M: measured value, E: estimated value, D: dissolved concentration, T: total concentration;
d) Emission of Cd from Zn or Zn and Pb production;
e) Only process discharges, no diffuse discharges (surface/storm water etc) included;
f) The total emission in 2002 consists of discharge of effluent from water purification plant and discharge of other water from the plant area (historic contaminated). Since 2005, the discharge from water from the plant area has been stopped; since then all waste water is treated in the purification plant;
g) The effluent concentration of 4 µg $L^{-1}$is a weighted average Cd concentration for both types of water discharges (effluent: avg conc. 1.5 µg L^{-1}, P90: 2.3 µg L^{-1}; discharge: 2,736,115 m^3/year; other plant area water: avg concentration: 13.6 µg L^{-1}; total discharge: 571,334 m^3/year);
¶ Annual averages;
* Emission to the sea;
h) Measured by supervision authority.

Table 3.65 Aquatic emissions from Cd oxide producing plants in the EU-16

Plant N°	Production volume	Production emission¶	Emission factor	Conc. In effluent©	Number of emission days	Concentration in effluent(a)	Effluent flow(a)	Low flow receiving water (b)	Year
	tonnes y^{-1}	kg y^{-1}	g $tonne^{-1}$			mg l^{-1}	m^3 d^{-1}	m^3 d^{-1}	
12	4,498	0(d)	0	0		20	0	0	2002

a) Mean annual;
b) 10th percentile of flow rate or 1/3 of annual mean flow rate (EC, 2003);
c) M: measured value, E: estimated value, D: dissolved concentration, T: total concentration;
d) No emissions to water; thermal/dry process;
¶ Annual averages.

Release to air

Table 3.66 Atmospheric emissions from Cd metal producing plants in the EU-16

Plant N°	Production volume	Production emission amount¶	Emission factor	Year
	tonnes y^{-1}	kg $year^{-1}$	g $tonne^{-1}$	
1	485	30.4(a)(b)	62.7	2002
6	420	10.0(a) (c)	23.8	2002
7	209	54.2(a) (d)	259	2002

¶ Annual averages;
a) Cd emission from whole plant (including Zn and/or Pb production);
b) Total emissions: stack and diffuse emissions; diffuse emissions: 60-70% of total; stack emissions: 30-40% of total emissions;
c) All emissions from point sources and fugitive emissions from roof openings for the whole zinc production process (extensive monitoring programme 2001/2002). Emissions from cadmium production are difficult to separate;
d) Total emissions from the zinc smelter; approx. 90 emission points to air. Approximately 90% of the emission comes from 20% of the emission points which all are equipped with abatement systems (demisters or scrubbers).

Table 3.67 Atmospheric emissions from Cd oxide producing plants in the EU-16

Plant N°	Production volume	Production emission amount¶	Emission factor	Year
	tonnes $year^{-1}$	kg $year^{-1}$	g $tonne^{-1}$	
12(a)	n.d.	6.6(a)	n.d.	2005
12	n.d.	11.7(b)	n.d.	2004

¶ Annual averages;
a) Cd in stack emissions is recently measured (year 2005): average Cd concentration: 55 µg/m^3 (punctual measurement, in-house methods; no further information available);
b) Cd in stack emissions measured by external laboratory (year 2004; no further information available); average Cd concentration : 97 µg/m^3;
n.d. No data available.

Waste

Table 3.68 Waste information for Cd metal producing plants in the EU-16

Plant N°	Type of waste produced	Quantity of waste	Cd content	Waste disposal type	Year
		(tonnes y^{-1})	%		
1	No waste produced Recycling of liquids directly into the leaching process. Recycling of solid wastes (scalings) by the residue recycling.	Not applicable	Not applicable	Internal recycling	2002
	Sludge out off the water purification is used as secondary raw material.	n.d.	n.d.	Internal recycling	2002
6	No waste related to cadmium production	Not applicable	Not applicable	Not applicable	2002
7	Normally no waste is produced during production of Cd metal. The Cd is a by product from the hydrometallurgical Zn metal production from Zn concentrates. In the Cd foundry some dross is produced but the material is recycled to the production. Sludges from the water treatment plants are deposited in mountain cavern deposits together with the other process wastes, however, the metal containing hydroxide cake from the weak acid treatment plant is recycled to the zinc process.	Not applicable	Not applicable	Internal recycling	2002

n.d. No data available.

Table 3.69 Waste information for Cd oxide producing plants in the EU-16

Plant N°	Type of waste produced	Quantity of waste	Cd content	Waste disposal type	Year
		(tonnes y^{-1})	%		
12	n.d.	n.d.	n.d.	n.d.	2002

n.d. No data available.

3.1.2.3.2 Release during processing and use

NiCd batteries' production and recycling

As described in Section 2.2.1 the number of companies producing NiCd batteries has further decreased in recent years. Five NiCd battery producers and three NiCd battery recyclers are still in operation. At present, updates on environmental emissions to water and air have been submitted by 3 NiCd battery producers and 3 recyclers (year 2002). Please note that the previous update of exposure information for these sectors was 1999/2000. The data are summarised in **Table 3.70**, **Table 3.71**, **Table 3.72** and **Table 3.73**. Waste information was collected from battery manufacturing and recycling plants. The data are presented in **Table 3.74** and **Table 3.75**.

Production of NiCd batteries

- Three out of five remaining NiCd battery producing plants submitted information on emissions to water (site 2, 3, 4). It should be noted however that emissions from site 2 include emissions from battery manufacturing as well as Cd recycling. The site is involved in both activities and wastewater emissions cannot be split between two factories. The total Cd emission to the aquatic environment from NiCd battery producing plants is 49.1 kg $year^{-1}$. It should be noted as well that the updated emissions are derived on the basis of annual average effluent concentrations, as opposed to the emissions given in the original TRAR document (see Section 3.1.2.2.1) in which P90's values were calculated on monthly average effluent concentrations.
- Two companies (site 2, 4) provided information on air emissions (stack emissions). The total Cd emission to the air compartment from this sector is 8.5 kg $year^{-1}$. As mentioned before, site 2 is both a NiCd battery producing and Cd recycling site. The reported emission figure of 5 kg $year^{-1}$ is originating from battery manufacturing only. For site 3 no information is provided since air emissions are not monitored. According to the company, there are no requirements for air monitoring in the permit since the plant runs a wet process (most emissions are to water).
- Fugitive emissions are not monitored.
- Number of emission days to water and air varies between 330 and 344 days.
- Measured effluent concentrations (annual mean), effluent discharge rates and type of receiving surface water (tide influenced river, sea, river) are reported for all companies.
- New information with respect to on-site treatment of waste water in a WWTP is not submitted. It is assumed that all waste waters are treated in an on-site WWTP/municipal STP before being discharged into surface waters.
- The following Cd containing waste arises from battery production: old batteries, powders, sludge, plates, other. In general all materials are recycled (external recycling in Cd recycling plants). In some cases sludge can also be land-filled.
- The flow of the receiving surface water –necessary to calculate a site specific dilution factor- is available for 3 companies (site 2, 3, 4).

Recycling of NiCd batteries

- Three NiCd battery recycling plants (site 1, 2, 2bis) reported information on emissions to water. Site 1 reports very low emissions to water for the year 2002 i.e. 0.13 kg $year^{-1}$.

Moreover, wastewater emissions -and emission factors- from this site are further reduced in 2003/2004 (0.06 kg $year^{-1}$) due to efforts to conform to ISO 14000, for which the site has been certified in February 2005 (details are included in the section below: ‘significant changes in emission reduction measures’). The information for site 2bis is already included in the NiCd battery producing section, since waste water emissions could not be split between NiCd-battery manufacturing and recycling plant. Site 2 states that no site emissions are discharged to surface water. All waste waters are collected and treated off-site in an external waste water treatment plant (total volume of waste water: 100 m^3/year, no further update data available) (1996 data: 35 tonnes fluid waste per year; Cd content: 20 ppm (total Cd); effluent concentration of off-site STP: 0.2 mg L^{-1}).

- Three Cd recycling plants (site 1, 2, 2bis) provided information on air emissions (stack emissions). Site 1 reports air emissions of 3.97 kg Cd/year for the year 2002. In analogy with water emissions, air emissions –and emission factors- are further reduced in 2003/2004 i.e. to 0.91 kg $year^{-1}$ as a result of measures taken to obtain an ISO 14000 certificate (building coverage, aspiration devices) (details are included in the section below: ‘significant changes in emission reduction measures’). The total Cd emission to the air compartment from the site 2bis is 0.85 kg $year^{-1}$. Please note that the reported figure for this site –NiCd battery manufacturing and Cd recycling plant- is related to recycling only. The very low emission of 0.002 kg Cd/year for site 2 is validated on the basis of the submitted air measurements’ report (IUTA-Prüfbericht, 2004). The low emission figure is a result of very low Cd concentrations detected in the stack emissions (Cd conc. 2.5 µg/m^3) combined with a low gas flow rate (78 m^3/hour maximum).
- Fugitive emissions are not monitored.
- Number of emission days to water and air is 330-360 days.
- Since for site 2 wastewater is not discharged locally (near the site), but collected and treated off-site, other water related emission information for this site (effluent discharge rate, type of receiving water and flow rate of surface water) is not relevant. The information relevant for site 2bis is reported in the section on NiCd battery manufacturing. Measured effluent concentrations (90P value/annual mean), effluent discharge rate and type and flow (low flow rate) of receiving surface water (river) are reported for site 1.
- Waste arising from the recycling of NiCd batteries e.g. batteries plastic boxes, metallic boxes, concentrated electrolytes, Fe/Cd electrodes is recycled or land-filled. Waste arising from the treatment of stack (air) emissions and waste water (dust filters, sludges) is recycled.

Significant changes in production/emission reduction measures since 1999/2000 are reported as follows:

- NiCd battery manufacturing plants: not available
- Cd recycling site 1: Invested improvements in building coverage and investment of aspiration device with a capacity of 60,000 m^3/hour to prevent diffuse emissions to air (since 2002). Improvements are ongoing in 2005. Wastewater and air emissions: efforts to conform to ISO 14000, for which the site has been certified in February 2005. The main changes that took place at the level of waste water emissions are the following: a) Because of the negative impact of the presence of cooling liquid -originating from electric vehicles batteries- and hydrocarbons -sometimes present in the electrolyte from batteries- on the WWTP efficiency, it was decided to collect the cooling liquid –during the batteries dismantlement- separately and send it for recycling. The electrolyte collecting system was modified by adding a hydrocarbon separator. The following actions were undertaken to

reduce air emissions: a) high efficiency systems were modified: i.e. two rows of filters were installed instead of one; in this manner maintenance operations are secured, peaks are avoided and Cd emissions are reduced. b) Furthermore, work was done on the empowerment of the operators using these air treatment systems by setting up luminous devices, which indicate the state of sealing. The use of these 'warnings' improved the follow up of the installations as well as immediately reduced the delays due to maintenance intervention.

- Cd recycling site 2: Installation of active carbon filter between furnaces and chimney (installed between 2002 and today).

Release to water

Table 3.70 Aquatic emissions from NiCd batteries producing plants in the EU-16

plant N°	Consumption volume (expressed as Cd)	Emission¶	Emission factor	Col in effluent(c)	Number of emission days	Concentration in effluent(a)	Effluent flow(a)	Low flow receiving water (b)	Year
	tonne $year^{-1}$	kg $year^{-1}$	g $tonne^{-1}$			mg l^{-1}	m^3 d^{-1}	m^3 d^{-1}	
2*/2bis	453	11.5(d)*	25.4	M (T)	330	0.11	326	432,000*	2002
3	454	13.7	30.2	M (T)	330	0.06	655	17 10^6	2002
4	771	23.9	31.0	M (T)	344	0.10	673	1,244,160	2002
6	No update data	No update data							
7	No update data	No up data							

a) Mean annual;
b) 10^{th} percentile of flow rate or 1/3 of annual mean flow rate (EC, 2003);
c) M: measured value, E: estimated value, D: dissolved concentration, T: total concentration;
d) Emissions from battery manufacturing plant and Cd recycling plant combined, emissions cannot be split between two factories;
¶ Annual averages;
* Emission to the sea.

Table 3.71 Aquatic emissions from NiCd batteries recycling plants in the EU-16

Plant N°	Production volume (expressed as Cd)		Emission¶	Emission factor Inc. in effluent(c)	Number of emission days	Concentration in effluent(a)	Effluent flow(a)	Low flow receiving water (b)	Year
	Tonne $year^{-1}$	kg $year^{-1}$	g $tonne^{-1}$			mg l^{-1}	m^3 d^{-1}	m^3 d^{-1}	
1	853	0.13	0.15	M (T)	191	0.37 (90P) 0.16 (avg)	4.2	11,232	2002
1	816	0.06	0.07	M (T)	177	0.24 (90P) 0.1 (avg)	3.3	11,232	2004
2	62	0(d)	0	0	360	0	0	0	2002
2bis	See data on-site is in Table 3.7								

a) Mean annual effluent flow for the year 2002 is 4.2 m^3 d^{-1} and for 2004 is 3.3 m^3 d^{-1};
b) 10^{th} percentile of flow rate or 1/3 of annual mean flow rate (EC, 2003);
c) M: measured value, E: estimated value, D: dissolved concentration, T: total concentration; ¶annual averages;
d) No site emission to water. Cleaning water as well as processing water are collected internal (about 100 m^3/year) and send to an external waste water treatment plant.

Release to air

Table 3.72 Atmospheric emissions from NiCd batteries producing plants in the EU-16

Plant N°	Consumption volume (expressed as Cd)	Production emission amount¶	Emission factor	Year
	tonne $year^{-1}$	kg $year^{-1}$	g $tonne^{-1}$	
2	453	5.0[(a)]	11.04	2002
3	454	n.d.[(b)]	n.d.	2002
4	771	3.5	4.54	2002
6	No update data	No update data		
7	No update data	No update data		

¶ Annual averages; n.d.: no data available;
a) Emission from battery manufacturing only; air emissions are broken down between two plants; battery manufacturing and Cd recycling;
b) Air emissions are not monitored. No requirement in the permit since the plant runs a wet process, therefore most emissions are releases in the water.

Table 3.73 Atmospheric emissions from NiCd batteries recycling plants in the EU-16

Plant N°	Production volume (expressed as Cd)	Production emission amount¶	Emission factor	Year
	tonne $year^{-1}$	kg $year^{-1}$	g $tonne^{-1}$	
1	853	3.97	4.55	2002
1	816	0.91	1.10	2004
2	771	0.0019 [(a)]	0.00002	2002
2bis	453	0.85 [(b)]	8.30	2002

¶ Annual averages;
a) Submitted air emissions are checked versus the analysis report and proved to be correct. Air emissions are that low due to the fact that in air emission no considerable amount of Cd can be found (conc. 2.5 µg/m^3) and the fact that the gas stream is very low due to technical reasons (78 m^3/hour maximum); analysis performed by external laboratory;
b) Emissions from Cd recycling unit on the site of battery manufacturing plant 2.

Waste

Table 3.74 Waste information for NiCd batteries producing plants in the EU-16

Plant N°	Type of waste produced	Quantity of waste	Cd content	Waste disposal type	Year
		(tonnes y^{-1})	%		
2	Old batteries	20.6	7%	Recycling plant	2002
	Powders (from sludge recycling)	25	95%	Recycling plant	
	Plates	38	27%	Recycling plant	
	Other (filters etc)	6	5%	Incineration	

Table 3.74 continued overleaf

Table 3.74 continued Waste information for NiCd batteries producing plants in the EU-16

Plant N°	Type of waste produced	Quantity of waste	Cd content	Waste disposal type	Year
		(tonnes y^{-1})	%		
3	Old batteries Sludge (filtercakes) Plates Others (filters etc.)	72 218 51 17	7-10% 57% water, 4% Cd on dry weight 48% 20%	External recycling plant Special (CET1) landfill External recycling plant	2002
4	Old batteries Sludge (filtercakes) Plates Others (filters etc.)	185 187 117 1	13% 50% water, 9.7% Cd on dry weight 18% 5%	External recycling plant External recycling plant External recycling plant	2002
6	No update data	No update data			
7	No update data	No update data			

Table 3.75 Waste information for NiCd batteries recycling plants in the EU-16

Plant N°	Type of waste produced	Quantity of waste	Cd content	Waste disposal type	Year
		(tonnes y^{-1})	%		
1	Batteries plastic boxes Batteries metallic boxes Fe/Cd electrodes after treatment; Concentrated electrolytes Process slag, air treatment dust, used filters, rainwater sludges.	256 169.5 262.7 186.2	0.33 mg kg^{-1} 0.1 mg kg^{-1} 0.5 mg kg^{-1} 4.2 mg kg^{-1}.	Industrial landfill Recycling Industrial landfill Neutralisation Internal treatment.	2002
2	n.a.	n.a.	n.a.	n.a.	2002
2bis	Old batteries Powders Plates	1,024 25 38	9% 95% 27%	Recycling	2002

Production of Cd containing pigments

Compiled updated emission information for the three remaining Cd pigments producers was submitted (year 2003). A summary of releases to water and air is given in **Table 3.76** and **Table 3.77**. Waste information is presented in **Table 3.78**.

- The three remaining Cd pigments producing plants (site A, B, C) reported information on emissions to water (emission factors not available). The total Cd emission to the aquatic environment in 2003 is 10.9 kg $year^{-1}$. Please note that year 2004 waste water emission data have been provided by site C; Cd emission from this site amounts to 4.4 kg $year^{-1}$ (as opposed to 6.9 kg $year^{-1}$ for the year 2003).
- All companies presented information on air emissions (stack emissions) (site-specific emission factors not available). The total EU emission to the air compartment from cadmium pigments producers is 11.0 kg Cd/year.
- Information on fugitive emissions is not provided.
- The number of emission days to water and air varies between 318-365 days.
- Measured effluent concentrations (annual mean), effluent discharge rates and type of receiving surface water (river) are reported for all companies. The effluent from site C is analysed daily (usually a 24 hours composite sample). Effluent samples are analysed by Atomic Absorption using either 'flame' or 'graphite furnace'. The laboratory participates in the Aqua check scheme (Water Proficiency Testing and Laboratory Performance Monitoring) as a means of ensuring accurate results for metals in aqueous effluents.
- New information with respect to the on-site treatment of waste water in a WWTP is submitted for all sites. For Cd pigments producing sites in general, the on-site treatment of aqueous effluent is an integral part of the production process. The treatment of the aqueous effluent is a chemical/physical process involving pH change to precipitate Cd, followed by filtration to remove Cd carbonate. For site C specifically, all aqueous waste is collected and treated by raising the pH to 9 using sodium carbonate solution in a stirred treatment vessel. This precipitates the soluble Cd as carbonate. The resultant suspension is filtered through a filter press to remove suspended solids. The filtrate is tested for suspended solids, re-filtered and then passed to a (settling) 'pool' that allows a continuous discharge of effluent to the receiving river over 365 days/year.
- Sludge from the treatment of waste water and other solid wastes are land-filled.
- The flow of the receiving surface water –necessary to calculate a site specific dilution factor- is available for all companies.

Significant changes in production/emission reduction measures since 1996 are reported as follows:

- The most significant changes are for losses to solid wastes. Figures submitted for the previous draft of the RAR were lower because at that time waste solids from treatment of production waste water were sent to zinc refiners for recovery of zinc and cadmium. Environmental pressures have forced the closure of the relevant zinc refiners, and the waste solids now have to be sent to landfill.

Release to water

Table 3.76 Aquatic emissions from Cd pigments producing Plants in the EU-16

Plant N°	Production/ consumption volume	Processing emission¶	Emission factor	Conc. in effluent(c)	Number of emission days	Concentration in effluent(a)	Effluent flow(a)	Low flow receiving water (b)	Year
	tonne year^{-1}	kg year^{-1}	g tonne^{-1}			mg l^{-1}	m³ d^{-1}	M³ d^{-1}	
A	n.d.	1.0	n.d.	M(T)	365	0.02	145	3,333	2003
B	n.d.	3.0	n.d.	M(T)	318	0.02(f)	498	1,681,920	2003
C	n.d.	6.9 (d)	n.d.	M(T)	365	0.12(e)	156	45,000	2003
C	n.d.	4.4	n.d.	M(T)	365	0.08 (90P) 0.05 (avg)	240	45,000	2004

a) Mean annual;
b) 10th percentile of flow rate or 1/3 of annual mean flow rate (EC, 2003);
c) M: measured value, E: estimated value, D: dissolved concentration;
d) Waste water consists of process waste water and rainwater collected from buildings and exterior storage areas;
e) Average Cd concentration in effluent for the year 2004 is 0.05 mg L^{-1}; 90P value: 0.08 mg L^{-1}. Total discharge: 87480 m³/d. T: total concentration;
f) P90 in effluent for the year 2004: 0.054 mg L^{-1}; ¶annual averages; n.d.: no data available.

Release to air

Table 3.77 Atmospheric emissions from Cd pigments producing plants in the EU-16

Plant N°	Production/consumption volume	Processing emission ¶	Emission factor	Year
	tonne year^{-1}	kg year^{-1}	g tonne^{-1}	
A	n.d.	2.50	n.d.	2003
B	n.d.	5.60	n.d.	2003
C	n.d.	2.90	n.d.	2003

¶ Annual averages;
n.d. No data available.

Waste

Table 3.78 Waste information for Cd pigments producing plants in the EU-16

Plant N°	Type of waste produced	Quantity of waste	Cd content	Waste disposal type	Year
		(tonnes y^{-1})	%		
A	Solid waste and sludge	15	n.d.	landfill	2002
B	Solid waste and sludge	6.8	n.d.	landfill	2002
C	Solid waste and sludge	7.3	n.d.	landfill	2002

n.d. No data available.

Production of Cd containing stabilisers

As a result of the Vinyl 2010 commitment the number of producers in the EU-16 dropped to only a few. Only 2 companies currently acknowledged to the Rapporteur that some production still took place at their sites located in Italy. Emission data are summarised in **Table 3.79** and **Table 3.80**. Waste information is presented in **Table 3.81**.

- The two remaining Cd stabiliser producing plants (site X, Y) reported information on emissions to water (emission factors < 9.0-< 41.0 g $tonne^{-1}$). The total Cd emission to the aquatic environment in 2002 is < 1.4 kg $year^{-1}$.
- All companies presented information on air emissions (stack emissions) (emission factors < 1.3-38 g $tonne^{-1}$). The total EU emission to the air compartment from cadmium stabiliser producers is < 0.74 kg Cd/year. The analytical method used to measure Cd in air emissions from site Y is the following: MIP P-PRO-101 rev 2, 2003.
- Information on fugitive emissions is not provided.
- Depending on the site, the number of emission days to water varies between 220-365 days. The number of emission days to air varies between 50-220 days. The number of production days for site Y is 40-60 days.
- Measured effluent concentrations (annual mean), effluent discharge rates and type of receiving surface water (municipal STP, river, canal) are reported for both companies. For site Y, the analysis of waste water (ICP, dl: 5 µg L^{-1}) is done every 15 days on an average sample collected during this period with an automatic sampling system (internal laboratory). Two times per year the analysis is performed by a certified external laboratory on punctual sampling (EPA 200.8, 1994; dl: 1 µg L^{-1}).
- New information with respect to on-site treatment of waste water in a WWTP is submitted by company Y. This site has a physico-chemical treatment plant (comprising the following main units: homogenisation basin ($600m^3$), complex additivation, flocculation, sedimentation, filter press for sludges and sand filters for treated water) followed by active carbon filters. For site X, wastewaters are treated in an on-site WWTP (type is unknown) before being discharged to a municipal STP.
- Solid waste is land-filled.
- The flow of the receiving surface water –necessary to calculate a site specific dilution factor is available for both companies.

Release to water

Table 3.79 Aquatic emissions from Cd stabiliser producing plants in the EU-16

Plant N°	Production/ consumption volume	Production emission amount¶	Emission factor	Conc. in effluent(c)	Number of emission days	Concentration in effluent(a)	Effluent flow(a)	Low flow receiving water (b)	Year
	tonnes year^{-1}	kg year^{-1}	g tonne^{-1}			mg l^{-1}	m^3 d^{-1}	m^3 d^{-1}	
X	17	< 0.70(d)	<41	M (T)	220	On-site WWTP : < 0.005 Municipal STP : < 0.00037(e)	370	831,050	2002
Y	77	< 0.69	<9.0	M (T)	365	< 0.005(f)	352	86,400	2002
Y	77	< 0.69	<9.0	M (T)	365	< 0.001(g)	352	86,400	2002

a) Mean annual;
b) 10th percentile of flow rate or 1/3 of annual mean flow rate (EC, 2003);
c) M: measured value, E: estimated value, D: dissolved concentration, T: total concentration;
d) Emission to municipal STP;
e) Cd concentration in effluent from municipal STP; calculated from Cd concentration in effluent from on-site WWTP; taking into account removal at STP: 60%; extra dilution: 2000 m^3/d/370 m^3/d = 5.4.; ¶annual averages;
f) Analysis performed by internal laboratory (two times a month) method MIP-P-PRO-101 rev 2 year 2003;
g) Analysis performed by certified external laboratory (two times a year), method EPA 200.8 (1994).

Release to air

Table 3.80 Atmospheric emissions from Cd stabiliser producing plants in the EU-16

Plant N°	Production/consumption volume	Production emission amount¶	Emission factor	Year
	tonnes year^{-1}	kg year^{-1}	g tonne^{-1}	
X	17	0.64	38.0	2002
Y	77	<0.10(a)	<1.3	2002

¶ Annual averages;
a) Analysis performed by internal laboratory.

Waste

Table 3.81 Waste information for Cd stabiliser producing plants in the EU-16

Plant N°	Type of waste produced	Quantity of waste	Cd content	Waste disposal type	Year
		(tonnes y^{-1})	%		
X	Solid waste	37 kg Cd	37 kg Cd	offsite inertisation and land-filling	2002
Y	n.d.	n.d.	n.d.	n.d.	2002

n.d. No data available.

Use of Cd/CdO in alloys, plating and other uses

For these uses, no site-specific update information was submitted to the Rapporteur.

3.1.2.3.3 Releases during the production of other non-ferrous metals

In this section, the Cd releases from four sites that stopped Cd metal production and that submitted emission information are briefly discussed. An overview of Cd emissions to water and air for each of the four non-ferrous metal producing sites is presented in Annex VI.

From this information, it can be concluded that, although the production of Cd metal stopped, Cd emissions to water and air can still be substantial -up to 427 kg Cd/year to water and 56.6 kg Cd/year to air respectively. The Cd emissions arise from the production of other non-ferrous metals (i.e. Zn and Pb). No production volumes related to other non-ferrous metals were submitted, so no corresponding emission factors could be calculated.

3.1.3 Predicted environmental concentrations (PEC)

3.1.3.1 Local exposure assessment: in production, processing and use scenarios excluding those related to batteries

Point sources have a major impact on the environmental concentration on a local scale.

Local exposure concentrations are calculated from emission data submitted by Industry (Industry Questionnaire, 1997) according to the EU-Technical Guidelines Document (TGD, 1996). Calculated values are compared with measured concentrations near Cd emitting plants (Ind. Questionnaire, 1997) and where large differences occur, results are analysed and evaluated.

3.1.3.1.1 Aquatic compartment

<u>Calculated local concentrations</u>

Calculation of local PEC-values for the aquatic compartment is performed according to the method described in the TGD (1996). On a local scale it is assumed that wastewater will pass through a STP before being discharged into the environment. Once discharged, complete mixing of the effluent in the surface water is assumed. The calculation involves several sequential steps: it includes the calculation of the discharge concentration (if not available) of a STP to a water body, the dilution effect and the removal from the aqueous medium by adsorption to suspended matter. Volatilisation and degradation are ignored because these processes are not applicable for Cd. Local sedimentation of Cd is ignored. Input data were submitted via the Industrial Questionnaire (1997).

The first step in the assessment of the local PEC values in the aquatic environment is the determination of the site-specific effluent concentration. If not available, it was calculated from reported daily releases to surface water (kg d^{-1}) and the local effluent flow rate (m^3 d^{-1}).

$$Ceffluent_{STP} = \frac{EMISSIONlocal}{EFFLUENTlocal_{STP}} .10^3$$

EMISSIONlocal:	Local emission amount from point source (kg d^{-1})
$EFFLUENTlocal_{STP}$:	effluent discharge rate of STP (m^3 d^{-1})
$Ceffluent_{STP}$:	Cd concentration in effluent of STP (mg L^{-1}).

If no effluent discharge rate was submitted, a default value of 2,000 $m^3\ d^{-1}$ (TGD, 1996) was used.

In the second step, the concentration in the receiving surface water is calculated. Complete mixing of the effluent with the receiving water is assumed. The calculation of the dilution factor is based on the given flow rate of the receiving water-body (or default: 18,000 $m^3\ d^{-1}$) and on the given discharge rate of the industrial STP (or default: 2,000 $m^3\ d^{-1}$). In the absence of both data, a default dilution factor of 10 is used for emissions to freshwater. A default dilution factor of 100 is used for emissions to the sea.

$$D = \frac{EFFLUENTlocal_{STP} + FLOW}{EFFLUENTlocal_{STP}}$$

D:	Dilution factor
$EFFLUENTlocal_{STP}$:	Effluent discharge rate of local STP ($m^3\ d^{-1}$)
FLOW:	Flow rate of the receiving water ($m^3\ d^{-1}$)

The local available concentration of Cd in water is estimated taking into account the fraction of chemical that is adsorbed to suspended matter (TGD, 1996). The local concentration in the receiving surface water during the emission period is then calculated with the equation:

$$Clocal_{water} = \frac{Ceffluent_{STP} \cdot 1,000}{(1 + K_p \cdot C_{susp} \cdot 10^{-6}) * D}$$

$Clocal_{water}$:	Local concentration in surface water during emission period (µg L^{-1})
$Ceffluent_{STP}$:	Cd-concentration in local STP effluent (µg L^{-1})
K_p :	Solids-water partition coefficient of suspended matter (130000 L kg^{-1}).
C_{susp} :	Concentration of suspended matter in watercourse (default = 15 mg L^{-1})
D:	Dilution factor (default 10)

The value of K_p can be derived from the ratio of dissolved to total Cd concentrations in waterbodies. The dissolved fraction is generally the fraction passing a 0.45 µm membrane filter. The K_p-value varies with environmental conditions. Factors having a large influence on the actual K_p-value are the pH, the total metal concentration, the water hardness and the nature and concentration of complexing agents. A range of measured K_p values is presented in **Table 3.82**. In the calculations presented here, a European average value of K_p = 130 10^3 L kg^{-1} is used.

Table 3.82 The solid- water partition coefficient of suspended matter (K_p) in different freshwaters

Location	K_p (L kg^{-1}) average	K_p (L kg^{-1}) minimum	K_p (L kg^{-1}) maximum	Source
Flanders	17 10^3	0.28 10^3	280 10^3	VMM, 1997
the Rhine, Meuse and Schelde rivers in The Netherlands	n.a.	30 10^3	300 10^3	Ros and Slooff, 1990
4 locations in the Netherlands 1983-1986	129 10^3	n.a.	n.a.	Crommentuijn et al., 1997a
7 locations in the Netherlands 1988-1992	151 10^3	n.a.	n.a.	Crommentuijn et al., 1997a
3 locations in the Netherlands 1992-1994	224 10^3	n.a.	n.a.	Crommentuijn et al., 1997a
St Lawrence River basin 1991-1992	100 10^3	7.9 10^3	794 10^3	Quemerais and Lum, 1997

n.a. Not available

The calculated surface water concentrations are actual contributions to the receiving water. The local PEC values are obtained by adding the regional PEC value for water to the calculated local concentration in surface water.

$$PEClocal_{water} = Clocal_{water} + PECregional_{water}$$

$PEClocal_{water}$: Predicted environmental concentration during emission episode (µg L^{-1})
$Clocal_{water}$: Local concentration in surface water during emission episode (µg L^{-1})
$PECregional_{water}$: Regional concentration in surface water (0.11 µg L^{-1} Table 3.157)

The local PEC values of Cd in surface water are presented in **Table 3.83**. The local PEC values range from 0.11 to 5.54 µg L^{-1} for Cd/CdO-producing plants and from 0.11 to 2.86 µg L^{-1} for Cd/CdO-processing plants.

Table 3.83 The local PEC_{water} (dissolved fraction) for Cd-producing and -processing plants in the EU-16. PEC's include background Cd

use-	N°	Production emission¶	Processing emission¶	Dilution factor	$Clocal_{water}$	$PEClocal_{water}$	Year
Category		kg $year^{-1}$	kg $year^{-1}$		µg L^{-1}	µg L^{-1}	
Cd-production	1	23.9		12	1.26	1.37	1996
	2	614		320	0.47	0.58	1996
	*3**	15.7		100(a)*	0.03*	0.14*	1996
	*4**	21.6		100(a)*	0.41*	0.52*	1996
	5	77.8		10(a)	5.4	5.5	1996
	6	0.18		29,500	7.8 10^{-6}	0.11	1996
	*7**	70		100(a)*	0.20*	0.31*	1996
	8	11		930	0.01	0.12	1996
	*9**	17.4		100(a)*	0.02*	0.13*	1999
	10	0(1)		0(1)	0(1)	0.11	1996
	11	0(2)		0(2)	0(2)	0.11	1996
	*13**	372		100(a)*	0.58*	0.69*	1996
CdO-producers	11		0(2)	0(2)	0(2)	0.11	1996
	12		0(2)	0(2)	0(2)	0.11	1993
Cd-stabilisers	F		0.03	500	0.0007	0.11	1996
	G		0.5	25	0.18	0.29	1996
	H		0.78	100	0.027	0.14	1996
	I		0.1	10	0.01	0.12	1996
	J		0	0	0	0.11	1996
	K		4.1	10	0.58	0.69	1996
	L		0	0	0	0.11	1996
	M		0	0	0	0.11	1996

Table 3.83 continued overleaf

Table 3.83 continued The local PEC_{water} (dissolved fraction) for Cd-producing and -processing plants in the EU-16. PEC's include background Cd

use-	N°	Production emission¶	Processing emission¶	Dilution factor	$Clocal_{water}$	PEClocalwater	Year
Category		kg year-1	kg year-1		µg L-1	µg L-1	
	windows manufacturer		0	0	0	0.11	1996
Cd-pigments	A		0.6	50	0.14	0.25	1996
	B		4.02	1,000	0.001	0.11	1996
	C		5.9	700	0.04	0.15	1996
	D		0.9	250	0.03	0.14	1996
	E		13.4	24,800	0.001	0.11	1996
Cd-plating	EU		250	10(a)	2.75	2.9	1996
Cd-alloys	EU		61.3	10(a)	1.7	1.81	1996

* Emission to the sea; ¶annual averages;
n.a. Not available;
1) No water emissions: waste waters are recycled;
2) No water emissions: dry process;
a) Default value: 10 (freshwater), 100 (sea water).

Measured local concentrations

Monitoring data from Cd-producing plants were submitted via the Industrial Questionnaire (1997). In general, most of these plants have implemented a monitoring program to control the effluent concentrations and the concentrations in the receiving water flow at and around the point of discharge. In **Table 3.84** measured and calculated data are presented as dissolved concentrations. Submitted measured values are generally total concentrations and are often limited to one value per site rather than ranges. Moreover, measurements do not always refer to the same year as the one for which PEC values are calculated (e.g. site 2). In order to be able to compare measured and calculated values, total measured values are converted to dissolved values assuming a dissolved fraction of 33% of the total measured Cd concentration (dissolved fraction = $1/((1+K_p \cdot C_{susp} \cdot 10^{-6})$ with K_p = 130 10^3 L kg^{-1}, C_{susp} = 15 mg L^{-1}; TGD, 1996). Measured concentrations range from < 0.1 µg L^{-1} to 10 µg L^{-1}. At some plants measurements were performed at different locations and Cd-concentrations were found to decrease with distance from the point of discharge.

Only few comparisons between predicted and measured concentrations can be made. Model predictions fit observations except for the plants that emit their effluents to the sea. Environmental characteristics of both receiving water and effluent water have a very important influence on the final dissolved Cd concentrations in the receiving waterbody. Dilution factors of 1.0 to 3.4 do not seem realistic when effluents are emitted to the sea. Factors influencing the final dissolved exposure concentration are the amount and composition of suspended matter, water hardness, pH and Cd concentration of the receiving water before the point of discharge. Predictions of local concentrations can only be improved if local conditions are assessed in detail.

Table 3.84 The measured local Cd concentrations in the effluent receiving water and the local PEC_{water} concentrations for Cd-producing and -processing plants in the EU-16

Use-	Plant N°	Production	Processing	$PEClocal_{water}$		Year
Category		emission amount	emission amount	calculated	measured(2)	
		kg y^{-1}	kg y^{-1}	µg L^{-1}	µg L^{-1}	
Cd-production	1	23.9		1.37	1.0	1996
	2	614		0.59	0.1 (1994)	1996
	3*	15.7		0.15*	1.5-10 (500m-1km)	1996
	4*	21.6		0.52*	1.6 (10m, 1995)	1996
	5	77.8		5.5	5	1996
	6	0.18		0.11	0.15	1996
	7*	70		0.32*	0.03 (1997)(a)	1996
	8	11		0.12	n.a.	1996
	9*	17.4		0.13	< 0.05 (2000)	1999
	10	0(1)		0.11	n.a.	1996
	11	0(1)		0.11	n.a.	1996
	13*	372		0.69*	3 (50m)	1996
CdO-producers	11		0(1)	0.11	n.a.	1996
	12		0(1)	0.11	n.a.	1993
Cd-stabilisers	F		0.03	0.11	n.a.	1996
	G		0.5	0.29	n.a.	1996
	H		0.78	0.14	n.a.	1996
	I		0.1	0.13	n.a.	1996
	J		0	0.11	n.a.	1996
	K		4.1	0.69	n.a.	1996
	L		0	0.11	n.a.	1996
	M		0	0.11	n.a.	1996
	window manufacturer		0	0.11	n.a.	1996
Cd-pigments	A		0.6	0.25	n.a.	1996
	B		4.02	0.11	n.a.	1996
	C		5.9	0.15	n.a.	1996
	D		0.9	0.14	n.a.	1996
	E		13.4	0.11	n.a.	1996
Cd-plating	EU		250	2.9	n.a.	1996
Cd-alloys	EU		61.3	1.81	n.a.	1996

* Emission to the sea;
n.a. Not available;
1) No water emissions: dry process or waste waters are recycled;
2) If total concentrations are measured, dissolved concentrations are estimated to be 33% of total Cd concentration ($Kp = 130\ 10^3$ L kg^{-1}, $C_{susp} = 15$ mg L^{-1});
a) Measured at 40 m depth (emission at 30 m depth), several km away from the emission point.

3.1.3.1.2 The sediment

Following the standard approach as laid down in the TGD, the local concentration in the sediment is predicted based on the local concentrations in the water as

$$PEClocal_{sediment} = K_p \; PEClocal_{water} . \; 10^{-3}$$

in which the K_p (L $kg^{-1}{}_{dw}$) equals the solid- water partition coefficient of suspended matter. The average Kp value for suspended matter (130,000 $Lkg^{-1}{}_{dw}$) however strongly over predicts sediment concentrations. As an example, the average Cd concentrations in surface water in Europe is about 0.14 µg Cd/Land the average sediment Cd concentration is 1.32 mg Cd/kg_{dw}[41]. The predicted average sediment concentration using the average Kp of suspended matter is 0.14 · 130,000/1,000 = 18.2 mg Cd/kg_{dw} and which is about 14-fold above the average measured concentrations. As an alternative, one could use the 'best fit' Kp of sediments, defined as the ratio of the average sediment to average water Cd concentrations. This 'best fit' Kp yields 10,000 L $kg^{-1}{}_{dw}$ (=1.32/0.14 · 1,000). Another alternative is to use a measured regional PEC for the sediment to which a local added fraction is added, formally

$$PEClocal_{sediment} = PECregional_{sediment} + K_p \; Clocal_{water} . \; 10^{-3}$$

in which the K_p (L $kg^{-1}{}_{dw}$) equals the solid- water partition coefficient of suspended matter. This option has been preferred because (i) of the preference for measured rather than predicted sediment concentrations and (ii) because the contribution of the local discharge to the sediment concentrations is taken into account via suspended matter Kp in line with the TGD.

The measured PEC regional is taken as an average of 90^{th} percentiles of surveys: 2.66 mg Cd/kg_{dw} (see **Table 3.189**).

The local $PEC_{sediment}$ are readily calculated from the data in **Table 3.83** and the above-mentioned equation and presented in **Table 3.85**. The $Clocal_{sediment}$ (K_p Clocal $_{water}$. 10^{-3}) is included to illustrate the contribution of the local discharge onto the sediment PEC.

The local $PEC_{sediment}$ range from 2.7 to 707.8 mg $kg^{-1}{}_{dw}$ for Cd-producing plants and from 2.7 to 359.6 mg kg^{-1} for Cd-processing plants.

Table 3.85 The local $PEC_{sediment}$ for Cd-producing and –processing plants in the EU-16. The PEC's include background Cd. All values are expressed as total Cd concentrations and thus not corrected for bioavailability

Use category	Plant n°	Production emission¶	Processing emission¶	$Clocal_{sediment}$	$PEClocal_{sediment}$	Year
		kg $year^{-1}$	kg $year^{-1}$	mg $kg^{-1}{}_{dw}$	mg $kg^{-1}{}_{dw}$	
Cd-producers[(e)]	1	23.9		163.7	166.4	1996
	2	614		61.4	64.1	1996
	3*	15.7		4.4	7.1	1996

Table 3.85 continued

41 Median of averages, median or geometric means (of min-max) of all European surveys listed in Tables 3.184 and 3.187. Observations near point sources and industrial activities are excluded and only the most recent data are included when data were reported for various periods. Concentrations in water refer to the dissolved fraction (see Table 3.184) but also include the data with 'unknown fractionation' (i.e. dissolved or not; this means that the median Cd water concentration can somewhat be overestimated).

Table 3.85 continued The local $PEC_{sediment}$ for Cd-producing and –processing plants in the EU-16. The PEC's include background Cd. All values are expressed as total Cd concentrations and thus not corrected for bioavailability

Use category	Plant n°	Production emission¶	Processing emission¶	$Clocal_{sediment}$	$PEClocal_{sediment}$	Year
		kg year-1	kg year-1	mg kg-1dw	mg kg-1dw	
	4*	21.6		52.9	55.6	1996
	5	77.8		705.1	707.8	1996
	6	0.18		0.0	2.7	1996
	7*£	70		26.4	29.1	1996
	8	11		1.4	4.1	1996
	9*	17.4		1.8	4.5	1999
	10	0(1)		0.0	2.7	1996
	11	0(1)		0.0	2.7	1996
	13*	372		74.9	77.6	1996
CdO-producers	11		0(1)	0.0	2.7	1996
	12		0(1)	0.0	2.7	1993
Cd-stabilisers	F		0.03	0.1	2.8	1996
	G		0.5	22.9	25.6	1996
	H		0.78	3.5	6.2	1996
	I		0.1	1.7	4.4	1996
	J		0	0.0	2.7	1996
	K		4.1	75.3	78.0	1996
	L		0	0.0	2.7	1996
	M		0	0.0	2.7	1996
	window manufacturer		0	0.0	2.7	1996
Cd-pigments	A		0.6	18.8	21.5	1996
	B		4.02	0.1	2.8	1996
	C		5.9	5.2	7.9	1996
	D		0.9	3.8	6.5	1996
	E		13.4	0.1	2.8	1996
Cd-plating	EU		250	356.9	359.6	1996
Cd-alloys	EU		61.3	220.4	223	1996

* Emission to the sea;
¶ Annual averages;
n.a. Not available;
1) No water emissions: waste waters are recycled;
2) No water emission: dry process;
£ Based on 1996 monitoring results (sediment analyses 0-3cm), the value of 1.9 mg Cd/kg dwt is proposed for the local exposure assessment by the company (Industry/company data submission, Aug. 2004).

3.1.3.1.3 Atmospheric compartment

Calculated local concentrations

Local PEC-values for the atmospheric compartment are calculated according to the OPS model proposed in the TGD (1996) for a general standard environment. The PEC values are represented as an average concentration at 100 m from the source. In general the atmospheric compartment receives its input from direct emission to air. Local Cd concentrations in the air are assessed by calculating the amount emitted to the air by the Cd producing and processing plants:

$$Clocal_{air,\,ann} = Clocal_{air} \cdot \frac{Temission}{365}$$

$$Clocal_{air} = Elocal_{air} \cdot Cstd_{air}$$

$Elocal_{air}$:	Local direct emission rate to air during emission period (kg d^{-1})
$Cstd_{air}$:	Concentration in air at source strength of 1 kg d^{-1} (ng m^{-3}) default: 278 (TGD, 1996)
Temission :	Number of days per year that emission takes place (d y^{-1})
$Clocal_{air}$:	Local concentration in air during emission period (ng m^{-3})
$Clocal_{air,\,ann}$:	Annual average concentration in air, 100 m from point source (ng m^{-3})

Input data are the total daily emissions of the individual Cd-producing plants and EU emission data of industry processing Cd in alloys (ERL, 1990) and plating (WS Atkins, 1998).

The calculated concentrations in air are actual contributions to the receiving atmosphere. The local PEC values are obtained by adding the regional PEC values for air to the calculated local concentration in the atmosphere.

$$PEClocal_{air,ann} = Clocal_{air,\,ann} + PECregional_{air}$$

$PEClocal_{air,ann}$:	Annual average predicted environmental concentration in air (ng m^{-3})
$PECregional_{air}$:	Regional concentration in the air (0.55 ng m^{-3}; Table 3.157)

The results of the predicted local atmospheric Cd concentrations at 100 m from the point sources are listed in **Table 3.86**. Calculated local PEC values range from 0.8 to 1,282 ng m^{-3} with the highest values emitted by Cd producing pyrometallurgical plants. For the Cd processing industry, a very high value was found for the processing of Cd in alloys. Since information on-site specific or EU level was not available, it is based on estimated EU-emission amounts. Site-specific information is needed to validate the results.

Table 3.86 Calculated local PEC_{air} concentrations for Cd-producing and processing plants in EU-16

Use-category	Plant N°	Production emission amount¶ kg year^{-1}	Processing emission amount¶ kg year^{-1}	Number of emission days(1)	Annual average air concentration (100 m) ng m^{-3}	$PEClocal_{air,ann}$ (100 m) ng m^{-3}	Year
Cd-production	1	54		365	41	42	1996
	2	1,683		365	1,282	1,282	1996
	3	800		70	609	610	1996
	4	3.03		15	2.3	2.9	1996
	5	946		243	721	721	1996
	6	6.24		105	4.8	5.3	1996
	7	200		365	152	153	1996
	8	28.6		151	21.8	22	1996
	9	110		365	83.8	84	1996
	10	3.32		316	2.5	3.1	1996
	11	1.61		32	1.2	1.8	1996
	13	24.6		123	18.7	19	1996
CdO-producers	11		0.30	251	0.228	0.8	1996
	12		0.31	256	0.236	0.8	1993
Cd-stabilisers	F		0.09	20	0.069	0.6	1996
	G		0.8	48	0.609	1.2	1996
	H		0.5	60	0.381	0.9	1996
	I		0.1	13	0.076	0.6	1996
	J		0.7	13	0.533	1.1	1996

Table 3.86 continued overleaf

Table 3.86 continued Calculated local PEC_{air} concentrations for Cd-producing and processing plants in EU-16

Use-category	Plant N°	Production emission amount¶ kg year-1	Processing emission amount¶ kg year-1	Number of emission days(1)	Annual average air concentration (100 m) ng m-³	PEClocalair,ann (100 m) ng m-³	Year
	K		0.04	12	0.030	0.6	1996
	L		n.a.	155	n.a.	0.6	1996
	M		0	155	0	0.6	1996
	window manufacturer		n.a.	350	n.a.	0.6	1996
Cd-pigments	A		1.15	230	0.876	1.4	1996
	B		2.37	231	1.8	2.4	1996
	C		3.6	276	2.7	3.3	1996
	D		5.8	230	4.4	5.0	1996
	E		0.2	85	0.152	0.7	1996
Cd-plating	EU		0	155	0	0.6	1996
Cd-alloys	EU		770	62	586	587	1996

n.a. Not available;
¶ Annual averages;
1) B-Tables, TGD (1996) when data not available.

Measured local concentrations

Measured atmospheric concentrations in the surroundings of the production-sites are available and are presented in **Table 3.87**. Concentrations in the air vary according to the distance from the emission point and the prevailing wind direction. Measured data range from 0.23 ng m^{-3} to 78 ng m^{-3}. Distances from the point source range from 100 m to 2,400 m. Calculated values of these sites vary from 0.6 to 1,300 ng m^{-3} at a distance of 100 m from the point source. They are the sum of the calculated local atmospheric concentration, due to plant emission, and the background concentration, which is, according to the TGD (1996), the regional PEC value (0.561 ng m^{-3}, **Table 3.157**). Due to the difference in distance between the measured and calculated values, comparison of both values for each site is not possible. Trends in the measured Cd concentrations over the last decade are presented in **Annex J**.

Table 3.87 Calculated and measured local PEC_{air} concentrations for Cd-producing and processing plants in EU-16

Use-category	N°	Production emission amount kg y^{-1}	Processing emission amount kg y^{-1}	$PEClocal_{air}$ (100 m) ng m^{-3}	Measured ann.avg. air concentration ng m^{-3}	Year
Cd-producers	1	54		42	44 (300m, 1993)	1996
	2	1,683		1,282	78 (600m)	1996
	3	800		610	n.a.	1996
	4	3.03		2.9	4 (1,000 m,1994)	1996
	5	946		721	30 (1,200 m)	1996
	6	6.24		5.3	1 (2,400 m)	1996
	7[£]	200		153	11 (4,000 m)	1996
	8	28.6		22	11 (300m, 1996)	1996
	9	110		84	0.23(2,000 m,1993)	1996
	10	3.32		3.1	< 40 (100m)	1996
	11	1.61		1.8	n.a.	
	13	24.6		19	n.a.	1996
CdO-producers	11		0.30	0.8	n.a.	1996
	12		0.31	0.8	5.4 (150m, 1994)	1993
Cd- stabilisers	F		0.09	0.6	n.a.	1996
	G		0.8	1.2	n.a.	1996
	H		0.5	0.9	n.a.	1996
	I		0.1	0.6	n.a.	1996
	J		0.7	1.1	n.a.	1996
	K		0.04	0.6	n.a.	1996
	L		n.a.	0.6	n.a.	1996
	M		0	0.6	n.a.	1996

Table 3.87 continued overleaf

Table 3.87 continued Calculated and measured local PEC_{air} concentrations for Cd-producing and processing plants in EU-16

Use- category	N°	Production emission amount kg y-1	Processing emission amount kg y-1	PEClocalair (100 m) ng m-³	Measured ann.avg. air concentration ng m-³	Year
	window manufacturer		n.a.	0.6	n.a.	1996
Cd- pigments	A		1.15	1.4	n.a.	1996
	B		2.37	2.4	n.a.	1996
	C		3.6	3.3	n.a.	1996
	D		5.8	5.0	8 (200 m)	1996
	E		0.2	0.7	n.a.	1996
Cd-plating	EU		0	0.6	n.a.	1996
Cd-alloys	EU		770	587	n.a.	1996

n.a. Not available;

£ The results of recent measurements during February-May 2003 indicate figures of 0.7 to 8.50 ng Cd/m³ (3 month average) (Industry/company data subsmission, Aug. 2004).

3.1.3.1.4 Terrestrial compartment

Calculated local concentrations

According to the TGD, the local PEC_{soil} is calculated as an average concentration over a certain time period in agricultural soil, fertilised yearly with sludge from a STP and receiving continuous aerial deposition (dry and wet) from a nearby point source, for a period of 10 years. For the terrestrial ecosystem, the concentration is calculated for a depth of 0.2 m. Sludge from Cd producing plants is however not applied to agricultural land but is recycled internally or by an external plant (IZA-Europe, pers. communication). Application of sludge from processing sites/scenarios is unlikely to take place[42] but may occur if the Cd is emitted via a sewer to a municipal sewage treatment plant. This route of emission is taken into account in the regional assessment as diffuse Cd flux (see Section 3.1.3.4.2). Therefore, the Cd input to soil through sludge from the Cd producing plants is omitted in these local calculations and atmospheric deposition is the only source of Cd input into the terrestrial compartment. Atmospheric deposition of Cd is calculated assuming that all Cd is deposited within an area of 100 km² around the source and that the deposition occurs in a continuous flux.

The PEClocal is the sum of the regional Cd concentration in soil (PECregional) and the atmospheric deposition minus the leaching losses. The PEClocal is solved from the dynamic Cd balance in the 0-0.2 top layer of the soil as:

$$PEClocal_{soil} = \frac{Dair}{k} - (\frac{Dair}{k} - PECregional_{soil})\exp(-kt)$$

where

Dair = aerial deposition flux per kg of soil (mg kg^{-1} d^{-1})
t = time (3,650 days)

[42] In line with national and EU legislation sludges from on-site WWTP of Cd processors are likely to be classified as hazardous (e.g. see for the sector of metal treatment in IPPC, 2004; EC legislation in: EC, 1991 and EC, 2000)

k = first order rate constant for removal from top soil (d^{-1})

$PECregional_{soil}$= the regional Cd concentration in soil (0.36 mg kg^{-1}_{ww}; **Table 3.157**) and which is calculated for an agricultural scenario assuming a realistic worst case Cd input scenario.

The aerial deposition flux is

$$Dair = \frac{DEPtotalann}{DEPTHsoil \cdot RHOsoil}$$

DEPtotalann = annual average total deposition flux (mg m^{-2} d^{-1})

DEPTHsoil = mixing depth of soil (0.20 m)

RHOsoil = bulk density of soil (1,700 kg m^{-3})

Dair = aerial deposition flux per kg of soil (mg kg^{-1} d^{-1})

$$DEPtotalann = 0.01\ (Elocalair + Estpair) \cdot Temission/365$$

Elocalair = local direct emission rate to air during emission episode (kg d^{-1})

Estpair = local indirect emission to air from STP during episode (0 kg d^{-1})

Temission = number of days per year that the emission takes place

DEPtotalann = annual average total deposition flux (mg m^{-2} d^{-1})

The factor 0.01 is used in the previous calculation to convert the source strength (kg d^{-1}) to deposition (mg m^{-2} d^{-1}) assuming a deposition area of 100 km^2 (TGD, 1996, p. 300).

Removal from the top soil is by leaching only and the first order rate constant is given as

$$k = \frac{Finfsoil \cdot RAINrate/365}{K_D \cdot DEPTHsoil \cdot RHOsoil}$$

Finfsoil = fraction of rain water that infiltrates into soil (0.25)

RAINrate = rate of wet precipitation (700 mm y^{-1})

K_D = solid:liquid Cd distribution in soil (280 L kg^{-1}, see below)

k = pseudo first-order rate constant for leaching from soil layer (d^{-1})

The solid-liquid Cd distribution coefficient (K_D; L kg^{-1}) in soil is defined as

$$K_D = \frac{[Cd]_S}{[Cd]_l}$$

in which $[Cd]_s$ represents the Cd concentration in the solid phase of the soil (µg kg^{-1}) and $[Cd]_l$ the Cd concentration in pore water (µg L^{-1}). The Cd K_D values vary strongly with soil properties. The Cd K_D values have been measured in different soils. **Table 3.10** lists a number of these studies and shows regression equations between the K_D values and soil properties. The K_D values are generally obtained from Cd adsorption studies in soil suspensions. Main methodological differences between studies are the type and concentration of the background electrolyte, the solid:liquid ratio and the equilibration time. A variation of about two orders of magnitude of the K_D of Cd between different soil types was found. The soil pH is a dominant factor controlling mobility of Cd. From the regression lines between the K_D and soil properties (see **Table 3.88**) it can be predicted that the K_D decreases between 3.2 and 5.1 fold per unit pH decrease. Some studies show that the K_D significantly increases if the soil organic matter content increases (see **Table 3.88**).

The McBride model was based on data of Gerritse and Van Driel (1984), who measured K_D values of Cd for 33 temperate soils, at three different ionic strengths of soils extractants (water extract, dilute salt extract of ionic strength (IS) 0.011M and dilute salt extract of IS 0.11M). The relationship between $\log K_D$ and pH that was derived for the salt extract of intermediate IS (0.011M) - which best matches the IS of many soil solutions - was in best agreement with the log K_D-pH relationships derived by Römkens and Salomons (1998) and Smolders et al. (unpublished) for *in situ* K_D values (see **Table 3.88**). The K_D values in the water extract were higher than in the dilute salt extracts, which can be ascribed to a general ionic strength effect. Due to this effect, Cd concentrations in water extracts tend to underestimate the Cd concentrations in the soil solution as the IS is usually lower in a water extract than in the soil solution. It was found for 18 (contaminated) topsoils that the concentration in a water extract was on average 2.4 times lower than the Cd concentration in the pore water (Degryse F, personal communication). As McBride et al. (1997) used the water extract data of Gerritse and Van Driel (1984), their model probably overestimates in situ K_d values and hence underestimates Cd concentrations in the soil solution.

The best estimates on leaching losses are probably made using *in situ* pore water concentrations, and not using the soluble Cd concentrations in suspension studies. However, no large data sets on *in situ* K_D values are available. In this model K_D was assumed 280 L kg^{-1} which is a typical value for a soil with pH 6.5 and 2% organic matter (the average predicted K_D for these characteristics is 500 L kg^{-1} based on all equations in **Table 3.88**, and 320 L kg^{-1} without the McBride equation).

Table 3.88 The solid-liquid Cd distribution coefficient (K_D) in different topsoils†

K_D (L kg^{-1})	Notes	Source
$\log K_D$=-1.00+0.51pH+0.51log(%OM)	adsorption K_D measured in 0.001*M* $CaCl_2$, n=63 (Danish agricultural soils, subsoils included)	Christensen, 1989
$\log K_D$=0.89+log(%OM/100)+0.52pH	adsorption K_D in $NaNO_3$ 0.01M, n=15 (soils from New Jersey)	Lee et al., 1996
$\log K_D$ =-1.8+log(%OM)+0.59pH	adsorption K_D in 0.005N salts; n=33 (Dutch, French and British soils, some polluted soils included)	Gerritse and Van Driel, 1984
$\log K_D$=-1.16+0.56pH	*in situ* (pore-water based) K_D, n=100 (unpolluted agricultural and forest soils from the Netherlands)	Römkens and Salomons, 1998
$\log[Cd]_S$=3.62-0.50pH-0.45log(%OM*10)+0.96log$[Cd]_{Tot}$	metal concentration in water extract; n=33 (contaminated soils from various sources)	McBride et al., 1997
$\log K_D$=-1.34+0.64pH	*in situ* (pore-water based) K_D, n=28 (unpolluted grassland soils from Belgium)	Smolders et al. (unpublished)
$\log K_D$=-2.09+0.61pH+0.936log(%C)	adsorption K_D in $CaCl_2$ 0.010M n=58 (unpolluted grassland soils from Belgium)	Smolders et al. (unpublished)

† The study of Römkens and Salomons (1998) include subsurface horizons;
%OM Percentage organic matter;
%C Percentage carbon;
$[Cd]_S$ Metal concentration in water extract (µg l^{-1});
$[Cd]_{Tot}$ Total metal concentration in soil (mg kg^{-1}).

Results of the calculations are presented in **Table 3.89**. The PEC_{soil} values range from 0.36 mg kg_{ww}^{-1} to 0.85 mg kg_{ww}^{-1}.

Table 3.89 Calculated total local PEC_{soil} for Cd-producing and processing plants in EU-16. PEC's include background Cd

Use-Category	Plant N°	Emission to air¶ kg d^{-1}	Number of emission days(1)	$PEClocal_{soil}$ mg kg_{ww}^{-1}	Year
Cd-production	1	0.15	365	0.37	1996
	2	4.6	365	0.85	1996
	3	11.4	70	0.59	1996
	4	0.2	15	0.36	1996
	5	3.9	243	0.63	1996
	6	0.06	105	0.36	1996
	7	0.5	365	0.41	1996
	8	0.2	151	0.36	1996
	9	0.3	365	0.39	1996
	10	0.01	316	0.36	1996
	11	0.05	32	0.36	1996
	13	0.2	123	0.36	1996
CdO-producers	11	0.001	251	0.36	1996
	12	0.001	256	0.36	1993
Cd recycling	1	0.02	260	0.36	1996
	2	0	230	0.36	1997
Cd-stabilisers	F	0.005	20	0.36	1996
	G	0.02	48	0.36	1996
	H	0.008	60	0.36	1996
	I	0.008	13	0.36	1996
	J	0.1	13	0.36	1996
	K	0.003	12	0.36	1996
	L	n.a.	155	0.36	1996
	M	0	155	0.36	1996
	window manufacturer	n.a.	350	0.36	1996
Cd-pigments	A	0.01	230	0.36	1996
	B	0.01	231	0.36	1996
	C	0.01	276	0.36	1996
	D	0.03	230	0.36	1996
	E	0.002	85	0.36	1996
Cd-plating	EU	0	155	0.36	1996
Cd-alloys	EU	12.4	62	0.58	1996

n.a. Not available;
¶ Annual averages; B-Tables (TGD, 1996) when data not available.

Measured local concentrations

At this moment, there are no measured local soil concentrations submitted by the Cd producing- or processing industries.

3.1.3.2 Local exposure assessment: batteries' related scenarios

Point sources can have a major impact on the environmental concentration on a local scale. Local exposure concentrations are calculated from emission data submitted by Industry (Industry Questionnaires, 2000/2001) according to the EU-Technical Guidelines Document. (TGD, 1996). In this report local PECs are calculated for life cycle stages 1 (NiCd batteries producers) and 4 (Cd recyclers) of the life cycle of NiCd batteries. Local exposure during production of battery raw materials is not considered in this section but is addressed in the Section 3.1.3.1. Calculated values will be compared with measured concentrations near Cd emitting plants (Industry Questionnaires, 2000/2001) and where large differences occur, results are analysed and re-evaluated. For the disposal life cycle stage a generic exposure assessment is performed for incineration.

3.1.3.2.1 Aquatic compartment

Calculated local concentrations

Input data were submitted via Industry Questionnaires (2000/2001).

Calculation of local PEC-values for the aquatic compartment is performed according to the method described in the TGD (EC, 2003). The general lines are the same as those given in the TGD (1996, see Section 3.1.3.1.1). However, application of the revised TGD implies a number of changes. These are:

The calculation of the dilution factor is based on the given low-flow rate (or 10th percentile) of the receiving water body and on the given effluent discharge rate. Where only average river flows are available, the flow for dilution purposes should be estimated as one third of this average (EC, 2003). In the absence of both data, a default dilution factor of 10 is used for emissions to freshwater. A default dilution factor of 100 is used for emissions to the sea.

It must be noted that with the assumption of complete mixing of the effluent in the surface water no account is taken of the fact that in reality in the mixing zone higher concentrations will occur. For situations with relatively low dilution factors this mixing zone effect can be accepted. For situations with very high dilution factors, however, the mixing zones may be very long and the overall area that is impacted by the effluent before it is completely mixed can be very substantial. Therefore, in case of site-specific assessments the dilution factor that is applied for calculation of the local concentration in surface water should not be greater than 1000 (EC, 2003).

In short:

The calculated surface water concentrations are actual contributions to the receiving water. The local PEC values are obtained by adding the regional PEC value for water (modelled value) to the calculated local concentration in surface water.

$$PEClocal_{water} = Clocal_{water} + PECregional_{water}$$

$PEClocal_{water}$:	Predicted environmental concentration during emission episode (µg/L)
$Clocal_{water}$:	Local concentration in surface water during emission episode (µg/L)
$PECregional_{water}$:	Regional concentration in surface water (0.11µg L^{-1}, calculated value, no changes made see Table 3.57)[43]

In the calculations, a European average value of suspended matter partitioning coefficient: K_p = 130,000 l/kg is used.

The local PEC values of Cd in surface water are presented in **Table 3.90** and **Table 3.91**.

Table 3.90 Local PECwater for NiCd batteries producing plants and Cd recycling plants in the EU emitting to the surface water after on-site WWTP

Use category	N°	Production/ processing emission (average)	Ceffluent	Dilution factor Site-specific	Clocal water Site-specific	PEClocal water Site-specific	Max. Dilution factor (revised TGD)	Clocal water D=1,000	PEClocal water D=1,000	Year
NiCd batteries		kg/y	mg L^{-1}	-	µg L^{-1}	µg L^{-1}	-	µg L^{-1}	µg L^{-1}	
	2[a]	7.3	0.12	1,178	0.034	0.15	1,000	0.041	0.15	2000
	3	30.5 (36,29)	0.12	13,542	0.0030	0.12	1,000	0.041	0.15	2000
	4	21.9 (31.88)	0.13	771	0.06	0.18	N.A.	N.A.	N.A.	2000
	6[b]	No emissions to water (recycled)	N.A.	N.A.	N.A.	N.A	N.A.	N.A.	N.A.	1999
	7[c]	No emissions to water (recycled)	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	1999
Cd recyclers[d]										
	1	0.126	0.45	1,889	0.08	0.19	1,000	0.153	0.27	2000
	2[d]	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	1999

N.A. Not applicable;
a) Company 2 emits to the marine environment;
b) All process wastewater is collected and sent to recycling company;
c) Emissions to water from cleaning operations are disposed in alkaline solution and externally recycled;
d) Only two recyclers (instead of three) have been listed under Cd-recyclers. The reason is that one company is both recycler and producer. A further breakdown in the submitted figures between the producing process and the recycling process was not feasible. For this reason this company have been listed with the other producers;
e) No “open” treatment steps; no emissions to air. The wastewater is collected and treated off-site. No further information was available. The sludge from the treatment is land-filled.

Plant 1 and plant 5 discharge their effluent after on-site treatment into the public sewer system (STP). These discharges will undergo a dilution step in the STP. The corresponding dilution factor is calculated based on the effluent flow rate and a default sewage flow of 2,000 m^3/day. In addition to the dilution factor the cadmium removal efficiency of the STP has to be taken into

[43] The effect of an increase in MSW cadmium content up to 24 mg kg^{-1} $_{dry\ wt.}$ (‘future’ scenarios) will have only a minor influence on the currently derived PECs regional for air, water and soil (see EUSES outprints in Annex V). Therefore there is no need to revise the current PEC reg, water and the PEC reg, air in order to derive the PEC values for the future situation.

account. According to CBS (2002) a removal efficiency of 60% can be used. The final site specific dilution factor is obtained using the site specific flow rate of the receiving surface water and the effluent flow of the STP. The results of the calculations are presented in **Table 3.91**.

Table 3.91 Local PECwater for NiCd batteries producing plants in the EU emitting to the surface water after on site WWTP and followed by STP

Input	Plant N° 1	Plant N° 5
Reference year		2,000
Processing emission (kg year^{-1})	4.9	59.7
Effluent flow (m^3/day)	127	5
Conc. effluent (mg L^{-1})	0.43	0.03
Size of STP (m^3/day)	2,000	2,000
Removal of cadmium in STP (%)	60	60
Flow rate receiving water (m^3/day)	1.9.10^6	2.2.10^6
Output		
Calculated dilution factor in STP	16.7	401
Calculated conc. effluent STP (mg L^{-1})	0.010	0.00003
Calculated site specific dilution factor in receiving water	894	1,101
Clocal water site specific (µg L^{-1})	0.0037	0.00001
PEClocal water site specific	0.12	0.114
Clocal water (D = 1,000)	N/A.	0.00001
PEClocal water site (D = 1,000)	N/A	0.114

N/A Not applicable.

The local PEC values -calculated on the basis of site-specific dilution factors- range from 0.11 to 0.18 µg L^{-1} for NiCd batteries producing plants and 0.19 µg L^{-1} for Cd recycling plants. It should be noted that the 0.11 µg L^{-1}value -for NiCd batteries producing plant 5 - equals the regional PEC. The draft revised TGD (2002) states that in case of site-specific assessments the dilution factor that is applied for calculation of the local concentration in surface water should not be greater than 1,000 (assumption of complete mixing, mixing zones). Therefore, for NiCd producing plants 2, 3 and Cd recycling plant 1 a local concentration in surface water is calculated based on the maximum dilution factor of 1,000. The results from this exercise indicate that for these plants the PEC values in surface water equals 0.15 µg L^{-1}for the NiCd batteries producing plants and 0.27 µg L^{-1}for the Cd recycling plant.

Measured local concentrations

Monitoring data from Cd-producing plants were submitted via the Industrial Questionnaire (2000/2001). In general, most of these plants have implemented a monitoring program to control the effluent concentrations. Only a limited number of measured Cd concentrations are available in the receiving surface water of the plants. Submitted measured values are generally total concentrations. In order to be able to compare measured and calculated values, total measured values are converted to dissolved values assuming a dissolved fraction of 33% of the total measured Cd concentration. In **Table 3.92** measured and calculated data are presented as dissolved concentrations.

Table 3.92 Measured local Cd concentrations in the effluent receiving water and the local PEC_{water} concentrations for Cd-producing and processing plants in EU

Use-category	Plant N°	Production Emission amount kg year^{-1}	Processing Emission amount kg year^{-1}	$PEClocal_{water}$ calculated µg L^{-1}	Measured µg L^{-1}	Year
NiCd-batteries	1[g]		4.9	0.12	N.A.	1999
	2[a]		7.3	0.15	0.153 (P_{90} downstream of discharge)	2000
	3		30.5	0.15	N.A.	2000
	4		21.9	0.17	N.A.	2000
	5		0.07	0.11	N.A.	1999
	6[b]		No emissions to water (recycled)	N/A	N.A.	1999
	7[c]		No emissions to water (recycled)	N/A	N.A.	1999
Cd recycling[d]	1	0.126		0.16	upstream: 75.9 µg L^{-1}[f] (20 m before emission point) downstream: 85.8 µg L^{-1} (80 m after emission point)	2000
	2[e]	0		N/A	N.A.	1999

N.A. Not available;
N/A Not applicable;
a) Company 2 emits to the marine environment. Measured data from the harbour;
b) All process wastewater is collected and sent to recycling company;
c) Emissions to water from cleaning operations are disposed in alkaline solution and externally recycled;
d) Only two recyclers (instead of three) have been listed under Cd-recyclers. The reason is that one company is both recycler and producer. A further breakdown in the submitted figures between the producing process and the recycling process was not feasible. For this reason this company have been listed with the other producers;
e) No "open" treatment steps; no emissions to air. The wastewater is collected and treated off-site. No further information was available. The sludge from the treatment is land-filled;
f) It should be noted that the river already has high Cd levels (see upstream from discharge) probably due to pollution from old metallic slag heaps;
g) Company stopped NiCd production.

Most of the plants did not have measured data. For plant 2, emitting to the marine environment, measured data were reported. From these data the 90th percentile was taken resulting in a Cd concentration of 0.153 µg L^{-1}which is in accordance with the modelled concentration. Recycling plant 1 reported measured Cd concentrations in surface water upstream and downstream from the plant for several years. Although the cadmium concentration downstream increases significantly it is highly unlikely that this increase is caused by a plant emitting 0.126 kg year^{-1} with an average effluent flow of 5 m^3/day. It is more likely that the elevated cadmium concentrations in the river are due the input from contaminated groundwater and/or run-off water originating from historical metallurgical slag heaps present at the industrial site of the former zinc processing plant. This hypothesis is supported by the increase in zinc concentration in the same order as cadmium, while the recycling plant does not emit zinc.

MSW incinerator: current situation (24.4% incineration)

Since the collection of site-specific data on MSW incinerators was outside the scope of this report a local scenario has been developed for a hypothetical incinerator based on the information provided in **Table 3.25** and **Table 3.33**. On average 25 incinerators are present in one region incinerating 2,794 ktonnes of MSW per year which result in an average capacity of 111,760 tonnes MSW/plant.year. The amount of wastewater generated is of the order of 0.5-2.5 m^3 per tonne of municipal waste incinerated (Williams, 1998). Reimann (2002) reported a water consumption of 1.1 m^3/tonne for the FGCS and 0.25 m^3 per tonne boiler water. Stubenvoll et al. (2002) reported amounts of waste water between 0.3-0.4 m^3/tonne. If it is assumed that an incinerator is in operation for 330 days per year a daily emission between 169 and 846 m^3 can be calculated (111,760 · 2.5 (or 0.5)) /330. Using these two values and assuming a default river flowrate of 18,000 m^3/day (TGD default) a generic dilution factor between 22 (=18,846/846) and 107 (= 18,169/169) can be calculated.

Although it was impossible to gather site-specific information for every incinerator in Europe, for some incinerators site-specific information on type of receiving water and flow rate was available (see **Table 3.93**). The dilution factors provided in this table were calculated using the minimum effluent flow of 169 m^3/ day and the maximum flow rate of 846 m^3/day.

Table 3.93 Calculated site specific dilution factors for some MSW incinerators in the EU

Incinerator	Receiving water	Flow rate m^3 day^{-1}	846 m^3 day^{-1}	169 m^3 day^{-1}
			Dilution factor	
United Kingdom				
Edmonton Incinerator London Waste Ltd	Thames	5,702,400	6,740	33,743
Lewisham Incinerator London	Thames	5,702,400	6,740	33,743
Stoke on Trent Incinerator MES Environmental Ltd	Trent	54,432	64	323
Nottingham Incinerator Waste Recycling Group	Trent	5,814,000	6,872	34,403
France				
Brive	Corrèze	864,000	1,021	5,113
Chartres	Eure	432,000	511	2,557
Toulouse	Garonne	17,280,000	20,426	102,250
Bordeaux	Garonne	60,480,000	71,489	357,871
Pau	Gave de Pau	> 57,888	> 68	344
Orléans	Loire	73,008,000	86,298	432,001
Angers	Maine	11,059,200	13,072	65,440
Chaumont (close to the source)	Marne	17,280	20	103
Créteil	Marne (at mouth in Seine)	4,242,240 – 8,320,320	5,014 – 9,835	25,103 – 49,234
Caen	Orne	2,790,720	3,299	16,514
Maubeuge	Sambre	43,200 – 259,200	51 – 306	257 – 1,534

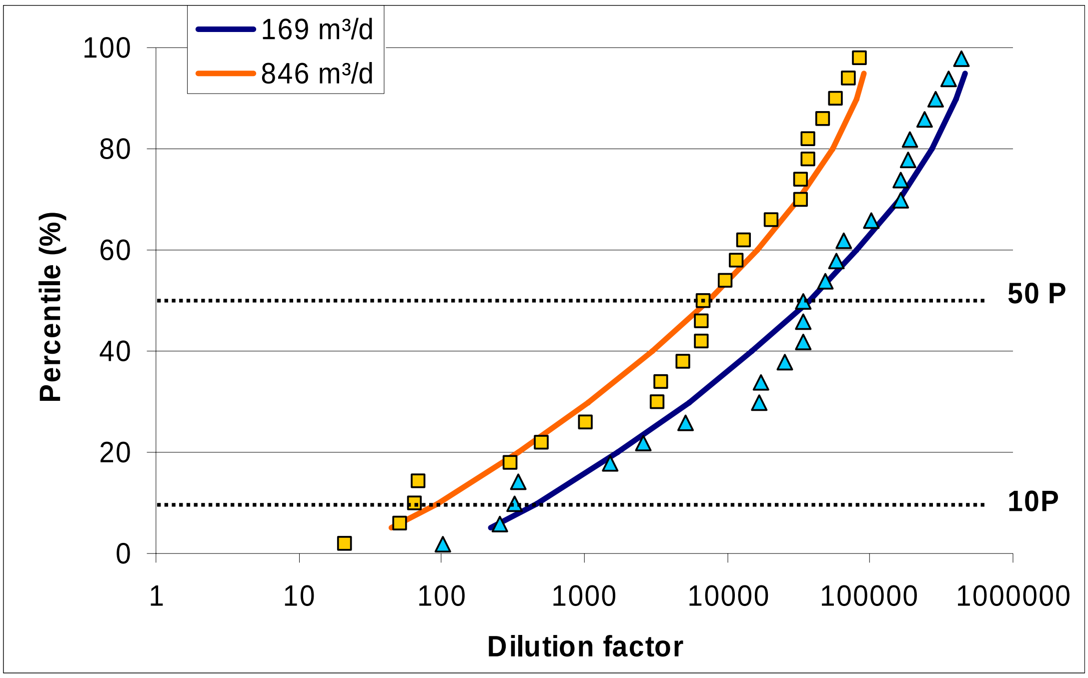
Table 3.93 continued overleaf

Table 3.93 continued Calculated site specific dilution factors for some MSW incinerators in the EU

Incinerator	Receiving water	Flow rate m³ day⁻¹	846 m³ day⁻¹	169 m³ day⁻¹
France				
Strasbourg	Rhine	9,936,000	11,745	58,794
Lyon Sud	Rhone	40,262,400 – 49,334,400	47,591 – 58,315	238,240 – 291,921
Bellegarde	Rhone	31,104,000	36,766	184,048
Lyon Nord	Saone	27,993,600 – 31,795,200	33,089 – 37,583	165,644 – 188,138
Le Mans	Sarthe	2,937,600 (à Spay, 5 km van Le Mans)	3,472	17,383
St. Thibault des Vignes Carrières/S. Guerville Issy les Moul. St Ouen Ivry Argenteuil	Seine	27,648,000	32,681	1 63,599

From the previous table it is clear that a lot of incinerators are discharging their effluents into large rivers frequently resulting in a dilution factor larger than 1,000. In order to obtain both a realistic worst case dilution factor and a typical dilution factor the cumulative distribution function of dilution factors have been elaborated and the 10th percentile and the 50th percentile are taken respectively.

Figure 3.11 Cumulative distribution function of dilution factor based on reported flowrates.



From **Figure 3.11** it can be calculated that the realistic worst case dilution factors (10th P) range between 93 and 459. Typical dilution factors (50th P) range between 7,370 and 36,840.

In order to take this variation in dilution factors over to the risk characterisation phase two scenarios are withheld:

- Realistic worst case dilution factor of 100
- Typical dilution factor of 1,000

As effluent concentration for the local PEC calculations the 90th P value has been chosen of the measured influent concentration and a removal efficiency of 98.8%.

Effluent concentration = 0.47 mg Cd/L (90th influent) · (1-0.988) = 0.0056 mg Cd/L

In Scenario 1 (DF = 100), the amount of waste water generated is 846 m^3/tonnes/day. With an effluent concentration of 0.0056 mg L^{-1}and 330 operating days a yearly load of 1.6 kg can be calculated (846 m^3/day · 330 days/year · 0.0056 mg L^{-1}= 1.6 kg Cd/year). In a similar way the cadmium load associated with 169 m^3 of waste water per day (Scenario 2 with DF = 1,000) can be calculated (169 m^3/day · 330 days/year · 0.0056 mg L^{-1}= 0.3 kg Cd/year).

Table 3.94 Local PEC water (total cadmium) for MSW incineration plants in the EU. Scenario 1: Dilution factor 100. Scenario 2: Dilution factor 1000

	Emission	Ceffluent	Dilution factor[a]	Clocal water	PEClocal water
	kg year^{-1}	mg L^{-1}	-	µg L^{-1}	µg L^{-1}
Scenario 1	10th percentile measured dilution factors				
	1.6	0.0056	100	0.019	0.13
Scenario 2	50th percentile measured dilution factors				
	0.3	0.0056	1,000	0.0019	0.12

a) Dilution in receiving water

The Cd emissions and the calculated PEClocalwater in **Table 3.94** represents the impact of all cadmium containing sources in the MSW and not NiCd batteries only. PEClocal surface water of 0.12 µg L^{-1}(total cadmium) is calculated for a reasonable worst case scenario (90th P Cd concentration) with a typical dilution factor of 1,000. This value is very close to the regional background of 0.11 µg L^{-1}. If the calculations are performed with the realistic worst case dilution factor (i.e. 100) PEClocalwater is 0.13 which is only slightly above the regional PEC value (0.11 µg L^{-1}).

In order to evaluate if having NiCd batteries in the MSW stream or not significantly influences the PEClocalwater values, these PEClocalwaters have been recalculated assuming in the first scenario that NiCd batteries only contributed 10% to the overall cadmium content of the waste and in a second scenario it was assumed that Cd from NiCd batteries accounted for 50 % of the total Cd load observed in MSW (see **Table 3.95**).

Table 3.95 Local PEC water (total cadmium without the NiCd contribution) for MSW incineration plants in the EU. Scenario 1: Dilution factor 100. Scenario 2: Dilution factor 1,000

	Dilution factor Scenario 1	Clocal water	PEClocal water	Dilution factor Scenario 2	Clocal water	PEClocal water
		$\mu g\ L^{-1}$	$\mu g\ L^{-1}$	-	$\mu g\ L^{-1}$	$\mu g\ L^{-1}$
	Assumption NiCd contribution: 10% of the total Cd load					
Scenario 1 & 2	100	0.017	0.13	1,000	0.002	0.11
	Assumption NiCd contribution: 50% of the total Cd load					
Scenario 1 & 2	100	0.009	0.12	1,000	0.0009	0.11

a) Dilution in receiving water

From **Table 3.95** it is clear that removing the NiCd battery fraction from the MSW does not significantly reduce the PEClocal water. This is not surprisingly since on average 95% of the PEClocal water is coming from the regional background concentration, which is 0.11 $\mu g\ L^{-1}$on a calculated basis.

MSW incinerator scenario sensitivity analysis (effluent concentration = 0.009 mg L^{-1})

As part of the sensitivity analysis (see subsection “Sensitivity analysis” under Section 3.1.2.2.5) a scenario of a incinerator with a effluent concentration of 0.009 mg L^{-1}(derived from the maximum reported influent concentration of 0.76 mg $L^{-1}$and assuming a removal efficiency of 98.8%) is included (see **Table 3.96**).

Effluent concentration = 0.76 mg Cd/L (max con. influent) · (1-0.988) = 0.009 mg Cd/L

In scenario 1 (DF = 100), the amount of waste water generated is 846 m^3/tonnes/day With an effluent concentration of 0.009 mg $L^{-1}$and 330 operating days a yearly load of 2.5 kg can be calculated (846 m^3/day · 330 days/year · 0.009 mg L^{-1}= 2.5 kg Cd/year). In a similar way the cadmium load associated with 169 m^3 of waste water per day (Scenario 2 with DF = 1,000) can be calculated (169 m^3/day · 330 days/year · 0.009 mg L^{-1}= 0.5 kg Cd/year).

Table 3.96 Local PEC water (total cadmium) for MSW incineration plants in the EU

	Emission	Ceffluent	Dilution factor[a]	Clocal water	PEClocal water
	kg $year^{-1}$	mg L^{-1}	-	$\mu g\ L^{-1}$	$\mu g\ L^{-1}$
Scenario 1	10^{th} percentile measured dilution factors				
	2.5	0.009	100	0.03	0.14
Scenario 2	50^{th} percentile measured dilution factors				
	0.5	0.009	1,000	0.003	0.12

a) Dilution in receiving water

PEClocal surface water of 0.12 $\mu g\ L^{-1}$(total cadmium) is calculated for a worst case scenario (max Cd concentration) with a typical dilution factor of 1,000. This value is very close to the regional background of 0.11 $\mu g\ L^{-1}$. If the calculations are performed with the realistic worst case dilution factor (i.e. 100) PEClocalwater is 0.14 which is only slightly above the regional PEC value (0.11 $\mu g\ L^{-1}$), MSW incinerator: future situation (100% incineration)

In a similar way the cadmium emission to surface water from future incinerators can be calculated. The assumption has been made that due to expected higher cadmium content in the MSW a higher effluent concentration is expected to occur (this is the case if the removal efficiency will be kept at 98.8%). For the two future scenarios the following effluent concentrations have been used to perform the calculations (based on **Table 3.37**):

- For the scenario with 10% batteries' collection efficiency the following overall cadmium effluent concentration has been used: 0.0135 mg Cd/L (= 1.13 · 0.012)
- For the scenario with 75% collection efficiency the following overall cadmium effluent concentration has been used: 0.007 mg Cd/L (= 0.62 · 0.012)

In Scenario 1 (DF = 100) for the 10% collection scenario, the amount of waste water generated is 846 m^3/tonnes/day With an effluent concentration of 0.0135 mg $L^{-1}$and 330 operating days a yearly load of 3.75 kg can be calculated (846 m^3/day · 330 days/year · 0.0135 mg L^{-1}= 3.75 kg Cd/year). In a similar way the cadmium load associated with 169 m^3 of waste water per day (Scenario 2 with DF = 1,000) can be calculated (169 m^3/day · 330 days/year · 0.0135 mg L^{-1}= 0.75 kg Cd/year).

In Scenario 1 (DF = 100) for the 75% collection scenario, the amount of waste water generated is 846 m^3/tonnes/day. With an effluent concentration of 0.007 mg $L^{-1}$and 330 operating days a yearly load of 1.9 kg can be calculated (846 m^3/day · 330 days/year · 0.007 mg L^{-1}= 1.9 kg Cd/year). In a similar way the cadmium load associated with 169 m^3 of waste water per day (Scenario 2 with DF = 1,000) can be calculated (169 m^3/day · 330 days/year · 0.007 mg L^{-1}= 0.4 kg Cd/year).

Table 3.97 Local PECwater for MSW incineration plants in the EU. Future scenarios: collection rate: 10% and 75% (total cadmium concentrations). Dilution Scenario 1: Dilution factor 100. Dilution Scenario 2: Dilution factor 1000

Use category	Emission	Ceffluent	Dilution factor[a]	Clocal water	PEClocalwater
MSW Incineration plant	kg/y	mg L^{-1}	-	µg L^{-1}	µg L^{-1}
10% collection Dilution Scenario 1	3.75	0.0135	100	0.045	0.16
10% collection Dilution Scenario 2	0.75	0.0135	1,000	0.0045	0.12
75% collection Dilution Scenario 1	1.9	0.007	100	0.023	0.14
75% collection Dilution Scenario 2	0.4	0.007	1,000	0.0023	0.12

a) Dilution in receiving water

A PEClocal surface water[28] of 0.12 µg L^{-1}(total cadmium) under a collection scenario of 10% and 75% is calculated for a scenario in which a dilution factor of 1,000 is relevant. For the

[28] PEC reg, water, future = PEC reg, water, current. Indeed, the effect of an increase in MSW cadmium content up to 24 mg kg^{-1} $_{dry\ wt.}$ ('future' scenarios) will have only a minor influence on the currently derived PECs regional for air, water and soil (cfr EUSES outprints in Annex V). Therefore there is no need to revise the current PEC reg, water and the PEC reg, air in order to derive the PEC values for the future situation.

realistic worst case (DF = 100) PEC local water varies between 0.14 and 0.16 µg $L^{-1}$for the respective scenarios of 75% collection and 10% collection.

In case the NiCd batteries would be completely removed from the MSW stream (for the 10% collection scenario the contribution of NiCd batteries is 63% and for the 75% collection scenario a contribution of 32% is assumed) similar PEClocal water values as presented in **Table 3.89**, for the assumption that NiCd batteries contributed in the current situation only 10% of the total cadmium load, are obtained.

Landfill current situation (leachate concentration = 5 µg L^{-1})

In the following paragraph the results from the local exposure assessment for a generic landfill (life cycle stage 5: disposal; landfills **Table 3.50**) are presented. Since the collection of site specific data on landfills was out of the scope of this report, local PEC values have been calculated for two hypothetical sites:

- Scenario 1: a landfill where the collected landfill leachate is discharged directly in the surface water
- Scenario 2: a landfill where the collected landfill leachate is discharged into a municipal STP before going into the surface water

The contamination of the groundwater compartment (PEC groundwater, added) due to fugitive emissions of landfills has not been quantified on a local scale in this report since no guidance is available to perform these calculations.

In the case of Scenario 1 (direct discharge to surface water) a generic dilution factor can be calculated from the leachate volume generated daily (100 m^3/day, see subsection "Overall cadmium emissions from landfilling MSW" under Section 3.1.2.2.5) and the default flowing rate of a river being 18,000 m^3/day resulting in a dilution factor of 180.

In Scenario 2 the landfill leachate is discharged in the public sewer system (STP). These discharges will undergo a dilution step in the STP. The corresponding dilution factor is calculated based on the landfill effluent flow rate and a default sewage flow of 2,000 m^3/day. In addition to the dilution factor the cadmium removal efficiency of the STP has to be taken into account. According to CBS (2002) a removal efficiency of 60% can be used for STP's. Finally the effluent of the STP is diluted in the receiving water. For the latter a default dilution factor of 10 can be used (based on a default flow rate of the receiving surface water of 18,000 m^3/day and a default effluent flow of the STP of 2,000 m^3). The results of the calculations are presented in **Table 3.98**.

Table 3.98 Local PEC water for MSW landfills emitting directly to the surface water (Scenario 1) or indirectly through a STP (Scenario 2). Cadmium leachate concentration is 5 µg L^{-1}. Comparison of both scenarios

Input	Scenario 1	Scenario 2
Effluent Flow (m^3/d)	100	100
Conc. effluent (µg L^{-1})	5	5
Size of STP (m^3/d)	N/A	2,000
Removal of cadmium in STP (%)	N/A	60
Flow rate receiving water (m^3/d)	18,000	18,000

Table 3.98 continued overleaf

Table 3.98 continued Local PEC water for MSW landfills emitting directly to the surface water (Scenario 1) or indirectly through a STP (Scenario 2). Cadmium leachate concentration is 5 µg L^{-1}. Comparison of both scenarios

Input	Scenario 1	Scenario 2
Dilution factor from STP to river	N/A	10
Output		
Calculated dilution factor in STP	N/A	21
Calculated conc. effluent STP (µg L^{-1})	N/A	0.095
Calculated generic dilution factor in receiving water	180	10
Clocal water generic (µg L^{-1})	0.009	0.003
PEClocal water generic	0.12	0.12

N/A Not applicable.

Table 3.99 Local PEC water for MSW landfills emitting directly to the surface water (scenario 1) or indirectly through a STP (scenario 2: STP). Cadmium leachate concentration is 5 µg L^{-1}. Total cadmium concentrations

Use category	Ceffluent	Dilution factor[a]	Clocal water	PEClocalwater
	mg L^{-1}	-	µg L^{-1}	µg L^{-1}
Scenario 1 (direct discharge, no STP)				
MSW Landfill (total cadmium)	0.005	180	0.009	0.12
Scenario 2 (STP)				
MSW Landfill (total cadmium)	0.005	10	0.003	0.12

a) Dilution in receiving water

A PEClocal surface water of 0.12 (total cadmium) is calculated for both scenarios which is only slightly above the regional PEC (= 0.11 µg L^{-1}).

In case all NiCd batteries would be removed from the MSW the influence on the PEClocal water would be negligible (see **Table 3.100**).

Table 3.100 Local PEC water for MSW landfills emitting directly to the surface water (Scenario 1) or indirectly through a STP (Scenario 2: STP). Cadmium leachate concentration is 5 µg L^{-1}. Total cadmium without the NiCd contribution

Use category	Ceffluent	Dilution factor[a]	Clocal water	PEClocalwater
	mg L^{-1}	-	µg L^{-1}	µg L^{-1}
Scenario 1 (direct discharge, no STP)				
MSW Landfill (NiCd batteries contributed for 10%)	0.0045	180	0.008	0.12
MSW Landfill (NiCd batteries contributed for 50%)	0.003	180	0.005	0.12

Table 3.100 continued overleaf

Table 3.100 continued Local PEC water for MSW landfills emitting directly to the surface water (Scenario 1) or indirectly through a STP (Scenario 2: STP). Cadmium leachate concentration is 5 µg L^{-1}. Total cadmium without the NiCd contribution

Scenario 2 (STP)				
MSW Landfill (NiCd batteries contributed for 10%)	0.0045	10	0.003	0.12
MSW Landfill (NiCd batteries contributed for 50%)	0.003	10	0.002	0.12

a) Dilution in receiving water.

<u>Landfill scenario sensitivity analysis (leachate concentration = 50 µg L^{-1})</u>

As part of the sensitivity analysis (see subsection "Sensitivity analysis" under Section 3.1.2.2.5) a scenario of a landfill with a leachate concentration of 50 µg $L^{-1}$is included. As is the case in the previous paragraph both a landfill with and without a STP is being considered.

Table 3.101 Local PEC water for landfills emitting directly to the surface water (scenario 1) or indirectly through a STP (Scenario 2). Cadmium leachate concentration is 50 µg L^{-1}

Input	Scenario 1	Scenario 2
Effluent Flow (m^3/d)	100	100
Conc. effluent (µg L^{-1})	50	50
Size of STP (m^3/day)	N/A	2,000
Removal of cadmium in STP (%)	N/A	60
Flow rate receiving water (m^3/day)	18,000	18,000
Dilution factor from STP to river	N/A	10
Output		
Calculated dilution factor in STP	N/A	21
Calculated conc. effluent STP (µg L^{-1})	N/A	0.95
Calculated generic dilution factor in receiving water	180	10
Clocal water generic (µg L^{-1})	0.094	0.032
PEClocal water generic	0.21	0.15

N/A Not applicable.

Table 3.102 Local PECwater for MSW landfills emitting directly to the surface water (Scenario 1) or indirectly through a STP (Scenario 2). Cadmium leachate concentration is 50 µg L^{-1}. Total cadmium concentrations

Use category	Cleachate	Dilution factor[a]	Clocal water	PEClocalwater
	mg L^{-1}	-	µg L^{-1}	µg L^{-1}
Scenario 1 (direct discharge, no STP)				
MSW Landfill (total cadmium)	0.05	180	0.094	0.21
Scenario 2 (STP)				
MSW Landfill (total cadmium)	0.05	10	0.032	0.15

a) Dilution in receiving water

A PEClocal surface water of 0.21µg L^{-1}(total cadmium) is calculated for landfill sites that discharge directly in surface water. In case the landfill discharged to a STP an overall PEC of 0.15 µg $L^{-1}$is obtained.

In case all NiCd batteries would be removed from the MSW the influence on the PEClocal water would be negligible at the exception of the case where NiCd batteries as to their Cd content contribute to 50% of the MSW (see **Table 3.103**). In the latter case, direct discharge of leachate from MSW landfills would no longer result in risk (see **Table 3.266**).

Table 3.103 Local PECwater for MSW landfills emitting directly to the surface water (Scenario 1) or indirectly through a STP (Scenario 2). Cadmium leachate concentration is 50 µg L^{-1}. Total cadmium without the NiCd contribution

Use category	Cleachate	Dilution factor[a]	Clocal water	PEClocalwater
	mg L^{-1}	-	µg L^{-1}	µg L^{-1}
Scenario 1 (direct discharge, no STP)				
MSW Landfill (NiCd batteries contributed for 10%)	0.045	180	0.085	0.20
MSW (NiCd batteries contributed for 50%)	0.025	180	0.047	0.16
Scenario 2 (STP)				
MSW Landfill (NiCd batteries contributed for 10%)	0.045	10	0.028	0.14
MSW Landfill MSW (NiCd batteries contributed for 50%)	0.025	10	0.016	0.13

a) Dilution in receiving water.

3.1.3.2.2 Sediment compartment

The $PEClocal_{sediment}$ is calculated according to the formula presented below (see Section 3.1.3.1.2):

$$PEClocal_{sediment} = PECregional_{sediment} + K_p\ Clocal_{\ water}.\ 10^{-3}$$

in which the K_p (L $kg^{-1}{}_{dw}$) equals the solid- water partition coefficient of suspended matter (Kp = 130,000 L $kg^{-1}{}_{dw}$).

The measured PEC regional as mentioned in Section 3.1.3.4.3 is taken as an average of 90^{th} percentiles of different surveys (Flanders, France, The Netherlands, Spain and Sweden) and is 2.66 mg $kg^{-1}{}_{dry\ wt.}$ (see **Table 3.189**). This value represents a realistic worst case for the EU ambient Cd concentrations in sediment (natural Cd + historical Cd) and is used as the PECregional in the risk characterisation.

The local $PEC_{sediment}$ are readily calculated from the data in **Table 3.90** and the aforementioned equation and presented in **Table 3.104**. The $Clocal_{sediment}$ (K_p Clocal $_{water}$. 10^{-3}) is included to illustrate the contribution of the local discharge onto the sediment PEC.

The local $PEC_{sediment}$ range from 2.66 (i.e. the PECregional) to 10.46 mg $kg^{-1}{}_{dry\ wt.}$ for NiCd batteries-producing plants and is 22.6 mg $kg^{-1}{}_{dry\ wt.}$ for one Cd-recycling plant. Local sediment concentrations calculated for plants 2, 3 and recycler 1 are on the basis of the maximum dilution factor of 1,000.

Table 3.104 Local PECsediment for NiCd batteries producing plants and Cd recycling plants in the EU (without correction for bioavailability)

Use category	N°	Production emission	Processing emission	Clocal sediment D=1,000 or site specific	PEClocalsediment D=1,000 or site specific	Year
NiCd batteries		kg $year^{-1}$	kg $year^{-1}$	mg kg^{-1} dry wt	mg kg^{-1} $_{dry\ wt.}$	
	1		4.9	0.5	3.16	1999
	2[a]		7.3	5.3	7.96	2000
	3		30.5	5.3	7.96	2000
	4		21.9	7.8	10.46	2000
	5		0.07	0.003	2.66	1999
	6[b]		No emissions to water (recycled)	N/A	N/A	1999
	7[c]		No emissions to water (recycled)	N.A	N/A	1999
Cd recyclers[d]	1	0.126		19.9	22.6	2000
	2[e]	0		N/A	N/A	1999

N.A. Not available;
N/A Not applicable;
a) Company 2 emits to the marine environment;
b) All process wastewater is collected and sent to recycling company;
c) Emissions to water from cleaning operations are disposed in alkaline solution and externally recycled;
d) Only two recyclers (instead of three) have been listed under Cd-recyclers. The reason is that one company is both recycler and producer. A further breakdown in the submitted figures between the producing process and the recycling process was not feasible. For this reason this company have been listed with the other producers;
e) No “open” treatment steps; no emissions to air. The wastewater is collected and treated off-site. No further information was available. The sludge from the treatment is land-filled.

MSW incinerator: current situation

The local PEC sediment was calculated for two scenarios (dilution factor 100 and 1,000) (see **Table 3.105**)

Table 3.105 Local PECsediment for MSW incineration plants in the EU (without correction for bioavailability)

	Emission	Dilution factor[a]	Clocal water	Clocal sediment	PEClocal sediment
	kg $year^{-1}$		µg L^{-1}	mg kg^{-1} $_{dry\ wt.}$	mg kg^{-1} $_{dry\ wt.}$
Scenario 1	10^{th} percentile measured dilution factors				
	1.6	100	0.019	2.53	5.19
Scenario 2	50^{th} percentile measured dilution factors				
	0.3	1,000	0.0019	0.25	2.91

a) Dilution in receiving water

The Cd emissions and the calculated PEClocal sediment in **Table 3.105** represent the impact of all cadmium containing sources in the MSW and not NiCd batteries only. PEClocal sediment value of 2.91 mg kg^{-1}. dry wt (total cadmium) is calculated for the typical scenario (dilution factor of 1,000) which is very close to the regional background of 2.66 mg kg^{-1} $_{dry\ wt.}$ If the calculations are performed with the realistic worst case dilution factor (i.e. 100) PEClocal sediment is 5.19 mg kg^{-1} $_{dry\ wt.}$

Similar to the aquatic compartment the PEClocalsediment has also been calculated for the assumption that all NiCd batteries would be removed from the MSW waste stream (see **Table 3.106**).

Table 3.106 Local PEC sediment (total cadmium without the NiCd contribution) for MSW incineration plants in the EU (without correction for bioavailability). Scenario 1: dilution factor 100. Scenario 2: dilution factor 1000

	Dilution factor[a]	Clocal sediment	PEClocal sediment	Dilution factor[a]	Clocal sediment	PEClocal sediment
		mg kg^{-1} dry wt.	mg kg^{-1} dry wt.	-	mg kg^{-1} dry wt.	mg kg^{-1} dry wt.
	Assumption NiCd contribution: 10% of the total Cd load					
Scenario 1&2	100	2.21	4.87	1,000	0.03	2.69
	Assumption NiCd contribution: 50% of the total Cd load					
Scenario 1&2	100	1.17	3.93	1,000	0.13	2.79

a) Dilution in receiving water

From **Table 3.106** it is clear that removing the NiCd battery fraction from the MSW does not have a large impact on the calculated PEC sediment values. For those scenarios with a dilution factor of 1,000 the cadmium sediment concentrations are similar (2.69-2.79). If a dilution factor of 100 is applied the calculated sediment concentration is only slightly lower (3.93 versus 4.87) when it is assumed that NiCd batteries contribute for 50% of the total cadmium load.

<u>MSW incinerator scenario sensitivity analysis (effluent concentration = 0.009 mg L^{-1})</u>

The local PEC sediment was also calculated for the scenario developed with the maximum effluent concentration (i.e. 0.009 mg L^{-1}) (see **Table 3.107**) as part of the sensitivity analysis.

Table 3.107 Local PECsediment (without correction for bioavailability) for MSW incineration plants in the EU

	Emission	Dilution factor[a]	Clocal water	Clocal sediment	PEClocal sediment
	kg year^{-1}		µg L^{-1}	mg kg^{-1} dry wt.	mg kg^{-1} dry wt.
<u>Scenario 1</u>	10th percentile measured dilution factors				
	2.5	100	0.03	3.95	6.6
<u>Scenario 2</u>	50th percentile measured dilution factors				
	0.5	1,000	0.003	0.39	3.1

a) Dilution in receiving water

PEClocal sediment value of 3.1 mg kg^{-1}. dry wt (total cadmium) is calculated for the typical scenario (dilution factor of 1,000) which is very close to the regional background of 2.66 mg kg^{-1} $_{\text{dry wt.}}$ If the calculations are performed with the realistic worst case dilution factor (i.e. 100) PEClocal sediment is 6.6 mg kg^{-1} $_{\text{dry wt.}}$

MSW incinerator: future situation

Table 3.108 Local $PEC_{sediment}$ (without correction for bioavailability) for a generic MSW incineration plant in the EU. Future scenarios: collection rate: 10 and 75%. Total cadmium concentrations. Dilution Scenario 1: Dilution factor 100. Dilution Scenario 2: Dilution factor 1,000

Use category	Emission	Dilution factor[a]	Clocal water	Clocal sediment	PEClocal sediment
MSW Incineration plant	kg/y	-	µg L^{-1}	mg kg^{-1} dry wt	mg kg^{-1}.dry wt
10% collection Dilution Scenario 1	3.75	100	0.0455	5.9	8.6
10% collection Dilution Scenario 2	0.75	1,000	0.0046	0.6	3.3
75% collection Dilution Scenario 1	1.9	100	0.023	4.2	6.8
75% collection Dilution Scenario 2	0.4	1,000	0.0023	0.3	3.0

a) Dilution in receiving water

The results from the local exposure assessment for MSW incineration plants predict a PEClocal sediment of 3.0-3.3 mg kg^{-1} $_{dry\ wt.}$ (total cadmium) for the different future scenarios (collection rate: 75% and 10% respectively) if a dilution factor of 1,000 is relevant. In case only a dilution factor of 100 can be applied PEClocal sediment varies between 6.8 and 8.6 mg $kg^{-1}$$_{dry\ wt.}$

In case the NiCd batteries would be completely removed from the MSW stream (for the 10% collection scenario the contribution of NiCd batteries is 63% and for the 75% collection scenario a contribution of 32% is assumed) similar PEClocal sediment values as presented in **Table 3.106**, for the assumption that NiCd batteries contributed in the current situation only 10% of the total cadmium load, are obtained.

Landfill current situation

Table 3.109 Local PEC sediment (without correction for bioavailability) for MSW landfills emitting directly to the surface water (Scenario 1) or indirectly through a STP (Scenario 2: STP). Cadmium leachate concentration is 5 µg L^{-1}

Use category	Dilution factor[a]	Clocal water	Clocal sediment	PEClocal sediment
	-		mg kg^{-1} $_{dry\ wt.}$	mg kg^{-1} $_{dry\ wt.}$
Scenario 1 (direct discharge, no STP) MSW Landfill (total cadmium)	180	0.009	1.17	3.8
Scenario 2 (STP) MSW Landfill (total cadmium)	10	0.003	0.39	3.1

a) Dilution in receiving water.

The results from the local exposure assessment for MSW landfills show a PEClocal sediment of 3.1 mg kg^{-1}.$_{dry\ wt.}$ (total cadmium) if the leachate is sent to an STP and 3.8 mg kg^{-1} $_{dry\ wt.}$ if there is no STP.

In case all NiCd batteries would be removed from the MSW the influence on the PEClocal sediment would be negligible (see **Table 3.110**).

Table 3.110 Local PEC sediment (without correction for bioavailability) for MSW landfills emitting directly to the surface water (scenario 1) or indirectly through a STP (scenario 2: STP). Cadmium leachate concentration is 5 µg L^{-1}. Total cadmium without the NiCd contribution

Use category	Dilution factor[a]	Clocal water	Clocal sediment	PEClocal sediment
	-	µg L^{-1}	mg kg^{-1} dry wt	mg kg^{-1} dry wt
Scenario 1 (direct discharge, no STP)				
MSW Landfill (NiCd batteries contributed for 10%)	180	0.008	1	3.7
MSW Landfill (NiCd batteries contributed for 50%)	180	0.005	0.65	3.3
Scenario 2 (STP)				
MSW Landfill (NiCd batteries contributed for 10%)	10	0.003	0.39	3.1
MSW Landfill (NiCd batteries contributed for 50%)	10	0.002	0.26	2.9

a) Dilution in receiving water.

Landfill scenario sensitivity analysis (leachate concentration = 50 µg L^{-1})

As part of the sensitivity analysis (see subsection "Sensitivity analysis" under Section 3.1.2.2.5) a scenario of a landfill with a leachate concentration of 50 µg $L^{-1}$is included. As is the case in the previous paragraph both a landfill with and without a STP is being considered.

Table 3.111 Local $PEC_{sediment}$ (without correction for bioavailability) for MSW landfills emitting directly to the surface water (Scenario 1) or indirectly through a STP (Scenario 2). Cadmium leachate concentration is 50 µg L^{-1}. Total cadmium

Use category	Dilution factor[a]	Clocal water	Clocal sediment	PEClocal sediment
	-	µg L^{-1}	mg kg^{-1} $_{dry\ wt.}$	mg kg^{-1} $_{dry\ wt.}$
Scenario 1 (direct discharge, no STP) MSW Landfill (total cadmium)	180	0.094	12.2	14.9
Scenario 2 (STP) MSW Landfill (total cadmium)	10	0.032	4.2	6.8

a) Dilution in receiving water.

The results from the local exposure assessment for MSW landfills with a leachate concentration of 50 µg Cd/L show a PEClocal sediment of 6.8 mg kg^{-1} $_{dry\ wt.}$ (all waste) if the leachate is sent to an STP and 14.9 mg $kg^{-1}$$_{dry\ wt.}$ if there is no STP.

Table 3.112 Local PEC sediment (without correction for bioavailability) for MSW landfills emitting directly to the surface water (Scenario 1) or indirectly through a STP (Scenario 2: STP). Cadmium leachate concentration is 50 µg L^{-1}. All cadmium without the NiCd contribution

Use category	Dilution factor[a]	Clocal water	Clocal sediment	PEClocal sediment
	-	µg L^{-1}	mg kg^{-1} dry wt	mg kg^{-1} dry wt
Scenario 1 (direct discharge, no STP)				
MSW Landfill (NiCd batteries contributed for 10%)	180	0.085	11.1	13.7
MSW Landfill (NiCd batteries contributed for 50%)	180	0.047	6.1	8.8
Scenario 2 (STP)				
MSW Landfill (NiCd batteries contributed for 10%)	10	0.028	3.6	6.3
MSW Landfill (NiCd batteries contributed for 50%)	10	0.016	2.1	4.7

a) Dilution in receiving water.

For the scenario with a direct discharge of a leachate cadmium concentration of 50 µg $L^{-1}$the PEClocal sediment originating from cadmium emitting sources other than NiCd batteries is predicted to range between 8.8 and 13.7 mg kg^{-1} $_{\text{dry wt.}}$ If the landfill leachate is sent to an STP for treatment the local sediment concentrations range between 4.7-6.3 mg kg^{-1} $_{\text{dry wt.}}$

3.1.3.2.3 Atmospheric compartment

Calculated local concentrations

Local PEC-values for the atmospheric compartment are calculated according to the OPS model proposed in the TGD (1996) for a general standard environment (see Section 3.1.3.1.3).

Input data are the total daily emissions of the individual NiCd batteries-producing plants and Cd recycling plants (Industry questionnaires 1999/2000). The calculated concentrations in air are actual contributions to the receiving atmosphere. The local PEC values are obtained by adding the regional PEC values for air to the calculated local concentration in the atmosphere.

$$PEClocal_{air} = Clocal_{air} + PECregional_{air}$$

$PEClocal_{air}$: predicted environmental concentration in air during emission episode (ng/m^3)
$Clocal_{air}$: local concentration in the air during emission episode (ng/m^3)
$PECregional_{air}$: regional concentration in the air (0.561 ng/m^3)

The results of the predicted local atmospheric Cd concentrations at 100 m from the point sources are listed in **Table 3.113** Reported data are based on new emission data from Industry Questionnaire, 2000/2001. Calculated local PEC values range from 0.561 to 22.6 ng/m^3 for NiCd batteries producers and from 0.561 to 1.91 ng/m^3 for Cd recycling plants. It should be noted that for producing company 1 and 3 it was stated that emissions to air were negligible and mainly through effluents. Recycler 2 also declared that there are no “open treatment” steps in its procedure, so there are no stack emissions to air.

Table 3.113 Calculated local PECair concentrations for NiCd batteries producing plants and Cd recycling plants in the EU

Use category	Plant n°	Production emission amount (kg/y)	Processing emission amount (kg/y)	Number of emission days (d)	Annual average air concentration (100 m) ng/m³	PEClocal air (100 m) ng/m³	Year
NiCd batteries							
	1		N.A.	225	N.A.	0.561	1999
	2[a]		1.6	330	1.22	1.78	2000
	3[b]		N.A.	315	N.A.	0.561	2000
	4		13.5	330	10.28	10.9	2000
	5		7	230	5.3	5.9	1999
	6		0.036	250	0.03	0.64	1999
	7		28.99	300	22.1	22.64	1999
Cd recyclers[c]							
	1	1.77		350	1.35	1.91	2000
	2 [d]	0		240	0	0.561	1999
Total			> 53				

N.A. Not available;
a) Company 2 emits to the marine environment;
b) Wet processes. Mainly emissions to effluents;
c) Only two recyclers (instead of three) have been listed under Cd-recyclers. The reason is that one company is both recycler and producer. A further breakdown in the submitted figures between the producing process and the recycling process was not feasible. For this reason this company have been listed with the other producers;
d) No "open" treatment steps; no emissions to air.

Measured local concentrations

Measured atmospheric concentrations in the surroundings of the production-sites are scarce and are presented in **Table 3.114**.

From this table it can be concluded that the measured data at a distance of 100 m from the point source for plant 4 and plant 6 are in the same order of magnitude as the calculated data (4 ng/m^3 versus 10.9 ng/m^3 and 0.7 ng/m^3 versus 0.64 ng/m^3).

Table 3.114 Calculated and measured local PEC_{air} concentrations for NiCd producing and Cd recycling plants in EU

Use-category	N°	Production emission amount kg year^{-1}	Processing emission amount kg /$^{-1}$	$PEClocal_{air}$ (100 m) ng/m³	Measured ann.avg. air concentration ng/m³	Year
NiCd-batteries	1		N.A.	0.56	N.A.	1999
	2[a]		1.6	1.78	N.A	2000
	3[b]		N.A.	0.56	N.A.	2000
	4		13.5	10.9	4 (100 m from plant)	2000
	5		7	5.9	N.A.	1999
	6		0.036	0.64	0.7 (0.2-2.5) (100 m from plant)	1999
	7		28.99	22.64	N.A.	1999

Table 3.114 continued overleaf

Table 3.114 continued Calculated and measured local PEC_{air} concentrations for NiCd producing and Cd recycling plants in EU

Use-category	N°	Production emission amount kg year^{-1}	Processing emission amount kg /$^{-1}$	$PEClocal_{air}$ (100 m) ng/m^3	Measured ann.avg. air concentration ng/m^3	Year
Cd recycling[c]	1	1.77		1.91	N.A.	2000
	2[d]	0		0.56	N.A.	1999

N.A. Not available;
a) Company 2 emits to the marine environment;
b) Wet processes. Mainly emissions to effluents;
c) Only two recyclers (instead of three) have been listed under Cd-recyclers. The reason is that one company is both recycler and producer. A further breakdown in the submitted figures between the producing process and the recycling process was not feasible. For this reason this company have been listed with the other producers;
d) No "open" treatment steps; no emissions to air.

MSW incinerator: current situation

In the following section the results from the local exposure assessment for MSW incineration plants (life cycle stage 5: disposal; incineration) is presented. The local air emission for incineration plants is calculated using an allocation key based on the number of incinerators in each country and the country specific air emission amounts. The results presented below are based on emission data for incineration scenario 24.4% only (realistic case); it is assumed that for incineration scenario 100% (worst case), taking into account a proportional increase in incineration plants over Europe, analogous results can be expected.

Table 3.115 Calculated local PECair concentration for MSW incineration plant in the EU. Current situation. Total cadmium concentrations

Country	Emission amount	Number of emissions days	Annual average air concentration (100 m)	PEClocal air (100m)
	kg year^{-1}	days	ng/m^3	ng/m^3
Austria	1.4[c]	330	1.07	1.63
Belgium	3.5	330	2.7	3.2
Denmark	9.7	330	7.4	8.0
Finland	14	330	10.7	11.2
France[a]	16.4	330	12.5	13.1
France[b]	36.7	330	27.95	28.5
Germany	5	330	3.8	4.4
Italy	5.7	330	4.3	4.9
Luxembourg	22	330	16.8	17.3
The Netherlands	4.8	330	3.7	4..2
Norway	5.1	330	3.9	4.5
Portugal	1.6	330	1.2	1.8
Spain	6.8	330	5.2	5.7

Table 3.115 continued overleaf

Table 3.115 continued Calculated local PECair concentration for MSW incineration plant in the EU. Current situation. Total cadmium concentrations

Country	Emission amount	Number of emissions days	Annual average air concentration (100 m)	PEClocal air (100m)
	kg $year^{-1}$	days	ng/m^3	ng/m^3
Sweden	0.2	330	0.2	0.7
UK	1.5	330	1.1	1.7
EU 10% scenario	9.1	330	6.9	7.5

a) Generic scenario;
b) Based on P90 measured data;
c) According to the latest information (Stubenvoll et al., 2002) total Cd emissions in Austria from incinerators amount to 4.2 kg. Since there is a total of 3 plants, on average, 1.4 kg per plant is emitted.

From this table it can be concluded that the PEClocal in air at a distance of 100 m from the point source of the incineration plant range between 0.7 and 28.5 ng/m^3 (7.5 ng/m^3 for the average EU situation). It should be noted that this concentration is valid for all MSW incinerated (not exclusively batteries). The influence of removing the NiCd batteries on the overall emissions is given in **Table 3.116**.

Table 3.116 Calculated local PECair concentration for MSW incineration plant in the EU). Current situation. Total cadmium without the NiCd contribution

Country	Emission amount	Number of emissions days	Annual average air concentration (100 m)	PEClocal air (100m)
	kg $year^{-1}$	days	ng/m^3	ng/m^3
	Assumption NiCd contribution: 10% of the total Cd load			
Austria	1.26	330	1.0	1.5
Belgium	3.2	330	2.4	3.0
Denmark	8.7	330	6.3	7.2
Finland	12.6	330	9.6	10.2
France[a]	14.7	330	11.2	11.8
France[b]	33	330	25.1	25.7
Germany	4.5	330	3.4	4.0
Italy	5.1	330	3.9	4.5
Luxembourg	19.8	330	15.1	15.6
The Netherlands	4.3	330	3.3	3.8
Norway	4.6	330	3.5	4.1
Portugal	1.4	330	1.1	1.6
Spain	6.1	330	4.7	5.2
Sweden	0.18	330	0.14	0.7
UK	1.4	330	1.1	1.6
EU 10% scenario	8.2	330	6.3	6.8

Table 3.116 continued overleaf

Table 3.116 continued Calculated local PECair concentration for MSW incineration plant in the EU). Current situation. Total cadmium without the NiCd contribution

Country	Emission amount	Number of emissions days	Annual average air concentration (100 m)	PEClocal air (100m)
	kg year^{-1}	days	ng/m^3	ng/m^3
	Assumption NiCd contribution: 50% of the total Cd load			
Austria	0.7	330	1.07	1.63
Belgium	1.8	330	1.4	1.9
Denmark	4.9	330	3.7	4.2
Finland	7	330	5.4	5.9
France[a]	8.3	330	6.3	6.8
France[b]	18.4	330	14	14.6
Germany	2.5	330	1.9	2.4
Italy	2.9	330	2.2	2.7
Luxembourg	11	330	8.4	8.9
The Netherlands	2.4	330	1.9	2.4
Norway	2.5	330	2.0	2.5
Portugal	0.8	330	0.6	1.1
Spain	3.4	330	2.6	3.1
Sweden	0.1	330	0.1	0.6
UK	0.8	330	0.6	1.1
EU 10% scenario	4.5	330	3.5	4.0

a) Generic scenario;
b) Based on P90 measured data.

Removing the contribution from NiCd batteries to the MSW (10-50%), PEC local in air range between 0.6 and 25.7 ng/m^3.

For the future[44] and the 100% incineration scenarios it is assumed that the number of incineration plants is proportionally increased to the amount of MSW to incinerate. And since higher local air emissions due to higher cadmium content of the MSW are not expected to occur when the FGCS are working well (shift of the cadmium to incineration residues) **Table 3.111** can also be used for these scenarios.

3.1.3.2.4 Terrestrial compartment

Calculated local concentrations

According to the TGD, the local PEC_{soil} is calculated as an average concentration over a certain time period in agricultural soil, fertilised yearly with sludge from a STP and receiving continuous aerial deposition (dry and wet) from a nearby point source, for a period of 10 years.

[44] PEC reg, air, future = PEC reg, air, current. Indeed, the effect of an increase in MSW cadmium content up to 24 mg kg^{-1} $_{\text{dry wt.}}$ (‘future’ scenarios) will have only a minor influence on the currently derived PECs regional for air, water and soil (cfr EUSES outprints in Annex V). Therefore there is no need to revise the current PEC reg, water and the PEC reg, air in order to derive the PEC values for the future situation.

For the terrestrial ecosystem, the concentration is calculated for a depth of 0.2 m. Sludge from Cd producing plants is however not applied to agricultural land but is recycled internally or by an external plant (IZA-Europe, pers. communication). Application of sludge from processing sites/scenarios is unlikely to take place[45] but may occur if the Cd is emitted via a sewer to a municipal sewage treatment plant. This route of emission is taken into account in the regional assessment as diffuse Cd flux (no changes made, see Section 3.1.3.4.2). Therefore, the Cd input to soil through sludge from the Cd producing plants is omitted in these calculations and atmospheric deposition is the only source of Cd input into the terrestrial compartment. The fate of sludge from Cd processors is unknown. Atmospheric deposition of Cd is calculated assuming that all Cd is deposited within an area of 100 km^2 around the source and that the deposition occurs in a continuous flux.

The PEClocal is the sum of the regional Cd concentration in soil (PECregional) and the atmospheric deposition minus the leaching losses. The PEClocal is solved from the dynamic Cd balance in the 0-0.2 m top layer of the soil as (see Section 3.1.3.4.2):

$$PEClocal_{soil} = \frac{Dair}{k} - \left(\frac{Dair}{k} - PECregional_{soil}\right)\exp(-kt)$$

where

Dair =	aerial deposition flux per kg of soil (mg kg^{-1} days)
t =	time (3,650 days)
k =	first order rate constant for removal from top soil (d^{-1})
$PECregional_{soil}$=	the regional Cd concentration in soil (0.36 mg kg^{-1} wet wt) and which is calculated for an agricultural scenario assuming a realistic worst case Cd input scenario.

Results of the calculations are presented in **Table 3.117**. The PEC_{soil} values are 0.36mg $kg^{-1}_{wet\ wt.}$ - 0.37 mg $kg^{-1}_{wet\ wt.}$ PEC_{soil} values for NiCd batteries producers and Cd recyclers are very similar and are mainly determined by the PECregional value for soil of 0.363 mg $kg^{-1}_{wet\ wt.}$ Since atmospheric deposition is the only source of Cd input to the terrestrial compartment (sludge is recycled or land-filled) and emissions to air are relatively low (0.0014-0.10 kg/day; emission days: 225-350 days)), this emission route is of minor importance in comparison to the regional Cd concentration in soil. Referring to the scenarios of production, processing and use (reference year: 1996) in Section 3.1.3.1.4, local PEC_{soil} values for Cd producing plants (with higher air emissions) of 0.36-0.85 mg $kg^{-1}_{wet\ wt.}$ were calculated.

[45] In line with national and EU legislation sludges from on-site wwtp of Cd processors are likely to be classified as hazardous (e.g. see for the sector of metal treatment in IPPC, 2004; EC legislation in: EC, 1991 and EC, 2000)

Table 3.117 Calculated local PECsoil for NiCd producing plants and Cd recycling plants

Use category	Plant n°	Emission to air	Number of emission days	PEClocal soil	Year
		kg/day		mg kg^{-1} wet wt	
NiCd batteries					
	1	N.A.	225	0.36	1999
	2[a]	0.005	330	0.36	2000
	3[b]	N.A.	315	0.36	2000
	4	0.04	330	0.37	2000
	5	0.03	230	0.37	1999
	6	0.00014	250	0.36	1999
	7	0.097	300	0.37	1999
Cd recyclers[c]	1	0.01	350	0.36	2000
	2[d]	0	240	0.36	1999

N.A. Not available;
a) Company 2 emits to the marine environment;
b) Wet processes; no emissions to air. Mainly emissions to effluents;
c) Only two recyclers (instead of three) have been listed under Cd-recyclers. The reason is that one company is both recycler and producer. A further breakdown in the submitted figures between the producing process and the recycling process were not feasible. For this reason this company have been listed with the other producers;
d) No "open" treatment steps; no emissions to air.

Measured local concentrations

At this moment, only company 3 reported measured local soil concentrations of < 12 mg kg^{-1} $_{\text{dry wt.}}$

MSW incinerator: current situation

In the following section the results from the local exposure assessment for the terrestrial compartment for MSW incineration plants (life cycle stage 5: disposal; incineration) are presented. The only route of exposure for the terrestrial compartment is aerial deposition since it is assumed that the sludge from the on-site wastewater treatment plant is land-filled. As mentioned previously the local air emission for incineration plants is calculated using an allocation key based on the number of incinerators in each country and the country specific air emission amounts.

From **Table 3.118** it can be concluded that the local PEC soil surrounding incineration plants in the EU range from 0.363 mg kg^{-1} wet wt to 0.374 mg kg^{-1} $_{\text{wet wt.}}$ (total cadmium) which is almost similar to the regional PEC soil concentration of 0.363 mg kg^{-1} $_{\text{wet wt.}}$ Removing NiCd batteries in the MSW will not significantly reduce the cadmium soil concentration (calculations not shown).

Table 3.118 Calculated total local PECsoil for MSW incineration plants

Country	Emission amount	Number of emissions days	Clocalsoil	PEClocal soil
	kg $year^{-1}$	days	mg kg^{-1} wwt	mg kg^{-1} wwt.
Austria	1.4[c]	330	0.00041	0.363
Belgium	3.5	330	0.0012	0.364
Denmark	9.7	330	0.0028	0.366
Finland	14	330	0.0041	0.367
France[a]	16.4	330	0.0048	0.368
France[b]	36.7	330	0.0107	0.374
Germany	5	330	0.0015	0.365
Italy	5.7	330	0.0017	0.363
Luxembourg	22	330	0.0064	0.369
The Netherlands	4.8	330	0.0014	0.364
Norway	5.1	330	0.0015	0.364
Portugal	1.6	330	0.0005	0.363
Spain	6.8	330	0.0020	0.365
Sweden	0.2	330	0.00006	0.363
UK	1.5	330	0.0004	0.363
EU 10% scenario	9.1	330	0.0027	0.366

a) Generic scenario;
b) Based on P90 measured data;
c) According to the latest information (Stubenvoll et al., 2002) total Cd emissions in Austria from incinerators amount to 4.2 kg. Since there is a total of 3 plants, on average 1.4 kg per plant is emitted.

Landfills

The leachate from landfills may be treated in municipal treatment plants from which sludge may be applied to land. Figures for the amounts going to agricultural land have been added to the tables in the assessment, but no calculations of soil concentrations have been included (there is no calculation of soil levels related to landfill, as there are no air emissions).

Regulations on the metals content of sludges for agriculture come into play here (see Section 2.3). Moreover, as the case in (the 'global' RAR related) Section 3.1.3.1.4, the TRAR/batteries' related sections does not include local 'sludge application scenario'. Only diffuse emissions (averaged over whole EU) are considered in the assessment. The contribution of sludge application to (arable) land is considered and included in the PEC, reg, soil see Section 3.1.3.4.2.

3.1.3.3 Local exposure: all scenarios: update data (reference year 2002)

3.1.3.3.1 Aquatic compartment: calculated PECs

Surface water

Introduction

Calculation of local PEC-values for the aquatic compartment is performed according to the method described in the TGD (EC, 2003; see also Section 3.1.3.2.1). Input data were submitted via the Industry Questionnaire (2004).

Cd metal and Cd oxide production

Cd metal production

An overview of the calculated local Cd concentrations in surface water is presented in **Table 3.119**. From this table it can be concluded that for Cd metal producers in Europe:

- Daily emissions to surface water vary between 0.001 kg Cd/day (site 6) and 0.16 kg Cd/day (site 7; year 2002).
- Update information for on-site WWTP cadmium removal efficiency is not provided.
- Total Cd concentrations in on-site WWTP effluent vary between 0.0007 mg L^{-1}(annual mean site 6, direct discharge to large tide influenced river) and 0.05 mg L^{-1}(annual mean site 7, discharge to the sea; year 2002).
- Dilution factors vary between 2.3 (site specific dilution factor ditch, site 1) and 1,000 (maximum site specific dilution factor large river, site 6). Site specific dilution factors were derived for 2 sites. Production-site 7 discharges its wastewater to a marine environment for which a default dilution factor of 100 is applied.
- Local dissolved Cd concentrations in water vary between 0.0002 µg L^{-1}(site 6, large tidal river, maximum dilution factor of 1,000) and 0.53 µg L^{-1}(site 1, ditch, very small dilution factor).
- Calculated PECtotal levels in surface water vary between 0.11 µg L^{-1}(calculated regional $background_{total}$ = 0.11 µg L^{-1}) and 0.64 µg L^{-1}.

Table 3.119 The local PEC_{water} (dissolved fraction) for Cd metal producing plants in the EU-16. PEC's include background Cd

N°	Production emission¶	Concentration in effluent	Type of receiving water	Dilution Factor	$Clocal_{water}$	$PEClocal_{water}$	Year
	kg d^{-1}	mg l^{-1}			µg L^{-1}	µg L^{-1}	
1	0.03(c)	0.004	ditch	2.3	0.53	0.64	2002
6	0.001	0.0007	Tide influenced river	1,000(b) (ss: 11,087)	0.0002	0.11	2002
7*	0.16*	0.05	sea	100(a)*	0.17*	0.28*	2002
7*	0.10*	0.03	sea	100(a)*	0.10*	0.21*	2004

a) Default dilution factor: 10 (freshwater), 100 (sea water);
b) Site specific dilution factor restricted to a maximum of 1,000 (revised TGD - EC, 2003);
c) The total emission in 2002 consists of discharge of effluent from water purification plant and discharge of other water from the plant area (historic contaminated). Since 2005, the discharge from water from the plant area has been stopped; since then all waste water is treated In the purification plant;
ss Site specific dilution factor;
* Emission to the sea: values are only indicative; no assessment is done for the marine environment;
¶ Annual averages.

Cd oxide production

An overview of the calculated local Cd concentrations in surface water is presented in **Table 3.120**. From this table it can be concluded that for Cd oxide producers in Europe:

- Due to the fact that the production of cadmium oxide is a totally dry process; discharge of waste water from the site does not take place.
- As a result the PEClocal in surface water is 0.11 µg L^{-1}(calculated regional background).

Table 3.120 The local PEC_{water} (dissolved fraction) for Cd oxide producing plants in the EU-16. PEC's include background Cd

N°	Production emission¶	Concentration in effluent	Type of receiving water	Dilution Factor	$Clocal_{water}$	$PEClocal_{water}$	Year
	kg d^{-1}	mg l^{-1}			µg L^{-1}	µg L^{-1}	
12	0(a)	0	n.a.	n.a.	0	0.11	2002

¶ Annual averages;
n.a. Not applicable;
a) No emission to water; thermal/dry process.

Production and recycling of NiCd batteries

Production of NiCd batteries

An overview of the calculated local Cd concentrations in surface water is presented in **Table 3.121**. From this table it can be concluded that for NiCd battery producers in Europe:

- Daily emissions to surface water vary between 0.03 kg Cd/day (site 2) and 0.07 kg Cd/day (site 4).
- Update information for on-site WWTP cadmium removal efficiency is not provided.
- Total Cd concentrations in on-site WWTP effluent vary between 0.06 mg L^{-1}(annual mean site 3, direct discharge to large river) and 0.11 mg L^{-1}(annual mean site 2, discharge to the sea).

- Dilution factors are set to 1,000 (maximum site specific dilution factor, site 2, 3, 4). Site specific dilution factors were derived for 3 sites.
- Local dissolved Cd concentrations in water vary between 0.02 µg L^{-1}(site 3, river, maximum dilution factor of 1,000) and 0.04 µg L^{-1}(site 2, sea, maximum dilution factor of 1,000).
- Calculated PECtotal levels in surface water vary between 0.13 µg L^{-1}(calculated regional $background_{total}$ = 0.11 µg L^{-1}) and 0.15 µg L^{-1}. Please note that in this update, annual mean effluent concentrations -as provided by industry- are used for PEClocal water derivation, as opposed to the original TRAR on NiCd batteries (see Section 3.1.3.2.1), in which P90 effluent concentrations were calculated based on monthly average concentrations.

Table 3.121 The local PEC_{water} (dissolved fraction) for NiCd batteries producing plants in the EU-16. PEC's include background Cd

N°	Production emission¶	Concentration in effluent	Type of receiving water	Dilution Factor	$Clocal_{water}$	$PEClocal_{water}$	Year
	kg d^{-1}	mg l^{-1}			µg L^{-1}	µg L^{-1}	
2*/2bis	0.03*	0.11	sea	1,000(b) (ss: 1,326)*	0.04	0.15	2002
3	0.04	0.06	Tide influenced river	1000(b) (ss: 25,951)	0.02	0.13	2002
4	0.07	0.10	river	1,000(b) (ss: 1,850)	0.03	0.14	2002
6	No update data						
7	No update data						

* Emission to the sea: values are only indicative; no assessment is done for the marine environment;
¶ Annual averages;
b) Site specific dilution factor restricted to a maximum of 1,000 (revised TGD - EC, 2003); ss: site specific dilution factor.

Recycling of NiCd batteries

An overview of the calculated local Cd concentrations in surface water is presented in **Table 3.122**. From this table it can be concluded that for NiCd battery recyclers in Europe:

- Daily emissions to surface water vary between 0 kg Cd/d (Cd recycling plant 2; off-site treatment of waste water) and 0.0007 kg Cd/d (site 1, year 2002 value). All waste waters from site 2 are collected and treated off-site in an external waste water treatment plant. Recent -year 2004- measurements for site 1 indicate that waste water emissions are reduced by a factor two due to various measures taken to conform to ISO 14000. Please note that emission information and PEC $local_{water}$ for site 2bis is already included in the NiCd battery producing section since waste water emissions could not be split between the NiCd-battery manufacturing and the recycling plant.
- Update information for on-site WWTP cadmium removal efficiency is not provided.
- Total Cd concentrations in on-site WWTP effluent vary between 0 mg L^{-1}(site 2) and 0.37 mg L^{-1}(90P site 1, year 2002, discharge to river). Please note that the 90P Cd concentration in the effluent of site 1 is reduced to 0.24 mg L^{-1}in the year 2004.
- The dilution factor for site 1 is set to 1,000 (maximum site specific dilution factor; TGD - EC, 2003). Site specific dilution factors were derived for this site (site 1).

- Calculated PECtotal levels in surface water vary between 0.11 µg L^{-1}(site 2, calculated regional $background_{total}$ = 0.11 µg L^{-1}) and 0.24 µg L^{-1}(site 1, year 2002 data). On the basis of year 2004 information for site 1, a $PEClocal_{water}$ of 0.19 µg $L^{-1}$is calculated.

Table 3.122 The local PEC_{water} (dissolved fraction) for NiCd batteries recycling plants in the EU-16. PEC's include background Cd

N°	Production emission¶	Concentration in effluent	Type of receiving water	Dilution Factor	$Clocal_{water}$	$PEClocal_{water}$	Year
	kg d^{-1}	mg l^{-1}			µg L^{-1}	µg L^{-1}	
1	0.0007	0.37 (90P) 0.16 (avg)	river	1,000(b) (ss: 2,672)	0.13	0.24	2002
1	0.0003	0.24 (90P) 0.1 (avg)	river	1,000(b) (ss: 3,443)	0.08	0.19	2004
2	0(a)	0	n.a.	n.a.	0	0.11	2002
2bis	See data on-site 2/2bis in Table 3.21						

¶ Annual averages;
n.a. Not applicable;
a) No site emission to water. Cleaning water as well as processing water are collected internal (about 100 m^3/year) and send to an external waste water treatment plant;
b) Site specific dilution factor restricted to a maximum of 1,000 (revised TGD - EC, 2003); ss: site specific dilution factor.

Production of Cd containing pigments

An overview of the calculated local Cd concentrations in surface water is presented in **Table 3.123**. From this table it can be concluded that for Cd pigment producers in Europe:

- Daily emissions to surface water vary between 0.003 kg Cd/day (site A) and 0.02 kg Cd/day (site C). Please note that for site C year 2004 data have also been provided; emission to surface water is 0.01 kg/d (as opposed to 0.02 kg/day for year 2003).
- Update information for on-site WWTP cadmium removal efficiency is not provided.
- Total Cd concentrations in on-site WWTP effluent vary between 0.02 mg L^{-1}(annual mean for the sites A and B, direct discharge to river) and 0.12 mg L^{-1}(annual mean site C, direct discharge to river). Site C reports a 90P effluent concentration of 0.08 mg $L^{-1}$for the year 2004.
- Dilution factors vary between 24 (site specific factor river, site A) and 1,000 (maximum site specific dilution factor river, site B). Site specific dilution factors were derived for all sites.
- Local dissolved Cd concentrations in water vary between 0.01 µg L^{-1}(site B, river, maximum dilution factor of 1,000) and 0.27 µg L^{-1}(site A, river, site specific dilution factor). Note that for site $Clocal_{water}$ for the year 2003 and 2004 are similar; i.e. 0.14 µg L^{-1}. Different dilution factors have been calculated for both years due to the large difference in effluent discharge rates: year 2003: 156 m^3/day; year 2004: 240 m^3/day. Since for the year 2004 a higher effluent discharge is reported, the subsequent dilution in the receiving water is smaller.
- Calculated PECtotal levels in surface water vary between 0.12 µg L^{-1}(calculated regional $background_{total}$ = 0.11 µg L^{-1}) and 0.38 µg L^{-1}.

Table 3.123 The local PEC_{water} (dissolved fraction) for Cd pigments production plants in the EU-16. PEC's include background Cd

N°	Processing emission¶	Concentration in effluent	Type of receiving water	Dilution factor	$Clocal_{water}$	$PEClocal_{water}$	Year
	kg d^{-1}	mg l^{-1}			µg L^{-1}	µg L^{-1}	
A	0.003	0.02	river	24	0.27	0.38	2003
B	0.01	0.02	river	1,000(b) (ss: 3378)	0.01	0.12	2003
C	0.02	0.12	river	289	0.14	0.25	2003
C	0.01	0.08 (90P) 0.05 (avg)	river	189	0.14	0.25	2004

¶ Annual averages;
Avg Average
90P 90th percentile
b) Site specific dilution factor restricted to a maximum of 1,000 (revised TGD - EC, 2003); ss: site specific dilution factor.

Production of Cd containing stabilisers

An overview of the calculated local Cd concentrations in surface water is presented in **Table 3.124**. From this table it can be concluded that for Cd stabiliser producers in Europe:

- Daily emissions to surface water vary between 0.003 kg Cd/day (site X) and 0.01 kg Cd/day (site Y).
- Update information for on-site WWTP cadmium removal efficiency is not provided.
- Total Cd concentrations in on-site WWTP effluent vary between < 0.001 mg L^{-1}(maximum value, site Y, discharge to canal, external laboratory detection limit) and < 0.005 mg L^{-1}(maximum value, site X, discharge to municipal STP). Taking into account a second treatment step for site X (STP: 60% removal) and extra dilution of 5.4 in a municipal STP lowers the Cd concentration from < 0.005 mg $L^{-1}$to < 0.00037 mg L^{-1}.
- Dilution factors vary between 246 (site specific factor river, site Y) and 417 (site specific dilution factor river, site X). Site specific dilution factors were derived for 2 sites.
- Local dissolved Cd concentrations in water vary between 0.0003 µg L^{-1}(site X, river after STP, site specific dilution factor) and 0.007 µg L^{-1}(site Y, canal, site-specific dilution factor, based on detection limit internal laboratory).
- Calculated PECtotal levels in surface water vary between 0.11 µg L^{-1}(calculated regional $background_{total}$ = 0.11 µg L^{-1}) and 0.12 µg L^{-1}.

Table 3.124 The local PEC_{water} (dissolved fraction) for Cd stabilisers production plants in the EU-16. PEC's include background Cd

N°	Production emission¶	Concentration in effluent	Type of receiving water	Dilution Factor	$Clocal_{water}$	$PEClocal_{water}$	Year
	kg d^{-1}	mg l^{-1}			µg L^{-1}	µg L^{-1}	
X	0.003	On-site WWTP: < 0.005 Municipal STP: < 0.00037(a)	river after municipal STP	417	0.0003	0.11	2002
Y	0.01	< 0.005(b)	canal	246	0.007	0.12	2002
Y	0.01	< 0.001(c)	canal	246	0.001	0.11	2002

¶ Annual averages;

a) Cd concentration in effluent from municipal STP; calculated from Cd concentration in effluent from on-site WWTP; taking into account removal at STP: 60%; extra dilution= 5.4 (ratio of effluent discharge rate STP: default 2000 m^3/day and on-site WWTP discharge rate: 370 m^3/day);

b) Analysis performed by internal laboratory (two times a month) method MIP-P-PRO-101 rev 2 year 2003;

c) Analysis performed by certified external laboratory (two times a year), method EPA 200.8 (1994).

Use of Cd/CdO in alloys, plating and other uses

For these uses, no update information was submitted to the Rapporteur.

Calculation of Predicted Environmental Concentration for Sewage Treatment Plants (PEC_{stp})

The first step in the assessment of the local PEC values in the aquatic environment is the determination of the site-specific effluent concentration after on-site WWTP treatment. If not available, it is calculated from reported daily releases to surface water and local effluent discharge rate.

$$Clocal_{effluent} = \frac{EMISSIONlocal_{water} \times 10^6}{EFFLUENTlocal_{STP}}$$

$Clocal_{effluent}$: Concentration in effluent water (mg L^{-1})
$EMISSIONlocal_{water}$: Local emission rate to water (kg/day)
$EFFLUENTlocal_{STP}$: Effluent discharge rate of local STP (l/day)

If no effluent discharge rate is submitted, a default value of 2,000 m^3/day is used.

In case measured Cd concentrations in WWTP effluent are available, 90th percentile values are preferably used to account for a realistic worst case situation. If not available, annual means are used.

Additional removal of Cd needs to be considered if the industrial waste water undergoes an additional treatment in a municipal STP.

Since site specific information on type of WWTP, removal efficiency, Cd concentration in sludge and destination of sludge is not provided in the recently submitted industry questionnaires (2004), the paragraph extracted from Section 3.1.2.2.1 is still considered as valid for Cd metal/CdO producing and processing plants (see below).

"Wastewater treatment at Cd-producing and -processing plants involves filtration and precipitation. Liquid effluents from the different stages during production and processing of Cd are collected and treated with sodium carbonate at alkaline pH to precipitate Cd. Filtration aids and flocculating agents are added. The sludge is then filtered from the solution. The filtrate is neutralised prior to discharge to the environment. At industrial non-ferrous metal producing sites and waste water treatment plants (WWTP) a cadmium removal efficiency of at least 90% is reported based on physico-chemical techniques only, to achieve total cadmium concentrations within the range 1 – 0.1 mg L^{-1}(IPPC report, 2000). EUSES calculations give a corroborating removal rate (WS Atkins, 1998 and RPA, 2001): the Simple Treat model run with the Kp value of 130,000 l/kg yields the following distribution in the waste water treatment plant: 90% in sludge and 10% in water.

However, for municipal STP in practice, the average removal efficiency can vary widely from > 80% (based on measurements of influent and effluent cadmium concentrations and the water flows; VMM, pers. com. 2002) to 60% (CUWVO, 1986; in: CBS/Milieucompendium, 2000). The latter, lower figure will be used in this report".

Calculation of the STP concentration for evaluation inhibition to microorganisms (EC, 2003)

The removal of a chemical in the STP is computed from a simple mass balance. For the aeration tank, this implies that the inflow of sewage (raw or settled, depending on the equipment with a primary sedimentation tank) is balanced by the following removal processes: degradation, volatilisation and outflow of activated sludge into the secondary settler. Activated sludge flowing out of the aeration tank contains the chemical at a concentration similar to the aeration tank, which is the consequence of complete mixing. It consists of two phases: water, which is virtually equal to effluent flowing out of the solids-liquid separator (this is called the effluent of the STP), and suspended particles, which largely settle to be recycled into the aeration tank. Assuming steady state and complete mixing in all tanks (also the aeration tank), the effluent concentration approximates the really dissolved concentration in activated sludge. It is assumed that only the dissolved concentration is bioavailable, i.e. the actual concentration to which the micro-organisms in activated sludge are exposed. For the risk characterisation of a substance upon micro-organisms in the STP, it can therefore be assumed that homogeneous mixing in the aeration tank occurs which implies that the dissolved concentration of a substance is equal to the effluent concentration:

$$PEC_{stp} = Clocal_{effluent}$$

$Clocal_{effluent}$: Total concentration of substance in STP effluent (mg L^{-1})
PEC_{stp}: PEC for microorganisms in the STP (mg L^{-1})

Cd metal production

An overview of $PEC_{WWTP/STP}$ is given in **Table 3.125**. From this table it can be concluded that the PEC_{WWTP} for Cd metal producing plants varies between 0.7 µg $L^{-1}$and 50 µg L^{-1}(dissolved fraction).

Table 3.125 The local PEC $_{WWTP/STP}$ (total fraction) for Cd metal producing plants in the EU-16

N°	Production emission¶	On-site WWTP Off-site municipal STP	Removal efficiency	PEC_{WWTP}/PEC_{STP} (dissolved fraction)	Year
	kg d^{-1}		%	µg L^{-1}	
1	0.03	On-site WWTP (physico-chemical as pre-treatment, biological BDS and SRB as polishing) (a)	n.d.	3.6	2002
6	0.001	On-site WWTP	n.d.	0.7	2002
7*	0.16*	On-site WWTP	n.d.	50	2002
7*	0.10*	Site WWTP	n.d.	30	2004

a) WWTP with physico-chemical pre-treatment followed by biological process based on fully adapted, specialised and dedicated micro-organisms. Cannot be compared with STPs based on 'standard' microorganisms communities;
* Emission to the sea;
¶ Annual averages;
n.d. No data available.

Cd oxide production

Since the production of cadmium oxide is a totally dry process; discharge of waste water from the site does not take place.

Table 3.126 The local $PEC_{WWTP/STP}$ (total fraction) for Cd oxide producing plants in the EU-16

N°	Production emission¶	On-site WWTP Off-site municipal STP	Removal efficiency	PEC_{WWTP}/PEC_{STP} (dissolved fraction)	Year
	kg d^{-1}		%	µg L^{-1}	
12	0(a)	n.a.	n.a.	0	2002

¶ Annual averages;
n.a. Not applicable;
a) No emission to water; thermal/dry process.

Production of NiCd batteries

An overview of $PEC_{WWTP/STP}$ is given in **Table 3.127**. From this table it can be concluded that the PEC_{WWTP} for NiCd battery producing plants vary between 63 µg $L^{-1}$and 107 µg L^{-1}(dissolved fraction).

Table 3.127 The local $PEC_{WWTP/STP}$ (total fraction) for NiCd batteries producing plants in the EU-16

N°	Production emission¶	On-site WWTP Off-site municipal STP	Removal efficiency	PEC_{WWTP}/PEC_{STP} (dissolved fraction)	Year
	kg d^{-1}		%	µg L^{-1}	
2*/2bis	0.03	On-site WWTP	n.d.	107	2002
3	0.04	On-site WWTP	n.d.	63	2002

Table 3.127 continued overleaf

Table 3.127 continued The local $PEC_{WWTP/STP}$ (total fraction) for NiCd batteries producing plants in the EU-16

N°	Production emission¶	On-site WWTP Off-site municipal STP	Removal efficiency	PECWWTP/PECSTP (dissolved fraction)	Year
	kg d^{-1}		%	µg L^{-1}	
4	0.07	On-site WWTP	n.d.	103	2002
6	No update data				
7	No update data				

* Emission to the sea;
¶ Annual averages;
n.d. No data available.

Recycling of NiCd batteries

An overview of $PEC_{WWTP/STP}$ is given in **Table 3.128**. Update data are available for site 1 and site 2. For the latter site, the waste waters are collected and transported to be treated in an external waste water treatment plant. Therefore no site emissions occur. For site 1, the PEC_{WWTP} is 370 µg L^{-1}(90P, year 2002). For the year 2004, a lower PEC_{WWTP} of 240 µg L^{-1}(90P) is reported.

Table 3.128 The local $PEC_{WWTP/STP}$ (total fraction) for NiCd batteries recycling plants in the EU-16

N°	Production emission¶	On-site WWTP Off-site municipal STP	Removal efficiency	PEC_{WWTP}/PEC_{STP} (dissolved fraction)	Year
	kg d^{-1}		%	µg L^{-1}	
1	0.0004	On-site WWTP	n.d.	370 (90P)	2002
1	0.0002	On-site WWTP	n.d.	240 (90P)	2004
2	0[(a)]	n.a.	n.a.	0	2002
2bis	See data on-site 2/2bis in Table 3.127				

¶ Annual averages;
n.d. No data available;
n.a. Not applicable;
a) No site emission to water. Cleaning water as well as processing water are collected internal (about 100 m^3/year) and send to an external waste water treatment plant.

Production of Cd containing pigments

An overview of $PEC_{WWTP/STP}$ is given in **Table 3.129**. From this table it can be concluded that the PEC_{WWTP} for Cd pigments producing plants vary between 19 µg $L^{-1}$and 121 µg L^{-1}(dissolved fraction).

Table 3.129 The local $PEC_{WWTP/STP}$ (total fraction) for Cd pigments producing plants in the EU-16

N°	Processing emission¶	On-site WWTP Off-site municipal STP	Removal efficiency	PEC_{WWTP}/PEC_{STP} (dissolved fraction)	Year
	kg d^{-1}		%	µg L^{-1}	
A	0.003	On-site WWTP	n.d.	19	2003
B	0.01	On-site WWTP	n.d.	19	2003
C	0.02	On-site WWTP	n.d.	121	2003
C	0.01	On-site WWTP	n.d.	80	2004

¶ Annual averages;
n.d. No data available.

Production of Cd containing stabilisers

An overview of $PEC_{WWTP/STP}$ is given in **Table 3.130**. From this table it can be concluded that the PEC_{WWTP} for Cd stabiliser producing plants vary between 5 µg L^{-1}and 19 µg L^{-1}(dissolved fraction). The PEC_{STP} for stabiliser plant X –discharging to a municipal STP- is 0.4 µg L^{-1}.

Table 3.130 The local $PEC_{-WWTP/STP}$ (total fraction) for Cd stabiliser producing plants in the EU-16

N°	Production emission¶	On-site WWTP Off-site municipal STP	Removal efficiency	PEC_{WWTP}/PEC_{STP} (dissolved fraction)	Year
	kg d^{-1}		%	µg L^{-1}	
X	0.003	On-site WWTP	n.d.	5	2002
X		Off-site municipal STP	60	0.4(a)	2002
Y	0.01	On-site WWTP	n.d.	< 5(b)	2002
	l.01	On-site WWTP	n.d.	< 1(c)	2002

¶ Annual averages;
n.d. No data available;
a) PECSTP calculated taking into account 60% removal at STP and extra dilution at municipal STP of 5.4 (ratio of effluent discharge rate STP: default 2000 m^3/day and on-site WWTP discharge rate: 370 m^3/day);
b) Effluent analysis performed by internal laboratory (two times a month) method MIP-P-PRO-101 rev 2 year 2003;
c) Effluent analysis performed by certified external laboratory (two times a year), method EPA 200.8 (1994).

Use of Cd/CdO in alloys, plating and other uses

For these uses, no update information was submitted to the Rapporteur.

Calculation of $PEC_{sediment}$

The $PEClocal_{sediment}$ is calculated according to the formula presented below (see Section 3.1.3.1.2):

$$PEClocal_{sediment} = PECregional_{sediment} + K_p\ Clocal_{water}.\ 10^{-3}$$

in which the K_p (L kg$^{-1}{}_{dw}$) equals the solid- water partition coefficient of suspended matter (Kp =130,000 l/kg).

The measured PEC regional is taken as an average of 90th percentiles of surveys: 2.66 mg Cd/kg_{dw} (no changes made; **Table 3.189**, value not corrected for bioavailability).

The local $PEC_{sediment}$ are readily calculated from the data in **Table 3.119-Table 3.124** and the above-mentioned equation and presented in **Table 3.131-Table 3.136**. The $Clocal_{sediment}$ (K_p $Clocal_{water}$. 10^{-3}) is included to illustrate the contribution of the local discharge onto the sediment PEC.

Cd metal production

- Local Cd concentrations in sediment vary between 0.03 mg kg^{-1} dw (site 6, tide influenced river, maximum dilution 1,000) and 68.8 mg kg^{-1} dw (site 1, ditch). Elevated Cd concentrations in surface water lead to high concentrations in sediment due to the methodology used to calculate the Csediment (see partitioning on the basis of Csurface water, see subsection "Calculation on $PEC_{sediment}$" under Section 3.1.3.3).
- Calculated PECtotal levels in sediment vary between 2.7 mg kg^{-1} dw (measured regional $background_{total}$ = 2.66 mg kg^{-1} dw) and 71.5 mg kg^{-1} dw.

Table 3.131 The local $PEC_{sediment}$ (without correction for bioavailability) for Cd metal producing plants in the EU-16. PEC's include background Cd

N°	Production emission¶	$Clocal_{water}$	$Clocal_{sediment}$	$PEClocal_{sediment}$	Year
	kg d^{-1}	µg L^{-1}	mg kg^{-1}_{dw}	mg kg^{-1}_{dw}	
1	0.03	0.53	68.8	71.5	2002
6(b)	0.001	0.0002	0.03	2.7	2002
7*(a)	0.16	0.17*	21.9	24.5	2002
7*(a)	0.10	0.10*	13.6	16.2	2004

a) Default dilution factor: 10 (freshwater), 100 (sea water);
b) Site specific dilution factor restricted to a maximum of 1,000 (revised TGD - EC, 2003);
* Emission to the sea: values are only indicative; no assessment is done for the marine environment;
¶ Annual averages.

Cd oxide production

- Since no emissions to water take place at the CdO producing plant, the Clocal sediment and PEClocal sediment is 0 mg kg^{-1} dw and 2.7 mg kg^{-1} dw respectively.

Table 3.132 Local $PEC_{sediment}$ (without correction for bioavailability) for Cd oxide producing plants in the EU-16. PEC's include background Cd

N°	Production emission¶	$Clocal_{water}$	$Clocal_{sediment}$	$PEClocal_{sediment}$	Year
	kg d^{-1}	µg L^{-1}	mg kg^{-1}_{dw}	mg kg^{-1}_{dw}	
12	0(a)	0	0	2.7	2002

¶ Annual averages;
a) No emission to water; thermal/dry process.

Production of NiCd batteries

- Local Cd concentrations in sediment vary between 2.8 mg kg^{-1} dw (site 3, tide influenced river, maximum dilution 1,000) and 4.7 mg kg^{-1} dw (site 2, sea, maximum dilution 1,000).
- Calculated PECtotal levels in sediment vary between 5.5 mg kg^{-1} dw (measured regional $background_{total}$ = 2.66 mg kg^{-1} dw) and 7.4 mg kg^{-1} dw. Please note that site 2 is involved in

both production and recycling of NiCd batteries. No split in aquatic emissions could be done. Please note that in this update document, annual mean effluent concentrations, as provided by industry, are used for PEClocal water derivation, and consequently also the derivation of PEClocal sediment, as opposed to the original TRAR on NiCd batteries (see Section 3.1.3.2.1), in which P90 effluent concentrations were calculated based on monthly average concentrations.

Table 3.133 The local $PEC_{sediment}$ (without bioavailability correction) for NiCd batteries producing plants in the EU-16. PEC's include background Cd

N°	Production emission¶	$Clocal_{water}$	$Clocal_{sediment}$	$PEClocal_{sediment}$	Year
	kg d^{-1}	µg L^{-1}	mg $kg^{-1}{}_{dw}$	mg $kg^{-1}{}_{dw}$	
2*(b)/2bis	0.03*	0.04	4.7	7.4	2002
3(b)	0.04	0.02	2.8	5.5	2002
4	0.07	0.03	4.5	7.2	2002
6	No update data				
7	No update data				

* Emission to the sea: values are only indicative; no assessment is done for the marine environment;
¶ Annual averages;
b) Site specific dilution factor restricted to a maximum of 1,000 (revised TGD - EC, 2003).

Recycling of NiCd batteries

- Local Cd concentrations in sediment vary between 0 mg kg^{-1} dw (site 2, no direct, local on-site emissions to water) and 16.3 mg kg^{-1} dw (site 1, river, maximum dilution 1,000, year 2002 data).
- Calculated PECtotal levels in sediment vary between 2.66 mg kg^{-1} dw (measured regional $background_{total}$ = 2.66 mg kg^{-1} dw) and 19.0 mg kg^{-1} dw.

Table 3.134 The local $PEC_{sediment}$ (without correction for bioavailability) for NiCd batteries recycling plants in the EU-16. PEC's include background Cd

N°	Production emission¶	$Clocal_{water}$	$Clocal_{sediment}$	$PEClocal_{sediment}$	Year
	kg d^{-1}	µg L^{-1}	mg $kg^{-1}{}_{dw}$	mg $kg^{-1}{}_{dw}$	
1	0.0007	0.13	16.3	19.0	2002
1	0.0003	0.08	10.6	13.2	2004
2(a)	0	0	0	2.7	2002
2bis	See data on-site 2/2bis in Table 3.133				

¶ Annual averages;
a) No site emission to water. Cleaning water as well as processing water are collected internal (about 100 m^3/year) and send to an external waste water treatment plant.

Production of Cd containing pigments

- Local Cd concentrations in sediment vary between 0.8 mg kg^{-1} dw (site B, river, max. dilution 1,000) and 34.7 mg kg^{-1} dw (site A, river). Please note that update emission information (90P) submitted for site C for the year 2004 gives similar results for $Clocal_{sediment}$: 18.7 mg kg^{-1} dw as opposed to 18.4 mg kg^{-1} dw.

- Calculated PECtotal levels in sediment vary between 3.5 mg kg^{-1} dw (measured regional $background_{total}$ = 2.66 mg kg^{-1} dw) and 37.4 mg kg^{-1} dw.

Table 3.135 The local $PEC_{sediment}$ (without correction for bioavailability) for Cd pigments production plants in the EU-16. PEC's include background Cd

N°	Processing emission¶	$Clocal_{water}$	$Clocal_{sediment}$	$PEClocal_{sediment}$	Year
	kg d^{-1}	µg L^{-1}	mg kg^{-1}_{dw}	mg kg^{-1}_{dw}	
A	0.003	0.27	34.7	37.4	2003
B(b)	0.01	0.01	0.8	3.5	2003
C	0.02	0.14	18.4	21.0	2003
C	0.01	0.14	18.7	21.3	2004

¶ Annual averages;
b) Site specific dilution factor restricted to a maximum of 1,000 (revised TGD - EC, 2003).

Production of Cd containing stabilisers

- Local Cd concentrations in sediment vary between 0.04 mg kg^{-1} dw (site X, river after STP, site specific dilution factor) and 0.9 mg kg^{-1} dw (site Y, canal).
- Calculated PECtotal levels in sediment vary between 2.7 mg kg^{-1} dw (measured regional $background_{total}$ = 2.66 mg kg^{-1} dw) and 3.6 mg kg^{-1} dw.

Table 3.136 The local $PEC_{sediment}$ (without correction for bioavailability) for Cd stabilisers production plants in the EU-16. PEC's include background Cd

N°	Production emission¶	$Clocal_{water}$	$Clocal_{sediment}$	$PEClocal_{sediment}$	Year
	kg d^{-1}	µg L^{-1}	mg kg^{-1}_{dw}	mg kg^{-1}_{dw}	
X(a)	0.003	0.0003	0.04	2.7	2002
Y	0.01	0.007(b)	0.9	3.6	2002
Y	0.01	0.001(c)	0.2	2.8	2002

¶ Annual averages;
a) Cd concentration in effluent from municipal STP; calculated from Cd concentration in effluent from on-site WWTP; taking into account removal at STP: 60%; extra dilution: 2000 m^3/day/370 m^3/day = 5.4;
b) Effluent analysis performed by internal laboratory (two times a month) method MIP-P-PRO-101 rev 2 year 2003;
c) Effluent analysis performed by certified external laboratory (two times a year), method EPA 200.8 (1994).

Use of Cd/CdO in alloys, plating and other uses

For these uses, no update information was submitted to the Rapporteur.

Summary of calculated PECs for surface water

In **Table 3.137** a summary is given of the calculated Clocal and PECs in WWTP/STP, surface water and sediment for Cd metal and CdO producing and processing sectors. A detailed description of the results for each sector is provided in subsections "Surface water", "Calculation of predicted environmental concentration for sewage treatment plants (PEC_{stp})" and "Calculation on $PEC_{sediment}$" under Section 3.1.3.3 of this document.

Table 3.137 Summary of calculated PECs in surface water for Cd/CdO producing/processing sectors. Clocalsediment and PEClocalsediment are not corrected for bioavailability

N°	PEC_{WWTP}/PEC_{STP} (total fraction)	$Clocal_{water}$	$PEClocal_{water}$	$Clocal_{sediment}$	$PEClocal_{sediment}$
	$\mu g\ L^{-1}$	$\mu g\ L^{-1}$	$\mu g\ L^{-1}$	$mg\ kg^{-1}_{dw}$	$mg\ kg^{-1}_{dw}$
Cd metal production					
1	3.6(c)	0.53	0.64	68.8	71.5
6	0.7	0.0002	0.11	0.03	2.7
7*	50	0.17*	0.28*	21.9	24.5
7* (year 2004 data)	30	0.10*	0.21*	13.6	16.2
Cd oxide production					
12(a)	0	0	0.11	0	2.7
NiCd battery production					
2*/2bis	107	0.04	0.15	4.7	7.4
3	63	0.02	0.13	2.8	5.5
4	103	0.03	0.14	4.5	7.2
6	No update data	No update data	No update data	No update data	No update data
7	No update data	No update data	No update data	No update data	No update data
NiCd battery recycling					
1	370	0.13	0.24	16.3	19.0
1 (year 2004 data)	240	0.08	0.19	10.6	13.2
2(b)	0	0	0.11	0	2.7
2bis	See data on-site 2/2bis under NiCd battery production				
Cd pigments production					
A	19	0.27	0.38	34.7	37.4
B	19	0.01	0.12	0.8	3.5
C	121	0.14	0.25	18.4	21.0
C (year 2004 data, 90P)	80	0.14	0.25	18.7	21.3
Cd stabiliser production					
X WWTP	5				
X STP	0.4	0.0003	0.11	0.04	2.7
Y	< 5(d)	0.007	0.12	0.9	3.6
Y	< 1(e)	0.001	0.11	0.18	2.8

* Emission to the sea: values are only indicative; no assessment is done for the marine environment;

a) No emission to water; thermal/dry process;

b) No site emission to water. Cleaning water as well as processing water are collected internal (about 100 m^3/year) and send to an external waste water treatment plant;

c) Effluent concentration from biological based wastewater purification system contains fully adapted, specialised and dedicated micro-organisms. Cannot be compared with STPs based on 'standard' micro-organisms communities;

d) Effluent analysis performed by internal laboratory (two times a month) method MIP-P-PRO-101 rev 2 year 2003;

e) Effluent analysis performed by certified external laboratory (two times a year), method EPA 200.8 (1994).

Measured data in the aquatic compartment

Surface water

Table 3.138 Summary of calculated versus measured levels in surface water for Cd/CdO producing/processing sectors

N°	Emission amount	PEClocal$_{water}$ Calculated Dissolved Cd	Measured[(1)] (estimated dissolved Cd unless stated differently)	Remarks	Year
	kg d^{-1}	µg L^{-1}	µg L^{-1}		
Cd metal production					
1	0.03	0.64	1.0	25 m downstream from discharge point; spot sampling: 3 times/week, analytical method NEN 6426, Ditch is influenced by historical contamination, pH: 7.7-7.9	2002-2003
6	0.001	0.11	n.d.		
7*	0.16*	0.28	0.1-1.65 µg L^{-1}(total Cd) 0.08-1.3 µg L^{-1}(estimated dissolved fraction in seawater)	different sampling points nearest to the outlets of the WWTPs, year 2002, concentration of suspended matter in seawater: 0.5-4 mg L^{-1}(avg 2 mg L^{-1}), dissolved concentration is estimated to be 79% of total concentration (Kp=130,000 l/kg, Csusp=2 mg L^{-1}) (external laboratory data, NIVA).	2002
7*	0.10*	0.21	0.16-0.36 µg L^{-1}(total Cd) 0.13-0.28 µg L^{-1} (estimated dissolved fraction in seawater)	different sampling points nearest to the outlets of the WWTPs, year 2004, concentration of suspended matter in seawater: 0.5-4 mg L^{-1}(avg 2 mg L^{-1}), dissolved concentration is estimated to be 79% of total concentration (Kp=130,000 l/kg, Csusp=2 mg L^{-1}) (external laboratory data, NIVA).	2004
Cd oxide production					
12[(a)]	0	0.11	n.d.		2002
NiCd battery production					
2*/2bis	0.03*	0.15	n.d.		2002
3	0.04	0.13	n.d.		2002
4	0.07	0.14	n.d.		2002
6	No update data				
7	No update data				

Table 3.138 continued overleaf

Table 3.138 continued Summary of calculated versus measured levels in surface water for Cd/CdO producing/processing sectors

N°	Emission amount	PEClocal$_{water}$ Calculated Dissolved Cd	Measured(1) (estimated dissolved Cd unless stated differently)	Remarks	Year
	kg d^{-1}	µg L^{-1}	µg L^{-1}		
NiCd battery recycling					
1	0.0007	0.24	19.8	200 m downstream from discharge point, year 2002, River is influenced by contamination; i.e. infiltration and run-off waters from old metallurgical slag heaps. Upstream conc: 9.9 µg dissolved Cd/l; 200 m upstream from discharge point.	2002
1	0.0003	0.19	10.6	200 m downstream from discharge point, year 2004, River is influenced by contamination; i.e. infiltration and run-off waters from old metallurgical slag heaps. Upstream conc: 13.9 µg dissolved Cd/l; 200 m upstream from discharge point.	2004
2(b)	0	0.11	n.d.		2002
2bis	See data on-site 2/2bis under NiCd battery production				
Cd pigments production					
A	0.003	0.38	n.d.		2003
B	0.01	0.12	n.d.		2003
C	0.02	0.25	n.d.		2003
Cd stabiliser production					
X WWTP	0.003				
X STP		0.11	n.d.		2002
Y	0.01	0.12(b)	< 1.65 µg L^{-1}	upstream and downstream value, < 5 µg total Cd/l = dl, ICP, pH: 7.9; hardness: 120-123 mg $CaCO_3$/l; DOC: 7-11 mg L^{-1}	2002
Y	0.01	0.11(c)	< 1.65 µg L^{-1}	upstream and downstream value, < 5 µg total Cd/l = dl, ICP, pH: 7.9; hardness: 120-123 mg $CaCO_3$/l; DOC: 7-11 mg L^{-1}	2002

* Emission to the sea: values are only indicative; no assessment is done for the marine environmentn.d.: no data available; dl: detection limit

1) If total concentrations are measured, dissolved concentrations are estimated to be 33% of total Cd concentration (Kp = 130 103 L kg-1, Csusp = 15 mg L-1);

a) No emission to water; thermal/dry process;

b) No site emission to water. Cleaning water as well as processing water are collected internal (about 100 m^3/year) and send to an external waste water treatment plant;

b) Effluent analysis performed by internal laboratory (two times a month) method MIP-P-PRO-101 rev 2 year 2003;

c) Effluent analysis performed by certififed external laboratory (two times a year), method EPA 200.8 (1994).

Sediment

Table 3.139 Summary of calculated versus measured levels in sediment for Cd/CdO producing/processing sectors (without correction for bioavailability)

N°	Emission amount	PEClocal$_{sediment}$ calculated	Measured	Remarks	Year
	kg d^{-1}	mg $kg^{-1}{}_{dw}$	mg $kg^{-1}{}_{dw}$		
Cd metal production					
1	0.03	71.5	upstream: 5 mg kg^{-1} dw At discharge point: 1.6 mg kg^{-1} dw	(Recent) dredging occurred downstream of the discharge point. Ditch is influenced by historical contamination. TOC: < 1% AVS: U: 23.7 µmol/g dw D: 2.6 µmol/g dw (sampling: 25.11.2002, 100m upstream and downstream discharge point) (EURAS, 2003; external laboratory)	2002-2003
6	0.001	2.7	0.64 mg kg^{-1} dw (300 m upstream) 1.14 mg kg^{-1} dw (1,800 m downstream)	n.d.	2002
7*	0.16*	24.5	At discharge point: 1.1 mg kg^{-1} dw; further in the open sea: 2.1-3.2 mg kg^{-1} dw	jarosite discharge prior to 1986; since deposition in mountain caverns, significant decrease in top 1-cm sediment concentrations (external laboratory data, NIVA).	1996 (measured data) 2002 (calculated PEC)
7*	0.10*	16.2	At discharge point: 1.1 mg kg^{-1} dw; further in the open sea: 2.1-3.2 mg kg^{-1} dw	jarosite discharge prior to 1986; since deposition in mountain caverns, significant decrease in top 1-cm sediment concentrations (external laboratory data, NIVA).	1996 (measured data) 2002 (calculated PEC)
Cd oxide production					
12(a)	0	2.7	n.d.	n.d.	2002

Table 3.39 continued overleaf

Table 3.139 continued Summary of calculated versus measured levels in sediment for Cd/CdO producing/processing sectors (without correction for bioavailability)

N°	Emission amount	PEClocal$_{sediment}$ calculated	Measured	Remarks	Year
	kg d^{-1}	mg $kg^{-1}{}_{dw}$	mg $kg^{-1}{}_{dw}$		
NiCd battery production					
2*/2bis	0.03*	7.4	n.d.	The sediments of the harbour are heavily contaminated by industrial activity in the vicinity of the harbour. The total amount of metals present in the sediments is estimated to 1,000 tonnes. No relationship between the present metal emissions and the metal content of the harbour sediments can be established.	2002
3	0.04	5.5	n.d.	n.d.	2002
4	0.07	7.2	4.6	3 km downstream from discharge point, year 2001 data 3.3 mg kg^{-1} dw; 100 m upstream from discharge point; year 2001 data.	2002
6	No update data				
7	No update data				
NiCd battery recycling					
1	0.0007	19.0	133	200 m downstream from discharge point, year 2002 River is influenced by contamination; i.e. infiltration and run-off waters from old metallurgical slag heaps. Upstream conc: 55 mg kg^{-1} dw; 200 m upstream from discharge point.	2002
1	0.0003	13.2	224	200 m downstream from discharge point, year 2002 River is influenced by contamination; i.e. infiltration and run-off waters from old metallurgical slag heaps. Upstream conc: 88 mg kg^{-1} dw; 200 m upstream from discharge point.	2004
2[(b)]	0	2.7	n.d.	n.d.	2002
2bis	See data on-site 2 under NiCd battery production				

Table 3.39 continued overleaf

Table 3.139 continued Summary of calculated versus measured levels in sediment for Cd/CdO producing/processing sectors (without correction for bioavailability)

N°	Emission amount	PEClocal$_{sediment}$ calculated	Measured	Remarks	Year
	kg d^{-1}	mg $kg^{-1}{}_{dw}$	mg $kg^{-1}{}_{dw}$		
Cd pigments production					
A	0.003	37.4	n.d.	n.d.	2003
B	0.01	3.5	n.d.	n.d.	2003
C	0.02	21.0	n.d.	n.d.	2003
Cd stabiliser production					
X WWTP	0.003				
X STP		2.7	n.d.	n.d.	2002
Y	0.01	3.6(c)	n.d.	n.d.	2002
Y	0.01	2.8(d)	n.d.	n.d.	2002

* Emission to the sea: values are only indicative; no assessment is done for the marine environment;
¶ Annual averages; n.d.: no data available; TOC: total organic carbon; AVS: acid volatile sulfides; U: upstream; D: downstream;
a) No emission to water; thermal/dry process;
b) No site emission to water. Cleaning water as well as processing water are collected internal (about 100 m^3/year) and send to an external waste water treatment plant;
c) Effluent analysis performed by internal laboratory (two times a month) method MIP-P-PRO-101 rev 2 year 2003;
d) Effluent analysis performed by certified external laboratory (two times a year), method EPA 200.8 (1994).

Comparison of PECs with measured data

Measured Cd concentrations in surface water, presented in **Table 3.138**, are available for Cd metal production-site 1 and 7, Cd recycling site 1 and Cd stabiliser production-site Y.

- The dissolved Cd concentration of 1 µg L^{-1} measured in the ditch downstream from the discharge point of Cd metal production-site 1 is in the same range as the predicted concentration of 0.64 µg L^{-1}. The measured data should however be treated with caution due to the 'large influence of historic contamination in the ditch surrounding this site' (company statement).
- Measured Cd concentrations in the receiving marine environment are available for Cd metal production-site 7. Measurements are performed at several locations: nearby the discharge point and some kilometres away from the emissions point in the open sea. Total Cd concentrations varying between 0.1 µg L^{-1} and 1.65 µg L^{-1} are reported. The concentration of suspended solids in the seawater is on average 2 mg L^{-1} (0.5-4 mg L^{-1}). On the basis of this information, dissolved concentrations can be estimated from total concentrations as 79% of total Cd concentration (Kp = 130 10^3 L kg^{-1}, C_{susp} = 2 mg L^{-1}). Dissolved Cd concentrations varying between 0.08 µg L^{-1} and 1.3 µg L^{-1} are calculated. The maximum measured dissolved Cd concentration of 1.3 µg L^{-1} is situated a factor of five above the PEClocal$_{water}$ derived for this site of 0.28 µg L^{-1} (dissolved fraction).
- Cd recycler site 1 reports measured total Cd concentrations in the receiving river 200 m downstream from the discharge point of 60 µg total Cd/l (i.e. 19.8 µg dissolved Cd/l) (year 2002). The site reports that these data are influenced by historical contamination; i.e. infiltration and run-off waters from old metallurgical slag heaps in front of the plant. Therefore they should be treated with caution. The measured dissolved Cd concentration in the river of 19.8 µg L^{-1} is eighty fold the calculated PEC$_{water}$ (0.24 µg L^{-1}). Data for the year 2004 indicate that although there is a decline in Cd concentrations in the receiving river i.e.

10.6 µg L^{-1}, the measured value is still a factor of 60 above the modelled PEC of 0.19 µg L^{-1}. It should be noted however that the upstream measurement for this site is 13.9 µg Cd/l which is in the same order of magnitude as the downstream measurement.

- Cd stabiliser site Y reports measured total Cd concentrations in the receiving river of < 5 µg L^{-1}(5 µg L^{-1}being the detection limit). This value corresponds to < 1.65 µg dissolved Cd/l. The calculated $PEClocal_{water}$ of 0.12 µg $L^{-1}$is situated a factor of 14 below the measured Cd concentration of 1.65 µg L^{-1}. It should be noted however that the measured value is a maximum.

In conclusion, it can be noted that only limited measured information is (made) available.

Moreover, submitted measured data are stated by the companies to be (heavily) influenced by other sources (incl. historic contamination e.g. by infiltration from deposited waste).

In general measured Cd concentrations in surface water are situated above the modelled local values for the receiving surface water.

It should be noticed that in general the analytical methods (detection limit > 0.10 µg L^{-1}) used are not adequate to accurately and reliably measure (very low) concentrations in the environment.

The measured (estimated dissolved) concentrations, including 'background' concentrations, range from 0.08 to 1.3 µg $L^{-1}$for cadmium production-sites. The range of calculated local C_{water} and PEC values in water is respectively 0.00026 – 0.53 µg/l and 0.11-0.64 µg L^{-1}(the latter figures including the calculated 0.11 µg L^{-1}regional background level). Comparison of these local measured data for sites emitting to surface water with the calculated local PEC_{water} values of the corresponding sites shows good corroboration (the difference is maximum a factor 3.5 lower to factor 4.6 higher).

The measured data for NiCd battery recycler (site 1; for 2002 and 2004) 19.8 - 10.6 µg $L^{-1}$are two orders of magnitude higher as the corresponding calculated $Clocal_{water}$ and PEC values for this site are 0.13 - 0.08 µg $L^{-1}$and 0.24 – 0.19 µg L^{-1}(factors up to 152 - 132 difference).

For other sectors/plants no comparison is possible due to lack of measured data.

Both calculated and measured values will be taken forward to the risk characterisation bearing however in mind the limitations of these values.

Measured Cd concentrations in sediment (without correction for bioavailability), presented in **Table 3.139**, are available for Cd metal production-site 1, 6 and 7, NiCd battery manufacturing site 4 and Cd recycling site 1.

- For Cd metal production-site 1, the measured Cd concentration in sediment sampled upstream and at the discharge point is 5 mg kg^{-1} dw and 1.6 mg kg^{-1} dw respectively. Measured Cd concentrations are situated a factor of 14-45 below the $PEClocal_{sediment}$ of 71.5 mg kg^{-1} dw. This site also submitted information on AVS and organic carbon content of the sediments. Using these data, the exposure assessment could further be refined. As the methodology to perform the bioavailability correction for Cd is still under development, the correction will be performed in a next phase of the update RA process.
- Cd metal production-site 6 provides recent upstream and downstream measurements in sediments of 0.64 mg Cd/kg dw and 1.14 mg Cd/kg dw respectively (year 2002). As for site 1, the measured Cd concentrations are 2.4-4.2 times below the calculated $PEClocal_{sediment}$ of 2.7 mg kg^{-1} dw.

- For Cd metal production-site 7, discharging to a marine environment, Cd concentrations in sediment are reported near the discharge point for the year 1996: 1.1 mg kg^{-1} dw and in the open sea: 2.1-3.2 mg kg^{-1} dw. The same observation is made as for the other Cd metal producing plants. Measured Cd concentrations are situated 7.7-22.3 times below the modelled sediment concentration i.e. 24.5 mg kg^{-1} dw.
- NiCd battery manufacturing site 4 provides recent upstream and downstream measurements in sediments of 3.3 mg kg^{-1} dw and 4.6 mg kg^{-1} dw respectively (year 2001). The measured Cd concentrations are situated below, but in the same order of magnitude as the calculated PEClocal sediment of 7.2 mg kg^{-1} dw. Please note that the downstream sample is situated 3 km from the discharge point.
- Cd recycling site 1 provides recent upstream and downstream measurements in sediments of 55 mg kg^{-1} dw and 133 mg kg^{-1} dw respectively (year 2002). The measured Cd concentrations are 3-7 fold the calculated PEClocal sediment of 19.0 mg kg^{-1} dw. Please note that the measured data are influenced by historical contamination (infiltration and run-off waters from old metallurgical slag heaps). The sediment data for the year 2004 show an increase in Cd concentrations: upstream concentration: 88 mg kg^{-1} dw; downstream value 224 mg kg^{-1} dw. These data are 7-17 fold the modelled value of 13.2 mg kg^{-1} dw.

In conclusion, it is noted that only limited measured information is (made) available.

Moreover, it is stated by the companies that submitted measured data are (heavily) influenced by other sources (including historic contamination e.g. by infiltration from deposited waste).

In general, measured values are situated below the corresponding modelled $PEClocal_{sediment}$.

This may be due to the fact that the calculated PECsediment, derived using the partitioning methodology and $Kp_{suspended\ solids,}$ overestimates the real situation.

The measured concentrations in sediment (in the range 1.1 to 5 mg kg^{-1} dw) are for the Cd metal producers a factor 4.2 to 22.3 lower than the calculated values (range 2.7 to 71.5 mg kg^{-1} dw). Clocal sediment varies between 0.03 and 68.8 mg kg^{-1} dw. Only for one site (site 1): more detailed information on AVS and SEM concentrations on Cd, Cu and Pb are available.

For NiCd battery producers no comparison is possible due to lack of representative measured data (i.e. data for site 4 are not considered valid/useful given the distance from the discharge point).

For the NiCd recycler's site 1 measured data are a factor 7 to 17 higher than the calculated values. $Clocal_{sediment}$ is 10.6 to 16.3 mg kg^{-1} dw. Measurements only relate to Cd concentration in sediment. No data are available on AVS and SEMs on other metals, neither the sampling date(s).

For other sectors/plants no comparison is possible due to lack of measured data.

Both calculated and measured data will be taken forward to the risk characterisation bearing however in mind the limitations of these values.

3.1.3.3.2 Terrestrial compartment

Calculated PEC for soil

Calculations are made following the equations given in Section 3.1.3.1.4.

The local PEC_{soil} are readily calculated from the release data and the above-mentioned equation and are presented in **Table 3.140-Table 3.145**.

Cd metal production

- Daily stack emissions to air vary between 0.03 kg Cd/d (site 6) and 0.15 kg Cd/d (site 7).
- Calculated annual average deposition rates vary between $2.74 \cdot 10^{-4}$ mg/m^2/day and $1.48 \cdot 10^{-3}$ mg/m^2/day
- The main exposure route is aerial deposition for Cd metal producers; sludge from the on-site waste water treatment system is not applied to agricultural land but is recycled or land-filled (industry information).
- Calculated added local concentrations in soil vary between 0.003 mg kg^{-1} ww (site 6) and 0.02 mg kg^{-1} ww (site 7).
- Calculated PEC_{local} in soil vary between 0.36 mg kg^{-1} ww (calculated regional background soil = 0.36 mg kg^{-1} ww) and 0.38 mg kg^{-1} ww (based on calculated aerial deposition rates). For site 7, the selected measured annual average aerial deposition rate of 0.008 mg/m^2/day was used for PECsoil derivation. The PECsoil level, on the basis of measured deposition rates, for this site is 0.45 mg kg^{-1} ww. Please note that using measured deposition rates for $PEClocal_{soil}$ derivation addresses a reasonable worst case situation. Measured deposition data are influenced by blown up dust and other undefined inputs.

Table 3.140 Calculated total local PEC_{soil} for Cd-metal producing plants in EU-16. PEC's include background Cd

N°	Emission to air¶	Number of emission days	$Clocal_{soil}$	$PEClocal_{soil}$ (modelled aerial deposition rates)	$PEClocal_{soil}$ (measured aerial deposition rates)	Year
	kg d^{-1}		mg kg$_{ww}^{-1}$	mg kg$_{ww}^{-1}$		
1	0.08(a)(b)	365	0.01	0.37	-	2002
6	0.03(a)(c)	365	0.003	0.36	-	2002
7	0.15(a)(d)	365	0.02	0.38	0.45	2002

¶ Annual averages;
a) Cd emission from whole plant (including Zn and/or Pb production);
b) Total emissions: stack + diffuse emissions; diffuse emissions: 60-70% of total; stack emissions: 30-40% of total emissions;
c) All emissions from point sources and fugitive emissions from roof openings for the whole zinc production process. Emissions from cadmium production are difficult to separate;
d) Total emissions from the zinc smelter; approximately 90 emission points to air. Approximately 90% of the emission comes from 20% of the emission points which all are equipped with abatement systems (demisters or scrubbers).

Cd oxide production

- Daily stack emission to air is 0.026 kg Cd/day (year 2005; in-house methods) and 0.045 kg/day (year 2004; stack air measurements performed by external laboratory).
- The calculated annual average deposition rate is $1.81 \cdot 10^{-4}$ mg/m^2/day (year 2005) and $3.19 \cdot 10^{-4}$ mg/m^2/day (year 2004).
- The main exposure route is aerial deposition for Cd oxide producers.
- Calculated added local concentration in soil is 0.002 mg kg^{-1} ww (year 2005) and 0.003 mg kg^{-1} ww (year 2004).

- Calculated PEC_{local} in soil is 0.36 mg kg^{-1} ww (calculated regional background soil = 0.36 mg kg^{-1} ww).

Table 3.141 Calculated total local PECsoil for Cd-oxide producing plants in EU-16. PEC's include background Cd (0.36 mg kg^{-1} ww)

N°	Emission to air¶	Number of emission days	$Clocal_{soil}$	$PEClocal_{soil}$	Year
	kg d^{-1}		mg kg_{ww}^{-1}	mg kg_{ww}^{-1}	
12	0.026[(a)]	256	0.002	0.36	2005
12	0.045[(b)]	256	0.003	0.36	2004

¶ Annual averages;
a) Cd in stack emissions is recently measured (year 2005); average Cd concentration: 55 µg/m^3 (punctual measurement; in-house methods);
b) Cd in stack emissions measured by external laboratory (year 2004); average Cd concentration: 97 µg/m^3.

Production of NiCd batteries

- Daily stack emissions to air vary between 0.01 (site 4) and 0.02 kg Cd/day (site 2, battery manufacturing plant only). Site 3 did not provide any emission information, since air emissions are not monitored (not obliged in permit).
- The calculated annual average deposition rates vary between $9.59 \cdot 10^{-5}$ (site 4) and $1.37 \cdot 10^{-4}$ mg/m^2/day (site 2)
- The main exposure route is aerial deposition for NiCd battery producers; sludge from the on-site waste water treatment system is not applied to agricultural land but is recycled or land-filled (industry information).
- Calculated added local concentration in soil is 0.001 mg kg^{-1} ww (site 2, 4).
- Calculated PEC_{local} in soil is 0.36 mg kg^{-1} ww (calculated regional background soil = 0.36 mg kg^{-1} ww) (site 2, 4).

Table 3.142 Calculated total local PECsoil for NiCd batteries producing plants in EU-16. PEC's include background Cd

N°	Emission to air¶	Number of emission days	$Clocal_{soil}$	$PEClocal_{soil}$	Year
	kg d^{-1}		mg kg_{ww}^{-1}	mg kg_{ww}^{-1}	
2	0.02[(a)]	330	0.001	0.36	2002
3	n.d.[(b)]	330	n.d.	n.d.	2002
4	0.01	344	0.001	0.36	2002
6	No update data				
7	No update data				

¶ Annual averages;
n.d. No data available;
a) Emission from battery manufacturing only; air emissions are broken down between two plants; battery manufacturing and Cd recycling;
b) Air emissons are not monitored. No requirement in the permit since the plant runs a wet process, therefore most emissions are releases in the water.

Recycling of NiCd batteries

- Daily stack emissions to air vary between $5.3 \cdot 10^{-6}$ kg Cd/d (site 2) and 0.01 kg Cd/day (site 1, year 2002 data).
- Calculated annual average deposition rates vary between $5.21 \cdot 10^{-8}$ mg/m^2/day and $1.09 \cdot 10^{-4}$ mg/m^2/day
- The main exposure route is aerial deposition for Cd recyclers; sludge from the on-site waste water treatment system is not applied to agricultural land but is recycled or land-filled (industry information).
- Calculated added local concentrations in soil vary between $5.6 \cdot 10^{-7}$ mg kg^{-1} ww (site 2) and 0.0012 mg kg^{-1} ww (site 1, year 2002 data).
- Calculated PEC_{local} in soil is 0.36 mg kg^{-1} ww (calculated regional background soil = 0.36 mg kg^{-1} ww).

Table 3.143 Calculated total local PECsoil for NiCd batteries recycling plants in EU-16. PEC's include background Cd

N°	Emission to air¶	Number of emission days	$Clocal_{soil}$	$PEClocal_{soil}$	Year
	kg d^{-1}		mg kg_{ww}^{-1}	mg kg_{ww}^{-1}	
1	0.01	355	0.0012	0.36	2002
1	0.003	336	0.0003	0.36	2004
2	$5.3 \cdot 10^{-6}$(a)	360	$5.6 \cdot 10^{-7}$	0.36	2002
2bis	0.003(b)	330	0.0003	0.36	2002

¶ Annual averages;

a) Submitted air emissions are checked versus the analysis report and proved to be correct. Air emissions are that low due to the fact that in air emission no considerable amount of Cd can be found (conc. 2.5 µg/m^3) and the fact that the gas stream is very low due to technical reasons (78 m^3/hours maximum);

b) Emissions from Cd recycling unit on the site of battery manufacturing plant 2.

Production of Cd containing pigments

- Daily stack emissions to air vary between 0.01 kg Cd/day (site A, C) and 0.02 kg Cd/day (site B).
- Calculated annual average deposition rates vary between $6.85 \cdot 10^{-5}$ mg/m^2/day and $1.53 \cdot 10^{-4}$ mg/m^2/day
- The main exposure route is aerial deposition for Cd pigments producers. Sludge from the treatment of waste water is land-filled.
- Calculated added local concentrations in soil vary between 0.0007 mg kg^{-1} ww (site A) and 0.002 mg kg^{-1} ww (site B).
- Calculated PEC_{local} in soil is 0.36 mg kg^{-1} ww (calculated regional background soil = 0.36 mg kg^{-1} ww).

Table 3.144 Calculated total local PECsoil for Cd pigments producing plants in EU-16. PEC's include background Cd

N°	Emission to air¶	Number of emission days	$Clocal_{soil}$	$PEClocal_{soil}$	Year
	kg d^{-1}		mg kg_{ww}^{-1}	mg kg_{ww}^{-1}	
A	0.01	230	0.0007	0.36	2003
B	0.02	318	0.002	0.36	2003
C	0.01	250	0.0008	0.36	2003

¶ annual averages Production of Cd containing stabilisers.

- Daily stack emissions to air vary between 0.002 kg Cd/day (site Y) and 0.003 kg Cd/day (site X).
- Calculated annual average deposition rates vary between $2.74 \cdot 10^{-6}$ mg/m^2/day and $1.75 \cdot 10^{-5}$ mg/m^2/day
- The main exposure route is aerial deposition for Cd stabiliser producers. Although site X discharges its waste water to a municipal STP; the sludge is not applied to agricultural soil (see subsection "Calculated PEC for soil" under Section 3.1.3.3.2). Site-specific information on the destination of sludge is not available.
- Calculated added local concentrations in soil vary between $2.9 \cdot 10^{-5}$ mg kg^{-1} ww (site Y) and 0.0002 mg kg^{-1} ww (site X).
- Calculated PEC_{local} in soil is 0.36 mg kg^{-1} ww (calculated regional background soil = 0.36 mg kg^{-1} ww).

Table 3.145 Calculated total local PECsoil for Cd stabiliser producing plants in EU-16. PEC's include background Cd

N°	Emission to air¶	Number of emission days	$Clocal_{soil}$	$PEClocal_{soil}$	Year
	kg d^{-1}		mg kg_{ww}^{-1}	mg kg_{ww}^{-1}	
X	0.003	220	0.0002	0.36	2002
Y	0.002	50	$2.9 \cdot 10^{-5}$	0.36	2002

¶ Annual averages.

Use of Cd/CdO in alloys, plating and other uses

For these uses, no update information was submitted to the Rapporteur.

Measured levels in soil

There are no measured local soil concentrations submitted by the Cd/CdO producing- or processing industries.

Measured aerial deposition rates are available for the Cd metal producing sites. A comparison between calculated and measured deposition levels is provided in **Table 3.153** (see subsection "Measured levels" under Section 3.1.3.3.3).

3.1.3.3.3 Atmospheric compartment

Calculation of $PEClocal_{air}$

Local PEC-values for the atmospheric compartment are calculated according to the OPS model proposed in the TGD (EC, 2003) for a general standard environment.

Input data are the total daily emissions of the individual Cd-producing and processing plants (Industry questionnaires, 2004).

The calculated concentrations in air are actual contributions to the receiving atmosphere. The local PEC values are obtained by adding the regional PEC values for air to the calculated local concentration in the atmosphere.

$$PEClocal_{air,ann} = Clocal_{air,\ ann} + PECregional_{air}$$

$PEClocal_{air,ann}$: annual average predicted environmental concentration in air (ng m^{-3})
$PECregional_{air}$: regional concentration in the air (0.55 ng m^{-3}; **Table 3.157**)

The results of the predicted local atmospheric Cd concentrations at 100 m from the point sources are listed in **Table 3.146-Table 3.149**.

Cd metal production

- Daily stack emissions to air vary between 0.03 kg Cd/day (site 6) and 0.15 kg Cd/day (site 7). Please note that in general for the Cd metal production-sites the total emissions are reported i.e. emissions from stack and diffuse sources. Moreover, emissions due to refining/production of other non-ferro metals may be included (to different extent from site to site).
- Calculated annual average Cd concentrations at a distance of 100 m from the point source vary between 7.6 ng/m^3 (site 6) and 41.3 ng/m^3 (site 7).
- Calculated $PEClocal_{air}$ values vary between 8.2 and 41.8 ng/m^3 (calculated regional background = 0.55 ng/m^3).

Table 3.146 Calculated total local PECair for Cd-metal producing plants in EU-16. PEC's include background Cd

N°	Emission to air	Number of emission days	Annual average air concentration	$PEClocal_{air,ann}$	Year
	kg d^{-1}		(100 m) ng m^{-3}	(100 m) ng m^{-3}	
1	0.08[(a)(b)]	365	23.2	23.7	2002
6	0.03[(a)(c)]	365	7.6	8.2	2002
7	0.15[(a)(d)]	365	41.3	41.8	2002

¶ Annual averages;
a) Cd emission from whole plant (including Zn and/or Pb production);
b) Total emissions: stack + diffuse emissions; diffuse emissions: 60-70% of total; stack emissions: 30-40% of total emissions;
c) All emissions from point sources and fugitive emissions from roof openings for the whole zinc production process. Emissions from cadmium production are difficult to separate;
d) Total emissions from the zinc smelter; approximately 90 emission points to air. Approximately 90% of the emission comes from 20% of the emission points which all are equipped with abatement systems (demisters or scrubbers).

Cd oxide production

- The daily stack emissions to air for CdO production-site 12 amount to 0.026 kg/day (year 2005, in house methods). On the basis of Cd measurements in the stacks, performed by an external laboratory, an emission amount of 0.045 kg/day could be calculated for the year 2004.
- The calculated annual average Cd concentration at a distance of 100 m from the point source is 5.0 ng/m^3 (year 2005) and 8.9 ng/m^3 (year 2004).
- The calculated PEClocal air is 5.6 ng/m^3 (year 2005) and 9.4 ng/m^3 (year 2004).

Table 3.147 Calculated total local PECair for Cd-oxide producing plants in EU-16. PEC's include background Cd

N°	Emission to air	Number of emission days	Annual average air concentration	$PEClocal_{air,ann}$	Year
	kg d^{-1}		(100 m) ng m^{-3}	(100 m) ng m^{-3}	
12[(a)]	0.026	256	5.0	5.6	2005
12[(b)]	0.045	256	8.9	9.4	2004

¶ Annual averages;
a) Cd in stack emissions is recently measured (year 2005); average Cd concentration: 55 µg/m^3 (punctual measurement, in-house methods);
b) Cd in stack emissions measured by external laboratory (year 2004); average Cd concentration: 97 µg/m^3.

Production of NiCd batteries

- Daily stack emissions to air vary between 0.01 kg Cd/day (site 4) and 0.02 kg Cd/day (site 2, battery manufacturing plant only). Data are not available for site 3 since there is no requirement to monitor air emissions.
- The calculated annual average Cd concentration at a distance of 100 m from the point source vary between 2.7 ng/m^3 (site 4) and 3.8 ng/m^3 (site 2).
- Calculated $PEClocal_{air}$ varies between 3.2 ng/m^3 and 4.4 ng/m^3 (calculated regional background = 0.55 ng/m^3).

Table 3.148 Calculated total local PECair for NiCd battery producing plants in EU-16. PEC's include background Cd

N°	Emission to air	Number of emission days	Annual average air concentration	$PEClocal_{air,ann}$	Year
	kg d^{-1}		(100 m) ng m^{-3}	(100 m) ng m^{-3}	
2	0.02[(a)]	330	3.8	4.4	2002
3	n.d.[(b)]	330	n.d.	n.d.	
4	0.01	344	2.7	3.2	2002
6	No update data				
7	No update data				

¶ Annual averages;
n.d. No data available;
a) Emission from battery manufacturing only; air emissions are broken down between two plants; battery manufacturing and Cd recycling;
b) Air emissions are not monitored. No requirement in the permit since the plant runs a wet process, therefore most emissions are releases in the water.

Recycling of NiCd batteries

- Daily stack emissions to air vary between $5.3 \cdot 10^{-6}$ kg Cd/day (site 2) and 0.01 kg Cd/day (site 1, year 2002 data). Year 2004 data for site 1 show a significant reduction in air emissions -i.e. 0.003 kg Cd/y- as a result of measures taken to obtain an ISO 14000 certificate (building coverage, aspiration devices). The reported very low air emissions of site 2 are verified and proved to be correct (very low Cd concentrations and gas flow rate; analysis done by extern laboratory).
- The calculated annual average Cd concentrations at a distance of 100 m from the point source vary between 0.001 ng/m^3 (site 2) and 3.0 ng/m^3 (site 1).
- Calculated $PEClocal_{air}$ vary between 0.6 ng/m^3 and 3.6 ng/m^3 (calculated regional background = 0.55 ng/m^3).

Table 3.149 Calculated total local PECair for NiCd battery recycling plants in EU-16. PEC's include background Cd

N°	Emission to air¶	Number of emission days	Annual average air concentration	$PEClocal_{air,ann}$	year
	kg d^{-1}		(100 m) ng m^{-3}	(100 m) ng m^{-3}	
1	0.01	355	3.0	3.6	2002
1	0.003	336	0.69	1.2	2004
2	$5.3 \cdot 10^{-6}$(a)	360	0.001	0.6	2002
2bis	0.003(b)	330	0.6	1.2	2002

¶ Annual averages;

a) Submitted air emissions are checked versus the analysis report and proved to be correct. Air emissions are that low due to the fact that in air emission no considerable amount of Cd can be found (conc. 2.5 µg/m^3) and the fact that the gas stream is very low due to technical reasons (78 m^3/hour maximum);

b) Emissions from Cd recycling unit on the site of battery manufacturing plant 2.

Production of Cd containing pigments

- Daily stack emissions to air vary between 0.01 kg Cd/day (site A, C) and 0.02 kg Cd/day (site B).
- Calculated annual average Cd concentrations at a distance of 100 m from the point source vary between 1.9 ng/m^3 (site A, C) and 4.3 ng/m^3 (site B).
- Calculated $PEClocal_{air}$ values vary between 2.5 and 4.8 ng/m^3 (calculated regional background = 0.55 ng/m^3).

Table 3.150 Calculated total local PECair for Cd pigment producing plants in EU-16. PEC's include background Cd

N°	Emission to air ¶	Number of emission days	annual average air concentration	$PEClocal_{air,ann}$	Year
	kg d^{-1}		(100 m) ng m^{-3}	(100 m) ng m^{-3}	
A	0.01	230	1.9	2.5	2002
B	0.02	318	4.3	4.8	2002
C	0.01	250	2.2	2.8	2002

¶ annual averages Production of Cd containing stabilisers.

- Daily stack emissions to air vary between 0.002 kg Cd/day (site Y) and 0.003 kg Cd/day (site X).

- Calculated annual average Cd concentrations at a distance of 100 m from the point source vary between 0.08 ng/m^3 (site Y) and 0.5 ng/m^3 (site X).
- Calculated $PEClocal_{air}$ values vary between 0.6 and 1.0 ng/m^3 (calculated regional background = 0.55 ng/m^3).

Table 3.151 Calculated total local PECair for Cd stabiliser producing plants in EU-16. PEC's include background Cd

N°	Emission to air ¶	Number of emission days	Annual average air concentration	$PEClocal_{air,ann}$	Year
	kg d^{-1}		(100 m) ng m^{-3}	(100 m) ng m^{-3}	
X	0.003	220	0.5	1.0	2002
Y	0.002	50	0.08	0.6	2002

¶ Annual averages.

Use of Cd/CdO in alloys, plating and other uses

For these uses, no site-specific update information was submitted in time to the Rapporteur.

Measured levels

Table 3.152 Summary of calculated versus measured levels in air for Cd/CdO producing/processing sectors

N°	Emission amount	$PEClocal_{air}$ Calculated (100 m)	Measured ann.avg. air concentration	Remarks	Year
	kg d^{-1}	ng m^{-3}	ng m^{-3}		
Cd metal production					
1	0.08	23.7	5.6	300 m from emission point, measured with pourbaix (isokinetic) low volume sampler, year 2003 data.	2003: measured 2002: modelled
6	0.03	8.2	1.8	300 m NNW of Cd refinery (border of the site). Sampling device: DIGITEL DHA-80 (Riemer Messtechnik), high volume sampler, 500 l/min, 24 hours; pore size: 5µm (in-house analysis). Data are influenced by neighbouring harbour and industrial activities.	2002
7	0.15	41.8	8.5 (± 14.94 st.dev.) (450 m NNW) 0.97 (± 1.06 st. dev.) (626 m SW)	3 month period; 4 sampling points; 14 measurements per point; ICP-MS, NILU method U-22, Norwegian Institute of Air research (NILU), year 2003 data (external laboratory)	2003: measured 2002: modelled

Table 3.152 continued overleaf

Table 3.152 continued Summary of calculated versus measured levels in air for Cd/CdO producing/processing sectors

N°	Emission amount	$PEClocal_{air}$ Calculated (100 m)	Measured ann.avg. air concentration	Remarks	Year
	kg d^{-1}	ng m^{-3}	ng m^{-3}		
Cd oxide production					
12	0.026	5.6	n.d.	n.d.	2005
12	0.045	9.4	n.d.	n.d.	2004
NiCd battery production					
2	0.02	4.4	n.d.	n.d.	2002
3	No data	No data	4	200 m from stack, downwind. Measurements are carried out according to NFX 43.261 and NFX 43.006.	
4	0.01	3.2	0.3	50 m from property line to the NW; in direction of prevailing wind	2002
6	No update data				
7	No update data				
NiCd battery recycling					
1	0.01	3.6	126 (300 m N) 37 (300 m S) wind direction: from N or from S	Cd in PM 10; Sampling apparatus: High Volume System (Digitel DA 80); flow rate: 500 l/mn, 24 hours/day, more than 350 d/y. Analytical method: ICP, spectrophotometer.	2002
1	0.003	1.2	21 (300m N)* 15 (300m S) wind direction: from N or from S	Cd in PM 10; Sampling apparatus: High Volume System (Digitel DA 80); flow rate: 500 l/mn, 24 hours/day, more than 350 d/y. Analytical method: ICP, spectrophotometer	2004
2	$5.3 \cdot 10^{-6}$	0.6	n.d.	n.d.	2002
2bis	0.003	1.2	n.d.	n.d.	2002
Cd pigments production					
A	0.01	2.5	n.d.	n.d.	2003
B	0.02	4.8	n.d.	n.d.	2003
C	0.01	2.8	n.d.	n.d.	2003

Table 3.152 continued overleaf

Table 3.152 continued Summary of calculated versus measured levels in air for Cd/CdO producing/processing sectors

N°	Emission amount	PEClocal$_{air}$ Calculated (100 m)	Measured ann.avg. air concentration	Remarks	Year
	kg d^{-1}	ng m^{-3}	ng m^{-3}		
Cd stabiliser production					
X	-	1.0	n.d.	Cd concentration in air of the surroundings of the plant is considered to be negligible or very close to zero.	2002
Y	0.002	0.6	n.d.	n.d.	2002

n.d. No data available;

* The reduction in air concentrations in 2004, as compared to 2002, is a result of the measures taken to reduce point and diffuse air emissions from the site (improvement in building coverage/aspiration device and improved air treatment systems (two rows of filters) (ISO 14000 certificate).

Reduction in emission data of 2002 (and possibly later year(s)) compared to previously reported and assessed data of 1996 should be seen in the light of the information given in Section 3.1.2.3 and per sector in the paragraph starting with 'significant changes in production/emission reduction measures'.

Table 3.153 Summary of calculated versus measured aerial deposition levels for Cd/CdO producing/processing sectors

N°	Emission amount	Aerial deposition calculated	Aerial deposition measured	Remarks	Year
	kg d^{-1}	mg/m^2.day	mg/m^2.day		
Cd metal production					
1	0.08	$8.33 \cdot 10^{-4}$	0.1	average of 8 sampling points, average distance 1 km, deposition measurements with Bergerhoff collecting measurements, year 1996-1998). No individual data for points provided. The data are influenced by excavation activities on the plant area.	2002-2003
6	0.03	$2.74 \cdot 10^{-4}$	6.4 mg/m^2.d (300 m NNW) 4.5 mg/m^2.d (1.2 km ENE) 2.4 mg/m^2.d (750 m S) 2.7 mg/m^2.d (1 km WNW) 1.7 mg/m^2.d (1.2 km SW)	sampling in accordance with VDI 2119, Bergerhoff system, duration 1 month. Data are influenced by neighbouring harbour and industrial activities.	2002
7	0.15	0.0015	0.008	location: 500 m NNW, NILU, method ISO/DIS 4222.2 standard, n=12	2002

Table 3.153 continued overleaf

Table 3.153 continued Summary of calculated versus measured aerial deposition levels for Cd/CdO producing/processing sectors

N°	Emission amount	Aerial deposition calculated	Aerial deposition measured	Remarks	Year
	kg d^{-1}	$mg/m^2.d$	$mg/m^2.d$		
Cd oxide production					
12	0.026	$1.81 \cdot 10^{-4}$	n.d.		2005
12	0.045	$3.19 \cdot 10^{-4}$	n.d.		2004
NiCd battery production					
2	0.02	$1.37 \cdot 10^{-4}$	n.d.		2002
3	n.d.	n.d.	n.d.		2002
4	0.01	$9.59 \cdot 10^{-5}$	n.d.		2002
6	No update data				
7	No update data				
NiCd battery recycling					
1	0.01	$1.09 \cdot 10^{-4}$	n.d.		2002
1	0.003	$2.49 \cdot 10^{-5}$	n.d.		2004
2	$5.3 \cdot 10^{-6}$	$5.21 \cdot 10^{-8}$	n.d.		2002
2bis	0.003	$2.33 \cdot 10^{-5}$	n.d.		
Cd pigments production					
A	0.01	$6.85 \cdot 10^{-5}$	n.d.		2003
B	0.02	$1.53 \cdot 10^{-4}$	n.d.		2003
C	0.01	$7.95 \cdot 10^{-5}$	n.d.		2003
Cd stabiliser production					
X	0.003	$1.75 \cdot 10^{-5}$	n.d.		2002
Y	0.002	$2.74 \cdot 10^{-6}$	n.d.		2002

n.d. No data available

Comparison of PECs with measured data

Measured Cd concentrations in air, presented in **Table 3.152**, are available for Cd metal production-site 1, 6 and 7; NiCd battery producing site 3, 4 and Cd recycling site 1.

- For metal production-site 1, the measured annual average Cd concentration in air at a distance of 300 m from the emission point is 5.6 ng/m^3. The sampling is performed with a pourbaix low volume sampler (year 2003 data). The measured value is a factor of 4 below the modelled air concentration determined at 100 m from the emission point i.e. 23.7 ng/m^3.
- Metal production-site 6 reports measured annual average air concentration at a distance of 300 m NNW of the border of the site of 1.8 ng/m^3 (sampling device used: high volume sampler; 500 l/min, 24 hours, pore size: 5 µm). The measured value is situated a factor of 4.6 below the modelled PEC_{air} of 8.2 ng/m^3 (100 m from site). Please note that these data are influenced by neighbouring industrial activities.

- Measured Cd concentrations in the surrounding air compartment are available for Cd metal production-site 7. Measurements are performed at two different locations: 450 m NNW of site: 8.5 ± 14.9 ng/m^3 and 626 m SW of the site: 0.97 ± 1.06 ng/m^3 (year 2003 data). The highest measured concentrations are situated a factor of 4.9 below the modelled PECs. Measurements are performed according to NILU method U-22; and analysed by ICP-MS (National Environment Institute, 2003).

- Although NiCd battery producer 3 reports that there are no air emission data available (not required); measured Cd concentrations at a distance of 200 m from the stack are reported: 4 ng/m^3 (measurements carried out according to National standards NFX 43.261 and NFX 43.006).

- Battery manufacturing site 4 reports a measured annual Cd concentration in air of 0.3 ng/m^3 at a distance of 50 m from the property line in the prevailing wind direction. The measured value is a factor of 10 below the modelled PEC_{air} at 100 m from the site of 3.2 ng/m^3.

- Measured Cd concentrations in the surrounding air compartment are available for NiCd battery recycling site 1. Measurements are performed at two different locations: 300 m N of site: 126 ng/m^3 and 300 m S of the site: 37 ng/m^3 (year 2002). The wind direction is from North or South. The sampling is performed with a high volume sampler, flow rate: 500 l/min, 24 hours/day, > 350 days/year; analytical method: ICP, spectrophotometer, Cd in PM10. The highest measured concentration is situated a factor of 35 above the modelled PEC of 3.6 ng/m^3. The lowest concentration is situated a factor of 10 above the modelled PEC_{air}. Year 2004 data indicate that Cd concentrations in air are reduced in comparison with previous years: 21 ng/m^3 (300 m N) and 15 ng/m^3 (300 m S) respectively. These values are situated a factor of 12.5-17.5 above the modelled air concentrations. The plant indicates that impact from other industrial sources is probable (but cannot be quantified).

In conclusion, only limited measured information is (made) available.

Moreover, measured data are stated by the companies to be (very probably) influenced by other sources (e.g. other industrial sources, traffic etc.). However, only for one site, Cd metal producer site 7, the identification and approximate contribution of these other sources could be made based on the results of an extensive air monitoring programme. For recycler site 1 similar investigations are in preparation in collaboration with the national authority.

In general, the measured annual air concentration at a certain distance from the site is situated below the modelled $PEClocal_{air}$. This may be due to the different distances from the source (the calculated value assumes 100 m whereas the measured values were at 300 – 450 m) or different reference years (e.g. 2003 measured versus 2002 for the calculated).

For the three production companies of cadmium metal, measured concentrations, including ‘background’ concentrations, range from 1.8 to 8.6 ng/m^3. The range of calculated local C_{air} and PEC values in air is 8.2 - 41.8 ng/m^3. For corresponding sites a comparison of these local monitoring data with the calculated local C_{air} values shows that the calculated C_{air} is a factor 4 to 5 higher than the measured concentration at the respective site.

For battery producers some comparison is only possible for site 4 where the calculated value 3.2 ng/m^3 is a factor 10.6 higher than the (limitedly documented) measured data (0.3 ng/m^3).

The measured cadmium concentrations in air near the NiCd recyclers (site 1), ranging from 37 to 126 ng/m^3 (2002) and from 15 to 21 ng/m^3 (2004) are a factor 17.5 to 35 higher than the calculated local C_{air} for this site (0.6 to 3 ng/m^3).

Both calculated and measured data will be taken forward to risk characterisation bearing however in mind the limitations of these values.

Measured aerial deposition rates, presented in **Table 3.153**, are available for Cd metal production-site 1, 6 and 7.

- For metal production-site 1, the measured annual average deposition rates at a distance of 1 km from the emission point is 0.1 mg/m^2.day (year 1996-1998 data). The measured data are situated two orders of magnitude above the modelled deposition rates of $8.33 \cdot 10^{-4}$ mg/m^2.day (year 2002 data, based on stack emissions only). The sampling is performed at 8 different sampling points, located on average 1 km from the site. Bergerhoff collection methods are used to perform the sampling. It should be noted that the measured data are influenced by excavation activities in the plant area.
- Metal production-site 6 reports measured annual average deposition rates at different locations: 6.4 mg/m^2.day (300 m NNW); 4.5 mg/m^2.day (1.2 km ENE); 2.4 mg/m^2.day (750 m S); 2.7 mg/m^2.day (1 km WNW) and 1.7 mg/m^2.day (1.2 km SW). Relevant values (1.7-4.5 mg/m^2.day; within 1,000 m range as described in the TGD) are situated three orders of magnitude above the modelled aerial deposition value for the site of $2.74 \cdot 10^{-3}$ mg/m^2.day. The sampling is performed in accordance with national guidelines VDI 2119 using Bergerhoff system, duration: 1 month. Please note that the deposition monitoring data are influenced by neighbouring harbour and industrial activities.
- Metal production-site 7 reports a measured annual average deposition rate of 0.008 mg/m^2.day measured at 500 m NNW of the site. The measured Cd deposition rate is five fold the deposition rate modelled by EUSES (i.e. 0.0015 mg/m^2.day). The sampling is performed in accordance with ISO/DIS 4222.2 standard.

In conclusion, since metal production-sites 1 and 6 indicate that:

- the reported measured deposition rates are influenced by excavation activities on the plant area (site 1) and neighbouring harbour and industrial activities (site 6);
- fugitive emissions from both sites are reported to be minor in comparison with stack emissions (site 1) or are already included in the stack air emission estimation (site 6);
- the data from site 1 are rather outdated (1996-1998) (and in the meantime: excavation activities at the site are stopped),

It is judged that the measured aerial deposition rates for sites 1 and 6 do not fulfil the reliability and relevance criteria for further use of the data in $PEClocal_{soil}$ modelling. Hence only the average aerial deposition rate reported for site 7 is taken forward for modelling purposes.

3.1.3.3.4 Secondary poisoning

No changes made.

3.1.3.4 Regional and continental exposure assessment

3.1.3.4.1 Regional and continental concentrations calculated according to the TGD

Calculation of the regional environmental exposure concentration is based on both point and diffuse sources over a wider (regional) area. The regional PEC also provides the Cd background concentration (anthropogenic and natural) that is incorporated in the calculation of the local PEC.

The point Cd emissions are rather well documented (see Section 3.1.3.1). Some diffuse Cd emissions can also be rather well quantified such as Cd input from fertilisers or the total losses to the air based on deposition data (see **Table 3.178** and **Table 3.180**). Total Cd emissions during use and from disposal of Cd containing products are more difficult to quantify. Emissions of Cd from waste incineration and land-filling have been estimated in the TRAR/batteries' related sections.

Data of the OECD 1995 questionnaire (Pearse, 1996) and, for The Netherlands, the RIVM 1997 data are used for calculating the regional and continental PEC values in the various environmental compartments. These data were not complete and the missing data were completed with emission data that were estimated by ERL (ERL, 1990), or other sources as indicated in **Tables 3.154**, **3.155** and **3.156**.

Annual atmospheric emissions in the EU-16 amount to at least 124 tonnes Cd (see **Table 3.154**). This value does not include natural sources of Cd emission (15 tonnes y^{-1}, ERL 1990) such as emissions from Mount Etna, sea spray, forest fires, weathering of Cd rich soils, etc. The contribution of the natural sources is included in the background which is added to the continental PEC's (see Section 3.1.1). The emission of the EU non-ferrous metal producers and of Cd processors is 14.4 tonnes Cd. This value corresponds well with the sum of the emissions of these industries estimated in each country. The major sources of atmospheric Cd emissions in the environment are oil/coal combustion (43%) and iron and steel production (24.7%). Large differences are noticed in estimated Cd emissions from oil/coal combustion. As an example ERL estimates 7.1 tonnes Cd emission from oil/coal combustion for the UK whereas the OECD data estimate 48.2 tonnes Cd emission for the UK (Pearse, 1996) and Berdowski et al. (1998) 4.5 tonnes Cd/year. Total Cd emission in the EU from oil/coal combustion is 49.3 tonnes (ERL, 1990) or 54 (see **Table 3.154**, data of Berdowski et al. (1998) and ERL (1990)). A roughly estimated EU average value of measured deposition is 1 g Cd g ha^{-1} y^{-1} (see **Table 3.180**). This is equivalent to 356 tonnes Cd on the EU wide area. This value indicates that the atmospheric Cd emissions (including natural) are about 2 fold underestimated. On the other hand, net deposition may also be overestimated because even wet-only deposition data can include Cd that is resuspended from soil. Analytical quality of measured data is also a major issue in this assessment. The EU average Cd deposition rate is predicted about 0.4 g Cd ha^{-1} y^{-1} (see **Table 3.180**) and which is equivalent to 0.06 µg Cd/Lin collected rain water (assume 700 mm rainfall y^{-1}). Limits of quantification of Cd in water samples are often about 0.05 µg Cd/Lin monitoring programmes.

Annual emissions in water are at least 39 tonnes Cd (see **Table 3.155**). The available data are not comparable between EU countries since not all emissions were taken into account in each country. As an example, the Swedish Cd emission from municipal wastewater is 0.3 tonnes Cd/year. An extrapolation of this number to the EU on population basis, yields 12.7 tonnes Cd/year. It is unknown to what extent this value reflects a net emission to water.

Waste water contains natural Cd (e.g. surface water contains 0.05µg L^{-1}, dissolved natural Cd, see Section 3.1.3.4.3) and carry Cd that is recycled within the environment (dust, organic matter, etc.). Data on Cd emission from waste water treatment plants in the different EU countries are scarcely available. The older data provided by ERL (ERL, 1990) estimated Cd emissions from non ferrous metal producers and Cd processors as large as 72 tonnes Cd/year. The updated data (Pearse, 1996) yield estimated emissions of only 11.1 tonnes Cd/year (see **Table 3.155**, all data refer to emissions after the STP). Stormwater and combined sewer overflows may not be entirely covered. Emissions to water through runoff from soil are not accounted in **Table 3.155**. The anthropogenic part of these emissions is, however, included in the PECwater calculations because the model (EUSES 1.0) assumes that a fraction of the emissions to soil is released to water. The natural part of these processes is included via the background Cd concentration that is added to the predicted added concentrations (see Section 3.1.1. Emissions of Cd to water from natural processes are estimated to be of the same order of magnitude or even larger than the anthropogenic emissions. The natural background of Cd (dissolved fraction only) is estimated 0.05 µg $L^{-1}$for the entire of Europe. At default values of water volumes in the European continent (320 10^9 m^3) and the mean residence time of 166 days, this natural flux is equivalent to 35 tonnes Cd $year^{-1}$ (dissolved Cd) or about 100 tonnes Cd $year^{-1}$ (total). Natural Cd in water is obviously not all derived from runoff and erosion because other biogeochemical processes, such as fluxes of natural organic transfer, introduce metals into freshwater bodies.

Fertiliser Cd and atmospheric deposition are the major sources of Cd in agricultural **soils**. Soils receive a considerable fraction of total Cd emitted to the atmosphere. The fraction surface area that is agricultural soil in EU is 0.27, therefore 0.27 · 124 tonnes Cd (34 tonnes Cd) emitted annually ends up in agricultural soils. Fertiliser Cd is estimated to be 231 tonnes y^{-1} in the EU. The amount of Cd used in agriculture through sludge application is at least 13.6 tonnes y^{-1} (see **Table 3.156**).

The Cd released to natural and industrial soil is assumed to consist of atmospheric deposition only. The fraction natural soil (surface based) is 0.6 and the fraction industrial soil is 0.1. Emissions to the natural soils are therefore 0.6 · 124 =74 tonnes Cd/year and to industrial soil 0.1 · 126 = 12.4 tonnes Cd/year.

Table 3.154 Direct atmospheric Cd emission in the EU-16 (tonnes Cd/y). Data combined from different source documents as indicated in footnotes. Note that EU totals of the non-ferrous metals producers do not match the sum of the emissions of each country. The EU totals are the most recent data and are based on confidential questionnaires

	Cd alloys[5] and batteries production and recycling[12]	Cd/CdO production	Other non-ferrous metals	Production of iron and steel	Oil/coal combustion	Processing phosphates	Municipal incineration[13]	Wood/peat combustion	Other (cement, glass prod., traffic)
Austria	0[5]	0.1[4,11]		0.1[4,11]	2.0[11]		0.086	1.4[4]	2.9[11]
Belgium	0[5]	2[4,11]		1.9[11]	3[11]	0.1[4]	0.063		0.8[11]
Denmark	0.02[5]	0[9]		0.2	0.45[11]		0.300		1.4[11]
Finland	n.d.[5]	0.4[11]		0.7[4]	0.9[11]	n.d.	0.014		1.6[11]
France	0.24[5]	0.23[11]		3.9[5,11]	7.4[11]	0.03[11]	1.92		0.02[4]
Germany	0.18[5]	5.3[11]		10.5[11]	14.23[11]		0.300		1.4[11]
UK	0.26[5]	6.7[11]		2.9[11]	4.47[11]	0.03[4]	0.019		1.4[11]
Greece	0[5]	0.02[11]		0.7[11]	1.6[11]		0[5]		2.25[11]
Ireland	0[5]	0.05[11]		0.23[11]	0.6[11]		0[5]		0.7[11]
Italy	0.04[5]	2.2[5]		4.6[5]	6.3[5]		0.351		> 0.4[5,11]
Luxemburg				0.9[11]	0.24[11]		0.022		
The Netherlands	0.01[5]	0.85[6,8]			0.3[11]		0.053		0.7[11]
Norway	n.d.	0.26[11]		0.28[11]	0.13[11]	n.d.	0.041	n.d.	1.5[11]
Portugal	0[5]	0.02[11]		0.34[11]	1.4[11]		0.003		1.2[11]

Table 3.154 continued overleaf

Table 3.154 continued Direct atmospheric Cd emission in the EU-16 (tonnes Cd/y). Data combined from different source documents as indicated in footnotes. Note that EU totals of the non-ferrous metals producers do not match the sum of the emissions of each country. The EU totals are the most recent data and are based on confidential questionnaires

	Cd alloys[5] and batteries production and recycling[12]	Cd/CdO production	Other non-ferrous metals	Production of iron and steel	Oil/coal combustion	Processing phosphates	Municipal incineration[13]	Wood/peat combustion	Other (cement, glass prod., traffic)	
Spain	0.01[5]	0.04[11]		2.34[11]	10.5[11]	0.57[11]	0.054		> 2.8[5,11]	
Sweden	n.d.	1.4[4,11]		1.2[11]	0.4[11]		0.005	0.3[4]		
EU total	0.853[5, 12]	3.9[2]	9.7[3]	31	54	0.7	3.2	1.7	> 19	TOTAL
% of total	0.6%	3.1%	7.7%	24.7%	43.0%	0.6%	2.6%¶	1.4%	15.1%	> 124

n.d. No data;
1) Norwegian Zn producer's data (1994-1996);
2) Industry questionnaire of 1997;
3) Industry update based on 1995-1996 data and subtracting the emissions from Cd/CdO industry (Van Assche, 1998);
4) OECD Cd questionnaire, 1995 (Pearse, 1996);
5) Emission data by ERL (1990);
6) RIVM, 1997;
7) Data from 1991 and given by Pearse (1996);
8) This value is estimated to consist of 0.05 tonnes Cd from non-ferrous industry and 0.8 tonnes Cd from iron and steel production;
9) No non-ferrous metals producing industry in DK;
10) Cd-Bilanz 1994 (Umweldbundesamt, 1996);
11) Berdowsky et al., 1998;
12 & 13) Measured and modelled emissions (see TRAR/batteries' related sections).

Table 3.155 Cd emissions in the EU-16 to water (tonnes Cd/y). Data combined from different source documents as indicated in footnotes. Note that EU totals of the non-ferrous metals producers and of country totals do not match the sum of the emissions of each country. The EU totals are the most recent data and are based on confidential questionnaires

	Cd plating[12] & batteries production & recycling[15]	Cd/CdO production	Other non-ferrous metals	Production of iron and steel	Oil/coal combustion/ traffic	Processing phosphates	Municipal incineration [13]	MSW operational landfills [14]	Metal mining	Other (chem. industry, municipal wastewater)	TOTAL
Austria				n.d.			0.004	0.004	0		0.008
Belgium		0.5[4]		0.4[4]		1.8[4]	0.012	0.0074	0		2.7
Denmark		0[9]		0.1[5]			0.016	0.001	0		0.1
Finland		0.1[4]		n.d.	n.d.	n.d.	0.001	0.007	n.d.		0.1
France		2.4[4]		0.1[4]		7.3[4]	0.097	0.096			9.8
Germany		0.2[10]		6.3[5]			0.108	0.99			6.5
UK		0.6[1]		3.0[5]			0.023	0.114			3.6
Greece		0.1[5]		0.1[5]	-[5]	-[5]	0	0.014	n.d.	-[5]	0.2
Ireland		0[5]		< 0.05	-[5]	-[5]	0	0.006	n.d.	-[5]	< 0.05
Italy		0.025[1]		3.6[5]			0.018	0.085			3.6
The Netherlands		0.4[6]			0.1[6]	x[11]	0.035	0.006	0	0.8[6]	1.3
Norway		0.9[1]		n.d.			0.003	0.008	0		0.9
Portugal		0.1[5]		0.1[5]	-[5]	-[5]	0.003	0.011	n.d.		0.2
Spain		>2.5		1.8[5]	-[5]	-[5]	0.012	0.072	n.d.		> 4.3
Sweden		0.1[4]		0.1[4]	-[4]	-[4]	0.013	0.017	1.1[4]	0.3[4]	1.6
EU total	0.2[12]+**0.065**[15]	1.2[2]	9.7[3]	> 15.6	> 0.1	9.1	0.354	0.55	> 1.1	> 1.2	> 39.2

n.d. No data;
1) Zn producer's data of these countries(1994-1996);
2) Industry questionnaire of 1997;
3) Industry update based on 1995-1996 data and subtracting the emissions from Cd/CdO industry (Van Assche, 1998);
4) OECD Cd questionnaire, 1995 (Pearse, 1996);
5) Emission data by ERL (1990);
6) Milieucompendium, 2001;
7) Data from 1988 and given by Pearse (1996);
8) This value is estimated to consist of 0.05 tonnes Cd from non-ferrous industry and 0.8 tonnes Cd from iron and steel production;
9) No non-ferrous metals producing industry in DK;
10) Cd-Bilanz 1994 (Umweldbundesamt, 1996);
11) Gypsum waste from the P fertiliser industry (15 tonnes Cd in 1985), this is expected to decrease to 1.2 tonnes in 1994 and 0 tonnes in 2000 (Speed, 1993);
12) WS Atkins (1998);
13), 14) and 15) Data from the TRAR/batteries' related sections.

Table 3.156 Annual Cd input into agricultural soils from phosphate fertilisers and sludge in European countries. Underlined values are used when different values were available for the same country

	Cd from phosphate fertilisers	Cd from sludge[3]
	tonnes y^{-1}	tonnes y^{-1}
Austria	2.9[1]	0.1
Belgium	1.5[6]	>6
Denmark	0.707[6]	0.12
Finland	0.2[1]	0.07
Finland		0.042[5]
France	92[2]	1.58
Germany		1.27
Germany	20.4[1]	2.4[1]
Germany¶	22.1[4]	3.2[4]
Greece	10[2]	
Ireland	7.4[6]	0.01
Italy	44[2]	
The Netherlands	3[1]	0.4
Norway	0.072[6]	
Portugal	5[2]	
Spain	30[2]	
Sweden	1.1[1]	0.1
Sweden		0.13 (1996)
UK	11.3[1]	1.88 (1996)
EU total	231	> 13.6

1) Data based on the OECD questionnaire (Pearse, 1996);
2) Landner et al. (1996), data from 1990;
3) Source: report from the commission to the council and the European Parliament on the implementation of community waste legislation Directive 86/278/EEC on sewage sludge for the period 1995-1997, data from 1997 unless otherwise stated;
4) Kiene (1999);
5) Finnish Environment Institute (1997);
6) Hutton et al. (2001).

Computations of continental exposure concentrations are made by means of multimedia fate models based on the fugacity concept. These models are box models, consisting of a number of compartments, air, water, sediment and soil, which are considered homogeneous and well mixed. A chemical released into the model is distributed between the compartments according to the properties of both the chemical and the model environment. For metals the following types of fate processes are distinguished in the continental assessment:

- emission direct and indirect (STP)

¶ The current average Cd content in P fertilisers might also be 35 mg Cd/kg P_2O_5 or 79 mg Cd/kg P (personal communication). At an application rate of 407,000 tonnes P fertiliser per year, this makes a Cd input of 32 tonnes Cd/year

- advective transport: deposition, run-off, and erosion.

The input of chemicals is regarded in the model as continuous and equivalent to continuous diffuse emission. For metals, all individual compounds are assumed to transform into the ionic species. The results from the models are steady-state concentrations, which can be regarded as estimates of long-term average exposure levels (TGD, 1996).

In the **continental** model, it is assumed that all Cd emissions enter into the continental environment. It is also assumed that no inflow of air and water across the boundaries of the continent occurs. Continental exposure concentrations are calculated based on the combined anthropogenic Cd emissions from all EU-16 countries (**Tables 3.154 - 3.156**) and on the background level of Cd

$$PECcontinental = C\_continental + background\ Cd$$

The C_contintental is the Cd concentration at continental scale that is related to Cd emissions by man (EUSES 1.0 calculations, see below). Background Cd is, by definition, the natural background for surface water and air and is the ambient Cd concentration measured in areas away from point source for soils and sediments (see Section 3.1.1).

Regional calculations are performed using a similar box model for a generic regional environment. This environment is not an actual region, but a hypothetical site with predefined environmental characteristics, the so-called ‘standard environment’. A general standard region is represented by a typical densely populated area with an area of 200 · 200 km² and 20 million inhabitants, located in the margin of Western Europe (sum of EU Member States = continental scale). By default, it is assumed that 10% of the European production and use of Cd takes place within this area. Therefore:

continental emission = 90% of total European emission

regional emission = 10% of total European emission

The PECregional is calculated from

$$PECregional= C\_regional + PECcontinental$$

The C_regional is the Cd concentration at regional scale that is related to Cd emissions by man (EUSES 1.0 calculations, see below).

For the soil compartment, however, a second model was used in which country specific Cd emission data were used (see Section 3.1.3.4.2).

C_continental and C_regional are calculated with EUSES 1.0 (1997). The output of the model gives in fact the predicted added environmental concentrations at continental and regional scale ($PEC_{con,add}$ and $PEC_{reg,add}$). Therefore C_continental is considered as the calculated $PEC_{con,add}$, and C_regional is calculated as the difference between $PEC_{reg,add}$ and $PEC_{con,add}$.

In the model calculations, the use of the physico-chemical properties of Cd are not appropriate, and estimated partition coefficients for soil, sediments and suspended matter are used instead (TGD Appendix VIII, 1996). The solid/liquid distribution coefficient in soil, K_D, was set to 280 L kg^{-1} (see Section 3.1.3.1.4), the solid/water partition coefficient, K_p, of sediment and suspended matter were both set at 130 10^3 L kg^{-1} (see Section 3.1.3.1.1, European average). The sensitivity of PEC_{water} and PEC_{sed} to the choice of K_p is tested with additional model calculations, assuming the K_p of sediment and suspended matter equal to 17 10^3 L kg^{-1} or 224 10^3 L kg^{-1}. The concentration of suspended solids was set to 15 mg L^{-1} in each scenario, both for the continental and the regional compartment.

Volatilisation is ignored for Cd, therefore the Henry-coefficient was set to 0 Pa m^3 mol^{-1}. Most of the Cd present in the atmosphere will be bound to aerosols. The vapour pressure was set to 10^{-10} Pa to ensure that the metal fraction associated to aerosols was equal to one. Biotic and abiotic degradation rates were considered not to be relevant and set to zero.

Two models are used to estimate the Cd concentration in agricultural soil. The first method follows the procedure of the TGD (1996) and is calculated by EUSES 1.0 (1997). The second model is based on the mass balance of Cd including detailed Cd immision onto soil (country based) from fertilisers, sludge and atmospheric deposition and including output through leaching and plant uptake. This model is described in detail in Section 3.1.3.4.2.

In the TGD model (Model I for soil), input sources for soil contamination include direct emission to soil, deposition from the atmosphere and emission of sewage sludge to agricultural soil. Three types of soil are distinguished: agricultural, natural and industrial. The Cd emissions from agricultural practice (fertilisers) are assumed not to affect natural or industrial soil. The diffuse Cd emissions from atmospheric deposition, traffic etc. are distributed between these 3 types of soil proportionally to the surface areas of the three types of soil. According to the TGD (1996) the fraction of surface area that is agricultural soils is 0.27, the fraction natural soil 0.6, and the fraction industrial soil 0.1.

The continental and calculated regional emission data and resulting regional PEC values are presented in **Table 3.157** (details see **Annex I**). The calculated values are averages for a general regional and general continental environment.

Table 3.157 Emission values, total concentration and total PEC values for the regional and continental environment

Input continental (anthropogenic):	
amount released to air	111.6 tonnes y^{-1}
amount released to surface water	35.2 tonnes y^{-1}
amount released to agricultural soil (1)	207.9 tonnes y^{-1} + 12.2 tonnes y^{-1} (sludge application)
amount released to natural soil(1)	0 tonnes y^{-1}
amount released to industrial soil(1)	0 tonnes y^{-1}
Input regional (anthropogenic):	
amount released to air	12.4 tonnes y^{-1}
amount released to surface water	3.9 tonnes y^{-1}
amount released to agricultural soil(1)	23.1 tonnes y^{-1} + 1.4 tonnes y^{-1} (sludge application)
amount released to natural soil(1)	0 tonnes y^{-1}
amount released to industrial soil(1)	0 tonnes y^{-1}

Table 3.157 continued overleaf

Table 3.157 continued Emission values, total concentration and total PEC values for the regional and continental environment

Results		C_continental concentration	background(2)	C_regional
Concentration in air	ng m^{-3}	0.15	0	0.40
Concentration in agricultural soil	mg kg_{wwt}^{-1}	0.175	0.266	1.43 (not used)*
Concentration in natural soil	mg kg_{wwt}^{-1}	0.018	0.266	0.048 (not used)*
Concentration in industrial soil	mg kg_{wwt}^{-1}	0.018	0.266	0.048 (not used)*
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
Concentration in surface water	µg L^{-1}	0.01	0.05	0.05
Concentration in sediment	mg kg_{wwt}^{-1}	0.48	0.77	2.64
K_p sediment/suspended matter = 17 10^3 L kg^{-1}				
Concentration in surface water	µg L^{-1}	0.06	0.05	0.24
Concentration in sediment	mg kg_{wwt}^{-1}	0.39	0.77	1.54
K_p sediment/suspended matter = 224 10^3 L kg^{-1}				
Concentration in surface water	µg L^{-1}	0.006	0.05	0.03
Concentration in sediment	mg kg_{wwt}^{-1}	0.48	0.77	2.76
PEC values		PEC continental		PEC regional
PEC air	ng m^{-3}	0.15		0.55
PEC agricultural soil	mg $kg^{-1}{}_{wwt}{}^{-1}$	0.441		0.363 (model 2)*
PEC natural soil	mg kg_{wwt}^{-1}	0.284		0.322
PEC industrial soil	mg kg_{wwt}^{-1}	0.284		0.322
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
PEC surface water (dissolved fraction)	µg L^{-1}	0.06 (selected)		0.11 (selected)
PEC sediment	mg kg_{wwt}^{-1}	1.25 (selected)		3.88 (selected)
K_p sediment/suspended matter = 17 10^3 L kg^{-1}				
PEC surface water (dissolved fraction)	µg L^{-1}	0.11		0.35
PEC sediment	mg kg_{wwt}^{-1}	1.16		2.70
K_p sediment/suspended matter = 224 10^3 L kg^{-1}				
PEC surface water (dissolved fraction)	µg L^{-1}	0.06		0.09
PEC sediment	mg kg_{wwt}^{-1}	1.25		4.01

* See note in text for discussion;
1) Not including atmospheric deposition;
2) Natural (water and air) or ambient (soil and sediment) background Cd, see Section 3.1.3.4.3.

The estimated $C_{regional}$ for agricultural soils is high and exceeds ambient Cd concentrations (see Section 3.1.3.4.4). The PEC's calculated by EUSES 1.0 refer to the 'steady state' concentrations in the environment. Cadmium has a very long residence time in soil (elimination half-life is about 380 years with default parameters) and, therefore, steady state may not be achieved within the next centuries. The assumption in the model is that 10% of the continental emissions take place within the area of a standard regional system, i.e. 10% of the continental emissions (mainly diffuse emissions) are deposited in only 1% of the total European area. Fertiliser application is the dominant source of Cd in agricultural soils (**Table 3.156** and **Table 3.157**) and is 231 tonnes

Cd y^{-1}. The fraction of surface area that is agricultural is 0.27; therefore the area of agricultural soil in that region is $0.27 \cdot 4\ 10^4$ km^2 = $1.08\ 10^4$ km^2. The predicted emission of Cd trough fertiliser at the regional scale is 10% of 231 tonnes y^{-1} or the flux is 23.1 tonnes/($1.08\ 10^4$ km^2)= 25.5 g Cd ha y^{-1}. This is about tenfold higher than the emission data found for most European countries (see **Table 3.178**). The parameter values in EUSES could be adjusted but there are a number of reasons to use alternative (existing) soil mass balances (see Section 3.1.3.4.2) rather than EUSES (e.g. modelling the transient state rather than the steady state, modelling Cd losses from background Cd due to crop off take and leaching, etc.). Input and output parameters of the alternative model will be selected to represent different land use (agricultural) scenarios in EU. Therefore, $PECregional_{soil}$ for agricultural soils will be calculated with an alternative model and the outcome of this model (=0.36 mg Cd/kg_{ww}) will be used instead of the values given in **Table 3.15**. The $PECregional_{soil}$, calculated with the alternative model is lower than the $PECcontinental_{soil}$.that is calculated with EUSES (see **Table 3.157**). This is unusual but is inherent to the EUSES assumption that Cd output from soil (leaching) is calculated for the added Cd only, i.e. it assumes that ambient Cd in soil cannot be removed from soil. This is incorrect as the availability of added and ambient Cd is not strongly different (see Section 3.2.3) and ambient Cd in soil is the major source of Cd in leachates and crop Cd. The alternative model (see Section 3.1.3.4.2) assumes that all Cd in soil (natural background and historic additions and current additions) can be equally lost from soil by leaching or crop off take, leading to higher Cd output than estimated by EUSES. The EUSES calculations, will, however be used to estimate the $PECregional_{soil}$ for natural soils and industrial soils because the alternative model has not been used to derive specific values for such soils. No fertiliser emissions take place on these soils, i.e. the regional emissions for natural and industrial soils in EUSES may represent realistic values in contrast with agricultural soils (see above). Even though the EUSES predicted values refer to steady state conditions for the industrial and natural soils (i.e. concentration in a far future), these choices will not affect the conclusion of this risk assessment as will be shown in Section 3.3.

Increasing the K_p value of suspended matter and sediment by a factor 13, from $17\ 10^3$ l kg^{-1} to $224\ 10^3$ l kg^{-1}, decreases the predicted regional Cd concentration in surface water by a factor 4, from 0.35 µg L^{-1} to 0.09 µg L^{-1}, which corresponds to the background concentration. The PECsediment only increases by a factor 1.5. At lower K_p, more Cd remains in solution (higher Cd concentration in dissolved fraction) and less Cd will be sorbed on particles (lower Cd concentration in sediment/suspended matter).

Varying the solid-liquid Cd distribution coefficient (K_D) in soil tenfold above or below the selected value strongly affects the PECsoil values as calculated with EUSES, but affects the PECwater by maximally 20%. The PECsoil values predicted with EUSES are sensitive to the K_D because EUSES predicts concentrations at steady states which are reached after varying periods depending on the K_D (which control the output). In other words, PECsoils compared for different K_D values are compared at different times after contamination.

Cadmium disposal scenarios have been calculated in the Targeted Risk Assessment Report on batteries (see batteries' related sections).

Contribution of batteries' related life-cycle steps

In order to compare the global regional Cd emissions with the regional/continental Cd emissions during the life cycle of NiCd batteries an overview of these releases is given in **Tables 3.158-3.167**. The regional/continental cadmium emission of the disposal phase originating from all products containing cadmium in MSW can be found in **Table 3.35** (incineration current situation), **Table 3.39** (incineration future situation) and **Table 3.55** (landfills).

Table 3.158 Summary of regional releases in kg year^{-1} of Cd to different environmental compartments during the total life cycle of a NiCd battery (realistic scenario: 24.4% incineration and 75.6% land-filling. Scenario 10 mg kg^{-1} $_{dry\ wt.}$)

Life cycle stages	Regional releases in kg year^{-1}				
	Air	Water	Urban/ind. soil/agr. soil	Ground-water	Total release
1 Manufacturing of NiCd batteries and/or battery packs	29	35.4	0	0	64.4
2 Incorporation into battery powered devices and applications	0	0	0	0	0
3 Use, recharging and maintenance by end users	/	/	/	/	/
4 Recycling ▪ Collection ▪ Processing ▪ Recovery	1.8	0.1	0	0	1.9
5. Disposal (10-50% NiCd batteries contribution)					
▪ Incineration (24.4%)	32-162	4-18	N/A	N/A	36-180
▪ Land-filling (75.6%)	N/A	5-24	6-28	1-6	12-62
Total	63-193	45-78	6-28	1-6	115-308

/ No direct emissions. Indirect cadmium emissions associated with the energy consumption used to recharge the batteries are deemed negligible;
N/A Not applicable.

Table 3.159 Summary of regional releases in kg year^{-1} of Cd to different environmental compartments during the total life cycle of a NiCd battery (worst case scenario: 100% incineration. Scenario 10 mg kg^{-1} $_{dry\ wt.}$)

Life cycle stages	Regional releases in kg year^{-1}			
	Air	Water	Urban/ind. soil/agr. soil	Total release
1 Manufacturing of NiCd batteries and/or battery packs	29	35.4	0	64.4
2 Incorporation into battery powered devices and applications	0	0	0	0
3 Use, recharging and maintenance by end users	/	/	/	/
4 Recycling Collection ▪ Processing ▪ Recovery	1.8	0.1	0	1.9

Table 3.159 continued overleaf

Table 3.159 continued Summary of regional releases in kg $year^{-1}$ of Cd to different environmental compartments during the total life cycle of a NiCd battery (worst case scenario: 100% incineration. Scenario 10 mg kg^{-1} $_{dry\ wt.}$)

Life cycle stages	Regional releases in kg $year^{-1}$			
	Air	Water	Urban/ind. soil/agr. soil	Total release
5. Disposal (10-50% NiCd batteries contribution)				
▪ Incineration (100%)	140-701	14-72	N/A	154-773
▪ Land-filling (0%)	N/A	N/A	N/A	N/A
Total	171-730	50-108	0	220-839

/ No direct emissions. Indirect cadmium emissions associated with the energy consumption used to recharge the batteries are deemed negligible;
N/A Not applicable.

Table 3.160 Summary of regional releases in kg $year^{-1}$ of Cd to different environmental compartments during the total life cycle of a NiCd battery (worst case scenario: 100% land-filling. Scenario 10 mg kg^{-1} $_{dry\ wt.}$)

Life cycle stages	Regional releases in kg $year^{-1}$				
	Air	Water	Urban/ind. soil/agr. soil	Ground-water	Total release
1 Manufacturing of NiCd batteries and/or battery packs	29	35.4	0	0	64.4
2 Incorporation into battery powered devices and applications	0	0	0	0	0
3 Use, recharging and maintenance by end users	/	/	/	/	/
4 Recycling ▪ Collection ▪ Processing ▪ Recovery	1.8	0.1	0	0	1.9
5. Disposal (10-50% NiCd batteries contribution)					
▪ Incineration (0%)	N/A	N/A	N/A	N/A	N/A
▪ Land-filling (100%)	N/A	7-26	6-30	1-6	14-62
Total	31	43-62	6-30	1-6	81-129

/ No direct emissions. Indirect cadmium emissions associated with the energy consumption used to recharge the batteries are deemed negligible;
N/A Not applicable.

Table 3.161 Summary of regional releases in kg year^{-1} of Cd to different environmental compartments during the total life cycle of a NiCd battery (Future scenario: 100% incineration. Scenario 13.2 mg kg^{-1} $_{dry\ wt.}$)

Life cycle stages	Regional releases in kg year^{-1}			
	Air	Water	Urban/ind. soil/agr. soil	Total release
1 Manufacturing of NiCd batteries and/or battery packs	29	35.4	0	64.4
2 Incorporation into battery powered devices and applications	0	0	0	0
3 Use, recharging and maintenance by end users	/	/	/	/
4 Recycling ▪ Collection ▪ Processing ▪ Recovery	1.8	0.1	0	1.9
5. Disposal (32 % NiCd batteries contribution) ▪ Incineration (100%) ▪ Land-filling (0%)	449 N/A	62 N/A	N/A N/A	511 N/A
Total	480	98	0	577

/ No direct emissions. Indirect cadmium emissions associated with the energy consumption used to recharge the batteries are deemed negligible;
N/A Not applicable.

Table 3.162 Summary of regional releases in kg year^{-1} of Cd to different environmental compartments during the total life cycle of a NiCd battery (Future scenario: 100% incineration. Scenario 24 mg kg^{-1} $_{dry\ wt.}$)

Life cycle stages	Regional releases in kg year^{-1}			
	Air	Water	Urban/ind. soil/agr. soil	Total release
1 Manufacturing of NiCd batteries and/or battery packs	29	35.4	0	64.4
2 Incorporation into battery powered devices and applications	0	0	0	0
3 Use, recharging and maintenance by end users	/	/	/	/
4 Recycling ▪ Collection ▪ Processing ▪ Recovery	1.8	0.1	0	1.9
5. Disposal (63 % NiCd batteries contribution) ▪ Incineration (100%) ▪ Land-filling (0%)	883 N/A	218 N/A	N/A N/A	1,101 N/A
Total	914	254	0	1,167

/ No direct emissions. Indirect cadmium emissions associated with the energy consumption used to recharge the batteries are deemed negligible;
N/A Not applicable.

Table 3.163 Summary of continental releases in kg $year^{-1}$ of Cd to different environmental compartments during the total life cycle of a NiCd battery (realistic scenario: 24.4 % incineration and 75.6 % land-filling. Scenario 10 mg kg^{-1} $_{dry\ wt.}$)

Life cycle stages	Continental releases in kg $year^{-1}$				
	Air	Water	Urban/ind. soil/agr. soil	Ground-water	Total release
1 Manufacturing of NiCd batteries and/or battery packs	22	29.6	0	0	51.6
2 Incorporation into battery powered devices and applications	0	0	0	0	0
3 Use, recharging and maintenance by end users	/	/	/	/	/
4 Recycling ▪ Collection ▪ Processing ▪ Recovery	0	0	0	0	0
5 Disposal (10-60% NiCd batteries contribution) ▪ Incineration (24.4 %) ▪ Land-filling (75.6 %)	291-1,455 N/A	32-158 44-220	N/A 50-250	N/A 11-52	323-1,613 105-522
Total	313-1,477	106-408	50-250	11-52	479-2,187

/ No direct emissions. Indirect cadmium emissions associated with the energy consumption used to recharge the batteries are deemed negligible;
N/A Not applicable.

Table 3.164 Summary of continental releases in kg $year^{-1}$ of Cd to different environmental compartments during the total life cycle of a NiCd battery (worst case: 100% incineration- Scenario 10 mg kg^{-1} $_{dry\ wt.}$)

Life cycle stages	Continental releases in kg $year^{-1}$			
	Air	Water	Urban/ind. soil/agr. soil	Total release
1 Manufacturing of NiCd batteries and/or battery packs	22	29.9	0	51.6
2 Incorporation into battery powered devices and applications	0	0	0	0
3 Use, recharging and maintenance by end users	/	/	/	/
4 Recycling ▪ Collection ▪ Processing ▪ Recovery	0	0	0	0
5 Disposal (10-50% NiCd batteries contribution) ▪ Incineration (100%) ▪ Land-filling (0%)	1,262-6,308 N/A	130-649 N/A	N/A N/A	1,392-6,957 N/A
Total	1,284-6,330	160-679	0	1,444-7,009

/ No direct emissions. Indirect cadmium emissions associated with the energy consumption used to recharge the batteries are deemed negligible;
N/A Not applicable.

Table 3.165 Summary of continental releases in kg year^{-1} of Cd to different environmental compartments during the total life cycle of a NiCd battery (worst case scenario: 100% land-filling-Scenario 10 mg kg^{-1} $_{dry\ wt.}$)

Life cycle stages	Continental releases in kg year^{-1}				
	Air	Water	Urban/ind. soil/agr. soil	Ground-water	Total release
1 Manufacturing of NiCd batteries and/or battery packs	22	29.6	0	0	51.6
2 Incorporation into battery powered devices and applications	0	0	0	0	0
3 Use, recharging and maintenance by end users	/	/	/	/	/
4 Recycling ▪ Collection ▪ Processing ▪ Recovery	0	0	0	0	0
5 Disposal (10-50 % NiCd batteries contribution) ▪ Incineration (0%) ▪ Land-filling (100%)	N/A N/A	N/A 50-238	N/A 54-272	N/A 12-57	N/A 116-567
Total	22	80-268	54-272	12-57	168-619

/ No direct emissions. Indirect cadmium emissions associated with the energy consumption used to recharge the batteries are deemed negligible;
N/A Not applicable.

Table 3.166 Summary of continental releases in kg year^{-1} of Cd to different environmental compartments during the total life cycle of a NiCd battery (Future scenario: 100% incineration. Scenario 13.2 mg kg^{-1} $_{dry\ wt.}$)

Life cycle stages	Continental releases in kg year^{-1}			
	Air	Water	Urban/ind. soil/agr. soil	Total release
1 Manufacturing of NiCd batteries and/or battery packs	22	29.6	0	51.6
2 Incorporation into battery powered devices and applications	0	0	0	0
3 Use, recharging and maintenance by end users	/	/	/	/
4 Recycling ▪ Collection ▪ Processing ▪ Recovery	0	0	0	0
5 Disposal (32 % NiCd batteries contribution) ▪ Incineration (100%) ▪ Land-filling (0%)	4,037 N/A	554 N/A	N/A N/A	4,591 N/A
Total	4,059	584	0	4,643

/ No direct emissions. Indirect cadmium emissions associated with the energy consumption used to recharge the batteries are deemed negligible;
N/A Not applicable.

Table 3.167 Summary of continental releases in kg $year^{-1}$ of Cd to different environmental compartments during the total life cycle of a NiCd battery (Future scenario: 100% incineration. Scenario 24 mg kg^{-1} $_{dry\ wt.}$)

Life cycle stages	Continental releases in kg $year^{-1}$			
	Air	Water	Urban/ind. soil/agr. soil	Total release
1 Manufacturing of NiCd batteries and/or battery packs	22	29.6	0	51.6
2 Incorporation into battery powered devices and applications	0	0	0	0
3 Use, recharging and maintenance by end users	/	/	/	/
4 Recycling ▪ Collection ▪ Processing ▪ Recovery	0	0	0	0
5 Disposal (54% NiCd batteries contribution) ▪ Incineration (100%) ▪ Land-filling (0%)	 7,948 N/A	 1,960 N/A	 N/A N/A	 9,908 N/A
Total	7,970	1,990	0	9,960

/ No direct emissions. Indirect cadmium emissions associated with the energy consumption used to recharge the batteries are deemed negligible;
N/A Not applicable.

The C_continental and C_regional for the NiCd battery life cycle are calculated with EUSES 1.0. Three different scenarios are considered (realistic case: 24.4% incineration; 75.6% land-filling, worst case incineration: 100% incineration, 0% land-filling and worst case land-filling: 100% land-filling, 0% incineration). The contribution from the NiCd batteries to MSW varies between 0.1 and 0.5 for the current scenarios. In addition the future scenarios with a battery contribution of 32% and 63% have also been calculated. The output of the model gives in fact the predicted added environmental concentrations at continental and regional scale ($PEC_{con,\ add}$ and $PEC_{reg,\ add}$). Therefore C_continental is considered as the calculated $PEC_{con,\ add}$, and C_regional is calculated as the difference between $PEC_{reg,\ add}$ and $PEC_{con,\ add.}$

The results are presented in the **Tables 3.168-3.176**.

Current situation

It can be concluded that for all scenarios investigated the added regional/continental concentrations calculated on the basis of the emissions from the NiCd batteries life cycle only (indicated in bold) are very small. Due to the rather high Cd background concentrations for some environmental compartments (soil, sediment, surface water) the resulting PECregional and PECcontinental for these compartments are comparable to the overall regional/continental PECs (see **Table 3.157**).

Table 3.168 Contribution of NiCd batteries (fraction 0.1) to the overall Cd emission values, total concentration and total PEC values for the regional and continental environment (incineration 24.4%; land-filling 75.6%). Scenario 10 mg kg^{-1} dry wt

Input continental (anthropogenic):				
amount released to air		313 kg year^{-1}		
amount released to surface water		106 kg year^{-1}		
amount released to agricultural soil		50 (sludge from STP landfill)		
amount released to natural soil		0		
amount released to industrial soil		0		
Input regional (anthropogenic):				
amount released to air		63 kg year^{-1}		
amount released to surface water		45 kg year^{-1}		
amount released to agricultural soil(1)		6 (sludge from STP landfill)		
amount released to natural soil(1)		0		
amount released to industrial soil(1)		0		
Results		C_continental concentration	background(2)	C_regional
Concentration in air	ng m^{-3}	$3.8 \cdot 10^{-13}$	0	$6.8 \cdot 10^{-12}$
Concentration in agricultural soil	mg kg_{wwt}^{-1}	0.0001	0.266	0.00137
Concentration in natural soil	mg kg_{wwt}^{-1}	0.00006	0.266	0.0011
Concentration in industrial soil	mg kg_{wwt}^{-1}	0.00006	0.266	0.0011
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
Concentration in surface water	µg L^{-1}	$1.5 \cdot 10^{-5}$	0.05	0.00024
Concentration in sediment	mg kg_{wwt}^{-1}	0.0007	0.77	0.0122
PEC values		PEC continental		PEC regional
PEC air	ng m^{-3}	$3.8 \cdot 10^{-13}$		$7.8 \cdot 10^{-12}$
PEC agricultural soil	mg $kg^{-1}_{wwt}{}^{-1}$	0.266		0.267
PEC natural soil	mg kg_{wwt}^{-1}	0.266		0.267
PEC industrial soil	mg kg_{wwt}^{-1}	0.266		0.267
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
PEC surface water (dissolved fraction)	µg L^{-1}	0.05		0.050
PEC sediment	mg kg_{wwt}^{-1}	0.77		0.78

1) Not including atmospheric deposition;
2) Natural or ambient background Cd, Section 3.1.3.4.3.

Table 3.169 Contribution of NiCd batteries (fraction 0.5) to the overall Cd emission values, total concentration and total PEC values for the regional and continental environment (incineration 24.4%, land-filling 75.6%). Scenario 10 mg kg^{-1} dry wt

Input continental (anthropogenic)				
amount released to air		1,477 kg $year^{-1}$		
amount released to surface water		408 kg $year^{-1}$		
amount released to agricultural soil		250 (sludge from STP landfill)		
amount released to natural soil		0		
amount released to industrial soil		0		
Input regional (anthropogenic)				
amount released to air		193 kg $year^{-1}$		
amount released to surface water		78 kg $year^{-1}$		
amount released to agricultural soil(1)		28 (sludge from STP landfill)		
amount released to natural soil(1)		0		
amount released to industrial soil(1)		0		
Results		C_continental concentration	background(2)	C_regional
Concentration in air	ng m^{-3}	$1.81 \cdot 10^{-12}$	0	$2.1 \cdot 10^{-11}$
Concentration in agricultural soil	mg kg_{wwt}^{-1}	0.00046	0.266	0.005
Concentration in natural soil	mg kg_{wwt}^{-1}	0.00028	0.266	0.003
Concentration in industrial soil	mg kg_{wwt}^{-1}	0.00028	0.266	0.003
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
Concentration in surface water	µg L^{-1}	$6.5 \cdot 10^{-5}$	0.05	0.0006
Concentration in sediment	mg kg_{wwt}^{-1}	0.0032	0.77	0.03
PEC values		PEC continental		PEC regional
PEC air	ng m^{-3}	$1.81 \cdot 10^{-12}$		$2.3 \cdot 10^{-11}$
PEC agricultural soil	mg $kg^{-1}{}_{wwt}{}^{-1}$	0.266		0.27
PEC natural soil	mg kg_{wwt}^{-1}	0.266		0.27
PEC industrial soil	mg kg_{wwt}^{-1}	0.266		0.27
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
PEC surface water (dissolved fraction)	µg L^{-1}	0.05		0.051
PEC sediment	mg kg_{wwt}^{-1}	0.773		0.80

1) Not including atmospheric deposition;
2) Natural or ambient background Cd, Section 3.1.3.4.3.

Table 3.170 Contribution of NiCd batteries (fraction 0.1) to the overall Cd emission values, total concentration and total PEC values for the regional and continental environment (incineration 100%, land-filling 0%). Scenario 10 mg kg^{-1} dry wt

Input continental (anthropogenic)				
amount released to air		1,284 kg $year^{-1}$		
amount released to surface water		160 kg $year^{-1}$		
amount released to agricultural soil (1)		0 (sludge from STP is land-filled)		
amount released to natural soil(1)		0		
amount released to industrial soil(1)		0		
Input regional (anthropogenic)				
amount released to air		171 kg $year^{-1}$		
amount released to surface water		50 kg $year^{-1}$		
amount released to agricultural soil		0		
amount released to natural soil		0		
amount released to industrial soil		0		
Results		C_continental concentration	background(2)	C_regional
Concentration in air	ng m^{-3}	$1.57 \cdot 10^{-12}$	0	$1.84 \cdot 10^{-11}$
Concentration in agricultural soil	mg kg_{wwt}^{-1}	0.00024	0.266	0.0028
Concentration in natural soil	mg kg_{wwt}^{-1}	0.00025	0.266	0.0029
Concentration in industrial soil	mg kg_{wwt}^{-1}	0.00025	0.266	0.0029
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
Concentration in surface water	µg L^{-1}	0.00004	0.05	0.0004
Concentration in sediment	mg kg_{wwt}^{-1}	0.002	0.77	0.02
PEC values		PEC continental		PEC regional
PEC air	ng m^{-3}	$1.57 \cdot 10^{-12}$		$2 \cdot 10^{-11}$
PEC agricultural soil	mg $kg^{-1}{}_{wwt}{}^{-1}$	0.266		0.269
PEC natural soil	mg kg_{wwt}^{-1}	0.266		0.269
PEC industrial soil	mg kg_{wwt}^{-1}	0.266		0.269
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
PEC surface water (dissolved fraction)	µg L^{-1}	0.050		0.050
PEC sediment	mg kg_{wwt}^{-1}	0.772		0.79

1) Not including atmospheric deposition;
2) Natural or ambient background Cd, Section 3.1.3.4.3.

Table 3.171 Contribution of NiCd batteries (fraction 0.5) to the overall Cd emission values, total concentration and total PEC values for the regional and continental environment (incineration 100%, land-filling 0%). Scenario 10 mg kg^{-1} dry wt

Input continental (anthropogenic):				
amount released to air		6,330 kg year^{-1}		
amount released to surface water		679 kg year^{-1}		
amount released to agricultural soil (1)		0 (sludge from WWTP is land-filled)		
amount released to natural soil(1)		0		
amount released to industrial soil(1)		0		
Input regional (anthropogenic):				
amount released to air		730 kg year^{-1}		
amount released to surface water		108 kg year^{-1}		
amount released to agricultural soil		0		
amount released to natural soil		0		
amount released to industrial soil		0		
Results:		C_continental concentration	background(2)	C_regional
Concentration in air	ng m^{-3}	$7.8 \cdot 10^{-12}$	0	$7.9 \cdot 10^{-11}$
Concentration in agricultural soil	mg kg_{wwt}^{-1}	0.0012	0.266	0.012
Concentration in natural soil	mg kg_{wwt}^{-1}	0.0012	0.266	0.012
Concentration in industrial soil	mg kg_{wwt}^{-1}	0.0012	0.266	0.012
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
Concentration in surface water	µg L^{-1}	0.00019	0.05	0.0015
Concentration in sediment	mg kg_{wwt}^{-1}	0.0096	0.77	0.074
PEC values		PEC continental		PEC regional
PEC air	ng m^{-3}	$7.8 \cdot 10^{-12}$		$8.7 \cdot 10^{-11}$
PEC agricultural soil	mg $kg^{-1}{}_{wwt}^{-1}$	0.27		0.28
PEC natural soil	mg kg_{wwt}^{-1}	0.27		0.28
PEC industrial soil	mg kg_{wwt}^{-1}	0.27		0.28
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
PEC surface water (dissolved fraction)	µg L^{-1}	0.05		0.052
PEC sediment	mg kg_{wwt}^{-1}	0.78		0.85

1) Not including atmospheric deposition;
2) Natural or ambient background Cd, Section 3.1.3.4.3.

Table 3.172 Contribution of NiCd batteries (fraction 0.1) to the overall Cd emission values, total concentration and total PEC values for the regional and continental environment (land-filling 100%, incineration 0%). Scenario 10 mg kg^{-1} dry wt

Input continental (anthropogenic):				
amount released to air		22 kg $year^{-1}$		
amount released to surface water		80 kg $year^{-1}$		
amount released to agricultural soil (1)		54 (sludge from STP landfill)		
amount released to natural soil(1)		0		
amount released to industrial soil(1)		0		
Input regional (anthropogenic):				
amount released to air		31 kg $year^{-1}$		
amount released to surface water		43 kg $year^{-1}$		
amount released to agricultural soil		6 kg $year^{-1}$ (sludge from STP (landfill)		
amount released to natural soil		0		
amount released to industrial soil		0		
Results:		C_continental concentration	background(2)	C_regional
Concentration in air	ng m^{-3}	$2.7 \cdot 10^{-14}$	0	$3.3 \cdot 10^{-12}$
Concentration in agricultural soil	mg kg_{wwt}^{-1}	$5 \cdot 10^{-5}$	0.266	0.00098
Concentration in natural soil	mg kg_{wwt}^{-1}	$4.2 \cdot 10^{-6}$	0.266	0.00052
Concentration in industrial soil	mg kg_{wwt}^{-1}	$4.2 \cdot 10^{-6}$	0.266	0.00052
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
Concentration in surface water	µg L^{-1}	$6.4 \cdot 10^{-6}$	0.05	0.00019
Concentration in sediment	mg kg_{wwt}^{-1}	0.00032	0.77	0.0093
PEC values		PEC continental		PEC regional
PEC air	ng m^{-3}	$2.7 \cdot 10^{-14}$		$3.3 \cdot 10^{-12}$
PEC agricultural soil	mg $kg^{-1}{}_{wwt}{}^{-1}$	0.266		0.267
PEC natural soil	mg kg_{wwt}^{-1}	0.266		0.267
PEC industrial soil	mg kg_{wwt}^{-1}	0.266		0.267
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
PEC surface water (dissolved fraction)	µg L^{-1}	0.050		0.05
PEC sediment	mg kg_{wwt}^{-1}	0.770		0.78

1) Not including atmospheric deposition;
2) Natural or ambient background Cd, Section 3.1.3.4.3.

Table 3.173 Contribution of NiCd batteries (fraction 0.5) to the overall Cd emission values, total concentration and total PEC values for the regional and continental environment (land-filling 100%, incineration 0%). Scenario 10 mg kg^{-1} dry wt

Input continental (anthropogenic):				
amount released to air		22 kg $year^{-1}$		
amount released to surface water		268 kg $year^{-1}$		
amount released to agricultural soil (1)		272 (sludge from STP landfill)		
amount released to natural soil(1)		0		
amount released to industrial soil(1)		0		
Input regional (anthropogenic):				
amount released to air		31 kg $year^{-1}$		
amount released to surface water		62 kg $year^{-1}$		
amount released to agricultural soil		30kg $year^{-1}$ (sludge from STP (landfill)		
amount released to natural soil		0		
amount released to industrial soil		0		
Results:		C_continental concentration	background(2)	C_regional
Concentration in air	ng m^{-3}	$2.7 \cdot 10^{-14}$	0	$3.3 \cdot 10^{-12}$
Concentration in agricultural soil	mg kg_{wwt}^{-1}	0.00023	0.266	0.0028
Concentration in natural soil	mg kg_{wwt}^{-1}	$4.2 \cdot 10^{-6}$	0.266	$5.2 \cdot 10^{-4}$
Concentration in industrial soil	mg kg_{wwt}^{-1}	$4.2 \cdot 10^{-6}$	0.266	$5.2 \cdot 10^{-4}$
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
Concentration in surface water	µg L^{-1}	$2.43 \cdot 10^{-5}$	0.05	$3.11 \cdot 10^{-4}$
Concentration in sediment	mg kg_{wwt}^{-1}	0.0012	0.77	0.0156
PEC values		PEC continental		PEC regional
PEC air	ng m^{-3}	$2.7 \cdot 10^{-14}$		$3.3 \cdot 10^{-12}$
PEC agricultural soil	mg $kg^{-1}{}_{wwt}{}^{-1}$	0.266		0.296
PEC natural soil	mg kg_{wwt}^{-1}	0.266		0.267
PEC industrial soil	mg kg_{wwt}^{-1}	0.266		0.267
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
PEC surface water (dissolved fraction)	µg L^{-1}	0.05		0.05
PEC sediment	mg kg_{wwt}^{-1}	0.77		0.79

1) Not including atmospheric deposition;
2) Natural or ambient background Cd, Section 3.1.3.4.3.

Future situation (incineration only)

The overall effect of a future possible increase in the total cadmium content of the MSW up to 24 mg $kg^{-1}{}_{dry\ wt.}$ is represented in **Table 3.174**.

Table 3.174 Contribution of all MSW waste to the overall Cd emission values, total concentration and total PEC values for the regional and continental environment (Future scenario 100% incineration). Scenario 24 mg kg^{-1} dry wt

Input continental (anthropogenic):				
amount released to air		12,638 kg $year^{-1}$		
amount released to surface water		3,140.6 kg $year^{-1}$		
amount released to agricultural soil (1)		0		
amount released to natural soil(1)		0		
amount released to industrial soil(1)		0		
Input regional (anthropogenic):				
amount released to air		1,433 kg $year^{-1}$		
amount released to surface water		381.5 kg $year^{-1}$		
amount released to agricultural soil		0		
amount released to natural soil		0		
amount released to industrial soil		0		
Results:		C_continental concentration	background(2)	C_regional
Concentration in air	ng m^{-3}	$1.55 \cdot 10^{-11}$	0	$1.55 \cdot 10^{-10}$
Concentration in agricultural soil	mg kg_{wwt}^{-1}	0.0023	0.266	0.023
Concentration in natural soil	mg kg_{wwt}^{-1}	0.0024	0.266	0.024
Concentration in industrial soil	mg kg_{wwt}^{-1}	0.0024	0.266	0.024
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
Concentration in surface water	µg L^{-1}	0.00047	0.05	0.0034
Concentration in sediment	mg kg_{wwt}^{-1}	0.023	0.77	0.17
PEC values		PEC continental		PEC regional
PEC air	ng m^{-3}	$1.55 \cdot 10^{-11}$		$1.7 \cdot 10^{-10}$
PEC agricultural soil	mg $kg^{-1}{}_{wwt}^{-1}$	0.268		0.29
PEC natural soil	mg kg_{wwt}^{-1}	0.268		0.29
PEC industrial soil	mg kg_{wwt}^{-1}	0.268		0.29
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
PEC surface water (dissolved fraction)	µg L^{-1}	0.050		0.054
PEC sediment	mg kg_{wwt}^{-1}	0.79		0.97

1) Not including atmospheric deposition;
2) Natural or ambient background Cd, Section 3.1.3.4.3.

It can be concluded that the effect of an increase in MSW cadmium content up to 24 mg kg^{-1} $_{dry\ wt.}$ will have only a minor influence on the currently derived PECs regional for air, water and soil. Therefore there is no need to revise the current PEC reg, water and the PEC reg, air in order to derive the PEC values for the future situation (see Section 3.1.3.2). The specific future contribution of NiCd batteries to the overall PEC is given in **Tables 3.175-3.176** and is overall low.

Table 3.175 Contribution of NiCd batteries (fraction 0.32) to the overall Cd emission values, total concentration and total PEC values for the regional and continental environment (Future scenario 100% incineration). Scenario 13.2 mg kg^{-1} dry wt

Input continental (anthropogenic):				
amount released to air		4,059 kg $year^{-1}$		
amount released to surface water		584 kg $year^{-1}$		
amount released to agricultural soil (1)		0		
amount released to natural soil(1)		0		
amount released to industrial soil(1)		0		
Input regional (anthropogenic):				
amount released to air		480kg $year^{-1}$		
amount released to surface water		98 kg $year^{-1}$		
amount released to agricultural soil		0		
amount released to natural soil		0		
amount released to industrial soil		0		
Results:		C_continental concentration	background(2)	C_regional
Concentration in air	ng m^{-3}	$4.97 \cdot 10^{-12}$	0	$5.2 \cdot 10^{-11}$
Concentration in agricultural soil	mg kg_{wwt}^{-1}	0.00074	0.266	0.0077
Concentration in natural soil	mg kg_{wwt}^{-1}	0.00077	0.266	0.0081
Concentration in industrial soil	mg kg_{wwt}^{-1}	0.00077	0.266	0.0081
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
Concentration in surface water	µg L^{-1}	0.00013	0.05	0.001
Concentration in sediment	mg kg_{wwt}^{-1}	0.0065	0.77	0.053
PEC values		PEC continental		PEC regional
PEC air	ng m^{-3}	$4.97 \cdot 10^{-12}$		$5.7 \cdot 10^{-11}$
PEC agricultural soil	mg $kg^{-1}{}_{wwt}{}^{-1}$	0.267		0.274
PEC natural soil	mg kg_{wwt}^{-1}	0.267		0.275
PEC industrial soil	mg kg_{wwt}^{-1}	0.267		0.275
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
PEC surface water (dissolved fraction)	µg L^{-1}	0.050		0.051
PEC sediment	mg kg_{wwt}^{-1}	0.777		0.83

1) Not including atmospheric deposition;
2) Natural or ambient background Cd, Section 3.1.3.4.3.

Table 3.176 Contribution of NiCd batteries (fraction 0.63) to the overall Cd emission values, total concentration and total PEC values for the regional and continental environment (Future scenario 100% incineration). Scenario 24 mg kg^{-1} dry wt

Input continental (anthropogenic):				
amount released to air		7,970 kg $year^{-1}$		
amount released to surface water		1,990 kg $year^{-1}$		
amount released to agricultural soil (1)		0		
amount released to natural soil(1)		0		
amount released to industrial soil(1)		0		
Input regional (anthropogenic):				
amount released to air		914 kg $year^{-1}$		
amount released to surface water		254 kg $year^{-1}$		
amount released to agricultural soil		0		
amount released to natural soil		0		
amount released to industrial soil		0		
Results		C_continental Concentration	Background(2)	C_regional
Concentration in air	ng m^{-3}	$9.77 \cdot 10^{-12}$	0	$9.86 \cdot 10^{-11}$
Concentration in agricultural soil	mg kg_{wwt}^{-1}	0.0015	0.266	0.015
Concentration in natural soil	mg kg_{wwt}^{-1}	0.0015	0.266	0.015
Concentration in industrial soil	mg kg_{wwt}^{-1}	0.0015	0.266	0.015
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
Concentration in surface water	µg L^{-1}	0.00030	0.05	0.0022
Concentration in sediment	mg kg_{wwt}^{-1}	0.015	0.77	0.11
PEC values		PEC continental		PEC regional
PEC air	ng m^{-3}	$9.77 \cdot 10^{-12}$		$1.1 \cdot 10^{-10}$
PEC agricultural soil	mg $kg^{-1}{}_{wwt}{}^{-1}$	0.268		0.28
PEC natural soil	mg kg_{wwt}^{-1}	0.268		0.28
PEC industrial soil	mg kg_{wwt}^{-1}	0.268		0.28
K_p sediment/suspended matter = 130 10^3 L kg^{-1}				
PEC surface water (dissolved fraction)	µg L^{-1}	0.050		0.053
PEC sediment	mg kg_{wwt}^{-1}	0.79		0.90

1) Not including atmospheric deposition;
2) Natural or ambient background Cd, Section 3.1.3.4.3.

3.1.3.4.2 An alternative model predicting regional and continental concentrations in agricultural soils

Model description

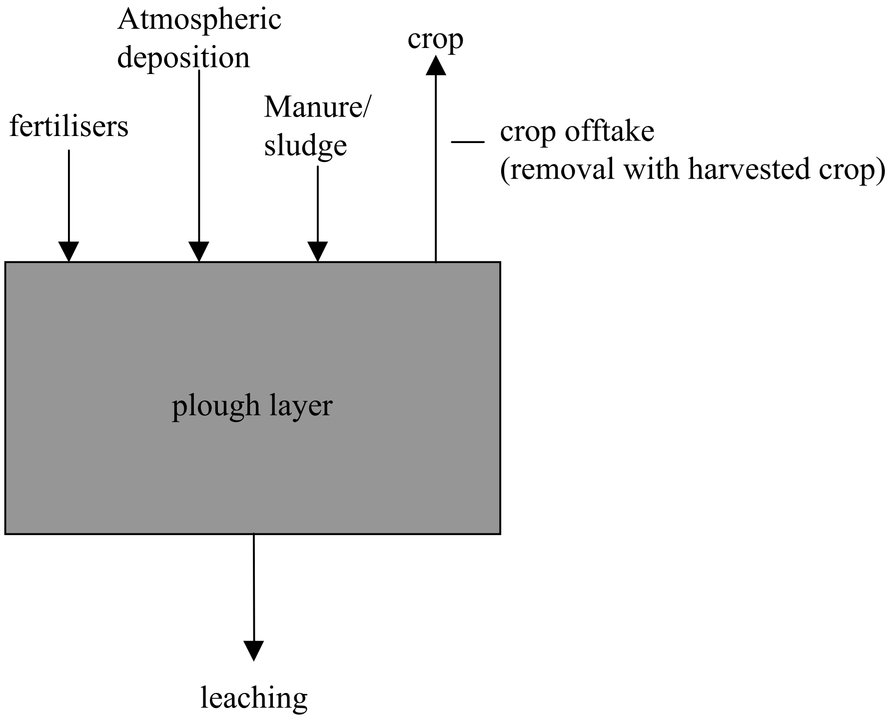
The predicted environmental Cd concentration in soil (PEC_{soil}) is a critical parameter in the risk assessment of Cd. The Cd exposure to the general population is predominantly controlled by dietary intake of Cd (see the human health part of this Risk Assessment Report, in separate document) and, hence, by Cd in crops used for food production. Food Cd concentrations are related to soil Cd and increasing trends in soil Cd may result in increasing trends in dietary intake. It is known that Cd availability is not greatly reduced upon ageing in soil and, therefore, a reduced Cd input in soil does not warrant reduced crop Cd concentrations if soil Cd input still exceeds the Cd losses from the soil (Smolders et al., 1999 and references therein). Whereas Cd in air and in the aquatic compartments have reduced since the late 70's in Europe, soil Cd concentrations may still increase with time (see the human health part of this Risk Assessment Report, in separate document). The relationship between Cd input in the agricultural environment and the resulting Cd concentrations in soil is discussed in this section.

A wealth of information exists on Cd balances in agricultural soils and this information will be used in an alternative soil Cd model. The alternative model is based on the Cd mass balance in the plough layer. The mass balance model calculates trends in soil Cd concentrations from the annual input-output balance and the existing Cd in soil. Cadmium mass balances in agricultural soils have been described before (Tjell and Christensen, 1992, Jensen and Bro-Rasmussen, 1992, Moolenaar and Lexmond, 1998, Hellstrand and Landner, 1998, Kiene, 1999) and are reproduced here with small modifications and updated information. The Cd mass balance offers distinct advantages over the EUSES 1.0 model for predicting soil Cd since the former (i) includes the main pathways of cadmium to and from agricultural soils and (ii) uses local Cd input rates that are measured and (iii) predicts future soil Cd concentrations at any time after t=0 in contrast with the EUSES predictions which are steady state concentrations that may only be reached after several decades. No distinction will be made between regional or continental scales, and the balances will be constructed for a number of conditions that are relevant in European agriculture.

The Cd mass balance is presented graphically in **Figure 3.12**. The Cd input in the agricultural soils mainly originates from the atmospheric deposition, from the fertilisation with phosphate fertilisers and from the application of manure or sludge. The main Cd fluxes out of the plough layer are leaching losses and removal of Cd with the harvested crop (= crop offtake). The input of Cd through manure or sludge application recycles some of the Cd that was previously removed from soil by crop offtake (see below).

It can be discussed that the Cd mass balance should be made on the whole rooting zone (i.e. 1 m) rather than on the plough layer. Losses of Cd by leaching out of the plough layer may indeed not be a reduction of risk for crop uptake as Cd may be retained in deeper horizons where it is still available for root uptake. However, because information on soil properties of deeper horizons is often lacking (e.g. total Cd, pore water concentrations, net water flux out of the rooting zone, rooting depth) it was preferred to focus on the plough layer only.

Fig. 3.12 The Cd input-output balance in agricultural soils



The Cd concentration in the topsoil at year i ($Cd_{soil,i,}$ mg $kg^{-1}{}_{dw}$) is calculated from the net Cd balance (input-output, g ha^{-1} y^{-1}) in year i-1 and the soil Cd concentration in year i-1 as

$$Cd_{soil,i} = Cd_{soil,i-1} + (\text{input-output})/(1{,}000 \cdot W_{soil})$$

in which W_{soil} represents the soil weight of the plough layer (kg_{dw} ha^{-1}). In all calculations presented below, W_{soil} is assumed to be 3 10^6 kg_{dw} (i.e., 0.23 m ploughing depth and 1,300 kg_{dw} m^{-3} bulk density). All data are calculated on dry soil weight basis. No data were found for Cd losses by erosion and it is furthermore assumed that these Cd losses are marginal. This model does not assume that a fraction of the wet deposition is lost to the aquatic environment (see. assumption in the EUSES 1.0 model). Input and output of Cd are discussed in detail below before predicting future trends in soil Cd.

Input of Cd in agricultural soil

Fertilisers

Phosphate fertilisers contain appreciable levels of Cd. The phosphate rock is the source of Cd and only a limited fraction of Cd is lost to the by-products during manufacture of high analysis fertiliser. As a result, the final Cd content in fertilisers, expressed on a unit P basis, is not very different from that in the rock phosphate, and the Cd:P ratio in the rock phosphate determines the fertiliser Cd content (McLaughlin et al., 1996). The Cd:P concentration ratio in rock phosphate varies from 1 to 640 mg Cd/kgP. Typical low Cd rock phosphates (<100 mg Cd/kgP) are those from Florida and Russia (Kola). Many rock phosphates from Africa (Morocco, Togo) contain average to high Cd levels (100-350 mg Cd/kgP). More details on Cd levels in rock phosphates can be found in the compilation made by McLaughlin et al. (1996). The fertiliser industry has developed a process to remove cadmium from the phosphoric acid, which is used in the production of many phosphate fertilisers. However, this process has not been incorporated at industrial scale (IFA, 1998).

Based on data from 1990, the annual Cd input from phosphate fertilisers in the EEC countries was estimated to be 275 tonnes (Landner et al., 1996). This number was obtained from phosphate fertiliser consumption data and Cd concentration in these fertilisers ranging between 128 and 176 mg Cd/kgP in different European countries. Current annual Cd input from phosphate fertiliser is somewhat reduced because of lower fertiliser consumption and because the Cd content in fertiliser is restricted (231 tonnes y^{-1}, **Table 3.156** and **3.178**). Between 1990 and 1995, annual consumption of phosphate fertilisers in West Europe has reduced from 4.5 million tonnes P_20_5 to 3.6 million tonnes P_20_5 (Statistics of the International Fertiliser Industry Association, Paris). During the last decade, several countries adopted limits of Cd content in fertilisers (see **Table 3.177**). **Table 3.178** lists input of Cd to agricultural soils from phosphate fertilisers in Europe. Most of the data are based on the OECD questionnaire (Pearse, 1996). The total Cd load in those EU-16 countries that responded to the 1995 questionnaire is about half of the value that was estimated based on the 1990 data (details not shown). The 1990 data are given for those EU countries that did not respond to the OECD questionnaire.

The annual Cd flux to agricultural soils from phosphate application varies from < 0.1g ha^{-1} (Finland) to 4.5g ha^{-1} (The Netherlands). Most of the data are calculated from total P consumption per country, the Cd concentrations in fertilisers and the total arable surface in that country. Since these fluxes are country averages, they do not reflect the variance that exists between cropping systems. The highest Cd flux (The Netherlands) is a local value for an experimental arable farm using only mineral fertilisers (Moolenaar and Lexmond, 1998). The high flux of 3.2 g Cd $ha^{-1}y^{-1}$ in France is based on data from the late 1980's. The present use of phosphate rock fertiliser in agriculture is further declining in Europe mainly due to the high production of manure and compost.

Table 3.177 Maximum permissible and currently applied Cd concentrations P fertilisers in European countries (sources: International Fertiliser Industry Association, pers. comm.; Hutton et al., 2001 and references therein); value of Germany is based on a personal communication for the Umweltbundesamt (2002)

Country	Limit (mg Cd/kgP)	From	Currently applied (mg Cd/kgP)
Austria	170 (max 20 g Cd $ha^{-1}2y^{-1}$ on arable land, max 10 g Cd $ha^{-1}2y^{-1}$ on grassland)	1994	57
Belgium	210(voluntary)	1994	75
Denmark	110	1995	34
Finland	50	1992	2.5
Germany	90 (voluntary)	1984	80
Norway	100	1992	5.3
Sweden	100, above 5 mg kg^{-1} P, an environmental fee is raised of 30 SEK per g Cd	1994	< 20
UK			34

Other fertilisers than P fertilisers contain low and negligible Cd concentrations with the exception of trace element fertilisers (McLaughlin et al., 1996). The general impact of these fertilisers on total Cd input in agricultural soils is most likely low. Lime may contain elevated Cd levels where it is a by-product of industrial processing. KEMI (1996) reports Cd levels in Danish lime around 1 mg Cd/kg. An annual lime application of 300 kg is then equivalent to 0.3 g Cd ha^{-1}. In Sweden, lime applications are estimated to import 0.02 g ha^{-1} y^{-1} (Hellstrand and Landner, 1998).

Table 3.178 Annual Cd input into agricultural soils from phosphate fertilisers in European countries

Country	Cd input		Source*
	tonne	g ha^{-1}	
Austria	2.9	1.1	1
Austria		0.8	7
Belgium	1.5	0.59-1.40	7
Denmark	0.707	0.79-1.44	7
France	92	3.2	2
Finland	0.2	<0.1	1
Finland		0.02-0.1	2
Finland	0.052	0.03	5
Finland		0.025	7
Germany	20.4	1.7	1
Germany¶	22.1	1.28	6
Greece	10	2.8	2
Ireland	9	1.8	2
Ireland	7.4	1.67	7
Italy	44	3.0	2
The Netherlands	3	1.5	1
The Netherlands		4.5	3
Norway	0.072	0.12-0.21	7
Portugal	5	1.4	2
Spain	30	1.5	2
Sweden	1.1	0.5	1
Sweden		0.8	2
Sweden		0.20	4
United Kingdom	11.3	0.9	1
United Kingdom		1.0-2.1	7
EEC (1990)	231	2.5	2

* Source;
1) Pearse, 1996, data based on the OECD questionnaire (1995), conversion to Cd flux (g ha^{-1} y^{-1}) made by Landner et al., 1995;
2) Landner et al., 1996, data from 1990;
3) Moolenaar and Lexmond, 1998;
4) Hellstrand and Landner, 1998;
5) Finnish Environment Institute, 1997;
6) Kiene, 1999;
7) Hutton et al., 2001.

¶ The current average Cd content in P fertilisers might also be 35 mg Cd/kg P_2O_5 or 79 mg Cd/kg P (personal communication). At an application rate of 407,000 tonnes P fertiliser per year, this makes a Cd input of 32 tonnes Cd/year.

Manure, compost and sludge

The Cd input into agricultural soil by application of animal manure recycles some of the Cd that was previously taken up by crops. Therefore, Cd input from manure is only a net input into agricultural soil at a continental scale if there is a net import of animal feed crops. No data were found on the net total Cd import in Europe by this pathway. In Sweden, it was estimated that a total of 155 kg Cd is imported annually through animal feeds to farms with animal production. This corresponds to a Cd influx of 0.05g Cd ha^{-1} y^{-1} at the national level (Hellstrand and Landner, 1998). Moolenaar and Lexmond (1998) estimated the average net Cd influx from imported animal feed (feed concentrates) as 0.05 g Cd ha^{-1} y^{-1} for a mixed farming system in The Netherlands. Kiene (1999) calculated the total Cd input via slurry and dung (gross input, no net input) to be 13 tonnes y^{-1} in Germany, equivalent to 0.76 g Cd $ha^{-1}y^{-1}$. Since these values are much lower than the total Cd load from P fertilisers, it is unlikely that manure application is an important net source of Cd in agriculture at the European level. A similar reasoning is made for compost.

Table 3.18 shows the Cd input into agricultural soils from manure application. The country average fluxes range from 0.4-2.1 g Cd ha^{-1} y^{-1}. In The Netherlands, the Cd input from application of manure and compost is higher than that from the use of mineral fertilisers. This reflects the importance of the intensive livestock industry in that country (Pearse, 1996).

It should be noted that the Cd:P ratio in manure is lower than that in most mineral fertilisers. Moolenaar and Lexmond (1998) report Cd:P ratios of 18 mg Cd/kgP in poultry manure and 47 mg Cd/kgP in cattle manure. Manure samples from Belgium were found to contain 70 mg Cd/kgP (cattle) or 43 mg Cd/kgP (pig, Landner et al., 1996). Therefore, lower Cd input values are found in these farming systems where P from mineral fertiliser is (partly) replaced by P from manure. Local excesses in areas of intensive livestock industry have resulted in almost zero P-fertiliser consumption in some areas (e.g. Flanders, Belgium). In Sweden, more than 50% of total P fertilisation was applied as manure-P in 1994-1995 (Hellstrand and Landner, 1998).

The application of sludge is an important source of Cd where it is applied. In the European countries listed in **Table 3.179**, sewage sludge Cd load is estimated to be lower than fertiliser Cd load (exception: Belgium, **Table 3.179**). The country average fluxes of Cd from sewage sludge application are below 0.2 g ha^{-1} y^{-1} for those countries for which data were found. However, it must be stressed that these fluxes are country averages (i.e. total load divided by the area of arable land for each country) and are not reflecting the much higher flux where it is applied. These fluxes vary widely and depend on local restrictions on the use of sludge in agriculture. Legislation in EU-16 countries is either based on maximal Cd concentrations in sludge (i.e. 1.2-10 mg Cd/kg) or maximum Cd fluxes (e.g. 3-15 g $ha^{-1}y^{-1}$). Some countries restrict a cumulative load (OECD, 1994). Total Cd input from sludge in the EU-16 is estimated to be at least 11.6 tonnes y^{-1} (see **Table 3.156**).

Table 3.179 Annual Cd input into agricultural soils from manure, sludge, lime and compost in European countries. All flux data are country averages, i.e. total load divided by area of arable land and, hence, do not reflect the flux where it is applied

Country	Manure and compost		Sludge		Lime	Source
	tonne	g ha^{-1}	tonne	g ha^{-1}	g ha^{-1}	
Austria	1.3		0.1	0.04		1, 3
Austria		0.95				2
Belgium		1.7	> 6			1, 3
Belgium		0.78-2.66		< 0.01		5
Denmark			0.12	0.06		3
Denmark				1.45	0.4	5
Finland	0.2		0.07	0.02-0.05		3
Finland		0.322			0.035	5
Germany			1.27			3
Germany			2.4			1
Germany¶	14.1	0.82	3.2	0.19		4
The Netherlands	4.2	2.1	0.4	0.2		1, 3
Norway					0.02	5
Sweden	0.6-0.7	0.05(5)	0.1			1
Sweden			0.13			3
UK		0.4	2.3		0.375-0.503	1

* Source;
1) Pearse, 1996, data based on the OECD questionnaire (1995), conversion to Cd flux (g ha-1 y-1) made by Landner et al., 1996;
2) Dachler and Kernmaeyr, 1997;
3) Source: report from the commission to the council and the European Parliament on the implementation of community waste legislation Directive 86/278/EEC on sewage sludge for the period 1995-1997, data from 1997;
4) Kiene (1999);
5) Hutton et al. (2001).

Atmospheric deposition

The atmospheric deposition has been a major source of Cd in European agricultural soils in the past. As a result of increased emission control, atmospheric Cd deposition notably decreased over the last decades (see also Section 3.1.3.4.3). Therefore, only more recent data (> 1985) are included in this section. Total atmospheric deposition includes wet and dry deposition. It can be

¶ In Germany, the total production of municipal STP sludge is at the moment approximately 3 million tonnes y^{-1} (in dry weight). The following table indicates the fate of the sludge (rates are from year 1996). The source for the data is Umweltbundesamt (2001).

Use in agriculture	44.1%
Use for landscaping	11.8%
Composting	10%
Incineration	19.5%
Deposition into landfills	11.4%
Other	3.2%

argued that the dry Cd deposition is not completely a net Cd input into soil on a regional or larger scale. Dry deposition contains Cd that was previously removed from other locations. Total deposition in rural areas is, however, dominated by wet deposition (CCRX, 1991).

Table 3.180 shows the measured atmospheric Cd deposition in rural areas of different EU-16 countries. The deposition values range between 0.15 and 4 g ha^{-1} y^{-1}, depending on country and on sampling method. The deposition values generally decrease from North- to Central Europe. No deposition data for southern European countries were found. The EU-16 average is calculated based on total atmospheric emission data at EU-16 scale (see **Table 3.154**) and an area of 3.56 10^6 km². The calculated EU-16 average is 0.4 g ha^{-1} y^{-1} and is lower than most measured data (e.g. Dutch averages, about 1 g ha^{-1} y^{-1}). It is unknown if the net deposition is overestimated (even wet-only deposition data can include Cd that is resuspended from soil) or if the estimated total Cd emission is underestimated.

Table 3.180 Atmospheric Cd deposition in rural areas of European countries (measured, Eu-16 average is calculated)

Country	Cd deposition g ha^{-1} y^{-1}	Comments	Source
Austria	2.6[1]	Lower Austria (1987)	BFL, 1997
Austria	0.4-0.6[2]	original reference from 1994	BFL, 1997
Austria	2.1	National mean (wet+dry deposition)	Hutton et al., 2001
Belgium	3.6[3]	1 rural site at Belgian coast; 1995-1997	VMM, 1999
Belgium	1.1[5]		Landner et al., 1995
Denmark	1.5[3]		Jensen and Bro-Rasmussen, 1992
Denmark	1.1[5]		Landner et al., 1995
Denmark	0.41	bulk deposition (wet deposition)	Hutton et al., 2001
Finland	0.2-0.4[1]	original reference from 1995	Landner et al., 1995
Finland	0.09-0.35	gradually from north to south Finland	Hutton et al., 2001
France	2[4]	southern France, 1985-1986	Jensen and Bro-Rasmussen, 1992
Germany	1.4-4.0	field measurements ("wet only" and "bulk")	Bachmann et al., 1998
Germany	4	wet only measurements	Kiene, 1999
The Netherlands	1.2[4]	average of 14 sampling points in 1992	CCRX, 1994
The Netherlands	0.9[5]		Landner et al., 1995
Norway	0.2-1.2	north -south, 1985-1986	Jensen and Bro-Rasmussen, 1992
Norway	0.37	average value for Norway	Hutton et al., 2001
Sweden	0.6-1.1[2]	two districts in Sweden, original reference from 1994	Eriksson et al., 1996
Sweden	0.15-0.6[4]	north -south, 1996	Hellstrand and Landner, 1998
Sweden	0.4-1.5[5]		Landner et al., 1995

Table 3.180 continued overleaf

Table 3.180 continued Atmospheric Cd deposition in rural areas of European countries (measured, Eu-16 average is calculated)

Country	Cd deposition g ha-1 y-1	Comments	Source
UK	2[5]		Landner et al., 1995
UK	1.8	median value of 29 rural sites	Hutton et al., 2001
EU-16-average predicted	0.4	126 tonnes y^{-1} deposited over 3.56 10^6 km^2	This study

1) Methodology unknown;
2) Deposition calculated from Cd in moss;
3) Total deposition;
4) Wet deposition;
5) Based on OECD questionnaire (Pearse, 1996) with recalculations made in Landner et al., 1995.

Output of Cd from agricultural soils

Leaching

The Cd losses by leaching out of the plough layer are difficult to quantify in agricultural soils. The estimated losses of Cd from the plough layer are generally smaller than 1% per year (Landner et al., 1995). Therefore, downward movement of Cd is only detectable in long-term observations.

Detailed Cd leaching studies at the field scale have been performed for a number of polluted soils (e.g. Streck and Richter, 1997 and references therein). No such studies or model predictions were found for agricultural soils at an ambient Cd concentration. Therefore, Cd losses by leaching are estimated here based on a simplified model that is commonly used in Cd mass balance studies. The annual leaching losses L (g Cd $ha^{-1}y^{-1}$) is estimated as the Cd concentrations in pore water multiplied by the annual net water flux (also called the precipitation excess), formally:

$$L = [Cd]_l 10F$$

in which $[Cd]_l$ represents the Cd concentration in the liquid (µg L^{-1}) and F is the annual precipitation excess (m). A typical value for F in temperate regions is 0.2 m y^{-1}. The concentration of Cd in pore water is calculated from the solid-liquid distribution coefficient K_D (L/kg) and the soil Cd concentration (see Section 3.1.3.1.4).

Despite a high correlation between K_D and soil properties (see **Table 3.88**, Section 3.1.3.1.4), large systematic variations in predicted K_D values exist among the different studies. As an examples, for a typical arable soil of the temperate regions with pH 6.5 and 2% OM (1.2%C), predicted K_D values range between 90 and 1,560 L kg^{-1} depending on the regression equations. Effectively, the uncertainty in the K_D results in an equal uncertainty in the predicted annual Cd losses per unit of excess precipitation.

Table 3.181 shows the predicted Cd leaching from an agricultural soil at an ambient Cd concentration for different soil properties. This table shows that the predicted Cd leaching strongly depends on the soil pH and on the type of regression equation. As will be shown below, this uncertainty will imply that it is impossible to predict if Cd will accumulate in soil or not in low Cd input cropping systems. Therefore, we feel that more accurately estimating average Cd losses by leaching is critical for predicting future trends in average soil Cd in Europe.

There is little experimental evidence that could be used to validate the model that estimates Cd leaching losses. The predicted annual Cd losses from the plough layer (0.3-26 g ha^{-1} y^{-1}) are generally higher than those estimated in most other soil Cd balances (typically < 2 g ha^{-1} y^{-1}, Tjell and Christensen, 1992, Jensen and Bro-Rasmussen, 1992, Moolenaar and Lexmond, 1998, Hellstrand and Landner, 1998). Nicholson et al., (1996) estimated Cd leaching from the unlimed long-term park grass soils of Rothamsted (UK) using the Cd mass balance. The increase of Cd in the 0-22.5 cm horizon during 1913-1983 was compared with the Cd input by atmospheric deposition (estimated) and by phosphate fertilisers (based on analysis). After accounting for a small (measured) Cd loss by crop offtake, the leaching losses were found to vary between 0.7-3.1 g ha^{-1} y^{-1}(untreated) and 2.4-4.9 g ha^{-1} y^{-1} (P-treated). The authors estimated a range for the atmospheric Cd input from the average and maximum net annual increase of Cd in 4 different untreated plots of the Rothamsted long-term trials (Jones et al., 1987). Obviously, even the maximum net Cd accumulation in these plots (i.e. 5.4 g ha^{-1} y^{-1}) is likely lower than the atmospheric Cd input because of Cd losses from these plots. Therefore, the highest estimated Cd leaching from the park grass plots (i.e. 3.1-4.9 g ha^{-1} y^{-1}) may still be conservative values. Using our model, we calculated the average annual Cd losses from the P treated plots from the soil properties (soil pH values as given in Nicholson et al., 1994), 0.2 m annual water flux out of the topsoil and the K_D estimated with the model of Römkens and Salomons, 1998. Our model predicted 7.1 g ha^{-1} y^{-1} for the P treated plots, i.e. not too much higher than the 4.9 g ha^{-1} y^{-1} estimated by Nicholson et al., 1996.

Table 3.181 The annual Cd leaching from the plough layer (L, in g $ha^{-1}y^{-1}$). The Cd leaching is calculated for a soil with 0.3 mg kg^{-1} total Cd (background concentration) and an annual net water flux out of the plough layer of 0.2 m. The different models used for estimating the K_D of Cd in soil are referred to in Table 3.88

Soil pH	%OM	K_D model	L g ha^{-1} y^{-1}
6.5	2	Christensen, 1989	2.0
6.5	4		1.4
5.5	2		6.6
6.5	2	Lee et al., 1996	1.6
6.5	4		0.8
5.5	2		5.3
6.5	2	Gerritse and Van Driel, 1984	2.8
6.5	4		1.4
5.5	2		10.8
6.5	2	Römkens and Salomons, 1998	2.0
6.5	4		2.0
5.5	2		7.2
6.5	2	McBride et al., 1997	0.4
6.5	4		0.3
5.5	2		1.2

Table 3.181 continued overleaf

Table 3.181 continued The annual Cd leaching from the plough layer (L, in g $ha^{-1}y^{-1}$). The Cd leaching is calculated for a soil with 0.3 mg kg^{-1} total Cd (background concentration) and an annual net water flux out of the plough layer of 0.2 m. The different models used for estimating the K_D of Cd in soil are referred to in Table 3.88

Soil pH	%OM	KD model	L g ha-1 y-1
6.5	2	Smolders et al. (in situ data, unpublished)	0.9
6.5	4		0.9
5.5	2		4.0
6.5	2	Smolders et al. (adsorption data, unpublished)	6.6
6.5	4		3.4
5.5	2		26

Crop offtake

Crop offtake of Cd is the amount of Cd that is removed from the soil with the harvested part of the plant. The crop offtake of Cd is generally small in agricultural conditions and does not largely influence the soil Cd balance. The crop offtake in three different crop rotation systems in agricultural districts of Sweden varied from 0.17 to 0.62 g Cd ha^{-1} y^{-1} (averages for each rotation, Eriksson et al., 1996). The crops included in the rotations were carrots, potatoes, barley, oil seed, oat and winter wheat. Detailed farm-gate and field-scale Cd balances were calculated for arable, dairy and mixed farming systems at two locations in The Netherlands (Moolenaar and Lexmond, 1998). On the arable farm, crop offtake varied from 0.6-0.9 g Cd ha^{-1} y^{-1} (averages for a rotation including potato, sugar beets, chicory and onion, winter wheat and spring barley). Crop offtake in grassland was 1.4 g Cd ha^{-1} y^{-1} but most of this returns to the soil as manure. The farm-gate balance of the mixed-farming system showed that the net Cd loss with milk and meat/animal was less than 0.01 g Cd ha^{-1} y^{-1}. The crop offtake can also be calculated from typical yields and crop Cd concentrations. **Table 3.182** shows such estimates for wheat grain and potatoes in several European countries. It can be deducted from the table that harvesting wheat grain removes, on average, 0.4 g ha^{-1}. A potato yield removes around 1.2 g Cd ha^{-1}

Table 3.182 The Cd content in selected agricultural crops and the estimated annual crop offtake

Crop	Crop Cd† µg kg^{-1}	Comment	Typical yield (tonnes)	Crop offtake g ha^{-1}
wheat grain	38 (M)	UK[2], n=393	7.7	0.29
	58 (M)	France[3], n=16	6.5	0.38
	70 (M)	The Netherlands[4], n=84	8.8	0.62
	40-69 (M)	Sweden[1], n=354, averages of three data sets	6.0	0.24-.0.41
	56 (M)	Germany[5], n=886	6.9	0.39
potato tuber	51 (M)	Sweden[1], n=69	30	1.53
	30 (M)	The Netherlands[4], n=94	35	1.05

† Mean;
m Median;
Source;
1) Eriksson et al., 1996;
2) Chaudri et al., 1995;
3) Mench et al., 1997;
4) Wiersma et al., 1986;
5) Weigert et al., 1984.

For modelling purposes, crop offtake is assumed proportional to soil Cd and, hence, future crop offtake values are changed proportionally to the change in soil Cd. No changes in crop offtake are assumed with long-term changes in soil properties (e.g. soil pH).

Future trends in soil Cd: the regional PEC_{soil} in 8 different scenarios

The Cd mass balance in the plough layer will be calculated for a number of scenarios representative of European agriculture. These scenarios are indicative for average conditions.

Three different input scenarios are combined with a low or high output scenario each. The difference in output scenario is mainly based on a different soil pH, either pH 6.8 (low output) or pH 5.8 (high output). Leaching losses are calculated with the K_D model of Römkens and Salomons (1998) and assuming 0.2 m annual water flux out of the plough layer and 2% organic matter. The soil Cd concentration at t=0 is derived from measured Cd concentrations in areas well away from point sources (see **Table 3.190**). The Cd content in soil at t=0 refers to natural Cd (from geological origin) and some Cd that was added in the past (fertiliser Cd and Cd from atmospheric deposition).

The low input scenarios 1 and 2 represent agricultural conditions of northern Europe (Sweden, Finland and Denmark) and Cd input/offtake and soil Cd data were selected to correspond with preceding tables. Scenario 3 and 4 represent central European agricultural conditions (e.g. UK, France, The Netherlands, Germany) using average Cd fluxes from P fertilisers and atmospheric deposition in these countries. The offtake values were selected from Moolenaar and Lexmond, 1998 (either mixed farming or arable farming) and a typical soil Cd concentration was selected for these countries. Scenario 5 and 6 represents high input farming systems, which may be found in e.g. wheat/corn rotations. Applications of P in these systems are typically 30 kg P ha^{-1} (i.e. data of France, Italy and Germany, Harris, 1998) and it is assumed that the P fertiliser contains 150 mg Cd/kg P. The atmospheric deposition (3 g Cd ha^{-1} y^{-1}) represents a high value for European rural areas (see above). The offtake is low and represents farming systems with high Cd recycling (i.e. corn used for roughage). A worst case scenario 7 is included: this scenario may represent land use in some Mediterranean agricultural areas where very low output prevails. The Mediterranean biogeographical region comprises up to 9% of the Pan- European area (Roekaerts, 2002). This region can be characterised by a limited excess drainage (0.05m/year rather than 0.2 m/year; note default value of TGD is 0.175 m/year) and a large K_d value (calcareous soils which prevail in Mediterranean areas, pH 7.5). The scenario is considered as worst case because the very low output is coupled with high input as described above. High input of fertiliser is unusual for these areas because of lower crop yields (unless combined with irrigation, for which the low excess drainage may not be realistic). Data of Cd deposition in these areas are not available, and a realistic worst case assumption of 3 g/ha/year was made. The scenario 8 is an attempt to represent an average for the whole of Europe. Average Cd inputs are derived from the tables given above and the EU-16 average Cd deposition is based on the net emission at the regional scale (see **Table 3.180**). The average Cd input from fertiliser may be based on the 1990 data and, as discussed above, this value may overestimate current input of Cd from fertilisers. The average Cd output is difficult to estimate. The leaching losses are based on a soil pH of 6.5 and the crop offtake is an average for scenarios 1-6.

The soil Cd is predicted to increase in 6 scenarios (between 2.8 and 46%) and decrease in two scenarios (11 and 19%) after 60 years of exposure to current inputs. At the EU scale (average), soil Cd is predicted to increase by 6% after 60 years. This increase is lower than the historical increasing trends in soil Cd in Europe (see the human health part of this Risk Assessment Report, in separate document). The (realistic) worst case of scenario (5) predicts soil Cd concentration =

0.411 mg Cd/kg_{dw}. This is equivalent to 0.363 mg Cd/kg_{ww} (standard environment characteristics, TGD) and is used as the $PECregional_{soil}$.

The soil Cd concentration at t=0 has a major impact on the PECsoil. This is obviously related to the fact that the amount of background Cd in soil is several folds higher than the annual Cd addition. For example, the 90th percentile of the Cd concentrations in cultivated soils in France is 0.8 mg kg^{-1} (Baize, 1999; see **Table 3.190**). This concentration would increase to 0.875 mg Cd/kg_{dw} after 60 years, assuming a high input/low output scenario as in scenario 5. However, we do not prefer to use upper percentiles (=local situation) as a realistic worst case for PECregional since the risk scenarios in soil (see Section 3.3) are mainly important for human food chain contamination (regional/continental) and food items are not grown in one location in this scenario (see the human health part of this Risk Assessment Report, in separate document). The upper percentiles of background Cd in soil are certainly more relevant for local exposure to Cd but the $PEClocal_{soil}$ should then be contrasted to PNEC values derived for these scenarios (e.g. human diets dominated by home-grown food, see the human health part of this Risk Assessment Report, in separate document). The $PEClocal_{soil}$ values obviously span a wider range than the $PECregional_{soil}$ values in **Table 3.183**. It can be shown that the risk characterisation of diffuse Cd emissions in agricultural scenarios (fertiliser Cd, atmospheric deposition) is controlled by the regional and continental assessment and not by local risk assessment, even if the local Cd background is 3-4 fold larger than assumed in **Table 3.183**. Moreover, soils with high natural background Cd are usually soils that have large clay content and have a high pH, both factors known to reduce risk of Cd for foodchain contamination (see the human health part of this Risk Assessment Report, in separate document) or secondary poisoning (see Section 3.2.7) and which are the critical pathways of Cd in soil.

In the context of the continued review, under the Fertilisers Directive (76/116/EEC), of risks posed to human health and the environment by cadmium in fertilisers, Member States were encouraged to perform national risk assessments during summer/autumn 2000. To ensure conformity, a suggested template of procedures had been established. Eight Member States (Austria, Belgium, Denmark, Finland, Greece, Ireland, Sweden and the United Kingdom) and Norway submitted risk assessments. These were analysed and summarised in a consultants report to the Commission (Hutton et al.) in January 2001.

Compared to the accumulation calculations performed within this report, a longer time horizon, 100 years, was chosen by most Member States. The time period (60 or 100 years) only weakly affects the PEC_{soil}. As an example, the EU average PECsoil (60 years) = 0.318 mg Cd/kg dw whereas the PEC_{soi} (100 years) = 0.329 mg Cd/kg d.w. Different algorithms for K_D were chosen based on national soil properties. Also, a majority of the MS modelled scenarios with different cadmium concentration in fertilisers, e.g. "low", national average" and "high/EU average". Finally, many MS chose to use different input values for cadmium via fertilisers in order to assess the importance of crop rotation or regional agriculture practices.

Predictions of PEC_{soil} after 60 or 100 years, performed by Austria, Belgium, Denmark, Finland, Norway, Sweden and the UK are given as an illustration in **Table 3.22**. Ireland presented a risk assessment using default input parameters, while the input and output values in the Greek risk assessment are difficult to comprehend. Therefore the results of these assessments are not integrated in **Table 3.183**.

Despite the differences in input values, the consultant found the following consistent trends in the various assessments, based on current fertiliser input levels[46]:

- for low fertiliser cadmium concentrations (between 2.5 to 40 mg Cd/kg P), cadmium in soil tends to accumulate relatively slowly, or decreases after 100 years of application due to net removal rates (leaching, crop uptake) exceeding inputs
- for fertilisers with Cd concentrations of 60 mg kg^{-1} P and above, accumulation in agricultural soils over 100 years is more pronounced (between 17 and 43% increase after 100 years).

The future soil Cd content might be slightly overpredicted by some countries because they included animal manure as a net input in soil. Cadmium input from manure is, however, only a net input at the country level if there is a net import of minerals added to animal feed. The Cd input in soil from animal feed is low compared to the input from P-fertilisers (see **Table 3.183**). The soil Cd content in some Belgian regions is predicted to increase by more than a factor two over 60 years. These values are based on Cd deposition data near former industrial sites (atmospheric deposition 36 g ha^{-1} y^{-1}) where resuspension is a possible source of atmospheric Cd.

Low Cd input values through fertiliser addition are currently applied in northern European countries (Sweden, Finland and Denmark). As seen from **Table 3.177**, these countries introduced maximum permissible Cd concentrations in the mid 1990's. The calculations represent the present day situation, where risk reduction measures strongly influence the Cd input by fertilisers, and not a worst case scenario.

Some countries have predicted steady state soil Cd concentrations which are significantly above those calculated by the alternative model for the 6 regions (e.g. Austria: soil Cd at steady state = 1.13 mg Cd/kg dw). But steady state concentrations are only reached after very long periods (e.g. about 930 years, recalculated for Austrian data) during which soil properties (pH) land use (crop offtake) may change and that undoubtedly affect the soil Cd balance. In other words, the assumption of constant parameter values in predicting soil Cd concentrations in the very far future is highly questionable.

It is difficult to judge if the Cd balance in European soils is at a steady state or not. Current European Cd inputs in agricultural soil (2-3 g ha^{-1} y^{-1}) have strongly reduced from historical inputs (e.g. 7-9 g ha^{-1} y^{-1} in Denmark between 1923-1980, Tjell and Christensen, 1985; at least 8-10 g ha^{-1} y^{-1} in UK, P treated park grass soils 1913-1983, Nicholson et al., 1996). In the low input scenarios, predicted trends are extremely sensitive to changes in soil pH. Lowering the soil pH increases predicted Cd leaching and results in a predicted downward trend of soil Cd. No other soil Cd balance has predicted a reduction in soil Cd.

It can be concluded that the current Cd input in European agricultural soils is reduced from historical input and that the European soil Cd concentration is predicted to change by between a 19% decrease to a 46% increase in 60 years. However, there is always uncertainty in the input-output data and it now appears that estimating Cd leaching losses is critical for drawing firm conclusions. An average steady state obviously does not preclude that a strong increase in soil Cd is found in local areas. The steady state in soil Cd may not be reached in agricultural

[46] MS have also made predictions for fertiliser Cd concentrations that are larger than currently applied values to evaluate the effect of new regulations on future trends in soil Cd. For example, Denmark predicted that future soil Cd may increase by 53%-74% in 100 years if fertiliser Cd contains 140 mg Cd/kg P (60 mg Cd/kg P205) and which is fourfold above the current concentrations in Denmark.

systems that have characteristics as given in scenario 5, 6 and 7. These systems have a high Cd input from fertilisers, even where fertiliser Cd is below the legal limits of e.g. Germany and Belgium.

Predicting future trends in crop Cd is even more difficult than predicting future trends in soil Cd. It is very likely, for example, that soil acidification may have more effect on crop Cd concentrations than the slow changes in soil Cd. Trends in crop Cd concentrations are not included in this report because annual variations in crop Cd can be higher than changes over long periods of time. Andersson and Bingefors (1985) found an increase of a factor two in grain Cd content (winter wheat) between 1918 and 1980, while the annual variations in the grain Cd content were up to a factor five. Large annual variations in crop Cd are also observed by Kjellstrom et al. (1975) (see the human health part of this Risk Assessment Report, in separate document). Soil Cd typically explains a minor part of the variance in crop Cd. As an example: Swedish field data show that soil Cd only explains 3-19% of the variability of crop Cd concentrations (Eriksson et al., 1996).

Table 3.183 The predicted environmental concentration of Cd in agricultural soil (PEC_{soil}, -plough layer only) after 60 years of exposure to current Cd influx in agricultural soils. Seven scenarios are selected that may be representative for European agriculture. Predictions are made using the Cd mass balance approach described in the text. The full description of the scenarios is given in the text

scenario	Cd input (g ha^{-1} y^{-1})				Cd output (g ha^{-1} y^{-1}) at t=0			net Cd balance	Cd soil at t=0	PEC_{soil} after 60 years
	P fertiliser	Atmospheric deposition	Animal feed	Total	Crop offtake	Leaching	Total	g $ha^{-1}y^{-1}$	mg $kg^{-1}{}_{dw}$	
1. low input-low output	1.1	0.6	0.05	1.75	0.3	1.1	1.4	+0.35	0.250	0.257
2. low input-high output	1.1	0.6	0.05	1.75	0.5	4.1	4.6	-2.85	0.250	0.203
3. average input-low output	2.0	2.0	0.1	4.1	0.66	1.6	2.26	+1.84	0.350	0.385
4. average input-high output	2.0	2.0	0.1	4.1	0.8	5.7	6.5	-—4	0.350	0.310
5. high input--low output	4.5	3.0	-	7.5	0.3	1.3	1.6	+5.9	0.300	0.411
6. high input-high output	4.5	3.0	-	7.5	0.3	4.9	5.2	+2.3	0.300	0.339
7. high input-very low output (worst case Mediterranean)	4.5	3.0	-	7.5	0.3	0.1	0.4	+7.4	0.300	0.439
8. EU average	2.5	0.4[1]	0.05	2.95	0.5	2.0	2.5	+0.45	0.300	0.318

Table 3.183 continued overleaf

Table 3.183 continued The predicted environmental concentration of Cd in agricultural soil (PEC_{soil}, -plough layer only) after 60 years of exposure to current Cd influx in agricultural soils. Seven scenarios are selected that may be representative for European agriculture. Predictions are made using the Cd mass balance approach described in the text. The full description of the scenarios is given in the text

Predicted environmental concentrations in agricultural soils as calculated[3] in the Risk assessments on Cd in fertilisers performed by EU Member States and Norway (Hutton et al., 2001) at current Cd application rates through fertilisers (Table 3.177)			
	Current Cd concentration in the soil	PEC_{soil} after 60 years (mg $kg^{-1}{}_{dw}$)	PEC_{soil} after 100 years (mg $kg^{-1}{}_{dw}$)
UK	0.23	-	0.27
Austria	0.242	-	0.345
Belgium	0.22-0.35	0.114-0.772[2]	-
Denmark	0.144-0.249	-	0.076-0.273
Finland	0.21	-	0.145-0.228
Sweden	0.23 (wheat + potatoes) 0.33 (carrots)	-	0.20-0.30 (wheat + potatoes)[4] 0.30-0.35 (carrots)
Norway	0.24	-	0.19-0.21

1) 126 tonnes y^{-1} deposited over 3.56 10^6 km^2 = 0.4 g ha^{-1} y^{-1};
2) Based on Cd deposition data near former industrial sites (atmospheric deposition 36 g ha^{-1} y^{-1}) where resuspension is a possible source of atmospheric Cd;
3) Calculations are based on net Cd inputs from different sources (P-fertilisers, atmospheric deposition, manure, sludge application and/or liming). Cadmium output is based on Cd offtake by several crops and leaching estimated by different K_D models;
4) Calculations based on the algorithm of McBride et al. (1997).

3.1.3.4.3 Measured regional data in the environment

Aquatic systems

Cadmium enters rivers and lakes because of both natural and anthropogenic factors. Weathering and erosion processes may wash Cd from geological sources into rivers. Industrial and municipal effluents are discharged into rivers and lakes. There is direct deposition of atmospheric Cd onto surface waters as well as run-off of Cd-bearing water from the soil and from landfills. Acidification of soil and water may increase the mobilisation of Cd in the environment which would otherwise remain adsorbed to rock and soil particles (Pearse, 1996). Measured Cd concentrations in freshwaters and in suspended matter are presented in **Tables 3.184**, **3.185** and **3.186**. Measured Cd concentrations in freshwater sediments are presented in **Table 3.187**.

Most of the data presented in these tables originate from national or regional monitoring programs. The following data treatment was applied to derive statistics (e.g. 90th percentiles) from the data in the following consecutive steps:

- Data are sorted per country as a surrogate for region
- When measurements were reported as being smaller than the detection limit (DL), a value of half the DL was assigned to this measurement.
- Outliers: a statistical approach was used for defining outliers in an attempt to exclude the contribution of local emissions from diffuse emissions. The uncertainty related to either including or excluding outliers will be taken forward to the risk characterisation where the effect of outlier analysis on the risk factors will be compared[47]. In this section, however, percentiles only refer to the database obtained after outlier exclusion. Outliers are selected based on the TGD (EC, 2003) using the equation: $\log(X_i) > \log(P75) + K(\log(P75) - \log(P25))$ where X_i is the concentration above which a measured value may be considered an outlier, Pi is the value of the ith percentile of the statistic and K is a scaling factor. This filtering of data with a scaling factor K = 1.5 is used in most statistical packages, but the factor can be subject dependent. A value of 1.5 was chosen in this report. Outliers are detected by calculating the P75 and P25 statistics on the entire dataset, i.e. not per sampling site. Outlier calculation per sampling site detects measurement errors.
- Derivation of statistics: the revised TGD (EC, 2003) recommends calculating the PECregional as the mean of 90th percentiles within a region. The 90th percentiles refer to observations at one sampling site. Almost all data referred to below do not give data organised per sampling site but rather list data without reference to a site. In order of preference we calculated the statistics as: xth percentile= mean of xth percentiles within the region; if this was not possible, then xth percentile= xth percentile of the data within the dataset. The P90 value is calculated from the rank in the observed frequency distribution and not from the rank in a curve fitted to the frequency distribution. This means that the P90 is not affected by the exact values of data at lower percentiles
- Data are presented as dissolved (D) concentrations. If the original data refer to total concentrations, then dissolved concentrations are estimated (ED) assuming that the dissolved Cd concentration in freshwater is 33% of the total Cd concentration in water (see Section 3.1.2.3.1: dissolved fraction = $1/((1+K_p \cdot C_{susp} \cdot 10^{-6})$ with $K_p = 130\ 10^3$ L kg^{-1}, C_{susp} = 15 mg L^{-1}; TGD, 1996). In Swedish oligotrophic lakes, about 60-100% of the Cd is dissolved (< 2.4 nm) at pH 4.5-6.0 and about 10-60% at pH 6-7 (Parkman et al., 1998).

[47] However, the methodology proposed by the rapporteur i.e. exclusion of outliers that are detected by statistical approach only was not endorsed by MSs (see ECB document 'mi_302+303_tc0404_env').

Fractionation is unknown (U) for the large Scandinavian database of Skjelkvåle et al. (1999). For all these data, the dissolved fraction is set at 100%. As will be shown in the risk characterisation, this conservative assumption does not affect the conclusion for regional risk.

Priority is given to the most recent data for risk characterisation. All data below are drawn from the original databases and secondary information about regional averages (or 90P values) are not used if the background information (i.e. detection or reporting limit[48]) is missing. The data of surface water are classified in reliability classes (RI1: most reliable, RI4, least reliable) to aid the risk characterisation. The detection limit (DL) is most critical. As the PNECwater is 0.19 µg L^{-1}(see Section 3.2), we propose that a dataset with DL ≥ 0.1 µg L^{-1} (dissolved) is less reliable within the risk characterisation.

RI 1: the detection limit is < 0.1 µg L^{-1} (dissolved), the Cd fractionation is known as dissolved or estimated dissolved and water hardness data are known. This allows the risk characterisation to be corrected for water hardness.

RI 2: the detection limit is < 0.1 µg L^{-1} (dissolved), the Cd fractionation is known as dissolved or estimated dissolved; hardness is unknown and no correction for hardness can be made.

RI 3: the detection limit is < 0.1 µg L^{-1} (dissolved), the Cd fractionation is known as dissolved, estimated dissolved or is assumed as dissolved when no information regarding the Cd fractionation was given.

RI 4: the detection limit ≥ 0.1 µg L^{-1} (dissolved) and data are considered on a case-by-case basis because the detection limit is too large.

In what follows the datasets of various European countries are described and discussed. Several databases contain series with different detection limits and a specific data analysis was performed, discussed below, to allow classification in the above-mentioned reliability classes Data are presented in **Tables 3.184, 3.186 and3.187** The underlined values are taken forward to the risk characterisation and are summarised in **Table 3.185** and **Table 3.188** in which the average of 90th percentiles are calculated per region. .

- Belgium

Flanders region: Monitoring data of total cadmium were obtained from the Flemish Environment Agency (VMM; http://www.vmm.be). For the purpose of this risk assessment, data for the years 2000-2002 are used. After analysis of the dataset and exclusion of the outliers, the dataset contained 3,591 measurements. The DL ranges from 0.1 to 1.2µg L^{-1}. Only 6% of the data were above the detection limit. This means that the 90th percentile of that dataset, 0.5µg L^{-1}(total) i.e. 0.17 µg L^{-1}(estimated dissolved) is unreliable.

Additionally, a qualitative description of the data-set was provided by VMM (pers. com., 2004). The monitoring network in Flanders contains a large number of sampling locations distributed over various types of surface waters in Flanders (834 sampling points in 2002). Total cadmium levels have been analysed and the data show that most higher cadmium levels are concentrated in the Kempen (i.e. the results of Dommel, Molse Neet and the Scheppelijke Neet are conspicuous). In 1997, 24% of the measurements were above the detection limit (mainly 0,2 and 1 µg L^{-1}). In 2002, 13% of the results were above the detection limit (between 0,1 and 1,2 µg L^{-1}). Calculation of the average of 90th percentiles on the datasets of 1997 and 2002 separately and without any data exclusion and by setting data lower than detection limit at half the detection limit, yields a

[48] The reporting limit (RL) is the lowest reported Cd concentration if no detection limit is indicated.

90th percentile (total cadmium) of 1.0µg L^{-1}in 1997 as well as in 2002 (VMM, pers. com., 2005). Given however that these P90's are within the range of the DL, these cannot be considered as reliable for the risk characterisation.

The monitoring data for the Walloon region were generated and reported by the Scientific Institute for Public Services (ISSeP). The dataset contains 690 values for the dissolved Cd content and 39 for the total Cd content of Walloon surface waters. The DL is reported to range from 0.1 to 0.3 µg $L^{-1}$for the dissolved Cd content and is equal to 1 µg $L^{-1}$for the total Cd concentration. The reporting limit exceeds the critical value of this report, however the P90-value is still useful as it exceeds the critical reporting limits (notice that all values below the reporting limit have been set to half the reporting limit). After excluding the outliers following the procedure mentioned above a dataset of 659 values remained ranging from 0.05 to 1.53 µg L^{-1}. Statistics were calculated once for the entire dataset.

Recently more (detailed) data for the Walloon region (years 2000, 2002 and 2004) were submitted via Industry's commentary file (ICdA, 2005) but could not be taken into account in this assessment[49]

- Denmark

For Denmark, data concerning Cd concentrations in surface waters were found in a survey of the national lakes for the Nordic Council of Ministers by Skjelkvåle et al. (1999). Measurements were performed in the year 1995 with the ICP-MS method. 0.03 µg $L^{-1}$was reported as the DL. The method was subjected to quality control. The statistics of the report for Denmark are based on 19 not-statistically selected lakes, and are therefore only indicative of the general levels of Cd in Danish lakes. For this reason, Skjelkvåle et al. (1999) only reported the 50th percentile. The maximum measured concentration is 0.266 µg L^{-1}, the lowest reported value is below the DL.

- Finland

A first dataset was found in the survey of the national lakes for the Nordic Council of Ministers by Skjelkvåle et al. (1999). Measurements were performed in the year 1995 with the ICP-MS method. 0.03 µg $L^{-1}$was reported as the DL. The method was subjected to quality control. 464 lakes were selected at random keeping in mind basic requirements concerning size and location. The data can be considered to represent the entire country.

A second dataset was obtained from the cooperation project "Ecogeochemical mapping of Eastern Barents region 1999-2000" (Salminen et al., 2004). The dataset reports the dissolved cadmium content of 339 measurements. The lowest reported value is 0.005 µg L^{-1}, the highest 0.48 µg L^{-1}. No DL is indicated.

- France

A number of monitoring data (52 in total), representative for the Rhône-mediterranean basin, were gathered from the "Réseau des Données sur l'eau du Bassin Rhône-Méditerranée-Corse"(RNB-eauRMC). This dataset for the region of the Rhône-Méditerranée for the year 2001 contains no actual measured data for Cadmium. All data are reported as smaller than the DL of 0.5 µg L^{-1}.

Data for the Seine were gathered from the Réseau National de Donnéés sur l'Eau (RNDE) and can be consulted on the web at http://www.rnde.tm.fr/. The dataset contains 9 values for the years 1998 to 2000. No DL is indicated and values range from 0.025 to 0.073 µg L^{-1}.

[49] Data were submitted in August 2005 and thus well beyond the agreed deadline for new data submission to be incorporated within the RAR following the CSTEE opinion.

Data for the Rhine-Meuse basin are reported by the Office International de l'Eau (1999) for the years 1995 to 1999. Data were obtained from 104 measurements. No information regarding the method of detection or DL is reported.

The datasets for France were designated RI 4. The reporting limits are unknown or exceed 0.1 µg L^{-1} or the dataset is not considered representative for a region.

- Germany

The dataset from the Elbe for the year 2000 originates from the Wassergütestelle Elbe (Hamburg). It reports the total Cd concentrations and consists of 114 measurements. The DL is reported as 0.05 µg $L^{-1}$and values range from 0.05 to 0.7 µg $L^{-1}$for total Cd concentrations. 111 values are reported as higher than the DL. Statistics were calculated once for the entire dataset.

A large dataset was obtained from the "Hessisches Landesamt für Umwelt und Geologie" (HLUG), containing recent information (2001) on cadmium concentrations in a large number of rivers in Germany (26 in total). The data can be presumed to represent the entire country. The dataset consists of 531 measurements. The fractionation of the measured cadmium is not indicated. The lowest reported values range from 0.1 to 0.5 µg L^{-1}, the highest is 64.2 µg L^{-1}. One measuring site was excluded, however, according to the aforementioned selection procedure. This resulted in a dataset of 520 values with a range of 0.1-0.98 µg L^{-1}. No DL is reported. Statistics were calculated by averaging over the different measuring sites, following the TGD, revised 2002 procedure. The reliability of the database is, overall, low because the fractionation is unknown, the detection limit is unknown and the majority of the data within a site are reported as a constant value (e.g. 0.5 µg L^{-1}), suggesting that this is the reporting limit. Because of lack of information on DL's, it was considered unreliable to divide the lowest values by 2. This database will not be taken forward to the Risk Characterisation because of all these uncertainties.

A third dataset for the year 1998 was obtained from the "Joint Water Commission of the Federal Länder (LAWA), Federal institute of Hydrology, Berlin. This dataset contains 2,614 measurements of 89 rivers. Data for different measurement points are available for some of these rivers. The 90th percentiles for some of the major rivers are given here. If 90th percentiles of different measuring points for a river are available, only the average of these 90th percentiles is indicated. Cadmium concentrations are reported for the total cadmium concentration and the DL ranges from 0.05 to 0.5 µg L^{-1}.

In addition, data concerning the Cd content of German surface waters were extracted from the COMMPS database (Combined Monitoring-based and Modelling-based Priority Setting scheme) of the European Commission (European Commission, 1999). This smaller dataset contains 33 values for the year 1996. Measurements were performed for the dissolved cadmium content and range from 0.02 to 0.21 µg L^{-1}. No DL is reported. Statistics were calculated once for the entire dataset.

- Greece

Data concerning the Cd content of Greek surface waters were extracted from the COMMPS database (Combined Monitoring-based and Modeling-based Priority Setting scheme) of the European Commission (European Commission, 1999). This dataset contains 39 values for the year 1998. Data refer to total concentrations (Dr. Lekkas, personal communication) and no DL is given. The reported values range from 0.06 to 1.89 µg L^{-1}. Statistics were calculated once for the entire dataset. For reference: Estrela et al. (2000) report an average value for the Axios river of 0.25 µg L^{-1}. No information regarding the original dataset, method of detection or DL is given.

- Italy

Data concerning the Cd content of Italian surface waters were extracted from the COMMPS database (Combined Monitoring-based and Modelling-based Priority Setting scheme) of the European Commission (European Commission, 1999). This dataset contains 6 values for the year 1996. The fractionation of the measured Cd content is not indicated and no DL is given. The reported values range from 0.5 to 2 µg L^{-1}. No information is available about the location of sampling. Statistics were calculated once for the entire dataset.

Because of the small amount of data for the year 1996, data for the year 1995 from the same database are also given. Notice the large difference in measured values between the 2 years. Questions can be raised regarding the representative ness of this dataset for the entire country. Statistics were calculated once for the entire dataset.

For reference: Breder (1988) reported dissolved Cd concentrations in Italian rivers to range from 0.004 to 0.113 µg L^{-1}in the years 1980 – 1982. Furthermore, Breder (1988) reports values in the Po river to range from 0.028 to 0.19 µg L^{-1}in the year 1983 with an average of 0.065 µg $L^{-1}$and the Cd content of Italian lakes to range from 0.004 to 0.013 µg L^{-1}. Jensen and Bro-Rasmussen (1992) report the average Cd content in the Tiber as 0.015 µg $L^{-1}$and in the Arno 0.1 µg L^{-1}. Because of the large difference between the dataset and the literature date, the dataset should not be taken forward to the risk analysis (RI 4).

- The Netherlands

Monitoring data for the Netherlands were gathered by the Rijkswaterstaat (RWS; executive organisation of the Dutch Ministry of Transport, Public Works and Water Management). The dataset presented here contains 333 values for the measured total Cd content of Dutch surface waters for the year 2002. Data are obtained from the "Waterstat" database on the internet to be found on http://www.actuelewaterdata.nl/. The data can be presumed to represent the entire country (data from 27 sampling sites). The DL is reported as 0.05 µg L^{-1}. Statistics were calculated by averaging the 90^{th} percentiles of measurements at each sampling point, following the TGD, revised 2002 procedure.

A second dataset for regional waters was obtained, containing 1692 data from 242 sampling points. Total Cd concentrations are reported. The reporting limit varies from 0.01 to 0.3 µg L^{-1}total Cd depending on the regional water management authority. Data were screened according to the aforementioned selection procedures (i.e. excluding data from regional water management authorities with RI 4 and excluding outlier data). This resulted in a dataset of 1492 values from 228 sampling points, with total Cd concentrations ranging from 0.005 to 0.56 µg L^{-1}(RL 0.01-0.24 µg L^{-1}). Including outlier data, total Cd concentrations range from 0.005 to 21 µg L^{-1}. Statistics were calculated by averaging the 90^{th} percentiles of measurements at each sampling point, following the TGD, revised 2002 procedure. The analysis by the responsible Dutch Water Authorities for these waters yielded a P90 of 0.73 µg L^{-1}(total) or 0.24 µg L^{-1}(estimated dissolved) which is about 3-fold above the P90 value calculated here and which was mainly related to the either or not including data with large detection limits. The MSR has returned this data analysis to the responsible Dutch Water Authorities but no further comments were received.

An additional dataset on total Cd content of Dutch surface waters for the year 1997 can be extracted from the COMMPS database (Combined Monitoring-based and Modeling-based

Priority Setting scheme) of the European Commission (European Commission, 1999). However, in the presence of more recent datasets, NL proposed to base the risk characterisation on the latter and preferred not to use the older COMMPS dataset to this aim (COM302+303_env_NL4, 19.11.04).

For reference:

Crommentuijn et al. (1997a) report a background concentration for the 90th percentile of dissolved Cd in the Netherlands of 0.08 µg L^{-1}.

Ros and Slooff (1990) report values for the dissolved Cd concentration of 0.18 - 0.026 and 0.34-0.059 µg $L^{-1}$for the Rhine (near Lobith) respectively the Meuse (near Eysden) in the years 1983 to 1986.

The "Coordinatie-Commissie voor de metingen van Radioactiviteit en Xenobiotische stoffen" (CCRX, 1994) reports the following 90th percentiles for the Cd content in the year 1992: 0.1, 0.8, 0.38, 0.2, 0.15, 0.09 and 0.2 µg $L^{-1}$for the Rhine (near Lobith), the Meuse (near Eysden), the Westerscheldt Schaar van Ouden Doel, the Nieuwe Waterweg Maassluis, the Nieuwe Waterweg Haringvlietsluizen, the Netherlands IJ23 and the Netherlands NZK KM2 respectively. The fractionation of the measured Cd is not given.

Pearse (1996) reports the following 90th percentiles for the Cd content of the year 1993: 0.1 and 0.6 µg $L^{-1}$for the Rhine (near Lobith) and the Meuse (near Eysden) respectively. The fractionation of the measured Cd is not reported.

- Norway

A first dataset was found in the survey of the national lakes for the Nordic Council of Ministers by Skjelkvåle et al. (1999). Measurements were performed in the year 1995 with the ICP-MS method. 0.02 µg $L^{-1}$was reported as the DL. The method was subjected to quality control. 985 lakes were selected at random keeping in mind basic requirements concerning size and location. The data can be considered to represent the entire country.

- Portugal

Data for Portugal were found in the Portuguese Database for Water (the National Information System for Water, to be found on the web at http://snirh.inag.pt). Values are presented here for the total Cd content of Portuguese surface waters in the year 2002. Detection limits vary per region from 0.1 to 5 µg L^{-1}total Cd or from 0.03 to 1.7 µg L^{-1}estimated dissolved Cd. In the whole dataset, 84% of the measurements are smaller than the DL, but for some of the surface waters more than 90% of the data are below the DL. As such, the DL strongly determines the statistics derived from this dataset. The dataset for Portugal, although very extensive, will not be fully included in the risk characterisation, because the detection limits exceed 0.1 µg L^{-1}. Statistics were calculated by averaging over the different regions, following the TGD, revised 2002 procedure.

- Spain

A dataset was found for one region of Spain: Andalusia. Data originate from the "Consejeria de medio ambiente en Andalusia" and were reported on the web by the Spanish Ministry of Environment. (http://www.mma.es). The database consists of 330 measurements of the cadmium concentrations of Spanish surface waters for the year 1994. The fractionation of the measured Cd is not indicated. The DL was 0.3 µg L^{-1}. Reported concentrations range from < 0.3 to 68 µg $L^{-1}$with 39% of the dataset being smaller than the DL. High values are encountered because of a historical contamination of the Guadalquivir. The results can, therefore, not be considered to represent ambient Cd concentrations of Spanish waters. Statistics were calculated once for the entire dataset but the data are not taken forward to the risk characterisation in this report because of the influence of data with historical contamination.

Recent data for Spain were submitted (Ministerio de medio ambiente, 2005) but could not be taken into account in this assessment[50].

Additional data were extracted from the COMMPS database (Combined Monitoring-based and Modeling-based Priority Setting scheme) of the European Commission (European Commission, 1999). This dataset contains 11 values for the year 1996. The fractionation of the measured Cd content is not indicated and no DL is given, but the reporting limit, as well all the values in the dataset, equal 0.1 µg L^{-1}. Therefore, the COMMPS dataset for Spain will not be included in the risk characterisation (RI 4). Statistics were calculated once for the entire dataset.

Notice the large difference between the 2 datasets. Keeping in mind the overall measured concentrations in Europe, one is inclined to rely stronger on the dataset from the COMMPS database.

For reference: Jensen and Bro-Rasmussen (1992) report the Cd concentrations of the Ebro as 0.12 µg L^{-1}. No additional information is provided.

- Sweden

Data were gathered by the Swedish University of Agricultural Sciences and can be consulted on the web at http://info1.ma.slu.se/. Data are presented for the year 2000 for lakes and for the years 1995 – 2001 for rivers. DLs vary but all cover the very low range of encountered values. Reported values range from 0.002 to 2.03 µg $L^{-1}$for rivers and from 0.001 to 4.46 µg $L^{-1}$for lakes. Statistics were calculated for the 2 datasets separately by averaging over the different regions, following the TGD, revised 2002 procedure.

A second dataset was found in the survey of the national lakes for the Nordic Council of Ministers by Skjelkvåle et al. (1999). Measurements were performed in the year 1995 with the ICP-MS method. 0.003 µg $L^{-1}$was reported as the DL. The method was subjected to quality control. 820 lakes were selected at random keeping in mind basic requirements concerning size and location.

- The United Kingdom

Data for the Cd content of British surface waters were gathered by the U.K Environmental Change Network (ECN) and can be found on the web at http://www.ecn.ac.uk/index.html Data are presented for the year 1995 and consist of 10 measurements. The fractionation of the measured Cd is not indicated. The DL is reported as 0.02 µg L^{-1}. Reported values range from < 0.02 to 0.46 µg $L^{-1}$with 30% of the values reported as smaller than the DL. Statistics were calculated once for the entire dataset.

Data were also extracted from the COMMPS database (Combined Monitoring-based and Modeling-based Priority Setting scheme) of the European Commission (European Commission, 1999). This dataset contains 1,363 values for the year 1996. Measurements were performed on the dissolved Cd content and the lowest reported values range from 0.02 to 0.2 µg L^{-1}. No DL was indicated. Measured concentrations range from 0.02 µg $L^{-1}$to 346 µg L^{-1}. After excluding the

[50] Data were submitted in May 2005 and thus well beyond the agreed deadline for new data submission to be incorporated within the RAR following the CSTEE opinion.

outliers a dataset was obtained with 1244 values ranging from 0.02 to 1.38 µg L^{-1}. Statistics were calculated once for the entire dataset.

A 3rd database (WIMS) was received from the Environment Agency and contains 7108 Cd measurements in freshwater for the year 2003. Measurements were performed on the dissolved Cd content. The detection limit varies from 0.01 to 1 µg L^{-1}. Sampling points with DL > 0.1 µg $L^{-1}$and sampling points with only one measurement were rejected. This resulted in a dataset of 6,905 values from 728 sampling points, with dissolved Cd concentrations ranging from 0.005 to 158 µg L^{-1}. Of these values, 5,388 are reported as '< 0.1 µg L^{-1}'. Because of the high number of measurements found under the DL, an outlier analysis on the full dataset was not useful because it resulted in a limit value at the DL. Therefore, it is proposed here to make an outlier analysis on the sub-dataset of measurements found above the DL. It should be noted that this results in a very conservative outlier analysis and only 20 P90 values of the 729 were rejected. Statistics were calculated by averaging the 90th percentiles of measurements at each sampling point, following the TGD, revised 2002 procedure.

Table 3.184 Measured or estimated dissolved Cd concentrations in surface water. Underlined data are used for risk characterisation

Location (source/database)	Cd fractionation[1]	Sampling period	n	Reporting limits [µg L-1]	90th percentile [µg L-1]	50th percentile [µg L-1]	10th percentile [µg L-1]	Statistics[2]	RI
Belgium									
Flanders (VMM)	ED	2000-2002	3591	0.03 - 0.4	(0.17: unreliable, only 6% of data>DL)	-	-	*	4
Walloon (ISSeP)	D	1999-2000	681	0.1 – 0.3	0.66	0.10	0.05	**	4
Denmark									
Denmark (Skjelkvåle et al., 1999)	U	1995	19	0.03	-	0.05	-	***	-
Finland									
Finland (Skjelkvåle et al.,1999)	U	1995	464	0.030	0.03	<0.03	<0.03	***	2
Eastern Barents Region (Salminen et al., 2004)	D	1999-2000	339	0.005	0.085	0.020	0.005	**	2
France									
Rhône-Méditerranée (RNB-eauRMC)	U	2001	52	0.5	0.25	0.25	0.25	**	4
Seine (RNDE)	D	1998 -2000	9	0.025	0.06	0.03	0.03	**	4
Rhine-Meuse (Office International de l'eau)	U	1995-1999	104	-	0.85	-	0.05	***	4

Table 3.184 continued overleaf

Table 3.184 continued Measured or estimated dissolved Cd concentrations in surface water. Underlined data are used for risk characterisation

Location (source/database)	Cd fractionation[1]	Sampling period	n	Reporting limits [µg L-1]	90th percentile [µg L-1]	50th percentile [µg L-1]	10th percentile [µg L-1]	Statistics[2]	RI
Germany									
Elbe (Wassergütestelle Elbe)	ED	2000	114	0.02	0.12	0.07	0.07	**	2
Germany (HLUG)	U	2001	520	0.1 - 0.5	0.46	0.45	0.44	*	4
Danube (LAWA)	ED	1998	52	0.03 - 0.07	0.03	-	-	*	2
Mosel (LAWA)	ED	1998	26	0.02 - 0.03	0.03	-	-	*	2
Oder (LAWA)	ED	1998	52	0.07	0.10	-	-	*	2
Rhein (LAWA)	ED	1998	194	0.02 - 0.07	0.03	-	-	*	2
Ruhr (LAWA)	ED	1998	22	0.07	0.11	-	-	*	2
Saar (LAWA)	ED	1998	76	0.03	0.03	-	-	*	2
Weser (LAWA)	ED	1998	67	0.02 - 0.13	0.09	-	-	*	4
Germany (COMMPS)	D	1996	33	0.02	0.11	0.05	0.02	**	2

Table 3.184 continued overleaf

Table 3.184 continued Measured or estimated dissolved Cd concentrations in surface water. Underlined data are used for risk characterisation

Location (source/database)	Cd fractionation[1]	Sampling period	n	Reporting limits [µg L^{-1}]	90th percentile [µg L^{-1}]	50th percentile [µg L-1]	10th percentile [µg L-1]	Statistics[2]	RI
Greece									
Greece (COMMPS)	ED	1998	39	0.02	0.18	0.08	0.03	**	3
Italy									
Italy (COMMPS)	U	1996	6	0.5	1.74	0.75	0.52	**	4
Italy (COMMPS)	U	1995	7	0.5	11.42	2.86	0.56	**	4
The Netherlands									
The Netherlands (RWS)	ED	2002	333 (27 sampling sites)	0.02	0.07	0.03	-	*	2
The Netherlands (regionale wateren)	ED	2002	1492 (228 sampling sites)	0.003-0.08	0.06	-	-	*	2
Norway									
Norway (Skjelkvåle et al., 1999)	U	1995	985	0.02	0.055	<0.02	<0.02	***	2

Table 3.184 continued overleaf

Table 3.184 continued Measured or estimated dissolved Cd concentrations in surface water. Underlined data are used for risk characterisation

Location (source/database)	Cd fractionation[1]	Sampling period	n	Reporting limits [µg L-1]	90th percentile [µg L-1]	50th percentile [µg L-1]	10th percentile [µg L-1]	Statistics[2]	RI
Portugal									
Arade (SNIRH)	ED	2002	6	0.33	-	0.17	-	**	4
Ave/ Leca (SNIRH)	ED	2002	22	0.33	0.17	0.17	0.17	**	4
Cavado/rib Costeiras (SNIRH)	ED	2002	39	0.33	0.17	0.17	0.17	**	4
Douro (SNIRH)	ED	2002	219	0.17 - 0.33	0.17	0.17	0.08	**	4
Guadiana (SNIRH)	ED	2002	35	1.7	0.83	0.83	0.83	**	4
Lima/ Neiva (SNIRH)	ED	2002	24	0.33	0.17	0.17	0.17	**	4
Lis/rib. Costa (SNIRH)	ED	2002	92	0.17	0.43	0.08	0.08	**	4
Minho/ Ancora (SNIRH)	ED	2002	41	0.33	0.17	0.17	0.17	**	4
Mira (SNIRH)	ED	2002	4	1.7	-	0.83	-	**	4

Table 3.184 continued overleaf

Table 3.184 continued Measured or estimated dissolved Cd concentrations in surface water. Underlined data are used for risk characterisation

Location (source/database)	Cd fractionation[1]	Sampling period	n	Reporting limits [µg L-1]	90th percentile [µg L-1]	50th percentile [µg L-1]	10th percentile [µg L-1]	Statistics[2]	RI
Portugal									
Mondego (SNIRH)	ED	2002	193	0.17	0.21	0.08	0.08	**	4
Rib. Algarve (SNIRH)	ED	2002	8	0.33	0.17	0.17	0.17	**	4
rib. Oeste (SNIRH)	ED	2002	57	0.03	0.02	0.02	0.02	**	3
Sado (SNIRH)	ED	2002	27	1.7	0.83	0.83	0.83	**	4
Tejo (SNIRH)	ED	2002	280	0.03 -1.7	0.83	0.83	0.02	**	4
Vouga/ rib. Costeiras (SNIRH)	ED	2002	127	0.17	0.28	0.08	0.08	**	4
Spain									
Andalusia (MMA)	U	1994	330	0.3	7	1	0.1	**	4
Spain (COMMPS)	U	1997	11	0.1	0.1	0.1	0.1	**	4

Table 3.184 continued overleaf

Table 3.184 continued Measured or estimated dissolved Cd concentrations in surface water. Underlined data are used for risk characterisation

Location (source/database)	Cd fractionation[1]	Sampling period	n	Reporting limits [µg L-1]	90th percentile [µg L-1]	50th percentile [µg L-1]	10th percentile [µg L-1]	Statistics[2]	RI
Sweden									
Sweden - rivers (SLU)	U	1995-2001	6,975	0.002	0.052	0.023	0.007	*	1
Sweden - lakes (SLU)	U	2000	1,204	0.001	0.027	0.011	0.006	*	1
Sweden (Skjelkvåle et al., 1999)	ED	1995	820	0.003	0.052	0.01	0.003	***	2
The United Kingdom									
The UK (ECN)	U	1995	10	0.02	0.31	0.10	0.01	**	3
The UK (COMMPS)	D	1996	1,244	0.02 – 0.2	0.43	0.17	0.10	**	4
The UK (WIMS)	D	2003	6,905 (728 sampling sites)	0.01-0.1	0.15	0.10	0.08	*	2

1) Cd fractionation: D: dissolved Cd; ED: estimated dissolved Cd. If total concentrations are measured, dissolved concentrations are estimated to be 33% of the total Cd concentration (see Section 3.1.3.1.1); U: unknown Cd (presumed as 100% dissolved);

2) Statistics;

* The statistics (=percentiles) are averages of corresponding values of the different sampling sites per region (TGD - EC, 2003);

** The statistics are the percentiles of the entire dataset due to a lack of geographically-referenced data;

*** Statistics are reported by the author of the respective dataset.

Reported average Cd concentrations in European surface waters range from 0.03 µg L^{-1}(Sweden) to 0.14 µg L^{-1}(U.K; **Table 3.185**). Notice that reported Cd concentrations increase as the uncertainty (RI) increases. We propose to use the data of RI 3 as a trade off between data richness and quality. Countries from northern, western and southern Europe are included and as such a general view of the ambient Cd concentration in European surface waters is obtained. The dataset for the Seine (France; n=9, P90= 0.06 µg L^{-1}) is not included as it comprises a very limited area and, as such, does not represent the entire region. If included, the effect on the resulting statistics would be minimal.

The average of the average 90th percentiles per region is 0.12 µg $L^{-1}$and is a first approximation of a $PEC_{regional}$. This value is slightly above the 90th percentile obtained in the EU-wide systematic survey of FOREGS study (0.10 µg L^{-1}, see below). The statistics of the datasets with RI 4 are not summarised as the uncertainty regarding these data is too large.

It is most likely that all surface waters contain some Cd that is emitted by man. Natural background Cd in surface water can therefore only be estimated indirectly. Scandinavian rivers and lakes probably contain minor quantities of Cd added by man since atmospheric Cd deposition data are lowest in the Scandinavian countries (see **Table 3.180**). The median Cd concentration in Scandinavian lakes is 0.01 µg Cd/L(Skjellkvåle et al., 1999). This value may not be representative for natural Cd in other regions since weathering of natural Cd from minerals may certainly vary between regions. Surface sediments in EU lakes contain 3.6-30-fold higher Cd concentrations than deeper sediments (see below: sediment data). These enrichment factors could be combined with actual Cd concentrations in the lakes to calculate pre-industrial Cd concentrations. An overall view of Cd concentrations in European aquatic systems is provided by the FOREGS Geochemical Baseline Program (FGBP). This program has been initiated to provide high quality environmental geochemical baseline data for Europe. The data presented here are based on samples of stream water collected throughout Europe. High quality and consistency of the obtained data are ensured by using standardised sampling methods and by treating and analysing all samples in the same laboratories. The FGBP is authorised by the directors of the Geological Surveys within FOREGS (Forum of European Geological Surveys) and can be found on the web at http://www.eurogeosurveys.org/foregs/.The cadmium concentration was measured using the ICP-MS method with a DL of 0.002 µg L^{-1}. 807 samples were taken randomly throughout Europe to obtain an overall view of the Cd concentration. The survey yielded a median concentration of 0.01 µg $L^{-1}$and a 90th percentile of 0.10 µg L^{-1}.

We propose a (high) estimate of 0.05 µg L^{-1} as a general natural background Cd in freshwater (dissolved fraction). This value is used as the natural background concentration in the calculation of $PECcontinental_{water}$. A high estimate of the natural background can be considered as a conservative choice because it is added to the calculated concentrations. The choice of this background is, however, not very relevant for local risk characterisation since the PNEC is about 4-fold higher than the natural background. The risk characterisation at regional scale is performed with measured data.

Table 3.185 Measured Cd concentrations in surface water classified per reliability index (RI) taken forward to the risk characterisation. The statistics (90th percentile and average) are the averages of corresponding values of the regional data from Table 3.184 which meet the criteria of reliability*. Datasets with RI=4 were discussed on a case-by-case basis above. Datasets with RI>1 include also data of classes with lower RI index (i.e. cumulative number of data)

RI*	Region	n	90th percentile [µg L^{-1}]	Average [µg L^{-1}]
1	Sweden	8,179	0.0395	0.03
2	Finland	803	0.057	-
	Germany	608	0.07	-
	Norway	985	0.055	-
	Sweden	8,999	0.044	0.03
	The Netherlands	1,825	0.07	0.04
	Greece	39	0.18	0.12
3	Finland	803	0.06	-
	Germany	608	0.07	-
	Greece	39	0.18	0.12
	The Netherlands	1,825	0.07	0.04
	Norway	985	0.06	-
	Sweden	8,999	0.04	0.03
	UK (ECN)	10	0.31	0.14
	UK (WIMS)	6,905	0.15	
4	Belgium	4,272	-	-
	Finland	803	-	-
	France	165	-	-
	Germany	1,295	-	-
	Italy	13	-	-
	The Netherlands	405	-	-
	Norway	985	-	-
	Portugal	1,174	-	-
	Spain	11	-	-
	Sweden	3,353	-	-
	UK(COMMPS)	1,244	-	-

*RI 1 DL<0.1 µg L^{-1}, Cd fractionation: D or ED (D: dissolved Cd; ED: estimated dissolved Cd) and water hardness known;
RI 2 DL<0.1 µg L^{-1}, Cd fractionation: D or ED;
RI 3 DL<0.1 µg L^{-1}, Cd fractionation: D, ED or U (Unknown=assumed dissolved);
RI 4 All data;
N Number of values in the dataset.

An important fraction of total Cd in freshwater is adsorbed on suspended matter. The Cd concentrations in suspended matter typically range between 1 and 10 mg $kg^{-1}{}_{dw}$ (see

Table 3.186). Higher values are typically recorded in the river Maas that carries Zn ore particles. The dissolved fraction Cd ranges 10-40% in the rivers Rhine, Meuse and Schelde (Ros and Slooff, 1990), about 50% in the rivers Rhine and Arno (Breder, 1988) and 30-40% in Tiber and Elbe (Breder 1988). In lake Constance and Zurich, the percentage dissolved Cd is 80 and 84% respectively. High dissolved fractions are found in acid waters, in which total concentrations are also elevated.

The Cd concentrations in EU freshwater generally decrease since the end of the 1970s. Breder (1988) noticed the largest drop in dissolved Cd concentration in the lower course of the Rhine between 1977 and 1984. Ros and Slooff (1990) demonstrated that Cd concentrations in great Dutch rivers (total and dissolved and on suspended matter) decreased 4-fold from 1983 to 1986. Since 1990, the decrease in Cd is generally less pronounced (Milieucompendium, 2001; see also **Annex J**). The total Cd concentration in the Schelde at the border Belgium-Netherlands decreased from 3.5 $\mu g\ L^{-1}$ in 1975 to about 0.4 $\mu g\ L^{-1}$ in 1988 (no further trend).

Seasonal changes in Cd concentrations occur in lakes. Borg (1987) investigated 59 forest lakes in northern Sweden. The Cd concentrations are 2.4 fold higher in winter than in than in summer. During summer, there is higher production of phytoplankton and the higher input of particulate matter from the watershed. Therefore, more metal becomes particle bound and settles to the lake sediment.

A negative correlation between Cd concentrations and pH is observed in Swedish rivers and in lakes. Cadmium concentrations in Swedish surface waters increase from north to south along with acidification and air-born Cd. Different fractions of Cd in five soft water forest lakes with differing pH (average 4.85-6.61) in southern Sweden were measured. Most of the Cd in water was in dialysable form, especially in the more acidic lakes. This Cd form increases with decreasing pH, resulting in increased total Cd levels (Parkman et al., 1998).

Table 3.186 Measured cadmium concentrations in suspended matter

Location	Concentration (mg kg^{-1}dw)	Moment	Year	Source
Germany Danube, Jochenstein	0.41 0.32-0.50	average (n=2) min-max	1998	LAWA database[1]
Germany Danube	0.82	average of 90th percentiles	1998	LAWA database[1, 2]
Germany Elbe, Grauerort	1.81 0.73-5.10	average (n=12) min-max	1998	LAWA database[1]
Germany Elbe	7.11	average of 90 percentiles	1998	LAWA database[1, 2]
Germany Mosel, Koblenz	0.94 0.43-1.34	average (n=13) min-max	1998	LAWA database[1]
Germany Mosel	1.09	average of 90 percentiles	1998	LAWA database[1, 2]
Germany Rhine, Koblenz	0.76 0.39-1.18	average (n=26) min-max	1998	LAWA database[1]
Germany Rhine	0.94	average of 90 percentiles	1998	LAWA database[1, 2]
Germany Weser, Bremen	3.60 1.60-5.00	average (n=14) min-max	1998	LAWA database[1]
Germany Weser	3.65	average of 90th percentiles	1998	LAWA database[1, 2]
France: basin Artoie, Picardie	11.83	average (n=10)	1995-1999	Office International de l'Eau, 1999
France: basin Rhin-Meuse	1.33	average (n=10)	1995-1999	Office International de l'Eau, 1999
France: basin Seine, Normandie	2.56	average (n=10)	1995-1999	Office International de l'Eau, 1999
France: basin Loire, Bretagne	3.73	average (n=10)	1995-1999	Office International de l'Eau, 1999
France: basin Rhône-Méditeranée-Corse	1.09	average (n=10)	1995-1999	Office International de l'Eau, 1999
The Netherlands: Rhine Lobith	6.3 2.3	n.a.	1983 1986	Ros and Slooff, 1990

Table 3.186 continued overleaf

Table 3.186 continued Measured cadmium concentrations in suspended matter

Location	Concentration (mg kg-1dw)	Moment	Year	Source
The Netherlands: Rhine Lobith	3.0 3.5 3.0	n.a.	1988 1989 1990	CCRX, 1991
The Netherlands Rhine Lobith The Netherlands Maas Eysden The Netherlands Westerschelde Schaar van Ouden Doel The Netherlands Nieuwe Waterweg Maassluis The Netherlands Nieuwe Waterweg Haringvlietsluizen The Netherlands IJ 23 The Netherlands NZK KM2	4 34 1 7.5 6.5 2 2.2	90th percentile	1992	CCRX, 1994
The Netherlands: Rhine	7.5	90th percentile	2000	Milieucompendium, 2001
The Netherlands: Maas	19.1	90th percentile	2000	Milieucompendium, 2001
The Netherlands: Schelde	8.1	90th percentile	2000	Milieucompendium, 2001
The Netherlands: Rijkswateren	8.5	90th percentile	2000	Milieucompendium, 2001
The Netherlands: IJsselmeer	1.9	90th percentile	2000	Milieucompendium, 2001
The Netherlands: Maas Eysden	29 11	n.a.	1983 1986	Ros and Slooff, 1990
The Netherlands: Maas Eysden	133 19 32	n.a.	1988 1989 1990	CCRX, 1991
The Netherlands: Schelde Schaar van Ouden Doel	17 9	n.a.	1983 1986	Ros and Slooff, 1990

n.a. Information not available;
1) Source: Joint Water Commission of the Federal Länder (LAWA), Federal Institute of Hydrology, Berlin;
2) The LAWA database contains 2614 measurements of 89 rivers. Data for different measurement points are available for some of these rivers. The 90th percentiles for some of the major rivers are indicated as an example in this table. If 90th percentiles of different measurement points for a river are available, only the average of these 90th percentiles is indicated.

Sediment

The datasets of various European countries are described and discussed below. Data are presented in **Table 3.187**. Older (literature) data are summarised in **Table 3.188**. The averages of percentiles per region are summarised in **Table 3.189**. It should be noted that these measured data in the sediment refer to total cadmium concentrations and are thus not corrected for bioavailability.

A statistical approach was used for defining outliers in an attempt to exclude the contribution of local emission sources from diffuse emission sources. The uncertainty related to either including or excluding outliers will be taken forward to the risk characterisation where the effect of outlier analysis on the risk factors will be compared. In this section, however, percentiles only refer to the database obtained after outlier exclusion. Outliers are selected based on the TGD (EC, 2003) using the equation: $\log(X_i) > \log(P75) + K(\log(P75) - \log(P25))$ where X_i is the concentration above which a measured value may be considered an outlier, Pi is the value of the i^{th} percentile of the statistic and K is a scaling factor. This filtering of data with a scaling factor K = 1.5 is used in most statistical packages, but the factor can be subject dependent. A value of 1.5 was chosen in this report. Outliers are detected by calculating the P75 and P25 statistics on the entire dataset, i.e. not per sampling site. Outlier calculation per sampling site detects measurement errors.

- Belgium

Monitoring data of cadmium concentrations in Flemish sediments (Belgium) were obtained from the Flemish Environment Agency (VMM). Data can also be consulted at the website (http://www.vmm.be). After exclusion of the outliers (8), the dataset contained 512 values of the year 2001. Data range from 0.02 to 7.4 mg $kg^{-1}{}_{dw}$. Data were aggregated to obtain the statistics presented below as not enough data were available to calculate site-specific statistics.

Additional data were extracted from the COMMPS database. 20 values for the year 1995 yield the statistics presented below. The values range from 1.48 to 31.33 mg $kg^{-1}{}_{dw}$. Samples were taken in rivers burdened by a high historical pollution load, however, and the data are therefore not taken forward in this report.

For reference: Plasman and Verreet (1992) report Cd concentrations in the sediment of the Dijle river to range from 0.1 to 3 mg $kg^{-1}{}_{dw}$.

- France

Data were obtained of the Cd concentration of the sediment for the year 2001 from the Réseau National de Donnéés sur l'Eau (RNDE) and can be consulted on the web at http://www.rnde.tm.fr/ . Data were selected for 2 regions: Artois-Picardie (n = 126) and Rhône-Méditerranée (n = 66). For Artois-Picardie it was possible to calculate river-specific statistics. For the Rhône-Méditerranée only the main rivers and tributaries were included in the database. For the latter region, all individual data were used to calculate region-specific statistics.

Additional data were found in the COMMPS database and consist of 123 values for the year 1996 (after excluding the outliers). The measured Cd concentration ranges from 1 to 20 mg $kg^{-1}{}_{dw}$.

For reference, averaged data per basin reported by the Office International de l'Eau are included in the table. In addition Breder (1988) reports values of 2 mountain lakes of Dauphiné to range from 0.15 to 2.5 mg $kg^{-1}{}_{dw}$, which are not incorporated in the risk assessment, however.

- The Netherlands

Monitoring data for the Netherlands were gathered by the Rijkswaterstaat (RWS; executive organisation of the Dutch Ministry of Transport, Public Works and Water Management). The dataset presented here contains 12 values of 12 different points for the measured Cd concentration of sediments for the year 2000. Data are obtained from the "Waterstat" database to be found on http://www.actuelewaterdata.nl/. The reported values range from 0.05 to 4.89 mg $kg^{-1}{}_{dw}$.

Data for the year 1997 were found in the COMMPS database. It contains 6 values with a range of 0.63 to 4.68 mg $kg^{-1}{}_{dw}$ (after excluding one outlier).

For reference: Breder (1988) reports a Cd concentration in the sediment of the Ijsselmeer of 3 mg $kg^{-1}{}_{dw}$ and in the Ketelmeer of 34 mg $kg^{-1}{}_{dw}$. Crommentuijn et al. (1997a) report a background Cd concentration of Dutch sediments of 0.8 mg $kg^{-1}{}_{dw}$. Pearse (1996) reports Cd concentrations in Maas sediments to range from < 0.6 to 15 mg $kg^{-1}{}_{dw}$ for the year 1994.

- Spain

One dataset of 9 values was found for Spain in the COMMPS database. Values represent Cd concentration in the sediment for the year 1997 and range from 0.1 to 17.2 mg $kg^{-1}{}_{dw}$. The highest measurement was rejected however, considered as being an outlier, resulting in a dataset of 8 values with a range of 0.1-0.52 mg $kg^{-1}{}_{dw}$.

- Sweden

Data for the Cd concentration of Swedish sediments was gathered by the Swedish University of Agricultural Sciences (SLU) and can be consulted on the web at http://info1.ma.slu.se/. Data for the years 1998-2000 are presented here. The dataset consists of a total of 297 values measured in 99 distinct locations. As such, it can be considered to represent the entire country. Values range from 0.12 to 7.64 mg $kg^{-1}{}_{dw}$.

For reference: Pearse (1996) reports Cd concentrations in pre-industrial sediments of lake bed deposits to range from 0.3 to 0.6 mg $kg^{-1}{}_{dw}$. Jensen and Bro-Rasmussen (1992) report for northern Sweden background Cd concentrations in lake sediments of 0.1 to 0.4 mg $kg^{-1}{}_{dw}$ and Cd concentrations in the upper cm of the lake sediments to range from 0.1 to 2 mg $kg^{-1}{}_{dw}$. Parkman et al. (1998) reports Cd concentrations in the surface sediment of forest lakes in south-west Sweden to range from 1 to 6 mg $kg^{-1}{}_{dw}$ in the year 1977 and in central and northern Sweden to range from 0.4 to 2.4 mg $kg^{-1}{}_{dw}$ in the year 1979.

Table 3.187 Measured Cd concentrations in sediments. Underlined data are used for risk characterisation. All values are expressed as total Cd concentrations and thus not corrected for bioavailability

Location (source)	Sampling period	n	Range [mg $kg^{-1}{}_{dw}$]	90th percentile [mg $kg^{-1}{}_{dw}$]	50th percentile [mg $kg^{-1}{}_{dw}$]	10th percentile [mg $kg^{-1}{}_{dw}$]	Average [mg $kg^{-1}{}_{dw}$]	Statistics[1]
Belgium								
Flanders (VMM)	2001	512	0.02 – 7.4	1.59	0.27	0.03	0.68	**
Belgium (COMMPS)	1995	20	1.48 – 31.33	14.83	7.89	2.88	8.58	**
France								
AA-delta (Artois-Picardie) (RNDE)	2001	13	0.1 - 6.1	4.66	1	0.54	1.78	**
Boulonnais (Artois-Picardie) (RNDE)	2001	4	0.2 - 0.4	0.34	0.2	0.2	0.25	**
Bresle (Artois-Picardie) (RNDE)	2001	2	0.2 – 0.5	0.47	0.35	0.23	0.35	**
Canche (Artois-Picardie) (RNDE)	2001	7	0.1 – 1.1	0.68	0.2	0.1	0.34	**
Deule (Artois-Picardie) (RNDE)	2001	14	0.8 – 7.8	7.74	2.9	0.86	3.91	**
Lys (Artois-Picardie) (RNDE)	2001	13	0.2 – 0.9	0.9	0.5	0.2	0.55	**
Samber (Artois-Picardie) (RNDE)	2001	13	0.3 – 1.2	0.8	0.4	0.3	0.53	**
Scarpe (Artois-Picardie) (RNDE)	2001	15	0.4 – 9.7	3.84	1.8	0.42	2.4	**

Table 3.187 continued overleaf

Table 3.187 continued Measured Cd concentrations in sediments. Underlined data are used for risk characterisation. All values are expressed as total Cd concentrations and thus not corrected for bioavailability

Location (source)	Sampling period	n	Range [mg kg^{-1}_{dw}]	90^{th} percentile [mg kg^{-1}_{dw}]	50^{th} percentile [mg kg^{-1}_{dw}]	10^{th} percentile [mg kg^{-1}_{dw}]	Average [mg kg^{-1}_{dw}]	Statistics[1]
France								
Scheldt (Artois-Picardie) (RNDE)	2001	20	0.2 – 12	1.41	0.35	0.29	1.15	**
Somme (Artois-Picardie) (RNDE)	2001	23	0.2 – 4.3	1.32	0.4	0.2	0.71	**
Yser (Artois-Picardie) (RNDE)	2001	2	0.3 – 0.4	0.39	0.35	0.31	0.35	**
Artois-Picardie (RNDE)	2001	126	0.1 - 12	2.05	0.77	0.35	1.12	**
Rhône-Méditerranée (RNDE)	2001	66	0.01 – 4.2	0.93	0.12	0.01	0.37	**
France (COMMPS)	1996	123	1 - 20	5.6	2	1	2.91	**
Rhine-Meuse (Office International de l'eau)	1995-1999	135	-	-	-	-	1.23	**
Seine, Normandie (Office International de l'eau)	1995-1996	260	-	-	-	-	2.16	**
Loire, Bretagne (Office International de l'eau)	1995-1996	97	-	-	-	-	8.32	**
Adour, Garonne (Office International de l'eau)	1995-1996	365	-	-	-	-	2.38	**
Rhone-Méditerrannée-Corse (Office International de l'eau)	1995-1996	431	-	-	-	-	1.55	**

Table 3.187 continued overleaf

Table 3.187 continued Measured Cd concentrations in sediments. Underlined data are used for risk characterisation. All values are expressed as total Cd concentrations and thus not corrected for bioavailability

Location (source)	Sampling period	n	Range [mg kg^{-1}_{dw}]	90th percentile [mg kg^{-1}_{dw}]	50th percentile [mg kg^{-1}_{dw}]	10th percentile [mg kg^{-1}_{dw}]	Average [mg kg^{-1}_{dw}]	Statistics[1]
The Netherlands								
The Netherlands (RWS)	2000	12	0.05 – 4.89	3.75	1.49	0.08	1.92	**
The Netherlands (COMMPS)	1997	6	0.63 – 4.68	3.63	1.74	0.83	2.07	**
Spain								
Spain (COMMPS)	1997	8	0.1 – 6.13	2.20	0.34	0.18	1.05	**
Sweden								
Sweden (SLU)	1998-2000	297	0.12 –7.64	2.97	1.07	0.3848	1.4168956	**

1) Statistics;

** The statistics are the Xth percentile of the entire dataset.

Table 3.188 Literature data on the Cd concentrations in European sediments. All values are expressed as total Cd concentrations and thus not corrected for bioavailability

Location	Concentration $[mg\ kg^{-1}{}_{dw}]$	Moment	Year	Source
Germany: 12 lakes in southern Bavaria	0.4-5.9	max		Breder, 1988
Germany: 12 lakes in southern Bavaria	0.1-0.95	min		Breder, 1988
Lower and middle Rhine(*)	12.8, 16.1, 5.1		1972, 1979, 1985	Jensen and Bro-Rasmussen, 1992
European rivers: the lower Rhine	11.8	max		KEMI, 1997
Upper Rhine(*)	5.3, 3.1, 2.1		1972, 1979, 1985	Jensen and Bro-Rasmussen, 1992
Elbe(*)	17, 11.8		1972, 1985	Jensen and Bro-Rasmussen, 1992
Danube(*)	19.8, 2.1		1972, 1985	Jensen and Bro-Rasmussen, 1992
Weser(*)	13.6, 2.6		1972, 1985	Jensen and Bro-Rasmussen, 1992
Ems(*)	10.4, 1.7		1972, 1985	Jensen and Bro-Rasmussen, 1992
Main(*)	12, 3.9		1972, 1985	Jensen and Bro-Rasmussen, 1992
Neckar(*)	37.3, 11.9, 2.4		1972, 1979, 1985	Jensen and Bro-Rasmussen, 1992
N-Italy: lake Como	1.1			Breder, 1998
N-Italy: lake Maggiore	0.25-2.5			Breder, 1998
Italy: rivers, natural background	0.2-0.3			Breder, 1998
Italy: rivers, surface sediment	0.6-1.8			Breder, 1998
Lake Zürich, background	0.2			Breder, 1988
Lake Zürich, surface	6			Breder, 1988

The ambient Cd concentration in surface sediments away from point sources ranges between 0.1-34 mg Cd/kg_{dw} with most values in the 1-10 mg Cd/kg_{dw} range (0.38-3.8 mg Cd/kg_{ww}). All data from **Table 3.187** are taken forward to the risk characterisation and are summarised in **Table 3.189**. Countries from northern, western and southern Europe are included and as such a general view of the ambient Cd concentration in European sediments is obtained. The total average Cd concentration of European sediments is 1.32 mg Cd/kg_{dw}. 10% of the sediments contain Cd concentrations exceeding 2.66 mg $kg^{-1}{}_{dw}$.

Table 3.189 Measured Cd concentrations in sediments taken forward to the risk characterisation. The statistics (90th percentile and average) are the averages of corresponding values of the regional data from Table 3.187. All values are expressed as total Cd concentrations and thus not corrected for bioavailability

PEC regional	n	90th percentile [mg $kg^{-1}{}_{dw}$]	Average [mg $kg^{-1}{}_{dw}$]
Flanders	512	1.59	0.68
France	315	2.86	1.47
The Netherlands	18	3.69	2.00
Spain	8	2.20	1.05
Sweden	297	2.97	1.42

The average of 90th percentiles of measured Cd concentrations in various countries is 2.66 mg $kg^{-1}{}_{dw}$. This value represents a realistic worst case for the EU ambient Cd concentrations in sediment (natural Cd + historical Cd) and is used as the PECregional in the risk characterisation. The modelled PEC values for sediment are calculated from regional emission to sediments and a background concentration that is typical for EU (i.e. no realistic worst case). That typical ambient background concentration away from point sources is derived here as the median of the averages reported in **Table 3.189** and **Table 3.188** to encompass more countries. The resultant typical ambient background sediment Cd concentration is 2 mg Cd/kg_{dw} (= 0.77 mg Cd/kg_{ww}). This value is used in **Table 3.157** to calculate modelled PEC values.

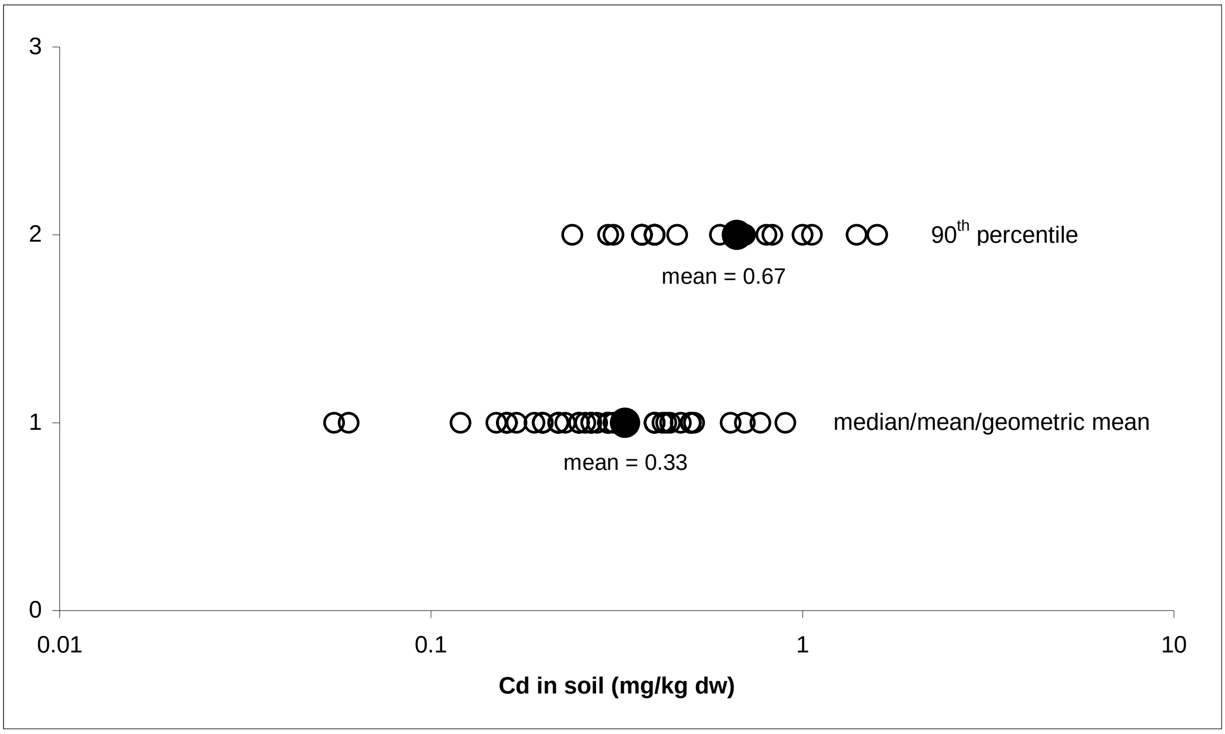
The Cd concentrations in the deeper layers of sediments in lakes range between 0.1-0.8 mg $kg^{-1}{}_{dw}$ (0.04-0.3 mg Cd/kg_{ww}). These concentrations may be representative for natural background. In lakes in SW Sweden concentrations in pre-industrial sediment layers, below 20 cm depth, are 0.3-0.6 mg $kg^{-1}{}_{dw}$ and 0.1-0.4 in middle and northern Sweden (Johansson, 1989 cited in KEMI, 1997). A generalised background concentration of 0.4 mg $kg^{-1}{}_{dw}$ was therefore proposed for Swedish lake sediments (Pearse, 1996). Surface sediments (0 - 20 cm) are enriched with Cd compared to deeper layers. Results from Swedish lakes show a gradient significantly decreasing from south to north and an enrichment factor of about 7, referring to the background in southern areas of Sweden. The enrichment factor in Lake Zurich is 30 (Breder, 1988). Concentrations in river sediments show a 3-6 fold enrichment compared with background concentrations in Italian rivers (Breder, 1988). However, in many non-polluted lakes of northern Europe a decrease in Cd concentration of surface sediments is found compared to concentrations in deeper sediment layers deposited during less acidic conditions. Borg et al. (1989) found Cd in the sediment to decrease at pH below 5. Decreasing pH values in the sediment pore water may also cause leakage of Cd from the sediments to the water phase. In acid forest lakes, Johansson (1980) found lower Cd concentrations in surface sediments (0-1cm) compared to in subsurface layers (1-3cm). Furthermore he found that the fixation of Cd to sediment decreased at pH < 5, increasing the residence time for Cd in the water phase.

In general, Cd concentrations of surface sediments show downward trends. Breder (1988) demonstrated for the river Rhine a decrease from 1977 to 1983 from 38.6 mg kg^{-1}_{dw} to 21.9 mg kg^{-1}_{dw} at the most contaminated site. At other locations of the river Rhine, a 2- to 5-fold decrease was recorded.

Terrestrial compartment

Measured Cd concentrations in soil are presented in **Table 3.190**. Little data were found for southern European countries[51]. The soil Cd concentrations in areas away from point sources range between 0.05 and 14 mg kg^{-1}_{dw} and most concentrations are found in the 0.1-1.8 mg kg^{-1}_{dw} range. **Figure 3.13** illustrates the concentration ranges that are listed in the **Table 3.190**.

Figure 3.13 Measured concentrations of Cd in soils in Europe. Points are averages, medians or geometric means (of min-max) or 90th percentiles of all European surveys listed in Table 3.190. Full points are the means of corresponding ranges. Observations near point sources and industrial activities are excluded and only the most recent data are included when data were reported for various periods



The data from **Table 3.190** can be subdivided in different regions as a tool for the risk characterisation. Regional ambient Cd concentrations can be derived for the different countries/regions according to two different methodologies:

- method 1: ambient Cd concentration = 90th percentile of all data from a single country/region (TGD, 1996);
- method 2: ambient Cd concentration = average of the 90th percentiles that have been derived for the different sites within the region of interest (TGD, revised 2002)

[51] For Spain measured data (*LÓPEZ ARIAS, M. & GRAU CORBÍ, J.M., 2004*) were submitted in May 2005 and thus well beyond the agreed deadline for new data submission to be incorporated within the RAR following the CSTEE opinion.

However, it is difficult to combine the data of all soils within a country because of the large differences between soils (e.g. sandy versus clay soils). Ideally, averages of 90^{th} percentiles should be calculated per soil type within a country or region.

An attempt was made to average the 90^{th} percentiles of German sand, löss and clay soils. The data were identified (wherever possible), selected and compiled from the data set "Hintergrundwerte für anorganische und organische Stoffe in Böden" (LABO, 1998). In this selection only the data related to the for this risk assessment most relevant 'soil-use' and 'soil-exposure' categories i.e. the data of the so-called 'Type 0' ("ohne Gebietsdifferenzierung") and 'Type II' ("verdichtete Raume") are included:

- average P90 for sandy soils: 0.56 mg kg^{-1}_{dw}
- average P90 for löss (loamy) soils: 0.67 mg kg^{-1}_{dw}
- average P90 for clay soils: 0.89 mg kg^{-1}_{dw}

All data from **Table 3.191** are taken forward to the risk characterisation as is presented in **Table 3.251**. Reported P90 values are averaged per country as a surrogate for region. No attempt was made to differ between soil classes. 10% of the soils contain Cd concentrations exceeding 0.86 mg kg^{-1}. Recent data for Spain are reported (Ministerio de medio ambiente, 2005) but could not be taken into account in this assessment.

A typical average Cd concentration (ambient Cd concentration) in soils located away from point sources is 0.30 mg kg^{-1}_{dw} (0.26 mg kg^{-1}_{ww}). This concentration is close to the average soil Cd concentrations of the different surveys. This concentration is used as the ambient background concentration that is included in the PEC_{soil}. The Cd concentration in the soil depends on the parent material of the soil, the localisation and the land use. Districts associated with Cambrian bedrock, have enhanced Cd concentrations in the soils. Shales and sandstone are important components of the Cambrian formation and have generally high Cd concentrations. Marine clays in western Sweden and the coarser textured sediments in the middle of Sweden generally have lower-than-average contents (KEMI, 1998). Little information is available to estimate the natural background of Cd. The archived soil collection of Rothamsted shows that soil Cd has increased about 0.1-0.2 mg Cd/kg between about 1850 and 1980 (Jones et al., 1987, see **Table 3.190**). A more detailed analysis of this trend is described in Section 4 (see the human health part of this Risk Assessment Report, in separate document).

Influence of atmospheric deposition in areas around industrial point sources is well demonstrated in the Shipman area in the UK. Shipman was the centre of Zn mining from the middle of the 17^{t}h until the middle of the 19th century. Very high Cd concentrations have been found in these soils. Atmospheric deposition is the dominant source of cadmium in forest soils (Pearse, 1996). In Sweden, concentrations of Cd in the mor layer (the top layer of podzolic soils, 5-8 cm thick, rich in organic matter) of forest soils increased threefold since the pre-industrial era (Pearse, 1996). The mor layer absorbs heavy metals very effectively, and metal concentrations reflect the historical deposition over many decades (Pearse, 1996). The enrichment factor decreases to the north, but even in the northern-most part of Sweden the soil content is somewhat affected by long-range atmospheric transport and deposition of Cd. The concentrations showed a large-scale pattern with the highest values in the south of Sweden and decreasing concentrations towards the north. Regional average Cd concentrations in the mor layer ranged from 1 mg kg^{-1}_{dw} in the south to 0.4 mg kg^{-1}_{dw} in the north. About 2 mg kg^{-1} has been measured in surface layers (0-20 cm) of peatlands (Hellstrand and Landner, 1998). Locally enhanced Cd concentrations in forest soils are attributed to larger point sources, such as the Rönnskär smelters. The concentrations in the mor layer are > 5 mg kg^{-1}, within a distance of 15 km from the Rönnskär smelter (Hellstrand and

Landner, 1998). There are indications of enriched concentrations also in the B-horizon of the soils (15-25 cm below surface), in southern Sweden (Hellstrand and Landner, 1998). Recent data indicate that Cd concentrations in the mor layer of Swedish forest soils are presently decreasing in most areas. In northern Sweden, decreasing concentrations in the mor layer are probably a result of the decreasing atmospheric deposition. In southern Sweden, acidification has caused increased leakage rates of Cd from soil surface layers which, together with decreased deposition, result in net outflow of Cd from the mor layers. This indicates that Cd is leaching from surface soils to deeper soil layers, and finally to the runoff water (Hellstrand and Landner, 1998).

Table 3.190 Measured total cadmium concentrations in soils

Location	Concentration (mg kg^{-1}dw)	Moment	Year	Source
Natural soils				
Sweden: concentration in forest mor layer	0.35	5th percentiles		Pearse, 1996
	0.64	50th percentiles		
	1.27	95th percentiles		
Netherlands: natural areas	0.05 - 1.8			Ros and Slooff, 1990
Germany: Niedersachsen (country area)				LABO, 1994
sandy soils	0.16	median (n=3379)		
	0.24	90th percentile		
loamy soils	0.19	median (n=1833)		
	0.30	90th percentile		
Germany: forest soil on sand	< 0.3	Median (n=164)		Hindel et al., 1997; LABO, 1998
	0.7	90th percentile		
Germany: forest soil on sandloam	< 0.3	Median (n=20)		Hindel et al., 1997; LABO, 1998
	0.4	90th percentile		
Agricultural soils				
Sweden: background concentration in agricultural soil	0.15			SEPA, 1987
Swedish agricultural soil	0.26	average		Pearse, 1996
	0.22	median		
	0.11-0.49	5 -95th percentiles		
Finland: normal agricultural topsoil	0.06	average		KEMI, 1997
Finland agricultural soil	0.2	average		Pearse, 1996

Table 3.190 continue overleaf

Table 3.190 continued Measured total cadmium concentrations in soils

Location	Concentration (mg kg^{-1}dw)	Moment	Year	Source
Agricultural soils				
Denmark: arable soil	0.22	median	1966	Tjell and Hovmand, 1978
	0.25	average (n=44)		
UK: Rothamsted	0.51-0.77	averages	1846-1980	Jones et al., 1987
agricultural soils	0.33-0.43		1881-1983	
	0.27-0.42		1882-1982	
	0.37-0.47		1870-1983	
soils under permanent grassland	0.19-0.27		1876-1984	
The Netherlands: agricultural soils	< 0.1 - 1.6			Pearse, 1996
The Netherlands: agricultural soils	0.30 - 0.87			Ros and Slooff, 1990
The Netherlands: arable soils	0.5	average (n=708)		Wiersma et al., 1986
	0.4	median		
	0.04-14	min-max		
Belgium: agricultural soils in Flanders			1994-1995	De Temmerman et al., 2000
sandy soil	0.25	median (n=222)		
	0.37	90th percentile		
sandy loam soil	0.3	median (n=270)		
	0.4	90th percentile		
loam soil	0.32	median (n=120)		
	0.46	90th percentile		
clay soil	0.27	median (n=19)		
	0.31	90th percentile		

Table 3.190 continue overleaf

Table 3.190 continued Measured total cadmium concentrations in soils

Location	Concentration (mg kg^{-1}dw)	Moment	Year	Source
Agricultural soils				
France: plough layer of agricultural soils	0.01	min	1995-1999	Baize, 1999
	0.30	median		
	0.39	average (n=10634)		
	0.69	90th percentile		
France: cultivated soils	0.02	min	1995-1999	Baize, 1999
	0.25	median		
	0.41	average (n=1063)		
	0.80	90th percentile		
France: all soils (surface and deep soils, agricultural and forest)	< 0.02	min	1995-1999	Baize, 1999
	0.16	average (n=768)		
	0.46	median		
	1.06	90th percentile		
Germany: agricultural soil on sand	< 0.3	median		Hindel et al., 1997; LABO, 1998
	0.6	90th percentile		
Germany: agricultural soil on loam	< 0.3	median		Hindel et al., 1997; LABO, 1998
	0.7	90th percentile		
Germany: agricultural soil on sandloam	< 0.3	median		Hindel et al., 1997; LABO, 1998
	0.7	90th percentile		
Germany: agricultural soils (Südoldenburg)	0.31	median (n=269)		Leinweber, 1996
	1.59	90th percentile		

Table 3.190 continue overleaf

Table 3.190 continued Measured total cadmium concentrations in soils

Location	Concentration ($mg\ kg^{-1}dw$)	Moment	Year	Source
Soils near point sources				
UK: Shipman (n=329)	97	average		Jensen and Bro-Rasmussen, 1992
	2 - 360	range		
Germany: Hamburg region	1.2	average		Lux et al., 1988
	< 0.1-27.8	min-max		
The Netherlands: organic matter layer of forest soils and borders of highway	1.13-4.91			CCRX, 1994
The Netherlands; subsoil of forest soils and borders of highway	< 0.35			
Unknown land use				
Sweden	0.22	average		Jensen and Bro-Rasmussen, 1992
	0.03-2.3	min-max		
N-Sweden: top soils	0.17-0.28	averages		KEMI, 1998
S-Sweden: top soils	0.23-0.31	averages		KEMI, 1998
Middle of-Sweden: top soils	0.22-0.28	averages		KEMI, 1998
Sweden (north, south and middle), top soils	0.26	average		KEMI, 1998
	0.40	90^{th} percentile		
Denmark	0.17	average		Jensen and Bro-Rasmussen, 1992
	0.11-0.32	min-max		
The Netherlands	0.4	average		Jensen and Bro-Rasmussen, 1992
The Netherlands: background concentrations	0.01 - 0.3			Ros and Slooff, 1990

Table 3.190 continue overleaf

Table 3.190 continued Measured total cadmium concentrations in soils

Location	Concentration (mg kg^{-1}dw)	Moment	Year	Source
Unknown land use				
The Netherlands: calculated background conc. for a standard soil with 10% OM and 25% clay.	0.8			Crommentuijn et al., 1997a
The Netherlands: Kempen (0 - 25 cm)	0.3 - 2.7			Ros and Slooff, 1990
The Netherlands: Kempen (0 - 2 cm)	0.2 - 100			Ros and Slooff, 1990
The Netherlands:				Van Driel and Smilde (1982)
clay soils	0.5	average (n=248)		
sandy soils	0.3	average (n=63)		
Belgium	0.28	average		Jensen and Bro-Rasmussen, 1992
Belgium: background concentration in Flanders	0.5	average (n=470)		Cornelis et al., 1993
	0.4-1.0	25-75th percentile		
	1.0	90th percentile		
France	0.2	average		Jensen and Bro-Rasmussen, 1992
UK	0.5	average		Jensen and Bro-Rasmussen, 1992
UK (England and Wales)	0.2, 0.7, 1.4	10,50,90th percentiles		McGrath and Loveland, 1992.
UK	0.49	mean	2000	Black et al., 2002
	0.3	median		
	11.2	max		
UK	0.44	mean		Ross et al. (draft)
	0.29	median		
	2.39	max		
Germany	0.3	average		Jensen and Bro-Rasmussen, 1992

Table 3.190 continue overleaf

Table 3.190 continued Measured total cadmium concentrations in soils

Location	Concentration (mg kg^{-1} dw)	Moment	Year	Source
Unknown land use				
Germany	0.44	average		Crössman and Wüstermann, 1992
Germany: Hessen	0.12 0.1-2.4	average min-max		Jensen and Bro-Rasmussen, 1992
Sweden, top soil (0-20 cm)	0.23 0.37	average (n=3067) 90th percentile		Eriksson et al., 1997
The Netherlands: top soil, all land uses (n=4094)	0.3 0.83	50th percentile 90th percentile	1993-1998	Brus et al., 2002

Table 3.191 Measured Cd concentrations in soils taken forward to the risk characterisation. The statistics (90th percentile) are the averages of corresponding values of the regional data from Table 3.190

Location	90th percentile [µg kg-1]
Belgium	0.51
France	0.85
Germany	0.65
Sweden	0.39
The Netherlands	0.83
The United Kingdom	1.40

Atmospheric compartment

Important sources of Cd in the atmosphere are natural sources, industrial point sources and the combustion of fuel and coal. Atmospheric Cd concentrations measured in various sites in the EU, are shown in **Table 3.192**.

The air Cd concentrations in remote areas are about 0.1 ng m^{-3}. Such values are found in northern Norway in 1978 and in southern Norway in 1985 (Jensen and Bro-Rasmussen, 1992). Recent levels in European rural areas vary from 0.1 to 0.5 ng m^{-3}, averaging 0.5 ng m^{-3} in Germany and the Netherlands. The natural background of Cd in air (pre-industrial background) is most likely lower than the ranges now found in rural areas. The estimated emission of Cd due to natural processes is 15 tonnes y^{-1} (sea spray, Mount Etna, forest fires, RL, 1990) whereas the current anthropogenic emissions are 126 tonnes y^{-1}. Therefore, natural background of Cd in air is probably 10 fold lower than the 0.1-0.5 ng m^{-3} range of rural areas. Because air Cd concentrations below 0.1 ng m^{-3} are hardly detectable and have no meaning in terms of risk, we choose to select a zero Cd concentration as the natural background.

Dutch measurements in 1982/83 demonstrate a decrease in the concentrations from south to north caused by Belgian emissions. A Norwegian study demonstrated, that the long-range Cd transport from Western Europe has decreased from 1978/79 to 1985, whereas transport from eastern Europe has not changed. In Germany, the mean concentration of Cd in the air decreased between 1979 and 1994 from 0.97 ng m^{-3} to 0.22 ng m^{-3} (Bieber, 1995) because of a decreasing content of total dust as well as a decreasing Cd content in dust. In The Netherlands, average concentrations ranged from 0.7 - 2 ng m^{-3} (Ros and Slooff, 1990). The Cd concentrations decreased from south to north. Since 1990, the average Cd concentration in The Netherlands decreased from 0.5 to 0.2 ng m^{-3} in 2000 (Milieucompendium, 2001). In general, no large differences are measured between industrial areas and rural area, but higher values are recorded around metal-processing industries. The air Cd in Belgium is generally higher than in other countries. This may reflect resuspension of historic polluted particles although it is possible that the detection limit is higher than 1 ng m^{-3} (no data were reported below 10 ng m^{-3}). More details on recent time trends in air Cd are given in Section 4 (see the human health part of this Risk Assessment Report, in separate document).

More recent measured cadmium concentrations in air for the Belgian region, Flanders, can be found in VMM (2004). Air monitoring data of remote/rural areas for EU-countries for more recent years (till 2003) are reported in EMEP (2004).

Table 3.192 Measured cadmium concentrations in air

Location	Cd concentration (ng m^{-3})	Moment	Year	Source
Sweden background concentrations	0.1			SEPA, 1987
N-Norway	0.1		1978	Jensen and Bro-Rasmussen, 1992
S-Norway	0.3		1978/1979	Jensen and Bro-Rasmussen, 1992
S-Norway	0.1		1985	Jensen and Bro-Rasmussen, 1992
The Netherlands: Witteveen	5			Hutton, 1982
The Netherlands: background concentrations	3-6			Ros and Slooff, 1990
The Netherlands: Rekken: background area	1, 4, 11	50,75,98th percentiles		Ros and Slooff, 1990
The Netherlands: 17 locations	1 - 11	average	1981-1983	Ros and Slooff, 1990
The Netherlands: 17 locations	1 - 10	50th percentile	1981-1983	Ros and Slooff, 1990
The Netherlands: 17 locations	4 - 21	95th percentile	1981-1983	Ros and Slooff, 1990
The Netherlands: 17 locations	5 - 59	98th percentile	1981-1983	Ros and Slooff, 1990
The Netherlands: 17 locations	10 - 73	max	1981-1983	Ros and Slooff, 1990
The Netherlands: 5 locations	0.71 - 1.27	min	1982-1983	Ros and Slooff, 1990
The Netherlands: 5 locations	2.9 - 11.6	max	1982-1983	Ros and Slooff, 1990
The Netherlands	0.5		1982-83	Jensen and Bro-Rasmussen, 1992
The Netherlands: 4 locations	1.1	average	1982-1983	CCRX, 1994
	0.71		1992	
	1.3		1982-1983	
	0.71		1992	
	1.7		1982-1983	
	0.53		1992	
	0.35		1992	

Table 3.192 continued overleaf

Table 3.192 continued Measured cadmium concentrations in air

Location	Cd concentration (ng m-³)	Moment	Year	Source
Belgium: Botrange	4 - 6	average	1972 - 77	Hutton, 1982
Belgium, 1984/88	< 10			Jensen and Bro-Rasmussen, 1992
Belgium: rural areas	10		1985-1995	VMM, 1997
Western Germany (5 sampling sites)	0.97 0.22		1979 1994	Bieber, 1995
Germany, Corviglia	2.1			Hutton, 1982
Germany	1 - 0.4		1979-1987	Jensen and Bro-Rasmussen, 1992
The Netherlands	0.5-0.2	n.a.	1990-2000	Milieucompendium, 2001
UK: 7 rural sites	1 - 2.7	average		Hutton, 1982
UK, Wales	0.4 - 0.1		1984-1987	Jensen and Bro-Rasmussen, 1992
France, Corsica	0.66		1986	Jensen and Bro-Rasmussen, 1992
Mediterranean Sea	0.36		1984	Jensen and Bro-Rasmussen, 1992
Central Europe: rural areas	0.1 - 0.8		late 1980s	KEMI, 1997
EU: annual, rural	0.1-4			OECD, 1994
EU: rural annual mean	< 1 - 5			KEMI, 1997
Near point sources				
Belgium: area around non-ferro plants	10, 27, 50		1992-1993	Ecolas, 1995
Belgium: area around non-ferro plants	10, 57, 120		1993-1994	Ecolas, 1995
Belgium: urban areas	10-20		1985-1995	VMM, 1997
Belgium: non-ferro industrial areas	10-100		1985-1995	VMM, 1997
Belgium: ferro industrial areas	10-20		1985-1995	VMM, 1997
Belgium: other industrial areas	10-20		1985-1995	VMM, 1997

Table 3.192 continued overleaf

Table 3.192 continued Measured cadmium concentrations in air

Location	Cd concentration (ng m^{-3})	Moment	Year	Source
Near point sources				
at the edge of a lead smelter in Belgium	60	max		OECD, 1994
at the edge of a lead smelter in Germany	29			
EU: annual, urban areas	2-150			OECD, 1994
EU: urban annual mean	5 - 15			KEMI, 1997
EU: industrial annual mean	15 -50			KEMI, 1997

3.1.3.4.4 Comparison of measured and calculated data

Table 3.193 summarises the typical regional Cd concentration in surface water, sediments, soils and air and shows regional and continental PEC's in these various compartments.

Both calculated regional and continental PEC's of freshwater are found in the typical range of measured Cd concentrations. The calculated regional PEC is close to the 90th percentile of Cd concentration in the dissolved fraction.

The modelled regional PEC's of the sediment are about 8 fold higher than the average Cd concentrations although the continental PEC is still in the typical range. Regional and continental PEC's are calculated for 'steady state' conditions with EUSES for the sediment. Steady state conditions in the environment can only be achieved after a very long period, presumably several centuries (see Section 3.1.3.4.1). Regional sediment Cd concentrations may exceed actual ambient concentrations because the indirect input via runoff from soil with steady state Cd concentrations is much larger than the actual input via runoff. The regional steady state soil Cd concentrations (EUSES predictions) were 4-5 fold above ambient soil Cd concentrations (see Section 3.1.3.4.1). Regional PEC's can also be above the typical Cd concentrations because of the assumption that only 1% of the total EU sediment volume collects Cd from 10% of the EU Cd releases into surface water.

The PEC's of soil, calculated with the alternative model, is close to the measured Cd concentrations. This correspondence is related to the fact that the model II predicts on average only 14% change in soil Cd in 60 years with current Cd emissions.

Air Cd is remarkably well predicted. Typical Cd concentrations in air are, however, only valid for rural areas.

Table 3.193 Typical measured regional Cd concentrations in the environment (away from point sources and remote areas = ambient Cd concentrations) and the regional and continental predicted environmental concentrations (PEC's). The measured concentrations and natural background are derived from compilations given in **Tables 3.184-3.192** as discussed in the previous section. PEC's are derived from **Table 3.157**.

Table 3.193 Typical measured regional Cd concentrations in the environment (away from point sources and remote areas = ambient Cd concentrations) and the regional and continental predicted environmental concentrations (PEC's). The measured concentrations and natural background are derived from compilations given in Tables 3.184-3.192 as discussed in the previous section. PEC's are derived from Table 3.157

Compartment	Measured Cd		Natural background	PECcontinental	PECregional
	Typical range	Average concentration (90th percentile)			
freshwater µg L^{-1} (dissolved fraction)	0.02-0.27	0.12$^{\$}$	<0.05	0.06	0.11
aq. sediment mg kg^{-1}_{ww}	0.38-3.8	0.51 (1.01)	0.04-0.3	1.25	3.88
aq. sediment mg kg^{-1}_{dw}	1-10	1.3 (2.6)	0.1-0.8	3.2	10
soil mg kg^{-1}_{ww}	0.1-1.6	0.26	unknown	0.28-0.44	0.36
soil mg kg^{-1}_{dw}	0.11-1.81	0.29		0.32-0.50	0.41
air ng Cd m^{-3}	0.1-0.5	~0.5	~0	0.15	0.55

$ Average of regionally averaged P90 values.

3.2 EFFECTS ASSESSMENT

3.2.1 Methods and definitions

3.2.1.1 Data quality

A wealth of information is available on the ecotoxicity of Cd. The data quality of that information varies between source documents. Not all source documents provide complete background information of the toxicity test. A Reliability Index (RI, score 1-4) was given to each test result based on a number of quality criteria. These criteria are described in the introduction of the sections on the terrestrial and aquatic compartments. In this way, the risk assessments can be made for various levels of data quality.

Not all data that were incorporated in the tables, have been used in the effect assessment (e.g. derivation of the Predicted No Effect Concentrations – PNEC's). A first selection was made based on the RI values of the test results. Secondly, some test results were not taken into account to avoid overrepresentation of similar data. As an example, some tests provide data at different exposure times. In these conditions, only the data at the highest exposure time were selected. If various endpoints are derived from one test (i.e. reproduction, growth and mortality), only the most sensitive endpoint was included. Similar toxicity tests are reported in different source documents (i.e. using the same organism, endpoint, soil or water and test conditions). For these cases, the lowest value is selected or a geometric mean value is calculated. All data selected for the effects assessment (PNEC calculation and summarising graphs and tables) are underlined in the tables presenting toxicity data.

3.2.1.2 Definitions of critical concentrations

A number of critical concentrations are derived from the dose response relationship of each test result. Based on guidelines of the TGD (TGD 1996, part II, p. 327), these concentrations are defined as:

No Observed Effect Concentration - NOEC. In order of preference, the NOEC is derived as:

- *Category 1*: the NOEC is the highest tested concentration at which the endpoint is not significantly different from the control treatment at the 5% level of significance, or at which the endpoint shows ≤ 10% significant adverse effect.
- *Category 2*: if the test shows a significant toxic effect at the lowest concentration tested, the NOEC is defined as LOEC/2 if the inhibition is ≤ 20%.
- The statistical analysis in the source document is used to identify NOEC's of category 1 and 2.
- *Category 3*: if no statistics are provided in the source document, the NOEC is determined as the highest concentration at which inhibition is ≤ 10%.
- *Category 4*: if no statistics are provided in the source document and there is more than 10% inhibition at the lowest tested concentration, the NOEC is determined as half the highest concentration at which the inhibition is > 10% but ≤ 20%.

There has to be a concentration-effect relationship to derive a NOEC, i.e. no NOEC is defined if the test does not show a toxic effect up to the highest concentration tested. If the % inhibition is > 20% at the lowest tested concentration, no NOEC can be derived.

Category 5: the NOEC is defined as the EC_{10}, the concentration at which 10% inhibition is found, as given in the source document. This value is often found by intra- or extrapolation.

Lowest Observed Effect Concentration (LOEC), the lowest tested concentration at which > 10% inhibition is found. The toxic effect must be statistically significant at the 5% level. The statistical analysis in the source document is used to find that concentration. If no statistics are provided in the source document but if there is a dose-effect relationship, the LOEC value is derived as the lowest concentration at which the inhibition is > 20% but ≤ 30%. In some exceptional cases, an insignificant toxic effect (or, when no statistics are provided, ≤ 20% inhibition) can be found at concentrations higher than the LOEC as defined above. In these cases, LOEC's are re-defined as the lowest concentration at which and above which significant toxicity (or, when no statistics were provided, > 20% inhibition) is found.

Along with the LOEC value, the % effect (inhibition) relative to the control is given. If the LOEC is found at the lowest concentration tested, this is given in the table (LT). Along the same lines, NOEC values found at the highest concentration tested (HT) are indicated. NOEC or LOEC data have not been included if they were found by extrapolation outside the test range, i.e. below the lowest or above the highest Cd application rate.

The $EC_{x \geq 50}$ ($LC_{x \geq 50}$) is the concentration at which at least 50% inhibition (mortality) is found. This value is calculated from the response curve given in the source document or is defined as the concentration at which the toxicity is 50% or more. The % effect is indicated in the tables.

The definitions of NOEC and LOEC are essential for a consistent approach. Some information is, however, lost using these definitions. Insensitive tests are not included in the effect assessment if the test failed to detect any toxic effect (no NOEC can be defined). Sensitive tests do not affect the derivation of the PNEC if the test showed 20% or more inhibition at the lowest concentration tested (no NOEC can be derived).

3.2.2 Aquatic compartment

3.2.2.1 General

3.2.2.1.1 Data quality: definitions of Reliability Indices (RI's)

A reliability index (RI) is given for each test based on a number of criteria. These criteria are given below and the IUCLID file contains the information which criteria were not met by each test.

- RI 1: standard test (OECD approved tests) and performed according to the standard procedures.
- RI 2: no standard test but complete background information is given, i.e. the following information is present:
  a) water hardness (either measured or calculated from Ca and Mg concentrations)

b) pH

c) the background Cd concentration in the test medium for all data < 1 µg L^{-1}

d) measured Cd concentrations or indications that nominal concentrations are close to measured concentrations

e) information that actual Cd concentrations were maintained during the test

f) statistical analysis of the dose-response relationship

g) no varying metal contamination along with increasing Cd application

h) the control must be tested along with at least two Cd concentrations above the control

i) information about the origin of the test organisms

j) information on the test concentration range

- RI 3: no standard test and one or more of the following information from the above-mentioned list is missing as background information: b), d), e), f), i), or j). All other information from that list is present.
- RI 4: no standard test and one or more of the following information from the above-mentioned list is missing as background information: a), c), g) or h).

  The requirement c) is critical since some tests have reported toxic effects below 1 µg L^{-1} nominal Cd concentrations. Background Cd concentrations in filtered water typically range between 0.05 and 0.2 µg L^{-1} and the lack of reporting the background concentration may underestimate the Cd concentration at which the first toxic effects are found. Some tests were included that did not show Cd toxicity up to the highest Cd concentration tested. These tests cannot be used for risk assessment (no NOEC can be found) and were considered unreliable (RI4) but were quoted in the tables for illustration.

3.2.2.1.2 Source of data and its limitations for risk assessment

A wealth of information is available on the toxicity of Cd to aquatic organisms. In this section, a compilation is made of different studies, which provide data of Cd toxicity to different species. Most of the tests were performed in laboratory conditions where Cd was added to the solution as soluble Cd^{2+} salts. Four tests on the toxicity of the CdO powder were found. The tests were performed using the filtrate of a dispersion of CdO powder. These tests are the OECD 203 fish acute toxicity test (Janssen Pharmaceutica, 1993b), the OECD 202 acute immobilisation test with Daphnia sp. (Janssen Pharmaceutica, 1993d) and the OECD 201 algae growth inhibition test (Janssen Pharmaceutica, 1993f, Lisec 1998b). The test results were reported as measured concentrations in the filtrates. It is most likely that Cd in the soluble fraction of the dispersion has the same speciation as that in a corresponding solution where Cd is added as soluble Cd^{2+} salts. Therefore, the toxicity tests using the filtrates of the CdO dispersion are treated equally as tests performed using soluble Cd^{2+} salts.

The CdO powder is only slightly soluble in water. The solubility decreases with increasing solution pH.

It is assumed that the dissolved fraction of a CdO dispersion represents the toxic Cd compound. The dissolved fraction of CdO has most likely the same speciation as the soluble Cd^{2+}salts dissolved in the same medium. It is therefore assumed that the toxicity of CdO can be assessed based on studies with Cd^{2+}salts, providing that the assessments are based on the dissolved fractions. Both the effect and exposure assessments of CdO in the aquatic environment are being made based on soluble fraction, as far as possible.

Cadmium toxicity in the aquatic environment can as well be overestimated or underestimated based on the laboratory data for various reasons. The major factors limiting a proper risk assessment are the unknown Cd speciation in environmental samples, the joint toxic actions of different pollutants, the process of long-term acclimation of organisms/populations to Cd and the general lack of information about the most toxic pathways of the higher trophic levels. A short discussion of these factors is given below.

Speciation

Cadmium can be present in an aquatic environment as inorganic species, including the free metal ion Cd^{2+}, as soluble complexes or sorbed on suspended particles. The free metal ion is considered as the most toxic species. Evidence for this concept was found in studies where metal speciation was altered by varying Cl^- concentration, affecting the concentration of $CdCl_n^{2-n}$ species (Sunda et al., 1978) or where synthetic chelates were added to the test solution (Allen et al., 1980). Other evidence on limited Cd toxicity of Cd complexed by dissolved organic matter is illustrated by the data of Giesy et al. (1977) discussed in Section 3.2.2.3. The toxicity of cadmium sorbed on suspended particles is far less than that of soluble Cd (see e.g. Van Leeuwen et al., 1985 discussed in Section 3.2.2.2). Soluble Cd is traditionally distinguished from insoluble forms by membrane (0.45 µm) filtration. Soluble cadmium in freshwater can be lower than 10% of total cadmium as discussed in the exposure section. Certainly, membrane filtered water samples should be used in risk analysis when concentrations are compared with toxic concentrations given in this compilation.

Data on Cd speciation in the soluble fraction of freshwater samples are limited. Complexation of Cd^{2+} by *inorganic ligands* is not pronounced in freshwater systems. Concentrations of inorganic ligands such as Cl^-, CO_3^{2-} and SO_4^{2-} are generally below 0.001 M in freshwaters (Stumm and Morgan, 1996). The computed fraction of Cd^{2+} to the total dissolved inorganic Cd species is about 0.5 (Stumm and Morgan, 1996). In exceptional cases, freshwaters may contain higher concentrations of ligands and lower free metal fractions. An example is the Lake IJssel in The Netherlands that was used for toxicity tests described below (Van Leeuwen et al., 1985). Lake IJssel is an artificial freshwater basin containing salts originating from the sea which was previously at that place. Complexation of Cd by dissolved organic ligands cannot be calculated unequivocally. Complexation is high at high concentrations of dissolved organic carbon and at low water hardness. Solution speciation of Cd undoubtedly affects toxicity but it is striking to note that the free metal ion is very rarely an order of magnitude smaller than the total concentration. Borg et al. (1989) studied Cd speciation in five soft water forest lakes in southern Sweden. Cadmium was predominantly in the soluble form in all of the lakes. In the circumneutral lakes, 35 to 82% of the soluble Cd was present in free ionic form, as inorganic complexes or as low molecular weight organic complexes. In the more acidic lakes, 83 to 100% of the soluble Cd was present in these forms. No data are available at the regional scale to account for Cd speciation in the dissolved fraction for risk assessment. In view of the much larger uncertainty of a toxic threshold concentration, we conclude that ignoring Cd speciation on the dissolved fraction will not cause large errors in risk assessment of Cd at a regional scale.

Mixed pollution

In the data compilation given below, only tests with single Cd contamination are included. However, elevated Cd levels in the environment are often associated with elevated Zn levels. The interaction between Zn and Cd can be antagonistic (Zn protecting Cd to become toxic) at moderate Zn levels. At Zn concentrations reaching toxic levels, Cd toxicity is more readily observed. In addition to simultaneous Zn pollution, in many environments other toxic substances exist that may affect Cd toxicity. A widespread approach to account for combined metal toxicity is to use the sum of the toxic unit of each pollutant (the concentration of a pollutant divided by its EC_{50}) as a gross toxicity indicator. In this approach it is assumed that the toxic actions of each contaminant are additive. The validity of such an approach was confirmed in a mesocosm experiment (Jak et al., 1996). The EC_{50} values of combined toxicity of 7 different heavy metals (including Cd) and arsenic on several plankton species were found between 0.53 and 0.98 'sum of toxic units' (Jak et al., 1996).

Acclimation

Populations previously exposed to Cd are more tolerant to elevated Cd than previously unexposed populations. An example of this process is found in a laboratory study with algae (Lawrence et al., 1989) reported in Section 3.2.2.4 and with slugs (Lam, 1996) reported in Section 3.2.2.3

Toxic pathways for higher trophic levels

Most studies report single species tests where Cd was added as Cd^{2+} salts. Cadmium toxicity in multi-species systems is certainly more complex because of altered food availability in toxic conditions and because of Cd exposure in various ways to higher trophic levels. The first process is illustrated in Section 3.2.2.3 by two studies reporting that the toxic action of Cd can decrease some populations and raise other populations in a multi-species system (Lawrence et al., 1989, DeNoyelles et al., 1980, Marshall and Mellinger, 1980). The question whether Cd in the diet or in water is the most toxic source is difficult to answer. Sörensen (1991) reports that in less contaminated environments, water rather than dietary uptake is the major route of Cd uptake. In contrast, as aquatic ecosystems become progressively more contaminated with Cd, the gastrointestinal route of Cd uptake becomes more important than the gill route (Sörensen, 1991). It must be stressed that this conclusion refers to Cd uptake and not to Cd toxicity. The importance of the food route on Cd toxicity can be indirectly found in data on Cd toxicity found in Sweden at very low Cd concentrations. In a field study in the River Emån (Sweden), sublethal toxicity was found in perch (*Perca fluviatilis*) collected downstream from a source of Cd pollution that ceased its discharge in the river in 1976 (Sjöbeck et al., 1984). The Cd concentrations downstream from the source were 0.1-0.2 $\mu g\ L^{-1}$ while upstream from the source the Cd concentrations were around 0.05 $\mu g\ L^{-1}$ (probably detection limit). The Cd concentrations in the liver of female downstream fish were 6-8 times higher than in those of upstream fish. Based on solution levels, no such large difference in liver Cd should be expected. Before 1976, solution Cd was however higher (about 1 $\mu g\ L^{-1}$) and it is likely that the downstream river sediment and benthic organisms had a high Cd burden at the time of fish and solution sampling (1981). The higher Cd load in the food rather than in solution may be the reason for increased liver Cd and Cd toxicity in the downstream fish compared to the upstream fish. This example indicates that a solution based risk assessment could underestimate exposure on-sites with historical pollution.

3.2.2.2 Acute and chronic toxicity to fish/amphibians

Table 3.194 Selected data with RI 1-3 for acute and chronic Cd toxicity to fish/amphibians. Sixty-three tests were reviewed from 27 source documents and 51 tests were selected

	Min	Median	Max	n
Acute tests				
$E(L)C_{x\geq 50}$ (µg L^{-1})	0.9	1,500	40,200	31
Chronic tests				
NOEC (µg L^{-1})	0.47	4.2	62	19
LOEC (µg L^{-1})	0.78	11	132	20
$E(L)C_{x\geq 50}$ (µg L^{-1})	3.4	20	650	7

Results of cadmium toxicity studies with fish reveal that toxic concentrations vary from the sub µg L^{-1} range to over 10 mg L^{-1} (see **Table 3.194**). Larger values are less relevant as many of the organisms in the environment exposed to such cadmium concentrations are already affected (see Section 3.2.2.1). The variability in toxicity among tests can be attributed to varying water quality (e.g. hardness, pH and organic load), life stage investigated, species differences, exposure time and acclimation of the test organisms.

The marked effects of water hardness on cadmium toxicity have been studied extensively. Toxicity test results of Canton and Slooff (1982) demonstrate that cadmium toxicity decreases as water hardness increases. For *Oryzias latipes* a NOEC value of 30 µg L^{-1} was recorded after 18 days exposure at a hardness of 200 mg $CaCO_3$/L. This value was fivefold lower in water with hardness of 100 mg $CaCO_3$/L. The effect of hardness became only significant after 4 days. McCarty et al. (1978) compared Cd toxicity to *Carassius auratus* in water with hardness 20 and 140 mg $CaCO_3$/L. A 20-fold lower LC_{50} value was recorded in soft test water. The effects of water hardness on the LC_{50} values are confounded by precipitation reactions that occur at the very high Cd concentrations. Pickering and Henderson (1966) also found changes in pH and acidity of the test water when cadmium salts were added to hard water. The water became milky, insoluble hydroxide and/or basic salts of cadmium were precipitated and lowered the pH of the test water. Carroll et al. (1979) compared cadmium toxicity in the presence of either Ca, Mg en Na salts at equal total salt concentrations. Calcium salts were most efficient in reducing the toxic action of Cd. Hall et al. (1986) compared Cd toxicity to *Pimephales promelas* in synthetic water with hardness 120 mg $CaCO_3$/L with that in well water with hardness 200 mg $CaCO_3$/L. The LC_{50} values were statistically not different in both media.

Toxicity values smaller then < 1 µg L^{-1} are found in very soft waters. Rombough and Garside (1982) tested Cd toxicity for alevins of *Salmo salar* in soft water with hardness ranging between 19 and 28 mg $CaCO_3$/L. Biomass production per female, an endpoint combining reproduction, survival of alevins and their growth, was significantly reduced at a Cd concentration of 0.78 µg L^{-1}. Chapman (1978) tested mortality of different juvenile stages of *Oncorhynchus tsahwytscha* in soft well water with hardness 23 mg $CaCO_3$/L. After 8.3 days, LC_{50} values of parr and smolts stages were found at Cd concentration of 0.9 and 1.6 µg Cd/L respectively. Benoit et al. (1976) exposed three generations of *Salvelinus fontinalis* to several concentrations of Cd in Lake Superior water (H 42-47 mg $CaCO_3$/L). The total weight of young produced per female of the second generation was significantly reduced at a Cd concentration of 1.7 µg L^{-1}. No effect was found at a concentration of 0.9 µg Cd/L. Sjöbeck et al. (1984) studied Cd toxicity to *Perca fluviatilis* in a field investigation of river Emån (Sweden, H 40-50 mg $CaCO_3$/L).

Downstream from a former source of Cd pollution, an activated immune defence system was found in perch compared to reference perch living in the same river upstream of the contamination source. Upstream of the source, Cd concentration is below 0.05 µg L^{-1} and downstream Cd concentrations are 0.1-0.2 µg L^{-1}. This test calls for a detailed analysis because it shows the lowest LOEC value in the entire data set of reviewed tests. The test is, however, excluded in the current risk assessment (RI 4) for various reasons. First of all, only two test concentrations (upstream/downstream) were studied. Secondly, the statistics of the experimental design are questionable; as only one reference site but three contaminated sites were studied (confounding factors cannot be excluded). Thirdly, the river was contaminated in the past with both Cd and Ni and it is unknown how these two metals interact. A fourth remark is that the uptake of food with elevated Cd (benthic organisms dwelling in the sediment with elevated Cd due to the historical pollution) might have been an important Cd exposure in this investigation (see also above in Section 3.2.2.1.2). This implies that the solution LOEC does not reflect the risk. Last of all, the authors note that it is difficult to evaluate the ecological significance of the sub lethal endpoint (Sjöbeck et al., 1984).

Canton and Slooff (1982) illustrate to what extent sensitivity to Cd varies among several species. The LC_{50} values vary from 30 to 3,800 µg L^{-1} at water hardness H= 100 mg $CaCO_3$ L^{-1} and from 20 to 11,100 µg L^{-1} at H= 200 mg $CaCO_3$ L^{-1} between 6 fish species. Phipps and Holcombe (1985) studied acute cadmium toxicity to 6 fish species and recorded a fish sensitivity factor (highest fish 96h LC_{50}/lowest fish 96h LC_{50}) of about 9. Dave et al. (1981) found rainbow trout to be more sensitive than zebrafish during their embryo-larval stage. Eaton et al. (1978) found greater sensitivity of two salmonid species, whereas Chapman (1978) noticed that steelhead was consistently more sensitive to cadmium than Chinook salmon. Pickering and Henderson (1966) found that 96h LC_{50} values for fathead minnows were significantly lower than those for bluegills. The LC_{50} values for fathead minnows were also lower than those for goldfish.

Different toxicity tests studied cadmium sensitivity at different life stages. Chapman (1978) found newly hatched alevins of both Chinook salmon and brook trout to be much more tolerant than later juvenile forms. Toxic Cd concentrations were very low (lowest LC_{50} value was found at 0.9µg L^{-1}) but it should be noted that tests were performed in very soft well water of only 23 mg $CaCO_3$/L. The toxicity tests of Eaton et al. (1978) indicated that larvae or juveniles were in all cases more sensitive than embryos. In contrast, Spehar (1976) demonstrated that stages of spawning and embryo production were the most sensitive for *Jordanella floridae*. Benoit et al. (1976) found males of brook trout to be more sensitive than females. At a cadmium concentration of 3.4 µg L^{-1}, both pre-exposed and not pre-exposed males became extremely hyperactive during spawning and suddenly died. Weights (growth) of 16-week old juveniles were also significantly less than weights of control fish. Hatch and survival of brook trout through the juvenile stage were not affected at 6.4 µg L^{-1}. Pickering and Gast (1972) found a statistically significant effect of cadmium toxicity at 27 µg Cd/L on hatchability of *Pimephales promelas*. At lower cadmium concentrations they also noticed a sudden increase in the number of eggs produced. Rombough and Garside (1982) found Atlantic salmon alevins to be considerably more sensitive to cadmium than the embryos. Alevins became substantially more sensitive near the completion of yolk absorption.

Increasing exposure time generally increases the Cd concentration in target organs, resulting in an increasing severity of observed effects (Pickering and Henderson 1966, Eaton et al., 1978, Spehar, 1976, Carroll et al., 1979, Phipps and Holcombe, 1985, McCarty et al., 1978). Carroll et al. (1979) recorded a 2- to 5-fold decrease in the LC_{50} value for *Salvelinus fontinalis* from 24 to 96 hours. McCarty et al. (1978) found a 2-fold reduction in the LC_{50}-value for *Carassius auratus* from 2 to 10 days.

Besides growth, reproduction and survival, other parameters have been studied when assessing toxicity of cadmium to fish. Muramoto (1981) observed vertebral column damage of *Cyprinus carpio* during 47 days. Bishop and McIntosh (1981) evaluated the use of ventilation rate and cough rate to predict the chronic toxicity of cadmium to bluegill. At cadmium concentrations lower than 1% of the LC_{50} value of bluegill, the ventilation rate and cough rate of bluegill were increased. Changes in cough rate were correlated with cadmium exposure. This test has not been selected for the risk assessment since it is an acute test. Arillo et al. (1984) investigated the biochemical responses to low cadmium concentrations in *Salmo gairdneri*. Blood, liver and mitochondrial enzymes are sensitive to cadmium and their activity was altered when exposed to 10 µg Cd/L. The activity of the enzymes antioxidase and lipid peroxidase was only reduced at a Cd concentration of 620 µg Cd/L. This test was neither selected because of unknown ecological relevance of the test results. Venugopal et al. (1997) found a reduction of more than 50% at this concentration. Karlsson-Norrgren et al. (1985) recorded a change in gill morphology at 10 µg Cd/L after 6 weeks of exposure. Lowe-Jinde and Niimi (1984) found short- and long-term effects of cadmium on glycogen reserves and liver size of rainbow trout.

In conclusion, lowest effect concentrations for fish were found at 0.8 µg L^{-1}. Toxicity is most pronounced in soft water. One reliable EC_{50} and one LOEC value were found below 1 µg L^{-1}. These values refer to tests performed at water hardness < 50 mg $CaCO_3$/L. Reproduction parameters are most sensitively affected by Cd.

Table 3.195 Toxicity to fish/amphibians. All underlined data are selected to discuss the critical concentrations (Table 3.194). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	Organism	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC ($\mu g\ L^{-1}$)	Cat.*	LOEC ($\mu g\ L^{-1}$) (%effect)	EC_{50} ($\mu g\ L^{-1}$) (%effect)	LC_{50} ($\mu g\ L^{-1}$) (%effect)	References	R.I.
$CdCl_2$	*Salmo salar*	municipal water charcoal filtered and UV sterilised; BC 0.13 µg Cd/L; pH 6.5-7.3; T 5-10; DO 11.1-12.5; Al 14-17; H 19-28	semi-static	M	24	A	mortality					34	Rombough and Garside, 1982	2
					46	C	total biomass	0.47	1	0.78(28)				2
$CdCl_2$	*Catostomus commersoni*	sand filtered Lake Superior Water; continuous flow; DO 10.3; H 45; Al 41; Ac 3; pH 7.6	T 18.1	M	30	C	standing crop (biomass)	4.2	1	12			Eaton et al., 1978	2
	Esox lucius		T 15.9		28	C	biomass	4.2	1	12.9				2
	Oncorhynchus kisutch (sac fry		T 10.1		27	C	biomass	1.3	1	3.4				2
	Oncorhynchus kisutch		T 9.7		27	C	biomass	4.1	1	12.5				2
	Salvelinus namaycush		T 9.6		31	C	biomass	4.4	1	12.3				2
	Salvelinus fontinalis		T 9.7		126	C	biomass	1.1	1	3.8				2
	Salmo trutta		T 9.7		60	C	biomass	3.8	1	11.7				2
	Salmo trutta (late eyed eggs)		T 10		61	C	biomass	1.1	1	3.7				2

Table 3.195 continued overleaf

Table 3.195 continued Toxicity to fish/amphibians. All underlined data are selected to discuss the critical concentrations (Table 3.194). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	*Organism*	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC (µg L-1)	Cat.*	LOEC (µg L-1) (%effect)	EC50 (µg L-1) (%effect)	LC50 (µg L-1) (%effect)	References	R.I.
$CdCl_2$	*Salvelinus fontinalis*	sterilised Lake Superior water; H 42-47; pH 7-8; Al 38-46; Ac 1-10; DO 4-12; T 9-15	continuous flow	M	3 years	C	mortality	1.7	1			3.4	Benoit et al., 1976	2
						C	growth (weight) of 16 week old juveniles	1.7	1		3.4(56)			2
						C	total weight of young /female of the 2nd generation	0.9	1	1.7(31)				2
						C	reproduction	6.4	1					2
$CdCl_2$	*Jordanella floridae*	untreated Lake Superior water; T 25; DO 8.3; H 44; Al 42; Ac 2.4; pH 7.1-7.8	continuous flow	M	4	A	mortality					2,500	Spehar, 1976	2
					100	C	mortality	8.1	1			16(72)		2
						C	growth	8.1	1	16(27)				2
						C	reproduction	4.1	1		8.1(52)			2
$CdCl_2$	*Salmo gairdneri*	aerated well water; T 10; O_2 7.5; H 375-390; pH 8-8.6	continuous flow	M	84	C	mortality	12	1	36 (10) HT			Lowe-Jinde and Niimi, 1984	2
Cd	*Salvelinus fontinalis*	reconstituted soft water: T 14-16°C; DO 9.3-11.4 mg L^{-1}; Cd(BG) <0.2 µg L^{-1}; pH 6.3-7.6; H 20	static renewal	M	10	C	survival	8	1	18			Jop et al., 1995	2
						C	growth	18	1					2
		river water: T 14-16°C; DO 8.7-12.2 mg L^{-1}; Cd(BG) <4 µg L^{-1}; pH 6.6-7.4; H 16-28	static renewal	M	10	C	survival	62	1	132				2

Table 3.195 continued overleaf

Table 3.195 continued Toxicity to fish/amphibians. All underlined data are selected to discuss the critical concentrations (Table 3.194). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

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$CdCl_2$	*Lepomis macrochirus*	dechlorinated, carbon-filtered tap water	Static; T 22; DO 8.5; H 18; Al 16; pH 7.4-7.7	M	4	A	mortality					2,300	Bishop and McIntosh, 1981	2
$CdCl_2$	*Pimephales promelas*	lake water; T 22.5; DO 7.5; H 44.4; Al 45.4; pH 7.1-7.8	continuous flow	M	4	A	mortality					1,500	Phipps and Holcombe, 1985	2
	Carassius auratus				4	A						748		2
	Ictalurus punctatus				4	A						4,480		2
	Lepomis macrochirus(juv)				4	A	mortality					6,470		2
$CdCl_2$	*Barytelphusa guerini*	tap water; pH 7.2-7.4; DO 7.8-8 mg L^{-1}, Al 102; H 112; male fish	semi-static	N	4	A	mortality					1,820	Venugopal et al., 1997	2

Table 3.195 continued overleaf

Table 3.195 continued Toxicity to fish/amphibians. All underlined data are selected to discuss the critical concentrations (Table 3.194). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	*Organism*	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC (µg L-1)	Cat.*	LOEC (µg L-1) (%effect)	EC50 (µg L-1) (%effect)	<u>LC50 (µg L-1) (%effect)</u>	References	R.I.
Cd-solution	*Oncorhynchus tsahwytscha*	continuous flow; aerated UV sterilised well water; T 11.6-12.8; Al 22; H 23; DO 10.2; pH 7.1; Cd < 0.2 µg L^{-1}	newly hatched alevins	M	4	A	mortality					> 27	Chapman, 1978	3
			swim-up alevins			A						1.3		3
			5-8m old parr			A						1.0		3
			smolts			A						> 2.9		3
			newly hatched alevins		8.3	A						> 27		3
			swim-up alevins			A						1.3		3
			5-8m old parr			A						<u>0.9</u>		3
			smolts			A						1.6		3
	Salmo gairdneri		newly hatched alevins		4	A						> 26		3
			swim-up alevins			A						1.8		3
			5-8m old parr			A						3.5		3
			smolts			A						> 2.9		3
			newly hatched alevins		8.3	A						> 26		3
			swim-up alevins			A						<u>1.6</u>		3
			5-8m old parr			A						2.0		3
			smolts			A						2.3		3
$CdCl_2$	*Brachydanio rerio*	synthetic water (changed ISO) ; T 24; DO >80%; H 100; pH 7.2	semi-static; adults	N	4	A	mortality					<u>3,500</u>	Bresch ., 1982	3
			larvae		24	C	reproduction			<u>10</u>(35)				
					36	C	reproduction	<u>1</u>	1					

Table 3.195 continued overleaf

Table 3.195 continued Toxicity to fish/amphibians. All underlined data are selected to discuss the critical concentrations (Table 3.194). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

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$CdCl_2$	*Salmo salar*	municipal water charcoal filtered and UV sterilised; BC 0.13 µg Cd/L; pH 6.5-7.3; T 5-10; DO 11.1-12.5; Al 14-17; H 19-28	semi-static	M	24	A	mortality					34	Rombough and Garside, 1982	2
					46	C	total biomass	0.47	1	0.78(28)				2
$CdCl_2$	*Catostomus commersoni*	sand filtered Lake Superior Water; continuous flow; DO 10.3; H 45; Al 41; Ac 3; pH 7.6	T 18.1	M	30	C	standing crop (biomass)	4.2	1	12			Eaton et al., 1978	2
	Esox lucius		T 15.9		28	C	biomass	4.2	1	12.9				2
	Oncorhynchus kisutch (sac fry		T 10.1		27	C	biomass	1.3	1	3.4				2
	Oncorhynchus kisutch		T 9.7		27	C	biomass	4.1	1	12.5				2
	Salvelinus namaycush		T 9.6		31	C	biomass	4.4	1	12.3				2
	Salvelinus fontinalis		T 9.7		126	C	biomass	1.1	1	3.8				2
	Salmo trutta		T 9.7		60	C	biomass	3.8	1	11.7				2
	Salmo trutta (late eyed eggs)		T 10		61	C	biomass	1.1	1	3.7				2
$CdCl_2$	*Salvelinus fontinalis*	sterilised Lake Superior water; H 42-47; pH 7-8; Al 38-46; Ac 1-10; DO 4-12; T 9-15	continuous flow	M	3 years	C	mortality	1.7	1			3.4	Benoit et al., 1976	2
						C	growth (weight) of 16 week old juveniles	1.7	1		3.4(56)			2
						C	total weight of young /female of the 2nd generation	0.9	1	1.7(31)				2
						C	reproduction	6.4	1					2
$CdCl_2$	*Jordanella floridae*	untreated Lake Superior water; T 25; DO 8.3; H 44; Al 42; Ac 2.4; pH 7.1-7.8	continuous flow	M	4	A	mortality					2,500	Spehar, 1976	2
					100	C	mortality	8.1	1			16(72)		2
						C	growth	8.1	1	16(27)				2
						C	reproduction	4.1	1		8.1(52)			2
$CdCl_2$	*Salmo gairdneri*	aerated well water; T 10; O_2 7.5; H 375-390; pH 8-8.6	continuous flow	M	84	C	mortality	12	1	36 (10) HT			Lowe-Jinde and Niimi, 1984	2

Table 3.195 continued overleaf

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Cd	*Salvelinus fontinalis*	reconstituted soft water: T 14-16°C; DO 9.3-11.4 mg L^{-1}; Cd(BG) <0.2 µg L^{-1}; pH 6.3-7.6; H 20	static renewal	M	10	C	survival	8	1	18			Jop et al., 1995	2
						C	growth	18	1					2
		river water: T 14-16°C; DO 8.7-12.2 mg L^{-1}; Cd(BG) <4 µg L^{-1}; pH 6.6-7.4; H 16-28	static renewal	M	10	C	survival	62	1	132				2
$CdCl_2$	*Lepomis macrochirus*	dechlorinated, carbon-filtered tap water	Static; T 22; DO 8.5; H 18; Al 16; pH 7.4-7.7	M	4	A	mortality					2,300	Bishop and McIntosh, 1981	2
$CdCl_2$	*Pimephales promelas*	lake water; T 22.5; DO 7.	continuous flow	M	4	A	mortality					1,500	Phipps and Holcombe, 1985	2
	Carassius auratus	5; H 44.4; Al 45.4; pH 7.1-7.8												
	Ictalurus punctatus				4	A						748		2
	Lepomis macrochirus(juv)													
					4	A						4,480		2
					4	A	mortality					6,470		2
$CdCl_2$	*Barytelphusa guerini*	tap water; pH 7.2-7.4; DO 7.8-8 mg L^{-1}, Al 102; H 112; male fish	semi-static	N	4	A	mortality					1,820	Venugopal et al., 1997	2

Table 3.195 continued overleaf

Table 3.195 continued Toxicity to fish/amphibians. All underlined data are selected to discuss the critical concentrations (Table 3.194). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	*Organism*	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC (µg L-1)	Cat.*	LOEC (µg L-1) (%effect)	EC50 (µg L-1) (%effect)	LC50 (µg L-1) (%effect)	References	R.I.
Cd-solution	*Oncorhynchus tsahwytscha*	continuous flow; aerated UV sterilised well water; T 11.6-12.8; Al 22; H 23; DO 10.2; pH 7.1; Cd < 0.2 µg L^{-1}	newly hatched alevins	M	4	A	mortality					> 27	Chapman, 1978	3
			swim-up alevins			A						1.3		3
			5-8m old parr			A						1.0		3
			smolts			A						> 2.9		3
			newly hatched alevins		8.3	A						> 27		3
			swim-up alevins			A						1.3		3
			5-8m old parr			A						0.9		3
			smolts			A						1.6		3
	Salmo gairdneri		newly hatched alevins		4	A						> 26		3
			swim-up alevins			A						1.8		3
			5-8m old parr			A						3.5		3
			smolts			A						> 2.9		3
			newly hatched alevins		8.3	A						> 26		3
			swim-up alevins			A						1.6		3
			5-8m old parr			A						2.0		3
			smolts			A						2.3		3

Table 3.195 continued overleaf

Table 3.195 continued Toxicity to fish/amphibians. All underlined data are selected to discuss the critical concentrations (Table 3.194). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	Organism	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC (µg L-1)	Cat.*	LOEC (µg L-1) (%effect)	EC50 (µg L-1) (%effect)	LC50 (µg L-1) (%effect)	References	R.I.
$CdCl_2$	*Brachydanio rerio*	synthetic water (changed ISO) ; T 24; DO >80%; H 100; pH 7.2	semi-static; adults	N	4	A	mortality					3,500	Bresch ., 1982	3
			larvae		24	C	reproduction			10(35)				
					36	C	reproduction	1	1					
$CdCl_2$	*Brachydanio rerio*	tap water; continuous flow; T 20	H 170	M	1	A	mortality					7,000	Canton and Slooff, 1982	3
					2	A						4,200		
		synthetic water (Dutch standard water); semi-static; T 24												
	Oryzias latipes		H 200		1	A	mortality					> 2,600		
					2	A						1,800		
					3	A						170		
					4	A						130		
					1	A	mortality and abn. behaviour					> 2,600		
					2	A						470		
					3	A						160		
					4	A						70		
			H 100		1	A	mortality							
					2	A						>2,800		
					3	A						350		
					4	A						350		
					1	A	mortality and abn. behaviour					> 2,800		
					2	A						320		
					3	A						120		
		synthetic water (Dutch standard water); semi-static; T 24			4	A						70		
			H 200		1	A	mortality					33,000		
					2	A						20,500		
					3	A						14,400		
	Poecilia reticulata				4	A						11,100		
							mortality and abn. behaviour							

Table 3.195 continued overleaf

Table 3.195 continued Toxicity to fish/amphibians. All underlined data are selected to discuss the critical concentrations (Table 3.194). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	Organism	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC (µg L-1)	Cat.*	LOEC (µg L-1) (%effect)	EC50 (µg L-1) (%effect)	LC50 (µg L-1) (%effect)	References	R.I.
					1	A						31,000		
					2	A						19,500		
					3	A	mortality					12,100		
					4	A						11,100		
			H 100		1	A						10,400		
					2	A	mortality and abn. behaviour					5,700		
					3	A						4,300		
					4	A						3,800		
					1	A						7,100		
		tap water; continuous flow; T 20			2	A						5,900		
					3	A	mortality					3,700		
					4	A						3,400		
			H 200		18	C	mortality and abn. behaviour	30	1	35(25)		50		
			H 100			C		6	1	23(25)		40		
			H 200		18	C		6	1	7(25)		20		
			H 100			C		3	1	13(25)		30		
	Oryzias latipes													
		tap water; continuous flow; T 20	H 170		1	A	mortality					4,000		
	Xenopus laevis				2	A						3,200		
					100	C	mortality	30	1			1,500		
							inhibition of larvae development	9	1		650			
							body weight	30	1					

Table 3.195 continued overleaf

Table 3.195 continued Toxicity to fish/amphibians. All underlined data are selected to discuss the critical concentrations (Table 3.194). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	Organism	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC (µg L-1)	Cat.*	LOEC (µg L-1) (%effect)	EC50 (µg L-1) (%effect)	LC50 (µg L-1) (%effect)	References	R.I.
$CdSO_4$	*Brachydanio rerio*	synthetic water (ISO 1977) ; T 25; pH 8.3; H 100	static; juvenile fish (0.25g each)	N	1	A	mortality					2,400	Dave et al., 1981	3
					4	A						1,700		3
	Salmo gairdneri		semi-static; T 8; embryo-larva		6	A						1,700		3
					48	C	median survival time	4	1	5(15)				3
$CdSO_4$	*Pimephaless promelas*	pond water diluted with carbon filtered demineralised tap water; H 201-204; DO 6.5-6.6; pH 7.6-7.7; Al 145-161; Ac 8-12; T 16-27	continuous flow; pond fish	M	60	C	survival of developing embryos	37	1	57(26)			Pickering and Gast, 1972	3
							hatchability of eggs							
						C	growth reproduction	37	1	57				3
						C	mortality	350	1					3
						C	survival of developing embryos	13	1	37(26)				3
					104	C	reproduction					68		3
			continuous flow; 3 week old fry from laboratory		60	C	growth	27	1	57(22)				3
							mortality							
						C		14	1	27(24)				3
					30	C		110	1					3
			static		4	A						30,000		3
			continuous flow		4	A						2,000		3
$CdCl_2$	*Brachydanio rerio*	synthetic water; T 25; pH 6.9-7.2; H 12.4	continuous flow	N	42	C	mortality			3 (40)LT		10 (60)	Karlsson-Norrgren et al., 1985	3
$CdCl_2$	*Cyprinus carpio*	tap water; T 18-19; pH 6.8; Al 14.8; H 18, BC 0.001 mg L^{-1}; food < 0.05 µg L^{-1}	semi-static	N	47	C	vertebral column damage			10LT			Muramoto, 1981	3

Table 3.195 continued overleaf

Table 3.195 continued Toxicity to fish/amphibians. All underlined data are selected to discuss the critical concentrations (Table 3.194). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	Organism	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC (µg L-1)	Cat.*	LOEC (µg L-1) (%effect)	EC50 (µg L-1) (%effect)	LC50 (µg L-1) (%effect)	References	R.I.
$CdSO_4$	*Salvelinus fontinalis*	synthetic soft water (EPA); pH 7.3 - 7.7; T 12	+ 3.10^{-3} M $CaCO_3$ H 340 - 344; Al 327-332	N	4	A	mortality					26	Carroll et al., 1979	3
			+ 3.10^{-3} M $CaSO_4$ H 332 - 348; Al 28-30			A						29		3
			+ 3.10^{-3} M $MgCO_3$ H 348 - 360; Al 314-324			A						3.8		3
			+ 3.10^{-3} M $MgSO_4$ H 324 - 336; Al 27-32			A						4.4		3
			+ 3.10^{-3} M Na_2SO_4 H 44 -46; Al 27-34			A						2.4		3
$CdCl_2$	*Pimephales promelas*	well water; pH 7.7; H 200; Al 140; T 22; BC negligible	static	N	2	A	mortality					100	Hall et al., 1986	3
					4	A						90		
$Cd(NO_3)_2$	*Gambusia affinis*	0.15µm filtered pond water rich in TOC; continuous flow; DO > 90%; Al 4; H 10; pH 5.6; Cd 0.02 µg L^{-1}	T 30.2	N	4	A	mortality					1,300	Giesy et al., 1977	3
			T 30.7			A						1,500		3
			T 28			A						2,600		3
		0.15 µm filtered well water pour in TOC; continuous flow; ; DO > 90%; Al 9.7; H 11.1; pH 6.5; Cd 0.023 µg L^{-1}	T 30.2			A						900		3
			T 28			A						2,200		3
$CdCl_2$	*Carassius auratus*	aerated dechlorinated and aged city water; T 22-25; Cd < 10 µg L^{-1}; Al 14-18; DO 90%	static; H 20	N	2	A	mortality					2,760	McCarty et al., 1978	3
					4	A						2,130		3
					10	A						1,780		3
			H 140		2	A						46,900		3
					4	A						46,800		3
					10	A						40,200		3

Table 3.195 continued overleaf

Table 3.195 continued Toxicity to fish/amphibians. All underlined data are selected to discuss the critical concentrations (Table 3.194). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	Organism	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC (µg L-1)	Cat.*	LOEC (µg L-1) (%effect)	EC50 (µg L-1) (%effect)	LC50 (µg L-1) (%effect)	References	R.I.
Supporting data														
$CdCl_2$	*Salmo gairdneri*	water; T 15; pH 7.4; DO 90%; H 320	continuous flow	N	4 months		activity of:						Arillo et al., 1984	
						C	liver enzymes	1	1	10(10)				4
						C	blood enzymes	1	1	10(36)				4
						C	mitochondrial enz	1	1		10(75)			4
							gill sialic acid content							
						C	mucus lysozyme	1	1	10(20)				4
						C		10	1					4
$CdSO_4$	*Brachydanio rerio*	synthetic water (ISO 1977) ; T 25; pH 8.3; H 100	semi-static; embryo-larva	N	10	C	median survival	50(HT)					Dave et al., 1981	4
Cd	*Brachydanio rerio*	OECD-203-test water; T 22; pH 7.42; DO 9.3; H 233.4	static	M	4	A	mortality			320(20)			Janssen Pharmaceutica, 1993a	4
CdO	*Brachydanio rerio*	OECD-203-test water; T 22; pH 7.82; DO 9.5; H 243.6	static	M	4	A	mortality	1600 (HT)					Janssen Pharmaceutica, 1993b	4
Cd	*Salvelinus fontinalis*	river water: T 14-16°C; DO 8.7-12.2 mg L^{-1}; Cd(BG) <4 µg L^{-1}; pH 6.6-7.4; H 16-28	static renewal	M	10	C	growth	132 (HT)					Jop et al., 1995	4
$CdCl_2$	*Lepomis macrochirus*	dechlorinated, carbon-filtered tap water	continuous flow; T 14.5-16; pH 7.8-8.2; DO 6.2-8.1; H 340-360; Al 248-264; Cd < 1 µg L^{-1}	N	3	A	cough rate			50(35)LT			Bishop and McIntosh, 1981	4
$CdCl_2$	*Barytelphusa guerini*	tap water; pH 7.2-7.4; DO 7.8-8 mg L^{-1}, Al 102; H 112; male fish	semi-static	N	30	C	activity of antioxidase				620(80)		Venugopal et al., 1997	4
						C	lipid peroxidase				620(52)			4

Table 3.195 continued overleaf

Table 3.195 continued Toxicity to fish/amphibians. All underlined data are selected to discuss the critical concentrations (Table 3.194). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	Organism	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC (µg L-1)	Cat.*	LOEC (µg L-1) (%effect)	EC50 (µg L-1) (%effect)	LC50 (µg L-1) (%effect)	References	R.I.
$CdCl_2$	*Pimephales promelas*	synthetic water (5% natural limestone spring water + 95% deionised water); static	T 25; DO 7.8; pH 7.5; Al 18; H 20	N	4	A	mortality					630-1,050	Pickering and Henderson, 1966	4
	Lepomis macrochirus													
	Carassius auratus					A						1,940		4
	Lebistes reticulatus													
	Lepomis cyanellus					A						2,340		4
	Pimephales promelas													
	Lepomis cyanellus					A						1,270		4
						A						2,840		4
		hard limestone spring water	T 25; DO 7.8; pH 8.2; Al 300; H 360			A						72,600-73,500		4
						A						66,000		4
Soluble Cd	*Perca fluviatilis*	River Emån water; T 20-22; H 40-50; pH 6.7; female fish	field study	M	whole life	C	immune defence				0.1-0.2(45-100)LT		Sjöbeck et al., 1984	4

T Temperature (°C);
H Hardness (as mg $CaCO_3$/L);
DO Dissolved oxygen (mg O_2/L);
Al Alkalinity (mg $CaCO_3$/L);
Ac Acidity (mg $CaCO_3$/L);
LT LOEC value found at lowest concentration tested
HT NOEC value found at highest concentration tested
* NOEC classification (see section 3.2.1.2);
** Days of exposure of embryos and larvae-juveniles

3.2.2.3 Acute and chronic toxicity to aquatic invertebrates

Table 3.196 Selected data with RI 1-3 for acute and chronic Cd toxicity to aquatic invertebrates. One hundred and two tests were reviewed from 42 source documents and 97 tests were selected

	Min	Median	Max	n
Acute tests				
$E(L)C_{x\geq50}$ (µg L^{-1})	7	166	74,000	61
Chronic tests				
NOEC (µg L^{-1})	0.16	2.0	11	22
LOEC (µg L^{-1})	0.28	1.9	25	19
$E(L)C_{x\geq50}$ (µg L^{-1})	1	5	32	14

A large number of acute tests were found for invertebrates. Only few chronic studies met all criteria for classification as RI 2. Certain invertebrates e.g. *Daphnia* and *Ceriodaphnia*, appear to be particularly sensitive to cadmium. Most chronic LOEC values of *Daphnia* range between 1 and 10 µg L^{-1}. The lowest LOEC value is found in well water (H 103 mg $CaCO_3$ /L, background Cd 0.08 µg L^{-1}, Chapman et al., 1980). The mean number of young per adult after 21 days exposure was reduced at only 0.29 µg L^{-1} (measured concentration). The NOEC in this test was 0.16 µg L^{-1}.

Toxicity of CdO powder was tested in the 48-hour acute test with *Daphnia magna*. The filtrate of a CdO dispersion was diluted in several series (57-750 µg Cd/L). There were no toxic effects up to 250 µg Cd/L and there was 70% mortality at 750 µg Cd/L).

A wide range of concentrations at which cadmium is toxic to freshwater invertebrates (see **Table 3.196**) is found. The acute $E(L)C_{x\geq50}$ values vary from 5 µg L^{-1} to 74 10^3 µg L^{-1}. Canton and Slooff (1982) found a lower LC_{50} value of 0.67 µg Cd/L and a NOEC value of 0.37 µg Cd/L. Both values are, however, unreliable because the authors state that it is an extrapolated value below the lowest test concentration (tested concentration range not reported). The extrapolation is based on concentration measurements with flame atomic absorption spectrophotometry (detection limit ~20 µg L^{-1}) does therefore not warrant reliable data. Differences in species, life stage, exposure time, type of flow system in which experiments were performed, changes in water quality, hardness, pH, alkalinity, temperature and organic fractions, impact cadmium toxicity.

Van Leeuwen et al. (1985) compared both mortality and reproduction characteristics in synthetic water and 50 µm filtered and sterilised IJssel water. The LC_{50} and LOEC values were both 7 times higher in natural water than in synthetic water. They explain the differences found by differences in speciation of cadmium. In natural water bioavailability of cadmium is reduced through sorption on suspended particles so that biological responses occur at higher cadmium levels. Giesy et al. (1977) also report the influence of particles on bioavailability of cadmium. They compare cadmium toxicity in soft well water containing low organic carbon concentrations to toxicity in soft surface waters containing high concentrations of naturally occurring organic compounds. Toxicity of cadmium was significantly smaller in the organic surface water than in the well water (LC_{50} values were 35 µg L^{-1} and 7 µg L^{-1} respectively). Different molecular organic fractions of this surface water were isolated by ultracentrifugation and were added to the well water. Addition of these fractions resulted in a decrease in Cd toxicity (an increase of the

LC_{50} value from 7 µg L^{-1} to 16.5 µg L^{-1}). Adding the smallest fraction (< 0.9 nm) however increased Cd toxicity. Both effects of cadmium sorption to suspended particles and cadmium complexation by dissolved organic carbon confirm the free ion theory as described above (see Section 3.2.2, introduction). Schuytema et al. (1984) compared Cd toxicity in soft well water with toxicity in a water-sediment system. In well water toxic concentrations were expressed as total measured concentrations, in the sediment-water system as dissolved measured concentrations. They found similar LC_{50} values in both systems demonstrating that the dissolved fraction in sediment-water systems is the bioavailable fraction. Hall et al. (1986) tested cadmium toxicity on different water flea species in both synthetic and well water. They report that the different water types did not affect the cadmium toxicity to the different species tested.

Acclimation of a species or a population generally decreases the sensitivity to toxic compounds. Lam (1996) collected adolescent *Brotia hainanensis* (snails) from sites either upstream or downstream of a Cd polluting source. The downstream snails were more tolerant to cadmium than upstream snails even after laboratory acclimation for one week. Similar interpopulation differences persisted in the first generation (F1) juveniles (< 2-day-olds) which were descendants of laboratory-cultured snails. These differences in metal tolerance in the F1 juveniles disappeared after the juveniles had been cultured under identical laboratory conditions for one week. Bodar et al. (1990) found *Daphnia magna* pre-exposed to sublethal Cd concentrations to become more resistant to cadmium.

Cadmium toxicity generally increases with increasing exposure time. Van Leeuwen et al. (1985) report a gradual decline in the LC_{50} values for daphnids with time from 10 µg L^{-1} to 2 µg L^{-1} in synthetic water until a constant level was reached after about 2 weeks. In 50 µm filtered Lake IJssel water the LC_{50} declined from 24 µg L^{-1} after 14 days to 14 µg L^{-1} after 21 days. Attar and Maly (1982) obtained LC_{50} values, which varied between 204 µg L^{-1} if calculated at 36 hours and 5 µg L^{-1} if calculated at 96 hours. Biesinger and Christensen (1972) found a fourteen-fold decrease of the LC_{50} value for *Daphnia magna*, in filtered Lake Superior water, from exposure day 2 to 21. Canton and Slooff (1982) performed a similar test in synthetic water and found an even bigger decrease of the LC_{50} value, from 30 µg Cd/L to 0.67 µg Cd/L. In the same test the NOEC data for mortality showed a similar trend. The background Cd of the test medium and test concentration range is unknown. Furthermore, it is not known if thresholds below 1 µg L^{-1} are calculated by extrapolation outside the tested concentration range. Therefore, these data are considered as unreliable. Spehar et al. (1978) record an eleven-fold decrease of the LC_{50} value for snails between 7 days and 28 days. For mayfly no significant effects on mortality were observed until the fourth week of exposure at which 3 µg L^{-1} caused 70% mortality.

The marked effects of increasing water hardness reducing cadmium toxicity are extensively reported (see Section 3.2.2.6.4).

The importance of species differences, over and within different trophic levels, is illustrated by the experiments of Canton and Slooff (1982), Baudouin and Scoppa (1974), Warnick and Bell (1969), Williams et al. (1985), Winner (1988), Fennikoh et al. (1978), Hall et al. (1986) and Ingersoll and Kemble (2000). Canton and Slooff (1982) studied short- and long-term toxicity of cadmium to different freshwater organisms of different trophic levels. Bacteria, algae, crustaceans, fishes and amphibians were studied. In both short- and long-term studies, *Daphnia magna* was the most sensitive organism. Baudouin and Scoppa (1974) compared cadmium toxicity to three most representative freshwater zooplankton (*Cyclops abyssorum prealpinus, Eudiaptomus padanus padanus, Daphnia hyalina*) of Lake Monate -an unpolluted subalpine lake of Italy- and also found *Daphnia sp*. to be the most sensitive. Williams et al. (1985) studied cadmium toxicity on ten freshwater macroinvertebrates. Results indicated a wide range of species sensitivity. Members of the crustacean (*Gammarus* sp.) appear the most sensitive

(LC_{50} 20 µg L^{-1}) whilst insect species of the orders *Plecoptera* and *Trichoptera* exhibit high short-period tolerance to cadmium poisoning (LC_{50} 520 10^3 µg L^{-1}). Warnick and Bell (1969) studied 3 aquatic insects from which mayfly (*Ephemerella subvaria*) is the most sensitive. Hall et al. (1986) compared the sensitivity of different water flea species to cadmium. No difference in species sensitivity was reported. Ingersoll and Kemble (2000) compared Cd toxicity to *Hyalella azteca* and *Chironomus tentans* in well water. They found *Hyalella azteca* to be the most sensitive.

Different toxicity tests demonstrate cadmium sensitivity to be depended on life stages. Wier and Walter (1976) found mature *Physa gyrina* to be much more tolerant than immature snails. Nebeker et al. (1986a) noted new-born *Daphnia*'s to be more resistant to Cd than test organisms of several days old. Sensitivity to Cd was also found to be dependent on the size of the neonates. Enserink et al. (1990) demonstrated larger neonates to be more resistant than smaller neonates.

Several reproduction parameters are used as toxic endpoints. Van Leeuwen et al. (1985) tested the effects of Cd on the number of offspring and the delay in the reproduction. Both parameters are based on individuals. From a 3-week life table study the authors calculated 'the intrinsic rate of natural reproduction' which integrates both age-specific survival and reproduction and found this a better test parameter. Bertram and Hart (1979) investigated the effect of cadmium on survival and reproduction capacity of *Daphnia pulex*. Cadmium at 5 µg L^{-1} reduced the average longevity. Reproduction parameters such as the number of broods per adult, the number of young per brood, the number of progeny per adult, the intrinsic rate of natural increase or the mean generation time were already affected at 1 µg L^{-1}. Elnabarawy et al. (1986) also found reproduction to be more sensitive to Cd than mortality for several daphnids. Both LOEC- and NOEC-values were below 1 µg L^{-1}. The same conclusion is drawn for the very low effect values on reproduction and growth found by Biesinger and Christensen (1972). A LOEC value of 0.17 µg Cd/Lfor reproduction was found by extrapolation beyond the test concentrations. Bodar et al. (1988a) note the change in the reproduction strategy of *Daphnia magna* which produce larger broods with smaller neonates at low cadmium concentrations (< 5 µg L^{-1}). At higher cadmium concentrations (> 5 µg L^{-1}) brood size and body size decline and the average number of days to the first brood increases.

Sublethal endpoints of *Daphnia* can be very sensitive to Cd. The haemoglobin content decreased by 20% when *Daphnia* was exposed to only 0.1 µg L^{-1} Cd for 16 days (Berglind, 1985). However, at Cd exposure between 0.2-1.6 µg L^{-1}, no differences with the control value were found. Bodar et al. (1988b) found a decrease of 60% in the chlorella consumption rate of *Daphnia magna* at a cadmium concentration of 5 µg L^{-1}.

In conclusion, Cd can affect primary consumers in the µg L^{-1} range and below. Reproduction was found to be the most sensitive endpoint. Different effect data smaller than 1 µg L^{-1} were found. However, several of those values are considered unreliable because they were obtained by extrapolation, or because they are expressed as nominal concentrations without information on background Cd concentration in the test medium.

Table 3.197 Toxicity to aquatic invertebrates. All underlined data are selected to discuss the critical concentrations (Table 3.196). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effect assessment

Test substance	Organism	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC ($\mu g\ L^{-1}$)	Cat.*	LOEC ($\mu g\ L^{-1}$) (%effect)	EC_{50} ($\mu g\ L^{-1}$) (%effect)	LC_{50} ($\mu g\ L^{-1}$) (%effect)	References	RI
Cd (filtrate of dispersion)	*Daphnia magna*	OECD 202-test medium; pH 7.76; DO 9.6; H 274; T 20.2	static	M	2	A	mortality			40(30)		110(70)	Janssen Pharmaceutica, 1993c	1 2
$CdCl_2$	*Daphnia magna*	synthetic water; T 25; pH 8; H 11; DO 69%	semi-static	M	1	A	mortality				1900		Kühn et al., 1989	2
					21	C	reproduction	0.6	1	1.9				2
$CdCl_2$	*Daphnia magna*	aerated well water; DO >70%; pH 8; T 22; H 300; Al 250	continuous	M	21	C	mortality	4.3	1			7.2 (100)	Knowles and McKee, 1987	2
						C	reproduction	0.8	1		2.1(54)			2
$CdCl_2$	*Aplexa hypnorum*	Lake Superior water; DO 7.5; T 24	continuous flow	M									Holcombe et al., 1984	
	mature		H 44.8; Al 40.7; pH 7.4-7.5;		4	A	mortality					93		2
	immature		H 45.3; Al 40.3; pH 7.3-7.6		26	C	growth	4.41	1		4.79(47)			2
						C	mortality+hatchability	4.41	1		4.79(62)			2
$CdCl_2$	*Physa integra*	untreated Lake Superior water; pH 7.1-7.7; T 15; DO 10-11; H 44-48; Al 40-44; Ac 1.9-3	semi-static	M	21	C	mortality	8.3	1				Spehar et al., 1978	2
	Ephemerella sp.				28	C						10.4		2
					28	C						3(70)		2
CdO (filtrate of dispersion)	*Daphnia magna*	OECD 202-test medium; pH 8.05; DO 9.3; H 226; T 19.1	static	M	2	A	mortality					750(70)	Janssen Pharmaceutica, 1993d	2
$CdCl_2$	*Daphnia magna*	dechlorinated Montreal city water; pH 6.95; T 20; Al 80; H 130; Cd 1µg L^{-1}	continuous flow	N	1.5	A	mortality					203.8	Attar and Maly, 1982	2
					2	A						58.16		2
					2.5	A						15.8		2
					3	A						8.88		2
					4	A						5		2
$CdCl_2$	*Daphnia magna*	synthetic water; static; pH 8-8.5	H 160-180; T 20	N	2	A	mortality					38	Lewis and Horning, 1991	2
	Daphnia pulex		H 80-100; T 20									42		2

Table 3.197 continued overleaf

Table 3.197 continued Toxicity to aquatic invertebrates. All underlined data are selected to discuss the critical concentrations (Table 3.196). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effect assessment

Test substance	*Organism*	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC (µg L-1)	Cat.*	LOEC (µg L-1) (%effect)	EC50 (µg L-1) (%effect)	LC50 (µg L-1) (%effect)	References	RI
$CdCl_2$	*Daphnia magna*	soft well water; H 26-32; Al 30; T 20; DO 7.5-9; pH 6.6-7.8	static	M	2	A	mortality					36	Schuytema et al., 1984	2
			continuous			A						49		2
		slurry; T 20; H 15-23; Al 10-15; DO 7.5-9; pH 6.1-7.1 (LC50 expressed on dissolved fraction)	100 mg L^{-1} total solids, static			A						39		2
			continuous			A						144		2
			1000 mg L^{-1} total solids, static			A						44		2
			continuous			A						97		2
Cd	*Ceriodaphnia dubia*	reconstituted soft water: T 14-16°C; DO 9.3-11.4 mg L^{-1}; Cd(BG) <0.2 µg L^{-1}; pH 6.3-7.6; H 20	static renewal	M	7	C	survival	19	1	41			Jop et al., 1995	2
						C	reproduction	10	1	19				2
		river water: T 14-16°C; DO 8.7-12.2 mg L^{-1}; Cd(BG) <4 µg L^{-1}; pH 6.6-7.4; H 16-28	static renewal	M	7	C	survival	19	1	39				2
							reproduction	11	1	19				2
$CdCl_2$	*Daphnia magna*	well water: T 20±2°C; DO 4.9-7.9; Cd(BG) 0.08	static renewal	M	21	C	reproduction (mean number of young per adult)						Chapman et al., 1980	
		pH 7.5, H 53								0.29				3
		pH 7.9, H 103						0.16	3	0.28				3
		pH 8.2, H 209						0.21	3	0.91				3
Cd	*Hyalella azteca*	well water: T 23°C; pH 7.8; H 280	flow-through	M	42	C	survival	0.51	1	1.9			Ingersoll and Kemble, 2000	3
							reproduction	1.9	1	3.2				3
	Chironomus tentans			M	20	C	weight	5.8	1	17.4				3
							biomass	5.8	1	17.4				3
							%emergence	5.8	1	17.4				3
							%hatch	5.8	1	17.4				3

Table 3.197 continued overleaf

Table 3.197 continued Toxicity to aquatic invertebrates. All underlined data are selected to discuss the critical concentrations (Table 3.196). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effect assessment

Test substance	*Organism*	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC (µg L-1)	Cat.*	LOEC (µg L-1) (%effect)	EC50 (µg L-1) (%effect)	LC50 (µg L-1) (%effect)	References	RI
$CdCl_2$	*Daphnia magna*	unchlorinated, carbon filtered well water, aerated to saturation; H 240; Al 230; pH 8; DO >5; T 23; Cd < 0.01 µg Cd/L	static	N	2	A	mortality					178	Elnabarawy et al., 1986	3
	Daphnia pulex					A						319		3
	Ceriodaphnia reticulata					A						184		3
	Daphnia magna		semi-static		14	C	reproductive impairment	2.5	1		7.5 (75)			3
	Daphnia pulex					C		7.5	1	25 (32)				3
	Ceriodaphnia reticulata				7	C		0.25	1	0.75 (20)				3
$CdCl_2$	*Daphnia magna*	20 µm cloth filtered Lake Superior water; pH 7.7; H 45.3; Al 42.3; DO 9; T 18;	semi-continuous flow; without food	N	2	A	mortality					65	Biesinger and Christensen, 1972	3
			with food		21	C	mortality					5		3
						C	weight/animal	1	3					3
						C	protein conc./animal	1	3					3
						C	GOT activity/animal			1(15)				3
$CdCl_2$	*Daphnia pulex*	Whatman N° 1 filtered Lake Champlain water; pH 7.7; Al 42.4; H 65; Cd < 1µg L^{-1}	static	N	3	A	mortality					62	Bertram and Hart, 1979	3
					4	A	mortality					47		3
			semi-continuous flow		104	C	longevity	1	3		5(57)			3
						C	brood size			1(37)LT				3
						C	generation time in days			1(19)LT				3
$CdCl_2$	*Daphnia magna*	Dutch standard water; T 19	semi-static H 200	M(>20µg L^{-1})	2	A	mortality					30	Canton and Slooff, 1982	3
			H 100		2	A	mortality					30		3
$CdSO_4$	*Ceriodaphnia dubia*	Synthetic water; H 90; Al 65; T 25	static	N	7	C	mortality	1.5	1	2(40)		3(70)	Winner, 1988	3
	Daphnia magna					C	reproduction	2	1	3(30)				3

Table 3.197 continued overleaf

Table 3.197 continued Toxicity to aquatic invertebrates. All underlined data are selected to discuss the critical concentrations (Table 3.196). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effect assessment

Test substance	*Organism*	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC (µg L-1)	Cat.*	LOEC (µg L-1) (%effect)	EC50 (µg L-1) (%effect)	LC50 (µg L-1) (%effect)	References	RI
$CdCl_2$	*Daphnia magna*	NPR synthetic water; pH 8.4; T 20; H 200	semi-static	N	21	C	intrinsic rate of natural increase	1	1	1.8(32.5)	32(100)		Van Leeuwen et al., 1985	3
						C	mortality	1	1	1.8 (17)		3.2 (88)		3
		50 µm filtered and sterilised Lake IJssel water; pH 8.1; T 20; H 224	semi-continuous flow	M	21	C	yield			0.3(36)LT				3
			semi-static	N	21	C	intrinsic rate of natural increase	3.2	1	10 (14.5)	32 (100)			3
$CdCl_2$	*Daphnia galeata mendotae*	10 µm filtered Lake Michigan water; T 18.5	semi-continuous flow	N	154	C	carrying capacity				7.7(50)		Marshall, 1978	3
						C	number of individuals	2	1	4(23)	8(58)			3
		H 120				C	average biomass							
						C	average birth rate	2	1	4(9)				3
						C	average death rate	2	1		4(71)			3
						C	brood size	2	1		4(70)			3
						C	dry weight	2	1	4(36)	5(54)			3
						C	life expectancy	4	1		8(71)			3
											5(50)			3
$CdCl_2$	*Daphnia magna*	culture medium; pH8.4; H 150; T 20	semi-continuous flow	N	25	C	mortality	2.5	4			10(60)	Bodar et al., 1988a	3
						C								
						C	biomass production/female	2.5	4		10(71)			3
							intrinsic rate of natural increase	5	3	10(34)	20(72)			3

Table 3.197 continued overleaf

Table 3.197 continued Toxicity to aquatic invertebrates. All underlined data are selected to discuss the critical concentrations (Table 3.196). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effect assessment

Test substance	*Organism*	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC (µg L-1)	Cat.*	LOEC (µg L-1) (%effect)	EC50 (µg L-1) (%effect)	LC50 (µg L-1) (%effect)	References	RI
$CdCl_2$	*Simocephalus serrulatus*	synthetic water; H 39-48; Al 26-42; Ac 1.9-5.7; pH 7-7.9	static T 20; <1d old	M	2	A	mortality					<u>24.5</u>	Spehar and Carlson, 1984	3
	Gammarus pseudolimnaeus	unfiltered river water; static; H 55-79 Ac 2-4.2; Al 41-65; pH 7.2-7.8	T 17; 0.1g		4	A						<u>68.3</u>		3
	Daphnia magna		T 20; <1d old		2	A						<u>166</u>		3
	Ceriodaphnia reticulata		T 20; <1d old		2	A						<u>129</u>		3
					9	C	reproduction	<u>3.4</u>	1	<u>7.2</u>				3
	Simocephalus vetulus		T 20; <1d old		2	A	mortality					<u>89.3</u>		3
	Simocephalus serrulatus		T 20; <1d old		2	A						<u>123</u>		3
	Gammarus pseudolimnaeus		T 17; 0.1g		4	A						<u>54.4</u>		3
	Hyalella azteca		T 7; 1µg		4	A						<u>285</u>		3
	Paraleptophlebia praepedita		T 12; 2µg		4	A						<u>449</u>		3
$CdCl_2$	*Dugesia sp.*	non aerated spring water; T 23; H 20	static	N	4	A	mortality					<u>4,900</u>	Fennikoh et al., 1978	3
	Cyclops sp.					A						<u>340</u>		3
	Cypridopsis sp.					A						<u>190</u>		3
	Hyalella sp.					A						<u>85</u>		3
	Procambarus sp.					A						<u>5,000</u>		3
$CdCl_2$	*Daphnia magna*	Dutch Standard water NPR 6503 (1980); pH 8.4; H 150; T 20	semi-continuous flow	N	2	A	mean survival time of embryos			1000(37) (LT)	10000(87)		Bodar et al., 1989	3

Table 3.197 continued overleaf

Table 3.197 continued Toxicity to aquatic invertebrates. All underlined data are selected to discuss the critical concentrations (Table 3.196). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effect assessment

Test substance	Organism	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC (µg L-1)	Cat.*	LOEC (µg L-1) (%effect)	EC50 (µg L-1) (%effect)	LC50 (µg L-1) (%effect)	References	RI
$CdCl_2$	*Daphnia magna*	Dutch Standard water NPR 6503 (1980); pH 8.4; H 150; T 20	semi-continuous flow	N	14	C	body weight				1(56)		Bodar et al., 1988b	3
						C	consumption rate	1	1		5(60)			3
$CdSO_4$	*Tubifex tubifex*	dilution water for BOD without phosphate buffer	pH 6.85; H 34.2; Al 1.5	N	2	A	mortality					31	Brkovic-Popovic and Popovic, 1977	3
		dilution water for BOD with phosphate buffer:	pH 6.85; H 34.2; Al 22.5			A						45		3
		drinking water	pH 7.32; H 261; Al 234; T 20			A						720		3
$Cd(NO_3)_2$	*Simocephalus serrulatus*	filtered (0.15µm) well water; Cd 0.023 µg L^{-1}; pH 6.5; H 11.1; Al 9.7; T 22; DO >80%	filtered well water	N	2	A	mortality					7	Giesy et al., 1977	3
			filtered well water + F1**			A						8.6		3
			filtered well water + F2**			A						12		3
			filtered well water + F3**			A						16.5		3
			filtered well water + F4**			A						3.6		3
		Skinface pond water; filtered through 0.15µm; Cd 0.02 µg L^{-1}; pH 5.6; H 10; Al 4; T 22; DO >80%				A						35		3
Cd-solution	*Gammarus pulex*	dechlorinated tap water; pH 7.7; T 12; H 152; DO >96%	continuous flow	M	4	A	mortality					20	Williams et al., 1985	3
	Asellus aquaticus					A						600		3
	Baetis rhodani					A						500		3
	Physa fontinalis					A						800		3
	Limnodrilus hoffmeisteri					A						2,400		3
	Ephemerella ignita					A						13,000		3
	Leuctra inermis					A						32,000		3
	Polycelis tenius					A						74,000		3
	Chironomus riparius					A						30,000		3
	Hydropsyche angustipennis					A						52,000		3

Table 3.197 continued overleaf

Table 3.197 continued Toxicity to aquatic invertebrates. All underlined data are selected to discuss the critical concentrations (Table 3.196). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effect assessment

Test substance	*Organism*	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC (µg L-1)	Cat.*	LOEC (µg L-1) (%effect)	EC50 (µg L-1) (%effect)	LC50 (µg L-1) (%effect)	References	RI
$CdCl_2$	*Daphnia magna*	well water; T 19.5; H 32-76; Al 31-69; pH 6.8-7.8	semi-static <4h old	M	2	A	mortality					109	Nebeker et al.,	3
			<24h old			A						46	1986a	3
			1d old			A						48		3
			2d old			A						164		3
			3d old			A						63		3
			4d old			A						82		3
			5d old			A						49		3
			6d old			A						23		3
$CdCl_2$	*Daphnia pulex*	synthetic water; pH 7.8; T 22	static; H 120; Al 110	N	2	A	mortality					90	Hall et al., 1986	3
	Daphnia magna					A						35		3
	Ceriodaphnia reticulata					A						110		3
	Daphnia pulex	well water; pH 7.7; T 22	static; H 200; Al 140;		2	A						90		3
	Daphnia magna					A						65		3
	Ceriodaphnia reticulata					A						80		3
$CdSO_4$	*Daphnia magna*	synthetic water (ISO 1977); pH 7.8; H 200; T 20-23	static	N	1	A	mortality					309	Dave et al., 1981	3
					2	A						69		3
					3	A						40		3
$CdSO_4$	*Cyclops abyssorum prealpinus*	5µm filtered Lake Monate water; pH 7.2; H 40.7; T 10		N	2	A	mortality					3,800	Baudouin and Scoppa, 1974	3
	Eudiaptomus padanus padanus					A						550		3
	Daphnia hyalina					A						55		3
$CdCl_2$	*Daphnia magna*	synthetic water; T 20; pH 8.3; H 250	semi-static; small neonates	N	2	A	mortality					98	Enserink et al., 1990	3
			large neonates			A						294		3

Table 3.197 continued overleaf

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Test substance	Organism	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC (µg L-1)	Cat.*	LOEC (µg L-1) (%effect)	EC50 (µg L-1) (%effect)	LC50 (µg L-1) (%effect)	References	RI
$CdCl_2$	*Daphnia magna*	synthetic water; T 20; pH 8.4; H 150	static;										Bodar et al., 1990	
			pre-exposed to control	N	2	A	mortality					320		3
			pre-exposed to 1µg Cd/L		2	A						391		3
			pre-exposed to 5 µg Cd/L		2	A						424		3
Cd-solution	*Physa gyrina*	synthetic water; T 20-22; DO 10-14; H 200; Al 130; pH 6.73; Cd < 0.5µg L^{-1}	static	N	1	A	mortality					7,600	Wier and Walter, 1976	3
	mature				2	A						4,250		3
					4	A						1,370		3
					9.5	A						830		3
					2	A						690		3
	immature				4	A						410		3
$CdCl_2$	*Brotia hainanensis*	aerated artificial pond water; T 20: pH 7.4;H 200	upstream adolescents	N	4	A	mortality					15,210	Lam, 1996	3
			downstream adolescents			A						35,940		3
			upstr. juv. <2d			A						770		3
			downstr. juv. <2d			A						1,090		3
			upstr. juv. >7d			A						1,180		3
			downstr. juv. >7d			A						1,220		3
$CdSO_4$	*Daphnia magna*	filtered aerated tubewell hard water; H 240, T 13; pH 7.6; DO 5.6; Al 400	static	M	2	A	mortality					1,880	Khangarot and Ray, 1989	3
$CdSO_4$	*Acroneuria lycorias*	carbon filtered Lake Superior tap water; pH 7-7.3; T 18.5; DO 8; Al 54-60; Ac 6-12; H 52-56		N	14	A	mortality					32,000	Warnick and Bell, 1969	3
	Ephemerella subvaria				4	A						2,000		3
	Hydropsyche betteni				10	A						32,000		3

Table 3.197 continued overleaf

Table 3.197 continued Toxicity to aquatic invertebrates. All underlined data are selected to discuss the critical concentrations (Table 3.196). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effect assessment

Test substance	Organism	Medium	Test conditions	Nominal/ Measured	Duration (d)	Acute/ chronic	Endpoint	NOEC (µg L-1)	Cat.*	LOEC (µg L-1) (%effect)	EC50 (µg L-1) (%effect)	LC50 (µg L-1) (%effect)	References	RI
Supporting data														
$CdCl_2$	*Pteronarcys dorsata*	untreated Lake Superior water; pH 7.1-7.7; T 15; DO 10-11; H 44-48; Al 40-44; Ac 1.9-3	semi-static	M	28	C	mortality	238 (HT)					Spehar et al., 1978	4
	Hydropsyche betteni				28	C		238 (HT)						4
$CdCl_2$	*Daphnia magna*	unchlorinated, carbon filtered well water, aerated to saturation; H 240; Al 230; pH 8; DO >5; T 23; Cd < 0.01 µg L^{-1}	semi-static	N	14	C	mortality	25(HT)					Elnabarawy et al., 1986	4
	Daphnia pulex					C		25(HT)						4
	Ceriodaphnia reticulata				7	C		25(HT)						4
$CdCl_2$	*Daphnia magna*	20 µm cloth filtered Lake Superior water; pH 7.7; H 45.3; Al 42.3; DO 9; T 18;	semi-continuous flow	N	21	C	reproductive impairment			0.17 (16)	0.7		Biesinger and Christensen, 1972	4
$CdCl_2$	*Daphnia magna*	Dutch standard water; T 19	semi-static H200	M(>20µg L^{-1})	20	C	mortality	0.37	5			0.67	Canton and Slooff, 1982	4
					20	C	reproduction	0.5	1		4.2			4/3
Cd	*Hyalella azteca*	well water: T 23°C; pH 7.8; H 280	flow-through	M	42	C	length	3.2 (HT)					Ingersoll and Kemble, 2000	4
							weight	3.2 (HT)						4
							biomass	3.2 (HT)						4
	Chironomus tentans			M	20	C	survival	17.4 (HT)						4
							number of eggs	17.4 (HT)						4
$CdSO_4$	*Daphnia magna*	synthetic water; H 90; Al 65; T 25	static	N	7	C	mortality	3(HT)					Winner, 1988	4
	Ceriodaphnia dubia					C	reproduction	0.5	2	1(45)				4/3
$CdCl_2$	*Daphnia magna*	hard synthetic water; H 250; T 20; DO 66-100%; pH 7.2-8.2	semi-static	N	16	C	growth	1.6(HT)					Berglind, 1985	4
$CdCl_2$	*Tetrahymena sp.*	Osterhouts medium		N	15 min.	A	ciliate chemotactic response inhibition			250	475		Berk et al., 1985	4

T Temperature (°C); Al Alkalinity (mg $CaCO_3$/L); ** Organic fractions F3 0.0032 - 0.0009 µm;
H Hardness (as mg $CaCO_3$/L); Ac Acidity (mg $CaCO_3$/L); F1 > 0.0183 µm; F4 < 0.0009 µm;
DO Dissolved oxygen (mg O_2/L); * NOEC classification (see section 3.2.1.2); F2 0.0183 - 0.0032 µm; GOT Glutamic oxalacetic transaminase;
LT LOEC value found at lowest concentration tested; HT NOEC value found at highest concentration tested

3.2.2.4 Toxicity to primary producers

Table 3.198 Selected data with RI 1-3 for Cd toxicity to primary producers. Twenty-nine tests were reviewed from 21 source documents and 20 tests were selected. All tests were considered to represent chronic exposure to Cd

	Min	Median	Max	n
NOEC (μg L^{-1})	0.85	6.9	31	8
LOEC (μg L^{-1})	1.9	18	100	9
E(L)$C_{x\geq50}$ (μg L^{-1})	6.1	59	1,000	12

Various studies reveal the toxicity of Cd, added as soluble salts, on algae, diatomic species, floating weeds and bacteria (see **Table 3.198**). Two studies are dealing with toxicity of CdO following the OECD-201 protocol for testing growth inhibition of algae (Janssen Pharmaceutica, 1993f, LISEC 1998b). These tests were performed in filtrates (0.1 µm or 0.45 µm pore size) of a CdO dispersion made up in the test medium. The metal oxide was dispersed in the test medium and membrane filtered. The Cd concentration in the filtrate was analysed and dilutions of the filtrate in test solution were inoculated with algae cells. Growth rate *of Selenastrum capricornutum* was reduced by 50% at Cd concentrations between 80-120 µg L^{-1} with CdO as test substance (LISEC 1998b, Janssen Pharmaceutica 1993f). A similar test was performed with filtrates of a dispersion of metallic Cd powder (LISEC 1998a, Janssen Pharmaceutica 1993e). The EC_{50} values for growth were 70-89 µg L^{-1} with Cd as test substance, similar to the values obtained with the CdO filtrates. This indicates that the filtrates of the CdO and metallic Cd dispersions have the same Cd speciation, i.e. predominantly Cd^{2+} ions.

Most reported LOEC values for algae or diatomic species range between 10 and 50 µg L^{-1} with some exceptions. Four effect concentrations were noted below that range. In general terms, metal toxicity to algae increases with decreasing nutrient supply, decreasing cell density and with decreasing concentrations of chelating agents (Chen and Lin, 1997). Those studies in which synthetic chelates have been used in solution are omitted from this review except when these concentrations are low enough to warrant little Cd complexation. It appears that Cd toxicity is far more pronounced in flow through systems compared to static experiments (Chen and Lin, 1997). The type of Cd^{2+} salts (Cl, NO_3^-, acetate or carbonate) was found not to affect Cd^{2+} toxicity (Wong et al., 1979).

Wong and co-workers (1979) followed growth (as cell number) in static conditions of *Ankistrodesmus falcatus* during 10 days after applying Cd^{2+} salts to a synthetic medium. The cell number was reduced to 60% of the control after 6 days exposure to 1,000 µg L^{-1}. At 500 µg L^{-1}, no toxic effect was yet clear. A NOEC of Cd at 500 µg L^{-1} is rather high compared to that of other studies (see **Table 3.199**). This could be attributed to a species effect: in a further comparative study on photosynthetic activity ($^{14}CO_2$ uptake) of four algae species (*Ankistrodesmus falcatus, Chlorella vulgaris, Scenedesmus quadricauda, Chlorella pyrenoidosa*) it was found that *A. falcatus* and *C. vulgaris* are rather tolerant to Cd (EC_{50} values at 700 and 600 µg L^{-1}) whereas *S. quadricauda* or *C. pyrenoidosa* are sensitive species (EC_{50} values below 20 and at 100 µg L^{-1}, Wong et al., 1979). Another factor that may explain the high NOEC in this test is the cell density. Metal toxicity often reduces at higher cell density because an increasing amount of metal becomes immobilised in the algal cell wall. A maximal initial cell density of 10,000 cells mL^{-1} is defined in the OECD-201 algal growth inhibition tests. The initial cell density in the test *A. falcatus* is about 20 fold above this limit (190,000 cells mL^{-1}). Therefore, we chose to define this test as unreliable. Klass et al. (1974) and Bringmann and Kühn (1980) also illustrate the sensitivity of *Scenedesmus quadricauda* to Cd. In the study of Klass et al. cell number was reduced to 48% of control at 6.1 µg L^{-1}. In this static experiment, cell density was rather low (ca. 10^5 cells/mL) and water hardness also low (25 mg L^{-1}), both factors contributing to high sensitivity. A drawback in the data interpretation of the test results is that average cell number (between 2-16 days after exposure) of the growing population is used as endpoint rather than cell number at one occasion. Bringmann and Kühn (1980) report a toxicity threshold concentration of Cd to *Scenedesmus quadricauda* of 31 µg L^{-1}. The effect at that concentration is very low (3%) and is considered as a NOEC here. Another *Scenedesmus* species (*S. subspicatus*) is affected by Cd concentrations around 30 µg L^{-1} (EC_{10} values in this case, Kühn and Pattard, 1990).

Toxicity of Cd to *Chlorella vulgaris* in static tests was reported by Wong et al. (1979), see above, Rosko and Rachlin (1977), Jouany et al. (1983) and Kosakowska et al. (1988). The study of Rosko and Rachlin reports an EC_{50} value for growth at 60 µg L^{-1} after 33 days of exposure. Neither pH (which increased from 7.5 to 9.5) nor Cd concentrations were monitored during growth in this static test. In the tests of Jouany et al. (1983) EC_{50} values for growth are 550-1,220 µg L^{-1}. In these tests, cell density was about two orders of magnitude higher than in the test of Rosko and Rachlin (1977). The test systems of Jouany et al. (1983) were either static or pseudodynamic (periodic addition of fresh medium). The Cd toxicity in the latter system was twofold higher (EC_{50} value twofold lower) than in the static system. In the tests of Kosakowska et al. (1988), the chlorophyll a content of the static system reduced by 77% compared to control in the presence of 393 µg Cd/L, the only concentration tested.

A very high sensitivity to Cd was reported for the diatomic species *Asterionella formosa* by Conway (1978). The test system was dynamic (continuous culture system, also called chemostat) in which the Cd addition starts when steady state conditions are reached, i.e. when algae growth rate matches the dilution rate. In an artificial medium matching the Lake Michigan composition, Cd reduced growth rate by an order of magnitude when measured steady state Cd concentration reached 2 µg L^{-1}. Unfortunately, the authors did not include a zero Cd treatment to show that steady state conditions were maintained during a further 9 days after initial steady state conditions. Therefore, these data are not included here. Nevertheless, static studies with the same diatomic species in (almost) the same medium revealed that significant inhibition of growth by 17% is reached at 4.1 µg L^{-1} after 24 hours (Conway and Williams, 1979). Another diatomic species, *Fragilaria crotonensis*, was unaffected by Cd up to 8.5 µg L^{-1}, the highest concentration tested.

The alga *Selenastrum capricornutum* is used in various standard algae tests (U.S. EPA, 1985, OECD, 1984). The static studies reported by Bartlett et al. (1974), Turbak et al. (1986), Lin et al. (1996), Chen and Lin (1997), Janssen Pharmaceutica (1993e&f) and LISEC (1998a,b) yield EC_{50} values for that species ranging between 18 and 341 µg L^{-1}. Lin et al. (1996) indicated that most standard tests have high P concentrations (> 0.1 mg L^{-1}) and showed that sensitivity to Cd increases tenfold under P limiting conditions. Chen and Lin (1997) compared Cd toxicity to *Selenastrum capricornutum* between a continuous system and the U.S. EPA static test. In an artificial medium, the growth rate declined to 50% of control at 13 µg L^{-1} in the continuous system within 24 hours. In the static experiment, the EC_{50} value for growth was 341 µg L^{-1}. The medium composition differed in the concentrations of $NaNO_3$, KH_2PO_4 and Na_2EDTA. The EDTA concentrations in both systems were low enough (below 1 µM) to ensure that almost no Cd is complexed by EDTA. Solution speciation calculation revealed that the difference in EC_{50} values between static and continuous systems is similar, whether based on total Cd concentration or on free metal (Cd^{2+}) concentration.

Lawrence et al. (1989) used a serial construction of two continuous systems. In the first continuous system, the green alga *Chlamydomonas reinhardii* was grown and that suspension was pumped into the second where the protozoan *Tetrahymena vorax* was grown. Once steady state cell numbers were reached in both continuous systems, Cd was added at various concentrations. LOEC's on cell number after 7 days were 10 µg L^{-1} and it appeared that the algae were a bit more sensitive to Cd than the protozoa. As a result of reduced grazing, the cell number of algae temporarily increased in the second continuous system at 40 µg L^{-1} Cd. Acclimation of the algae to 20 µg L^{-1} allowed the population to respond less drastically to 40 µg L^{-1} than increasing Cd from 0 to 40 µg L^{-1} in one step. It is unclear why the authors deliberately omitted Zn from the artificial solutions. It is likely that in Zn deficient conditions, Cd toxicity will be more pronounced. In a continuous *in situ* culture, shifts in populations of phytoplankton were observed upon Cd exposure. At Cd concentrations ranging between 2.9 and 4.2 µg L^{-1} (measured concentrations, almost all Cd soluble), cell densities of two *Dinobryon* species were reduced to less than 10% of control values. The densities of other plankton species (*Elakatothrix sp.* and *Rhabdoderma gorskii*) were increased significantly above those in the control systems (DeNoyelles et al., 1980). Since only one concentration was tested above the background, the data of this experiment cannot be used for the current risk assessment.

Varying solution pH between 4.3 and 6.2 marginally affected Cd toxicity to the green alga *Coelastrum proboscideum*. LOEC values were found at 27 µg L^{-1} (Müller and Payer, 1979).

Effects of Cd to duckweed (*Lemna paucicostata*) were assessed in three artificial media at varying pH (Nasu and Kugimoto, 1981). Toxic effects on the number of fronds after 1 week of growth started at 10 µg L^{-1} Cd and Cd toxicity was generally higher at higher pH.

In conclusion, Cd can affect primary producers in the 1-10 µg L^{-1} range but no tests showed toxicity below 1 µg L^{-1}. At nutrient limiting conditions and low cell density, species are likely to be most sensitive to Cd. With one exception, all tests were performed in artificial media, some of which had very similar composition as freshwater samples.

Table 3.199 Toxicity to aquatic primary producers. All underlined data are selected to discuss the critical concentrations (Table 3.198). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	Organism	Medium	Test conditions	Nominal/ measured	Duration (d)	Endpoint	NOEC (µg L^{-1})	Cat.*	LOEC (µg L^{-1}) (%effect)	EC_{50} (µg L^{-1}) (%effect)	References	RI
Cd	*Selenastrum capricornutum*	modified ISO 6341 medium; 0.2 µm filtered; T 20.3-25.6; pH 7.7-10.4 H 49	static	M	3	cell number	2.4	1	5(11)	23	LISEC, 1998a	1
filtrate of dispersion						growth rate	9.0	4		89		1
CdO	*Selenastrum capricornutum*	modified ISO 6341 medium; 0.2 µm filtered; H 49;pH 7-10		M	3	cell number			9.5(37)LT	18	LISEC, 1998b	1
filtrate of dispersion						growth rate	10.9	1	48(39)	79		1
Cd filtrate of dispersion	*Selenastrum capricornutum*	AM; H 23; pH 7-9		M	3	growth rate	15	4	60(46)	70	Janssen Pharmaceutica, 1993e	1
CdO filtrate of dispersion	*Selenastrum capricornutum*	AM H 23; pH 7-8		M	3	growth rate	50	1		120	Janssen Pharmaceutica, 1993f	1
$CdSO_4$	*Coelastrum proboscideum*	AM;H 32;T 31;pH 5.3;	static	M	1	biomass	6.3	1	27(36)		Müller and Payer 1979	2
$CdCl_2$	*Asterionella formosa*	AM; pH 8; H 121	static	M	1	growth rate	0.85	2	1.9(18)LT		Conway and Williams 1979	2
$CdCl_2$	*Chlamydomonas reinhardii*	AM;H 42;pH 6.7; T 20	continuous	N	7	steady state cell number	7.5	1	10(22)		Lawrence et al., 1989	3
$CdCl_2$	*Scenedesmus subspicatus*	AM;H 60;T 24; pH 8	static	N	3	biomass				62	Kühn and Pattard 1990	3
						growth rate (0-3d)				136		3
$Cd(NO_3)_2$	*Scenedesmus quadricauda*	AM; pH 7	static; T 27; H 55	N	7	biomass (OD)	31	1			Bringmann and Kühn, 1980	3
$CdCl_2$	*Lemna paucicostata*	AM; T 25	static;	N	7	number of fronds					Nasu and Kugimoto, 1981	
			pH > 6; H 120				5	2	10(19)			3
			pH 5.1; H 120				10	3	100(35)			3
			pH 5.1; H 700				10	3	50(20)			3
$Cd(NO_3)_2$	*Chlorella vulgaris*	AM; H=34;T=20	static	N	1	$^{14}CO_2$ uptake				600(50)	Wong et al., 1979	3
		AM; H=34;T=20	static		1					700(50)		3
	Scenedesmus quadricauda	AM; H=34;T=20	static		1					20(80)LT		3
	Chlorella pyrenoidosa	AM; H=34;T=20	static		1					100(50)		3

Table 3.199 continued overleaf

Table 3.199 continued Toxicity to aquatic primary producers. All underlined data are selected to discuss the critical concentrations (Table 3.198). Bold data are used to estimate the HC_5 (Table 3.206). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	Organism	Medium	Test conditions	Nominal/ measured	Duration (d)	Endpoint	NOEC ($\mu g\ L^{-1}$)	Cat.*	LOEC ($\mu g\ L^{-1}$) (%effect)	EC_{50} ($\mu g\ L^{-1}$) (%effect)	References	RI
$CdCl_2$	*Selenastrum capricornutum*	AM;H=15;pH=7.1;T=24	static	N	4	biomass			50(32)LT		Bartlett et al., 1974	3
$CdCl_2$	*Selenastrum capricornutum*	AM; pH 7.6; H 15; T 24	continuous static	N	1 1	growth rate growth rate				13 341	Chen and Lin, 1997	3 3
$CdCl_2$	*Selenastrum capricornutum*	AM; pH 7.5; H 15;T24;	static	N	1	growth rate				32	Lin et al., 1996	3
$CdCl_2$	*Selenastrum capricornutum*	AM;H=15;pH=7.1	static	N	14-21	biomass				57	Turbak et al., 1986	3
Supporting data												
$CdCl_2$	*Scenedesmus quadricauda*	AM; H 28; T 21-30	static	N	2-16	average cell number	0.6	1		6.1(52%)	Klass et al., 1974	4/3
$CdCl_2$	*Fragilaria crotonensis*	AM; pH 8; H 121	static	M	1	growth rate	8.5HT				Conway and Williams 1979	4
$Cd(NO_3)_2$	*Ankistrodesmus falcatus*	AM; H=34;T=20	static	N	6	cell number	500	3		1000(60%)	Wong et al., 1979	4/3
$CdCl_2$	*Chlorella vulgaris*	AM;H=82;T=21	static	N	33	cell number	0.75	3	18(28)	60(50)	Rosko and Rachlin, 1977	4/3/3
$Cd(NO_3)_2$	*Chlorella vulgaris*	AM Lefevre Czarda; T 20	static pseudo-dynamic	N	4 4	biomass (OD)				1220 550	Jouany et al., 1983	4 4
Cd-salt	*Dinobryon bavaricum* *Dinobryon sertularia* *Elakatothrix sp* *Rhabdoderma gorskii*	lake water	in situ continuous; epilimnion	M	12	cell density cell density			 3.5(+80%) 3.5(+40%)	3.5(>90) 3.5(>90)	DeNoyelles F. et al., 1980	4 4 4 4
$CdCl_2$	*Chlorella vulgaris* *Anabaena variabilis*	AM;H33;T 28	static	N	7	chlorophyll a content				393(77)LT 393(79)LT	Kosakowska et al., 1988	4

T Temperature (°C);
H Water hardness (mg $CaCO_3$/L);
AM Artificial medium;
OD Optical density;
LT LOEC value found at lowest concentration tested
HT NOEC value found at highest concentration tested
* NOEC classification (see Section 3.2.1.2).

3.2.2.5 Discussion

Table 3.200 lists all toxicity data of primary producers, aquatic invertebrates and fish/amphibians. This data set contains all individual data (i.e. no species means) that were underlined in **Tables 3.195**, **3.197** and **3.199**. This selection is based on data quality, i.e. data with RI 1-3 only. The selected data are retrieved from 168 different tests. This selection of results is used in this section to identify the factors that affect Cd toxicity, i.e. type of organism and environmental conditions.

Table 3.200 Summary of selected Cd toxicity data (µg Cd/L). All data have RI≤3 and are underlined in Tables 3.195, 3.197 and 3.199

	NOEC (chronic tests only)				
	min	5th perc.	median	max	n
fish/amphibians	0.47	0.86	4.2	62	19
aquat. invertebrates	0.16	0.21	2.0	11	22
primary producers	0.85	1.4	6.9	31	8
	LOEC (chronic tests only)				
	min	5th perc.	median	max	n
fish/amphibians	0.78	1.7	11	132	20
aquat. invertebrates	0.28	0.29	1.9	25	19
primary producers	1.9	3.1	18	100	9
	E-LC$_{x\geq50}$ (chronic tests only)				
	min	5th perc.	median	max	n
fish/amphibians	3.4	4.8	20	650	7
aquat. invertebrates	1	1.7	5	32	14
primary producers	6.1	9.9	59	1,000	12
	E-LC$_{x\geq50}$ (acute tests only)				
	min	5th perc.	median	max	n
fish/amphibians	0.9	2	1,500	40,200	31
aquat. invertebrates	7	24.5	166	74,000	61

The summary of selected data from chronic Cd tests reveals that the sensitivity to Cd decreases as:

aquatic invertebrates > fish/amphibians> primary producers.

The LOEC values indicate a considerably lower sensitivity of algae towards Cd than invertebrates or fish/amphibians. However, many of the tests with algae are performed in static (batch) conditions where high LOEC/NOEC values are associated with high cell densities. The much higher sensitivity obtained in the continuous systems (chemostats) indicates that algae may indeed be sensitively affected in the µg L^{-1} range (Conway, 1978; Chen and Lin, 1997).

The toxic effects of Cd become pronounced above 1 µg L^{-1}. In the selected data set with RI ≤ 3, only 6 of the 48 LOEC values and 1 of the 125 E(L)C_{50} values can be found below 1 µg L^{-1}. Two of these data refer to tests on fish in soft water (< 28 mg $CaCO_3$/L). In the data with RI 4, at least three more effect concentrations are found below 1 µg L^{-1}. These data were considered as not reliable, mainly because Cd background concentrations were unknown. Detecting Cd in solution below about 0.5 µg L^{-1} is intricate with conventional methods (i.e. flameless atomic absorption spectrometry, detection limit ≈ 0.1µg L^{-1}). The source document of Rombough and Garside (1982) is the only that mentions details on pre-concentration steps. These authors found a LOEC at 0.78 µg L^{-1}, significantly above the background of 0.13 µg L^{-1}. More information should be gathered using more sensitive techniques such as Inductively Coupled Plasma, Mass Spectrometry (ICP-MS detection limits around 0.05 µg L^{-1}) to assess possible toxic effects of Cd in the < 0.5 µg L^{-1} range. Some authors however stressed that threshold toxic Cd effects may not be found in chronic studies with Cd (Marshall, 1978; Van Leeuwen et al., 1985).

3.2.2.6 The $PNEC_{water}$

3.2.2.6.1 The NOEC data

Different species sensitivity distributions (SSD's) can be calculated for different selections of the data since the NOEC values have attached information such as data quality (the Reliability Index, RI) and properties of the test (species, water characteristics and endpoint). All data with RI = 4 (unreliable) were not included because critical information of the test was lacking. Statistical properties of the selected NOEC data are given in **Table 3.201**. The selected NOEC data are summarised in **Table 3.202**.

Table 3.201 Summary of the NOEC values (µg Cd/L) of chronic tests in the aquatic compartment for various levels of reliability (RI, defined in the introduction of Section 3.2.2)

	NOEC				
	min	5^{th} perc. of NOEC data	median	max	n
RI 1-3	0.16	0.34	3.4	62	49
RI 1-2	0.47	0.60	4.2	62	21
RI 1			2.4		1

3.2.2.6.2 Species sensitivity distributions at different levels of data quality

There are enough data from all three trophic levels to calculate the $PNEC_{water}$ by the assessment factor method (AFM) using the lowest assessment factor 10 (TGD, 1996, p. 330). The lowest NOEC value with a RI ≤ 3 is 0.16 µg L^{-1}. This would yield a $PNEC_{water}$ = 0.016µg L^{-1} (see **Table 3.206**). Rather than making a risk assessment based on one single NOEC value, it is possible to use the statistical extrapolation method (TGD, 1996, p. 469) if enough NOEC data are available. This condition is certainly met in the case of Cd and is preferred over the assessment factor method. The $PNEC_{water}$, derived with the assessment factor method, is in the range of background concentrations of membrane filtered freshwaters. The Cd toxicity has not been tested in that range. Moreover, Cd concentrations below 0.1-0.2 µg L^{-1} are difficult to measure with conventional methods (see Section 3.2.2.4.).

To evaluate the toxicity data, the statistical extrapolation method is used (Aldenberg and Slob, 1993). The fifth percentile (HC_5), with 50% confidence, of a species sensitivity distribution is calculated using the software package ETX 1.3a (RIVM, Bilthoven, The Netherlands). The HC_5 is calculated for 4 different approaches of data selection. The first approach is by using all the data (see **Table 3.202**), without calculation of species geometric mean values. The second method is by calculating ‘geometric mean’ NOEC values for each species, resulting in one NOEC per species (see **Table 3.203**). The third approach is by calculating ‘geometric mean’ NOEC’s on a case-by-case basis (see **Table 3.204**). At a special workshop, held in January 2001, in the framework of the EU Existing Substances programme, it was agreed that “for comparable data on the same endpoint and species the geometric mean should be used as the input value for the calculation using the SSD. If this is not thought to be possible, perhaps because results that are considered valid, are too variable, then consider grouping and combining the values, e.g. by pH ranges, and using reduced numbers of values. The full data set could also be used if necessary”. Geometric mean NOEC’s are thus calculated for the same species and the same endpoint, tested in similar media¶. This approach does not result in one NOEC per species. The fourth approach is by selecting the lowest NOEC for each species, resulting in one NOEC per species (see **Table 3.205**).

¶ Test media are considered to be similar if the difference in pH is 5% or less, if the difference in water hardness is 15% or less and if the difference in dissolved oxygen concentration, aluminium concentration, and temperature is 10% or less. Biomass and total weight of young per female are considered to be the same endpoint. Pond fish and laboratory fry (*P. promelas*) are considered to be the same species.

Table 3.202 Selected NOEC data of effects of Cd in freshwater. Data derived from Tables 3.195, 3.197 and 3.199 within quality class RI 1-3

Organism	Phylum/class	Order	Family	Medium	H	Nominal/ Measured	Duration (d)	Endpoint	NOEC (µg L^{-1})	References	R.I.
Salmo gairdneri	*Chordata*	*Salmoniformes*	*Salmonidae*	aerated well water; T 10; O_2 7.5; pH 8-8.6	375-390	M	84	mortality	12	Lowe-Jinde and Niimi, 1984	2
Salmo gairdneri	*Chordata*	*Salmoniformes*	*Salmonidae*	synthetic water (ISO 1977) ; T 25; pH 8.3	100	N	50	median survival time	4	Dave et al., 1981	3
Oncorhynchus kisutch	*Chordata*	*Salmoniformes*	*Salmonidae*	sand filtered Lake Superior Water; continuous flow; DO 10.3; Al 41; Ac 3; pH 7.6	45	M	27	biomass	1.3	Eaton et al., 1978	2
Salvelinus fontinalis	*Chordata*	*Salmoniformes*	*Salmonidae*	sand filtered Lake Superior Water; continuous flow; DO 10.3; Al 41; Ac 3; pH 7.6	45	M	126	biomass	1.1	Eaton et al., 1978	2
Salvelinus fontinalis	*Chordata*	*Salmoniformes*	*Salmonidae*	sterilised Lake Superior water; pH 7-8; Al 38-46; Ac 1-10; DO 4-12; T 9-15	42-47	M	3 years	total weight of young /female of the 2nd generation	0.9	Benoit et al, 1976	2
Salvelinus fontinalis	*Chordata*	*Salmoniformes*	*Salmonidae*	reconstituted soft water: T 14-16°C; DO 9.3-11.4 mg L^{-1}; Cd(BG) <0.2 µg L^{-1}; pH 6.3-7.6; H 20	20	M	10	survival	8	Jop et al., 1995	2
Salvelinus fontinalis	*Chordata*	*Salmoniformes*	*Salmonidae*	river water: T 14-16°C; DO 8.7-12.2 mg L^{-1}; Cd(BG) <4 µg L^{-1}; pH 6.6-7.4; H 16-28	16-28	M	10	survival	62	Jop et al., 1995	2
Salmo salar	*Chordata*	*Salmoniformes*	*Salmonidae*	municipal water charcoal filtered and UV sterilised; BC 0.13 µg Cd/L; pH 6.5-7.3; T 5-10; DO 11.1-12.5; Al 14-17	19-28	M	46	total biomass	0.47	Rombough and Garside, 1982	2
Catostomus commersoni	*Chordata*	*Cypriniformes*	*Catostomidae*	sand filtered Lake Superior Water; continuous flow; DO 10.3; Al 41; Ac 3; pH 7.6	45	M	30	standing crop (biomass)	4.2	Eaton et al., 1978	2
Esox lucius	*Chordata*	*Esociformes*	*Esocidae*				28	biomass	4.2		2
Salvelinus namaycush	*Chordata*	*Salmoniformes*	*Salmonidae*				31		4.4		2
Salmo trutta (late eyed eggs)	*Chordata*	*Salmoniformes*	*Salmonidae*				61		1.1		2
Jordanella floridae	*Chordata*	*Cyprinodontiformes*	*Cyprinodontidae*	untreated Lake Superior water; T 25; DO 8.3; Al 42; Ac 2.4; pH 7.1-7.8	44	M	100	reproduction	4.1	Spehar, 1976	2
Brachydanio rerio	*Chordata*	*Cypriniformes*	*Cyprinidae*	synthetic water (changed ISO) ; T 24; DO >80%; pH 7.2	100	N	36	reproduction	1	Bresch ., 1982	3
Oryzias latipes	*Chordata*	*Beloniformes*	*Adrianichthyidae*	tap water; continuous flow; T 20	200	M	18	mortality and	6	Canton and Slooff, 1982	3
					100			abn. behaviour	3		
Xenopus laevis	*Chordata*	*Anura*	*Pipidae*	tap water; continuous flow; T 20	170		100	inhibition of larvae development	9		3
Pimephaless promelas	*Chordata*	*Cypriniformes*	*Cyprinidae*	pond water diluted with carbon filtered demineralised tap water; DO 6.5-6.6; pH 7.6-7.7; Al 145-161; Ac 8-12; T 16-27	201-204	M	60	reproduction (pond fish)	13	Pickering and Gast, 1972	3
								reproduction (laboratory fry)			
							60		14		3
Daphnia magna	*Arthropoda*	*Cladocera*	*Daphnidae*	50 µm filtered and sterilised Lake IJssel water; pH 8.1; T 20; H 224	224	N	21	intrinsic rate of natural increase	3.2	Van Leeuwen et al., 1985	3
Daphnia magna	*Arthropoda*	*Cladocera*	*Daphnidae*	NPR synthetic water; pH 8.4; T 20	200	N	21	mortality	1	Van Leeuwen et al., 1985	3

Table 3.202 continued overleaf

Table 3.202 continued Selected NOEC data of effects of Cd in freshwater. Data derived from Tables 3.195, 3.197 and 3.199 within quality class RI 1-3

Organism	Phylum/class	Order	Family	Medium	H	Nominal/ Measured	Duration (d)	Endpoint	NOEC (µg L-1)	References	R.I.
Daphnia magna	*Arthropoda*	*Cladocera*	*Daphnidae*	synthetic water; T 25; pH 8; DO 69%	11	M	21	reproduction	0.6	Kühn et al., 1989	2
Daphnia magna	*Arthropoda*	*Cladocera*	*Daphnidae*	Synthetic water; Al 65; T 25	90	N	7	reproduction	2	Winner, 1988	3
Daphnia magna	*Arthropoda*	*Cladocera*	*Daphnidae*	well water: T 20±2°C; DO 4.9-7.9; Cd(BG) 0.08; pH 7.9	103	M	21	reproduction	0.16	Chapman et al., 1980	3
Daphnia magna	*Arthropoda*	*Cladocera*	*Daphnidae*	well water: T 20±2°C; DO 4.9-7.9; Cd(BG) 0.08; pH 8.2	209	M	21	reproduction	0.21	Chapman et al., 1980	3
Daphnia magna	*Arthropoda*	*Cladocera*	*Daphnidae*	unchlorinated, carbon filtered well water, aerated to saturation; Al 230; pH 8; DO >5; T 23; Cd < 0.01 µg Cd/L	240	N	14	reproductive impairment	2.5	Elnabarawy et al., 1986	3
Daphnia magna	*Arthropoda*	*Cladocera*	*Daphnidae*	aerated well water; DO >70%; pH 8; T 22; Al 250	300	M	21	reproduction	0.8	Knowles and McKee, 1987	2
Daphnia magna	*Arthropoda*	*Cladocera*	*Daphnidae*	culture medium; pH8.4; T 20	150	N	25	biomass production/female	2.5	Bodar et al., 1988a	3
Daphnia magna	*Arthropoda*	*Cladocera*	*Daphnidae*	20 µm cloth filtered Lake Superior water; pH 7.7; Al 42.3; DO 9; T 18	45.3	N	21	weight/animal	1	Biesinger and Christensen, 1972	3
Daphnia pulex	*Arthropoda*	*Cladocera*	*Daphnidae*	Whatman N° 1 filtered Lake Champlain water; pH 7.7; Al 42.4; Cd < 1µg L^{-1}	65	N	104	longevity	1	Bertram and Hart, 1979	3
Daphnia pulex	*Arthropoda*	*Cladocera*	*Daphnidae*	unchlorinated, carbon filtered well water, aerated to saturation; Al 230; pH 8; DO >5; T 23; Cd < 0.01 µg Cd/L	240	N	14	reproductive impairment	7.5	Elnabarawy et al., 1986	3
Aplexa hypnorum: immature	*Mollusca*	*Basommotophora*	*Physidae*	Lake Superior water; DO 7.5; T 24		M	26	growth	4.41	Holcombe et al., 1984	2
Physa integra	*Mollusca*	*Basommotophora*	*Physidae*	untreated Lake Superior water; pH 7.1-7.7; T 15; DO 10-11; Al 40-44; Ac 1.9-3	44-48	M	21	mortality	8.3	Spehar et al., 1978	2
Daphnia galeata mendotae	*Arthropoda*	*Cladocera*	*Daphnidae*	10 µm filtered Lake Michigan water; T 18.5	120	N	154	number of individuals	2	Marshall, 1978	3
Ceriodaphnia reticulata	*Arthropoda*	*Cladocera*	*Daphnidae*	unfiltered river water; static; Ac 2-4.2; Al 41-65; pH 7.2-7.8	55-79	M	9	reproduction	3.4	Spehar and Carlson, 1984	3
Ceriodaphnia reticulata	*Arthropoda*	*Cladocera*	*Daphnidae*	unchlorinated, carbon filtered well water, aerated to saturation; Al 230; pH 8; DO >5; T 23; Cd < 0.01 µg L^{-1}	240	N	7	reproductive impairment	0.25	Elnabarawy et al., 1986	3
Ceriodaphnia dubia	*Arthropoda*	*Cladocera*	*Daphnidae*	Synthetic water; Al 65; T 25	90	N	7	mortality	1.5	Winner, 1988	3
Ceriodaphnia dubia	*Arthropoda*	*Cladocera*	*Daphnidae*	reconstituted soft water: T 14-16°C; DO 9.3-11.4 mg L^{-1}; Cd(BG) <0.2 µg L^{-1}; pH 6.3-7.6; H 20	20	M	7	reproduction	10	Jop et al., 1995	2
Ceriodaphnia dubia	*Arthropoda*	*Cladocera*	*Daphnidae*	river water: T 14-16°C; DO 8.7-12.2 mg L^{-1}; Cd(BG) <4 µg L^{-1}; pH 6.6-7.4; H 16-28	16-28	M	7	reproduction	11	Jop et al., 1995	2
Hyalella azteca	*Arthropoda*	*Amphipoda*	*Hyalellidae*	well water: T 23; pH 7.8	280	M	42	Survival	0.51	Ingersoll and Kemble, 2000	3
Chironomus tentans	*Arthropoda*	*Diptera*	*Chironomidae*	well water: T 23; pH 7.8	280	M	20	weight	5.8	Ingersoll and Kemble, 2000	3
Selenastrum capricornutum	*Chlorophyceae*	*Chlorococcales*	*Scenedesmaceae*	modified ISO 6341 medium; 0.2 µm filtered; T 20.3-25.6; pH 7.7-10.4	49	M	3	cell number	2.4	LISEC, 1998a	1

Table 3.202 continued overleaf

Table 3.202 continued Selected NOEC data of effects of Cd in freshwater. Data derived from Tables 3.195, 3.197 and 3.199 within quality class RI 1-3

Organism	Phylum/class	Order	Family	Medium	H	Nominal/ Measured	Duration (d)	Endpoint	NOEC (µg L-1)	References	R.I.
Coelastrum proboscideum	*Chlorophyceae*	*Chlorococcales*	*Coelastraceae*	AM;T 31;pH 5.3;	32	M	1	biomass	6.3	Müller and Payer 1979	2
Asterionella formosa	*Bacillariophyceae*	*Pennales*	*Diatomaceae*	AM; pH 8	121	M	1	growth rate	0.85	Conway and Williams 1979	2
Chlamydomonas reinhardii	*Chlorophyceae*	*Volvocales*	*Chlamydomonaceae*	AM; pH 6.7; T 20	42	N	7	steady state cell number	7.5	Lawrence et al., 1989	3
Scenedesmus quadricauda	*Chlorophyceae*	*Chlorococcales*	*Scenedesmaceae*	AM; pH 7		N	7	biomass (OD)	31	Bringmann and Kühn, 1980	3
Lemna paucicostata	*Liliopsida*	*Arales*	*Lemnaceae*	AM; T 25		N	7	number of fronds		Nasu and Kugimoto, 1981	
				pH>6	120				5		3
				pH 5.1	120				10		3
				pH 5.1	700				10		3

T Temperature (°C);
H Hardness (as mg $CaCO_3$/L);
DO Dissolved oxygen (mg O_2/L);
Al Alkalinity (mg $CaCO_3$/L);
Ac Acidity (mg $CaCO_3$/L);
AM Artificial medium.

Table 3.203 'One species, one NOEC': selected NOEC data of effects of Cd in freshwater and calculation of 'geometric mean NOEC's. Data derived from Table 3.202

Organism	Phylum/class	Order	Family	NOEC (µg L^{-1})	
Salmo gairdneri	*Chordata*	*Salmoniformes*	*Salmonidae*	6.9	geometric mean of 4 and 12
Oncorhynchus kisutch	*Chordata*	*Salmoniformes*	*Salmonidae*	1.3	
Salvelinus fontinalis	*Chordata*	*Salmoniformes*	*Salmonidae*	4.7	geometric mean of 0.9, 1.1, 8 and 62
Salmo salar	*Chordata*	*Salmoniformes*	*Salmonidae*	0.47	
Catostomus commersoni	*Chordata*	*Cypriniformes*	*Catostomidae*	4.2	
Esox lucius	*Chordata*	*Esociformes*	*Esocidae*	4.2	
Salvelinus namaycush	*Chordata*	*Salmoniformes*	*Salmonidae*	4.4	
Salmo trutta (late eyed eggs)	*Chordata*	*Salmoniformes*	*Salmonidae*	1.1	
Jordanella floridae	*Chordata*	*Cyprinodontiformes*	*Cyprinodontidae*	4.1	
Brachydanio rerio	*Chordata*	*Cypriniformes*	*Cyprinidae*	1	
Oryzias latipes	*Chordata*	*Beloniformes*	*Adrianichthyidae*	4.2	geometric mean of 3 and 6
Xenopus laevis	*Chordata*	*Anura*	*Pipidae*	9	
Pimephaless promelas	*Chordata*	*Cypriniformes*	*Cyprinidae*	13.5	geometric mean of 13 and 14
Daphnia magna	*Arthropoda*	*Cladocera*	*Daphnidae*	1.0	geometric mean of 0.16, 0.21, 0.6, 0.8, 1, 1, 2, 2.5, 2.5 and 3.2
Daphnia pulex	*Arthropoda*	*Cladocera*	*Daphnidae*	2.7	geometric mean of 1 and 7.5
Aplexa hypnorum: immature	*Mollusca*	*Basommotophora*	*Physidae*	4.41	
Physa integra	*Mollusca*	*Basommotophora*	*Physidae*	8.3	
Daphnia galeata mendotae	*Arthropoda*	*Cladocera*	*Daphnidae*	2	
Ceriodaphnia reticulata	*Arthropoda*	*Cladocera*	*Daphnidae*	0.9	geometric mean of 0.25 and 3.4
Ceriodaphnia dubia	*Arthropoda*	*Cladocera*	*Daphnidae*	5.5	geometric mean of 1.5, 10 and 11
Hyalella azteca	*Arthropoda*	*Amphipoda*	*Hyalellidae*	0.51	
Chironomus tentans	*Arthropoda*	*Diptera*	*Chironomidae*	5.8	
Selenastrum capricornutum	*Chlorophyceae*	*Chlorococcales*	*Scenedesmaceae*	2.4	
Coelastrum proboscideum	*Chlorophyceae*	*Chlorococcales*	*Coelastraceae*	6.3	
Asterionella formosa	*Bacillariophyceae*	*Pennales*	*Diatomaceae*	0.85	
Chlamydomonas reinhardii	*Chlorophyceae*	*Volvocales*	*Chlamydomonaceae*	7.5	
Scenedesmus quadricauda	*Chlorophyceae*	*Chlorococcales*	*Scenedesmaceae*	31	
Lemna paucicostata	*Liliopsida*	*Arales*	*Lemnaceae*	7.9	geometric mean of 5, 10 and 10

Table 3.204 'Case-by-case selection': selected NOEC data of effects of Cd in freshwater and case-by-case calculation of 'geometric mean NOEC's. Bold, underlined data are selected for the HC_5 calculation. Data derived from Table 3.202

Organism	Medium	H	Endpoint	NOEC (µg L^{-1})		References
Salmo gairdneri	aerated well water; T 10; O_2 7.5; pH 8-8.6	375-390	mortality	12	*S. gairdneri*: no geometric mean calculation: different test medium	Lowe-Jinde and Niimi, 1984
Salmo gairdneri	synthetic water (ISO 1977) ; T 25; pH 8.3	100	median survival time	4		Dave et al., 1981
Oncorhynchus kisutch	sand filtered Lake Superior Water; continuous flow; DO 10.3; Al 41; Ac 3; pH 7.6	45	biomass	1.3		Eaton et al., 1978
Salvelinus fontinalis	sand filtered Lake Superior Water; continuous flow; DO 10.3; Al 41; Ac 3; pH 7.6	45	biomass	1.1	*S. fontinalis*: geometric mean calculation: same test medium, same endpoint (biomass)	Eaton et al., 1978
Salvelinus fontinalis	sterilised Lake Superior water; pH 7-8; Al 38-46; Ac 1-10; DO 4-12; T 9-15	42-47	total weight of young /female of the 2nd generation	0.9	geometric mean = 1.0	Benoit et al., 1976
Salvelinus fontinalis	reconstituted soft water: T 14-16°C; DO 9.3-11.4 mg L^{-1}; Cd(BG) <0.2 µg L^{-1}; pH 6.3-7.6; H 20	20	survival	8	*S. fontinalis*: geometric mean calculation: similar test medium, same endpoint (survival)	Jop et al., 1995
Salvelinus fontinalis	river water: T 14-16°C; DO 8.7-12.2 mg L^{-1}; Cd(BG) <4 µg L^{-1}; pH 6.6-7.4; H 16-28	16-28	survival	62	geometric mean = 22	Jop et al., 1995
Salmo salar	municipal water charcoal filtered and UV sterilised; BC 0.13 µg Cd/L; pH 6.5-7.3; T 5-10; DO 11.1-12.5; Al 14-17	19-28	total biomass	0.47		Rombough and Garside, 1982
Catostomus commersoni	sand filtered Lake Superior Water; continuous flow; DO 10.3; Al 41; Ac 3; pH 7.6	45	standing crop (biomass)	4.2		Eaton et al., 1978
Esox lucius			biomass	4.2		
Salvelinus namaycush				4.4		
Salmo trutta (late eyed eggs)				1.1		
Jordanella floridae	untreated Lake Superior water; T 25; DO 8.3; Al 42; Ac 2.4; pH 7.1-7.8	44	reproduction	4.1		Spehar, 1976
Brachydanio rerio	synthetic water (changed ISO) ; T 24; DO >80%; pH 7.2	100	reproduction	1		Bresch ., 1982
Oryzias latipes	tap water; continuous flow; T 20	200	mortality and	6	*O. latipes*: no geometric mean calculation: different test medium	Canton and Slooff, 1982
		100	abn. behaviour	3		
Xenopus laevis	tap water; continuous flow; T 20	170	inhibition of larvae development	9		Canton and Slooff, 1982
Pimephaless promelas	pond water diluted with carbon filtered demineralised tap water; DO 6.5-6.6; pH 7.6-7.7; Al 145-161; Ac 8-12; T 16-27	201-204	reproduction (pond fish)	13	*P. promelas*: geometric mean calculation: same test medium, same endpoint (reproduction)	Pickering and Gast, 1972
			reproduction (laboratory fry)	14	geometric mean = 13.5	
Daphnia magna	50 µm filtered and sterilised Lake IJssel water; pH 8.1; T 20; H 224	224	intrinsic rate of natural increase	3.2	*D. magna*: no geometric mean calculation: different endpoints	Van Leeuwen et al., 1985
Daphnia magna	NPR synthetic water; pH 8.4; T 20	200	mortality	1		Van Leeuwen et al., 1985
Daphnia magna	synthetic water; T 25; pH 8; DO 69%	11	reproduction	0.6	*D. magna*: no geometric mean calculation: different medium	Kühn et al., 1989
Daphnia magna	Synthetic water; Al 65; T 25	90	reproduction	2	*D. magna*: geometric mean calculation: similar medium, same endpoint (reproduction)	Winner, 1988

Table 3.204 continued overleaf

Table 3.204 continued 'Case-by-case selection': selected NOEC data of effects of Cd in freshwater and case-by-case calculation of 'geometric mean NOEC's. Bold, underlined data are selected for the HC_5 calculation. Data derived from Table 3.202

Organism	Medium	H	Endpoint	NOEC (µg L^{-1})		References
Daphnia magna	well water: T 20±2°C; DO 4.9-7.9; Cd(BG) 0.08; pH 7.9	103	reproduction	0.16	geometric mean = 0.6	Chapman et al., 1980
Daphnia magna	well water: T 20±2°C; DO 4.9-7.9; Cd(BG) 0.08; pH 8.2	209	reproduction	0.21	*D. magna*: no geometric mean calculation: different medium	Chapman et al., 1980t
Daphnia magna	unchlorinated, carbon filtered well water, aerated to saturation; Al 230; pH 8; DO >5; T 23; Cd < 0.01 µg Cd/L	240	reproductive impairment	2.5		Elnabarawy et al., 1986
Daphnia magna	aerated well water; DO >70%; pH 8; T 22; Al 250	300	reproduction	0.8		Knowles and McKee, 1987
Daphnia magna	culture medium; pH8.4; T 20	150	biomass production/female	2.5	*D. magna*: no geometric mean calculation: different medium	Bodar et al., 1988a
Daphnia magna	20 µm cloth filtered Lake Superior water; pH 7.7; Al 42.3; DO 9; T 18	45.3	weight/animal	1		Biesinger and Christensen, 1972
Daphnia pulex	Whatman N° 1 filtered Lake Champlain water; pH 7.7; Al 42.4; Cd < 1µg L^{-1}	65	Longevity	1	*D. pulex*: no geometric mean calculation: different medium	Bertram and Hart, 1979
Daphnia pulex	unchlorinated, carbon filtered well water, aerated to saturation; Al 230; pH 8; DO >5; T 23; Cd < 0.01 µg Cd/L	240	reproductive impairment	7.5		Elnabarawy et al., 1986
Aplexa hypnorum: immature	Lake Superior water; DO 7.5; T 24		Growth	4.41		Holcombe et al., 1984
Physa integra	untreated Lake Superior water; pH 7.1-7.7; T 15; DO 10-11; Al 40-44; Ac 1.9-3	44-48	Mortality	8.3		Spehar et al., 1978
Daphnia galeata mendotae	10 µm filtered Lake Michigan water; T 18.5	120	Number of individuals	2		Marshall, 1978
Ceriodaphnia reticulata	unfiltered river water; static; Ac 2-4.2; Al 41-65; pH 7.2-7.8	55-79	Reproduction	3.4	*C. reticulata*: no geometric mean calculation: different medium	Spehar and Carlson, 1984
Ceriodaphnia reticulata	unchlorinated, carbon filtered well water, aerated to saturation; Al 230; pH 8; DO >5; T 23; Cd < 0.01 µg L^{-1}	240	reproductive impairment	0.25		Elnabarawy et al., 1986
Ceriodaphnia dubia	Synthetic water; Al 65; T 25	90	Mortality	1.5	*C. dubia*: no geometric mean calculation: different medium, different endpoint	Winner, 1988
Ceriodaphnia dubia	reconstituted soft water: T 14-16°C; DO 9.3-11.4 mg L^{-1}; Cd(BG) < 0.2 µg L^{-1}; pH 6.3-7.6; H 20	20	Reproduction	10	*C. dubia*: geometric mean calculation: similar medium, same endpoint (reproduction)	Jop et al., 1995
Ceriodaphnia dubia	river water: T 14-16°C; DO 8.7-12.2 mg L^{-1}; Cd(BG) <4 µg L^{-1}; pH 6.6-7.4; H 16-28	16-28	Reproduction	11	geometric mean = 10.5	Jop et al., 1995
Hyalella azteca	well water: T 23; pH 7.8	280	Survival	0.51		Ingersoll and Kemble, 2000
Chironomus tentans	well water: T 23; pH 7.8	280	Weight	5.8		Ingersoll and Kemble, 2000
Selenastrum capricornutum	modified ISO 6341 medium; 0.2 µm filtered; T 20.3-25.6; pH 7.7-10.4	49	cell number	2.4		LISEC, 1998a
Coelastrum proboscideum	AM;T 31;pH 5.3;	32	Biomass	6.3		Müller and Payer 1979
Asterionella formosa	AM; pH 8	121	growth rate	0.85		Conway and Williams 1979
Chlamydomonas reinhardii	AM; pH 6.7; T 20	42	steady state cell number	7.5		Lawrence et al., 1989
Scenedesmus quadricauda	AM; pH 7		biomass (OD)	31		Bringmann and Kühn, 1980

Table 3.204 continued overleaf

Table 3.204 continued 'Case-by-case selection': selected NOEC data of effects of Cd in freshwater and case-by-case calculation of 'geometric mean NOEC's. Bold, underlined data are selected for the HC_5 calculation. Data derived from Table 3.202

Organism	Medium	H	Endpoint	NOEC (µg L^{-1})		References
Lemna paucicostata	AM; T 25		number of fronds		*L. paucicostata*: no geometric mean calculation: different medium	Nasu and Kugimoto, 1981
	pH>6	120		5		
	pH 5.1	120		10		
	pH 5.1	700		10		

T Temperature (°C);
H Hardness (as mg $CaCO_3$/L);
DO Dissolved oxygen (mg O_2/L);
Al Alkalinity (mg $CaCO_3$/L);
Ac Acidity (mg $CaCO_3$/L);
AM Artificial medium.

Table 3.205 'One species, one NOEC': lowest NOEC selection. Data derived from Table 3.202

Organism	Phylum/class	Order	Family	NOEC (µg L^{-1})
Salmo gairdneri	*Chordata*	*Salmoniformes*	*Salmonidae*	4
Oncorhynchus kisutch	*Chordata*	*Salmoniformes*	*Salmonidae*	1.3
Salvelinus fontinalis	*Chordata*	*Salmoniformes*	*Salmonidae*	0.9
Salmo salar	*Chordata*	*Salmoniformes*	*Salmonidae*	0.47
Catostomus commersoni	*Chordata*	*Cypriniformes*	*Catostomidae*	4.2
Esox lucius	*Chordata*	*Esociformes*	*Esocidae*	4.2
Salvelinus namaycush	*Chordata*	*Salmoniformes*	*Salmonidae*	4.4
Salmo trutta (late eyed eggs)	*Chordata*	*Salmoniformes*	*Salmonidae*	1.1
Jordanella floridae	*Chordata*	*Cyprinodontiformes*	*Cyprinodontidae*	4.1
Brachydanio rerio	*Chordata*	*Cypriniformes*	*Cyprinidae*	1
Oryzias latipes	*Chordata*	*Beloniformes*	*Adrianichthyidae*	3
Xenopus laevis	*Chordata*	*Anura*	*Pipidae*	9
Pimephaless promelas	*Chordata*	*Cypriniformes*	*Cyprinidae*	13
Daphnia magna	*Arthropoda*	*Cladocera*	*Daphnidae*	0.16
Daphnia pulex	*Arthropoda*	*Cladocera*	*Daphnidae*	1
Aplexa hypnorum: immature	*Mollusca*	*Basommotophora*	*Physidae*	4.41
Physa integra	*Mollusca*	*Basommotophora*	*Physidae*	8.3
Daphnia galeata mendotae	*Arthropoda*	*Cladocera*	*Daphnidae*	2
Ceriodaphnia reticulata	*Arthropoda*	*Cladocera*	*Daphnidae*	0.25
Ceriodaphnia dubia	*Arthropoda*	*Cladocera*	*Daphnidae*	1.5
Hyalella azteca	*Arthropoda*	*Amphipoda*	*Hyalellidae*	0.51
Chironomus tentans	*Arthropoda*	*Diptera*	*Chironomidae*	5.8
Selenastrum capricornutum	*Chlorophyceae*	*Chlorococcales*	*Scenedesmaceae*	2.4
Coelastrum proboscideum	*Chlorophyceae*	*Chlorococcales*	*Coelastraceae*	6.3
Asterionella formosa	*Bacillariophyceae*	*Pennales*	*Diatomaceae*	0.85
Chlamydomonas reinhardii	*Chlorophyceae*	*Volvocales*	*Chlamydomonaceae*	7.5
Scenedesmus quadricauda	*Chlorophyceae*	*Chlorococcales*	*Scenedesmaceae*	31
Lemna paucicostata	*Liliopsida*	*Arales*	*Lemnaceae*	5

The statistical extrapolation method (SEM, Aldenberg and Slob, 1993) was applied to the NOEC data (some grouped per species, see previous section), calculating the median 5th percentile (HC_5) of both the log-logistic and the log-normal distribution with the software package ETX 1.3a RIVM, Bilthoven, The Netherlands) (see **Table 3.206**).

Table 3.206 Calculation of critical concentrations (µg L^{-1}) using the assessment factor method (AFM) or the statistical extrapolation method (SEM, Aldenberg and Slob, 1993) for various levels of data quality

Data quality group	AFM: NOEC/AF µg Cd/L	
	AF=10	
RI 1-3	0.016	
RI 1-2	0.047	
	SEM: HC_5 at 50% (and 95%) confidence µg Cd/L	
	Logistic distribution	Normal distribution
Selection of all data, RI 1-2 (Table 3.202); n = 21	0.39 (0.15)	0.40 (0.16)
Selection of all data, RI 1-3 (Table 3.202); n = 49	0.35 (0.19)	0.34 (0.20)
One species, one value: geometric mean NOEC's (Table 3.203); n = 28	0.59 (0.30)	0.59 (0.32)
Case-by-case geometric mean calculation (Table 3.204); n = 44	0.38 (0.21)	0.38 (0.22)
One species, one value: lowest NOEC selection (Table 3.205); n = 28	0.31 (0.14)	0.31 (0.15)

Selection on data quality does affect the value of HC_5 between groups RI 1-3 and RI 1-2. The NOEC data with RI 1-3 yield a smaller HC_5 than those with RI 1-2. The group with RI 1-2 has obviously a higher quality label than the group RI 1-3. The latter group of data is, on the other hand, derived based on 28 species whereas the former is derived on 16 species (see **Table 3.202**). Many test results are classified as RI 3 mainly because the source document did not give statistical data analysis or because only nominal concentrations were given. These tests are still considered to be reliable (no critical information is missing). The choice between these two data groups is therefore a trade off between complete background information on tests with fewer species or more species with less complete background information. The latter is preferred here because the statistical extrapolation is based on the modelling of the species sensitivity distribution.

The choice of SSD (log-logistic or log-normal) does not affect the HC_5 (see **Table 3.206**). The choice of data selection (geometric mean calculation or not, lowest NOEC selection or not) influences the HC_5 by a factor two. The lowest HC_5 (0.31 µg L^{-1}) is calculated when only the lowest NOEC value is selected for each species. The highest HC_5 (0.59 µg L^{-1}) is calculated when the geometric mean NOEC is calculated for each species. The main drawback of both approaches is that they reduce information from the database. The lowest NOEC values are often found at low water hardness, in synthetic water or carbon filtered water. Selecting only these values creates a bias in the database which should be avoided for a generic risk assessment. However, hardness correction of the data may be used to set standards that vary by region (see Section 3.2.2.6.4). Selecting a geometric mean NOEC for each species may not protective for that species in all conditions. As an example, the geometric mean NOEC of *D. magna* is 1 µg Cd/Lwhereas several LOEC's of that species have been detected below 1 µg Cd/L(see **Table 3.197**). The alternatives for data selection are therefore using all RI 1-3 data or data of RI 1-3 with case-by-case averaging Some species might be overrepresented compared to others when all data are selected to calculate the HC_5. This is partly overcome by calculating geometric mean NOEC values on a case-by-case basis, where NOEC's are only averaged for the same species tested on the same endpoint in the same or a similar medium. As a trade-off between the last 2 alternatives, we propose to use the HC_5 of the largest group (RI 1-3), calculated based on case-by-case selected (geometric mean) NOEC values, i.e.

$$HC_5 = 0.38\ \mu g\ L^{-1}$$

The frequency distribution and HC_5 are illustrated in **Figure 3.14**.

Figure 3.14 The cumulative frequency distribution of the NOEC values of Cd toxicity tests of data quality group and RI 1-3 used to calculate the HC_5 (case-by-case geometric mean calculation; n = 44). Selected data and logistic distribution curve fitted on the data

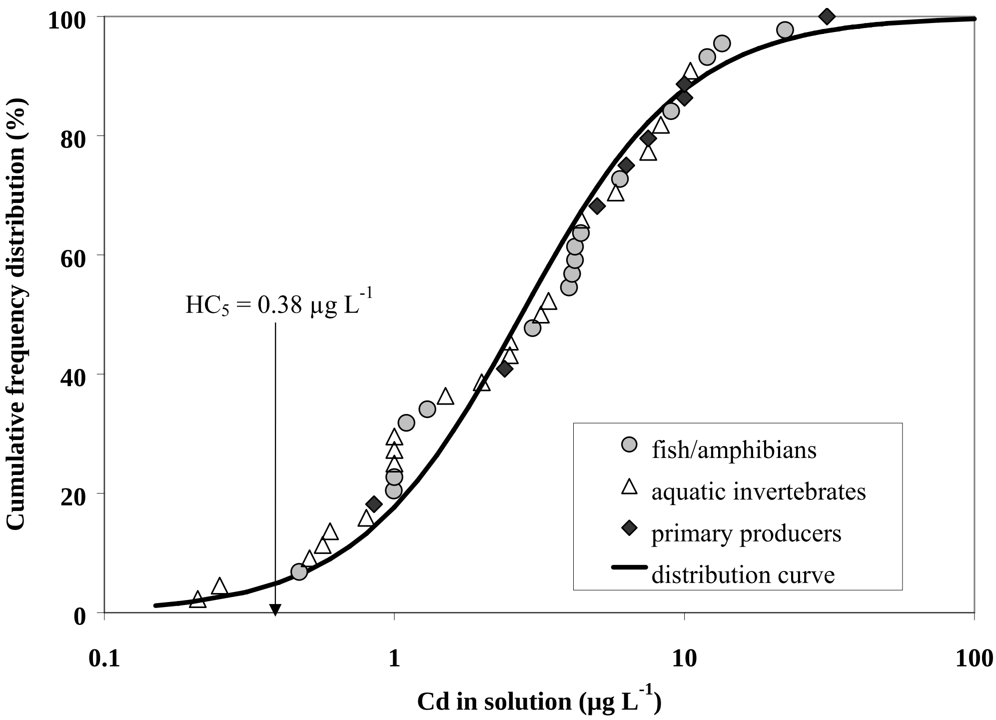


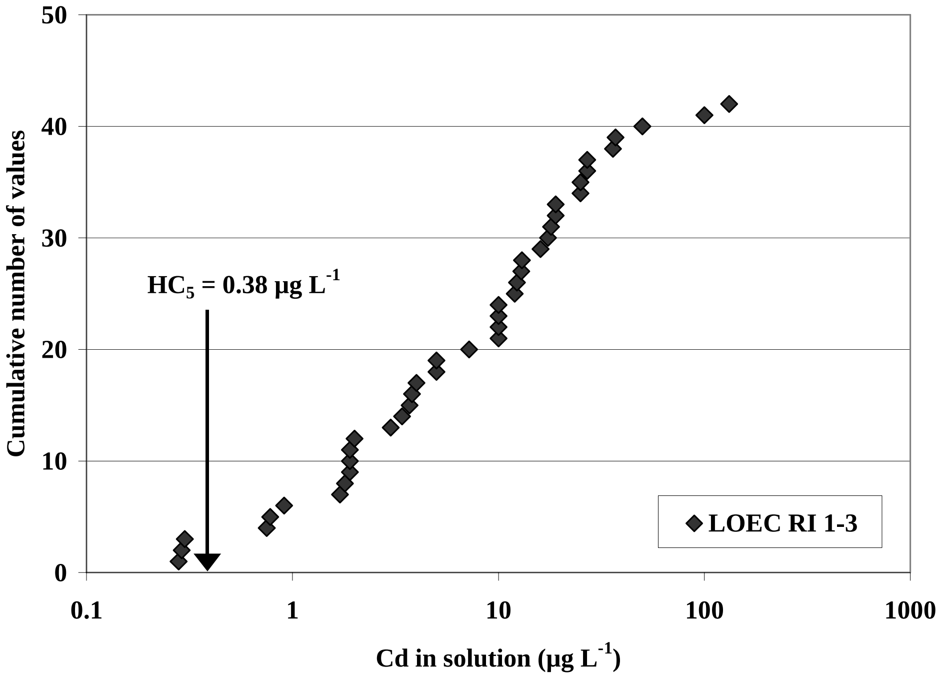
Figure 3.15 gives the cumulative number of the LOEC values of data quality group RI 1-3. LOEC values are found at higher Cd concentrations than NOEC values (not shown). Three LOEC's are found below the HC_5. Yield of a *Daphnia* population was reduced by 36% at 0.3 µg L^{-1} (measured concentration) after 21 days exposure in Lake IJssel water (Van Leeuwen et al., 1985). There was no statistical evaluation of the data and no NOEC value could be derived from that test (the LOEC was found at the lowest concentration tested). Furthermore, reproduction *Daphnia magna* was also significantly affected at 0.28 and 0.29 µg L^{-1} in well water at a hardness of 53 and 103 mg $CaCO_3$/L (Chapman et al., 1980).

A small number of other chronic tests has also demonstrated Cd toxicity at solution Cd concentrations below 0.5 µg Cd/L (e.g. Biesinger and Christensen, 1972; Sjöbeck et al., 1984). These data are less reliable as discussed in the Sections 3.2.2.2 and 3.2.2.3. Nevertheless, this review of toxicity data indicates that a toxicity threshold Cd concentration in freshwater, if detectable, may be very close to background Cd concentrations (typically 0.05-0.2 µg Cd/L in filtered freshwater). The number of ecological processes affected in the 0.1-0.5 µg Cd/L is, however, small as indicated by the LOEC frequency distribution.

The HC_5 is likely not overestimated due to speciation of Cd in the test media that would reduce Cd toxicity in the tests. One NOEC value of 0.8 µg L^{-1} was found in unfiltered well water

(Knowles and McKee, 1987). All other data (both NOEC or effect data) at concentrations below 1 µg L^{-1} were found in either synthetic media or in filtered environmental samples. Therefore, almost no Cd in these solutions has reduced availability due to sorption on suspended solids. This again justifies the use of filtered solutions in risk assessment of Cd in aquatic systems (see exposure section).

Figure 3.15 The cumulative number of LOEC values of selected tests of data quality group RI 1-3



3.2.2.6.3 Calculation of the generic PNECwater

The EU workshop on statistical extrapolation (17-18 January, 2001) proposed that the statistical extrapolation technique can be applied to derive a PNEC, but that an additional assessment factor should be applied to the HC_5. In order to derive a PNEC, this extra assessment factor should be between 5 and 1, to be judged on a case by case basis, and should remove uncertainty in extrapolating the PNEC to the field situation.

The data on which the HC_5 is calculated are selected NOEC's or geometric mean NOEC's, calculated on a case-by-case basis (see **Table 3.204**). The diversity of the data (44 NOEC values from 28 species and 16 different families, including warm and cold water fish, amphibians, crustaceans, algae and higher plants) is large enough to use the statistical extrapolation method to calculate the PNEC. Many of the tests are performed in synthetic water resulting in a lower degree of Cd complexation than in natural conditions.

All NOEC data are derived from real chronic studies. Test durations are between 7 days and 3 years, except for some algae tests, which should cover different life stages. The goodness-of-fit of the SSD's is tested with the Kolmogorov-Smirnov test. It indicated that the log-logistic distribution is accepted at the 1-5% and the log-normal distribution at the 1-10% significance levels when applied on the selected NOEC's.

Field data on Cd can hardly be used to derive threshold values for Cd in the environment because of the usual mixed metal pollution where Cd is found at high concentrations. Microcosm (model) ecosystems offer an alternative way of testing effects of Cd in field conditions. Results from such multi-species studies should be evaluated regarding their reliability, reproducibility, representativeness and relevance. Furthermore, the evaluation should include consideration of the reported endpoints, species and/or indices, including the statistical power of the test design. **Table 3.207** gives an overview of the description and results of nine multi-species (MS) studies. Using the US-EPA hardness correction (see next section), the NOEC and LOEC values of these MS studies can be compared to the HC_5 of single species NOECs (see **Table 3.208**). This reveals that the hardness corrected HC_5 values are within the range of the reported MS-NOEC values and below the reported MS-LOEC values, with one exception in the study of Marshall and Mellinger (1980). The study revealed a significant effect on 1 of the 16 species at 0.2 µg L^{-1} (nominal concentration, measured concentrations unknown).

Table 3.207 Overview of multi-species studies about effects of Cd (added as Cd^{2+}salt) in the aquatic environment

Reference (chronological order)	Test system	Replicates	Cd conc. range ($\mu g\ L^{-1}$, Nominal or Measured)	Water chemistry	Period	Results	Conclusion for Multi-Species study (MS)
1. Giesy et al., 1979	artificial streams: 91.5 m long, 0.3 m depth; mean water retention time = 2h; sediment present	2 for each treatment	0, 5, 10 (N) 0.02, 4-5, 8-10 (M)	hardness 11 mg L^{-1}as $CaCO_3$; pH = 6.5	1 year	at 5 and 10 µg Cd/l significant reductions in macrophytes biomass and periphyton; some invertebrate taxa eliminated, while other taxa increased in density chronic toxicity in crayfish and snails	5 µg $L^{-1}$is a MS-LOEC a MS- NOEC can not be derived (extrapolation factors > 2 are considered not reliable in Cd/CdO RAR) effects of Cd at 5 µg Cd/l in this very soft water is expected from single species studies
2. Marshall and Mellinger, 1980	closed 8 l carboys at 3-5 m or 6-8 m depth in Lake Michigan	2 for each treatment	0, 0.6, 1.2, 2.5, 5.0 (N, exp.1-4) 0, 0.2, 0.4, 0.8, 1.6 (N, exp. 5-6)	hardness 120 mg L^{-1}as $CaCO_3$; background Cd <0.1 µg Cd/l	3 weeks	for 16 species/categories of crustacean plankton sign. increases in density of 4 categ. at 0.6 or 1.2 µg Cd/l sign. decrease in density of 2 species at 0.6 µg Cd/l, one species sign. affected at 0.2 µg Cd/l lowest LOEC for total zooplankton density at 0.8 µg Cd/l- NOEC's varying with experiments (0.4-2.5 µg Cd/l) LOEC for 1 species at 0.2 µg L^{-1} LOEC for percentage similarity (biodiversity index): 1.2 µg L^{-1}(exp. 1&2), 0.6 µg L^{-1}(lowest tested conc., exp. 3&4)0.4 µg L^{-1}(exp. 5&6)	less reliable because no measured Cd concentrations in the critical Cd concentration range (<1 µg Cd/l) MS-NOEC's of total zooplankton density: 0.4-2.5 µg L^{-1} 1 individual species can be sign. affected at Cd = 0.2 µg L^{-1}
3. Marshall and Mellinger, 1980	10 m diameter open surface enclosures in L 223 of Canada's experimental lake area (~2m depth)	no	0, 1, 3, 10, 30 (N)	background Cd <0.1 µg Cd/l; hardness unknown	44-87 days	reduction in density of most of the 8 species/categories of custacean plankton at lowest Cd concentration tested increased density of 8 species/categories of rotifers at 1 or 3 µg L^{-1} LOEC for percentage similarity (biodiversity index) is 1 µg L^{-1}(lowest tested) EC1 of percent similarity is extrapolated from L223 and Lake Michigan enclosure data and is predicted 0.12 added Cd (background not included)	unreliable because no measured Cd concentrations, no replicates and no known water characteristics
4. DeNoyelles et al., 1980	continuous 5 l culture chambers, retention time 92-110 h, incubated at 1.74 m depth in L 239 of Canada's experimental lake area	2 for each treatment	0, 4 (N) unknown and 2.9-4.2 (M)	background Cd unknown; hardness unknown	188 h	density of 4 phytoplankton species: increased for 2 species and decreased for 2 other species	MS-NOEC is below 2.9-4.2 µg L^{-1}if based on most sensitive species less reliable because water hardness unknown
5. DeNoyelles et al., 1980	10 m diameter open surface enclosures in L 223 of Canada's experimental lake area (~2m depth)	no	0, 1, 3, 10, 30 (N) measured Cd : declined to half of nominal in 2 weeks (no other details available)²	background Cd <0.1 µg Cd/l; hardness unknown	2 weeks	density of 3 phytoplankton species: increased for 2 species at Cd = 1 and 3 µg L^{-1}, decreased for 1 species at lowest Cd rate and above (LOEC = 1 µg L^{-1})	MS-NOEC is below 1 µg L^{-1}if based on most sensitive species unreliable because no measured Cd, hardness unknown and no replicates

Table 3.207 continued overleaf

Table 3.207 continued Overview of multi-species studies about effects of Cd (added as Cd^{2+}salt) in the aquatic environment.

Reference (chronological order)	Test system	Replicates	Cd conc. range (µg L^{-1}, Nominal or Measured)	Water chemistry	Period	Results	Conclusion for Multi-Species study (MS)
6. Niederlehner et al., 1985	colonisation of barren polyurethane foam substrates by protozoan from a species source (collected on foam in a pond)	2 per treatment	0, 0.6, 1.3, 2.5, 5, 10 (N) 0.2, 0.4, 1.4, 2.7, 5.6, 9.5 (M)	dechlorinated tap water; hardness 70 mg L^{-1}as $CaCO_3$; background Cd 0.2 µg Cd/l	28 days	NOEC colonisation tests 0.4 µg L^{-1}, LOEC=1.4 µg L^{-1}(22% inhibition)²	reliable MS-NOEC=0.4 µg L^{-1}
7. Borgmann et al., 1989	3400 l indoor ecosystems (4 tanks) inoculated with *Daphnia magna* and phytoplankton	none at 5 and 15 µg L^{-1}, 2 at 1µg L^{-1}*, 3 at control*	0, 1, 5, 15 (N) 0.08-0.2, 1, 4.7, 12 (M)	tap water; hardness 130 mg L^{-1}as $CaCO_3$; background Cd < 0.3 µg Cd/l; pH 8.2-8.6	>10 weeks	no effects at 1 µg Cd/l on Daphnia ash free dry weight or chlorophyll concentration collapse of Daphnia population and Increase in Chlorophyll conc. at 5 µg /L both endpoints affected at 15 µg L^{-1}	less reliable MS-NOEC of 1 µg L^{-1}because no continuous replicates of control and 1 µg Cd/l treatment
8. Lawrence and Holoka, 1991	continuous 41 l culture chambers, retention time 2 days, incubated at 2 me depth in L 382, 302,204 of Canada's experimental lake area	2 per treatment	paired studies: 0, 0.2 (10 exp.) 0, 0.4 (3 exp) 0, 1 (2 exp) 0, 3 (2 exp)	background Cd in L 382 is < 0.002 µg L^{-1}, other lakes unknown; hardness less than about 10 mg L^{-1}as $CaCO_3$$ DOC < 1.2 mmol/l	2 weeks	6 categories of crustacean species calanoid and cyclopoid copepods: NOEC=1.0 µg L^{-1} 2 species: NOEC = 0.2 µg Cd/l 2 species (*D. galeata mendotae & Holpedium gibberum*): LOEC = 0.2 µg L^{-1}(lowest tested, 40% and 38% inhibition)	MS-NOEC below 0.2 µg L^{-1}if based on most sensitive species less reliable: no measured Cd concentrations in the critical Cd concentration range (<1 µg Cd/l)
9. Malley and Chang, 1991	lake 382 of Canada's experimental lake area	no	0.002 (pre-contamination years 1985-1986); 0.05-0.08 µg Cd/l (experimental years 1987-1988)	hardness less than about 10 mg L^{-1}as $CaCO_3$$ DOC<0.7 mmol/l	2 years	zooplankton community structure: no adverse effects on composition and population abundances	MS-NOEC = 0.08 µg L^{-1}, highest tested (less reliable-no replicates and unbounded, authors have indirect evidence for predicting effects at 0.2 µg Cd/l in soft water lakes)

* Control;
1 Continuous control,
2 Controls for the period before Cd was added; Cd in 4th unit (designed as 2nd continuous control) increased in time to 1 µg Cd/l (contamination ascribed to a welding joint);
$ The test reports Ca concentrations of about 2.2 mg L^{-1}but data on Mg are lacking, i.e. the hardness cannot be calculated unequivocally. The Ca/Mg molar ratio is typically about 3:1 in freshwater, yielding a hardness of about 7 mg $CaCO_3$/L. We have used a larger estimated Mg concentration (Ca/Mg molar ratio of 1), i.e. hardness of about 10 mg L^{-1}.

Table 3.208 Summarising table for multi-species studies (numbers refer to those in Table 3.207). The water hardness correction is described in Section 3.2.2.6.4. The HC_5 at the water hardness of the MS study is calculated based on hardness corrected NOEC data and retransformation with a lower hardness limit of H = 40 mg l^{-1} as $CaCO_3$). The model for the hardness correction is discussed in Section 3.2.2.6.4

Study number	Reliability	MS-NOEC (µg L^{-1})	MS-LOEC (µg L^{-1})	Hardness (mg L^{-1})	HC_5 at that hardness (µg L^{-1})
1	reliable	-	5	11	0.16
2	less reliable	< 0.2 (most sensit. species) 0.4-2.5 (crustacean density)	0.2 (most sensit. species) ≥ 0.8 (crustacean density)	120	0.34
3	unreliable	< 1 (most sensit species)	1 (most sensit. species)	no data	-
4	less reliable	< 2.9-4.2	2.9-4.2	no data	-
5	unreliable	< 1	1	no data	-
6	reliable	0.4	1.4	70	0.23
7	less reliable	1.0	5.0	130	0.37
8	less reliable	< 0.2 (most sensit. species)	0.2 (most sensit. species)	~10	0.16
9	less reliable	0.08	-	~10	0.16

The database of the 168 reliable tests on single species contains 3 reliable LOEC's below the HC_5 whereas the 9 multi species studies identified 1 LOEC below the hardness corrected HC_5. This suggests that NOEC and LOEC distributions overlap in the lower concentration range and that an additional assessment factor may be necessary. Therefore, we propose to include a assessment factor of 2 on the HC_5, yielding

$$PNEC_{water} = HC_5/2 = 0.19\ \mu g\ L^{-1}$$

One NOEC from the laboratory toxicity tests (RI 1-3) and one NOEC from the multi-species studies are below this $PNEC_{water}$. No LOEC's of the reliable single species or multi species studies is found below this $PNEC_{water}$. However, this generic $PNEC_{water}$ might not be protective for water with a very low water hardness (see Section 3.2.2.6.4). Finally, we note that the $PNEC_{water}$ derived with the Assessment Factor (AF) method is 4-14-fold below the value proposed above. This is related to the emphasis on the lowest NOEC value (with AF=10) with the AF method whereas the Statistcal Extrapolation method uses the weight of evidence.

3.2.2.6.4 $PNEC_{water}$ as a function of water characteristics

Water characteristics affect Cd toxicity. Toxicity of Cd generally increases with reducing water hardness, reducing concentrations of dissolved organic matter and increasing solution pH. Effects of dissolved organic matter on Cd toxicity cannot be described using the tests that are reviewed here since most tests did not report this water characteristic.

Toxicity of Cd^{2+} in solution is lower in more acid conditions because of H^+/Cd^{2+} competition at the membrane (e.g. data on *Lemna paucicostata*, Nasu and Kugimoto, 1981). Acidification leads to higher Cd emissions from catchments into water, but this is an effect on exposure, not on ecotoxicology of soluble Cd. In the presence of soluble Cd complexes (Cd complexed by dissolved organic matter), the situation is more complex because pH has effects on affinity of Cd^{2+} for the membrane and for the dissolved organic matter. Data suggesting that the effect of acidification is larger on releasing Cd^{2+} from soluble complexes than the opposite effect of decreasing Cd^{2+} affinity for the biota, have not been found. However, John et al. (1987) studied ^{109}Cd uptake (not toxicity) at varying pH and aquatic humus concentrations by *Salmo salar* in water reconstituted from a small marsh area in Oslo. The ^{109}Cd uptake was lowest at lowest pH at all but one DOC-level (Dissolved Organic Carbon). The pH effect was not significant at that DOC-level. The effects of pH on Cd toxicity were not identified in the selected tests of this report: a regression between the log ($EC_{x \geq 50}$) and pH showed non-significant effects for both the acute as chronic tests (P>0.05 for both regressions). The absence of effects of pH on Cd toxicity in this report might be due to the bias towards higher pH values (pH >7) of the aqueous media used in the selected tests.

Biotic ligand models (BLM's) have been developed to account for abiotic factors affecting metal toxicity. This model has been constructed and successfully validated to explain acute Cd toxicity to fish (fathead minnow and rainbow trout). Data for invertebrates (*C. dubia*) were not reliable enough to allow validation of a BLM and no BLM for algae was constructed (Hydroqual, 2003). Most of the data with fish show the importance of hardness on Cd toxicity, while effects of pH are of minor importance at pH >6.2. This BLM model can, however not be used in this document because the modifying factors for acute toxicity are not necessarily identical in chronic exposure and because the model is missing for invertebrates which are, most likely, the most sensitive group.

Considerable regional differences in water hardness of surface waters exist within the EU (see **Table 3.209**). Half of the surface waters in the northern European countries have a water hardness below 10 mg $CaCO_3$ L^{-1}, while in the western European countries almost 50% of the surface waters have a hardness above 200 mg $CaCO_3$ L^{-1}. Therefore, a water hardness correction of the $PNEC_{water}$ for risk characterisation at a local or regional scale might be useful.

Table 3.209 Water hardness (in mg $CaCO_3$ L^{-1}) distribution of surface waters in some EU countries

	10th percentile	25th percentile	50th percentile	90th percentile
Finland[a]	6.5	9	12	25
Sweden[b]	5	8	14	107
Norway[a]	0.7	1.7	4	18
Denmark[a]	14	86	155	272
France	48	83[e]217	335	
Belgium (Flanders)[c]	109	-	240,500	
Germany[d]	30	105	210	

a) Source: Skjelkvåle et al. (2001);
b) Source: Swedish University of agriculture;
c) Source: VMM;
d) Water hardness of groundwater instead of surface water (Hannappel et al., 2000);
e) 20th percentile.

The effect of water hardness (H) on Cd toxicity has been quantified by the US-EPA (US-EPA, 2001). For *Daphnia magna*, *Pimephales promelas* and *Salmo trutta* an increasing trend of chronic values with increasing water hardness was observed (see **Table 3.210**). The chronic value is the geometric mean of the NOEC and LOEC value for a given endpoint. To account for the apparent relationship of Cd chronic toxicity to hardness, an analysis of covariance was performed to calculate the pooled slope for hardness using the natural logarithm of the chronic value as the dependent variable, species as the treatment or grouping variable and the natural logarithm of hardness as the covariate or independent variable. This analysis was fit to the data of the 3 species for which chronic values are available over a range of hardness such that the highest hardness is at least 3 times the lowest, and the highest is also 100 mg L^{-1} higher than the lowest. Regression of the natural logarithm of the chronic value against the natural logarithm of water hardness gave a slope of 0.7712 for *D. magna*, 1.0034 for *P. promelas* and 0.5212 for *S. trutta*. The pooled slope for the three species is 0.7409, with 95% confidence limits of 0.3359 and 1.1459. The slope of 0.7409 was then used to adjust a range of chronic values to a reference hardness of 50 mg $CaCO_3$ L^{-1} following

$$\text{Chronic value}_{H=50} = \text{Chronic value}_{H}\left(\frac{50}{H}\right)^{0.7409} \qquad \text{Equation 3.1}$$

The water hardness correction covers a hardness range of 44-209 mg $CaCO_3$/L.

Table 3.210 Chronic values as a function of water hardness as reported by US-EPA (2001)

Species	Hardness (mg L^{-1} as $CaCO_3$)	Chronic value (µg L^{-1})
Daphnia magna	53	0.152
Daphnia magna	103	0.212
Daphnia magna	209	0.437
Salmo trutta	44	6.668
Salmo trutta	250	16.49
Pimephales promelas	44	10.0
Pimephales promelas	201	45.92

The effect of water hardness on Cd toxicity can also be observed in the current database. It has been frequently described in Sections 3.2.2.2-3.2.2.4 that water hardness is an important factor influencing Cd toxicity in water. Lowest LOEC or $EC_{x\geq50}$ values are often found in soft waters. The intrinsic variability of NOEC's across different studies limits the identification of the underlying relationship between hardness and toxicity in a meta-analysis in this report. Therefore, it is preferred to use the mean slope as used by US-EPA for the water hardness correction.

The water hardness correction equation of the US-EPA (US EPA, 2001; see above) is used to calculate the HC_5 as a function of water hardness. All NOEC values at hardness H are converted to NOEC values at a reference hardness of 50 mg $CaCO_3$ L^{-1} ($NOEC_{H=50}$) following

$$\text{NOEC}_{H=50} = \text{NOEC}_{H}\left(\frac{50}{H}\right)^{0.7409} \qquad \text{Equation 3.2}$$

Geometric mean values are calculated on the same data as in **Table 3.204** after normalisation of the data. The software package ETX 1.3a (RIVM, Bilthoven, The Netherlands) is used to calculate the HC_5 at the reference hardness of 50 mg $CaCO_3$ L^{-1}, assuming a log-logistic distribution. This HC_5 value is then divided by a assessment factor of 2 to yield a $PNEC_{water, regional}$ that is valid for waters with hardness of 50 mg $CaCO_3$ L^{-1}. The arguments to include an assessment factor 2 to convert a HC_5 to PNEC were given in the previous paragraph. Finally, Equation 3.2 is used again to recalculate the $PNEC_{water,regional}$ at different values of water hardness as:

$$PNEC_{water,regional} = 0.09\ (H/50)^{0.7409} \qquad \text{Equation 3.3}$$

It is proposed that this equation is not extrapolated below H = 40 mg $CaCO_3$/L, i.e. the $PNEC_{water,regional}$ for H < 40 mg $CaCO_3$/L = 0.08 µg Cd/L. The $PNEC_{water,regional}$ is graphically represented in **Figure 3.16**.

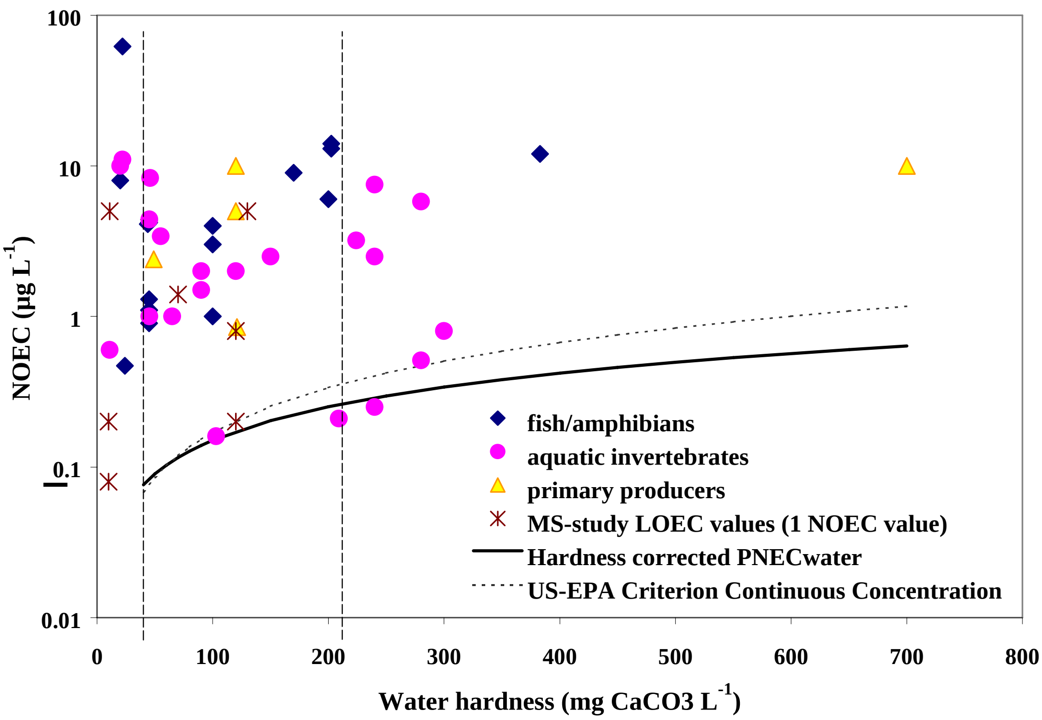
The extrapolation of the hardness correction below H = 40 mg $CaCO_3$/L is not proposed because this equation has not been tested in that hardness range. The $PNEC_{water,regional}$ = 0.08 µg Cd/L should then be evaluated for soft water. It is observed that:

- none of the 37 Cd toxicity tests in the database of the Cd RAR (including data with lower quality) that were performed between H = 7-10[1] and H=40 mg $CaCO_3$/L have identified adverse effects below the threshold of 0.08 µg Cd/L
- there are 2 multi-species studies (see **Table 3.207**) carried out in soft water lakes of Canada and which were designed to study fate and effects of Cd at low concentrations (0.05-0.2 µg Cd/L). The chemical properties of these waters (Ca = 2.2 mg L^{-1}, neutral pH, DOC about 8 mg C/L) are similar to that of soft water lakes in Scandinavian countries. The tests allow to conclude that 0.08 µg Cd/L is protective whereas adverse effects are found at about 0.20 µg Cd/L.
- We conclude that down to a water hardness of 7-10 mg $CaCO_3$/L there is no indication of Cd toxicity below 0.08 µg Cd/L.
- There are no data for the very soft waters (H below about 10 mg $CaCO_3$/L) and these areas may be unprotected by the proposed $PNEC_{water}$ for soft water.

Table 3.211 The $PNEC_{water,regional}$ (µg L^{-1}) for different values of water hardness (H, mg $CaCO_3$/L). The NOEC data were all first normalised to H=50 from which the HC_5 at a reference hardness was found. The PNECwater at that hardness contains a assessment factor of 2. The normalisation was then used to calculate the $PNEC_{water,regional}$ values at other values of H

	N	min. NOEC	median NOEC	$PNEC_{water}$
Data normalised to H 50 (method 2)	34	0.07		0.09
retransformed $PNEC_{water}$ = 0.09 $(H/50)^{0.7409}$				
H 40				0.08
H50				0.09
H100				0.15
H200				0.25

Figure 3.16 NOEC values of the laboratory studies , LOEC of multi-species studies (1 NOEC), water hardness corrected $PNEC_{water}$ and the US-EPA chronic criterion (US-EPA, 2001) as a function of water hardness. The dashed lines indicate the range of water hardness for which the US EPA (2001) hardness correction was derived



The water hardness correction method yields a $PNEC_{water,regional}$ at H = 50 mg $CaCO_3$/L of 0.09 µg Cd/L. Transforming this value to other water hardness using the slope of 0.7409, increases this threshold more than threefold between H = 40 and H = 200 (see **Figure 3.16**). We note that the US-EPA Cd criterion continuous concentration is very close to the regional $PNEC_{water}$.

Sorption of Cd^{2+} on suspended particles is higher in soft water than in hard water. As a result, the difference in HC_5 values between soft and hard water becomes smaller if the concentrations are based on total concentrations (dissolved and sorbed).

Although there is a relationship between Cd toxicity and water hardness, no correction of the $PNEC_{water}$ will be made to derive the generic $PNEC_{water}$. However, we suggest that for risk characterisation on a local/regional scale, $PNEC_{water}$ should be corrected to water hardness in order to better correspond to local/regional environmental conditions.

3.2.2.7 Conclusion

The $PNEC_{water}$ of Cd is derived from the median HC_5 value (Aldenberg and Slob, 1993) from 44 chronic NOEC values, some of which are geometric species means. These data are derived from 19 tests with fish/amphibians, 22 tests with aquatic invertebrates and 8 tests with primary producers, and represent 28 species in total. All these tests belong to data quality group RI 1-3. The NOEC values were obtained from laboratory based, single species studies and refer to the dissolved fraction. An assessment factor of two is applied on the HC_5. The $PNEC_{water}$ is

$$PNEC_{water} = 0.19\ \mu g\ Cd\ L^{-1}$$

No adverse effect of Cd below this PNEC was found in the 168 tests with RI 1-3 that have been reviewed. There is a trend that dissolved Cd is more toxic at lower water hardness. A correction of the PNEC for water hardness has been proposed that may be useful for local or regional risk characterisation. Multi-species NOEC's have been reported between 0.08 and 4.2 µg Cd L^{-1}. The lowest NOEC was found at very low water hardness. The hardness corrected $PNEC_{water}$ was within the range of MS NOEC values and below all MS LOEC's. This indicates that the HC_5 method is protective for ecosystem structure in case of Cd. No data were, however, found for very soft waters, i.e. at water hardness below about 10 mg $CaCO_3$/L. Current data suggest that a significant number of freshwaters in Norway, Finland and Sweden have water hardness below this threshold. So, a **conclusion (i)** is reached because there is a need for better information regarding the toxic effects of cadmium to aquatic organisms under low water hardness conditions (Cd toxicity testing in very soft waters).

3.2.3 Terrestrial compartment

3.2.3.1 General

3.2.3.1.1 Data quality: definitions of Reliability Indices (RI's)

For each test, a RI is given according to the following criteria:

- **RI 1**: standard test. Two such tests included are the OECD 207 acute toxicity test with *Eisenia fetida* in OECD-soil and the ISO 1994 "Soil quality effects of soil pollutants on Collembolla (*Folsomia candida*)" method for the determination of effects on reproduction.
- **RI 2**: no standard test but complete background information is given, i.e. the following information is present:
  a) soil pH
  b) soil organic matter or carbon content
  c) texture (class or texture fractions)
  d) total Cd content of the soil at zero Cd application if the NOEC or LOEC value is below 2µg g^{-1}
  e) equilibration time after soil contamination and prior to the test
  f) statistical analysis of the dose-response relationship
  g) no varying metal contamination along with increasing Cd application
  h) the control soil must be tested along with at least two Cd concentrations above the background concentration
  i) the soil must be homogeneously mixed with the metal prior to the test
- **RI 3**: no standard test and one or more of the following information from the above-mentioned list is missing as background information: b), c), e) or f). All other information from that list is present.
- **RI 4**: no standard test and one or more of the following information from the above-mentioned list is missing as background information: a), d), g), h) or i). The requirement d) is critical since some tests reporting LOEC values < 2 µg g^{-1} are considered unreliable. Background Cd concentrations in soil typically range between 0.1 and 0.5 µg g^{-1} and the

lack of reporting the background concentration may underestimate the total Cd concentration in soil at which the first toxic effects are found. Some tests were included that did not show Cd toxicity up to the highest Cd concentration tested. These tests cannot be used for risk assessment (no NOEC can be found) and were considered unreliable (RI4) but were quoted in the tables for illustration.

Tests performed in substrates that were judged as not representative for soils (e.g. pure quartz sand or farmyard manure) were not included in this effects assessment.

3.2.3.1.2 Source of data and its limitations for risk assessment

The original HEDSET contained no toxicity data for terrestrial organisms. A literature review was made on Cd toxicity to soil or litter microflora, soil fauna and higher plants.

Almost no tests have been made on the toxicity of CdO in soil. Many tests have however been performed with soluble Cd^{2+} salts. The relevance of soil toxicity tests with metal salts for a risk assessment of the metal oxide is discussed below. The tests with mixed metal pollution or with sludge are generally avoided in this review in order to avoid confounding factors for assessing the dose-response relationship. Mixed metal pollution is, however, more often found in the environment than single metal pollution. Other metals may have a synergistic or antagonistic effect on Cd toxicity. Increasing soil zinc is known to reduce Cd availability to plants. It has been advocated that plant Cd uptake studies at soil Cd:Zn ratio's that are strongly different from the usual 1:100 weight ratio are not relevant (Chaney et al., 1996). Antagonistic effects of Zn on Cd toxicity were shown for growth of the collemobollan *Folsomia candida* in artificial soil (Van Gestel and Hensbergen, 1997). The EC_{50} for growth was found at 1.5 of toxic units of Cd and Zn. The effects of Zn on Cd toxicity to reproduction were, however, only additive. Due to the lack of information on Cd:Zn interactions in Cd toxicity to soil microflora, soil fauna or higher plants, no predictions can be made to what extent single Cd toxicity studies may overestimate the Cd related toxicity at sites with moderate Cd-Zn metal contamination.

<u>Toxicity of Cd^{2+} salts versus toxicity of CdO</u>

Only one reliable study was found in which the toxicity of CdO was tested (Khan and Frankland, 1983). All other data are derived from studies using soluble Cd^{2+} salts in soil.

The toxicity of CdO in soil can be overestimated based on studies with soluble Cd^{2+} salts. Depending on the conditions prevailing in the soil, CdO transforms in soil to Cd^{2+} that sorbs to the soil sorption-sites. In this way, Cd derived from CdO becomes equally available as soluble Cd^{2+} salts after a certain equilibration time.

In order to quantify the transformation rate of CdO in soil, an experiment was set up in which 2 soils were amended with CdO at 50 μg Cd g^{-1} (Smolders et al., unpublished). The soil solution Cd concentration was monitored during a 3 month incubation period. The soil solution Cd concentrations were compared with these in soils that were amended with a Cd^{2+} salt at an equivalent total Cd application. The Cd concentrations in the CdO treated soil were between 71 and 86% of those in soil applied with the Cd^{2+} salt after 3 months incubation. Both soils were acids (pH $CaCl_2$ 4.4 and 5.4) which may have contributed to the rapid transformation.

Other evidence on the fate of CdO in soil can be found in studies on comparative toxicity of CdO versus Cd^{2+} salts and in isotopic exchange of Cd in soils contaminated with CdO. Calculations with MINTEQA2 (Allison et al., 1991) can provide the equilibrium speciation of CdO in soils but no model has yet been developed predicting its reaction rate.

Table 3.212 The Cd concentrations in membrane filtered soil solution of soils amended with CdO. The solution Cd concentrations are expressed as a percentage of the Cd concentration in the soil solution of the $Cd(N0_3)_2$ treated soil for corresponding soil types and equilibration times. Data in brackets at 99 days incubation are standard deviations (Smolders et al., unpublished)

	Soil solution Cd (% of Cd-salt treated soil)					
Cd source	Sandy pH 4.4			Clayey sand, pH 5.4		
	8 days	33 days	99 days	8 days	33 days	99 days
Untreated	0.3	0.2	0.6(0.1)	0.6	0.5	0.1(< 0.1)
CdO	103	76	71(12)	56	77	86(4)

In the study of Khan and Frankland (1983), a loamy sand soil (pH 4.6) was incubated for 15 days after contaminating with 10, 50, 100 and 500 µg g^{-1} Cd as $CdCl_2$ or with 100, 500 and 1,000 µg g^{-1} Cd as CdO. Yield of 42-day-old radish plants decreased consistently with increasing Cd rate. From the curves fitted to the shoot yield responses to both Cd compounds, the EC_{50} was predicted to be 70 µg g^{-1} for Cd added as $CdCl_2$ and 190 µg g^{-1} for the Cd added as CdO. Muramoto et al. (1991) measured Cd uptake in unpolished rice after applying various soluble and insoluble Cd forms. Cd application rates were 10 and 50 µg g^{-1}. The yield of rice (16 weeks) was reduced by 17% at the highest rate using $CdCl_2$ and by 8% using CdO. The Cd concentration in rice was not significantly different between $CdCl_2$ or CdO treated plants at the highest application rate. Webber (1973) compared Cd uptake in different plants from compost (pH 6.1) treated with various rates (0-500 µg g^{-1}) of Cd added as CdO or $CdSO_4$. The author concluded that CdO was at least as phytotoxic as $CdCl_2$. The Cd concentrations in the plant supplied with CdO were even higher than in those treated with $CdSO_4$.

Isotopic exchange using $^{109}Cd^{2+}$ is a method allowing calculating the fraction of the Cd in soils contributing to Cd^{2+} sorption /desorption reactions within defined conditions of time, solution composition and pH. A "radiolabile" fraction of 100% of total Cd in soil effectively means that all Cd in soil is equally available as recently added Cd^{2+}. In 33 polluted soils from U.K., Nakhone and Young (1993) found that this fraction varies from 6% to 102%. Many of these soils were contaminated by mine spoils and were characterised by a low fraction of "radiolabile" Cd. In the soils where the majority of Cd originated from sludge or from smelter fumes (Cd/CdO), the Cd labile pool varied from 29-102% (average 55%). In 10 Belgian soils with both background as elevated Cd levels, the "radiolabile" Cd pool was found to vary from 62-90% of aqua regia soluble Cd (Smolders et al., 1999). In a sandy soil sampled in the vicinity of a former Zn smelter in northern Belgium and which has been polluted through atmospheric deposition with mainly CdO, all aqua regia soluble Cd (10 µg g^{-1}) was found to be "radiolabile" (Vlassak V., personal communication).

Equilibrium calculations with MINTEQA2 (Allison et al., 1991) confirm that CdO is labile in soil and that Cd^{2+} becomes adsorbed. Effectively this prediction means that all Cd derived from CdO has the same speciation as Cd derived from soluble Cd salts. **Table 3.213** shows that in a soil contaminated with 50 µg g^{-1} Cd, added as CdO, almost all Cd is adsorbed and than all CdO has dissolved. This is surprising since CdO is considered as an insoluble product. In aqueous systems, CdO is indeed insoluble since the pH increases as the product dissolves, thereby reducing the solubility of the product. In soils, however, the pH is buffered and almost unaffected upon the dissolution of CdO.

All evidence gathered above indicates that, in the short term, CdO is less available than soluble Cd^{2+} salts but that the differences in availability between both Cd^{2+} forms are not very pronounced. For these reasons, a soil risk assessment for CdO based on soluble salt studies seems to be justified.

Table 3.213 Equilibrium speciation in soil contaminated with 50 $\mu g\ g^{-1}$ Cd added as CdO. The speciation is predicted with MINTEQA2 (Allison et al., 1991). The logK value of the reaction $Cd^{2+} + H_20 \rightarrow CdO$ (Monteponite) $+2H^+$ is –15.12 (database of MINTEQA2). Input parameters: soil moisture content = 0.2 g g^{-1}; soil solution composition $Ca(NO_3)_2$ 5 mM. Sorption of Cd^{2+} was assumed to occur on an infinite number of sites. At each soil pH, a solid:liquid concentration ratio K_D (solution Cd^{2+} activity based) was selected that represents a typical value (see Table 3.1.88)

speciation	Soil pH 5 K_d 50L/kg	Soil pH 6 K_d 200L/kg	Soil pH 7 K_d 800L/kg
CdO (% of total)	0.0	0.0	0.0
Cd^{2+} sorbed on soil solid (% of total)	99.3	99.8	99.9
Cd in soil solution (% of total)	0.7	0.2	< 0.1
Soil solution Cd^{2+} (μM) $Cd(NO_3)^+$ (μM)	 14.4 0.2	 3.61 0.05	 0.9 < 0.01

Influence of soil properties on Cd toxicity

Soil properties influence Cd toxicity. This is illustrated in this review in several tests that have been performed on a series of different soils. A general trend emerges that toxicity increases in soil when mobility of Cd is higher, i.e. soil toxicity increases as soil pH, or soil organic matter decrease. Exceptions to this rule have also been found (Mahler et al., 1978, see Section 3.2.3.4.).

The toxicity data were not converted to a standard soil in contrast with suggestions of the Technical Guidance Document (TGD, 1996, p.338). The suggested conversion corrects the data to a soil with a standard organic matter content of 3.4%. Whereas this conversion may be relevant for hydrophobic compounds, no information was found that bioavailability of metals in soil is predominantly related to soil organic matter content. Other normalisation equations that are used for defining maximum permissible concentrations in soils in Flanders-Belgium (Vlarebo, 1996) or in the Netherlands (Lexmond et al., 1986) are merely corrections for variance in background concentrations with soil properties. Since most LOEC data are substantially higher than background concentrations, no such normalisation equation can be advocated. We are not aware of any experimentally obtained relationship between soil properties and soil toxicity for Cd. Sauvé et al. (1998) demonstrated that toxicity of Pb and Cu on plants or on microbial processes correlates better with soil solution metal activity than with total concentrations. This indicates that soil solution metal activities represent the toxic dose in the soil. If this is the case, then soil toxicity data could be normalised based on e.g. soil properties that affect solid-liquid distribution of Cd. Crommentuijn et al. (1997b) however demonstrated that variation in Cd EC_{50} values for growth of the collembollan *Folsomia candida* increased when effects were expressed as Cd concentrations instead of total concentrations. The collembollan were exposed to Cd in artificial soils varying in pH and organic matter content, and hence, varying in Cd^{2+} sorption. It is unclear if the same is true for plants or soil microbial processes.

3.2.3.2 Toxicity to soil microflora

Table 3.214 Selected data for Cd toxicity to soil microflora. Fifty tests were reviewed from 18 source documents and 36 tests were selected

	Min	Median	Max	n
NOEC (μg g^{-1})	3.6	50	3,000	21
LOEC (μg g^{-1})	7.1	100	8,000	21
$E(L)C_{x\geq50}$ (μg g^{-1})	7.1	283	5,264	20

The soil microflora cycle C, N, P and S compounds in soil. Toxicity to some essential pathways in these cycles may result in plant nutrient deficiencies or unacceptable losses of nutrients to the environment.

Respiration is a process which is performed by a suite of soil organisms with varying sensitivities to soil contamination. Bond et al. (1976) measured respiration in a forest soil and litter microcosm for 24 days following soil contamination with 0, 0.01 and 10 μg g^{-1} Cd. The respiration rate between days 6-24 at the highest Cd rate was decreased by 36% compared with the control. No information was given on soil properties. Similar respiration studies with forest soil (0-4.5 cm) microcosms contaminated with 0, 0.6 and 6 μg g^{-1} Cd could not detect significant toxic effects on respiration rates followed over 23 days after contamination (Chaney et al., 1978). Interestingly, respiration rate decreased faster during incubation in control microcosms than in the Cd treated ones, resulting in significant higher respiration rates at 23 days in the Cd treated soils. To overcome the problems with high variability between the replicates, respiration of each microcosm was expressed as a percentage of that rate just prior to the treatment. Expressed this way, respiration was not significantly reduced by Cd up to the highest application rate at either 1.5 or 23 day's incubation. However, in treatments with 47 μg g^{-1} Zn added Cd addition at the highest dose reduced respiration rate faster than in the control soils at 36 hours after contamination. The added amount of Cd was not mixed in the microcosms (applied as a solution on the top layer) and, therefore, this test is not selected for effects assessment. Cornfield (1977) found evidence for increasing Cd toxicity with time on soil respiration. The respiration was followed for 8 weeks after contaminating the acid sandy soil with either 10 or 100 μg g^{-1} Cd. No toxic effects were noted for the 0-2 week’s incubation whereas respiration significantly reduced by 17 % at the lowest rate tested for the 0-8 week’s incubation. Saviozzi et al. (1997) found no Cd effects up to 50 μg g^{-1} on total respiration (28 days) in an inceptisol. Walter and Stadelman (1979) measured soil respiration for 24 hours in loamy sand previously grown for 14 weeks by maize plants. The soils were contaminated with Cd at 5 rates between 0 and 58 μg g^{-1} before plant growth. The LOEC was found at 29.1 μg g^{-1} at which respiration was 36% lower than in the nil treatment. Doelman and Haanstra (1984) compared toxic effects on respiration between five different soils amended with various Cd rates between 55 and 8,000 μg g^{-1}. Respiration rate was followed during approximately 18 months after contamination. In one soil (sandy soil) toxicity markedly reduced by ageing whereas no such clear trend was found in the other soils. The respiration rates at the end of the incubation period were insignificantly affected by Cd concentrations up to concentrations ranging from 150 to 3,000 μg g^{-1}. Increasing clay content and organic matter content reduced Cd toxicity in soil (Doelman and Haanstra, 1984). It is unclear why NOEC values in this study are much higher than the LOEC values for respiration from the studies cited above. In another study by the same authors (Haanstra and Doelman, 1984) glutamic acid (GLU) induced respiration was followed on the same soils (one soil not included). The time to reach a peak in respiration rate was chosen as the endpoint. The soils were all measured 18 months after Cd addition. Elevated Cd reduced GLU decomposition rate. In the sandy soil, a small but significant decrease in decomposition rate was already found at 55 µg g^{-1} (lowest concentration tested). In the other 4 soils, an inhibitory effect was only found at higher concentrations or not found (peat soil). A similar study on substrate (glucose and GLU) induced respiration was made on three different soils amended with various Cd rates between 1.8 and 229 µg g^{-1} (Reber 1989). In this study, the respiration rate of the treated soils was measured at the time where respiration rate increased maximally in the control soils. This endpoint proved to be very sensitive and statistically significant toxic effects (6% inhibition) were already found at Cd levels of 2.7-7.8 µg g^{-1}. More than 10% inhibition was found at 7-29 µg g^{-1} (LOEC values). It should be stressed that this endpoint should not be compared with, for example, cumulative respiration, an endpoint that is far less sensitive as can be derived from the studies cited above. Khan and Frankland (1984) measured toxic effects of Cd on cellulolytic activity in a loamy sand soil. The cellulolytic activity was measured using the dye release from a dyed cellophane film, encased in a nylon mesh and placed for 30 days in the soil. The soil was contaminated with various Cd rates between 0 and 100 µg Cd and incubated for 15 days prior to the test. The dye release was measured in a pot with or without growing plants. In the uncropped soils, the LOEC was 50 µg g^{-1} at which cellulolytic activity was 17% below that of the control. In the presence of plants, cellulolytic activity was more sensitive to Cd and the LOEC with oat plants was found at 10 µg g^{-1} (lowest concentration tested) where the inhibition was already 34%.

The *N-cycle* provides various pathways on which toxic effects can be monitored. Liang and Tabatabai (1978) measured NH_4^+-N induced nitrification as NO_3^-+NO_2^- accumulation after 10 days of incubation. Three soil types were contaminated with only one Cd application rate (560 µg g^{-1}). Nitrification decreased by between 67% and 94% compared with the nil treated soils. Bewley and Stotzky (1983) followed mineralisation and nitrification for 35 days after adding glycine to soils contaminated with 50, 100, 500 and 1,000 µg g^{-1} Cd. Nitrate accumulated at a lower rate in the Cd treated soil columns compared with the control. After 4 days, nitrate accumulation was 23% lower at the lowest Cd concentration tested (50 µg g^{-1}). After 35 days incubation, significant effects on nitrate accumulation were only found at the highest concentration tested. The Cd application was not well mixed in the soil columns and, therefore, these data were not selected for the effects assessment. Dušek (1995) measured ammonification and nitrification in two soils with and without NH_4^+ addition. Both soils were contaminated with 0, 10, 100 and 500 µg g^{-1} Cd. The LOEC's on maximum nitrate production rate were found at 100 µg g^{-1} or above. Walter and Stadelman (1979) measured ammonification on the same soil sample on which respiration was measured (see above). The ammonium accumulated after 50 days incubation was not sensitively affected up to the highest concentration tested (58 µg g^{-1}). Denitrification of nitrate in anaerobic conditions in a helium atmosphere was followed for a silt loam soil contaminated with various Cd rates between 0 and 500 µg g^{-1} (Bollag and Barabasz, 1979). Some samples were autoclaved and subsequently inoculated with *Pseudomonas*. Because of unknown effect of autoclaving soils on Cd availability, only the data obtained with the native soil microflora in unautoclaved soils are reported here. The various N forms (NO_3^-, NO_2^-, N_2O and N_2) were followed during 3 weeks of incubation. Removal of nitrate was slower and accumulation of the intermediates (NO_2^-, N_2O) was higher in the Cd treated soils. The presence of the intermediate N_2O (a greenhouse gas) was already higher at the lowest concentration tested (10 µg g^{-1}) after two or three weeks incubation. At a Cd level of 100 µg g^{-1}, the remaining quantities of NO_3^- + N_2O in the systems were about twice as high as in the control soil after 2 weeks incubation.

Toxic effects on *soil enzymes* are often used in soil toxicology, perhaps because of the ease of measurement. The enzymes reported here, urease, phosphatase and arylsulphatase, represent responsible parts of the N, P and S cycle respectively. Doelman and Haanstra (1986, 1989) and Haanstra and Doelman (1991) reported effects of Cd addition on enzyme activities in the five soils which were also used for the respiration studies (Doelman and Haanstra, 1984). The enzyme activities were recorded at a saturating substrate concentration in soils either 6 weeks or 18 months after Cd addition. Cd rates varied from 55 to 8,000 µg g^{-1}. The inhibition of the enzyme activity was plotted to the log of the added Cd concentration. A logistic response curve was plotted to the data and an EC_{50} was calculated by interpolation where curve fitting was possible. The EC_{50} values are given in **Table 3.215**. Toxicity of Cd increased with time (decrease of EC_{50}) for all combinations of soil and type of enzymes where response curves could be fitted. In all soils, except the peat soil, response curves were significant at 18 months after incubation and this incubation time was chosen for discussion below. The toxic effects of Cd were in general terms most pronounced in the sandy soil. Among the three enzymes, the urease activity was generally most sensitive to Cd (lowest EC_{50} values) except in the silty loam at pH 7.7. The EC_{50} value of urease in the sandy loam was 30 µg g^{-1} and is below the lowest concentration tested. The authors also reported the EC_{10} which were calculated with the experimental curves. These EC_{10} values range from < 1 to 280 µg g^{-1} for urease, from 16 to 8,000 µg g^{-1} for phosphatase and from 3.4 to 5,880 µg g^{-1} for arylsulphatase. Ten of the 14 EC_{10} values however fall below the lowest concentration tested (55 µg g^{-1}) and, hence, their statistical significance is questionable. The LOEC's were unfortunately not given in the original papers.

Biological *N_2 fixation* (either by free living cyanobacteria or as symbiotic associations) is very sensitive to soil pollution (Brookes, 1995). Toxic effects are found in soils treated with sewage sludge where, of course, multiple metal contamination is found. The LOEC values on yield of clover or on population of *Rhizobium leguminosarum* biovar *trifolii* are 0.8 µg g^{-1}, 1.0 µg g^{-1} and 6.0 µg g^{-1} Cd in three European long-term sludge treated plots (McGrath et al., 1995). The Zn levels on these sites are 130 µg g^{-1}, 200 µg g^{-1} and 180 µg g^{-1} respectively. All three Zn levels are below current limits of sludge treated soils in the EC. Effects of single metals on survival of *Rhizobium leguminosarum* biovar *trifolii* in soil was reported by Chaudri et al. (1992). This survival study used a farmyard manure treated plot of the Woburn Experimental Farm (U.K.). Two month after $CdSO_4$ application, no toxic effects were found on survival of the *Rhizobium* strains. After 18 months, however, the cell number was decreased in all soils and this decrease was most pronounced in the metal applied samples. The Cd NOEC was 4 µg g^{-1} and at 7.1 µg g^{-1} no more cells of the *Rhizobium* strains were detected. The nitrogen content in white clover plants grown on these soils decreased with increasing soil Cd content with a LOEC of 7.1 µg g^{-1}. In N-fertilised samples, no such decrease in plant N-content was found confirming toxicity on N_2-fixation. The evidence of metal toxicity on N_2-fixation which has been gathered in the last decade is however conflicting. NOEC values on N_2-fixation in sludge treated soils are often higher than the LOEC values given above (e.g. Ibekwe et al., 1995)

The toxicity tests for soil microflora lack standardisation that complicates mutual comparison of the tests described above. Toxicity of Cd generally decreases with increasing clay content, pH and organic matter content. The data compilation shows that N_2-fixation is probably the most sensitive soil microbial process. Toxic effects on N_2-fixation have been found at moderate Cd pollution, both in metal salt applied soils as in sludge treated soils.

Table 3.215 Toxicity to soil microflora. All underlined data are selected to discuss the critical concentrations (Table 3.214). Bold data are used to estimate the HC_5 (Table 3.225). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	Organism	Medium	pH[a]	%OC[b]	% clay	Equil. Period (d)	Duration (d)	Endpoint	NOEC (µg g^{-1})	Cat.*	LOEC (µg g^{-1}) (%effect)	$EC_{x\geq50}$ (µg g^{-1}) (%effect)	References	R.I.
CdOAc.	native soil microflora	phaeosem	6.9	1.3	21	>1 week	84(min.)	substrate induced respiration rate	3.6	1	7.1(15)	60	Reber, 1989	2
		neutral sandy hortisol	7	1.5	3		84(min.)	substrate induced respiration rate	3.6	1	7.1(15)	70		2
		acidic cambisol	5.6	1	7		84(min.)	substrate induced respiration rate	14.3	1	28.6(18)	>228(HT)		2
$CdCl_2$	native soil microflora	grassland soil	7.4	5.7	24	0	33	nitrification: NO_3^- production rate					Dušek, 1995	2
								$-NH_4^+$substrate	50	2	100(19)			
								$+NH_4^+$substrate	10	1	100(13)	500(60)		
			7.6	2.9	19		33	nitrification: NO_3^- production rate						
								$-NH_4^+$substrate	50	2	100(12)			
								$+NH_4^+$substrate	100	1	500 (45)			
$Cd(NO_3)_2$	native soil microflora	loamy sand	5.8	2.7	16	>98	1	24h respiration	14.6	1	29.1(36)		Walter and Stadelman, 1979	2
$CdCl_2$	native soil microflora	sand	7	1.1	2	560	1-2	glutamic acid decomposition time				150(56)	Haanstra and Doelman, 1984	2
		silty loam	7.7	2.6	19	560	1-2	glutamic acid decomposition time	55	1	150(15)			2
		clay	7.5	3.4	60	560	1-2	glutamic acid decomposition time	150	1	400(10)			2
$CdCl_2$	native soil microflora	sand	7	1.1	2	490	42-70	respiration	150	3	400(23)		Doelman and Haanstra, 1984	3
		sandy loam	6	6.1	9	301	42-70	respiration	150	1	400(20)			2
		silty loam	7.7	2.6	19	630	42-70	respiration	150	1	400(17)			2
		clay	7.5	3.4	60	560	42-70	respiration	3,000	1	8,000(34)			2
		peat	4.5	13.6	5	574	42-70	respiration	400	1	1,000(19)			2
$CdCl_2$	native soil microflora	sandy soil	7	1.1	2	42	5h	urease activity				340	Haanstra and Doelman, 1991	2
						560	5h	urease activity				120		
						42	1h	phosphatase activity				840		
						560	1h	phosphatase activity				330		
						42	2h	arylsulphatase activity				2,206		
						560	2h	arylsulphatase activity				121		
		sandy loam	6	6.1	9	42	5h	urease activity				>8,000		
						42	1h	phosphatase activity						
						42	2h	arylsulphatase activity				>8,000		

Table 3.215 continued overleaf

Table 3.215 continued Toxicity to soil microflora. All underlined data are selected to discuss the critical concentrations (Table 3.214). Bold data are used to estimate the HC_5 (Table 3.225). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	Organism	Medium	pHa	%OCb	% clay	Equil. Period (d)	Duration (d)	Endpoint	NOEC (µg g-1)	Cat.*	LOEC (µg g-1) (%effect)	ECx≥50 (µg g-1) (%effect)	References	R.I.
						560	2h	arylsulphatase activity				1,792		2
		silty loam	7.7	2.6	19	42	5h	urease activity				970		
						560	5h	urease activity				520		
						42	1h	phosphatase activity				5488		
						560	1h	phosphatase activity				235		
						42	2h	arylsulphatase activity				1,882		
						560	2h	arylsulphatase activity				137		
		clay	7.5	3.4	60	42	5h	urease activity				4,460		
						560	5h	urease activity				520		
						42	1h	phosphatase activity				9,744		
						560	1h	phosphatase activity				5,264		
						42	2h	arylsulphatase activity				9,486		
						560	2h	arylsulphatase activity				1,016		
		peat	4.5	13.6	5	42	5h	urease activity				3,260		
						560	5h	urease activity				490		
						42	2h	arylsulphatase activity				3,181		
$CdSO_4$	native soil microflora	sandy soil	4.9	2.2	5.2	0	56	respiration	5	2	10(17)		Cornfield 1977	3
$CdSO_4$	*Rhizobium leguminoasorum* bv. *trifolii*	sandy loam	6.5	/	9		540	cell number (survival)	4	3		7.1(100)	Chaudri et al., 1992	3
$CdCl_2$	native soil microflora	brown earth loamy sand	4.6	*1-20***	*0-15***	15	45	cellulolytic activity: unplanted soil	10	1	50(17)		Khan and Frankland, 1984	3
								oat grown soil			10(34)LT			3
								wheat grown soil			50(43)LT			3
$CdSO_4$	native soil microflora	organic soil	4.5	47		180	180	respiration rate	60	3		1,574	Frostegård et al., 1993	3
								ATP content	112	3		2,810		3
		sandy-loam	7.8	2.6		180	180	ATP content	112	3		708		3
$CdCl_2$	native soil microflora	inceptisol	5.2	1.4	8	0	28	substrate induced respiration	50	3	250(27)		Saviozzi et al., 1997	3
$Cd(NO_3)_2$	native soil microflora	silt loam	6.7	1.9	28	0	14	denitrification			10LT	100	Bollag and Barabasz, 1979	3

Table 3.215 continued overleaf

Table 3.215 continued Toxicity to soil microflora. All underlined data are selected to discuss the critical concentrations (Table 3.214). Bold data are used to estimate the HC_5 (Table 3.225). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	Organism	Medium	pHa	%OCb	% clay	Equil. Period (d)	Duration (d)	Endpoint	NOEC (µg g-1)	Cat.*	LOEC (µg g-1) (%effect)	ECx≥50 (µg g-1) (%effect)	References	R.I.
Supporting data														
$CdSO_4$	native soil microflora	sandy soil	4.9	2.2	5.2	0	14	respiration	100HT				Cornfield 1977	4
$CdCl_2$	native soil microflora	forest soil	4.8	1.1	*0-15***	0	1.5	respiration rate:					Chaney et al., 1978	
		(0-4.5cm)						47ppm Zn added	1.3		6.7(28)			4
								no Zn added	6.7HT					4
		loamy sand					23	with or without Zn added	6.7HT					4
$Cd(NO_3)_2$	native soil microflora	loamy sand	5.8	2.7	16	>98	50	ammonification: NH_4^+ found after 50 days incubation	58HT				Walter and Stadelman, 1979	4
$CdCl_2$	native soil microflora	Peat	4.5	13.6	5	560	1-2	glutamic acid decomposition time	1,000HT				Haanstra and Doelman, 1984	4
$CdSO_4$	native soil microflora	surface soil	4.8	3.8	9	0	4	nitrification: % NO_3^- of total N			50(30)LT	1,000(54)	Bewley and Stotzky, 1983	4
$CdSO_4$	native soil microflora	surface soil	5.8	2.8	23	0	10	nitrification: NO_3^- + NO_2^- accumulation after 10 days with addition of NH_4^+				560(94)LT	Liang and Tabatabai, 1978	4
			7.8	3.9	30		10	nitrification: NO_3^- + NO_2^- accumulation after 10 days with addition of NH_4^+				560 (70)LT		
			7.4	5.7	34		10	nitrification: NO_3^- + NO_2^- accumulation after 10 days with addition of NH_4^+				560(67)LT		
$CdSO_4$	native soil microflora	Lösslehm	6.10	1.56			30	microbial biomass	30(HT)				Beck, 1981	4
							52	nitrification	33(HT)					4
		Lösslehm degr	3.25	3.45			30	microbial biomass	30(HT)					4
		Lösslehm + kalk	7.25	1.47			30	microbial biomass	30(HT)					4
							38	nitrification	30(HT)					4
		Auengleye	7.50	2.91			30	microbial biomass	30(HT)					4
							37	nitrification	33(HT)					4
		Auenboden	7.20	1.95			30	microbial biomass	30(HT)					4
							37	nitrification	33(HT)					4
$CdCl_2$	native soil microflora	forest soil				0	24	respiration	0.01	2	10(36)		Bond et al., 1976	4

a) pH-water ;
b) %OC= %OM/1.7;
LT Lowest Tested concentration;
HT Highest Tested concentration;
* NOEC classification (see Section 3.2.1.2);
** estimated OC - clay content..

3.2.3.3 Toxicity to soil fauna

Table 3.216 Selected data for Cd toxicity to soil fauna. Forty tests were reviewed from 22 source documents and 37 tests were selected

	Min	Median	Max	n
NOEC (μg g^{-1})	5	32	320	13
LOEC (μg g^{-1})	5	59	326	12
$E(L)C_{x\geq50}$ (μg g^{-1})	27	102	3,680	28

The potential hazards of environmental pollutants to soil invertebrates have been assessed in acute and chronic toxicity tests. The toxicity of Cd (Cd^{2+} salts) has been tested with standard tests: the 14-day LC_{50} test using the earthworm *Eisenia fetida* (OECD 1984, EEC 1985) and the ISO test (ISO, 1994) with the collembolan *Folsomia candida.*

Table 3.216 summarises the reviewed literature data. Reproduction parameters are generally more sensitive to Cd than growth or survival. Spurgeon et al. (1994) grew adult *E. fetida* in contaminated OECD artificial soil (pH 6.3) for 8 weeks to test the effects of Cd [as $Cd(NO_3)_2$] on survival and cocoon production. Soil contamination ranged from 10 to 300 μg g^{-1}. The calculated LC_{50} was greater than 300 μg Cd/g soil (highest concentration tested). Cocoon production was unaffected at 5 μg g^{-1} but was reduced by 80% at 20 μg g^{-1}. The NOEC value for cocoon production in this soil is the lowest NOEC value for soil fauna found in this literature review. It was however noted by the authors (Spurgeon et al., 1994) that worms in all treatments lost weight after two weeks in the experiment. Using the same artificial soil, the EC_{50} of the growth of *E. fetida* was 33 μg Cd/g soil and there was no observed effect at 18 μg Cd/g soil (Van Gestel et al., 1991). Sexual development of *E. fetida* was inhibited at 10 μg Cd/g soil (lowest concentration tested) and a 50% effect was found at 27 μg Cd/g soil. The LC_{50} was 253 μg Cd/g soil. In studies by van Gestel et al. (1993) it was found that reproduction of *Eisenia* was more sensitive than growth. Khalil et al. (1996b) reported a LOEC of 10 μg Cd/g soil, the lowest concentration tested, and an EC_{50} of 35 μg Cd/g soil for cocoon production of the earthworm *Aporrectodea caliginosa* in natural soil 56 days after Cd addition. The LC_{50} was found at 540 μg Cd/g. Growth of this earthworm in that soil was reduced by 50% at 68 μg Cd/g (Khalil et al., 1996a).

Increasing exposure time generally increases toxicity in the laboratory tests. Van Gestel and van Dis (1988) recorded an increase in mortality with increasing exposure time, using the 14-day OECD test. Khalil et al. (1996b) and van Gestel et al. (1991) extended the exposure time of the earthworm to 8 and 12 weeks respectively. Both authors found a significant decrease of more than 50% of the LC_{50} during the exposure period. A short exposure time may therefore explain the higher LC_{50} values found by Neuhauser et al. (1985) in an artificial soil. An LC_{50} value of 1,843 μg g^{-1} was recorded in 2 weeks of exposure.

Fitzpatrick et al. (1996) compared the sensitivity to Cd in an artificial OECD-soil between two earthworm species. The LC_{50} of *Lumbricus terrestris* was lower than that of *Eisenia fetida* (256 versus 374 μg g^{-1} soil).

Soil characteristics influence Cd sorption and therefore its bioavailability and toxicity. Van Gestel and van Dis (1988) investigated the influence of pH on the toxicity of Cd to earthworms. Toxicity was assessed in a sandy soil limed from pH 4.1 to pH 7.0. The LC_{50} value at pH 4.1 was at least 3 to 4-fold lower than at pH 7.0. Bengtsson et al. (1986) studied the combined effects of Cd pollution and acidification of the soil on the earthworm *Dendrobaena rubida*. Tests were performed at pH 4.5, 5.5 and 6.5 in the C horizon of a sandy coniferous forest soil mixed with well decomposed cattle dung. Cocoon production was lower at pH 4.5 than at higher pH values in the nil treated soils. Cadmium significantly reduced cocoon production at pH 4.5. At pH 5.5 and 6.5 however, 10 µg Cd/g increased cocoon production whereas 100 µg Cd/g significantly decreased this productions at pH 5.5 only. Similar conclusions were made about effects of pH and Cd on success of hatching of the cocoons. No toxic effects of Cd on growth were found. At pH 6.5, growth was even increased by 100 µg Cd/g compared to control. Crommentuijn et al. (1997b) investigated the effects of pH and organic matter content on toxicity of Cd on growth and reproduction of the springtail *Folsomia candida*. The difference in soil properties affected the performance of the test organisms. Soluble Cd concentrations increased when pH or organic matter decreased in soil. The variation in Cd EC_{50} values for growth increased when effects were expressed as soluble Cd concentrations instead of total concentrations.

Kammenga et al. (1996), Korthals et al. (1996) and Parmelee et al. (1997) studied the effect of Cd pollution on nematodes. Korthals et al. (1996) recorded a NOEC value of 160 µg Cd/g (highest concentration tested) for survival of the natural nematode community in a sandy soil. Parmelee et al. (1997) found a comparable NOEC value of 200 µg g^{-1} (highest concentration tested) for survival in a forest topsoil. Kammenga et al. (1996) found a NOEC value for the juvenile/adult ratio of the nematode *Plectus acuminatus* of 32 µg g^{-1} in an artificial OECD-soil.

This data compilation seems to indicate that soil fauna are less sensitive to Cd than soil microflora. The LOEC values obtained with soil fauna are all higher than or equal to 5 µg g^{-1} whereas Cd toxicity to soil microbial processes or plants has been shown at lower Cd concentrations (see Section 3.2.3.2 and 3.2.3.4). Soil fauna could indeed be more resistant to Cd but it is striking to note that sensitive endpoints (e.g. reproduction) have rarely been tested in the 1-10 µg g^{-1} range. Some LOEC values of 10 µg g^{-1} are found at the lowest concentration tested for reproduction parameters of *Eisenia andrei* (van Gestel et al., 1991 and 1993). Three tests were found where Cd toxicity was measured below 10 µg g^{-1} (Khalil et al., 1996a, Spurgeon et al., 1994 and Parmelee et al., 1997). One of these tests showed Cd toxicity at 5 µg g^{-1} (Khalil et al., 1996a).

Table 3.217 Toxicity to soil fauna. All underlined data are selected to discuss the critical concentrations (Table 3.216). Bold data are used to estimate the HC_5 (Table 3.225). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	Organism	Medium	pH[a]	%OC[b]	Clay	Equil. Period (d)	Duration (d)	Endpoint	NOEC (μg^{-1})	Cat.*	LOEC ($\mu g\ g^{-1}$) (%effect)	$EC_{x\geq50}$ ($\mu g\ g^{-1}$) (%effect)	$LC_{x\geq50}$ ($\mu g\ g^{-1}$) (%effect)	References	R.I.
$CdCl_2$	*Folsomia candida*	OECD-soil	6.1$	5.9	20		42	fresh weight	50	1		322		van Gestel and Hensbergen, 1997	1
								reproduction	22	5		51			
$CdCl_2$	*Eisenia fetida*	OECD soil	7$	5.9	10.4	0		mortality					> 1,000HT	Van Gestel and van Dis, 1988	1
$CdCl_2$	*Folsomia candida*	OECD soil	6.6	5.9	20	0	35	mortality					972	Crommentuijn et al., 1995	1
								growth				633			
								number of juveniles				153			
								population increase				152			
$Cd(NO_3)_2$	*Eisenia fetida*	OECD-soil	6.5	5.8	20	0	14	mortality					374	Fitzpatrick et al., 1996	1
$Cd(NO_3)_2$	*Dendrobaena rubida*	C-horizon of sandy coniferous forest soil+well decomposed cattle dung	4.5	4.5-6.9		4 weeks	110	cocoon production	10	1		100(72%)		Bengtsson et al., 1986	2
			5.5					cocoon production				100(78%)			2
			6.5				270	hatching success	10	1	100(47)				2
			5.5					embryonic development			10LT				2
$CdCl_2$	*Lumbricus rubellus*	sandy loam soil	7.3	4.7	17	0	42	mortality	150	3			1,000(100)	Ma, 1982	3
								weight	150	3					
$CdCl_2$	*Folsomia candida*	OECD-soil	6.3$	5.9	20	0	42	mortality at 25% MC					1,275	van Gestel and van Diepen, 1997	3
								45%MC					868		
								55%MC					617		
								fresh weight at 25%MC	160	3	320(72)	523			3
								35%MC	320	1		640(73)			2
								45%MC	80	3	160(43)	253			3
								55%MC	160	3	320(29)	481			3
								reproduction at 25%MC				80(56)LT			3
								35%MC				80(57)LT			
								45%MC				80(46)LT			
								55%MC				80(43)LT			
$CdCl_2$	*Eisenia fetida*	sandy soil	4.1$	1	4.3	0	14	mortality					320-560	Van Gestel & van Dis, 1988	2

Table 3.217 continued overleaf

Table 3.217 continued Toxicity to soil fauna. All underlined data are selected to discuss the critical concentrations (Table 3.216). Bold data are used to estimate the HC_5 (Table 3.225). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	Organism	Medium	pHa	%OCb	Clay	Equil. Period (d)	Duration (d)	Endpoint	NOEC (µg-1)	Cat.*	LOEC (µg g-1) (%effect)	ECx≥50 (µg g-1) (%effect)	LCx≥50 (µg g-1) (%effect)	References	R.I.
$CdCl_2$	*Folsomia candida*	OECD soil; T 20; 50% WHC	5.4-5.9$	1.2	20	0	35	growth				246		Crommentuijn et al., 1997b	2
								reproduction				125			
			5.4$					mortality							
				2.1				growth				356	323		
								reproduction				44			
			5.7$					mortality							
				3.1				growth				389			
								reproduction				82	684		
			5.9$					mortality							
				4				growth				651			
								reproduction				193			
			5.9$					mortality					758		
				4.9				growth				615			
								reproduction				130			
			5.8$					mortality							
				5.9				growth				824	940		
								reproduction				193			
			3.1$					mortality							
				5.9				growth				302			
								reproduction				102	890		
			3.7$					mortality							
				5.9				growth				316			
								reproduction				102			
			4.3$					mortality					1261		
				5.9				growth				542			
								reproduction				164			
			5.7$					mortality							
				5.9				growth				697	743		
			7$					reproduction				177			
				5.9				growth				583			
			7.3					reproduction				113			
				5.9				growth				601	1276		
								reproduction				306			
$CdCl_2$	*Folsomia candida*	OECD soil	6	5.9	20	0	19	mortality	326	1	707		917	Crommentuijn et al., 1993	2
								number of offspring				/			
								growth	148	1	326	448			2

Table 3.217 continued overleaf

Table 3.217 continued Toxicity to soil fauna. All underlined data are selected to discuss the critical concentrations (Table 3.216). Bold data are used to estimate the HC_5 (Table 3.225). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	*Organism*	Medium	pHa	%OCb	Clay	Equil. Period (d)	Duration (d)	Endpoint	NOEC (µg-1)	Cat.*	LOEC (µg g-1) (%effect)	ECx≥50 (µg g-1) (%effect)	LCx≥50 (µg g-1) (%effect)	References	R.I.
							23	mortality	326	1	707		778		2
								number of offspring	71	1	148	159			2
								growth	148	1	326	376			2
							26	mortality	326	1	707		822		2
								number of offspring	71	1	148	204			2
								growth	326	1		707			2
							30	mortality	326	1	707		893		2
								number of offspring	71	1	148	227			2
								growth	148	1	326	541			2
							35	mortality	326	1			854		2
								number of offspring	148	1	326	807			2
								growth	326	1	707				2
$Cd(NO_3)_2$	*Eisenia fetida*	OECD soil	6	5.9	20	0	14	mortality					1843	Neuhauser et al., 1985	2
$Cd(NO_3)_2$	*Eisenia fetida*	OECD soil	6.3	5.9	20		56	cocoon production	5	1		46		Spurgeon et al., 1994	3
$CdCl_2$	*Eisenia andrei*	OECD soil	6.3	5.9	20	7	21	cocoon production			10(LT)			Van Gestel et al., 1993	3
								juvenile/adult ratio	10	3	18(38)				3
$CdSO_4$	*Aporrectodea caliginosa*	natural forest soil	7.05	12.5		0	42	growth			5(40)LT)	68		Khalil et al., 1996a	3
$CdSO_4$	*Aporrectodea caliginosa*	natural forest soil	7.05	12.7		0	56	mortality					540	Khalil et al., 1996b	3
								cocoon production			10(28)LT	35			3
$CdCl_2$	*Eisenia andrei*	OECD soil	6.7	5.9	20		84	growth	18	1		33		van Gestel et al., 1991	3
								mortality					253		3
								sexual development			10(37)LT	27			3
$CdCl_2$	*Plectus acuminatus*	OECD soil	5.5	5.9	20	5h	21	juvenile/adult ratio	32	1	100(24)	321		Kammenga et al., 1996	3
$Cd(NO_3)_2$	*Lumbricus terrestris*	OECD-soil	6.5	5.8	20	0	14	mortality					256	Fitzpatrick et al., 1996	3
$CdCl_2$	*Enchytraeus albidus*	OECD-soil	6.5	5.9	20	0	28	mortality					3,680	Römbke, 1989	3

Table 3.217 continued overleaf

Table 3.217 continued Toxicity to soil fauna. All underlined data are selected to discuss the critical concentrations (Table 3.216). Bold data are used to estimate the HC_5 (Table 3.225). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	*Organism*	Medium	pHa	%OCb	Clay	Equil. Period (d)	Duration (d)	Endpoint	NOEC (µg-1)	Cat.*	LOEC (µg g-1) (%effect)	ECx≥50 (µg g-1) (%effect)	LCx≥50 (µg g-1) (%effect)	References	R.I.
Supporting data															
$Cd(NO_3)_2$	*Eisenia fetida*	OECD soil	6.3	5.9	20		56	mortality	300HT					Spurgeon et al., 1994	4
$CdCl_2$	*Eisenia andrei*	OECD soil	6.3	5.9	20	7	21	growth	100HT					Van Gestel et al., 1993	4
$CdSO_4$	nematode community	top 10cm of an arable field on a sandy soil	4.1	1.9	4		14	mortality	160HT					Korthals et al., 1996	4
$CdSO_4$	trophic groups of nematode and microanthropod communities	top 10cm of A-horizon of mature oak-beech forest soil	3.8$	3.4	11	0	7	mortality	200HT					Parmelee et al., 1997	4
$Cd(NO_3)_2$	*Lumbricus terrestris*	artificial-soil				0	16	sperm-count				100		Cikutovic et al., 1993	4

a) pH-water;
$ pH-KCl;
b) OM = OC*1.7;
LT Lowest Tested concentration;
HT Highest Tested concentration;
MC Moisture content;
* NOEC classification (see Section 3.2.1.2)

3.2.3.4 Toxicity to higher plants

Table 3.218 Selected data for Cd toxicity to higher plants. Seventy-six tests were reviewed from 15 source documents and 54 tests were selected

	Min	Median	Max	n
NOEC ($\mu g\ g^{-1}$)	1.8	10	80	41
LOEC ($\mu g\ g^{-1}$)	2.5	40	160	44
E(L)$C_{x \geq 50}$ ($\mu g\ g^{-1}$)	2.8	100	320	34

Many studies report effects of Cd salts on plant development in potted soil. Only few studies were found in recent literature. There is currently a consensus that toxicity to plants due to single Cd pollution seldom occurs in the environment. In most cases, Cd pollution is associated with Zn pollution. Zinc is known to be more toxic to plants and plant growth effects in metal polluted areas are often attributed to Zn and not to Cd (Tiller, 1989). As stated above, we only report data that were obtained with single Cd pollution.

A summary of the literature review is given in **Table 3.218**. All data have been obtained using pot trials in greenhouse conditions. In most pot trials, Cd is homogeneously mixed in the whole soil prior to plant growth. In the experiments reported by Miles and Parker (1979) and by Kelly et al. (1979) however, the Cd^{2+} salts were incorporated by top dressing. These data are reported here but they were not selected for the effects assessment. Miles and Parker (1979) found that soil Cd in the top 2.5 cm of the pots was about twice as high as the intended average Cd level in soil. Near background Cd concentrations (< 1µg/g) were recorded in the base 2.5 cm of the pots. The strong toxic effects on growth of 3 of the 6 natural species tested at the lowest average concentration tested (10 $\mu g\ g^{-1}$) should therefore be treated with caution. Many threshold levels for Cd toxicity were obtained by Bingham et al. (1975) and by Mahler et al. (1978) using soils to which 1% sludge was incorporated. Sludge Cd was not the source for increasing Cd rates in soils (all soils obtained equal sludge rate). Bingham et al. (1975) report that the sludge was low in heavy metals without supplying the data. Mahler et al. (1978), from the same group of Bingham, report that 1% sludge application is equivalent to a metal application rate of 0.1 µg Cd/g, 6 µg Cu/g, 0.4 µg Ni/g and 20 µg Zn/g. These metal concentrations are all low and should not strongly increase the plant sensitivity to Cd. The data obtained by these two reports are interesting as they allow comparing differences in Cd toxicity between plant types (Bingham et al., 1975) and between soil types (Mahler et al., 1978). The data of Bingham et al. (1975) show that EC_{25} values vary from 4 $\mu g\ g^{-1}$ to 170 $\mu g\ g^{-1}$ between plant types. The EC_{25} values of rice were over 640 $\mu g\ g^{-1}$, the highest concentration tested. Mahler et al. (1978) showed that EC_{50} values vary from 105-320 $\mu g\ g^{-1}$ for chard and from 18-270 $\mu g\ g^{-1}$ for lettuce between the 8 soils. Among these 8 soils, 4 are acid (pH < 5.7), and 4 are calcareous (pH > 7.4). The Cd toxicity to chard is generally higher in acid soils (lower EC_{50}) than in calcareous soils, as expected based on the effect of pH on Cd sorption. However, Cd toxicity to lettuce is surprisingly generally higher in calcareous soils than in acid soils. Cd uptake in both plants is lower in the calcareous soils than in the acid soils. Why growth sensitivity of lettuce to absorbed Cd is so much higher in lettuce at higher soil pH is unknown. The other tests where Cd toxicity is compared between soil types support the general idea that Cd toxicity in soil is higher if the Cd sorption capacity of the soil is lower, i.e. at low pH, clay content and organic C content (Reber et al., 1989; Miller et al., 1976).

The low values of some LOEC values call for attention. The reliable LOEC values lower or equal to 4 µg g^{-1} are found by Miller et al. (1977), Reber (1989), Haghiri (1973) and by Bingham et al. (1975-with spinach only). These data generally relate to added Cd concentrations and Cd concentrations of the control soils were not given (generally below 1 µg g^{-1}). The LOEC values from the tests of Haghiri (1973) are derived as $EC_{>20}$ values without statistical information.

Two more source documents can be quoted here, which show Cd toxicity below 4 µg g^{-1} but of which data are not included in the table. The first report (Bingham et al., 1986) shows a significant yield reduction of 9 week-old Swiss chard upon adding 1 or 2.5 µg Cd/g to an unlimed sandy loam at pH 4. The yield reduction was 33% and 42% compared with the ‘control’ soil which was not a nil treatment but a soil supplied with 0.25 µg Cd/g. Because the ‘control’ soil was contaminated, no LOEC could be derived. The second report (Strickland et al., 1979) shows that yield of soybeans is reduced by over 30% upon adding Cd at 2.5 µg g^{-1}. The soil in which this effect was observed is, however an artificial substrate (quartz sand with 0.5% peat moss) wetted with dilute nutrient solution. Since this substrate represents an extreme example of a soil low in Cd sorption properties, we chose not to incorporate it in the table.

Table 3.219 Toxicity to higher plants. All underlined data are selected to discuss the critical concentrations (Table 3.218). Bold data are used to estimate the HC_5 (Table 3.225). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	Plant	Medium	pH[a]	%OC[b]	% clay	Equil. time prior to plant growth (d)	Growing period (d)	Pot (P) or field (F) trial	Endpoint	NOEC ($\mu g\ g^{-1}$)	Cat.*	LOEC ($\mu g\ g^{-1}$) (%effect)	$EC_{x\geq 50}$ ($\mu g\ g^{-1}$) (%effect)	References	R.I.
$CdCl_2$	*Picea sitchensis*	peaty gley	3.3	45	*40-100***	2	100	P	root length	1.8	1		2.8(59)	Burton et al., 1984	2
CdOAc	*Triticum aestivum*	phaeosem	6.9	1.3	21	>84	28	P	shoot dry weight	7.1	1	14.3(15)		Reber, 1989	2
		neutral sandy hortisol													
		acidic cambisol	7.0	1.4	3					29	1	57(15)			2
			5.6	0.9	7							3.6(11)			2
$CdCl_2$	*Glycine max*	silt loam	7.9	*1-20***	*0-28***	4 drying and rewetting cycles	28	P	shoot dry weight	10	3	100(22)		Miller et al., 1976	3
			6.0		*0-28***					10	3		100(69)		3
			5.5		*0-28***							10(26)			3
			6.5		*0-28***					5	4	10(12)	100(47)		3
		clay loam	6.1		*28-40***					10	3		100(66)		3
$CdCl_2$	*Zea mays*	loamy sand	6			4 drying and rewetting cycles	24	P	shoot dry weight			2.5(47)LT		Miller et. al, 1977	3
$CdCl_2$	*Raphanus sativus*	loamy sand	5.4	*1-20***	*0-15***	15	42	P	shoot dry weight	10	1	50(30)	70	Khan and Frankland, 1983	3
CdO												100(29)LT	190		3
$Cd(NO_3)_2$	*Lactuca sativa*	soil	3.9	1.2	8		42	P	shoot dry weight	2	2	32 (30)		Jasiewicz,1994	3
$CdCl_2$	*Avena sativa*	loamy sand	5.4	*1-20***	*0-15***	15	42	P	root dry weight			10(24)LT		Khan and Frankland, 1984	3
	Triticum aestivum					15	42	P	root dry weight				50(61)LT		
CdO	*Triticum aestivum*					15	42	P	root dry weight			100(47)LT			
$CdCl_2$	*Lactuca sativa*	humic sand	5.1	2.2			14	P	shoot fresh weight	32	1		136(50)	Adema and Henzen, 1989	3
		loam	7.5	0.8						3.2	1		33(50)		3
	Lycosperisicon esculentum	humic sand	5.1	2.2									16(50)		3
		loam	7.5	0.8						32	1		171(50)		3
	Avena sativa	humic sand	5.1	2.2						10	1		97(50)		3
		loam	7.5	0.8						10	1		159(50)		3

Table 3.219 continued overleaf

Table 3.219 continued Toxicity to higher plants. All underlined data are selected to discuss the critical concentrations (Table 3.218). Bold data are used to estimate the HC_5 (Table 3.225). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	Plant	Medium	pH[a]	%OC[b]	% clay	Equil. time prior to plant growth (d)	Growing period (d)	Pot (P) or field (F) trial	Endpoint	NOEC (µg g^{-1})	Cat.*	LOEC (µg g^{-1}) (%effect)	$EC_{x\geq 50}$ (µg g^{-1}) (%effect)	References	R.I.
$CdSO_4$	*Phaseolus vulgaris*	silt-loam soil amended with 1% clean sludge	7.5		*0-28***		up to maturity	P	bean dry weight	20	3	40 (25)		Bingham et al., 1975	3
	Glycine max								bean dry weight	2.5	3	5 (25)			3
	Triticum aestivum								grain weight	20	3	50 (25)			3
	Zea mays								kernel weight	10	3	18 (25)			3
	Lycosperisicon esculentum								ripe fruit weight	80		16(25)			3
	Cucurbita pepo								fruit weight	80	3	160 (25)			3
	Brassica oleracea								head weight	160(HT)	3				4
	Lactuca sativa								head weight	5	3	13 (25)			3
	Lepidium sativum								shoot weight	5	3	8 (25)			3
	Spinacia oleracea								shoot weight	1.25	3	4 (25)			4/3
	Brassica rapa								tuber weight	10	3	28 (25)			3
	Raphanus sativus								tuber weight	40	3	96 (25)			3
	Daucus carota								tuber weight	10		20 (25)			3
	Oryza sativa								grain weight	640(HT)					4
$CdSO_4$	*Lactuca sativa*	surface soils amended with 1% clean sludge	4.8	2.6	8.3	14	63	P	shoot dry weight	40	3	80(20)	260	Mahler et al., 1978	3
	Beta vulgaris					>77			shoot dry weight	20	3	80(35)	110		
	Lactuca sativa		5.0	3.3	14.6	14				40	3	160(22)	270		
	Beta vulgaris					>77				20	3	80(30)	135		
	Lactuca sativa		5.3	0.9	8.9	14				10	3	40(35)	100		3
	Beta vulgaris					>77				40	3	80(25)	110		
	Lactuca sativa		5.7	3.0	37.5	14				20	3	80(25)	160		
	Beta vulgaris					>77				40	3	160(40)	185		
	Lactuca sativa		7.4	1.4	18.7	14				20	3	80(35)	195		
	Beta vulgaris					>77				40	4	160(25)	320		
	Lactuca sativa		7.5	0.6	4.4	14				2.5	4	10(25)	80		
	Beta vulgaris					>77				20	3	80(25)	105		
	Lactuca sativa		7.7	0.9	40.6	14				5	3	10(30)	18		
	Beta vulgaris					>77				40	3	160(35)	195		
	Lactuca sativa		7.8	0.7	15.2	14				10	3	40(38)	58		
	Beta vulgaris					>77				80	3		320		

Table 3.219 continued overleaf

Table 3.219 continued Toxicity to higher plants. All underlined data are selected to discuss the critical concentrations (Table 3.218). Bold data are used to estimate the HC5 (Table 3.225). Data with reliability index 4 are given as supporting information but they are not used in the effects assessment

Test substance	Plant	Medium	pH[a]	%OC[b]	% clay	Equil. time prior to plant growth (d)	Growing period (d)	Pot (P) or field (F) trial	Endpoint	NOEC (µg g^{-1})	Cat.*	LOEC (µg g^{-1}) (%effect)	$EC_{x\geq50}$ (µg g^{-1}) (%effect)	References	R.I.
$CdCl_2$	*Glycine max*	silty clay loam	6.7	2.5	*28-40***		35	P	shoot dry weight				10(50)	Haghiri, 1973	3
	Triticum aestivum						35	P	shoot dry weight			2.5(21)LT			3
	Raphanus sativus						26	P	root dry weight			2.5(36)LT			3
	Lactuca sativa						37	P	shoot dry weight			2.5(40)LT			3
	Capsicum frutescens						112	P	pepper dry weight	10HT					4
	Apium graveolem						117	P	leaf dry weight	10HT					4
Supporting data															
$CdCl_2$	*Poa pratensis*	sandy	4.8	1.1	*0-15***	7-10	42	P	shoot dry weight	10	3		30(90)	Miles and Parker, 1979	4
	Liatris spicata								shoot dry weight			10(30)			
	Rhus radicans								shoot dry weight	10	3		30(63)		
	Andropgong scoparius								shoot dry weight			10(21)			
	Rudbeckia hirta								shoot dry weight				10(79)		
	Monarda fistulosa								shoot dry weight	10	3		30(68)		
$CdCl_2$	*Glycine max*	silt loam	4.5	*1-20***	*0-28***	4 drying and rewetting cycles	28	P	shoot dry weight	1	3		10(52)	Miller et al., 1976	4/3
			6.1		*0-28***					1	3	10(33)	100(66)		4/3
			7.0		*0-2**8*					1	3	10(33)	100(50)		4/3
		loamy sand	5.7		*0-28***					0.5	4		10(77)		4/3
$CdCl_2$	*Pinus strobus*	forest soil	4.8	1.1	*0-15***	several weeks	120	P	shoot dry weight	15	1		100(57)	Kelly et al., 1979	4
	Pinus taeda	0-14cm							shoot dry weight	15	3		100(55)		
	Liriodendron tulipifera	sandy							shoot dry weight	15	3		100(78)		
	Betula alleghaniensis								shoot dry weight	15	1		100(82)		
	Prunus virginiana								shoot dry weight	15	1		100(62)		
$Cd(NO_3)_2$	*Nicotinia tabacum*	sandy clay	5.3	0.9	9.4	21	60	P	total plant dry weight	5.4(HT)				Mench et al., 1989	4
	Nicotinia rustica								total plant dry weight	5.4(HT)					
	Zea mays								total plant dry weight	0.4		5.4(21)			

a) pH-water;
$ pH-KCl;
b) OM = OC*1.7;
LT Lowest Tested concentration;
HT Highest Tested concentration;
* NOEC classification (see Section 3.2.1.2);
** estimated OC - clay content.

3.2.3.5 Discussion

Table 3.220 lists all selected toxicity data of soil microflora, soil fauna and higher plants. This data set contains all data that were underlined in **Tables 3.215, 3.217** and **3.219**. This selection is based on data quality, i.e. data with RI 1-3 only, and on an attempt to avoid overrepresentation of data from the same test or the same organism (see introduction of effects assessment section). The selected data are retrieved from 167 different tests. This selection of results is used in this section to identify the factors that affect Cd toxicity, i.e. type of organism and environmental conditions. The data with RI 1-3 are considered to be reliable (no critical information is missing).

Table 3.220 Summary of selected Cd toxicity data for the terrestrial environment (µg g^{-1}). All data have RI ≤ 3 and a data selection was made to avoid overrepresentation of data from the same test or the same organism (see introduction of effects assessment section)

	NOEC				
	min	5th perc.	median	max	n
microflora	3.6	3.6	50	3,000	21
higher plants	1.8	2.5	10	80	41
soil fauna	5	8.0	32	320	13
	LOEC				
	min	5th perc.	median	max	n
microflora	7.1	7	100	8,000	21
higher plants	2.5	2.5	40	160	44
soil fauna	5	7.8	59	326	12
	E-LC$_{x≥50}$				
	min	5th perc.	median	max	n
microflora	7.1	57	283	5,264	20
higher plants	2.8	10	100	320	34
soil fauna	27	38	102	3,680	28

The median and 5th percentiles of the NOEC, LOEC and EC$_{x≥50}$ values of tests with higher plants are lower than corresponding values for microflora and soil fauna. This may indicate that Cd more sensitively affects higher plants than microbial processes or soil fauna. It must be stressed, however, that the low Cd concentration range (1-10 µg g^{-1}) has been tested in more detail with higher plants than with the other organisms.

3.2.3.6 The PNEC$_{soil}$

3.2.3.6.1 Species sensitivity distributions at different levels of data quality

The PNEC$_{soil}$ is calculated from the selected NOEC values. Different SSD's can be calculated for different selections of the data since the NOEC values have attached information such as data quality (the Reliability Index, RI) and properties of the test (species, soil characteristics and endpoint). The statistical properties of the NOEC data as a function of data quality is given in

Table 3.221. All data with RI=4 (unreliable) were not included because critical information of the test was lacking. The selected NOEC data are summarised in **Table 3.2.22**.

Table 3.221 The NOEC values (µg g^{-1}) of the terrestrial compartment for various levels of reliability (RI, defined in the introduction of effects assessment section). The selected data are underlined in preceding Tables 3.215, 3.217 and 3.219

NOEC					
	Min	5^{th} perc. of the NOEC data	Median	Max	n
RI 1-3	1.8	3.0	20	3,000	75
RI 1-2	1.8	3.6	40	3,000	22
RI 1			22		1

To evaluate the toxicity data, the statistical extrapolation method is used (Aldenberg and Slob, 1993). The fifth percentile (HC_5), with 50% confidence, of a species sensitivity distribution is calculated using the software package ETX 1.3a (RIVM, Bilthoven, The Netherlands). The HC_5 is calculated for three different approaches of data selection. The first approach is by using all the data (see **Table 3.222**), without calculation of species geometric mean values. The second approach is by calculating 'geometric mean' NOEC values for each species, resulting in one NOEC per species (see **Table 3.223**). The third approach is by calculating 'geometric mean' NOEC's on a case-by-case basis (see **Table 3.224**). Geometric mean NOEC's are calculated for the same species and the same endpoint, tested in similar¶ soils. This approach does not result in one NOEC per species. NOEC's of soil microbial assays have never been averaged across soils because of the intrinsic variability of the microbial population between soils.

¶ Soils are considered similar if their pH differs by maximum 0.2 units, and if the %OC and %clay difference is less than or equal to 1 and 8%.

Table 3.222 Selected data of effects of Cd in soil. Data derived from Tables 3.215, 3.217 and 3.219 within quality class RI 1-3

Organism	Phylum/class	Order	Family	Medium	pH[a]	Duration (d)	Endpoint	NOEC ($\mu g\ g^{-1}$)	References	R.I.
native soil microflora				phaeosem	6.9	84(min.)	substrate induced respiration rate	3.6	Reber, 1989	2
				neutral sandy hortisol	7	84(min.)	substrate induced respiration rate	3.6		2
				acidic cambisol	5.6	84(min.)	substrate induced respiration rate	14.3		2
native soil microflora				grassland soil	7.4	33	nitrification: NO_3^- production rate		Dušek, 1995	2
							$-NH_4^+$substrate	50		
							$+NH_4^+$substrate	10		
					7.6	33	nitrification: NO_3^- production rate			
							$-NH_4^+$substrate	50		
							$+NH_4^+$substrate	100		
native soil microflora				loamy sand	5.8	1	24h respiration	14.6	Walter and Stadelman, 1979	2
native soil microflora				silty loam	7.7	1-2	glutamic acid decomposition time	55	Haanstra and Doelman, 1984	2
				clay	7.5	1-2	glutamic acid decomposition time	150		2
native soil microflora				sand	7	42-70	respiration	150	Doelman and Haanstra, 1984	3
				sandy loam	6	42-70	respiration	150		2
				silty loam	7.7	42-70	respiration	150		2
				clay	7.5	42-70	respiration	3,000		2
				peat	4.5	42-70	respiration	400		2
native soil microflora				sandy soil	4.9	56	respiration	5	Cornfield 1977	3
Rhizobium leguminoasorum bv. *trifolii*				sandy loam	6.5	540	cell number (survival)	4	Chaudri et al., 1992	3
native soil microflora				brown earth loamy sand	4.6	45	cellulolytic activity: unplanted soil	10	Khan and Frankland, 1984	3
native soil microflora				organic soil	4.5	180	respiration rate	60	Frostegård et al., 1993	3
				sandy-loam	7.8	180	ATP content	112		3
native soil microflora				inceptisol	5.2	28	substrate induced respiration	50	Saviozzi et al., 1997	3
Folsomia candida	Arthropoda	Collembola	Isotomidae	OECD-soil	6.1[$]	42	reproduction	22	van Gestel and Hensbergen, 1997	1
Dendrobaena rubida	Annelida	Haplotaxida	Lumbricidae	C-horizon of sandy coniferous forest soil+well decomposed cattle dung	4.5	110	cocoon production	10	Bengtsson et al., 1986	2
					6.5	270	hatching success	10		2

Table 3.222 continued overleaf

Table 3.222 continued Selected data of effects of Cd in soil. Data derived from Tables 3.215, 3.217 and 3.219 within quality class RI 1-3.

Organism	Phylum/class	Order	Family	Medium	pH[a]	Duration (d)	Endpoint	NOEC (µg g-1)	References	R.I.
Lumbricus rubellus	Annelida	Haplotaxida	Lumbricidae	sandy loam soil	7.3	42	weight	150	Ma, 1982	3
Folsomia candida	Arthropoda	Collembola	Isotomidae	OECD-soil	6.3[$]	42	fresh weight at 25%MC	160	van Gestel and van Diepen, 1997	3
							35%MC	320		2
							45%MC	80		3
							55%MC	160		3
Folsomia candida	Arthropoda	Collembola	Isotomidae	OECD soil	6	35	number of offspring	148	Crommentuijn et al., 1993	2
Eisenia fetida	Annelida	Haplotaxida	Lumbricidae	OECD soil	6.3	56	cocoon production	5	Spurgeon et al., 1994	3
Eisenia andrei	Annelida	Haplotaxida	Lumbricidae	OECD soil	6.3	21	juvenile/adult ratio	10	Van Gestel et al., 1993	3
Eisenia andrei	Annelida	Haplotaxida	Lumbricidae	OECD soil	6.7	84	growth	18	Van Gestel et al., 1991	3
Plectus acuminatus	Nemata	Araeolaimida	Plectidae	OECD soil	5.5	21	juvenile/adult ratio	32	Kammenga et al., 1996	3
Picea sitchensis	*Pinopsida*	*Pinales*	*Pinaceae*	peaty gley	3.3	100	root length	1.8	Burton et al., 1984	2
Triticum aestivum	*Liliopsida*	*Cyperales*	*Poaceae*	phaeosem	6.9	28	shoot dry weight	7.1	Reber, 1989	2
				neutral sandy hortisol	7.0			29		2
Glycine max	*Mafnoliopsida*	*Fabales*	*Fabaceae*	silt loam	7.9	28	shoot dry weight	10	Miller et al., 1976	3
					6.0			10		3
					6.5			5		3
				clay loam	6.1			10		3
Raphanus sativus	*Mafnoliopsida*	*Capparales*	*Brassicaceae*	loamy sand	5.4	42	shoot dry weight	10	Khan and Frankland, 1983	3
Lactuca sativa	*Mafnoliopsida*	Asterales	Asteraceae	soil	3.9	42	shoot dry weight	2	Jasiewicz,1994	3
Lactuca sativa	*Mafnoliopsida*	Asterales	Asteraceae	humic sand	5.1	14	shoot fresh weight	32	Adema and Henzen, 1989	3
				loam	7.5			3.2		3
Lycosperisicon esculentum	*Mafnoliopsida*	Solanales	Solanaceae	loam	7.5			32		3
Avena sativa										
	Liliopsida	*Cyperales*	*Poaceae*	humic sand	5.1			10		3
				loam	7.5			10		3

Table 3.222 continued overleaf

Table 3.222 continued Selected data of effects of Cd in soil. Data derived from Tables 3.215, 3.217 and 3.219 within quality class RI 1-3

Organism	Phylum/class	Order	Family	Medium	pH[a]	Duration (d)	Endpoint	NOEC ($\mu g\ g^{-1}$)	References	R.I.
Phaseolus vulgaris	*Mafnoliopsida*	*Fabales*	*Fabaceae*	silt-loam soil amended with 1% clean sludge	7.5	up to maturity	bean dry weight	20	Bingham et al., 1975	3
Glycine max	*Mafnoliopsida*	*Fabales*	*Fabaceae*				bean dry weight	2.5		3
Triticum aestivum	*Liliopsida*	*Cyperales*	*Poaceae*				grain weight	20		3
Zea mays	*Liliopsida*	*Cyperales*	*Poaceae*				kernel weight	10		3
Lycosperisicon esculentum	*Mafnoliopsida*	*Solanales*	*Solanaceae*				ripe fruit weight	80		3
Cucurbita pepo										
Lactuca sativa	*Mafnoliopsida*	*Violales*	*Cucurbitaceae*				fruit weight	80		3
Lepidium sativum	*Mafnoliopsida*	*Asterales*	*Asteraceae*				head weight	5		3
Brassica rapa	*Mafnoliopsida*	*Capparales*	*Brassicaceae*				shoot weight	5		3
Raphanus sativus	*Mafnoliopsida*	*Capparales*	*Brassicaceae*				tuber weight	10		3
Daucus carota	*Mafnoliopsida*	*Capparales*	*Brassicaceae*				tuber weight	40		3
	Mafnoliopsida	*Apiales*	*Apiaceae*				tuber weight	10		3
Lactuca sativa	*Mafnoliopsida*	*Asterales*	*Asteraceae*	surface soils amended with 1% clean sludge	4.8	63	shoot dry weight	40	Mahler et al., 1978	3
Beta vulgaris	*Mafnoliopsida*	*Caryophyllales*	*Chenopodiaceae*				shoot dry weight	20		
Lactuca sativa					5.0			40		
Beta vulgaris								20		
Lactuca sativa					5.3			10		3
Beta vulgaris								40		
Lactuca sativa					5.7			20		
Beta vulgaris								40		
Lactuca sativa					7.4			20		
Beta vulgaris								40		
Lactuca sativa					7.5			2.5		
Beta vulgaris								20		
Lactuca sativa					7.7			5		
Beta vulgaris								40		
Lactuca sativa					7.8			10		
Beta vulgaris								80		

a pH-water;
$ pH-KCl;
MC Moisture content.

Table 3.223 'One species, one NOEC': selected NOEC data of effects of Cd in soil on fauna and higher plants, and calculation of "geometric mean" NOEC's. Data derived from Table 3.222

Organism	Phylum/class	Order	Family	Endpoint	NOEC (µg g^{-1})	
Dendrobaena rubida	Annelida	Haplotaxida	Lumbricidae		10	geometric mean of 10 and 10
Lumbricus rubellus	Annelida	Haplotaxida	Lumbricidae		150	
Folsomia candida	Arthropoda	Collembola	Isotomidae		113	geometric mean of 22, 80, 148, 160, 160, 320
Eisenia fetida	Annelida	Haplotaxida	Lumbricidae		5	
Eisenia andrei	Annelida	Haplotaxida	Lumbricidae		13	geometric mean of 10 znd 18
Plectus acuminatus	Nemata	Araeolaimida	Plectidae		32	
Avena sativa	*Avena sativa*	*Cyperale*	*Poaceae*		10	geometric mean of 10 and 10
Picea sitchensis	*Pinopsida*	*Pinales*	*Pinaceae*		1.8	
Triticum aestivum	*Liliopsida*	*Cyperales*	*Poaceae*		16	geometric mean of 7.1, 20, 29
Glycine max	*Mafnoliopsida*	*Fabales*	*Fabaceae*		7	geometric mean of 2.5, 5, 10, 10, 10
Raphanus sativus	*Mafnoliopsida*	*Capparales*	*Brassicaceae*		20	geometric mean of 10 and 40
Lactuca sativa	*Mafnoliopsida*	Asterales	Asteraceae		10	geometric mean of 2, 2.5, 3.2, 5, 5, 10, 10, 20, 20, 32, 40, 40
Lycosperisicon esculentum	*Mafnoliopsida*	Solanales	Solanaceae		51	geometric mean of 32 and 80
Phaseolus vulgaris	*Mafnoliopsida*	*Fabales*	*Fabaceae*		20	
Zea mays	*Liliopsida*	*Cyperales*	*Poaceae*		10	
Cucurbita pepo	*Mafnoliopsida*	*Violales*	*Cucurbitaceae*		80	
Lepidium sativum	*Mafnoliopsida*	*Capparales*	*Brassicaceae*		5	
Brassica rapa	*Mafnoliopsida*	*Capparales*	*Brassicaceae*		10	
Daucus carota	*Mafnoliopsida*	*Apiales*	*Apiaceae*		10	
Beta vulgaris	*Mafnoliopsida*	*Caryophyllales*	*Chenopodiaceae*		34	geometric mean of 20, 20, 20, 40,'40, 40, 40, 80

Table 3.224 'Case-by-case selection': selected NOEC data of effects of Cd in soil on fauna and higher plants,and case-by-case calculation of "geometric mean" NOEC's. Bold, underlined data are selected for the HC_5 calculation. Data derived from Table 3.222

Organism	Medium	pH	%OC	%clay	Endpoint	NOEC (µg g^{-1})	
Dendrobaena rubida	C-horizon of sandy coniferous forest soil+well decomposed cattle dung	4.5	4.5-6.9		cocoon production	10	no geometric mean: different endpoints
		6.5	4.5-6.9		hatching success	10	
Lumbricus rubellus	sandy loam soil	7.3	4.7	17	weight	150	
Folsomia candida	OECD soil	6	5.9	20	reproduction	148	geometric mean: similar soil, same endpoint, same species

Table 3.224 continued overleaf

Table 3.224 continued 'Case-by-case selection': selected NOEC data of effects of Cd in soil on fauna and higher plants, and case-by-case calculation of "geometric mean" NOEC's. Bold, underlined data are selected for the HC_5 calculation. Data derived from Table 3.222

Organism	Medium	pH	%OC	%clay	Endpoint	NOEC ($\mu g\ g^{-1}$)	
Folsomia candida	OECD-soil	6.1	5.9	20	reproduction	22	geometric mean = 57
Folsomia candida	OECD-soil	6.3	5.9	20	fresh weight	160	geometric mean: similar soil, same endpoint, same species
			5.9	20	fresh weight	320	geometric mean = 160
			5.9	20	fresh weight	80	
			5.9	20	fresh weight	160	
Eisenia fetida	OECD soil	6.3	5.9	20	cocoon production	5	
Eisenia andrei	OECD soil	6.3	5.9	20	juvenile/adult ratio	10	no geometric mean: different endpoints
Eisenia andrei	OECD soil	6.7	5.9	20	growth	18	
Plectus acuminatus	OECD soil	5.5	5.9	20	juvenile/adult ratio	32	
Picea sitchensis	peaty gley	3.3	45		root length	1.8	
Triticum aestivum	phaeosem	6.9	1.3	21	shoot dry weight	7.1	no geometric mean: different endpoints, different soils
Triticum aestivum	neutral sandy hortisol	7.0	1.4	3	shoot dry weight	29	
Triticum aestivum	silt-loam soil amended with 1% clean sludge	7.5			grain weight	20	
Glycine max	silt loam	7.9			shoot dry weight	10	no geometric mean: different endpoints, different soils
Glycine max	silt loam	6.0			shoot dry weight	10	
Glycine max	silt loam	6.5			shoot dry weight	5	
Glycine max	clay loam	6.1			shoot dry weight	10	
Glycine max	silt-loam soil amended with 1% clean sludge	7.5			bean dry weight	2.5	
Raphanus sativus	loamy sand	5.4			shoot dry weight	10	no geometric mean: different soils
Raphanus sativus	silt-loam soil amended with 1% clean sludge	7.5			tuber weight	40	
Lycosperisicon esculentum	Loam	7.5			shoot fresh weight	32	no geometric mean: different soils
Lycosperisicon esculentum	silt-loam soil amended with 1% clean sludge	7.5			ripe fruit weight	80	
Avena sativa	humic sand	5.1			shoot fresh weight	10	no geometric mean: different soils
Avena sativa	loam	7.5				10	
Phaseolus vulgaris	silt-loam soil amended with 1% clean sludge	7.5			bean dry weight	20	
Zea mays					kernel weight	10	
Cucurbita pepo					fruit weight	80	
Lepidium sativum					shoot weight	5	
Brassica rapa					tuber weight	10	
Daucus carota					tuber weight	10	

Table 3.224 continued overleaf

Table 3.224 continued 'Case-by-case selection': selected NOEC data of effects of Cd in soil on fauna and higher plants, and case-by-case calculation of "geometric mean" NOEC's. Bold, underlined data are selected for the HC_5 calculation. Data derived from Table 3.222

Organism	Medium	pH	%OC	%clay	Endpoint	NOEC ($\mu g\ g^{-1}$)	
Lactuca sativa	humic sand	5.1	2.2		shoot fresh weight	32	no geometric mean: different soils
	loam	7.5	0.8		shoot fresh weight	3.2	
Lactuca sativa	Soil	3.9	1.2	8	shoot dry weight	2	
Lactuca sativa	surface soils amended with 1% clean sludge	4.8	2.6	8.3	shoot dry weight	40	geometric mean: same endpoint, same species, similar soils
Lactuca sativa		5.0	3.3	14.6	shoot dry weight	40	geometric mean = 40
Lactuca sativa	surface soils amended with 1% clean sludge	5.3	0.9	8.9	shoot dry weight	10	
Lactuca sativa		5.7	3.0	37.5	shoot dry weight	20	
Lactuca sativa	surface soils amended with 1% clean sludge	7.4	1.4	18.7	shoot dry weight	20	geometric mean: same endpoint, same species, similar soils
Lactuca sativa	silt-loam soil amended with 1% clean sludge	7.5		14	shoot weight	5	geometric mean = 10
Lactuca sativa	surface soils amended with 1% clean sludge	7.5	0.6	4.4	shoot dry weight	2.5	no geometric mean: different soils
Lactuca sativa	surface soils amended with 1% clean sludge	7.7	0.9	40.6	shoot dry weight	5	
Lactuca sativa		7.8	0.7	15.2	shoot dry weight	10	
Beta vulgaris	surface soils amended with 1% clean sludge	4.8	2.6	8.3	shoot dry weight	20	geometric mean: same endpoint, same species, similar soils
Beta vulgaris		5.0	3.3	14.6	shoot dry weight	20	geometric mean = 20
Beta vulgaris	surface soils amended with 1% clean sludge	4.8	2.6	8.3	shoot dry weight	20	no geometric mean: different soils
Beta vulgaris		5.0	3.3	14.6	shoot dry weight	20	
Beta vulgaris		5.3	0.9	8.9	shoot dry weight	40	
Beta vulgaris		5.7	3.0	37.5	shoot dry weight	40	
Beta vulgaris		7.4	1.4	18.7	shoot dry weight	40	
Beta vulgaris		7.5	0.6	4.4	shoot dry weight	20	
Beta vulgaris		7.7	0.9	40.6	shoot dry weight	40	
Beta vulgaris		7.8	0.7	15.2	shoot dry weight	80	

There are enough data from all three trophic levels to calculate the $PNEC_{soil}$ by the assessment factor method (AFM) using the lowest assessment factor 10 (TGD, 1996, p. 339). The lowest NOEC value with a RI ≤3 is 1.8 μg g^{-1}. This yields a $PNEC_{soil}$ = 1.8/10 μg g^{-1} or 0.18 μg g^{-1}. That value is within the range of Cd background concentrations in soil. Rather than making a risk assessment based on one single NOEC value, it is possible to use the statistical extrapolation method (TGD, 1996, p. 469) if enough NOEC data are available. This condition is certainly met in the case of Cd and is preferred because it is based on information from a wide range of species and soil microbial processes. The need for additional assessment factors in that assessment will be discussed in the next section.

The statistical extrapolation method (SEM) was applied to the NOEC data (some geometric mean values, see above), calculating the median 5th percentile (HC_5) of both the log-logistic and the log-normal distribution with the software package ETX 1.3a (RIVM, Bilthoven, The Netherlands) (see **Table 3.225**).

Table 3.225 Calculation of critical concentrations (μg g^{-1}) using the assessment factor method (AFM) or the statistical extrapolation method (SEM; Aldenberg and Slob, 1993) for Various levels of data quality

Data quality group	AFM: NOEC/AF μg g^{-1}	
	AF = 10	
RI 1-2: whole data set (n=22)	0.18	
RI 1-3: w hole data set (n=75)	0.18	
RI 1- 3: microflora (n=21)	0.36	
RI 1-3: plants+invertebrates (n=54)	0.18	
	SEM: HC5 at 50% (and 95%) confidence μg g-1	
	Logistic distribution	Normal distribution
RI 1-2: whole data set (n=22)	1.8 (0.5)	1.9 (0.5)
RI 1-3: whole data set (n=75)	2.3 (1.3)	2.2 (1.4)
RI 1-' microflora		
Selection of NOEC's, RI 1-3 (Table 3.222); n = 21	2.3 (0.6)	2.3 (0.7)
RI 1-3 higher plants + invertebrates		
Selection of all NOEC's, RI 1-3 (Table 3.222); n = 54	2.5 (1.5)	2.5 (1.5)
One species, one value: geometric mean NOEC's (Table 3.222); n = 20	2.5 (1.0)	2.6 (1.1)
Case-by-case geometric mean calculation (Table 3.222); n = 49	2.7 (1.6)	2.6 (1.7)

Selection on data quality slightly affects the value of HC_5 between groups RI 1-3 and RI 1-2 (see **Table 3.225**; whole data set), illustrating that the frequency distributions of both data sets overlap (2.3 versus 1.8 μg Cd g^{-1}). The median NOEC is distinctly higher for RI 1-2 than for RI 1-3 (see **Table 3.221**), but the higher variance in the former data set results in a larger difference between the 5th percentile and the median. Many plant data are excluded from the group RI 1-2 (only 3 NOEC values of plants in that group) whereas plants seem to be the most sensitive group (see Section 3.2.3.5). Several Cd toxicity tests on higher plants are selected from older source documents (1970-1980) and the information on the test, such as statistical treatment, is often not complete in these documents. Statistical data analysis is a prerequisite for a test to enter class RI 2.

The HC_5 value of tests with RI 1-2 is based on 14 NOEC’s from 3 different soil microbial processes, 5 NOEC’s from 2 different invertebrate families (2 species), and 3 NOEC’s from 2 different plant families (2 species; **Table 3.226**). The RI 1-3 database consists of 24 NOEC’s from 7 soil microbial processes, 12 NOEC’s from 3 invertebrate families (5 species), and 41 NOEC’s from 9 plant families (16 species). The data with RI 1-2 have a higher quality label, but are derived from a limited number of species (only 4 different species and 3 different soil microbial processes). The majority of data within group RI 3 lack statistical data analysis to classify them as RI 2 (details not shown). In consequence, the choice for which data group is based on a preference for either a large diversity in species or for data supplied with statistical analysis of the test result (class 1 and 2 NOEC’s). The underlying assumption in the statistical extrapolation technique is that the logistic frequency distribution reflects species sensitivity distribution. Since the class RI 1-2 has limited species, it is proposed to use the class RI 1-3 as the basis for deriving the PNEC.

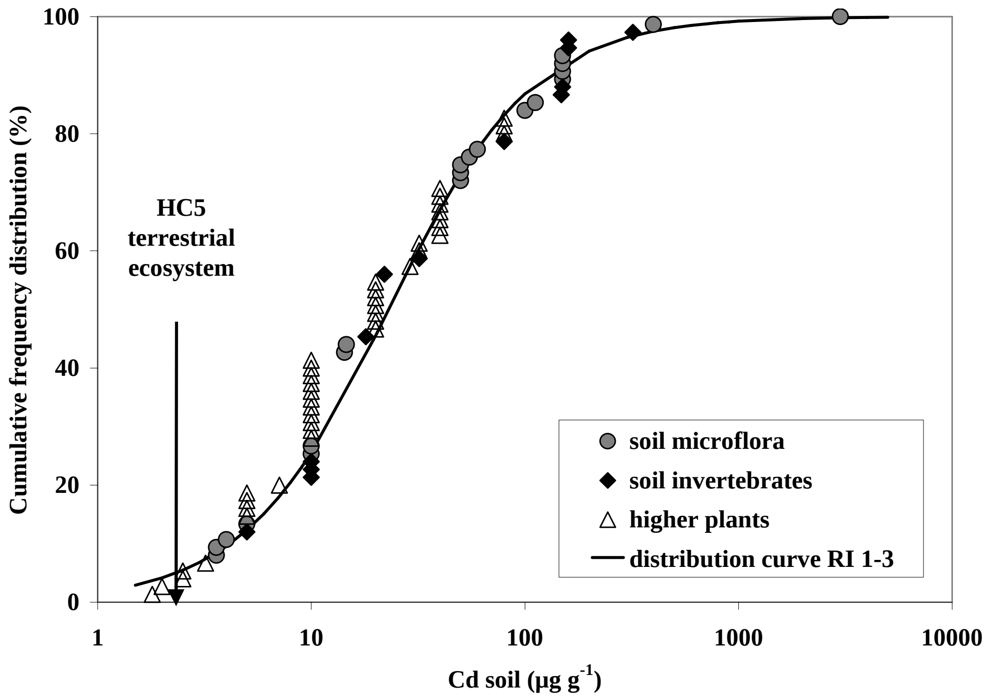
The terrestrial data set is split in two groups: microbial processes and soil invertebrates + higher plants. The endpoints for microbial processes are relevant at the ecosystem functioning level, while the endpoints for soil fauna and plants are relevant at the species level. The principle of splitting the terrestrial data in two groups is open to criticism: there is no scientific argument (e.g. field validation) for either option. For both groups, the choice of SSD does not affect the HC_5, nor does the choice of data selection (geometric mean calculation or not) for soil invertebrates and higher plants. However, the statistical uncertainty surrounding the HC_5 is smaller using the combined dataset. In contrast to the procedure used to derive a $PNEC_{water}$, the lowest NOEC selection approach was not performed because such a selection would not yield a representative data set for the terrestrial ecosystem (e.g. all clay soils would be excluded). The HC_5 for the microflora furthermore equals the HC_5 for soil fauna and plants.

Concluding we propose to use the HC_5 based on all NOEC's of the microflora data set, which is the lowest of all HC_5 values is, i.e.

$$HC_5 = 2.3\ \mu g\ Cd/g$$

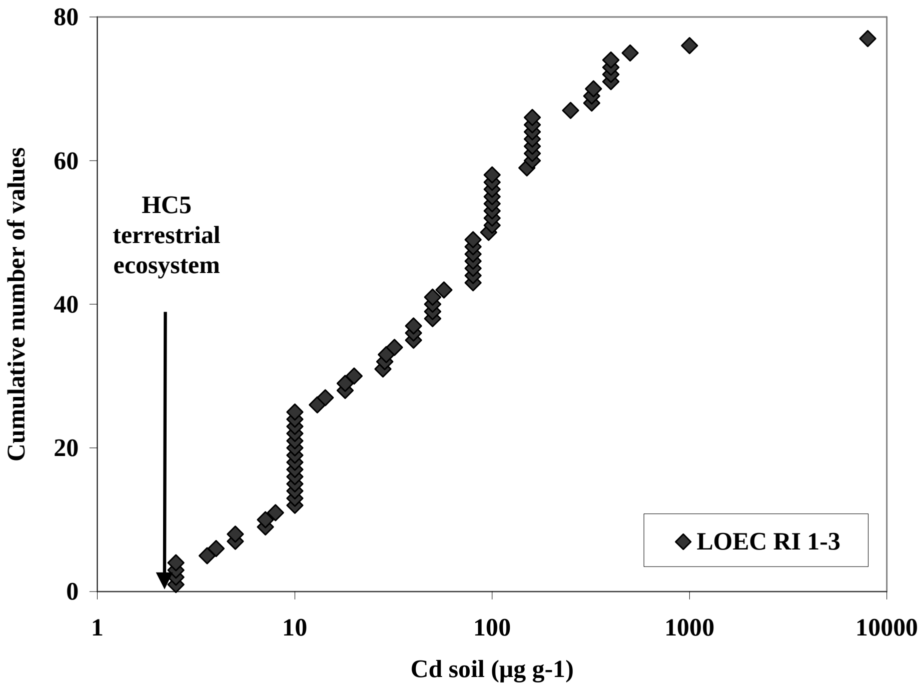
The frequency distribution and HC_5 are illustrated in **Figure 3.17**.

Figure 3.17 The cumulative frequency distribution of the selected NOEC values of Cd toxicity tests of soil microflora, invertebrates and higher plants. Observed data and logistic distribution curve for the whole RI 1-3 data set fitted on the data



The HC_5 for the terrestrial ecosystem, based on all NOEC's of the microflora group and on a logistic distribution, is 2.3 µg g^{-1}. The whole data set of terrestrial tests (including tests with RI = 4) contains no observations where toxicity was found below 2.3 µg g^{-1} (see **Figure 3.18**). The lowest toxicity data (2.5 µg Cd/g; 4 values) are classified as RI = 3 and were found on plant growth.

Figure 3.18 The cumulative number of LOEC values of selected tests of data quality group RI 1-3



3.2.3.6.2 Calculation of the generic $PNEC_{soil}$

The EU workshop on statistical extrapolation (17-18 January, 2001) proposed that the statistical extrapolation technique can be applied to derive a PNEC, but that an additional assessment factor should be applied to theHC_5, which is estimated as a median 5^{th} percentile of the NOEC distribution. This assessment factor may be chosen between 5 and 1 and should remove uncertainty in extrapolating the PNEC to the field situation. The uncertainty is related to the limited number of taxa included in the species sensitivity distribution, the unknown long term effects in the field and the possibility that mixed pollution renders cadmium more readily toxic.

Species diversity

The HC_5 value of the terrestrial ecosystem is derived from 5 different microbial processes. This HC_5 almost equals the HC_5 values based on the fauna and plant data (49 different tests) and the HC_5 of the whole RI 1-3 data set (derived from 65 different tests with 20 different species and 5 different soil microbial processes). The plants belong to 9 different families and 9 different orders and the invertebrates belong to 3 different families and 3 different orders. This diversity certainly meets the recommendation of the EU workshop (17-18 January, 2001) on statistical extrapolation that the data set should contain at least 8 different taxa for applying the statistical extrapolation technique. The entire database does, however, not contain community system data and is biased towards agricultural species.

Along the same lines, it can be argued that the data should be based on a diversity of soil properties. The tests on which the HC_5 value is based are performed in soils with pH 3.1-7.9% carbon 0.6-47 and % clay 2-70. This range in soil properties covers most of the European topsoils.

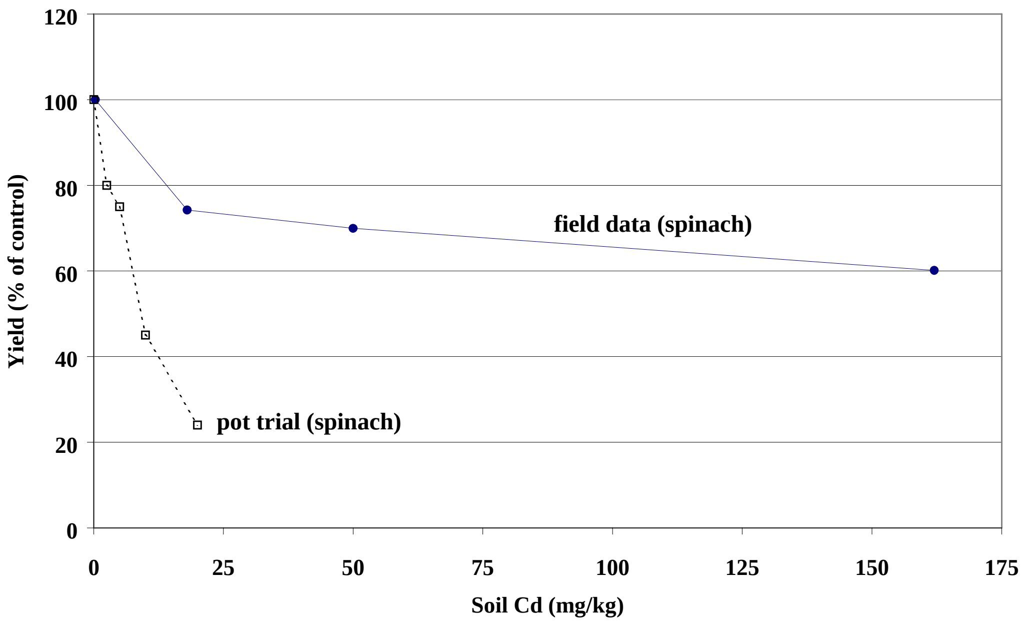
Lab to field extrapolation

There are only limited field data that allow deriving threshold concentrations of Cd in soil at the field scale. Cadmium is usually associated with other metals in the field and these other metals are more readily toxic than Cd itself. In most cases, Cd pollution is associated with Zn pollution. Effects of smelter contamination on plants or on earthworms are often attributed to Zn and not to Cd (Tiller, 1989; Spurgeon and Hopkin, 1995).

Few toxic effects of Cd-salts were found in the field observations (Sajwan et al., 1995, Kádár, 1995). In the former test, the top 7.5 cm of loamy sand microplots were contaminated with Cd up to 6.7 µg Cd/g (measured concentration) along with small doses of Ni (11 $\mu g\ g^{-1}$) and Se (0.2 $\mu g\ g^{-1}$). There were no growth effects observed in bush beans compared with the nil treatment where soil Cd was at 0.6 µg Cd/g (Sajwan et al., 1995).

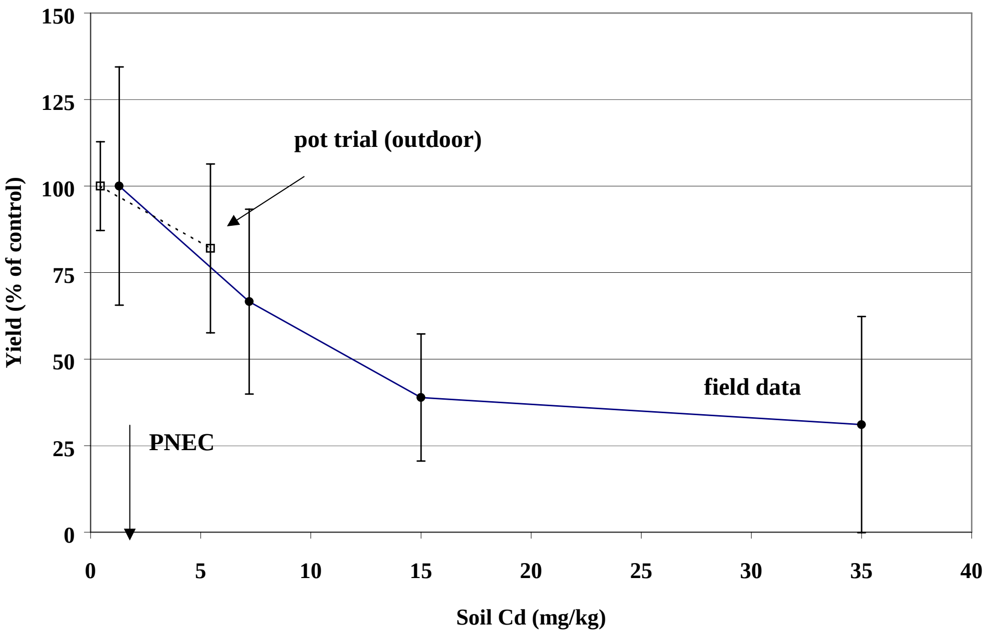
A field trial on the effects of metal salts was started in Nagyhörcsök (Hungary) in 1991 by Dr. I. Kádár. Cadmium (as $CdSO_4$) was applied to the soil at 4 rates above control with threefold replication (see **Table 3.226**). The soil is a calcareous chernozem, characterised by a high cation exchange capacity, high pH and high base saturation. More details on this field trial are described elsewhere (Kádár, 1995; Kádár et al., 1998). This type of soil is certainly *not* a worst case scenario for cationic metals, which are strongly sorbed in that type of soil. No toxic effect of Cd on plant growth was detected up to the highest rate during the first 4 years. Toxic effects were very pronounced in 1995 and 1996 in spinach and red beet, both plants belonging to the same family, and, to a lesser extent, in 1997 in wheat grain. Pot trial studies confirm that spinach is far more sensitive to Cd than corn, wheat or carrots (Bingham et al., 1975, see also **Table 3.219**). The NOEC's for spinach and red beet in the field were both 50 µg Cd/g, i.e. well above the HC_5 as derived from the laboratory tests. The average yield data (see **Table 3.226**) show that the average plant yield is already considerably reduced at this NOEC, but that this reduction is not large enough to yield a statistically significant effect. The intrinsically higher variability in field data biases the comparison of field NOEC's with laboratory NOEC's. Effect concentrations may, therefore, be a better basis for a lab-field comparison for plant growth. The response of spinach growth to Cd shows that yield is reduced with about 25% at 18 µg Cd/g (see **Table 3.226**). The EC_{25} of spinach grown in a pot trial s was 4 µg Cd/g, i.e. more than 4-fold lower in than in the field (Bingham et al., 1975; see also **Table 3.219** and **Figure 3.19**). The soil in that pot trial (pH 7.5) has a similar pH as in the field trial (7.3). No pot trial studies were found with red beet. The Bingham et al. study also reports the EC_{25} of Cd on wheat grain as 50 µg Cd/g (same soil as with spinach) whereas the highest Cd rate in the field did not even result in 25% reduction in wheat grain yield. The highest Cd rate in the field was 810 kg Cd/ha, equivalent to 456 µg Cd/ g EDTA extractable Cd (Kádár, 1995). The total Cd in that soil is most likely similar to EDTA extractable Cd. Concluding, the phytotoxic effect of Cd in the field trials in the Hungarian calcareous chernozem are found at higher concentration than in the pot trials of Bingham et al. (1975) with a calcareous silt loam.

Figure 3.19 Yield of spinach: field data (Hungary; Kádár et al., 1998) and pot trial data (Bingham et al., 1975). The soil pH was 7.3 in the field experiment and 7.5 in the pot trial



Another long-term field trial was started in 1988-1990 in Bordeaux (France) by Dr. M. Mench of the INRA Bordeaux. By 1990, there were 3 nominal Cd rates above control: 10, 20 and 40 µg Cd /g. The field has plots with pH 5.3-5.6 and plots with pH 6.7-7.0. The corn shoot yield data of 2000 are given in **Table 3.226**. Cadmium was more toxic in the most acid plots and had no significant effect on corn shoot yield up to 7-8 µg Cd/g. The LOEC's at 15 µg Cd/g are associated with a 50% (high pH) and 61% (low pH) lower shoot yield than the control. One pot trial with corn is reported in a similar soil as in the acid plots. Leaf and stem dry weight was reduced by 18% at 5.4 µg Cd/g, the highest concentrations tested (Mench et al., 1989; **Figure 3.20**). The field data suggest a similar inhibition of growth of corn by Cd as in the pot trials if the field data between control and the first Cd rate are interpolated.

Figure 3.20 Yield of corn: field data and pot trial data (pot trials with 17 kg soil; Mench et al., 1989)



Concluding, the few field data yield NOEC's that are well above the HC_5 of 2.3 µg Cd/g. Toxicity of Cd on plants grown in pot trials is equally or more pronounced than in the field. There is currently no indication of higher toxicity of Cd salts in the field than in the laboratory.

Goodness-of-fit

The goodness-of-fit of the SSD's is tested with the Kolmogorov-Smirnov test. The log-logistic and the log-normal distribution are accepted at the 1-10% significance levels when applied on the microbial data set on which the HC_5 is based. The lower 95% confidence level is 0.6 (log-logistic distribution) and 0.7 (log-normal distribution), which is considerably lower than the HC_5. The lower 95% confidence level in the combined dataset is 1.5 showing that the statistical uncertainty strongly reduces when combining all terrestrial data.

All these arguments given above suggest that an assessment factor ranging from 1 to 2 might be appropriate to derive a $PNEC_{soil}$ from the HC_5. Therefore we propose

HC_5	Assessment factor	$PNEC_{soil}$
2.3 µg g^{-1}	1	2.3 µg g^{-1}
2.3 µg g^{-1}	2	1.15 µg g^{-1}

It must be recalled that there is no single test in the entire database (including tests with RI 4) at which a toxic effect of Cd was found at or below the $PNEC_{soil}$ = 2.3 µg Cd /g. Furthermore, the $PNEC_{soil}$ based on secondary poisoning is below 1.15 µg Cd/g(see Section 3.2.7.3), and therefore a single value for the $PNEC_{soil}$ based on microbial processes is of no importance on the overall outcome of the risk characterisation for the soil compartment.

Table 3.226 Phytotoxicity of Cd salts in field trials

Test substance	Soil properties	Results*						
$CdSO_4$	Nagyhörcsök (Hungary): calcareous Chernozem; pH ($CaCl_2$) = 7.3; 3% org. matter; 5%$CaCO_3$; CEC 22 $cmol_c$/kg	1991: 1 single Cd application						Kádár et al., 1998
		(kg Cd/ha)	0	30	90	270	810	
		1994: soil Cd (µg)	0.3	18	50	162	not meas.	
		yield (tonnes FW/ha)						
		1991: corn		n.s.	n.s.	n.s.	n.s.	
		1992: carrot		n.s.	n.s.	n.s.	n.s.	
		1993: potato		n.s.	n.s.	n.s.	n.s.	
		1994: pea		n.s.	n.s.	n.s.	n.s.	
		1995: red beet	14.6[a]	7.4[a]	9.5[a]	3.7[b]	0.7[b]	
		1996: spinach	16.3[a]	12.1[a]	11.4[a]	9.8[b]	3.7[b]	
		1997: wheat grain	6.8[a]	n.d.	7.3[a]	6.4[a]	5.4[a]	
$Cd(NO_3)_2$	Borde aux (France)	1988-1990 Cd applications						Mench, pers. com. (2000)
	pH ($CaCl_2$) = 5.3-5.6; CEC 10 cmolc/k g	2000:soil Cd (mg Cd/kg)	1.3	7.2	15	35		
		2000: corn (g FW/plant)	59.9[a]	39.9[a]	23.3[b]	18.6[b]		
$Cd(NO_3)_2$	Bordeaux (France)	1988-1990 Cd applications						Mench, pers. com. (2000)
	pH ($CaCl_2$) = 6.7-7.0; CEC 15 $cmol_c$/kg	2000:soil Cd (mg Cd/kg)	1.2	8.3	15	32		
		2000: corn (g FW/plant)	35.6[a]	44.0[a]	17.9[b]	16.4[b]		

* Values in the same row with the same superscript do not differ significantly.
n.s. Not specified
n.d. Not determined

3.2.3.6.3 $PNEC_{soil}$ in relation to soil properties

Toxicity is well known to vary with soil properties, which justifies deriving PNEC values per soil type. As an example, a very low $EC_{x\geq50}$ value (2.8 µg g^{-1}) was found for root growth in a forest soil with pH 3.3 (Burton et al., 1984). Clearly, such soil should not be compared with arable soils at higher pH values for which $EC_{x\geq50}$ values are almost one order of magnitude higher. As discussed above, no empirical equation has been developed for Cd to normalise toxicity to a standard soil. In this section, an attempt will be made to calculate the PNEC for different soil classes. All selected NOEC data with RI ≤ 3 are used in this calculation. The number of classes is restricted to maintain a sufficient number of degrees of freedom. Two selection methods are tested: one is by pH and one is by soil texture.

The pH of the soil dominates the solid-liquid distribution of Cd in soil (see **Table 3.10**). It is often assumed that the metal concentration in soil solution represents the toxic dose for the ecosystem and, therefore, a correlation between metal toxicity and pH is to be expected. At higher pH, metal solubility is low and the HC_5 could be higher than at low pH where metals are more soluble. A significant correlation between the log NOEC values and soil pH was, however, not found ($P > 0.05$) for the data collated here (see **Figure 3.21**). A positive trend between log NOEC and soil pH emerges up to about pH 6 beyond which there seems to be no further trend.

The data were classified in two groups, data obtained at soil pH lower or equal to 6.0 and data obtained at soil pH above 6.0. Statistical properties of the data are given in **Table 3.227**. The HC_5 was calculated by statistical extrapolation of the log logistic distribution of the NOEC values (ETX 1.3a, RIVM, Bilthoven, The Netherlands). The HC_5 value is lower in the group pH > 6.0 (see **Table 3.227**). The mean log NOEC value is identical for both groups but the standard deviation of the log NOEC values is largest in the group pH > 6.0. Therefore, the extrapolated HC_5 value is smaller for the group pH > 6.0.

No correlation was found between log NOEC values and % clay in soil (details not shown). The NOEC values found in soils with less than 10% clay are somewhat lower than in soils with more than 10% clay. The lowest HC_5 value is found in soils with less than 10% clay. The median log NOEC is also lowest in this group, while the standard deviation is identical in both groups.

Figure 3.21 Semi log plot of the selected Cd NOEC values in soil (n=72) as a function of soil pH

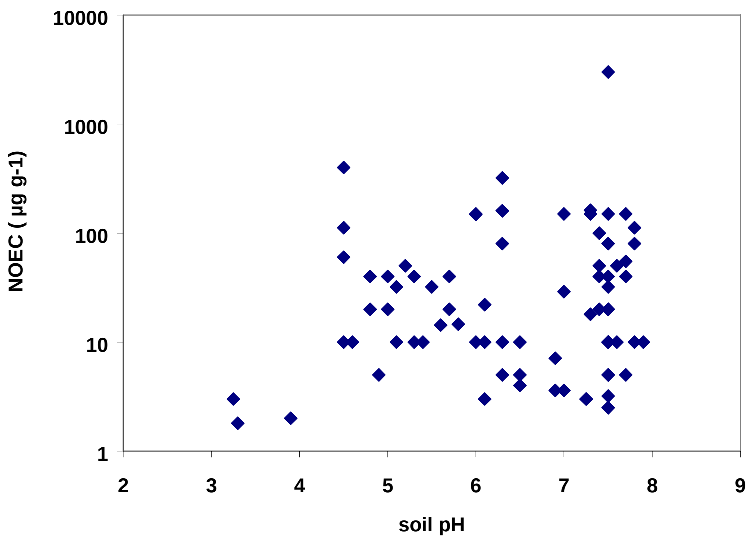


Table 3.227 The $PNEC_{soil}$ (µg Cd/g) calculated as the HC_5 value using the statistical extrapolation method (Aldenberg and Slob, 1993) on the NOEC data sorted by soil characteristics. The NOEC data were sorted either by soil texture or by soil pH

	n	Min. NOEC	Median NOEC	HC_5 (µg Cd/g)
classified by pH				
pH ≤ 6.0	25	1.8	20	2.7
pH > 6.0	50	2.5	20	2.0
classified by %clay				
% clay ≤ 10	18	2.0	17	1.5
% clay > 10	48	1.8	20	2.4

It is striking that the HC_5 values vary only slightly with soil properties whereas higher variability in toxicity between soil types is often found in comparative experiments (see e.g. plant data of Miller et al., 1976). That variability is reduced here for several reasons. Firstly, the effect of soil factors on the NOEC data is obscured by all other sources of variance, e.g. variance in sensitivity among species and endpoints. Secondly, a NOEC value relates to the *lack* of toxicity. Soil properties may, for example, have a more pronounced effect on the concentrations at which toxicity is found (LOEC and $EC_{x\geq50}$ values).

An attempt was made to unravel the effect of soil type on Cd toxicity using the effect data (LOEC and $EC_{x\geq50}$ values). The % effect was related to neither total soil Cd nor to soluble Cd concentrations. The soluble Cd concentrations are calculated from total concentrations based on a model relating soil properties with the solid-liquid distribution coefficient K_D. The model proposed by Römkens and Salomons, 1998 was used (see **Table 3.10**). This model estimates the K_D based on soil pH only. Few LOEC data were found for which the % effect was not clear from the data. The % inhibition for these data was assumed to be 30%.

The correlation coefficient between % inhibition and soluble Cd concentrations (R^2 = 0.02) is similar as between % inhibition and total soil Cd (R^2 = 0.04) and EC_{50} values seem to span an almost equal order of magnitude variability whether expressed as solubles or totals (see **Figure 3.22**). Other K_D models were tested (see **Table 3.10**) but none of these models yielded better correlations (details not shown). It is concluded that normalisation of terrestrial Cd toxicity data based on the solubility of Cd in soil is still not justified pending experimentally proven models.

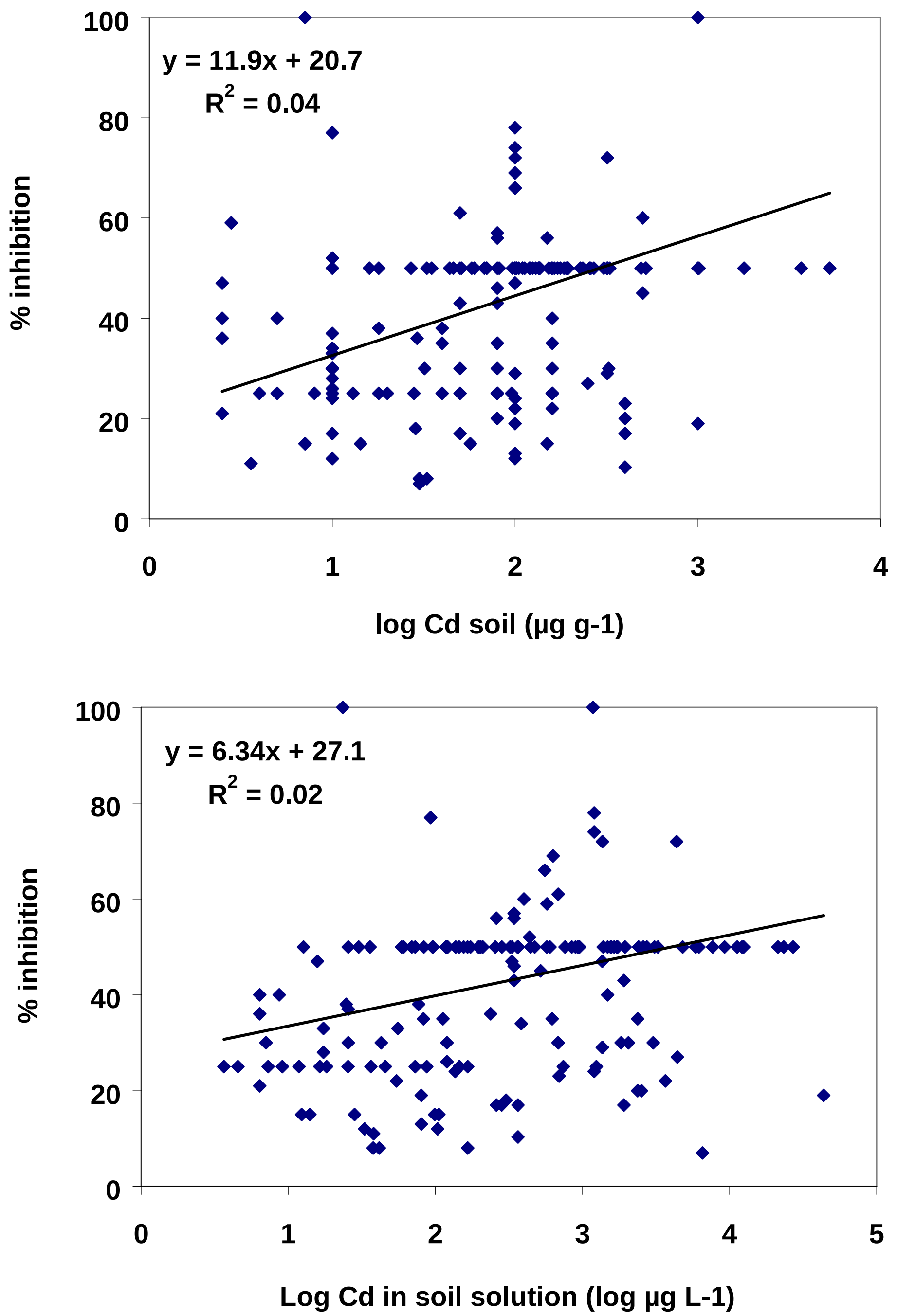
3.2.3.7 Conclusion

The $PNEC_{soil}$ of CdO is based on the 5^{th} percentile (HC_5) of a log-logistic distribution fitted to 21 NOEC's of microbial processes (5 different processes). The HC_5 of the microbial processes almost equals the HC_5 values based on the fauna and plant data (54 different tests) and the HC_5 of the whole data set of reliable tests (derived from 75 different tests with 20 different species and 5 different soil microbial processes). The NOEC data are derived from terrestrial toxicity tests with Cd^{2+} salts. The HC_5 is 2.3 µg g^{-1}. There is currently no justification for higher toxicity of Cd salts in the field then in the laboratory. Therefore, a PNEC can be proposed as the median HC_5 with an additional assessment factor ranging from 1 to 2. This yields:

$$PNEC_{soil} = 1.15\text{-}2.3\ \mu g\ Cd/g_{dw}$$

No adverse effects of Cd were found below 2.3 µg g^{-1} in the entire data set (including data that were considered unreliable). Soils with less than 10% clay have a slightly lower $PNEC_{soil}$ (1.5 µg g^{-1}) than soils with more than 10% clay (2.0 µg g^{-1}). Normalising the Cd toxicity data to soil solution Cd concentrations does not reduce the variance of toxic Cd concentrations between the tests.

Figure 3.22 The % inhibition of Cd in soil related to the soil total Cd concentrations (top) or to soil solution Cd concentrations (bottom). The soil solution concentrations are estimated from soil Cd concentrations based on soil pH (see main text for details)



3.2.4 Toxicity to benthic organisms

The fate of CdO powder in sediments is not documented. In the absence of this information, it is hypothesised that the metal behaves as the Cd^{2+} salt after equilibration. Only limited relevant data on the toxicity of Cd^{2+} to freshwater benthic organisms were found. These data refer to tests where uncontaminated sediment was spiked with Cd^{2+} salts. Several tests with field-contaminated sediments were found. These tests cannot be used for dose-response analysis because the sediments are contaminated with various other metals and with organic compounds. Some of these tests are nevertheless included as supportive information in the review given below. Tests with marine sediments were not included.

3.2.4.1 Influence of sediment properties on toxicity of Cd

There are 3 potential pathways for contaminants to reach benthic organisms: the sediment (e.g. ingestion), the overlying water and the interstitial (pore) water (e.g. across respiratory surfaces and body walls). The relative importance of each rout– depends on a number of factors - sediment characteristics such as type of organisms and feeding habitat (Power and Chapman, 1996).

The Cd mobility in anaerobic sediments is controlled by the concentration of acid-volatile sulphides (AVS) by the particulate organic carbon (POC) and by the dissolved organic carbon (DOC). In aerobic conditions, in which the AVS are virtually absent, Cd mobility depends on the content of the POC and of Fe and Mn-hydroxides. The toxicity of Cd most likely depends on its mobility in the sediment. Since the beginning of the 90's the role of AVS on metal toxicity in sediments has been studied intensively (Van den Berg et al., 1998, Pesch et al., 1995, Allen et al., 1993, Zhuang et al., 1994, Di Toro et al., 1992, Carlson et al., 1991). A relationship was found between cadmium toxicity and the AVS normalised Cd content. In general, toxicity was expected to be absent when the ratio of the simultaneously extractable metals (SEM) to the AVS < 1 (molar ratio) and to increase drastically from SEM/AVS ≥ 1. Metal toxicity above this value furthermore depend on water hardness, pH and solid phase properties. However, the molar ratio did not seem to be a good predictor of potential effects, because the ratio gives no indication about the absolute amount of SEM present in excess of AVS. Therefore, the molar difference was introduced as a better predictor. At a molar SEM-AVS difference < 0 no toxic effects are expected while at molar SEM-AVS difference > 0 toxic effects may occur. Recently, Di Toro et al. (2000) suggested another modification to the SEM-AVS procedure that significantly improves the prediction of organism mortality. The indicator of risk is the ratio of [SEM-AVS] to the organic carbon content (oc) of the sediment. The SEM-AVS relationships can, however, only be applied in anaerobic conditions and ignores spatial and temporal variations (Van den Berg et al., 1998, Zhuang et al., 1994).

There are exceptions to the AVS based normalisation for bioavailability of Cd in sediments. Lee et al. (2000) did not find a correlation between metal concentrations in animal tissue of four benthic organisms and metal concentrations in pore water. The metal concentrations in the animal tissue were correlated with the metal concentrations extracted from the sediment, indicating that exposure of these organisms principally occurred through ingestion of particles. Therefore, the AVS-based approach may be appropriate for protecting some, but not all, benthic organisms. One study furthermore identified Cd toxicity at SEM concentrations below the AVS (Hansen et al., 1996b). A marine sediment with an AVS level of about 17 mmol $kg^{-1}{}_{dw}$ was spiked with $CdCl_2$. Effects were found at 12 mmol SEM $kg^{-1}{}_{dw}$ on the abundances of *Nematoda* and *Annelida*. Although this effect concentration is found at rather high total metal concentration, it reveals that the AVS normalisation may not be applicable in all cases. The study was, however, carried out in marine sediments, and is therefore not used in our calculation of the $PNEC_{sediment}$.

3.2.4.2 Acute and prolonged toxicity to benthic organisms

Table 3.228 Selected data with RI 1-3 for Cd toxicity to benthic organisms. Seventeen tests were reviewed from 5 source documents and 14 tests were selected

	Min	Median	Max	n
NOEC (µg g_{dw}^{-1})	115	680	3,390	15
LOEC (µg g_{dw}^{-1})	334		1,079	2
$E(L)C_{x\geq50}$ (µg g_{dw}^{-1})	563	1,400	6,200	13

A summary of the literature review is given in **Table 3.228**. The Cd concentrations in the sediment/water systems are either expressed per unit sediment dry weight (µg $g^{-1}{}_{dw}$) or as the dissolved fraction in the liquid phase (µg L^{-1}). The main factors influencing toxicity results are physico-chemical characteristics of the test medium, test species (physiological behaviour), life stage of the test organisms, test design and preparation of the test medium. The criteria for defining reliability indices are explained for each source document in the IUCLID document. Data obtained from mixed polluted sediments were considered unreliable (RI 4).

Carlson et al. (1991) and Di Toro et al. (1992) studied the influence of the type of sediment on toxicity of Cd. Carlson et al. (1991) studied toxicity to *Lumbricus variegatus* in two lake sediments and one river sediment. The sediments were contaminated with Cd (40-16,000 µg $g^{-1}{}_{dw}$) by equilibrating the sediment with Cd spiked Lake Superior water. The LC_{50} values varied from 700-6,000 µg $g^{-1}{}_{dw}$. The LC_{50} values were positively related with the AVS—content, i.e. more AVS reduces Cd toxicity. Similar dose-response curves were obtained for the three sediments if the sediment Cd concentration was normalised per unit AVS. Cadmium was extracted with cold hydrochloric acid ($[Cd]_{SE}$), simultaneous with AVS. No toxicity was recorded when $[Cd]_{SE}/AVS<1$ (molar concentration ratio). Mortality increased sharply to 100% when $[Cd]/AVS\geq1$. Di Toro et al. (1992) performed similar tests with the same test species and sediments of the same three locations. They found no unique relationship between $[Cd]_{SE}$ (mg $kg^{-1}{}_{dw}$) and mortality of the test organisms for the different freshwater sediments. By contrast, a clear mortality-concentration relationship was observed when relating mortality to the $[Cd]_{SE}/AVS$ molar ratio. No mortality in excess of 20% was observed for sediments with $[Cd]_{SE}/AVS<1$. For sediments with $[Cd]_{SE}/AVS>1$-3, mortality increased significantly. Similar results were found by Hansen et al. (1996a) for mixed polluted sediments. The simultaneously extractable metals (SEM) however included Cd+Cu+Ni+Zn+Pb. The authors conclude that the AVS is a reactive pool that binds heavy metals and render them unavailable to biota. Hare et al. (1994) studied the in situ colonisation of Cd-spiked freshwater sediments by macroinvertebrates in a chronic field study. Lake sediments below the top 10 cm layer was sampled, spiked with Cd, transferred to 8-L test trays and then installed in the lake bottom at 15 m depth. The mean total abundance for all taxa in the test trays was not significantly related to Cd exposure. Taken individually (at species level), the abundances of most species also did not appear to be related to exposure up to the highest Cd exposure level (563 µg Cd/g_{dw}). Only the number of *Chironomus* (*salinarius gp*) sp., which is one of the most abundant *Chironomidae* species, was strongly reduced at 563 µg Cd/g_{dw}. Larvae of this species burrow deep in the sediment and have their guts filled with sediment, indicating a high exposure via sediment intake.

The physiological behaviour of the test species affects their sensitivity to Cd (Carlson et al. (1991), Di Toro et al. (1992) and Francis et al. (1984)). The sensitivity of the worm *Lumbricus variegatus* and the snail *Helisoma* sp. was measured in spiked sediments (Carlson et al., 1991, Di Toro et al., 1992). *Lumbricus* was found to be the most sensitive to Cd in 4 out of the 6 different freshwater sediments. The higher sensitivity of the worms was attributed to the extended exposure of the worms due their life strategy. *Lumbricus* is usually half buried in the sediment while the other half remains in the overlying water for respiration. The snails however remain on the surface of the sediment, decreasing their contact with Cd in the sediment. Francis et al. (1984) investigated the effect of Cd-enriched sediment on goldfish, leopard frog and largemouth bass in the embryonic and larvae stages. The sediment was contaminated between 1 and 1,000 mg $kg^{-1}{}_{dw}$. No effects on survival were found up to the highest level for goldfish and frog. There was, however, 14% mortality at hatching of the bass larvae at the highest Cd level. The authors attribute the higher sensitivity of bass to the extended contact time of embryos and larvae with the contaminated sediment. Eggs of largemouth bass are settled onto the sediment and larvae remain there after hatching. Embryos and larvae of goldfish and leopard frog however remain in the overlying water and are less exposed to Cd in the sediment.

Nebeker et al. (1986b) studied survival of *Hyalella azteca* in Cd-spiked water and in sediment. Tests were performed in static and flow through conditions. The Cd concentrations in the solutions of the flow through systems were far below those in the static system. In the flow-through test, Cd had no effect on mortality of *Hyalella azteca* whereas in the static test, effects are found in sediment/water systems containing 20 µg Cd L^{-1}. The gradient between the pore water and bottom water Cd concentrations is disturbed in flow-through systems. Therefore the pore water and bottom water concentrations decrease and the sediment appears to be less toxic.

Table 3.229 Toxicity to benthic organisms. All underlined data are selected for the effect assessment

Test substance	Organism	Medium	Test conditions	Nominal/ Measured	Equilibration period (d)	Duration (d)	Endpoint	NOEC µ– g^{-1}_{dw}	NOEC µg L^{-1}	Cat*	LOEC µg g^{-1}_{dw}	LOEC µg L^{-1}	$EC_{x\geq50}$ µg g^{-1}_{dw}	$EC_{x\geq50}$ µg L^{-1}	references	R.I.
Helisoma sp.		uncontaminated freshwater sediment from:	semi-static; sed./water:1:3 (vol)	M-total	/	10	mortality								Di Toro et al., 1992	
		Pequaywan Lake	AVS: 42 µmol/g					<u>3390</u>	1			<u>4520</u>				3
	Lumbricus variegatus	East River	AVS: 8.8 µmol/g					<u>2260</u>	1			<u>3340</u>				3
		West Bearskin Lake	AVS: 3.6 µmol/g					<u>340</u>	1			<u>790</u>				3
		Pequaywan Lake	AVS: 42 µmol/g					<u>3390</u>	1			<u>4520</u>				3
		East River	AVS: 8.8 µmol/g					<u>680</u>	1			<u>1130</u>				3
		West Bearskin Lake	AVS: 3.6 µmol/g					<u>340</u>	1			<u>680</u>				3
$CdCl_2$	*Hyalella azteca*	n–tural sediment (Soap Creek Pond - Oregon State University); 200 ml spiked natural sediment + 800 ml well water	static; T 19°C; sediment characteristics: 3% organic carbon, 15% sand, 29% silt, 56% clay; water ch–racteristics: pH 7.1, H 54 mg L^{-1} $CaCO_3$, BC < 0.5 µg L^{-1}. AVS unknown	M (diss.)	0.5	4	mortality	<u>167</u>	1.1	2	<u>334</u>(26)	3.2		6.6	Nebeker et al., 1986b	3
$CdCl_2$	*Micropterus salmoides*	natural stream sediment; 250 g_{dw} sediment □pproach□d-solution or distilled deionized water (control) +350 ml rec–nstituted water	DO 6.6-8.1 mg L^{-1}, T 22.1-22.5 °C, pH 7.9-8–4; sed: OM 2.3%, $Cd_{–}$ 1.02 mg kg^{-1}, Zn_T 108.2 mg kg^{-1}, Fe_T 5.52%; 5.52% sand, 35.4% silt, 12% clay	M	0.42	7	mortality	<u>540</u>	22	2	<u>1079</u> (14)	44 (14)			Francis et al., 1984	3
$CdNO_2$	*Chironomus (salinarius gp) sp.*	natural lake sediment (Lake Tantaré, Canada), sampled below the top 1-10 cm; spiked sediments in test trays replaced in the test location in the lake	field test; water characteristics: pH 5.5-5.6, H 3; sediment characteristics: AVS: 0.5 µmol/g_{dw}	N	/	14 months	abundance	<u>115</u>		1			<u>563 (80)</u>		Hare et al., 1994	2

Table 3.229 continued overleaf

Table 3.229 continued Toxicity to benthic organisms. All underlined data are selected for the effect assessment

Test substance	Organism	Medium	Test conditions	Nominal/ Measured	Equilibration period (d)	Duration (d)	Endpoint	NOEC µ– g⁻¹dw	NOEC µg L⁻¹	Cat*	LOEC µg g⁻¹dw	LOEC µg L⁻¹	EC$_{x\geq50}$ µg g⁻¹dw	EC$_{x\geq50}$ µg L⁻¹	references	R.I.
$CdCl_2$			sediment AVS content:	M	4	10	mortality								Carlson et al., 1991	2
	Lumbricus variegatus	Pequaywan Lake	38-32 µmol/g					3000		1			6000			
		East River sediment	6.8-7.3 µmol/g					800		1			1400			
		West Bearskin Lake	2.8-3.2 µmol/g					380		1			700			
	Helisoma sp.	Pequaywan Lake	38-32 µmol/g													
		East River sediment	6.8-7.3 µmol/g					3000		1			6200			
		West Be arskin Lake	2.8-3.2 µmol/g					2300		1			4100			
			test water: sand filtered Lake Superior water; T–21-22 °C, alkalinity 45–46 mg L⁻¹, hardness 44-45 mg L⁻¹, pH 7.9-8, dissol–ed oxygen concentration >6 mg L⁻¹, continuous flow; T 23°C; 1.5L Cd sol. + 1L sed.					380		1			810			
Supporting data																
$CdCl_2$	*Hyalella azteca*	contaminated freshwater sediment from Foundry cove	semi -static; sed./w ater:1:3 (vol) AVS: 0.1-47 µmol/g; SEM (Ni+Cd) 0.3-1000 µmol/g	M-total	/		mortality						17 (100)		Di Toro et al., 1992	4
$CdCl_2$	*Rana pipiens* *Carassius auratus*	natural stream sediment; 250 g_{dw} sediment pproachd-solution or distilled deionized water (control) +350 ml rec–nstituted water	DO 6.6-8.1 mg L⁻¹, T 22.1-22.5 °C, pH 7.9-8–4; sed: OM 2.3%, Cd– 1.02 mg kg⁻¹, Zn_T 108.2 mg kg⁻¹, Fe_T 5.52%; 5.52% sand, 35.4% silt, 12% clay	M	0.42	7	mortality	1074(HT) 1008(HT)	77 69						Francis et al., 1984	4 4
Cd^{2+}	*Hyalella azteca*	natural sediment: Foundry cove	% total organic carbon: 0.55-16.4 µg/g, total Cd: 0.4-38900 µg/g, total Cu: 18-143 µg/g, total Ni: 18-31500 µg/g, total Pb: 6.1-357 µg/g, total Zn: 65-403 µg/g, sum metals: 2.9-893, SEM: 0.2-779 µmol/g, AVS: 0.4-64.6 µmol/g, SEM/AVS: 0.02-139	M-total	/	10	mortality	72			363(20)				Hansen et al., 1996a	4

TOC Total organic carbon;
AVS Acid volatile sulphides;
SEM Simultaneously extractable metals
HT Highest Tested concentration;
H Water hardness (mg $CaCO_3$ L^{-1});
* NOEC classification (see section 3.2.1.2).

3.2.4.3 The $PNEC_{sediment}$

There is only one sediment toxicity test available within the data set that can be considered as a real chronic test (test duration of other tests are 4-10 days and use mortality as endpoint). The statistical extrapolation technique will therefore not be used on the NOEC data and two alternative methods will be proposed.

According to the TGD (TGD 1996, p.335), the $PNEC_{sediment}$ may be calculated using the equilibrium partitioning (EP) method in the absence of ecotoxicological data for sediment-dwelling organisms. Based on the equilibrium partitioning, the following formula is applied to calculate $PNEC_{sediment}$ (mg $kg^{-1}{}_{ww}$):

$$PNEC_{sediment} = \frac{K_{sed\text{-}water}}{RHO_{sediment}} \cdot PNEC_{water} \cdot 1000 \qquad \text{Equation 3.3}$$

with $PNEC_{water}$ expressed in mg L^{-1}, $RHO_{sediment}$ the bulk density of wet sediment (kg_{ww} m^{-3}), $K_{sed\text{-}water}$ the water-sediment partition coefficient (m^3 m^{-3}).

This equation can be transformed to a dry weight based $PNEC_{sediment}$ as

$$PNEC_{sediment} = K_p \cdot PNEC_{water} \cdot 10^{-3} \qquad \text{Equation 3.4}$$

in which K_p equals the solid-water partition coefficient of suspended matter, expressed in L kg^{-1}, and $PNEC_{water}$ expressed in µg L^{-1}. This transformation has assumed that the fraction Cd in the pore water can be neglected compared to the total amount of Cd in the sediment. Even at the lowest Kp assumed in the table below, this fraction is less than 0.01%. The $PNEC_{water}$ equals 0.19 µg L^{-1} (see Section 3.2.2.7). The K_p ranges 17 10^3 L kg^{-1}- 224 10^3 L kg^{-1} (typical value, 130 10^3 L kg^{-1} see Section 3.1.2.3.1, **Table 3.82**). The TGD stipulates an upper limit of Kp beyond which an additional safety factor of 10 should be included (either in PNEC or in PEC) to take the risk of direct ingestion into account. This upper limit is at Kp of about 2,000 L kg^{-1}. This situation is certainly the case for Cd, therefore the PNEC should be lowered by a factor of 10 in all cases, i.e. the $PNEC_{sediment}$ should be calculated in this case as

$$PNEC_{sediment} = K_p \cdot PNEC_{water} \cdot 10^{-4} \qquad \text{Equation 3.5}$$

This results in:

K_p (L kg^{-1})	$PNEC_{sediment}$ (mg Cd/kg_{dw})
17,000	0.32
130,000	2.5
224,000	4.3

The ‘generic’ $PNEC_{sediment}$ derived with the EP method using the typical Kp values of suspended matter is, therefore, 2.5 mg Cd/kg_{dw}

Another approach to calculate the $PNEC_{sediment}$ is using the assessment factor (AF) method. The NOEC of the chronic test (115 mg kg^{-1}) is divided by an AF of 50. The choice of an AF of 50 instead of 100 is justified by the number of acute toxicity data, showing no differences between species. This results in

$$PNEC_{sediment} = 115 \text{ mg kg}^{-1}/50 = 2.3 \text{ mg Cd/kg}_{dw}$$

The AF method yields a PNEC that is almost identical as the 'generic' $PNEC_{sediment}$ derived with the EP method. The AF method however predicts a PNEC which is even below the background value of the sediment in which the lowest chronic NOEC was found (2.8 mg Cd/kg_{dw}, Hare et al., 1994). The separation between the PNEC and effect concentrations (n=15) is higher than 100-fold, and this is large for natural elements. Additional chronic toxicity data (currently not found) could remove this concern by reducing the AF to 10 or below. However, it should be recalled that sediment toxicity tests spiked with Cd have little field relevance because Cd availability can remain low as long as the capacity of free sulphides (AVS) in the sediment is not exceeded. Mixed metal pollution is the rule rather than the exception in the field and the Cd availability in metal polluted sediment is larger than in clean sediment. The AVS normalisation method proposed by DiToro et al. (2000) for predicting chronic effects can be a useful alternative, but can hardly be used to set generic sediment criteria (see below).

The rapporteur of the present document has clear reservations against the AF method (see above) but has no other choice than selecting the AF above the EP method for a pragmatical reason: the EP method that includes the safety factor 10 leads to an enigma that risk is predicted in all local scenarios, even if emissions are zero and the Cd concentrations in water are within the *natural* background range. This enigma remains whatever the choice of Kp as will be demonstrated in the next paragraph.

The local risk characterisation method of the TGD uses the risk factor for sediment, defined as $PEClocal_{sed}/PNEC_{sediment}$. The $PEClocal_{sed}$ is calculated from the local water concentrations and the suspended matter-water partitioning coefficient (Eqn. 50 in the TGD). It can be shown that $PEClocal_{sed}/PNEC_{sediment}$ effectively eliminates the Kp factor in the nominator and denominator, leading to $PEClocal_{sed}/PNEC_{sediment}=10 \cdot PEClocal_{water}/PNEC_{water}$. In simple terms, this means that the risk is predicted (risk factor above 1.0) when the local water concentration is larger than the $PNEC_{water}/10$, i.e. risk for the sediment compartments is predicted when the Cd concentrations in the overlying water are above 0.019 $\mu g\ L^{-1}$. The natural background Cd concentration is estimated as 0.050 µg Cd/L (see Section 3.2.2.1.1) which means that risk is predicted even when emissions are zero and where the Cd concentrations in water are background. Different hypothesis can be forwarded to explain this enigma (i) the benthic organisms may be less sensitive to Cd than aquatic organisms; (ii) exposure via the pore water is the dominant route and the safety factor 10 is overly protective; (iii) the Cd concentrations in the pore water of sediment are lower than that in the overlying water in contrast with the TGD method that assumes equal concentrations in local scenarios (formation of metal sulphides that reduce Cd^{2+} activity in sediments compared to the overlying water can explain such reductions). The safety factor 10 could be disregarded to avoid the enigma with the EP method, however no consensus was reached at the Technical Meetings and it is proposed to use the AF method.

Concluding, it is proposed to select a PNEC derived with an AF as:

$$PNEC_{sediment} = 2.3 \text{ mg Cd/kg}_{dw}$$

There seems to be many studies that indicate that the SEM/AVS concept (see Section 3.2.4.1) may be used for evaluating site-specific toxicity of metals. There are, however, a number of comments on the SEM/AVS concept, which limits its use for a generic approach. Firstly, Ankley (1996) showed that in some cases there appeared to be a linear accumulation of metals with increasing sediment metal concentration irrespective of the SEM/AVS content. This questions the validity of the assumption that when the SEM/AVS < 1, the metals would not be bioavailable.

Secondly, both the qualities of the SEM-data and the AVS-data are under recent discussion. The experimentally determined SEM values may underestimate the actual concentration of metals (Cooper and Morse, 19998), while the AVS values from pooled sediment samples may overestimate the actual AVS concentration in the top, aerobic sediment layer (Van den Berg et al., 1998).

Thirdly, relative to the SEM/AVS concentrations, sediment guidelines based upon dry weight-normalised concentrations were equally or slightly more accurate in predicting both non-toxic and toxic results in laboratory tests (Long et al., 1998). These latter findings currently limit the value of the SEM/AVS ratio for risk assessment.

Fourthly, further research is required to the proposed SEM/AVS concept to better implement its significance (Ankley et al., 1996; Ankley, 1996; Mayer et al., 1996)

- for benthic organisms that have a habitat at or slightly above the sediment surface where aerobic conditions prevail, and the AVS-content will be very low;
- to protect aquatic systems from metal release associated with sediment suspension;
- for the transport of metals into the food web either from sediment ingestion or the ingestion of contaminated benthos; and
- for organisms that are capable of actively extracting substances from sediments, such as polychaetes, that may produce ligands for (essential) metals, to accelerate uptake.

Due to the several comments on the SEM/AVS concept, its use for a generic approach is not adopted in the present RAR. However, taking into account AVS in assessing the risk of Cd for site-specific purposes might be possible.

The two-tiered approach as proposed in the Zn RAR (draft version, June 2001; Annex 3.3.2.C) could be followed.

To apply the AVS-approach, the worst case approach should be followed, i.e. the highest SEM concentration, the lowest AVS concentration and the lowest f_{oc} value. Furthermore, before applying the AVS-approach, some answers should be found on questions about the representativeness of the studies used to develop the AVS approach, the cut off value of 100 μmol g^{-1}_{oc}, seasonal variations in SEM, AVS and f_{oc} and the presence of other metals.

In conclusion, the $PNEC_{sediment}$ is derived by the assessment factor method, i.e.

$$PNEC_{sediment} = 2.3 \text{ mg Cd/kg}_{dw}$$

will be used for risk characterisation.

Remark: After the TMIV'02 last visit discussion on cadmium in sediment a number of MSs (UK, F, DE) and Industry commented on the sediment assessment (see Risk Characterisation and Conclusions).

For UK and DE comments see Risk Characterisation (see Section 3.3.2).

F expressed it cannot accept a final **conclusion (iii)** based on PNEC derived from an assessment factor of 50. An additional test for the sediment compartment should be requested, in order to reduce the uncertainty of the hazard assessment of the sediment compartment. So, F suggests a general **conclusion (i)** for the sediment compartment (long-term assay on sediment spiked with cadmium). In addition F supports the proposal made by Industry (French CA, 21.01.03).

Industry proposes a stepwise approach (IZA Europe, ICdA CollectNiCad letter, 6 February, 2003). The first step is related to the incorporation of the results of the studies dealing with bioavailability of metals performed in the frame of the zinc risk assessment. If needed, a second step, an additional long-term assay on sediment could be performed.

3.2.5 Atmospheric compartment

No toxicity data of CdO in the atmospheric compartment were found.

3.2.6 Toxicity for micro-organisms in a sewage treatment plant (STP)

Toxicity data of Cd to micro-organisms are presented in **Table 3.230**. Two tests on the effect of Cd on sludge respiration were found. Both tests were performed according to the OECD 209-guidelines (respiration inhibition test). The tests were performed using metallic Cd powder and CdO powder. Accounting for the variability of the test results, it seems that both Cd and CdO have a similar toxic action (similar NOEC and LOEC values) when based on the soluble fraction. Cd only affects sludge respiration at about 1 mg Cd/L in the dissolved fraction. This concentration was found at a loading of 100 mg metallic Cd powder or 100 mg CdO powder per litre of sludge suspension.

The LOEC values in the dissolved fraction (~1 mg Cd/L) are high compared with LOEC values for aquatic species (mostly in the 10-100 µg Cd/L range). This may indicate a high tolerance of bacteria to Cd. Some toxicity tests were found with bacterial cultures. These bacteria are tested in artificial media and a high tolerance to Cd was found for *Pseudomonas putida, Zoogloea ramigera* and *Escherichia coli* (Bringman and Kuhn, 1980; Norberg and Molin, 1983; Zwarum 1973). The threshold toxic Cd concentration for *Pseudomonas putida* is 80 µg L^{-1} (Bringman and Kuhn, 1980), but this concentration refers to 3% inhibition and can be considered as a NOEC. Cd only affects the other species above 1 mg L^{-1} range. It is unknown to what extent the components of the media, in which the bacteria are tested, can reduce Cd toxicity through metal complexation. Therefore, none of the tests with bacterial cultures have been selected for deriving the $PNEC_{micro\text{-}organisms}$.

A $PNEC_{micro\text{-}organisms}$ is derived by dividing the lowest NOEC value of a respiration inhibition by an assessment factor of 10 (TGD, 1996, p.334).

This yields:

$$PNEC_{micro\text{-}organisms} = 20\ \mu g\ Cd/L$$

This concentration refers to the Cd in the dissolved fraction.

Table 3.230 Toxicity for micro-organisms in a sewage treatment plant or in artificial media

Test substance	Organism	Medium	Test conditions	Nominal/ Measured	Duration (d)	Endpoint	NOEC (µg Cd L^{-1})	LOEC (µg Cd L^{-1})	EC_{50} (µg Cd L^{-1})	References	R.I.
Cd	0.5 mm sieved activated domestic sludge	activated domestic sludge (1.6g L^{-1}) fed with synthetic sewage	pH 7.7-7.8; T 18.5-19.2	M-total (Cd) M-dissolved	0.125	respiration rate	32,600 <u>200</u>	100,000(11) <u>800</u> (11)		LISEC, 1998c	1
CdO	0.5 mm sieved activated domestic sludge	activated domestic sludge (1.6g L^{-1}) fed w ith synthetic sewage	pH 7.59-7.79; T 18.5-19.3	M-total (Cd) M-dissolved	0.125	respiration rate	27,300 <u>353</u>	77,800(26) <u>1,200</u>(26)		LISEC, 1998d	1
$CdCl_2$	*Escherichia coli*	artificial medium; pH 6	soy pepton 0.01%	N	1-6h	respiration	600	6,000		Zwarum, 1973	4
$Cd(NO_3)_2$	*Pseudomonas putida*	artificial medium; pH 7	static; T 25; H 80	N	0.67	biomass (OD)	80			Bringmann and Kühn, 1980	4
$CdCl_2$	*Zoogloea ramigera*	artificial medium; pH 7; H 81; T 26	static	N	0.87	cell number	1,000		3,000	Norberg and Molin, 1983	4

H Water hardness (mg $CaCO_3$/L);
OD Optical density.

3.2.7 Assessment of secondary poisoning

3.2.7.1 Source of data and limitations for risk assessment

Toxicity of Cd through secondary poisoning is assessed based on laboratory studies where organisms are exposed to variable Cd concentrations in their prey. A $PNEC_{oral}$ can be calculated from such studies. This $PNEC_{oral}$ can be combined with the bioconcentration factors (BCF's) or bioaccumulation factors (BAF's) of the prey to assess risks of secondary poisoning of the predator by Cd originating from soil, freshwater or sediment. This protocol is suggested by the TGD (TGD, 1996) and will be discussed together with an alternative approach for mammals and birds in Section 3.2.7.4).

The risk of secondary poisoning is focussed on mammals and birds and not on lower organisms. No or little data were found to calculate the $PNEC_{oral}$ for fish or aquatic invertebrates, benthic organisms or lower terrestrial organisms. A short discussion will, however, be given about secondary poisoning in fish or lower terrestrial organisms (see Sections 3.2.7.2.3 and 3.2.7.3.2).

A wealth of data is available on bioconcentration factors or bioaccumulation factors. Only a selection of the data is given here, merely as an illustration rather than to serve as a complete survey. The bioconcentration factors soil-plant (the soil-plant transfer factors) are reported separately in the human health part of this Risk Assessment Report, as this pathway is important for Cd exposure to the general population.

Some BCF and BAF values are derived from systems with mixed metal pollution. Mixed pollution is an additional factor that affects the Cd availability and, hence, the BCF or BAF. No reliability indices were given to the studies from which the BCF's or BAF's are calculated.

3.2.7.2 The aquatic compartment

3.2.7.2.1 The bioconcentration factor in water

The ability of an organism to concentrate a substance from the aquatic environment is expressed as the bioconcentration factor (BCF).

BCF-values calculated on the basis of steady-state uptake and depuration rate constants are indicated with an asterisk in the Tables. Most of the BCF values were, however simply calculated from the concentration ratio between water and biota. Many of the BCF's are calculated on a dry weight basis. The BCF's on dry weight basis are transformed to the wet weight basis if the dry weight percentage of the organism was given in the source document.

Results of Cd bioconcentration studies in water are presented in **Table 3.231**.

Table 3.231 The bioconcentration factor (BCF) of Cd in freshwater organisms. The Cd concentrations in the organisms are the product of BCF and Cd concentration in water

Test substance	Organism	Medium	Test conditions	Nominal/ measured	Duration (d)	Cd in water µg L^{-1}	BCF (L kg^{-1}_{ww} or L kg^{-1}_{dw}[a])	References	Remark
				Primary producers					
$CdCl_2$	periphyton (assembly of algae and detritus on rocks)	natural sediment and water of oligotrophic soft water lakes (Ontario)	field study; alkalinity 98 mg L^{-1}; DOC 601 µm L^{-1}; H 8.3 mg L^{-1}	M-total	116	0.09	130,000*[a]		
$CdCl_2$	*Elodea* sp.	tap + deionized water (50/50); T 20°C; DOC 0.9 mg L^{-1}; H 88 mg $CaCO_3$ L^{-1}; Cd 0.14 µg L^{-1}; Cu 4 µg L^{-1}; Zn 4 µg L^{-1}; Pb 0.2 µg L^{-1}	semi-static; pH 6; no aeration	M	16	0.5	60,600-151,500[(a)]	Van Hattum et al., 1989	
							4,560-11,400		
						2	89,000-300,000[(a)]		
							6,700-22,333		
						4.3	100,232-310,000[(a)]		
							7,535-23,143		
					14	11	1,636		
$CdSO_4$	*Chlorella vulgaris*	algae medium: H 6.2 mg $CaCO_3$ L^{-1}; Zn 48 µg L^{-1}, Cu 2.54 µg L^{-1}, Co 5.9 µg L^{-1}, Mn 91 µg L^{-1}; T 25°C; aerated with 5% CO_2		M	2.08	0.18	2,222[(a)]	Khummongkol et al., 1982	
$CdCl_2$	*Phytium* sp.	bal Medium A	5 g glucoseL-1, 4 g casamino acidL-1; pH 6.5; T 25°C	M	5	5	44,000[(a)]	Duddridge and Wainwright, 1980	
	Dictyuchus sterile						89,000[(a)]		
	Scytalidium lignicola								
	Phytium sp.						50,000[(a)]		
	Dictyuchus sterile		2 g glucoseL-1, 1.8 g casamino acidL-1; pH 6.5; T 25°C						
	Scytalidium lignicola	basal Medium B			7		38,000[(a)]		
							90,000[(a)]		
							48,000[(a)]		
				Primary consumers					
$CdCl_2$	*Daphnia magna*	Lake Louhilampi (Finland)	DOC 14.2 mg L^{-1}; pH 6.5; H 6 mg $CaCO_3$ L^{-1}	N	1	20	994*	Penttinen et al., 1995	
					3	20			
			DOC < 0.2 mg L^{-1}; pH 6.5; H 30 mg $CaCO_3$ L^{-1}				625		
		Artificial humic-free water			1	20	510*		

Table 3.231 continued overleaf

Table 3.231 continued The bioconcentration factor (BCF) of Cd in freshwater organisms. The Cd concentrations in the organisms are the product of BCF and Cd concentration in water

Test substance	Organism	Medium	Test conditions	Nominal/ measured	Duration (d)	Cd in water µg L^{-1}	BCF (L kg^{-1}_{ww} or L kg^{-1}_{dw} ^{a})	References	Remark
$CdCl_2$	*Daphnia magna*	Reconstituted water charcoal and 0.45 µm filtered	H 92 mg L^{-1}; Al 73 mg L^{-1}; pH 8	N	4	10		Stackhouse and Benson, 1989	no gut clearance
			Without HA				6,240[(a)]		
			+0.5 mg HA L^{-1}				5,520[(a)]		
			+5 mg HA L^{-1}				4,690[(a)]		
			+50 mg HA L^{-1}				2,200[(a)]		
$CdSO_4$	*Daphnia magna*	Ultrapure water; Alk: 100 mg L^{-1}; pH 8.3-8.8; T 20°C	Soft water: H 58 mg L^{-1}	N	28	7.5	7,333[(a)]	Winner and Gauss, 1986	no gut clearance;
			Hard water: H 230 mg L^{-1}		28		6,666[(a)]		no steady state
			Soft water: H 58 mg L^{-1}		20		4,733[(a)]		
			+ 0.75 mg HA L^{-1}		20		5,000[(a)]		
$CdSO_4$	*Daphnia magna*	Lake Superior water			4	(dissolved)		Poldoski J.E., 1979	no gut clearance
						0.0225	3,555		
						0.225	2,089		
						1	1,000		
						3.4	735		
						10.1	396		
pproach	*Asellus aquaticus*	Tap + deionized water (50/50); T 20°C; DOC 0.9 mg L^{-1}; H 88 mg $CaCO_3$ L^{-1}; Cd 0.14 µg L^{-1}; Cu 4 µg L^{-1}; Zn 4 µg L^{-1}; Pb 0.– µg L^{-1}	continuous flow; pH 5.9 - 7.6; DO 8.5 mg L^{-1}	M	30	0.87-11.3	17,560*	Van Hattum et al., 1989	
Secondary consumers									
$CdCl_2$	*Salmo salar*	municipal water charcoal filtered and UV sterilised; BC 0.13 µg CdL^{-1}; pH 6.5-7.3; T 5-10; DO 11. 1-12.5; Al 14-17; H 19-28	Alevins; T 8.9-9.3 °C	M	92	0.13	1,385[(a)]	Rombough and Garside, 1982	
						0.47	1,277[(a)]		
						0.78	1,282[(a)]		
						7.5	213[(a)]		
						8.2	213[(a)]		
						34	95[(a)]		
						79	60[(a)]		
						300	5[(a)]		

Table 3.231 continued overleaf

Table 3.231 continued The bioconcentration factor (BCF) of Cd in freshwater organisms. the Cd concentrations in the organisms are the product of BCf and Cd concentration in water

Test substance	Organism	Medium	Test conditions	Nominal/ measured	Duration (d)	Cd in water µg L^{-1}	BCF (L kg$^{-1}_{ww}$ or L kg$^{-1}_{dw}$[a])	References	Remark
$CdCl_2$	*Gasterosteus aculeatus*	Water; T 14.6 °C; pH 8.09; DO 94%; Alk 99.7 mg $CaCO_3L^{-1}$; H 120.6 mg $CaCO_3L^{-1}$	Semi-static	M	33.3	0.8	511	Pascoe and Mattey, 1977	no gut clearance
					16	2.6	172.5		
					15.3	4.5	216.3		
					16.3	9	101.3		
					30	29	34.03		
					22.2	50	23.14		
					7.6	90	14.36		
					21.5	290	14.77		
					13.3	910	5.24		
					36.8	2970	2.78		
					15.3	5180	2.04		
					2	8670	1.27		
					0.3	97500	0.51		
$CdCl_2$	*Cyprinus carpio*	tap water; T 18-19; pH 6.8; Al 14.8; H 18, BC 0.001 mg L^{-1}; food < 0.05 µg L^{-1}	semi-static; viscera	N	100	1	221[a]	Muramoto, 1981	
			gills				286[a]		
			vertebrae				122[a]		
			viscera			10	1,620[a]		
			gills				1,300[a]		
			vertebrae				418[a]		
			viscera			50	892[a]		
			gills				236[a]		
			vertebrae				11,500[a]		
			viscera			100	613[a]		
			gills				158[a]		
			vertebrae				59[a]		

Table 3.231 continued overleaf

Table 3.231 continued The bioconcentration factor (BCF) of Cd in freshwater organisms. The Cd concentrations in the organisms are the product of BCF and Cd concentration in water

Test substance	Organism	Medium	Test conditions	Nominal/ measured	Duration (d)	Cd in water µg L^{-1}	BCF (L kg^{-1}_{ww} or L kg^{-1}_{dw} [a])	References	Remark
$CdSO_4$	*Lepomis macrochirus*	Water; H 207 mg $CaCO_3 L^{-1}$; Ac 11 mg $CaCO_3 L^{-1}$; Alk 152 mg $CaCO_3 L^{-1}$; pH 7.7; DO 6.6 mg L^{-1}; T 16-29 °C	gill	M	330	2.3	< 2,174	Eaton, 1974	
			intestine and caecum				< 2,174		
			liver				< 4,348		
			kidney				< 4,348		
			gill			31	1,097		
			intestine and caecum				2,355		
			liver				6,484		
			kidney				6,065		
			gill			80	363		
			intestine and caecum				2,188		
			liver				4,175		
			kidney				2,313		
			gill			239	142		
			intestine and caecum				1,364		
			liver				1,826		
			kidney				634		
			gill			757	53		
			intestine and caecum				229		
			liver				363		
			kidney				165		
			gill			2140	37		
			intestine and caecum				176		
			liver				206		
			kidney				68		

Table 3.231 continued overleaf

Table 3.231 continued The bioconcentration factor (BCF) of Cd in freshwater organisms. The Cd concentrations in the organisms are the product of BCF and Cd concentration in water

Test substance	Organism	Medium	Test conditions	Nominal/ measured	Duration (d)	Cd in water µg L^{-1}	BCF (L kg^{-1}_{ww} or L kg^{-1}_{dw}[a])	References	Remark
$CdCl_2$	*Salvelinus fontinalis*	sterilised Lake Superior water; H 42-47; pH 7-8; Al 38-46; Ac 1-10; DO 4-12; T 9-15	continuous flow; first generation:	M	266			Benoit et al., 1976	
			kidney			0.06	33,333[a]		
			gill				11,666[a]		
			liver				6,666[a]		
			kidney			0.5	24,000[a]		
			gill				11,000[a]		
			liver				9,000[a]		
			kidney			3.4	14,118[a]		
			gill				2,206[a]		
			liver				2,941[a]		
			gonad				1,912[a]		
			spleen				882[a]		
			muscle				29.4[a]		
			red blood cells				29.4[a]		
			second generation:		735	3.4			
			kidney				1,2647[a]		
							2,647		
			gill				1,765[a]		
							1,471		
			liver				4,412[a]		
							2,294		

HA Humic acids;
* BCF-value calculated on the basis of steady-state uptake and depuration rate constants;
DOC Dissolved organic carbon;
H Water hardness (as mg $CaCO_3$/L).

The BCF's of Cd are highest for the primary producers and lowest for fish (see **Table 3.232**). The BCF's of algae are obtained by measuring Cd concentration in water and algae. The high BCF's do not necessarily reflect high Cd intake in algae because a significant proportion of Cd is sorbed to the cell wall. Several BCF values of the invertebrates might overestimate true intake if the analysis of the Cd content in the organisms was performed without gut clearance. The kidney and liver of fish concentrate most Cd within the fish total body.

Table 3.232 Comparison of freshwater BCF (L kg^{-1}) found in this study with data found by Taylor (1983)

	This review			Taylor (1983)	
	Min	Max	Median	Min	Max
algae wet weight	1,636	23,143	7,535	10	10,000
dry weight	2,222	310,000	11,5116		
invertebrates wet weight	396	17,560	994	10	2,000
dry weight	546	33,333	5,000		
vertebrates wet weight	0.51	6–84	229		
dry weight	5	33,333	233		
vertebrates -total body content- wet weight	0.51	5'1	15	1	3,000
dry weight	5	1,385	80		

The BCF's of algae, which were selected in this review, are higher than the BCF's that were reviewed from 40 laboratory studies by Taylor (1983). The reviewed BCF values for freshwater algae range between 10 and 10,000 L $kg^{-1}{}_{ww}$ (Taylor, 1983). This report finds BCF values ranging between 222-31,000 L $kg^{-1}{}_{ww}$ if all dry weigh based data are converted to wet weight data. For this conversion it was assumed that the average dry matter content is 10%. The BCF's for algae, which were collated here, were generally found in soft water. Low water hardness is known to increase availability of soluble metals such as Cd^{2+}. The range in fresh weight based BCF's of invertebrates is also somewhat above the range found by Taylor (1983). The whole-body fish BCF's cover a similar range in both studies.

Most important factors affecting the bioconcentration of Cd by aquatic organisms are the Cd concentration of the water, the hardness, pH, and the presence of complexing agents such as humic acid.

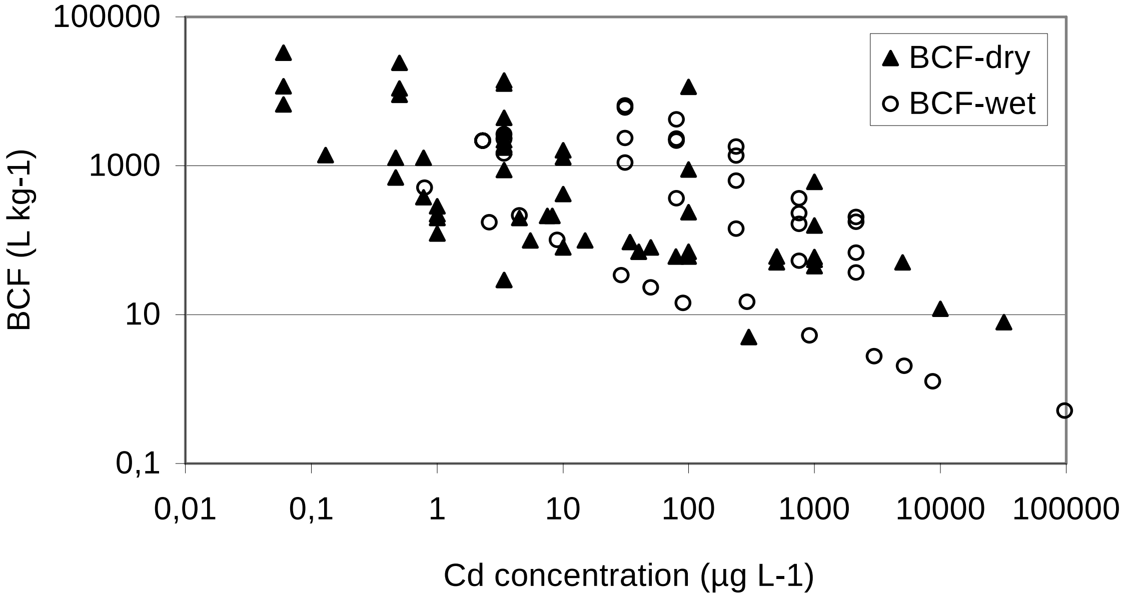
The influence of pH on the bioconcentration of Cd is illustrated by experiments of Lithner et al. (1995). A field study was performed in Swedish brooks. The bryophyte *Fontinalis antipyretica* was transplanted from a pristine brook to various polluted brooks, in the Rönnskär area, containing 0.12 to 0.29 µg Cd/L. After an exposure period of 14 days the BCF of the top shoots of the bryophytes was determined. An increase in BCF with increasing pH was observed. In acidified brooks (pH < 6) BCF values up to 10,000 L $kg^{-1}{}_{dw}$ were found. In neutral brooks (pH > 6) BCF values of more than 30,000 L $kg^{-1}{}_{dw}$ were recorded.

Increasing water hardness reduces the BCF of Cd. Penttinen et al. (1995) found a significant effect of hardness on bioconcentration of Cd by *Daphnia magna*. After an exposure period of 1 day in artificial water, the uptake rate constant was 5 times smaller in water with hardness of 30 mg $CaCO_3$/L than in water with hardness 6 mg $CaCO_3$ /L. However, Winner and Gauss (1986) found no significant change in Cd bioconcentration by *Selenastrum capricornutum* at water hardness values ranging from 57 to 230 mg $CaCO_3$ /L.

Humic acids (HA) associate with Cd and reduce the bioavailability and accumulation of Cd by aquatic organisms. The Cd in *Daphnia magna* decreased from 66 to 50 µg Cd/g_{dw} when 5 mg HA L^{-1} was added to the artificial water (Stackhouse and Benson, 1989). Increasing the HA content to 50 mg HA L^{-1} further decreased the Cd uptake by 65%.

Increasing Cd concentration in water reduce the BCF. Tissue Cd concentrations increase with increasing solution Cd but level off at high Cd concentrations (i.e. > 10 µg L^{-1}). As a result, the BCF's decrease at high Cd concentrations. This is well illustrated by the BCF values of fish presented in **Figure 3.23**. The decreasing trend was observed in all tissues.

Figure 3.23 The BCF values (L kg^{-1}) of fish or fish tissues as a function of the Cd concentration in water (µg L^{-1}). Data collated from experiments where solution Cd was artificially increased (see Table 3.231)



This trend was also observed in aquatic invertebrates (Poldoski, 1979) Cadmium content of *Daphnia magna* increased from 0.08 to 4 mg kg^{-1}_{ww} with increasing solution Cd between 0.023 and 10 µg Cd L^{-1}. The bioconcentration factor however decreased from 3,555 to 396 L kg^{-1}_{ww}. The BCF's of the insects *Pteronarcys dorsata, Hydropsyche betteni* and the snail *P. integra*. increased up to Cd concentrations of 10 µg Cd/L. Further increasing the Cd concentration in water resulted in a decrease of the BCF's. Van Hattum et al. (1989), however, found increasing BCF values of the isopod *Asellus aquaticus* with increasing solution Cd concentrations between 0.5 and 4.3 µg Cd/L.

In conclusion, the restricted survey of BCF's of aquatic organisms demonstrates that the BCF's are highest in primary producers and lowest in secondary consumers. Factors affecting the BCF are the water hardness, pH, the Cd concentration and the presence of Cd^{2+} complexing agents.

3.2.7.2.2 The bioaccumulation factor in water

Whereas bioconcentration is the net uptake due to water exposure only, bioaccumulation includes all routes (air, water, soil and food) (TGD, 1996). Several field studies and one laboratory experiment were found in which the BAF (L kg_{ww}^{-1}) was calculated for organisms, mainly invertebrates, exposed by both water and food. Bioaccumulation factors range from 4 to 170,000 L kg^{-1}_{dw}. Comparison of bioaccumulation factors and bioconcentration factors of aquatic invertebrates reveals the latter to be significantly lower.

Lithner et al. (1995) calculated BAF values ranging from 24,000 to 65,000(L $kg^{-1}{}_{dw}$) for 4 invertebrates living in Swedish lakes (heavy metal contaminated Rönnskär area). In the same area two fish species were captured to determine the Cd concentration of the liver. A BAF of 27,000 L $kg^{-1}{}_{dw}$ was found for liver of *Esox lucius* and of 164,000 L $kg^{-1}{}_{dw}$ for liver of *Perca fluviatilis*. These values are remarkably high but liver is known to concentrate Cd compared to the other tissues (see previous section). The dry weight based BCF values of whole fish (see **Table 3.332**: 5-1385 L kg^{-1}) seem to span a similar range as field derived BAF values of whole fish (4-2492 L kg^{-1}, see **Table 3.232** and **3.233**). A similar comment applies to the wet weight based BAF values (see **Table 3.232** and **3.233**).

Table 3.233 The BAF values for whole body vertebrates (L kg-1)

	Min	Max	Median
vertebrates -total body–content- *dry weight*	4	2,492	167
vertebrates -total body content- *wet weight**	1	623	42

* Calculated assuming a mean dry weight:wet weight ratio of 0.25 for whole fish.

Stephenson and Turner (1993) calculated a BAF of 170,000 L $kg^{-1}{}_{dw}$ for the amphipod *Hyalella azteca* in an oligotrophic Canadian lake containing 0.09 µg Cd/L. The fraction of body burden Cd derived from food (algae) was calculated to be 58%. This fraction was calculated based on the difference in Cd uptake rate from food only and from food and water. Munger and Hare (1997) found a BAF of 1,345 L $kg^{-1}{}_{dw}$ for the insect *Chaoborus punctipennis* in a laboratory test. They also studied the relative importance of water and food as Cd sources to the insect. In artificial lake water, a food chain was simulated, composed of the larvae of the insect, its crustacean prey (*’eriodaphnia dubia*), and the prey's algae food (*Selenastrum capricornutum*). Animals were exposed to a Cd concentration of 1.1 µg Cd^{2+} /L^1. *Chaoborus punctipennis* was exposed to both food and water and to food alone during a 14 day exposure period. Cadmium concentration in food, the crustacean prey, was 77 µg Cd/g_{dw} and remained stable throughout the experimental period. No significant difference in Cd content of the insect between both scenarios was found. This suggests that Cd uptake via the water is negligible for *Chaoborus punctipennis*.

From the same test it was possible to study the biomagnification. *Selenastrum capricornutum* exposed to 1.1 µg Cd^{2+} /L had a Cd content of 1,110 µg $g^{-1}{}_{dw}$ and was the food for *Ceriodaphnia dubia*. Exposure of the latter to the same Cd^{2+} concentration in the water and to Cd-enriched algae resulted in a body burden of 77 µg $g^{-1}{}_{dw}$. *Chaoborus punctipennis* contained 16 µg Cd/g_{dw} when fed by Cd-enriched *Ceriodaphnia* in water containing 1.1 µg Cd/L. These results suggest no biomagnification of Cd in the lower aquatic food chain.

3.2.7.2.3 Secondary poisoning within the aquatic compartment

The freshwater shrimp *Gammarus pulex* was exposed to Cd contaminated mycelium as a sole nutrient source (Duddridge and Wainwright, 1980). The mycelium was grown in a medium containing 1,000 µg Cd/L for 4 days prior to the feeding experiment. The shrimps were maintained in a solution containing background Cd or in a solution containing 7 µg Cd/L. In the latter case, the mycelium fed to the shrimps was not previously contaminated by Cd. A 4-day LC_{50} value was recorded when feeding the contaminated mycelium (150-170 mg Cd/kg_{dw}) to the shrimp and all shrimps died after 13 days in that treatment. The shrimps exposed to Cd in solution only, survived the treatment better and 50% mortality was observed at 12 days. The most toxic pathway (water or food) cannot be derived from this study as the food was contaminated at a higher Cd concentration (1,000 µg L^{-1}) than that in the solution of the shrimp feeding experiments (7 µg Cd/L). Another study with Cd in water only revealed a 4-day LC_{50} of 20 µg Cd/L for *Gammarus pulex* (Williams et al., 1985).

No $PNEC_{oral}$ can be calculated for secondary or primary consumers in the aquatic compartment since no NOEC's were found from feeding studies. Cd uptake through food intake may be more important than uptake from water for some organisms, such as amphipods and insects (Stephenson and Turner 1993, Munger and Hare 1997).

Table 3.234 The bioaccumulation factor (BAF) of Cd in freshwater: the Cd concentrations in the organisms are the product of BAF and Cd concentration in water

Test substance	Organism	Medium	Test conditions	Nominal/ measured	Duration (d)	Cd water µg L^{-1}	BAF (L kg^{-1}_{ww} or L kg^{-1}_{dw} [a])	References	Remark
				Primary consumers					
$CdCl_2$	*Hyalella azteca*	natural sediment and water of oligotrophic soft water lakes (Ontario)	field study; uptake via water + (periphyton) food; alkalinity 98 mg L^{-1}; DOC 601 µmL^{-1}; H 8.3 mg L^{-1}	M-total	116	0.09	170,000[(a)]*	Stephenson and Turner., 1993	field study
Cd-water	*Asellus aquaticus* *Libellulidae Sialis lutaria*	Surface water of lakes (Sweden)	Lakes neutral: pH 6.5; H 19 mg $CaCO_3L^{-1}$: Zn 15.2 µg L^{-1}, Cu 4.6 µg L^{-1}, Cd 0.14 µg L^{-1}, Pb 1.8 µg L^{-1}, As 7 µg L^{-1}; Acidified: pH 5.6; H 14 mg $CaCO_3L^{-1}$: Zn 14.4 µg L^{-1}, Cu 2.4 µg L^{-1}, Cd 0.1 µg L^{-1}, Pb 1.4 µg L^{-1}, As 2.6 µg L^{-1}	M	whole-life	0.10-0.14	65,000[(a)] 41,000[(a)] 27,000[(a)]	Lithner et al., 1995	field study/BAF's are arrhythmic means
Cd-water	*Chaeroborus punctipennis*	Canadian lakes	pH 4.62-7.27; H 7.1-74 mg $CaCO_3L^{-1}$; OC 1.29-14.6 mg L^{-1}; Cd 0.017-0.802 µg L^{-1}; Zn 0.523-2.4 µg L^{-1}	M	whole life	dissolved		Hare and Tessier, 1996	field study
						0.033	87,272[(a)]		
						0.021	11,429[(a)]		
						0.267	23,483[(a)]		
						0.043	21,860[(a)]		
						0.354	25,113[(a)]		
						0.036	53,889[(a)]		
						0.552	7,228[(a)]		
						0.802	1,783[(a)]		
						0.246	54,065[(a)]		
						0.035	31,714[(a)]		
						0.036	48,889[(a)]		
						0.075	25,067[(a)]		
						0.017	14,118[(a)]		
						0.127	20,475[(a)]		
						0.161	29,814[(a)]		
						0.061	21,967[(a)]		
						0.023	13,913[(a)]		
						0.017	38,235[(a)]		
						0.028	25,714[(a)]		
						0.045	7,778[(a)]		
						0.217	35,806[(a)]		
						0.134	42,687[(a)]		
						0.251	9,841[(a)]		
^{109}Cd	*Chaeroborus punctipennis*	Artificial lake water;	T 10°C, H 11.6 mg $CaCO_3$ L^{-1}; food: *Ceriodaphnia dubia*; Cd background concentration < 0.023 µg L^{-1}	M	14	1.1	1,345[(b)]	Munger and Hare, 1997	laboratory experiment
				Secondary consumers					
Cd-water	*Perca fluviatilis* *Esox lucius*	Surface water of lakes (Sweden)	Lakes circumneutral: pH 6.5; H 19 mg $CaCO_3L^{-1}$: Zn 15.2 µg L^{-1}, Cu 4.6 µg L^{-1}, Cd 0.14 µg L^{-1}, Pb 1.8 µg L^{-1}, As 7 µg L^{-1}; Acidified: pH 5.6; H 14 mg $CaCO_3L^{-1}$: Zn 14.4 µg L^{-1}, Cu 2.4 µg L^{-1}, Cd 0.1 µg L^{-1}, Pb 1.4 µg L^{-1}, As 2.6 µg L^{-1}	M	whole-life	0.10-0.29	164,000[(a)](liver) 27,000 [(a)](liver)	Lithner et al., 1995	field study

Table 3.234 continued overleaf

Table 3.234 continued The bioaccumulation factor (BAF) of Cd in freshwater: the Cd concentrations in the organisms are the product of BAF and Cd concentration in water

Test substance	Organism	Medium	Test conditions	Nominal/ measured	Duration (d)	Cd water µg L^{-1}	BAF (L kg^{-1}_{ww} or L kg^{-1}_{dw}[a])	References	Remark
Cd^{2+}water	*Perca fluviatilis*	River Eman water	field study; liver;	M	whole life	0.1-0.2	64,000-32,000[(a)]	Olsson and Haux, 1986	field study
Cd-water	*Lepomis macrohirus*	Palestina lake, Indiana (US); H= 275-300 mg $CaCO_3$ L^{-1}); shallow lake (2m); moderately contaminated and contaminated sites	field study; whole fish	M	whole life	0.9	111[a]	Murphy et al., 1978	field study
						17	182[a]		
	L. microlophus					0.9	144[a]		
						17	470[a]		
	L. gulosus					0.9	167[a]		
						17	82[a]		
	Micropterus salmoides					0.9	135[a]		
						17	64[a]		
	Pomoxis nigromaculatus					0.9	89[a]		
						17	33[a]		
	Notemigonus crysoleucas					0.9	213[a]		
						17	38[a]		
	Catostomus commersoni					0.9	133[a]		
						17	117[a]		
	Ictalurus nebulosus					17	166[a]		
	Amia calvla					17	3.5[a]		
Cd-water	*Lepomis. macrochirus*	Skinface pond (South Carolina, US); pH 4.6, 6 mg O_2 L^{-1}; uncontaminated	field study, whole fish	M	499 (after stocking)	0.17	240[a]	Wiener and Giesy, 1979	field study
Cd-water	*Cyprinus carpio*	Sakarya river basin (Turkey); pH ~7; EC 350-850 µS/cm	field study, whole fish, 4 sampling occasions	M	whole life	0.06-0.6	340-2,300[a]	Barlas, 1999	field study
	Barbus plebejus					0.06-0.6	280-2,500[a]		

Table 3.235 Secondary poisoning of Cd in freshwater

Test substance	Organism	Medium	Test conditions	Nominal/ measured	Duration (d)	Food mg kg^{-1}_{ww}	EC_{50} g/kg_{ww}	References
$CdCl_2$	*Gammarus pulex*	Dechlorinated tap water	Semi-static; T 15°C, constant aeration; fed *Phytium* mycelium	M	4	150-170[(a)]	150-170 (50)	Duddridge and Wainwright, 1980
					21		150-170 (100)	

3.2.7.3 The terrestrial compartment

3.2.7.3.1 Bioconcentration and bioaccumulation factors in soil

Bioconcentration of Cd in the terrestrial compartment is defined as the net result of the Cd uptake, distribution and elimination in an organism due to exposure to Cd in soil only.

Results of cadmium bioaccumulation studies in soil are presented in **Table 3.237** and a summary of the bioaccumulation factors is given in **Table 3.236**. All BAF values were calculated from the soil:biota concentration ratios. Most organisms are earthworms and the Cd levels are expressed on dry or wet weight basis. All the data on earthworms are obtained from specimens with guts voided prior to analysis.

Table 3.236 The bioaccumulation factors (BAF's) of soil dwelling organisms

	Min	Max	Median	5th percentile	n
Earthworms- wet weight basis (kg_{dw}/kg_{ww})	4	32	15	5	11
Earthworms- dry weight basis ($kg_{dw}/k–_{dw}$)	1.6	151	15	5	85
Arthropoda - dry weight basis (kg_{dw}/kg_{dw})	0.05	18.8	1.4	0.30	45

Cadmium is concentrated from the soil into earthworms organisms (BAF values all higher than 1). Most important factors affecting the bioaccumulation of Cd by earthworms are the Cd concentration of the soil, soil type, pH, soil organic matter and CEC.

The influence of the Cd content of the soil on the bioaccumulation of Cd is illustrated in most of the studies. Cadmium concentrations in earthworms increase with increasing Cd levels in a non-proportional way (i.e. Wright and Stringer, 1980; Ma, 1982). As a result, the BAF decreases with increasing soil Cd (see **Figure 3.24**). Wright and Stringer (1980) compared Cd content in earthworms and soil from pastures near a large Pb and Zn smelting plant and a control area 9-km away. Cadmium concentrations in the earthworms were several times the value in the soil. For all species, the Cd BAF values however were significantly lower at the contaminated site than at the control site. The soil Cd concentration in the contaminated site was 7-9 folds higher than in the control site. Spurgeon and Hopkin (1996) calculated the BAF of Cd for different earthworm species at 22 locations around a primary smelting plant. For all worm species, body burdens increased with increasing soil Cd levels. No evidence was found for species specific accumulation. The BAF values ranged from 2.59 to 115 kg_{dw}/kg_{dw}. There was an inverse relationship between the BAF's for earthworms and the concentration of Cd in soils. In addition, soil pH and OM were found to affect the BAF of Cd for earthworms. Beyer et al. (1982) examined Cd in earthworms (*Lumbricidae*) from agricultural sites amended with sewage sludge and from experimental control plots. Earthworms from sludge amended sites contained 12 times more Cd than worms from the control sites. The BAF values were lower in contaminated soil than in the control soils. Liming the soil slightly decreased the Cd body burden of the earthworms and high Zn concentrations in soil substantially reduced Cd in earthworms. Morgan and Morgan (1988) examined Cd content in worms in 12 heavily polluted soils of non-ferrous metalifferous mines. A significant correlation was found between the Cd in earthworm and total Cd content of the soils. Gish and Christensen (1973) measured Cd content of topsoil and earthworms near 2 highways (Maryland). Cd contents in both soil and worms decreased with increasing distance from the roadways. Andersen (1979) studied Cd uptake by *Allolobophora spp*. And *Lumbricus terrestris* in soil receiving sewage sludge. The sludge application *reduced* the Cd content in the worms whereas soil Cd concentrations were more than doubled by the sludge application.

The influence of soil type, pH, CEC and the organic matter content of the soil was studied by Ma (1982). The body burden of Cd in earthworms was higher in sandy soils (21-35 mg $kg^{-1}{}_{dw}$) than in loamy soils (12.2-32 mg $kg^{-1}{}_{dw}$), although the soil concentration of Cd was higher in the latter. The BAF increased with decreasing the pH, CEC and soil organic matter content. The soil pH was the most important soil factor for the BAF.

Hunter et al. (1987a) performed a field study in the vicinity of a major copper refinery housing copper/cadmium alloying plant. Invertebrates from contaminated and semi-contaminated (1 km from the plant) grasslands all showed significant elevation of total body Cd concentrations relative to the control site. Detrivorous soil macrofauna showed accumulation of Cd (10-20 times) with respect to concentrations in refinery site organic surface soil and plant litter. Herbivorous invertebrates showed body:diet concentration factors of 3-5 times. Biotransfer of Cd to carnivorous invertebrates reveals marked differences in Cd accumulation by predatory beetles and spiders. Seasonal changes in the abundance, species composition and age structure of invertebrate populations caused marked variation in Cd contamination levels throughout the year.

Figure 3.24 The bioaccumulation factors (BAF kg kg^{-1}) of earthworms as a function of the Cd concentration in soil (mg kg^{-1})

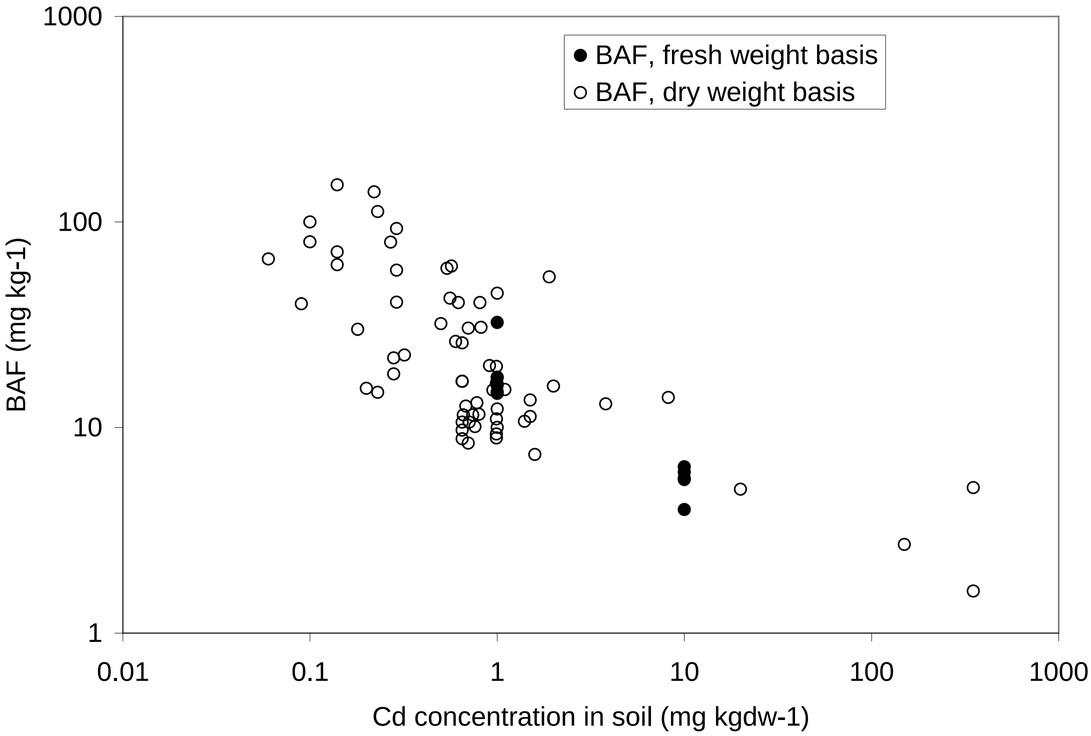


Table 3.237 Bioaccumulation factors in soil. The Cd concentrations in the biota are the product of BAF and soil Cd concentration

Test substance	Organism	Medium	Test conditions	Equilibration period (d)	Duration (d)	Soil mg kg^{-1}_{dw}	BAF (kg_{dw}/kg_{ww} or kg_{dw}/kg_{dw}[(a)])	References	Remark
Cd-soil	*Lumbricus terrestris*	control soil of orchard (Long Ashton); pH 6.5; average biomass 113.7 g/m²; Cd 1 µg/g_{dw}; Pb 92 µg/g_{dw}; Zn 89 µg/g_{dw}	control soil	/	whole life	1	14.64	Wright and Stringer, 1980	field study
			polluted soil			10	5.58		
	Allolobophora caliginosa	Polluted soil of pasture (Severnside); pH 6.8; average biomass 85.8 g/m²; Cd 10 µg/g_{dw}; Pb 147 µg/g_{dw}; Zn 617 µg/g_{dw}	control soil			1	32.45		
			polluted soil			10	6.43		
	Allolobophora tuberculata		control soil			1	17.55		
			polluted soil			10	/		
	Allolobophora chlorotica		control soil			1	14.91		
			polluted soil			10	5.65		
	Allolobophora longa		control soil			1	16.01		
			polluted soil			10	3.99		
	Allolobophora rosea		control soil			1	16.27		
			polluted soil			10	6.06		
Cd-soil	*Allalobophera* sp. + *Lumbricus* sp. + *Octolasium* sp.	soil	Bodine soil	/	whole life	0.32	22.5[a]	Van Hook, 1974	field study
			Captina soil			0.2	15.5[a]		
			Clairborne soil			0.28	21.8[a]		
			Emory soil			0.8	11.6[a]		
			Linside soil			0.28	18.2[a]		
			Rarklin soil			0.23	14.8[a]		
Cd-soil	*Lumbricus terrestris* + *Lumbricus rubellus* + *Lumbricus castaneus* + *Allolobophora caliginosa* + *Allolobophora chlorotica* + *Allolobophora rosea*	Polluted soil around a primary smelting place; pH 5.56-7.32; OM 15-29.9%		/	whole life	/	2.59[(a)]	Spurgeon and Hopkin, 1996	field study
							6.11[(a)]		
							3.81[(a)]		
							6.53[(a)]		
							5.99[(a)]		
							4.86[(a)]		
							23[(a)]		
							10.2[(a)]		
							11.4[(a)]		
							22.8[(a)]		
							64.3[(a)]		
							13.2[(a)]		
							19.8[(a)]		
							9.26[(a)]		
							32.6[(a)]		
							115[(a)]		

Table 3.237 continued overleaf

Table 3.237 continued Bioaccumulation factors in soil. The Cd concentrations in the biota are the product of BAF and soil Cd concentration

Test substance	Organism	Medium	Test conditions	Equilibration period (d)	Duration (d)	Soil mg kg^{-1}_{dw}	BAF (kg_{dw}/kg_{ww} or kg_{dw}/kg_{dw}[(a)])	References	Remark
Cd-soil	*Lumbricadea* sp.			/	whole life			Beyer et al., 1982	agricultural soil amended or not with sludge
		Landsdale1 loam	control; pH 5.9-6.3			0.06	66[(a)]		
			sludge; pH 5.5-6.2			3.8	13[(a)]		
		Hagerstown silt loam	control; pH 5.4-6.4; CEC 9 meq/100g; OM 3%			0.18	30[(a)]		
			sludge; pH 4.9-6; CEC 13 meq/100g; OM 4.9%			0.91/0.55	20[(a)]		
		Landsdale2 loam	control; pH 4.9-6.4; CEC 8 meq/100g; OM 2.5%			0.14/0.05	62[(a)]		
			Sludge; pH 4.6-6.3; CEC 8 meq/100g; OM 2.8%			1.9/1.6	54[(a)]		
		Readingston silt loam	control; pH 5.3-6.1; CEC 10 meq/100g; OM 2.6%			0.09/0.08	40[(a)]		
			sludge; pH 5.5-6.1; CEC 11 meq/100g; OM 3.8%			8.2/5.7	14[(a)]		
Cd-soil	*Lumbricus rubellus*	Topsoil of control soil	control	/	whole life	1	10[(a)]	Morgan and Morgan, 1988	field study
	Dendrodrilus rubidus	and12 heavily contaminated soils of non-ferrous metalliferous mines; pH 4.3-7.8; OC 1-27%; CEC 8-77 meq/100g	polluted			0.1-350	80[(a)]- 1.6[(a)]		
			control			1	45[(a)]		
			polluted			0.1-350	100[(a)]- 5.1[(a)]		

Table 3.237 continued overleaf

Table 3.237 continued Bioaccumulation factors in soil. The Cd concentrations in the biota are the product of BAF and soil Cd concentration

Test substance	Organism	Medium	Test conditions	Equilibration period (d)	Duration (d)	Soil mg kg^{-1}_{dw}	BAF (kg_{dw}/kg_{ww} or kg_{dw}/kg_{dw}[(a)])	References	Remark
Cd-soil	*Lumbricus terrestris* + *Allolobophora chlorotica* + *Allolobophora trapezoides* +	Topsoil along two highways (Maryland): B-W parkway; silt-clay; pH 6.97; OM 4.96-7.3	B-W parkway 3 m	/	whole life	1.59	7.4[(a)]	Gish and Christensen, 1973	field study
			6.1 m			0.78	13.2[(a)]		
	Allolobophora turgida	US-Highway1 ; pH 6.88-6.96; OM 4.8-6.36	12.2 m			0.68	12.7[(a)]		
			24.4 m			0.71	10.6[(a)]		
			48 8 m			0.74	11.5[(a)]		
			US-Highway1 3 m			0.95	15.2[(a)]		
			6.1 m			0.66	11.5[(a)]		
			12.2 m			0.76	10.1[(a)]		
			24.4 m			0.65	9.7[(a)]		
			48 8 m			0.7	8.4[(a)]		
Cd-soil	*Allolobophora longa*	experimental plots:		/	whole life			Andersen, 1979	micrplots
		soil 1: K-fertilised; pH 5.9	soil 1			0.29	40.7[(a)]		
			soil 2			0.14	71.4[(a)]		
		soil 2: NPK-fertilised (300 kg N/ha); pH 5.7	soil 3			0.65	8.8[(a)]		
	Allolobophora caliginosa		soil 4			0.99	9.3[(a)]		
			soil 1			0.29			
		soil 3 Vejen sewage sludge (30 T/ha containing 14.6 mg Cd/kg_{dw}); pH 5.8)	soil 2			0.14			
	Allolobophora rosea		soil 3			0.65	10.6[(a)]		
		soil 4: Lundtofte sewage sludge (30 T/ha containing 34.1 mg Cd/kg_{dw}); pH 6	soil 4			0.99	11[(a)]		
			soil 1			0.29	92.8[(a)]		
	Allolobophora chlorotica		soil 2			0.14	151.4[(a)]		
	Lumbricus terrestris		soil 3			0.65	16.8[(a)]		
			soil 4			0.99	19.8[(a)]		
			soil 3			0.65	16.8[(a)]		
			soil 4			0.99	16.4[(a)]		
			soil 1			0.29	58.3[(a)]		
			soil 3			0.65	25.8[(a)]		
			soil 4			0.99	8.88[(a)]		

Table 3.237 continued overleaf

Table 3.237 continued Bioaccumulation factors in soil. The Cd concentrations in the biota are the product of BAF and soil Cd concentration

Test substance	Organism	Medium	Test conditions	Equilibration period (d)	Duration (d)	Soil mg kg$^{-1}_{dw}$	BAF (kg$_{dw}$/kg$_{ww}$ or kg$_{dw}$/kg$_{dw}$[a])	References	Remark
Cd-soil	detrivorous invertebrates			/	whole life			Hunter et al., 1987a	field study
	Collembola								
			control			0.8	2.6[a]		
			1 km site			6.9	1.7[a]		
	Isopoda		refinery			15.4	3.4[a]		
			control			0.8	18.4[a]		
			1 km site			6.9	18.8[a]		
	Diplopoda		refinery			15.4	15.0[a]		
			control			0.8	7[a]		
			1 km site			6.9	2.1[a]		
	Oligochaeta		refinery			15.4	1.2[a]		
			control			0.8	5.1[a]		
			1 km site			6.9	4.9[a]		
	Diptera		refinery			15.4	6.9[a]		
			control			0.8	2.8[a]		
			1 km site			6.9	1.0[a]		
	herbivorous insects		refinery			15.4	1.6[a]		
	Orthoptera								
			control			0.8	0.24[a]		
	Formicidae		1 km site			6.9	0.046[a]		
			refinery			15.4	0.12[a]		
			control			0.8	1.5[a]		
	Hemiptera		1 km site			6.9	0.8[a]		
			refinery			15.4	2.4[a]		
			control			0.8	1.0[a]		
	Lepidoptera (larvae)		1 km site			6.9	0.5[a]		
			refinery			15.4	0.7[a]		
	Curculionidae		control			0.8	0.8[a]		
			1 km site			6.9	1.0[a]		
			refinery			15.4	1.4[a]		
	Carnivorous insects		control			0.8	0.8[a]		
	Coleoptera		1 km site			6.9	0.5[a]		
	Saphylinidae		refinery			15.4	1.0[a]		

Table 3.237 continued overleaf

Table 3.237 continued Bioaccumulation factors in soil. The Cd concentrations in the biota are the product of BAF and soil Cd concentration

Test substance	Organism	Medium	Test conditions	Equilibration period (d)	Duration (d)	Soil $mg\ kg^{-1}_{dw}$	BAF (kg_{dw}/kg_{ww} or kg_{dw}/kg_{dw}[(a)])	References	Remark
	Carabidae		control			0.8	0.8[(a)]		
			1 km site			6.9	0.7[(a)]		
			refinery			15.4	0.9[(a)]		
	predatory larvae		control			0.8	0.9[(a)]		
			1 km site			6.9	0.8[(a)]		
			refinery			15.4	1.0[(a)]		
	Araneida		control			0.8	2.8[(a)]		
	Lycosidae		1 km site			6.9	1.2[(a)]		
			refinery			15.4	1.4[(a)]		
	Linyphiidae		control			0.8	3.3[(a)]		
			1 km site			6.9	5.0[(a)]		
			refinery			15.4	6.6[(a)]		
	Opiliones		control			0.8	3.0[(a)]		
			1 km site			6.9	2.7[(a)]		
			refinery			15.4	5.8[(a)]		
			control			0.8	3.5[(a)]		
			1 km site			6.9	3.7[(a)]		
			refinery			15.4	6.0[(a)]		
$CdCl_2$	*Lumbricus rubellus*	sandy loam soil	17% clay; OM 8%; pH 7.3; CaCO3 5.5%; ; T 15°C moisture content 35-40%: food: dried alder leaves	/	84	0.5	32[(a)]	Ma, 1982	Laboratory study
	Allolobophora caliginosa					20	5[(a)]		
						150	2.7[(a)]		
Cd-soil				up to 1 decade	whole life				Field study
		marine clay loam;				1	12.3[(a)]		
			30% clay; CEC 26.3 meq/100g; OM 5.8%; pH 7.1; 0 T compost/ha			1.4	10.7[(a)]		
			30% clay; CEC 24.5 meq/100g; OM 6.7%; pH 7; 20 T compost/ha			1.5	11.3[(a)]		

Table 3.237 continued overleaf

Table 3.237 continued Bioaccumulation factors in soil. The Cd concentrations in the biota are the product of BAF and soil Cd concentration

Test substance	Organism	Medium	Test conditions	Equilibration period (d)	Duration (d)	Soil mg kg^{-1}_{dw}	BAF (kg_{dw}/kg_{ww} or kg_{dw}/kg_{dw}[(a)])	References	Remark
		sandy loam;	30% clay; CEC 25.1 meq/100g; 8.4%; pH 6.9; 40 T compost/ha			0.6	26.2[(a)]		
			10% clay; CEC 9.4 meq/100g; OM 2.8%; pH 6.6; 0 T compost/ha			0.7	30.4[(a)]		
			10% clay; CEC 10.5 meq/100g; OM 4%; pH 7; 20 T compost/ha			1	17.5[(a)]		
		riverine clay loam;	10% humus CEC 12.3 meq/100g; OM 4.9%; pH 7; 40 T compost/ha			1.1	15.3[(a)]		
			40% humus; CEC 26.4 meq/100g; OM 6.9%; pH 5.3; 0 T compost/ha			1.5	13.6[(a)]		
			40% humus; CEC 28.7 meq/100g; OM 9.2%; pH 5.8; 20 T compost/ha			2	15.9[(a)]		
			40% humus; CEC 28.7 meq/100g; OM 9.7%; pH 5.9; 40 T compost/ha						
		peaty sand;				0.23	112.2[(a)]		
			10% humus CEC 20.5 meq/100g; OM 12.4%; pH 4.7; 0 T compost/ha						
			10% humus CEC 19.2 meq/100g; OM 11.2%; pH 5.2; 20 T compost/ha			0.57	60.9[(a)]		
			10% humus CEC 18.3 meq/100g; OM 13.6%; pH 5.8; 40 T compost/ha						
						0.81	40.5[(a)]		
			7% humus CEC 13.5 meq/100g; OM 6.4%; pH 5.4; 0 T compost/ha						
		sandy podzolized soil;	7% humus CEC 12.7 meq/100g; OM 7.4%; pH 5.4; 20 T compost/ha			0.27	79.6[(a)]		
			7% humus CEC 23.2			0.56	42.6[(a)]		
						0.82	30.7[(a)]		

Table 3.237 continued overleaf

Table 3.237 continued Bioaccumulation factors in soil. The Cd concentrations in the biota are the product of BAF and soil Cd concentration

Test substance	Organism	Medium	Test conditions	Equilibration period (d)	Duration (d)	Soil mg kg^{-1}_{dw}	BAF (kg_{dw}/kg_{ww} or kg_{dw}/kg_{dw}[(a)])	References	Remark
		plaggen soil;	meq/100g; OM 8.1%; pH 5.7; 40 T compost/ha			0.22	140[(a)]		
			3% humus CEC 5.3 meq/100g; OM 2.8%; pH 4.8; 0 T compost/ha			0.54	59.4[(a)]		
			3% humus CEC 6.1 meq/100g; OM 3.7%; pH 5.5; 20 T compost/ha			0.62	40.5[(a)]		
			3% humus CEC 7.1 meq/100g; OM 4.3%; pH 6; 40 T compost/ha						

3.2.7.3.2 Secondary poisoning within the lower terrestrial foodchain

Russell et al. (1981) studied Cd toxicity to *Helix aspersa* by feeding with Cd-enriched food during 30 days. The Cd concentration in tissue increased with increasing Cd content of the food. Reproduction was unaffected by the Cd in food up to 10 mg $kg^{-1}{}_{dw}$ (concentration in food). Reproduction was significantly reduced at 25 mg $kg^{-1}{}_{dw}$.

A case study on Cd bioaccumulation in the lower food chain was made for the plant (wheat)-insect (aphids)-predator (lacewings) pathway (Merrington et al., 2001). A low Cd soil was fertilised with high Cd P-fertiliser and Cd concentrations, resulting in higher Cd in soil and in wheat shoots. Aphids feeding on the wheat plants of the fertilised soil had 3 times higher Cd concentrations than those feeding on the control plants. However, lacewings showed no significant accumulation of Cd and no differences in larval performance were recorded. This illustrates that this pathway does not lead to Cd bioaccumulation.

No $PNEC_{oral}$ will be derived for lower terrestrial organisms due to lack of sufficient data and because secondary poisoning is assessed for organisms of a higher trophic level (mammals and birds).

Table 3.238 Secondary poisoning within the lower terrestrial foodchain

Test substance	Organism	Medium	Test conditions	Endpoint	Nominal/ measured	Duration (d)	NOEC mg kg^{-1}_{dw}	LOEC mg kg^{-1}_{dw}	$EC_{x\geq50}$ mg kg^{-1}_{dw}	References
$CdCl_2$	*Helix aspersa*	moist quartz sand covered by a piece of woven glass towel; food: ground Purina Lab-Chow supplemented with $CaCO_3$;		shell growth	N	30	25	100 (20)	300 (95)	Russell et al., 1981
				reproduction			10	25 (28)	50 (69)	

3.2.7.4 The sediment compartment

3.2.7.4.1 Bioaccumulation in sediment

Most of the BAF's of benthic organism are lower than 1 (either fresh weight based or dry weight based, **Table 3.239**). The BAF's are smaller for vertebrates than for invertebrates. The BAF's of benthic organisms are generally smaller than BAF's for soil-invertebrate transfer (see **Figure 3.24**). Data on marine organisms indicate larger BAF values than given here (details not shown). However, BAF values of marine organisms are not used in this risk assessment.

Table 3.239 The BAF values of some benthic organisms

	Min	Max	Median
invertebrates, wet weight (kg_{dw}/kg_{ww})	0.38	0.44	0.43
invertebrates, dry weight (kg_{dw}/kg_{dw})	0.01	1.15	0.28
vertebrates, wet weight (kg_{dw}/kg_{ww})	0.006	0.18	0.07

The body burden Cd generally increases with increasing Cd concentration in the sediment but levels off at higher Cd contents of the sediment (Francis et al., 1984). Low BAF values can therefore be found at high Cd concentrations in the sediment. The Cd concentrations in the oligochaete *Lumbricus variegatus* were similar in field contaminated sediments, containing about 5 µg Cd g^{-1}_{dw}, and in sediments spiked up to 750 µg Cd g^{-1}_{dw} (Ankley et al., 1994; Peterson et al., 1996). The BAF values therefore differ by more than one order of magnitude between both systems. These observations were made for two different sediments (one from a pond, the other from a river) and differences in metal immobilisation between the sediments may explain different Cd availability in the sediments.

The influence of contact time in the sediment on the BAF was illustrated by data of Francis et al. (1984). Cd accumulation and toxicity in fish (largemouth bass) and amphibian (leopard frog) was measured in embryo-larval stages. Largemouth bass accumulated, at all sediment concentrations, significantly more Cd than leopard frog. The differences in BAF's between the species were attributed to differences in contact time of the organisms with the sediment. Bass eggs and larvae have direct contact with sediment throughout the exposure period whereas goldfish and leopard frog dwell in the water column above the sediment.

The BAF's collected in this review are based on a maximal exposure time of 50 days and may underestimate longer-term BAF values.

Van Hattum et al. (1993) studied the influence of temperature and pH on the uptake of Cd in *Asellus aquaticus*. No significant pH effects on Cd uptake were observed. Increasing temperature from 5-20°C, however, significantly increased Cd uptake about fourfold.

Table 3.240 Bioaccumulation of Cd in benthic organisms

Test substance	Organism	Medium	Test conditions	Nominal/ Measured	Equilibration period (d)	Duration (d)	Sediment mg kg^{-1}_{dw}	BAF (kg_{dw}/kg_{ww} or kg_{dw}/kg_{dw}[(a)])	References
Cd-sediment	*Lumbricus variegatus*	contaminated sediment from lower Fox river (Wisconsin)	40-60g_{dw} sediment + Lake Superior water; T 22°C; semi-static; Cu 64-90 mg kg^{-1}_{dw}; Zn 208-347 mg kg^{-1}_{dw}; Pb 102-150 mg kg^{-1}_{dw}; Cr 71-118 mg kg^{-1}_{dw}; no food addition	M-total	1	30	5.2	0.38	Ankley et al., 1994
							4.1	0.44	
							5.8	0.43	
$CdCl_2$	*Lumbricus variegatus*	Cd spiked natural sediment of small mesotrophic pond(Minnesota); 0.74 µmol/g_{dw} SEM and 4.6 µmol S/g_{dw}	org. density 10000 org/m²	M-total	11	14			Peterson et al., 1996
			SEM/AVS = 0.4				450	0.02[a]	
			SEM/AVS = 0.8				754	0.03[a]	
			org. density 25000 org/m²						
			SEM/AVS = 0.4				382	0.01[a]	
			SEM/AVS = 0.8				714	0.01[a]	
Cd-sediment	*Asellus aquaticus*	natural sediment from the polluted lake Ketelmeer and the uncontaminated lake Oostvaardersplassen (N□pproach□s) + mixture of tap and deionized water; 100 g_{ww} sediment + 400 ml water	semi-static; lake Ketelmeer: 2% OC; 1% clay, 13% silt; Pb 48 mg kg^{-1}_{dw}; Cu 27 mg kg^{-1}_{dw}; Zn 319 mg kg^{-1}_{dw}; Fe 5100 mg kg^{-1}_{dw}; T 5°C	M-total	7	50			Van Hattum et al., 1993
			T 10°C				5.3	0.28 [a]	
			T 20°C				5.3	1.02 [a]	
			pH 5 (T 20°C)				5.3	1.15 [a]	
			pH 8 (T 20°C)				5.3	1.1 [a]	
			lake Oostvaarders plassen: 5% OC; 8% clay, 70% s ilt; Pb 84 mg kg^{-1}_{dw}; Cu 25 mg kg^{-1}_{dw}; Zn 221 mg kg^{-1}_{dw}; Fe 16400 mg kg^{-1}_{dw};				5.3	1 [a]	
			T 5°C						
			T 10°C						
			T 20°C				1.2	0.25 [a]	
							1.2	0.5 [a]	
								0.5 [a]	

Table 3.240 continued overleaf

Table 3.240 continued Bioaccumulation of Cd in benthic organisms.

Test substance	Organism	Medium	Test conditions	Nominal/ Measured	Equilibration period (d)	Duration (d)	Sediment mg $kg^{-1}{}_{dw}$	BAF (kg_{dw}/kg_{ww} or kg_{dw}/kg_{dw}(a))	References
$CdCl_2$	*Rana pipiens*	natural stream sediment; 250 g_{dw} sediment ▯pproach▯d-solution or distilled deionized water (control) +350 ml reconstituted water	DO 6.6-8.1 mg L^{-1}, T 22.1-22.5 °C, pH 7.9-8.4; sed: OM 2.3%, Cd_T 1.02 mg kg^{-1}, Zn_T 108.2 mg kg^{-1}, Hg_T 0.052 mg kg^{-1}, Fe_T 5.52%; 5.52% sand, 35.4% silt, 12% clay	M	0.42	7	1	0.08	Francis et al., 1984
							10	0.034	
							100	0.0031	
							1000	0.013	
	Micropterus salmoides						1	0.18	
							10	0.072	
							100	0.15	
							1000	0.006	

dw Dry weight basis;
ww Wet weight basis;
a) Dry weight basis;
SEM Simultaneously extractable metals. This is the sum of the metals cadmium, lead, nickel, zinc and copper in the sediment simultaneously extracted with the AVS and is expressed in µmol/g_{dw}.; equilibration period: time of equilibration after spiking the pristine sediments or time of stabilisation after mixing the contaminated sediment and water, prior to exposure'.

3.2.7.5 Toxicity to mammalian and avian organisms

3.2.7.5.1 Derivation of the $PNEC_{oral}$

The TGD suggested method for risk assessment of secondary poisoning is based on modelling critical pathways such as the soil-worm-bird or water-fish-bird food chains (Romijn et al., 1994). The $PNEC_{oral}$ for mammals and birds is derived from feeding studies with Cd salt spiked diets. Nine feeding studies have been selected here (see **Table 3.242**). This compilation is based on sub-chronic and chronic studies and has excluded acute studies, mixed metal feeding studies and experiments where Cd was injected in the test animals. Four studies were selected with birds and 5 studies with mammals.

The $PNEC_{oral}$ can be calculated from the lowest NOEC using an assessment factor. The assessment factors for the feeding test are based on the TGD (TGD, 1996, p.350) and are 10 for the 90 day feeding test with mallard ducks (reproduction as endpoint) and 10 for the chronic study with monkey. The $PNEC_{oral}$ could also be calculated using statistical extrapolation. The underlying assumption is a log-logistic distribution of species sensitivity to dietary Cd (see **Table 3.241**). This approach has been used in the risk assessment of secondary poisoning of Spurgeon and Hopkin (1996) and Smit et al. (2000). No species mean NOEC's are calculated from the 2 studies with either rats and mallard ducks. The 2 studies on rats were performed with very different exposure time and the studies with mallard ducks have different endpoints. Averaging per species *increases* the HC_5 (50 and 95% confidence) of the mammal and bird data (not shown).

Table 3.241 Calculation of $PNEC_{oral}$ (mg kg^{-1} food) using the assessment factor method (AFM) or the statistical extrapolation method (SEM; Aldenberg and Slob, 1993)

	AFM	SEM	
	NOEC/AF	HC_5 at 50% (and 95%) confidence	significance*
	mg kg^{-1} food		
Mammals (n=5)	0.30	1.9 (0.14)	***
Birds (n=4)	0.16	0.75 (0.007)	***
Combined (n=9)	0.16	1.6 (0.35)	***

* Goodness of fit;
*** Is significant at 1% level of significance.

- The assessment factor method invariably leads to the lowest $PNEC_{oral}$. There is currently no guideline in the TGD to use the statistical extrapolation method to derive a PNECoral and it is proposed to use the AF method as a first approach to assess secondary poisoning.

The suggested $PNEC_{oral}$ is therefore calculated as the lowest NOEC in the database and using and AF of 10, yielding

$$PNEC_{oral} = 0.16 \text{ mg kg}^{-1} \text{ fresh weight}$$

and is expressed as the fresh weight based Cd concentration in the food of the predator. Note that this PNEC is situated at the lowest NOEC of this database and which is the NOEC of the feedings studies with mallard ducks discussed above.

Table 3.242 Mammalian and avian toxicity data from laboratory feeding studies. Concentrations are expressed per unit fresh weight of the food. Bold and underlined NOEC data are used to estimate the HC_5

Test substance	Organism	Medium	Duration (d)	Endpoint	NOEC (mg Cd/kg)	Cat*	LOEC (mg Cd /kg) (%effect)	References
				Mammals				
$CdCl_2$	2-5 y old rhesus monkey *Macaca mulatta*	pelleted food	3,280 (9 y)	growth	3	1	10 (~25)	Masaoka et al., 1994
$CdCl_2$	8 wk old Yorkshire barrows (pig) *Sus scrofa domesticus*	diet: mixture of yellow corn, soybean meal, meat and bone meal, dehydrated alfalfa meal, trace minerals and vitamins	42	growth	50	1	150 (60)	Cousins et al., 1973
$CdCl_2$	4 m old lamb *Ovis amon aries*	diet: mixture of primary corn, cotton seed hulls and soybean oil meal	191	growth	15	1	30 (20)	Doyle et al., 1974
$CdCl_2$	rat *Rattus norvegicus*	basal animal diet: Altromin-R, powdered	728 (2y)	grth	10	1	50	Löser, 1980
$CdCl_2$	5 wk old rat *Rattus norvegicus*	basal diet: wheat flour, casein, lard, minerals and vitamins	56	growth	15	2	30 (8)	Groten et al., 1991
				Birds				
$CdCl_2$	first-year adult mallard duck *Anas platyrhynchos*	commercial duck breeder mash coated with Cd dissolved in propylene glycol	90	spermatogenesis	1.6	1	15.2	White et al., 1978
$CdCl_2$	1 d old mallard duckling *Anas platyrhynchos*	food	84	kidney lesion haemoglobin concentrations	10 10	1	20 20	Cain et al., 1983
$CdSO_4$	6 m old White Leghorn laying hen *Gallus dometicus*	purified soybean-glucose diet	28	egg production	12	1	48 (39)	Leach et al., 1978
$CdCl_2$	Japanese quail (after hatching) *Coturnix c. japonica*	purified basal diet (35% soybean protein)	42	growth	38	2	75(15)	Richardson et al., 1974

* NOEC classification (see Section 3.2.1.2).

The risk of secondary poisoning of fish eating birds by Cd is predicted to be smaller than the direct effects of Cd in the aquatic environment (see Section 3.3). This is readily demonstrated using BCF's of fish in **Table 3.232**. Cadmium concentrations in whole fish at the proposed $PNEC_{water}$ = 0.19 µg Cd/l (see Section 3.2.2.7) is predicted to range between 0.0001 and 0.12 mg Cd/kg fresh weight using the whole range of BCF's (0.5-623 l/kg fresh weight, **Table 3.232** and **Table 3.233**). These Cd concentrations are below the $PNEC_{oral}$ for birds or birds and mammals. This assessment is made for freshwater systems and not for marine environments. Nephrotoxic lesions ascribed to Cd have been found in sea birds from areas that are relatively uncontaminated and where natural Cd may be the source (Nicholson et al., 1983; IPCS, 1992b). We propose that our assessment should not be used for the marine environment where the bioaccumulation of Cd differs from that in freshwater dominated systems.

The risk of secondary poisoning in the soil-worm-bird/mammal is predicted to be far more critical than the risk of soil Cd affecting plants, invertebrates or micro-organisms. This is readily demonstrated using the BAF's of Cd in earthworms (see **Table 3.236**). Cadmium concentrations in earthworms at the proposed $PNEC_{soil}$ = 2.3 mg Cd/kg (see Section 3.2.3.7) is predicted to range between 9.2 and 74 mg Cd/kg fresh weight using the whole range of BCF's (4-32 kg/kg fresh weight, see **Table 3.236**). All these concentrations are above the $PNEC_{oral}$ of birds, mammals or birds and mammals and even overlap the LOEC range of the feeding studies.

The model for secondary poisoning of mammals and birds in the soil-worm-birds/mammals may, however, be questioned in case of Cd: concentrations of Cd in earthworms sampled in uncontaminated areas typically range between 1-10 mg Cd/kg fresh weight (see **Table 3.237**) and are generally higher than the $PNEC_{oral}$ proposed here. It is either possible that soil Cd at background is indeed at risk for carnivorous mammals and birds or it is possible that the model that compares earthworm Cd with dietary Cd in feeding studies is overprotective. Beyer (2000) concluded on this approach that 'assessors have been overly cautious in evaluating toxicity of Cd'. Spurgeon and Hopkin (1996) used this model for risk assessment of secondary poisoning by Cd in the vicinity of a smelter and concluded that 'it is unlikely to describe risk to predators correctly'. Spurgeon and Hopkin (1996) have argued that the model is overly protective because of

(I) the problems of quantifying the BAF: a mean BAF would overestimate earthworm concentrations at more contaminated sites because the BAF decreases with soil Cd (see, for example, **Figure 3.24**).

(II) higher availability of Cd in metal salt spiked meals in the laboratory tests than Cd in worms

(III) use of unrepresentative species for the predators

Other authors suggest that the model is not sufficiently protective and that additional safety factors should be used to account for differences in metabolic rate between laboratory and field animals, differences in caloric content between the laboratory diets and field prey, differences in food assimilation efficiency, differences in bioavailability of the toxic compound etc. (see Smit et al., 2000 for references).

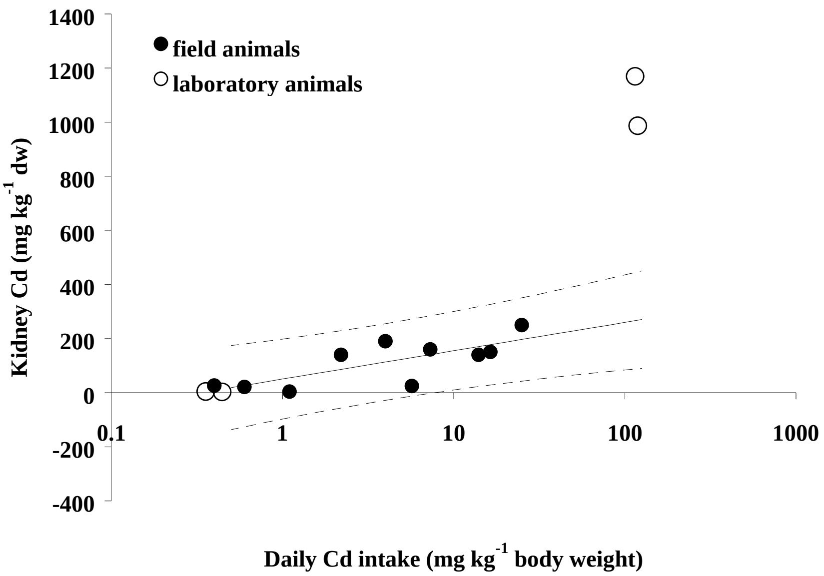
One of the key assumptions in the model is that equal food Cd concentration leads to equal effects in laboratory animals and field animals. None of the laboratory tests reviewed here have fed earthworms to the animals as the principal source of Cd. Earthworms from even uncontaminated areas have Cd concentrations close to effect concentrations in Cd salt spiked laboratory meals. The assumption of equal effects at equal total Cd intake can be tested indirectly by comparing internal Cd dose (body burden) between laboratory and field animals at equal Cd intake. This comparison will be made here.

Cadmium intake by wildlife is probably most documented in shrews (*Sorex araneus*) because this mammal usually has a high Cd body burden (Hunter et al., 1989). Shrews have a high dietary Cd intake rate and feed on invertebrates active at the ground surface supplemented with soil dwelling macrofauna (Hunter et al., 1987b). Earthworms can be the major source of dietary Cd in shrews (Ma et al., 1991). Kidney Cd concentrations up to 550 mg kg^{-1} dry weight have been observed in shrew (Hunter et al., 1989), i.e. close to critical concentration (see next section). Data on cadmium intake rates and body burden Cd have been compiled by Shore and Douben (1994) from 4 different studies. Kidney Cd concentrations increase with increasing Cd intake rate. This increase is linear at low intake rate but levels off at higher intake. Shore and Douben (1994) combined the data from four different studies and found a significant linear relation between the log Cd intake rate and the kidney Cd (see **Figure 3.25**, $P<0.015$). A laboratory feeding trial has been performed with shrew fed a $CdCl_2$ spiked diet (Dodds-Smith et al., 1992a&b). The body burden Cd (kidney Cd) after only 11 weeks exposure at the high Cd diets is significantly above that predicted by the log-linear regression line on field animals (see **Figure 3.25**). A drawback in this analysis is the extrapolation from the regression line since Cd intake rate in the laboratory trials is about fourfold higher than the highest Cd intake rate recorded in field shrew. Taken together, this analysis suggests that Cd is more available in laboratory spiked meals than in the diet of field animals.

A recent feeding study compared Cd availability to cattle from hay grown on a smelter affected substrate with hay spiked with Cd salts (spiking at corresponding concentrations). The kidney Cd of cattle fed hay grown on the smelter affected substrate was 3-fold above that of control animals whereas it was increased 12 fold in the Cd spiked hay treatment (Stuzynski et al., 2000). Clearly, Cd availability is higher in Cd salt spiked meals than in dietary Cd.

These arguments suggest that risk of secondary poisoning by Cd may be overestimated when based on Cd salt feeding studies. Therefore, an alternative approach will be used based on renal thresholds. The TGD allows that field data are used in this type of risk assessment provided that interpretation is made with caution (TGD 1996, p. 346). This effects assessment will only be made for mammals for which dose-response curves can be established. The assessment for terrestrial birds will be discussed in the risk characterisation because there no paired data of soil Cd /kidney Cd for birds were found.

Figure 3.25 Cd intake and kidney Cd in free living common shrew (*S. araneus*) and in laboratory cultivated shrew (control and Cd salt spiked diet). The log-linear regression and 95% prediction interval is made on field animal data (compilation of Shore and Douben, 1994). Data of laboratory animals is derived from Dodds-Smith et al. (1992 a&b)



3.2.7.5.2 An alternative approach for wildlife in the terrestrial environment based on renal thresholds

The alternative strategy to estimate the risks of secondary poisoning by Cd using renal threshold was formulated by Spurgeon and Hopkin, 1996. This strategy was not elaborated in that paper but this method was already adopted in pathway calculations of the US-EPA 503 sludge regulations (Chaney and Ryan, 1991).

The alternative method uses kidney Cd concentrations of wildlife as an indicator of Cd exposure and risk. The kidney is regarded as the critical organ in *chronic* Cd toxicity. With continued exposure, there is a continual increase in Cd concentration in the renal cortex until a critical value is reached and histopathological changes and renal dysfunction is found (proximal tubular cell necrosis, proteinuria and glycosuria; Scheuhammer, 1987 and references therein). This critical value should be regarded as a sublethal endpoint. The risk of secondary poisoning will be assessed by calculating the exposure at which this critical value is not exceeded for wildlife.

The proposed approach overcomes the uncertainties in the traditional approach which uses foodchain modelling (i.e. soil-worm-mammal modelling) because the proposed approach does *not* require assumptions about the diet (e.g. 100% earthworms) and about Cd bioavailability during transfer soil-food-wildlife (i.e. the BAF value and assumption of equal exposure at equal diet Cd between spiked meals and environmental Cd).

The *ecological relevance* of kidney damage as the critical endpoint in this assessment deviates from traditional endpoints such as growth or reproduction which have obvious ecological relevance. Indeed, the relationship between ecological fitness and kidney damage is unknown and which is the major difficulty in understanding effects of Cd in wildlife (Cooke and Johnson, 1996). The kidney has spare functional capacity and proteinuria or calciuria might be tolerated without progression to renal failure (Cooke and Johnson, 1996). Seabirds showing signs of nephrotoxicity were 'outwardly healthy' (Nicholson et al., 1983). A beaver population from the

Mulde (a tributary of the Elbe in Germany) had average kidney Cd concentrations of 467 µg/g dw (above the threshold proposed below). The fertility of this population was higher than 3 other population that had lower kidney Cd concentrations (Nolet et al., 1994). The authors conclude that the habitat quality seemed to determine the fertility and that Cd did not seem to interfere with fertility. Kidney damage in shrews (*S. araneus*) caught in a polluted smelter site was identified by electron microscopy although urine analyses showed no evidence for clinical renal dysfunction and animals were ‘in good condition’ (data of Hunter, 1984, quoted in Cooke and Johnson, 1996).

Dietary deficiencies can exacerbate Cd toxicity and one example was found where effects in wildlife due to Cd was related to kidney damage (as judged from exceedance of critical kidney Cd concentrations) and which was related to Ca deficiency (see bottom of this section: field validation). Therefore, we propose to use renal dysfunction as an endpoint with ecological relevance, realising that this endpoint leads to a more conservative approach than traditional endpoints in most conditions.

Kidney Cd of wildlife such as shrews, moles and badgers is markedly increased at sites with elevated Cd (Ma,1987; Ma and Broekhuizen,1989; Ma et al.,1991; Hendriks et al.,1995). Some of the wildlife field data do allow to estimate a dose (soil Cd) response (kidney Cd) slope. The critical soil Cd that is needed to reach the critical kidney Cd can be calculated with this slope. This critical soil Cd ($Cd_{soil,crit}$) could then be considered as an acceptable concentration in soil assessed for secondary poisoning. This approach would only yield assessments based on animals for which kidney Cd data are available at different Cd exposure. Alternatively, critical soil Cd concentrations could also be derived based on a proportional extrapolation from any paired set of soil/kidney Cd concentration data, allowing to include more species in the assessment. **Figure 3.26** illustrates this approach. The proportional extrapolation method contains a safety factor since kidney Cd only increases proportionally with the dose at low concentrations. The less than proportional increase of kidney Cd with soil Cd is observed in most studies and may be explained by e.g. avoidance or metal interactions for Cd absorption (most gradient studies are derived from sites with mixed metal pollution).

Kidney-Cd concentrations of wildlife are compiled in **Table 3.243**. The data are mean or median Cd concentrations for 9 different mammal species (no data found for birds). Paired sets of soil Cd/kidney-Cd were found for 8 mammal species. Most of these studies have measured Cd concentrations at 2 or more locations differing in metal exposure (smelters).

Figure 3.26 Two methods to estimate the critical Cd in soil (arrows) that would lead to critical Cd concentrations in the kidney of mammals: proportional extrapolation based on one data point (here: at lowest soil Cd) or extrapolation from a regression line fitted to all data. Data from Cd in common shrew (*S. araneus*) in a transect study (Hunter et al., 1989)

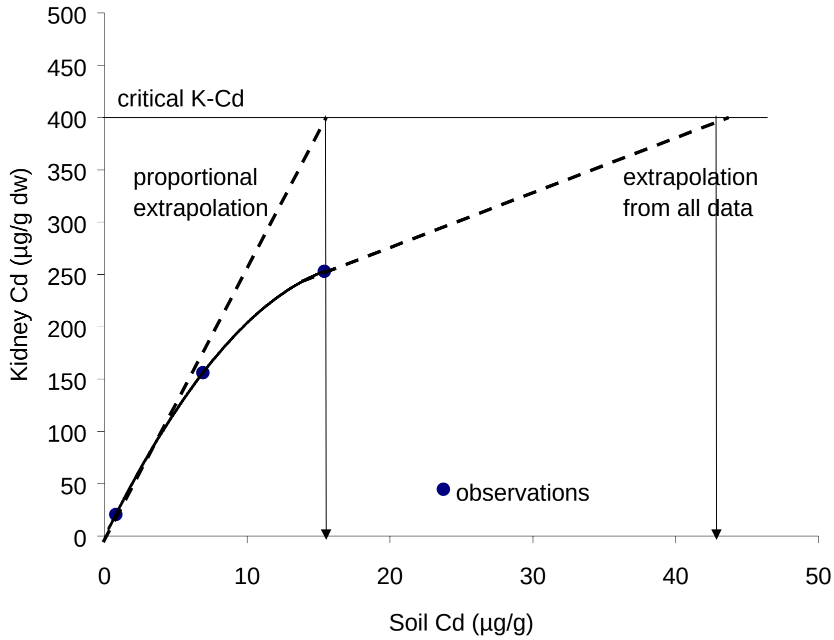


Table 3.243 Kidney Cd concentrations in mammals and predicted critical soil Cd concentrations at which renal threshold (K-Cd) may be exceeded. Predictions are based on proportional extrapolation (Figure 3.26). Bold and underlined data are used for risk assessment

Species		Site	Soil pH	Soil Cd µg/g	Kidney Cd µg/g dw	Predicted critical soil Cd (µg/g)		Reference:	Remark
						Critical K-Cd 200 µg/g dw	Critical K-Cd 400 µg/g dw		
badger	*Meles meles*	NL			9-213			Ma and Broekhuizen, 1989	n=15; 4-5 y old animals, habitat not close to floodplains of Meuse
					49-405				n=9; 4-5 y old animals, habitat close to floodplains of Meuse
beaver	*Castor fiber*	NL		24	55(113 in adults)	42.5	<u>85 (adults based)</u>	Nolet et al., 1994	soil:0-5 cm; Biesbosch estuary; young animals-modelling predicts K-Cd = 113 mg kg^{-1} dw in adults
		DE			467		-		
		DE		-	50	-	-		Elbe region: Mulde (adults)
		DE		-	30	-	-		Elbe region: Elbe (adults)
		DE		-	20	-	-		Elbe region: Elbe (adults)
				-		-			Elbe region: Heide (adults)
common shrew	*Sorex araneus*	UK	5.2	0.6	10.9	11.0	22.0	Read and Martin, 1993	soil: litter layer; K-Cd in mature animals
			5.4	1	37	5.4	10.8		
			4.4	2	9.3	43.0	86.0		
			5.05	1.7	41.3	8.2	16.5		
			4.9	3.3	154	4.3	<u>8.6</u>		
			4.85	19.9	142	28	56.1		
common shrew	*Sorex araneus*	UK		0.8	20.5	7.8	<u>15.6</u>	Hunter et al., 1989	soil: 0-5 cm
				6.9	156	8.8	17.7		
				15.4	253	12.2	24.3		

Table 3.243 continued overleaf

Table 3.243 continued Kidney Cd concentrations in mammals and predicted critical soil Cd concentrations at which renal threshold (K-Cd) may be exceeded. Predictions are based on proportional extrapolation (Figure 3.26). Bold and underlined data are used for risk assessment

Species		Site	Soil pH	Soil Cd µg/g	Kidney Cd µg/g dw	Predicted critical soil Cd (µg/g)		Reference:	Remark
						Critical K-Cd 200 µg/g dw	Critical K-Cd 400 µg/g dw		
common shrew	*Sorex araneus*	UK		0.75	25.7	5.8	11.7	Hunter and Johnson, 1982	soil: 0-5 cm
				3.1	139	4.5	8.9		
				8.5	193	8.8	17.6		
common shrew	*S. araneus*	NL	6.1	2.9	126-200	2.9	5.8	Ma et al., 1991	soil: 0-10 cm, Ao horizon Cd is 5.5 µg/g; range of means in season
			3.5	0.3	14-51	1.2	2.4		soil: 0-10 cm, Ao horizon Cd is 1.2 µg/g; range of means in season
common shrew	*Sorex araneus*	NL		1.8	11	32.7	65.5	Hendriks et al., 1995	soil:0-20 cm; Rhine floodplains
				6.4	21	61.0	121.9		
cottontail rabbit	*Sylvilagus floridanus*	U.S.		~6	166	7.2	14.5	Storm et al., 1994	Palmerton-site; soil: A1 horizon
				~60	380	31.6	63.2		
				~10	284	7.0	14.1		
cottontail rabbit	*Sylvilagus floridanus*	U.S.		0.1	5.3	3.8	7.5	Dressler et al., 1986	soil: 0-15 cm
				0.4	12.3	6.5	13.0		soil: 0-15 cm; soil received sludge
field vole	*Microtus agrestis*	UK		0.8	1.7	94.1	188.2	Hunter et al., 1989	soil: 0-5 cm
				6.9	23.9	57.7	115.5		
				15.4	88.8	34.7	69.4		
field vole	*Microtus agrestis*	UK		0.75	1.3	115.4	230.8	Hunter and Johnson, 1982	soil: 0-5 cm
				3.1	4.06	152.7	305.4		
				8.5	23.3	73.0	145.9		

Table 3.243 continued overleaf

Table 3.243 continued Kidney Cd concentrations in mammals and predicted critical soil Cd concentrations at which renal threshold (K-Cd) may be exceeded. Predictions are based on proportional extrapolation (Figure 3.26). Bold and underlined data are used for risk assessment

Species		Site	Soil pH	Soil Cd µg/g	Kidney Cd µg/g dw	Predicted critical soil Cd (µg/g)		Reference:	Remark
						Critical K-Cd 200 µg/g dw	Critical K-Cd 400 µg/g dw		
field vole	*Microtus agrestis*	NL	6.1	2.9	1-3	193.3	386.7	Ma et al., 1991	soil: 0-10 cm, Ao horizon Cd is 5.5 µg/g; range of means in season
			3.5	0.3	0.1-0.3	200.0	400.0		soil: 0-10 cm, Ao horizon Cd is 1.2 µg/g; range of means in season
mole	*Talpa europea*	NL	5.2	1.7	112	3.0	6.1	Ma, 1987	soil: 0-10 cm; Budel pasture
			6	6	224	5.4	10.7		
			6.5	9.2	221	8.3	16.7		
			4.1	0.3	186	0.3	0.6		soil: 0-10 cm; Budel heath site
			4	0.1	59	0.3	0.7		soil: 0-10 cm; Arnhem pasture
mole	*Talpa europea*	FI			186			Pankakoski et al., 1993	Helsinki metropolitan area, adult animals only
					82				rural area, adult anim pproacy
pygmy shrew	*Sorex minutus*	UK	5.2	0.6	7.9	15.2	30.4	Read and Martin, 1993	soil: litter layer; K-Cd in mature animals
			5.4	1	5.9	33.9	67.8		
			4.4	2	7.9	50.6	101.3		
			5.05	1.7	12.1	28.1	56.2		
			4.9	3.3	18.7	35.3	70.6		
			4.85	19.9	49.9	79.8	159.5		
white-tailed deer	*Odocoileus virginianus*	U.S.		6-100	70	17.1	34.3	Storm et al., 1994	Palmerton-site; soil A1 horizon
woud mouse	*Apodemus sylvaticus*	UK		0.8	2	80.0	160.0	Hunter et al., 1989	soil: 0-5 cm
				6.9	8.5	162.4	324.7		
				15.4	41.7	73.9	147.7		

Table 3.243 continued overleaf

Table 3.243 continued Kidney Cd concentrations in mammals and predicted critical soil Cd concentrations at which renal threshold (K-Cd) may be exceeded. Predictions are based on proportional extrapolation (Figure 3.26). Bold and underlined data are used for risk assessment

Species		Site	Soil pH	Soil Cd µg/g	Kidney Cd µg/g dw	Predicted critical soil Cd (µg/g)		Reference:	Remark
						Critical K-Cd 200 µg/g dw	Critical K-Cd 400 µg/g dw		
woud mouse	*Apodemus sylvaticus*	UK		0.75	1.46	102.7	205.5	Hunter and Johnson, 1982	soil: 0-5 cm
				3.1	5.5	112.7	225.5		
				8.5	7.4	229.7	459.5		

Critical concentration of Cd in kidney

There are several reviews of the critical kidney Cd concentrations in laboratory animals (IPCS, 1992a), small mammals (Cooke and Johnson, 1996) and birds (Furness, 1996). The individual studies will not be discussed here but attention will be given to the conflicting evidence that has suggested lower limits.

The WHO has reviewed several studies on test animals (mouse, rat, rabbit, pig, horse, monkey and bird; IPCS, 1992a). Histological tubular lesions are usually observed at 200-300 µg Cd/g wet weight. In some studies on rats, monkeys, horses and birds certain effects were seen at lower levels. The WHO concludes that 'if one wishes to establish a range of values for the critical concentration in individuals at which a small but significant part of the exposed population will show effects, animal studies indicate that a renal cortex level of about 100-200 µg/g wet weight is likely to coincide with such a range' (IPCS, 1992a). This range corresponds with whole kidney, dry weight based values of 400-800 µg/g dw (wet weight concentrations are about 0.2 time dry weight concentrations and whole kidney concentrations are about 0.8 times kidney cortex values).

There are reports of kidney damage in wildlife at concentrations below the range suggested by WHO. Nicholson et al. (1983) identified nephrotoxicity in seabirds at whole kidney concentrations of 100-200 µg/g dw, about fourfold lower than the WHO criterion. Kidneys, however, also contained Hg (5-15 µg/g dw). Starlings were injected $CdCl_2$ and showed similar kidney lesions compared to the seabirds at comparable tissue Cd concentrations. However, the Cd dosed animals may not be representative for the seabirds because of the acute exposure of the test animals. Chmielnicka et al. (1989) suggested that the WHO criterion should be revised after identifying nephrotoxicity in Cd dosed rats at kidney Cd concentrations of 30 µg/g wet weight (about 120 µg/g dw). However, this study was also based on an acute dose (injections during 8 weeks and histopathological effects in the liver after only 2 weeks), suggesting that it may not be relevant for a realistic chronic exposure (Beyer, 2000). Leffler and Nyholm (1996) reported nephrotoxicity in bank voles (*Clethrionomous glareolus*) collected close to the smelter in Rönnskärsverken (Sweden) and in a control site. The voles from the contaminated area had increased proteinuria and increased kidney Cd concentrations. The proteinuria was identified at only 4 µg/g wet weight (whole kidney, about 20 µg/g dw). A comment on that paper was written by Elinder (1997) about the very low value at which nephrotoxicity was found. Elinder concluded that this study was confounded, basically because the voles urinated more in the contaminated site. The authors have responded to this comment that other factors (other metals, biotope characteristics) may also have been involved in the proteinuria (Nyholm and Leffler, 1997).

We propose to use the lower limit of the WHO suggested critical range of Cd concentration for our assessment, i.e. 100 µg Cd/g wet weight in the renal cortex or 400 µg Cd/g dw. The WHO suggested range is based on the largest review of animal data and Cooke and Johnson (1996) similarly suggested 100 µg Cd/g wet weight as a critical concentration. This RAR repeats the WHO conclusions that mean renal cortex Cd should reach 200 µg/g wet weight to observe tubular proteinuria (see Section 4 of this report in a separate document). There is indeed conflicting evidence suggesting lower limits (Nicholson et al., 1983, Chmielnicka et al., 1989 and Leffler and Nyholm, 1996) but there are arguments that these studies may be less relevant for chronic exposure to Cd-only contamination in wildlife (see above).

Critical soil Cd concentrations for wildlife

The critical soil Cd concentration is defined as that concentration at which a critical kidney Cd concentration of 400 µg/g dw (whole kidney) is predicted using a proportional extrapolation from each paired soil/kidney Cd concentration set (see **Figure 3.26**). The lowest critical soil Cd concentration was selected from each transect study or when only a range in soil or kidney Cd concentrations was available (see **Table 3.243**). Different values were derived from the studies of Ma because the soil properties were markedly different between sites, clearly leading to different Cd exposure (see **Table 3.243**). Twenty (20) values of critical Cd concentrations were derived from 8 different mammal species. The frequency distribution of the 20 values illustrates that moles and shrews typically have high kidney Cd concentrations which is related to the high Cd intake rate (see **Figure 3.27**).

This compilation of field data will be used to derive a critical soil Cd concentration for terrestrial mammals ($Cd_{soil,\ crit}$). We propose to derive this value with statistical extrapolation. The distribution of values (see **Figure 3.27**) reflects site specific species sensitivity if it is assumed that there are no differences in renal threshold between species. In this regard, this distribution is conceptually equal to a distribution of Cd thresholds from toxicity tests in soil.

Figure 3.27 Cumulative frequency of the critical soil Cd concentration at which the critical kidney Cd concentration (400 µg/g dw) may be exceeded in the average population of different species. The line is the log-logistic curve fitted on all individual data

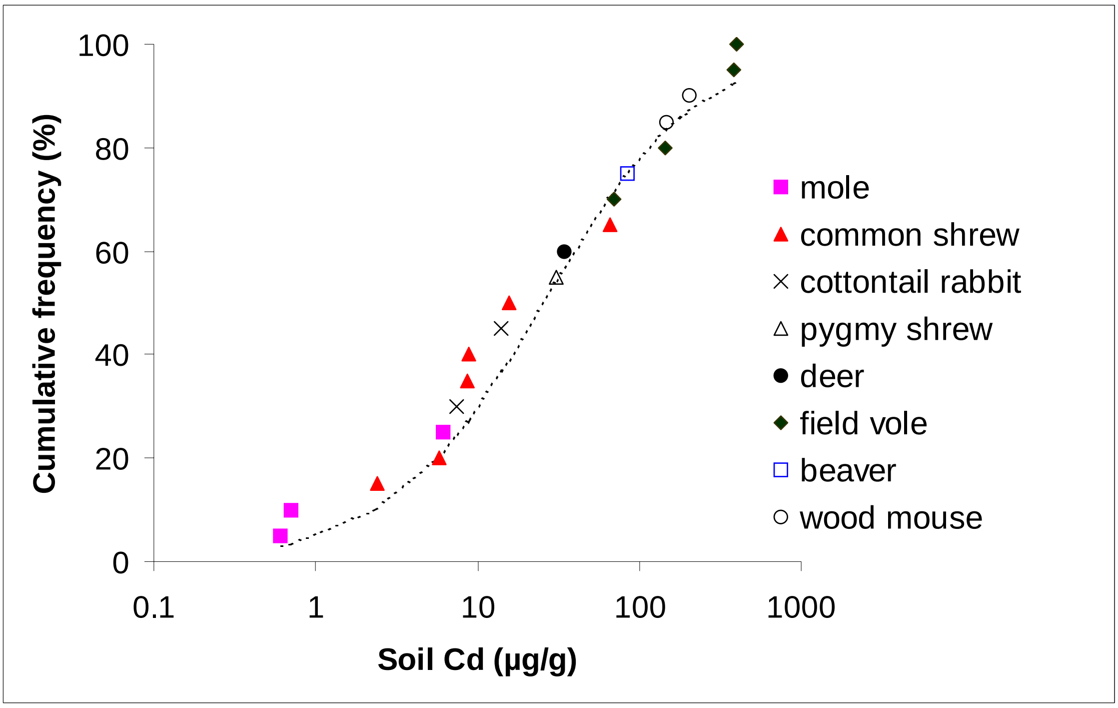


Table 3.244 Prediction of critical soil Cd for terrestrial mammals based on values at which the critical kidney Cd concentration (400 µg/g dw) may be exceeded in the average population of different species. The critical soil concentrations is either the lowest value in the database or the HC_5 predicted by statistical extrapolation (Aldenberg and Slob, 1993)

	Lowest value	Statistical extrapolation (log-logistic model)	
		HC_5 at 50% (and 95% confidence interval)	significance*
Critical soil Cd (µg/g)			
all data selected in Table 3.243 (n=20)	0.6	0.9 (0.2-2.3)	***
Excluding data from soils with pH < 4.2 (n=16)	5.8	3.3 (1.0-7.1)	***
Geometric means of species (n=8)	1.4	1.5 (0.1-5.7)	***

* Goodness of fit;
*** Is significant at 1% level of significance.

The statistical extrapolation method (log-logistic distribution) predicts that the HC_5 for protecting mammals is 0.9 µg/g. The HC_5 is higher when based on species mean values. Averaging data is not defensible: the data of Ma (1987, moles) and Ma et al. (1991, shrews) have shown that soil acidity leads to higher Cd concentration in the prey (earthworms) and higher body burden in the predator. Averaging data leads to a loss of information and species may not be protected in these soils. If the data from soils with reported pH <4.2 are excluded (i.e. 4 values excluded), the HC_5 increases from 0.9 to 3.3 µg Cd/g. Ma and van der Voet (1993) successfully predicted the Cd exposure to shrew for different values of soil pH and % organic matter. This model is useful to derive soil criteria that vary with soil properties. The model has not been incorporated in our assessment because it was validated with only 1 predator species and because soil properties are unknown for most other data. However, this generic HC_5 overestimates the risk associated to wildlife in pH neutral soils as indicated by the monitoring data of moles from Ma, 1987: while kidney Cd is already at 200 µg/g dw in acid soils near soil background values (0.3 µg/g), these kidney Cd concentrations are only found in pH neutral soils at soil Cd concentrations > 6 µg/g and which is well above the HC_5 of 0.9 µg/g.

The HC_5 for protecting mammals is about twofold *below* the $PNEC_{soil}$ derived for protecting plants, soil fauna and microflora. Effectively this assessment suggests that biotransfer of Cd from soil to higher trophic levels is the most critical pathway for Cd. This HC_5 value is mainly driven by the data on moles by Ma (1987) and, to a lesser extent, by data on shrews (Ma et al., 1991) and are valid for acid soils (soil pH < 4.1, see **Table 3.243**). These soils are relatively uncontaminated, i.e. the predicted critical soil Cd concentrations derived from these data contain a safety factor due to the proportional extrapolation. No data were found on moles or shrews in soils that are acid and that contain high Cd concentrations.

Assessment of secondary poisoning is obviously very complex. There is currently only little field evidence that attributes pathological injury to Cd (Beyer, 2000). This assessment here reveals that Cd may have a potential risk to mammals at only moderate soil Cd concentrations. Before reaching conclusions, this assessment should be evaluated. The assessment may underestimate risk for mammals because:

- the value of the renal threshold (400 µg/g dw) that may be too high according to some studies (see previous section for a discussion).

- the assumption that the renal threshold is the same for all species. There is, however, currently no evidence suggesting that this is the case (Beyer, 2000).
- average kidney Cd data of populations were used, and not upper percentiles. Effectively, the assessment would protect the average population of a species and not individuals. Some source documents have reported individual data. The number of individuals with kidney Cd concentrations above 400 µg/g dw is small and we have not found such values reported below the soil HC_5= 0.9 µg/g (details not shown).

On the other hand, this assessment has used margins of safety because:

- critical soil Cd concentrations are predicted by the proportional extrapolation (see **Figure 3.26**) and the lowest value was chosen from each study. The critical kidney Cd is never reached at or beyond the predicted 'critical soil Cd concentrations' in each transect. As an example, the critical soil Cd for the common shrew predicted from the transect study of Hunter et al. (1989) is 15.6 µg Cd/g (see **Table 3.243**). The observed kidney Cd at the largest soil Cd (15.4 µg Cd/g) is 253 µg/g, i.e. only 60% of the critical kidney Cd. A proportional extrapolation from the data at the highest Cd concentration predicts that soil Cd should reach 24.3 µg Cd/g before the critical kidney Cd is reached. This means that the most conservative critical soil Cd estimate (15.6 µg/g) has a margin of safety of 1.6 (=24.3/15.6) or higher (**Figure 3.26** suggests a factor of about 3). The HC_5 is driven by data where the kidney Cd was still below the renal threshold. In addition, there is only 1 documented population with a mean/median kidney Cd concentrations above the renal threshold (the beaver population in the contaminated Elbe region, no soil Cd concentration known).
- the renal dysfunction is a sublethal endpoint and field data suggest that its relationship with ecological fitness still has to be demonstrated (Cooke and Johnson, 1996). One study was found for birds where ecological effects can be related to renal dysfunction at kidney Cd concentrations above the proposed kidney threshold (see below: field validation).
- the HC_5 is driven by indicator organisms that are, probably, more documented than non-indicator organisms.
- the HC_5 is driven by the mole and shrew thresholds applicable to acid sandy soil (pH 4.2) and which represent a reasonable worst case scenario. The HC_5 excluding these soils is > 3 fold above the 'generic' HC_5.

Field validation

Cadmium toxicity (ecological effects) towards wildlife in the field was recently reported for the white-tailed ptarmigan *Lagopus leucurus* (bird) in a Cd contaminated area of the Colorado Rocky Mountains (Larison et al., 2000). Evidence for ecological effects related to Cd are: increased mortality in the contaminated area for the adult female birds compared to that in an uncontaminated area, higher mortality for metal-contaminated ptarmigans and a distinctly lower female:male ratio in the adult population in the contaminated area. Ptarmigans are herbivorous and commonly eat willow buds and recently grown shoots of willow, both food items that are elevated in Cd but low in calcium. The low calcium diet exacerbates Cd poisoning as shown for humans (Chapter 4). Elevated kidney Cd (> 400 µg/g dw, i.e. above the threshold chosen here) was found in adult birds in the contaminated area and which was associated with 8-10% lower bone calcium (and more fragile bones) compared to values in individuals with kidney Cd < 400 µg/g dw. The calcium metabolic disorders may be related to renal tubular damage The larger effects on adult females than on males is explained by the foraging habitat of females that dwell longer in the Cd contaminated area than males and by their larger calcium demand for egg-laying females. Soil Cd concentrations are not directly reported in that study. The area is known as the Colorado ore-belt and well over a thousand mines, mostly abandoned, are situated there. The rocks and mineralised materials in the mining area contain, on average, 75 µg Cd/g_{dw}. The concentrations of Cd encountered in the surface waters and sediments of that area are > 5 µg L^{-1} and 15.2 µg Cd/g_{dw} (Nash et al., 2001 and Church et al., 2000). All these data show that environmental Cd concentrations are > 7-fold above corresponding EU average (see Section 3.1.3.4) suggesting that also the soil Cd is > 7 fold above EU average (i.e. soil Cd > 2.1 µg Cd/g_{dw}). That soil Cd value is above the generic HC_5 of 0.9 µg Cd/g_{dw}.

<u>Conclusion</u>

We propose a critical soil Cd concentration to protect mammals from soil borne Cd as

$$Cd_{soil,crit} = 0.9 \text{ µg } Cd/g_{dw}$$

which is the HC_5 of values at which the critical kidney Cd concentration (400 µg/g dw) may be exceeded in the average population of 8 different species. This value is driven by the mole and shrew thresholds derived from data valid for acid sandy soils (pH 4.2). This value is below the $PNEC_{soil}$ for direct effects on higher plants, soil fauna or soil microbial processes. The risk characterisation of Cd in soil should be based on protecting mammals.

3.3 RISK CHARACTERISATION

3.3.1 Introduction

The risk characterisation is based on a comparison of the PEC with PNEC values. **Table 3.245** summarises the PNEC values that were calculated in the effects assessment (see Section 3.2).

Table 3.245 The PNEC values derived in Section 3.2

	Value	Units	Remark
$PNEC_{water}$	0.19	µg Cd/L	dissolved fraction
$PNEC_{water}$	$0.09 * (H/50)^{0.7409}$	µg Cd/L	for refined risk characterisation if hardness is known (see Section 3.2.2.6.4); dissolved fraction; not to be used below H=40
$PNEC_{soil}$	1.15-2.3	mg Cd/kg_{dw}	based on ecotoxicity
$PNEC_{soil}$	0.9 (selected)	mg Cd/kg_{dw}	based on secondary poisoning to mammals (local and regional)
$PNEC_{sediment}$	2.3	mg $kg^{-1}{}_{dw}$	PNEC is not corrected for bioavailability AVS and OC based normalisation could be used for regional as well as site-specific risk characterisation
$PNEC_{micro\text{-}organisms}$	20	µg Cd/L	dissolved fraction only
$PNEC_{oral}$	0.16	mg $Cd/kg_{diet\ fw}$	birds/mammals

Different effects assessments have led to different $PNEC_{soil}$ values for local risk estimates. The lowest PNEC for soil is based on the assessment of secondary poisoning to mammals. The risk of secondary poisoning is conventionally assessed separately from the direct toxic effect because the predators do not sample 100% of their food in the local environment. However, the $PNEC_{soil}$ for secondary poisoning is determined by effects on organisms with a reasonably small habitat (moles and shrews) and we propose that local soil Cd concentrations should not exceed this PNEC as well. Therefore the $PNEC_{soil}$ = 0.9 mg kg^{-1} is proposed for local risk assessment.

3.3.2 Risk characterisation for production and use (excluding batteries)

3.3.2.1 The aquatic compartment (including sediment and STP)

The risk factors (PEC/PNEC ratio) for local water (dissolved fraction) and sediment concentrations are given in **Table 3.246**. The PNEC was not corrected for water hardness because of lack of site-specific water hardness information. No bioavailability corrections were made for Cd in sediment because of lack of useful site-specific information.

Table 3.246 Local risk characterisation for water and sediment. The factor risk = PEC/PNEC. The PNECwater is 0.19 μg Cd/L and the PNECsediment is 2.3 mg Cd/kg_{dw} (Table 3.245). The factor risk for sediments is calculated for the concentration of added Cd (Clocalsediment, Table 3.85) and for the added and regional Cd (total Cd, i.e. PEClocalsediment, Table 3.85) without correction for bioavailability

	N°	$PEClocal_{water}$	Factor risk water	Factor risk sediment		year
Category		μg L^{-1}		Added	Total	
Cd-production	1	1.37	7.2	71.2	72.3	1996
	2	0.59	3.1	26.7	27.9	1996
	*3**	0.15*	0.8*	1.9	3.1	1996
	*4**	0.52*	2.7*	23	24.2	1996
	5	5.5	29	307	307.7	1996
	6	0.11	0.6	0.0	1.2	1996
	*7**£	0.32*	1.7*	11.5	12.7	1996
	8	0.12	0.7	0.6	1.8	1996
	*9**	0.13*	0.7*	0.8	2.0	1999
	10	0.11	0.6	0.0	1.2	1996
	11	0.11	0.6	0.0	1.2	1996
	*13**	0.69*	3.6*	33	33.7	1996
CdO-producers	11	0.11	0.6	0.0	1.2	1996
	12	0.11	0.6	0.0	1.2	1993
Cd-stabilisers	F	0.11	0.6	0.0	1.2	1996
	G	0.29	1.5	10.0	11.1	1996
	H	0.14	0.7	1.5	2.7	1996
	I	0.13	0.7	0.7	1.9	1996
	J	0.11	0.6	0.0	1.2	1996
	K	0.69	3.6	32.7	33.9	1996
	L	0.11	0.6	0.0	1.2	1996
	M	0.11	0.6	0.0	1.2	1996
	windows manufacturer	0.11	0.6	0.0	1.2	1996
Cd-pigments	A	0.26	1.4	8.2	9.3	1996
	B	0.11	0.6	0.0	1.2	1996
	C	0.15	0.8	2.3	3.4	1996
	D	0.14	0.8	1.7	2.8	1996
	E	0.11	0.6	0.0	1.2	1996
Cd-plating	EU	2.9	15	155.2	156.3	1996
Cd-alloys	EU	1.81	9.5	95.8	97	1996

* Emission to the sea;
n.a. Not available;
£ Recently delivered data were not yet taken into account, this will be done during the development of the Risk Reduction Strategy.

The table predicts elevated risks for the aquatic ecosystem at 11 locations/scenarios and risk to benthic organisms at all sites/scenarios. The risk for the Cd alloy processing sites is based on a generic scenario (see Section 3.1.2.1.1).

High risks are estimated for the sediment on the basis of PEC and PNEC values without correction for bioavailability, irrespective of the use of added or total Cd concentrations ($Clocal_{sediment}$ or $PEClocal_{sediment}$). Moreover, several sites in the production and processing area have a risk for benthic organisms irrespective of the regional background (see local added Cd, $Clocal_{sediment} > PNEC_{sediments}$).

Emissions to freshwater

There are 6 sites (covering 3 scenarios) and 2 further scenarios with risk factors above 1 based on calculated local concentrations. Measured Cd concentrations (see **Table 3.84**) in the receiving water remove some concern for two of the three sites where data are available: risk factors reduce to 5.6 (site 1), and 0.5 (site 2). The latter value, although measured, is judged less reliable than the calculated because it relates to a previous year (< 1996), is rather poorly documented and is therefore of questionable representativeness for the reference reporting year (1996). Risk at the Cd producing plant 5 is high (risk factor 29). This risk is substantiated by the measured Cd concentration (5 µg L^{-1}) which corresponds very well with the calculated PEC_{local} (5.5 µg L^{-1}). An unknown factor in the risk assessment is the sedimentation rate of Cd after the on-site STP. This factor is not included here and may be of importance for an improved risk characterisation. The variability of the $PEC_{regional}$ (which is added to C_{local} to estimate the PEC_{local}) can only add to the uncertainty of the risk for these sites where the added Cd (C_{local}, see **Table 3.5**) is below the PNEC, i.e. at 2 sites (site G and A). However, the difference between C_{local} and the PNEC is <0.05 µg L^{-1}, which is a small value for a regional PEC. Therefore, the uncertainty about the $PEC_{regional}$ is unlikely to be of importance for the risk characterisation at these sites.

Emissions to the sea

Using the PNEC freshwater risk factors are above 1 at the Cd producing plants 4, 7 and 13 that emit effluents to the sea. Measured Cd concentrations (see **Table 3.84**) at site 7 reduce the risk factor to below 1 but increase concern at site 4 and 13 (risk factor up to 16). However, this risk characterisation is only indicative as no PNEC was derived for marine species.

Based on PECs and PNEC without correction for bioavailability, the risks for benthic organisms are elevated at all sites. Risk is always predicted even if emissions are zero because the regional Cd concentration in sediment is above the $PNEC_{sediment}$ (i.e. 2.3 mg $kg^{-1}{}_{dw}$). The regional Cd concentration in sediment is the 90^{th} percentile of measured data. At 15 producing and processing sites/areas there is a predicted risk irrespective of the regional background (see local added Cd, $Clocal_{sediment} > PNEC_{sediments}$). Measured local Cd concentrations (not available) could remove concern. Moreover, the risk characterisation could also be refined by including indicators of Cd bioavailability. This can be achieved by measuring the organic carbon normalised excess of SEM over AVS. This refinement should use a worst case approach to account for seasonal variation in AVS and it is suggested that the AVS approach should be further validated (see Section 3.2.4.3) (**conclusion (i)**). Furthermore, an uncertainty analysis regards the impact of an EU-wide variability in $PEC_{regional}$ (as a default approach in the absence of site-specific data) on the risk characterisation at local level, is not yet included. Both aspects, bioavailability and variability impact, will be implemented in an update of the risk assessment report once the results of the **conclusion (i)** program are agreed at TC NES level (see separate document, 'RAR Stage II').

The risk for micro-organisms in sewage treatment plants is investigated for on-site as well as off-site sewage treatment plants (STP).

On-site waste water treatment plants

Information from the specific production and processing sites indicates that methods to remove cadmium from discharge to water are generally in place. However, no detailed data are available. The ratio of the effluent Cd concentration (see **Table 3.1**) to PNEC micro-organisms (see **Table 3.245**) predicts risk to the on-site STP for a number of sites in the production area (Cd metal) and in the processing areas, pigments, plating and alloys. The risk ratio ranges from 0.02 to 22 and is higher than 1 at 14 locations. There is a possibility that risk is overpredicted. Several toxicity tests (including sludge respiration test) showed that Cd affects micro-organisms of an STP at only about 1 mg Cd/L in the dissolved fraction (see Section 3.2.6). The $PNEC_{STP}$ was calculated from the lowest NOEC using an assessment factor, yielding a $PNEC_{micro\text{-}organisms}$ that is about 50-fold below the lowest LOEC and where sludge respiration was less than 30% affected (see Section 3.2.6). There is only 1 site (site 2 of the Cd producers) where the lowest NOEC is exceeded. Measured data may remove the concern. Wastewater treatment at the plants in the Cd metal production area are based on physical-chemical principles only (see also IPPC report on the best available techniques in the non ferrous metals industries, May 2000). Therefore, it is proposed that the conclusions related to the risk for micro-organisms in the on-site WWTP (STP) are considered as indicative only and are not taken forward to the section 5 (general conclusions).

Off-site waste water treatment plants (municipal sewage treatment plants)

For producers of Cd metal and CdO, no discharge occurs to municipal sewage system, as these sites do emit to surface/sea water or do not emit at all to the aquatic compartment[52]. Therefore, the risk assessment of Cd and CdO producers for off-site STP is not relevant. Risk to off-site STP is only relevant for the processors that potentially have emissions to sewer systems. Only three stabiliser production-sites have not reported flows of receiving water (see **Table 3.1**). The Cd concentration in the effluent of these sites is already lower than the $PNEC_{micro\text{-}organisms}$ suggesting no risk. The Cd plating and alloy scenario can potentially emit to off-site STP and the predicted Cd concentrations in the effluent is 0.081 and 0.05 mg Cd/L, respectively (**Table 3.1**). Assuming no further dilution in the STP (i.e. default effluent flow of 2,000 m^3 day^{-1} and default STP capacity of 2000 m^3 day^{-1}) and assuming 60% removal rate in STP, there remains still a risk (risk factor 1.6 (=0.0324/0.02) and 1.0 (=0.02/0.02)[53]). Apart from requests via the Lead company, no attempt was made by the Rapporteur to actively retrieve detailed data directly from the concerned sector. The predicted Cd concentrations in the effluents of the Cd pigment scenarios range from 0.002 to 0.08 mg Cd/L (**Table 3.1**). Assuming no further dilution in the STP (i.e. default effluent flow of 2,000 m^3 day^{-1} and default STP capacity of 2,000 m^3 day^{-1}) and assuming 60% removal rate in STP, there is a risk for the Cd pigment scenario with the highest Cd concentration in the effluent (Risk factor 1.6 (=0.032/0.02): **conclusion (iii)**).

52 For Cd metal producers: Industry statements, Zinc RAR; for CdO producers: no release of water effluent.

53 There is no dilution of the plating effluent in the water treatment plant in this scenario. As a dilution of 2 would remove the risk, UK suggested that it would be worth trying to obtain information on possible water volumes from that use (UK EA comments, Jan. 2003).

Regional and continental Cd concentrations

Calculated values

The predicted Cd concentrations in water have been calculated for a range in Kp values (see **Table 3.157**). At the average Kp values, the PEC/PNEC ratio's are 0.6 (regional) and 0.3 (continental). The PEC's are larger if the Kp is lower. At the lowest value of Kp (17 10^3 L kg^{-1}) PEC/PNEC ratio's are 1.8 (regional) or 1.7 (continental). The predicted concentrations in sediment have also been calculated for a range of Kp values. At the average Kp values, the PEC/PNEC ratio's are 4.4 (regional) and 1.4 (continental). The PEC's are lower if the Kp is lower. At the lowest value of Kp (17 10^3 L kg^{-1}) PEC/PNEC ratio's are 3 (regional) or 1.3 (continental). At the largest value of Kp (224 10^3 L kg^{-1}) PEC/PNEC ratio's are 4.5 (regional) and 1.4 (continental).

Measured values

It is proposed to refine the risk characterisation with measured data which may be more relevant given the uncertainties in emissions, their geographical distribution, the wide range in natural environments, contributions from historic pollution etc.

Water

Two assessment methods and a sensitivity analysis are presented. First of all, data from an EU-wide survey have been assessed. The FOREGS Geochemical Baseline Program (FGBP) study determined a mean Cd concentration in European surface waters of 0.01 µg L^{-1} and a 90^{th} percentile of 0.1 µg L^{-1}, leading to risk factors of 0.05 to 0.5.

Secondly, a compilation of recent (> 1995) data sets of EU countries has been made and data are classified in a tiered approach depending on the available background information (see **Table 3.184** and **Table 3.185**). The lowest number refers with data with highest quality, the higher number refer to data with lower quality but including those of the lowest number (i.e. a cumulative number of data). The first tier is a risk characterisation with the set of data with reliability index (RI) 1 which allow a 'bioavailability correction', i.e. a correction of the PNEC based on water hardness. However, it was only possible to make such corrections for water hardness for the dataset of Sweden with RI 1 and restricted to the data with hardness > 10 mg $CaCO_3$/L. In that case, risk factors were calculated for each monitoring point as the ratio of PEC to the hardness corrected PNEC. The 90^{th} percentile of these risk factors is below 1 and is represented in **Table 3.247**. The tiers 2 and 3 are the risk characterisations on data which do not allow bioavailability correction but for which the detection limit of Cd is at least 2-fold below the $PNEC_{water}$. The tier 2 used data for which fractionation (dissolved or not) was known, the tier 3 also included data where information on fractionation was unknown. In that latter case, data with unknown fractionation were assumed to be identical to dissolved concentrations which are considered a conservative approach. From the table it can be seen that risk factors are all below 1 in tier 2 unless no outlier exclusion is made in the UK database, in which case risk factor > 1 due to 20 sampling sites (of the 728 sites) with large Cd that are excluded in the analysis as proposed by the rapporteur (thus excluding outliers). It is unknown what the source of Cd is in these sites. However risk factors > 1 are also found in tier 3 and tier 4 (case-by-case analysis) for the U.K and the Walloon region.

Table 3.247 Regional risk characterisation for water in datasets varying in data quality (RI*). The factor risk = PEC/PNEC. The $PNEC_{water}$ is 0.19 µg Cd/L (Table 3.245). Risk characterisation of dataset with RI=1 included bioavailability corrections (hardness correction) and risk factor given is 90th percentile of risk factors. Datasets with RI>1 include also data of classes with lower RI index (i.e. cumulative number of data). Data refer to period 1995-2002 and details about data treatment are given in Table 3.184

					Supporting information: inclusion of outliers	
RI*	Country	n	90th percentile [µg L^{-1}]	Factor risk	90th percentile [µg L^{-1}]	Factor risk
1	Sweden	5,466	0.04$	0.54	0.04$	0.58
2	Finland	803	0.0575	0.30	0.0575	0.30
	Germany	608	0.07	0.39	0.07	0.39
	Norway	985	0.055	0.29	0.055	0.29
	Sweden***	8,999	0.044	0.23	0.044	0.23
	The Netherlands	1825	0.07	0.38	0.12	0.63
	Greece	39	0.18	0.93	0.18	0.93
	UK (WIMS)	6,905	0.15	0.79	0.87	4.6
3	Finland	803	0.06	0.30	0.06	0.30
	Germany	608	0.07	0.39	0.07	0.39
	Greece	39	0.18	0.93	0.18	0.93
	The Netherlands	1,825	0.07	0.38$	0.12	0.63
	Norway	985	0.06	0.29	0.06	0.29
	Sweden***	8,999	0.04	0.23	0.04	0.23
	U.K. (ECN)	10	0.31	1.6	0.31	1.6
	U.K. (WIMS)	6,905	0.15	0.79	0.87	4.6
4	Belgium; France, Italy,; Germany (datasets for the Main and Weser from the LAWA database); Portugal; Spain and The UK (COMMPS)			case-by-case (see text)		

* RI 1: DL<0.1 µg L^{-1}, Cd fractionation: D or ED (D: dissolved Cd; ED: estimated dissolved Cd) and water hardness known; RI 2: DL<0.1 µg L^{-1}, Cd fractionation: D or ED; RI 3: DL< 0.1 µg L^{-1}, Cd fractionation: D, ED or U (Unknown=assumed dissolved); RI 4: all data;

n Number of values in the dataset;

** Including the dataset of Skjelkvale et al. (1999) ; no hardness data known for individual points in this dataset;

$ The Dutch rapporteur expressed concern about the P90 values>PNEC at the monitoring sites on the rivers Schelde and Maas located at the border with Belgium (risk factors 1.6 and 1.1 respectively) while the average P90 values of these rivers in The Netherlands both show risk factors <1.0 (details not shown). Preference was given by the MSR to calculate the P90 value of the entire river system rather than to a P90 value of one site on a river because the TGD states that 'The mean of the 90th percentiles of the individual sites within one region is recommended for regional PEC determination';

$ The average of P90 values of different sampling sites for the RI=1 data. The factor risk is based on the 90th percentile of individual values as the hardness changes within the sampling sites.

The risk factor for the Swedish data with RI=1 is 0.54. This risk factor is obtained after correction for water hardness using the formula for water hardness correction as presented in Section 3.2.2.6.4 and using the proposed $PNEC_{water}$ for soft waters (from 40 mg L^{-1}down to 10 mg $L^{-1}CaCO_3$) of 0.08 µg Cd L^{-1}. Uncorrected, the risk factor would become 0.22. As the corrected risk factor is much higher than the uncorrected one, it is advisable to use values corrected for water hardness for soft waters, when available. There are no data of $PNEC_{water}$ for the very soft waters (H below about 10 mg $CaCO_3$/L) and these areas may be unprotected by the proposed $PNEC_{water}$ for soft water (0.08 µg Cd L^{-1}). Therefore, there is a need for testing the Cd toxicity in these very soft waters (**conclusion (i)** is drawn).

The data of Sweden in RI 2 and 3 are not corrected for water hardness.

Outliers have been removed in the calculation of P90 values to exclude local point sources in the regional assessment. The effect of either including or excluding outliers only marginally affects the risk characterisation except in UK (WIMS database) where the 20 outliers (of 728 sites) have a large impact on the average P90 (note: risk factor is 0.25 for the median P90 of the entire database, including these outliers). In all data-sets, the number of outliers was always less than 10% of the entire database. It is unknown what the source of Cd is in these outliers.

Datasets assigned as RI4 are considered least reliable because, most importantly, the reporting limit is near or above the PNEC. These databases will be considered on a case-by-case basis below. In some cases (Belgium, UK and France) it is still possible to make a risk characterisation for (part) of the region:

- Belgium

The Flemish region: 94% of the data in the 2000-2002 dataset of the Flemish Environment Agency (VMM) are smaller than the DL. The dataset has reporting limits exceeding 0.1 µg L^{-1}. The P90-value (0.17 µg L^{-1}) is within the reporting limits and is therefore considered unreliable. The Walloon region: the reporting limit exceeds the critical value of 0.1 µg L^{-1}defined in this report and even exceeds the PNEC, therefore this database was not included in **Table 3.247**. However the P90 value exceeds the critical reporting limit and can be considered as a reliable value because the P90 value is calculated from the rank in the observed frequency distribution and not from the rank in a curve fitted to the frequency distribution. This means that the P90 is not affected by the exact values of data at lower percentiles. All values below the reporting limit have been set to half the reporting limit. The P90 value indicates a risk for the Walloon region (risk factor: 3.5).

- France

The datasets for France were designated RI 4 and not included in the risk characterisation. The reporting limits are unknown or exceed 0.1 µg L^{-1} or the dataset is not considered representative for a region. A small dataset with reliable background information was available for the river Seine. That dataset was considered too small to represent the French rive dataset for the Seine has a P90 value of 0.06 and a corresponding risk factor of 0.32, i.e. no risk is predicted for the Seine River.

- Germany

The data for the Main and Weser contained sampling points for which the DL was higher or identical to 0.1 µg L^{-1}. However, the average P90 value for these rivers is 0.04 and 0.09 µg L^{-1-1} respectively, suggesting no risk.

- The UK

The COMMPS dataset for the UK (n=1244) was designated RI 4 as the reporting limits exceed 0.1 µg L $^{-1}$. It was, therefore, not included in the **Table 3.247**. The P90 value, however, exceeds the reporting limits and can be considered reliable for reasons discussed above. This P90 values indicates a risk for the UK (risk factor: 2.26). The risk factor increases to 5.36 by including the outliers (1.5% of the entire dataset).

- Italy

The Italian dataset was considered not to be representative for the Italian region. The few values largely exceed those encountered in literature and the reporting limits exceed 0.1 µg L^{-1}. The dataset itself is highly questionable as it indicates a 10-fold decrease of the risk factor from the year 1995 to the year 1996 (the risk factor decreases from 60 to 9.2). The dataset was designated RI 4 and not included in the risk characterisation.

- Portugal

The dataset for Portugal, although very extensive, was not included in the risk characterisation as the reporting limits exceed 0.1 µg L^{-1}. Moreover, 84% of the data have values< DL. The P90 values of different rivers are generally situated within the reporting limits interval and are, therefore, considered unreliable. The P90 value of the River Oeste might still be useful: the P90 value is 0.02 µg L^{-1} but this value is below the DL (0.03 µg L^{-1}). Since the DL is far below the PNEC, this P90 vlaues suggests no risk in that river.

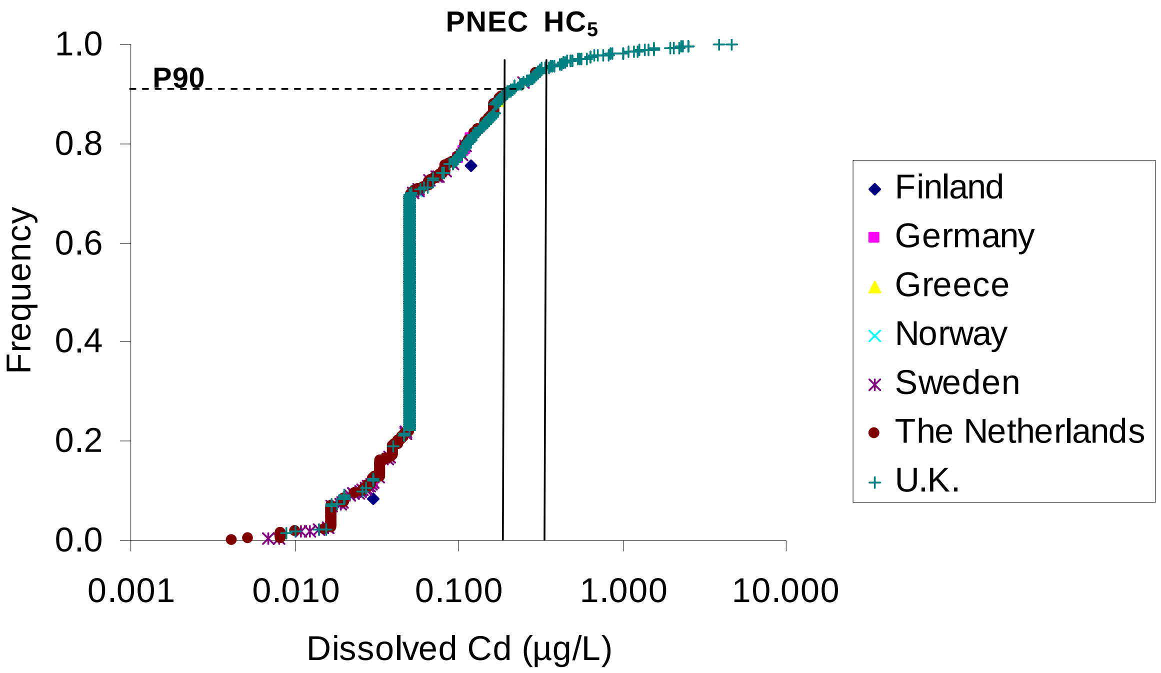
- Spain

The dataset for Andalusia was not included as it obtains high values because of a historical contamination of the Guadalquivir river. The results can, therefore, not be considered to represent ambient Cd concentrations of Spanish waters. The COMMPS dataset for Spain was not included as the reporting limit, as well all the values in the dataset, equal 0.1 µg L^{-1}. The resulting risk factor of 0.53 (=0.1/0.19), however, indicates no risk but the risk coefficient is highly uncertain.

Uncertainty analysis

The frequency distribution of individual 90th percentiles is plotted relative to the PNEC derived from the HC_5 with an assessment factor (AF) 1 or 2. The 90th percentiles refer to data with RI 3 with outliers excluded and the values are either 90th percentiles of individual sites (Sweden, Germany, The Netherlands, UK-WIMS database) or, when no such data are available, the 90th percentiles of a dataset in which each site was only reported once (Greece, UK-ECN database, Norway, Finland). The uncertainty surrounding the PNEC is related to several aspects: statistical aspects (confidence limits on the HC_5 estimated from the SSD) and more general concerns such as species representativity, the inherent uncertainty about NOEC values compared to benchmark values, mixed pollution etc. (see Section 3.2). These uncertainty factors have crystallised in the AF=2 which was agreed. The majority of 90th percentiles are below the PNEC while the risk cannot be excluded for about 10% of the P90 values (note that P90 values from data with RI4 such as Walloon region are not included). The choice of the assessment factor AF (i.e. either 0.19 µg L^{-1} by including the AF=2 as proposed or 0.38 µg L^{-1} with AF=1) only affects the conclusion of risk for a relatively limited number of data that fall in the range 0.19-0.38 µg L^{-1} (6% of the data used in **Figure 3.28**). In terms of regions at risk, it should be noted that the choice of the AF (1 or 2) does only affect the conclusion for the small ECN database of UK whereas for the remaining countries (including UK, using the larger WIMS database) the choice of the AF (1 or 2) does not affect the conclusion about risk, in contrast with the discussion about the exclusion of outliers. For datasets with lower reliability (RI 4), the risk factor is > 1 for UK (COMMPS dataset) and the Walloon region, and, again, this conclusion remains irrespective of the value of the AF for the PNEC.

Figure 3.28 Cumulative frequency of P90 values of dissolved Cd concentrations in EU surface waters. Relative to the PNEC derived from the HC_5 with an assessment factor (AF) 1 or 2. The AF=2 is agreed to be used for the PNEC and reflects most of the uncertainties. The P90 values refer to data with RI 3 and the values are either 90th percentiles of individual sites (Sweden, Germany, The Netherlands, UK-WIMS database) or, when no such data are available, the 90th percentiles of a dataset in which each site was only reported once (Greece, UK-ECN database, Norway, Finland). n=1020 with 70% of data from UK and 25% of the data from The Netherlands



To conclude: no regional risk is predicted based on the majority of 90th percentiles of dissolved Cd values in EU with reliability index 1 to 3 (i.e. acceptable detection limit). Regional risk for the aquatic ecosystem cannot be excluded in certain regions such as UK and the Walloon[54] region of Belgium. For the UK, the conclusion on risk is largely based on 20 of the 728 sites where elevated Cd was found and these outliers (unknown source) drive the conclusion about risk for the UK. This shows that the risk of Cd in freshwater is borderline. A **conclusion (iii)** is proposed. The overall conclusion is based on datasets evaluation with and without exclusion of outliers. The methodology proposed by the rapporteur i.e. exclusion of outliers that are detected by a statistical approach only was not endorsed by MSs. It should be noted however, that although a large number of measured data is available, more information is needed for better characterising the risks to surface water in EU. In particular data from eastern and southern Europe are underrepresented in the entire dataset, detection limits are often too high and the fractionation is often not reported. Current actions (e.g. Water Framework Directive) are already taking such measures. Special attention should be paid to waters with low hardness (H below 10 mg $CaCO_3$ L^{-1}).

[54] Industry analysed the data of 2000 showing that the P90 is largely affected by sites with historical pollution; the more recent databases revealed no risk, however this was not verified by MRS.

Table 3.248 Regional risk characterisation for sediment. The factor risk = PEC/PNEC. The $PNEC_{sediment}$ is 2.3 mg Cd/kg_{dw} (Table 3.245). All values are without correction for bioavailability

				Supporting information: inclusion of outliers	
	n	90th percentile [mg Cd/kg_{dw}]	Factor risk	90th percentile [mg Cd/kg_{dw}]	Factor risk
Belgium (VMM)	512	1.59	0.69	1.75	0.76
France	315	2.86	1.24	3.86	1.68
France - Artois-Picardië	126	2.05	0.89	37	16.08
France- Rhône-Méditerannée	66	0.93	0.4	0.93	0.4
Spain	8	2.20	0.96	8.3	3.63
Sweden	297	2.97	1.29	2.97	1.29
The Netherlands	18	3.69	1.60	11.48	3.31
Supporting information: 90th percentile of Cd in suspended matter		8.5	3.7		

Sediment

Analysis based on PEC and PNEC values without correction for bioavailability: the limited data presented in **Table 3.248** show risk factors varying from 0.4 to 1.6. The P90 value of the concentration of Cd in suspended matter in The Netherlands exceeds that of the P90 value of sediments. This suggests that risk factors based on suspended matter, as a model for newly deposited sediments, are even larger than those for whole sediment samples. The exclusion of outliers (see Section 3.1.3.4.3) largely affects the magnitude of the risk factors. For Belgium the risk factor increases from 0.69 to 0.76 by taking into account the outliers of the VMM dataset. 6.5% of the values in the VMM dataset (including outliers) exceed the $PNEC_{sediment}$. Including the COMMPS dataset would render a risk factor of 3.57. For France, the risk factor for the Artois-Picardië region is 0.89 and would augment to 16.08 if the outliers were taken into account with 19.8% of the values in the dataset (including outliers) exceeding the $PNEC_{sediment}$. The uppermost outlier is the Deule with a risk factor of 156. The risk factor for the Rhône-Méditerannée region is 0.4 with 1.5% of the values in the dataset exceeding the $PNEC_{sed}$. If only the outliers of the COMMPS dataset were taken into account, the risk factor for France would augment from 1.24 to 1.68. The limited dataset from RWS for The Netherlands counts 4 values (of the 12) exceeding the $PNEC_{sediment}$. When including the one outlier of the COMMPS dataset for The Netherlands, the risk factor for The Netherlands would augment from 1.6 to 3.31. When including the outlier of the COMMPS dataset for Spain, the risk factor for Spain augments from 0.96 to 3.63. The Swedish risk factor is 1.29 with 19.19% of the dataset exceeding the $PNEC_{sed}$. The total risk factor would augment from 1.16 to 2.03 by only taking into account the COMMPS values that were discerned as outliers in the limited datasets of The Netherlands and Spain.

A large uncertainty surrounds the $PNEC_{sediment}$ (2.3 mg Cd/kg_{dw}) and, hence, the risk characterisation. The PNEC was calculated from one single chronic toxicity test using an AF of 50. The AVS/SEM method might further specify the $PNEC_{sediment}$ value but this is subject of the **conclusion (i)** program on sediments.

Uncertainties surrounding the effects of Cd in sediments are related to the speciation of Cd in the sediment, e.g. the fraction of Cd present as insoluble sulphides. More information about the relationship between Cd speciation and Cd toxicity is given in the RAR Stage II: **conclusion (i)** bioavailability in sediment (see separate document).

3.3.2.2 The terrestrial compartment

The ratio PEC/PNEC for local soil risk assessment is given in **Table 3.249**. The selected $PNEC_{soil}$ value is 0.9 mg $kg^{-1}{}_{dw}$, which is the lowest $PNEC_{soil}$ value and which is based on secondary poisoning to mammals (see **Table 3.245**).

Risk is predicted at one location (site 2 of the Cd producers), the risk factors range from 0.5-1.1. This conclusion should be treated with caution. The local soil concentrations are calculated after 10 years exposure. The residence time of Cd in soil exceeds 100 years and predicted Cd concentrations after 50 years with current emissions will result in risk factors that are above 1 at the Cd producing sites 2, 3 and 5; **Conclusion (iii)**[55] Due to the long residence time of Cd in soil and the persistent availability (Smolders et al., 1999), such contamination should be avoided. Soil Cd is predicted to increase by more than 60% in 10 years at three sites (site 2, 3 and 5 of the Cd producers). These three sites have high emissions (> 800 kg Cd $year^{-1}$) and the highest emission factors are well above those of the other producers (> 3 kg Cd $tonne^{-1}$, **Table 3.2**). It is recommended that emission reduction measures should be adopted to reach emission factors that are similar to these of the other producers.

Table 3.249 Local risk characterisation for soil. The factor risk = PEC/PNEC. The PNEC value = 0.9 mg $kg^{-1}{}_{dw}$ is equivalent to 0.79 mg $kg^{-1}{}_{ww}$ (standard environmental characteristics, TGD) and is the lowest for local risk assessment based on toxicity mammals through secondary poisoning (Table 3.245)

Use-category	Plant N°	$PEClocal_{soil}$	Factor risk soil	Year
		mg $kg^{-1}{}_{ww}$		
Cd-production	1	0.37	0.5	1996
	2	0.85	1.1	1996
	3	0.59	0.7	1996
	4	0.36	0.5	1996
	5	0.63	0.8	1996
	6	0.36	0.5	1996
	7	0.41	0.5	1996
	8	0.36	0.5	1996
	9	0.39	0.5	1996
	10	0.36	0.5	1996
	11	0.36	0.5	1996
	13	0.36	0.5	1996
CdO-producers	11	0.36	0.5	1996
	12	0.36	0.5	1993

Table 3.249 continued overleaf

[55] This conclusion was adapted in light of the "2002 Update". Section 3.3.3.4.1.

Table 3.249 continued Local risk characterisation for soil. The factor risk = PEC/PNEC. The PNEC value = 0.9 mg kg^{-1}_{dw} is equivalent to 0.79 mg kg^{-1}_{ww} (standard environmental characteristics, TGD) and is the lowest for local risk assessment based on toxicity mammals through secondary poisoning (Table 3..245)

Use-category	Plant N°	PEClocal soil	Factor risk soil	Year
		mg kg^{-1}_{ww}		
Cd-stabilisers	F	0.36	0.5	1996
	G	0.36	0.5	1996
	H	0.36	0.5	1996
	I	0.36	0.5	1996
	J	0.36	0.5	1996
	K	0.36	0.5	1996
	L	0.36	0.5	1996
	M	0.36	0.5	1996
	window manufacturer	0.36	0.5	1996
Cd-pigments	A	0.36	0.5	1996
	B	0.36	0.5	1996
	C	0.36	0.5	1996
	D	0.36	0.5	1996
	E	0.36	0.5	1996
Cd-plating	EU	0.36	0.5	1996
Cd-alloys	EU	0.58	0.7	1996

The regional risk assessment of soils should be based on the measured soil Cd concentration (see **Table 3.190**) or using the regional PEC_{soil} that is calculated with the detailed model 2 (for agricultural soils) or with EUSES (= model 1) for natural and industrial soils (see **Table 3.250**).

Model 2 was developed to assess the risks of Cd in agricultural soils. The predicted soil Cd concentrations after 60 years with current emissions range from 0.20 to 0.44 mg kg^{-1}_{dw}. These concentrations are lower than the lowest $PNEC_{soil}$ for mammals (see **Table 3.250**).

Table 3.250 Regional risk characterisation for soil. The factor risk = PEC/PNEC. The PNEC value is based on secondary poisoning to mammals (Table 3.245). PEC values derived from Table 3.183

Scenario	PEC_{soil} after 60 years [mg kg^{-1}_{dw}]	$PNEC_{soil}$	Factor risk soil
Agricultural soils			
1. low input-low output (pH 6.8)	0.257	0.9	0.29
2. low input-high output (pH 5.8)	0.203	0.9	0.23
3. average input-low output	0.385	0.9	0.43
4. average input-high output	0.310	0.9	0.34
5. high input-low output	0.411	0.9	0.46

Table 3.250 continued overleaf

Table 3.250 continued Regional risk characterisation for soil. The factor risk = PEC/PNEC. The PNEC value is based on secondary poisoning to mammals (Table 3.245). PEC values derived from Table 3.183

Scenario	PECsoil after 60 years [mg kg-1dw]	PNECsoil	Factor risk soil
Agricultural soils			
6. high input-high output	0.339	0.9	0.38
7. high input-very low output (worst case Mediterranean)	0.439	0.9	0.49
8. EU average	0.318	0.9	0.35
Natural and Industrial soil (PEC_{soil}= PECsoil at steady state)			
	0.322	0.9	0.35

Measured values

Average soil Cd concentrations typically range between 0.1 and 1.6 mg $kg^{-1}{}_{dw}$. The average (or median) Cd concentrations in natural and agricultural soils have risk factors 0.1-1.0 (mean 0.4). Corresponding factors for the 90th percentiles are 0.4-1.6 (see **Table 3.251**). Soil Cd concentrations are often affected by soil type (texture and %OM) because background Cd is related to these properties. As an example, the 90th percentiles of German sand, loss and clay soils have been averaged (see Section 3.1.3.4.2 – terrestrial compartment). The data were selected and compiled from the data set “Hintergrundwerte für anorganische und organische Stoffe in Böden” (LABO, 1998). Risk factors are 0.62 for the sandy soils, 0.74 for the loamy (loss –ok) soils and 0.98 for the clay soils. Reported 90th percentiles of soil Cd are often, but not always, classified per soil groups. The lack of a harmonised way of reporting 90th percentiles obscures the regional EU risk characterisation.

Local concentrations are often higher than the $PNEC_{soil}$ values, either due to pollution or due to high background concentrations. High background concentrations (> 2 mg kg^{-1}) in soil are often associated with low plant availability (e.g. Mench et al., 1997). There is no information on Cd toxicity to the soil ecosystem or to mammals in such soils. Soils with historic Cd contamination (smelters) have Cd concentrations that are often several folds higher than the $PNEC_{soil}$ for soil organisms or for mammals. The elevated Cd in smelter affected soils is generally associated with elevated Zn concentrations. The usual Zn/Cd ratio is about 100 in these soils. The $PNEC_{soil}$ of Zn, added above background, is only 27 mg $kg^{-1}{}_{dw}$ (RAR Zn, 2004) whereas the $PNEC_{soil}$ of Cd is 0.9 mg $kg^{-1}{}_{dw}$. In a smelter affected soil containing 2.5 mg Cd/kg and 250 mg kg^{-1} Zn (background about 50 Zn kg^{-1}) it is likely that Zn and not Cd will be toxic to soil organisms.

Uncertainty analysis

If 90th percentiles of soil Cd concentrations are used, risk cannot be excluded in one region (see **Table 3.251**). Reported 90th percentiles are averaged per country as a surrogate for region. No attempt was made to discriminate soil classes. The risk is predicted for the UK when using the $PNEC_{soil}$ of 0.9 mg Cd/kg derived from the study of secondary poisoning. This $PNEC_{soil}$ has a large (statistical) uncertainty and the limited data available suggest that risk for secondary poisoning is mainly pronounced in very acid soils because data from such soil types has triggered the PNEC value (see Section 3.2.3.6.3). As an illustration, the $PNEC_{soil}$ increases from 0.9 mg Cd/kg to 3.3 mg Cd/kg if data on acid soils (pH <4.2) are excluded in the derivation of the PNEC (see Section 3.2.3.6.3). Practically this means that the risk in UK could be excluded if the P90 values do not refer to acid soils, which is unknown. This analysis is qualitative because there is no validated model to estimate risk to mammals taking soil pH into account (see Section 3.2.3.6.3). Moreover, even if risk to secondary poisoning can be excluded, risk to soil microbial process in UK soils cannot be excluded because it falls within the range of the proposed $PNEC_{soil}$ based on direct toxicity to soil microbial processes (see **Table 3.245**). Taken together, regional soil Cd concentrations predict risk in one EU country for which data are available, but the uncertainty surrounding the PNEC values for soil suggests that risk is borderline. A conservative **conclusion (iii)** is proposed.

Table 3.251 Regional risk characterisation for soil. The factor risk = PEC/PNEC. The $PNEC_{soil}$ is 0.9 mg Cd/kg_{dw} (Table 3.245)

Location	90th percentile [µg kg-1]	Factor risk
Belgium	0.51	0.56
France	0.85	0.94
Germany	0.65	0.73
Sweden	0.39	0.43
The Netherlands	0.83	0.92
The United Kingdom	1.40	1.56

3.3.2.3 Secondary poisoning

Effects of soil-borne Cd on mammals has already been included in the previous section since this pathway is more critical than direct effects on higher plants, soil fauna or soil microbial processes.

The PEC_{oral} for birds is calculated as ranges with PEC_{soil} and PEC_{water} and with the range in BAF and BCF values derived from the compilations in Section 3.2.7.

The PEC_{oral} of worms is 5.4-9.1 mg $kg^{-1}{}_{ww}$ (Table 3.252) if based on a median BAF for worms and is 1.4-19 mg $kg^{-1}{}_{ww}$ if based on the entire range of BAF's for worms. The $PNEC_{oral}$ for birds is 0.16 mg kg^{-1} diet, i.e. the PEC/PNEC ratio varies between 9 and 121, with most ratios consistently above 1. This suggests that Cd concentration in the worms may be at risk for the birds, even at ambient soil Cd concentrations.

The PEC_{oral} of fish is < 0.1-3.6 mg $kg^{-1}{}_{ww}$ if based on a median BCF for fish and is < 0.01-148 mg $kg^{-1}{}_{ww}$ if based on the entire range of BCF and BAF's for fish. The $PNEC_{oral}$ for birds is 0.16 mg kg^{-1} diet, i.e. the PEC/PNEC ratio varies between < 0.1-930 with most ratios, however, consistently below 1. This suggests that Cd concentration in the fish may be at risk for the birds in some situations. The PEC_{oral} at ambient Cd concentration in water (<0.3 µg Cd/L) is 0.004 mg Cd/kg_{ww} using the median BCF for fish and is 0.19 mg $kg^{-1}{}_{ww}$ based on the highest BAF or BCF value for whole fish. The first value is well below the $PNEC_{oral}$ for birds, the latter is 1.2 fold the $PNEC_{oral}$ suggesting potential risk at ambient concentrations. This conclusion should be put into perspective: BAF or BCF values of whole fish are typically about 100 L/kg_{ww} with few extremes above 500 L/kg_{ww} and at which risk factors are above unity (see **Table 3.232** and **3.233**).

For different reasons it is felt that even the large PEC/PNEC ratio in water (local) or soil (at local and ambient concentrations) for birds may not reflect a severe risk:

(I) Kidney or liver Cd concentrations in terrestrial birds are below concentrations that are assumed to be acceptable (Furness, 1996-see below for more details) despite that measured Cd concentrations in worms from uncontaminated areas often exceed the $PNEC_{oral}$;

(II) the $PNEC_{oral}$ is based on Cd salt spiked meals thereby overestimating Cd availability to the test animals (see Section 3.2.7.5.1);

(III) birds may not sample 50% of their food as worms in a contaminated area.

The risk of Cd to birds may be refined with field data and critical tissue concentrations. This assessment is yet not possible due to the lack of dose (soil/food Cd)-response (tissue concentration). Tissue concentrations of Cd in birds have been reviewed by Furness (1996). Kidney Cd concentrations in pelagic seabirds are several orders of magnitude higher than in terrestrial seabirds. We will not make any risk assessment here for marine birds as discussed in Section 3.2.7.4.1. Furness (1996) suggests a critical Cd concentration of 100 $\mu g\ g^{-1}{}_{ww}$ (about 400 $\mu g/g_{dw}$). This threshold is the same as suggested for mammals (see Section 3.2.7.5.1) Mean kidney Cd concentration in the kidney of terrestrial birds is below 11 $\mu g/g_{ww}$ and individual highest concentrations (70$\mu g\ g^{-1}{}_{ww}$) have been found in feral pigeons collected around Heathrow airport (presumably enriched with Cd from tire debris, Hutton and Goodman, 1980). A recent survey in Italy reported low kidney Cd concentration (< 8 $\mu g\ g^{-1}{}_{dw}$, or < 2 $\mu g\ g^{-1}{}_{ww}$) in top predators little owl and common buzzard (Battaglia et al., 2005). It has been surprisingly difficult to show elevated Cd in birds inhabiting environments supposedly polluted by Cd (Furness, 1996). Kidney Cd in top predators barn owl and kestrel from the metal polluted Kempen (NL) are 24 ± 26 $\mu g\ g^{-1}{}_{dw}$ and 4.8 ± 6 $\mu g\ g^{-1}{}_{dw}$ respectively (Gorree et al., 1995), i.e. well below the critical value. The only exception with clearly elevated Cd exposure in a contaminated area are the white tailed ptarmigan (*Lagopetus leucurus*) with kidney Cd concentrations up to about 200 $\mu g\ g^{-1}{}_{ww}$ (as observed in Colorado, U.S.A.) which is 2-fold above the toxic threshold (Larison et al., 2000). The large exposure is related to the diet (herbivorous with preference for willow) as discussed in Section 3.2.7.5.1. The corresponding concentrations in samples from a non-contaminated environment are maximally 40 $\mu g\ g^{-1}{}_{ww}$, i.e. below the toxic threshold. The elevated Cd exposure for that species is found in an area where soil Cd is estimated to be at least 2 mg Cd/kg (see Section 3.2.7.5.1). As none of the regional or local soil Cd concentrations in this study are > 2 mg Cd/kg, we conclude that risk of Cd for this species (rare in Europe) is unlikely at the PEC_{soil} considered.

Table 3.252 The predicted environmental concentrations in food (PEC_{oral}). The choice for the parameters and the risk for secondary poisoning are discussed in the text. $PEC_{oral}=(0.5PEC_{local}+0.5PEC_{regional})*BC(A)F$

	PEC_{local} min-max mg $kg^{-1}{}_{ww}$ (or $\mu g\ L^{-1}$)	$PEC_{regional}$ mg $kg^{-1}{}_{dw}$ (or $\mu g\ L^{-1}$)	BAF - BCF median (min-max) $kg_{dw}\ kg_{ww}{}^{-1}$ (or L $kg_{ww}{}^{-1}$)	PEC_{oral} mg kg^{-1} ww
soil-worm	0.36-0.85	0.36	15 (4-32)	5.4-9.1 (median BAF) 1.4-19.4 (range of BAF
water-fish	0.1-477	0.11	15 (0.5-623)	0.002-3.6 (median BCF) <0.001-148(range of BCF/BAF)

3.3.2.4 The atmospheric compartment

A quantitative risk characterisation for exposure of organisms to airborne cadmium is not done because there are no useful data on the effects of airborne cadmium in environmental organisms and thus no PNEC air could be derived. The PECs in air are used for the risk assessment of man indirectly exposed via the environment (see Section 4 of this report in a separate document). Inorganic cadmium air emissions are primarily associated with particulates in the air. Emission to air will settle out to soil. The impact of industrial air emissions at local scale is therefore included in the conclusions on the terrestrial compartment.

3.3.2.5 Conclusions[56]

Environmental Cd concentrations that were either modelled (based on local emissions from Cd/CdO production or processing and on diffuse emissions) or measured were combined with the effects assessment that was largely based on dose (Cd^{2+} salts)-response (chronic toxicity) studies. The effects assessment was based on protecting mammals from soil borne Cd. The following is concluded:

- Modelled freshwater dissolved Cd concentrations based on-site-specific emission data (without water hardness corrections) exceed the freshwater $PNEC_{water}$ at 11 sites where Cd is produced or processed, 3 of which have emissions into the sea. The measured Cd concentrations usually reduce concern. For one site risk is predicted if based on modelled concentrations but not if based on measured concentrations. However, the measured concentration refers to two years before the reference year and will therefore not be preferred over the modelled concentration. Risk at Cd containing alloy production-sites cannot be excluded. There is potential risk for *on-site* STP at a number of Cd producing[57] and processing sites (pigments, plating and alloys). Measured site-specific (toxicity) data may remove this concern
- There is potential Cd toxicity for off-site STP due to emissions from Cd plating, pigment and alloy industry.
- Modelled sediment concentrations (without bioavailability correction) result in elevated risks for benthic organisms[58] at all sites/scenarios. Risk is always predicted even if emissions are zero because the regional Cd concentration in sediment is above the $PNEC_{sediment}$. The regional Cd concentration in sediment is the 90th percentile of measured data. No risk is predicted using average or median sediment Cd concentration and if emissions are zero. On the other hand, at 15 producing and processing sites/areas i.e. 7 Cd-production-sites and 8 Cd-processing sites (i.e. stabiliser production, pigment production and the generic scenarios 'Cd plating' and 'Cd alloys'), there is predicted risk irrespective of the regional background (see local added Cd, $Clocal_{sediment}$ > $PNEC_{sediments}$). Measured local Cd concentrations (not available) could remove concern. A refined risk characterisation could be performed at these sites using an AVS and Organic Carbon based normalisation. To that latter perspective, a **conclusion (i)** was decided.

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[56] These conclusions were adapted in light of the "2002 Update". Section 3.3.3.4.1

[57] The type of the WWTP at the plants in the production area (Cd metal) being based on physical-chemical principles only, it is proposed that the conclusions related to the risk for micro-organisms in the on-site WWTP are considered as indicative only and are not taken forward to the Section 5 (general conclusions).

[58] After the TMIV'02 last visit discussion on cadmium in sediment a number of MSs (UK, F, DE) and Industry commented on the sediment assessment and the current conclusions drawn in line with the outcome of that last TM (for more details, see effects assessment and risk characterisation).

- predicted regional and continental Cd concentrations in water are below the $PNEC_{water}$ at a mean K_p value while the risk factor is 1.7 using a K_p value that is distinctly smaller than average. No regional risk is predicted based on the majority of 90th percentiles of measured data from monitoring programmes with acceptable detection limit. Regional risk for the aquatic ecosystem cannot be excluded in certain regions such as UK and the Walloon region of Belgium.
- In general, the current local standards for emissions to water mentioned in permits (maximum Cd concentration in the effluent and the volume of discharged effluent) should be reconsidered in the light of the derived PNECwater in order to prevent risk to the aquatic compartment.
- Regional predicted concentrations in the sediment are typically larger than the PNEC but overestimate measured concentrations. Risks for the 90th percentiles of the various European countries ranges from 0.69 to 1.6 (datasets excluding outliers). AVS/SEM analysis could remove the concern. To the latter perspective, **conclusion (i)** is decided.
- modelled local soil Cd concentrations indicate immediate risks for mammals at one Cd metal production-site. Long term predictions (> 20 years) show that current atmospheric emissions from 3 Cd metal producing sites can increase risk at the local scale. The emission factors of these sites should be reduced to those of other Cd producing plants. Given the total lack of information related to site-specific air emission data for the Cd alloy and Cd plating industry, long term risk at the local terrestrial scale cannot be excluded for these industry areas.
- predicted regional soil Cd concentrations that include different agricultural scenarios are below the $PNEC_{soil}$. The average (or median) measured Cd concentrations in natural and agricultural soils have risk factors 0.1-1.0 (mean 0.4). Corresponding factors for the 90th percentiles are 0.4-1.6. Risk cannot be excluded in one region but depends on the magnitude of the assessment factor chosen in the derivation of the $PNEC_{soil}$ (either 1 or 2, see Section 3.2.3.7). Averaging of all 90th percentiles within a region is clearly affected by the dominant soil types in each region because soil Cd concentration is affected by properties such as % clay and % organic matter.
- potential risk of Cd to terrestrial birds is predicted using soil-worm-bird or water-fish-bird modelling. Field data (body burden: kidney and liver Cd data) of terrestrial birds do not indicate Cd poisoning, even in contaminated areas and in top predators. Pelagic birds have reported kidney Cd concentrations above acceptable values but no risk characterisation of marine environments was made here.

3.3.3 Risk characterisation for battery related life cycle steps

3.3.3.1 Overview assumptions and built-in conservatism

Within the approach used in this report to estimate the cadmium emissions associated with waste management strategies such as land-filling and incinerations different assumptions have been made that lack validation due to the limited availability of data on this subject. As general premise realistic worst case conditions were taken as input values to perform the calculations but in other cases average values were used instead of worst case estimated in order to conserve the environmental realisms of the estimates. **Table 3.253** provides an overview of the assumptions and default values taken in this report and the associated level of conservatism introduced with them.

Table 3.253 Overview of the input values used in the emission calculations of MSW landfills and MSW incinerators

Subject	Parameter	Value	Best case	Typical	Realistic worst case	Worst case	Description
General data							
Information NiCd batteries	Cd content portable NiCd battery	13.8%					Average: referring to actual manufacturing and production data
Section 2.2.2.2	Cd content industrial NiCd battery	8%					Average: referring to actual manufacturing and production data
Section 2.2.2.4.2.2.	Weight portable NiCd battery	38 g					Average: referring to actual manufacturing and production data
Section 2.2.2.4.4.1	Sales data portable NiCd batteries	14,000 tonnes					Upper limits used
Section 2.2.2.4.4.2	Sales data industrial NiCd batteries	3,632 tonnes					Upper limits used
Section 2.2.2.4.4.3	Future sales portable NiCd batteries	13,500 tonnes					Real consumption numbers show a decrease: 11,793 tonnes in 2000 -11,265 tonnes in 2001
Section 2.2.2.5.1.1	Recycling data portable NiCd batteries	1,446 tonnes					Lowest limits used
Section 2.2.2.5.1.2	Recycling data industrial NiCd batteries	2,667 tonnes					Lowest limits used
Section 2.2.2.5.2	Recycling %	10%					
	Recycling %	75%					
NiCd manufacturing:recycling sites	Cd concentration effluent						90^{th} percentile (in general: of the individual raw measurements)
	Effluent flow						90^{th} percentile
	Flow receiving water						Minimal flow rate or 1/3 average flow rate
Municipal Solid Waste (MSW)	Cd content	$10g\ tonne^{-1}s$					90^{th} percentile
"Contribution of NiCd batteries to the cadmium content of municipal solid waste: current situation" under Section 3.1.2.2.5.	Moisture content	30%					Van der Poel (1999) and other references (see text)
	Contribution NiCd battery	10%					Typical percentages are between 10-20 %
	Contribution NiCd battery	50%					Maximum NiCd battery contribution measured was 4.3g Cd/tonnes $_{dry\ wt.}$ MSW (Germany) used on the 90^{th} percentile value of 10 g Cd /tonnes $_{dry\ wt.}$
"Waste management strategies in Europe" under Section 3.1.2.2.5	MSW incinerated/landfilled current situation						Average for EU.
	MSW incinerated/landfilled 100 % incineration						Additional scenario added for the sensitivity analysis

Table 3.253 continued overleaf

Table 3.253 continued Overview of the input values used in the emission calculations of MSW landfills and MSW incinerators

Subject	Parameter	Value	Best case	Typical	Realistic worst case	Worst case	Description
MSW incineration	Volume fluegass	5,500 Nm^3/tonnes					Range reported in literature 5,000-6,000
“Current emissions” under Section 3.1.2.2.5.	Cd concentration in flue gass						Most often average values were used, In some cases concentrations were P90 values
Above Table 3.27	Waste water generated	2,5 m^3/tonnes					Range reported in literature 0.5-2.5 m^3. For the regional PEC calculations this maximum value have been used. For the local calculations both min and max have been used.
Table 3.27	Cd concentration in waste water before treatment	0.3 mg L^{-1}					Average of measured data used for regional calculations
	Cd concentration in waste water before treatment	0.42 mg L^{-1}					90th percentile of measured data used for local calculations
	Cd concentration in waste water before treatment	0.76 mg L^{-1}					Max value used for sensitivity analysis
	Removal efficiency Cd	98.8%					Based on 104 measurements and the comparison of both average evalues of influent/effluent as maximum values
Table 3.30	Cd percentage in fly ash	87%					Average value based on different literature data
	Cd percentage in bottom ash	13%					Average value based on different literature data
MSW landfill “Overall cadmium emissions from landfilling MSW” under Section 3.1.2.2.5. Table 3.1.	Cd concentration in leachate	5 µg L^{-1}					Eggenberger and Waber (2000), Flyhammar, 1995, EREF, 1999. 90th percentile Germany < 5, 80th percentile Switserland < 3, 50th percentile Sweden = 5 and < 5, 50th percentile USA/France: 2,5-7 landfills (Germany) (Krümpelbeck, 1999, average concentrations): 1.5 years: 11µg L^{-1} 21-30 years: 2.8 µg L^{-1} landfills (Sweden) (Flyhammar et al., 1998): 1-2 years: 40 µg L^{-1} 20-22 years: 6 µg L^{-1}

Table 3.253 continued overleaf

Table 3.253 continued Overview of the input values used in the emission calculations of MSW landfills and MSW incinerators

Subject	Parameter	Value	Best case	Typical	Realistic worst case	Worst case	Description
	Leachate volume	2,500 m^3/ha					Maximum value based on average to reasonable worst case precipitation of 800 mm/y
Table 3.44	Rainfall	800 mm/y					Rainfall representative for Mid Europe and the Scandinavian countries, reasonable worst case for South Europe
Table 3.51	Surface landfill	14,7 ha					Average value of reported landfill surface areas
Sewage Treatment plant	Removal efficiency Cd	60%					Average value (CBS, 2002)
Regional calculations							
NiCd manufacturing:recycling sites	Allocation to region						Highest emittor chosen
Incineration MSW	Regional air emissions						Average or 90P values have been used.
	Regional water emissions						Maximum amount of water generated, average influent concentration and typical removal percentage used for calculations
Landfilling MSW	Regional water emissions						Maximum leachate volume (2,500 m^3/ha,y) used in combination with average Cd concentration (5 μg L^{-1}) and average landfill surface (14,7 ha)
Local calculations							
Incineration MSW	Aquatic compartment						P90 value of measured influent concentrations
Section 3.1.3.2.1 Figure 3.11 (below Table 3.93)	Dilution factor	100					Based on the 10^{th} percentile of calculated DF with the maximum value of waste water generated (2.5 m^3/tonne)
	Dilution factor	1,000					Based on the 50^{th} percentile of measured data and the maximum volume of waste water generated (2.5 m3/tonne). Could in fact also be considered as a realistic worst case since 75 % of the incinerators have a DF > 1,000
	Size plant	112 ktonnes					Large plant

Table 3.253 continued overleaf

Table 3.253 continued Overview of the input values used in the emission calculations of MSW landfills and MSW incinerators

Subject	Parameter	Value	Best case	Typical	Realistic worst case	Worst case	Description
	Terrestrial and atmospheric compartment						Country specific air emissions have been used. Sometimes based on P90 values measured data, sometimes highest emission factor and sometimes measured data represented average conditions.
Landfilling MSW	Surface landfill	20 ha					Future landfills are expected to be large (at least 20ha), High surface equals high volume of leachate generated with average Cd leachate concentration (5µg L^{-1}).
Below Table 3.49	Leachate volume	100 m^3/d					Based on large landfill surface area and high leachate volume (2,024 m3/ha/y) during operational phase
	Dilution factor	180					Based on the release of the leachate in a river with TGD standard flow rate of 18,000 m^3/d
	Local water emission						Based on large landfill surface area, high leachate volume (2,024 m^3/ha/y) during operational phase, average Cd leachate concentration (5 µg L^{-1})
Future emissions	Landfill leachate concentration	50 µg L^{-1}					According to the performed geochemical modelling on mature waste, carbonate precipitation is likely to prevent cadmium concentrations rising above 60 to 90 µg L^{-1}. The laboratory results indicated, however, that for the aerobic columns, cadmium concentrations generally remained below 10 µg L^{-1}suggesting that the retention mechanism is probably not precipitation alone. The leachate concentration of 50 µg L^{-1}can be considered as a conservative/realistic worst case leachate concentration because in this case we are assuming that aerobic precipitation is the only metal retention mechanisms
"Forecasts of future battery waste arisings" under Section 3.1.2.2.5.	Future Cd content	13.2 g $tonne^{-1}$					Based on 75 % collection but already 9 g $tonne^{-1}$ Cd due to other sources. Also future sales figures (13,500 tonnes) kept constant while evidence of decreasing trend) The same trend is supposed in 'consumption' figures
		24 g $tonne^{-1}$					Based on 10 % collection but already 9 g $tonne^{-1}$ Cd due to other sources, Also future sales figures (13,500 tonnes) kept constant while evidence of decreasing trend) The same trend is supposed in 'consumption' figures

3.3.3.2 The aquatic compartment (including sediment and STP)

The risk factors (PEC/PNEC ratio) for **local water** and **sediment** concentrations are given in **Table 3.254** for the NiCd producers and recyclers and from **Table 3.255-Table 3.260** for incinerators and landfills. By lack of relevant data, corrections for water hardness could not be done for the risk characterisation.

3.3.3.2.1 Risk characterisation NiCd producing/recycling plants

Table 3.254 Local risk characterisation NiCd producing/recycling plants for water, sediment and STP. The factor risk = PEC/PNEC. The $PNEC_{water}$ is 0.19 µg Cd/L. The $PNEC_{sediment}$ is 2.3 mg kg^{-1} $_{dry\ wt.}$ The factor risk is calculated for the concentration of added Cd ($Clocal_{sediment}$) and for the added and regional Cd (total Cd, i.e. $PEC_{sediment}$) without correction for bioavailability. The PNEC for micro-organisms is 20 µg L^{-1}(Table 3.245)

Use-	N°	PEClocal water site specific	Factor risk water site specific	PEClocal water DF=1,000	Factor risk water DF=1,000	PEClocalsediment DF=1,000 or site specific	Factor risk sediment DF=1,000 or site specific Total	Factor risk sediment DF=1,000 or site specific Added	$C_{effluent}$	Factor risk STP	Year
Category		µg L^{-1}		µg L^{-1}		mg kg^{-1} $_{dry\ wt.}$			(mg L^{-1})		
NiCd-batteries	1	0.12	0.63	N/A	N/A	3.2	1.4	0.2	0.019[a]	0.95	1999
	2*	0.15	0.79	0.15	0.79	8.0	3.5	2.3	0.12	n.r	2000
	3	0.12	0.63	0.15	0.79	8.0	3.5	2.3	0.12	n.r.	2000
	4	0.18	0.94	N/A	N/A	10.5	4.6	3.4	0.13	n.r.	2000
	5	0.11	0.58	0.114	0.58	2.7	1.2	0	0.00007[a]	0.005	2000
	6	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	n.r.	1999
	7	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	n.r.	1999
Cd recyclers	1[b]	0.19	1.0	0.27	1.4	22.6	9.8	8.6	0.45	n.r.	2000
	1[c]	0.13	0.68	0.17	0.89	19.8	8.6	7.5	0.17	n.r.	2000
	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1999

N/A Not applicable – Factory 6 & 7 have no emissions to water – See Table 3.5;
a) Influent concentration STP = effluent concentration plant*DF STP);
b) Based on P90 of daily measurements;
c) Based on average effluent concentration and average effluent flow rate;
n.r. Not relevant;
* Emission to the sea.

Aquatic compartment

Freshwater and marine

For the NiCd batteries producing plants emitting in fresh water ecosystems there are no sites with a risk factor larger than one. Plant 4 has a risk factor of 0.94. Although the P90 of concentrations in the effluent is calculated on monthly average values (and not on daily measurements) the risk factor of 0.94, calculated on the basis of several ‘parameter’ worst case assumptions, is judged as being ‘without concern’ for aquatic organisms. For the NiCd recycling sites there is one site with an elevated risk, plant 1. If the risk characterisation is performed with the average flow rate and average cadmium concentration a risk factor of 0.89 is obtained (scenario 1b). This indicates that at plant 1, although operating fully in line with the current legislation and local permit, risk to aquatic organisms can potentially occur at specific spatial-temporal conditions.

NiCd producing plant 2 emits effluents to the marine environment. The risk factor is below 1 at that site (based on the PNEC freshwater). However, the risk characterisation is indicative only, as no PNEC was derived for marine species.

Uncertainty analysis

It should be noted that an assessment factor of 2 has been included in the PNEC water derivation due to remaining uncertainty.

The uncertainty surrounding the PNEC is related to several aspects:

- Statistical aspects: for cadmium an effect database of 168 reliable tests on single species is available which contains 3 reliable LOEC’s below the derived HC_5 (0.38 µg L^{-1}) whereas the 9 multi species studies identified 1 LOEC below this hardness corrected HC_5. This suggests that NOEC and LOEC distributions overlap in the lower concentration range and that an additional assessment factor may be necessary.
- The inherent uncertainty about NOEC values compared to the benchmark values
- Species representativity
- Mixed pollution (etc. see Section 3.2)

These factors have crystallised in the AF=2 which was agreed.

The uncertainty around the PNEC water influences the risk conclusion for the NiCd recycling plant. If no assessment factor is applied the site would not have a local risk anymore (RCR = 0.5-0.7) for the water compartment.

Using measured regional values

Aforementioned exposure estimations and risk assessment are based on calculated $PEC_{regional}$ (i.e. 0.11 µg L^{-1}). Preference should, however, be given to measured values when available. However in the absence of reliable and representative regional measured data in the vicinity of the individual sites the RCR values have also been calculated (results not shown) using the average of the measured P90 values for different countries (i.e. 0.12 µg L^{-1}) and also using the median of the measured P90 values (i.e. 0.07 µg L^{-1}), The use of the average measured regional PEC concentration (0.12 µg L^{-1}) does not change the risk conclusions for the NiCd producing sites. Only in the case of recycler 1 the observed risk ratio of 1 for a site specific dilution changes into a no risk scenario (RCR = 0.79) when the median measured regional concentration is used as regional background.

Sediments (assessment without bioavailability correction)

Based on PECs and PNEC not corrected for bioavailability, the risks for benthic organisms are elevated at sites 1 to 5 for the NiCd producing plants and recycler 1. Risk factors based on 'total' (i.e. locally added and regional background contribution) vary between 1.2 and 9.8.

It should be noted that a risk is always predicted even if emissions are zero because the regional Cd concentration in sediment is above the $PNEC_{sediment}$. The regional Cd concentration in sediment is the 90th percentile of measured data. (2.66 mg kg^{-1} $_{dry\ wt.}$) No risk is predicted when the EU average or median sediment Cd concentration is used as regional Cd concentration. Based only on local emissions (i.e. without the background contribution), no risk is predicted at some sites if local background is low as suggested by risk factors based on locally added Cd only (e.g. plant 1). At several producing and processing sites (plant 2, 3 and 4), however, there is predicted risk irrespective of the regional background (see local added Cd, $Clocal_{sediment}$ > $PNEC_{sediments}$). Measured local Cd concentrations (not available) could remove the concern.

Moreover, the risk characterisation could also be refined by including indicators of Cd bioavailability. This can be achieved by measuring the organic carbon normalised excess SEM Cd over AVS. This refinement should use a worst case approach to account for seasonal variation in AVS and it is suggested that the AVS approach should be further validated (see Section 3.2.4.3). To that end a **conclusion (i)** was decided by the Technical Meeting. Furthermore, an uncertainty analysis regards the impact of an EU-wide variability in $PEC_{regional}$ (as a default approach in the absence of site-specific data) on the risk characterisation at local level, is not yet included. Both aspects, bioavailability and variability impact, will be implemented in an update of the risk assessment report once the results of the **conclusion (i)** program are agreed at TC NES level (see separate document, 'RAR Stage II').

STP (off-site)

In this study, the risk for micro-organisms in sewage treatment plants is investigated for off-site sewage treatment plants (STP) only[59].

Only two plants discharge in a STP system. The ratio of effluent concentration to the PNEC $_{micro-organisms}$ (20 µg L^{-1}) is suggested as the indicator of risk for a STP (TGD, 1996). This ratio is lower than 1 for both plants. However, for the reference year 1999, the risk factor calculated for NiCd producing plant 1 is close to 1 (0.95)[60]. There is a possibility that the risk is over predicted. Several toxicity tests (including sludge respiration test) showed that Cd affects micro-organisms of an STP at only about 1 mg Cd/L in the dissolved fraction. The $PNEC_{STP}$ was calculated from the lowest NOEC using an assessment factor, yielding a $PNEC_{micro-organisms}$ that is about 50-fold below the lowest LOEC and where sludge respiration was less than 30% affected

59 Remark: the type of the on-site STP (WWTP) at the battery production-sites is essentially based on physical-chemical principles only (see information in Table 3.7).

60 For the year 2000, due to the implementation of a new wastewater treatment plant and the changing in the production process and cleaning method, a significant reduction in total emission towards the municipal STP is reported (see Section 3.1.2.2.1) and based on measured data (concentration of Cd in effluent and the effluent flow) a lower PEC local and risk factor can be calculated.

(section 3.2.6). There is no site where effluent concentrations exceed about 1 mg Cd/L or the lowest NOEC (200 µg L^{-1}).

For the other sites the STP risk factor is irrelevant because for these sites the industrial effluents are rejected to surface water after physico-chemical treatment on-site.

3.3.3.2.2 Risk characterisation MSW incinerators

Since cadmium emissions from incinerators reflect always all cadmium sources a comparative risk assessment has been made. First, the risk associated with the total cadmium emissions is given. This analysis is followed by the calculation of the risks associated with the total cadmium without NiCd batteries.

Freshwater

Table 3.255 Local risk characterisation incinerators for water and STP (at dilution factor 100 and 1,000). The factor risk = PEC/PNEC. The $PNEC_{water}$ is 0.19 µg Cd/L. The $PNEC_{sediment}$ is 2.3 mg kg^{-1} $_{dry\ wt.}$ The PNEC for micro-organisms is 20 µg L^{-1}(Table 3.245). Total cadmium concentrations. (Dilution Scenario 1 = DF 100 and Dilution Scenario 2 = DF 1000)

	PEC local water DF = 100	Factor risk water DF = 100	PEC local water DF = 1,000	Factor risk water DF = 1,000	Ceffluent	Factor risk STP
	µg L^{-1}	-	mg L^{-1}	-	mg L^{-1}	
Dilution Scenario 1 & 2	0.13	0.68	0.12	0.63	0.005	0.25

No risks are expected for aquatic organisms when the current estimated emission from a hypothetical local incineration plant is considered (for both dilution factor 100 and 1,000). If the effluent of a incinerator plant is released after an on-site WWTP with high Cd removal efficiency (98.8%) in a STP no toxicity to the off-site STP micro-organisms is predicted. Removing all NiCd batteries from the MSW stream has a negligible influence on the obtained risk ratios (see **Table 3.256**).

Table 3.256 Local risk characterisation incinerators for water (at dilution factor 100 and 1,000). The factor risk = PEC/PNEC. The $PNEC_{water}$ is 0.19 µg Cd/L. The $PNEC_{sediment}$ is 2.3 mg kg^{-1} $_{dry\ wt.}$ The PNEC for micro-organisms is 20 µg L^{-1}(Table 3.245). Total cadmium without NiCd contribution. (Dilution Scenario 1 = DF 100 and Dilution Scenario 2 = DF 1000)

	PEC local water DF = 100	Factor risk water DF = 100	PEC local water DF = 1,000	Factor risk water DF = 1,000
	µg L^{-1}	-	µg L^{-1}	-
	Assumption NiCd batteries contributed 10 % to the overall Cd load			
Dilution Scenario 1 & 2	0.13	0.68	0.11	0.58
	Assumption NiCd batteries contributed 50 % to the overall Cd load			
Dilution Scenario 1 & 2	0.12	0.63	0.11	0.58

Uncertainty analysis

PNEC

It should be noted that an assessment factor of 2 has been included in the PNEC derivation due to remaining uncertainty. The inclusion or exclusion of this assessment factor does not influence the risk conclusions for the MSW incinerator scenarios.

Using measured regional values

Aforementioned exposure estimations and risk assessment are based on calculated PEC $_{regional}$ (i.e. 0.11 µg L^{-1}). Preference should, however, be given to measured values when available. However in the absence of reliable and representative regional measured data in the vicinity of the individual sites the RCR values have also been calculated (results not shown) using the average of the measured P90 values for different countries (i.e. 0.12 µg L L^{-1}) and also using the median of the measured P90 values (i.e. 0.07 µg L L^{-1}). The use of the average measured regional PEC concentration (0.12 µg L L^{-1}) or the median regional PEC concentration (0.07 µg L^{-1}) does not change the risk conclusions.

Dilution factors

The risk conclusions are based on a realistic worst case dilution factor of 100 and a typical value of 1,000. In case the dilution factor would be below 25 at an effluent concentration of 0.0056 mg L^{-1} L^{-1} or more, a risk would be predicted.

Cadmium removal efficiencies

The risk conclusions are based on the use of an on-site WWTP with a removal efficiency of 98.8% and an influent concentration of 0.47 mg $L^{-1}L^{-1}$. In case the removal efficiency is lower than 95.1% while the influent concentration is 0.47 mg L^{-1} or more, a risk would be predicted.

3.3.3.2.3 Sediments (assessment without bioavailability correction)

Table 3.257 Local risk characterisation incinerators for sediments (at dilution factor 100 and 1,000). The factor risk = PEC/PNEC. The $PNEC_{sediment}$ is 2.3 mg kg^{-1} $_{dry\ wt.}$ The factor risk is calculated for the concentration of added Cd ($Clocal_{sediment}$) and for the added and regional Cd (total Cd, i.e. $PEC_{sediment}$) without correction for bioavailability. Total cadmium concentrations. (Dilution Scenario 1 = DF 100 and Dilution Scenario 2 = DF 1000)

	PEC local sediment DF = 100	Factor risk sediment DF = 100 Total	Factor risk sediment DF = 100 Added	PEC local sediment DF = 1,000	Factor risk sediment DF = 1,000 Total	Factor risk sediment DF = 1,000 Added
	mg kg^{-1} dry wt.	-	-	mg kg^{-1} dry wt.	-	
Dilution Scenario 1 & 2	5.19	2.3	1.1	2.91	1.3	0.09

For all hypothetical local incineration scenarios a risk for sediment organisms is predicted. It should be noted that risk is always predicted even if local emissions are zero because the regional Cd concentration (90th percentile of measured data i.e. 2.66 mg $kg^{-1}$$_{dry\ wt.}$ is already above the PNEC sediment. The risk factor based on total vary is 2.1 for the realistic worst case situation when a DF of 100 can be applied and is 1.1 for a DF of 1,000. Based only on local emissions (i.e. without the background contribution), no risk is predicted for the scenario with the dilution factor of 1,000.

Table 3.258 Local risk characterisation incinerators for sediments (at dilution factor 100 and 1,000). The factor risk = PEC/PNEC. The $PNEC_{sediment}$ is 2.3 mg kg^{-1} $_{dry\ wt.}$ The factor risk is calculated for the concentration of added Cd ($Clocal_{sediment}$) and for the added and regional Cd (total Cd, i.e. $PEC_{sediment}$) without correction for bioavailability. Total cadmium without NiCd contribution

	PEC local sediment DF = 100	Factor risk sediment DF = 100 Total	Factor risk sediment DF = 100 Added	PEC local sediment DF = 1,000	Factor risk sediment DF = 1,000 Total	Factor risk sediment DF = 1,000 Added
	mg kg^{-1} $_{dry\ wt.}$	-	-	mg kg^{-1} $_{dry\ wt.}$	-	
	Assumption NiCd batteries contributed 10 % to the overall Cd load					
Dilution Scenario 1 & 2	4.87	2.1	0.96	2.69	1.2	0.01
	Assumption NiCd batteries contributed 50 % to the overall Cd load					
Dilution Scenario 1 & 2	3.93	1.7	0.48	2.79	1.2	0,01

Removing all NiCd batteries from the MSW stream has only a minor impact on the risk conclusions.

These results are based, however, on no correction for the bioavailability of cadmium in sediments (SEM/AVS method). A **conclusion (i)** program is ongoing. Furthermore, an uncertainty analysis regards the impact of an EU-wide variability in PEC reg (as a default approach in the absence of site-specific data) on the risk characterisation at local level, is not yet included. Both aspects, bioavailability and variability impact, will be implemented in an update of the risk assessment report once the results of the **conclusion (i)** program are agreed at TC NES level (see separate document).

3.3.3.2.4 Future scenarios and sensitivity analysis MSW incinerators

Future scenario

Table 3.259 Local risk characterisation incinerator for water and STP (at dilution factor 100 and 1,000). Future scenarios: collection rate: 10 and 75%. The factor risk = PEC/PNEC. The $PNEC_{water}$ is 0.19 µg Cd/L. The PNEC for micro-organisms is 20 µg L^{-1}(Table 3.245). Total cadmium concentrations

Scenario	PEC local water DF = 100	Factor risk water DF = 100	PEC local water DF = 1,000	Factor risk water DF = 1,000	Ceffluent	Factor risk STP
	µg L^{-1}	-	µg L^{-1}	-	mg L^{-1}	
MSW Incineration plant (10%; total cadmium)	0.16	0.84	0.12	0.63	0.0135	0.68
MSW Incineration plant (75%; total cadmium)	0.14	0.74	0.12	0.63	0.007	0.35

Table 3.259 indicates no risks for the future hypothetical incineration plant (both scenarios) for aquatic organisms if a dilution factor of 1,000 is applicable. Performing the exercise for the different collection scenarios (10 and 75%) with a dilution factor of only 100 indicates also no risk for the aquatic compartment for both the 10% and 75% recycling scenario. No toxicity to off-site STP micro-organisms from the MSW local incineration plant is predicted for the future scenarios.

Removing all NiCd batteries resembles the current scenario as presented in **Table 3.256** (i.e. assumption at start that 10% of the Cd load is due to NiCd batteries).

Uncertainty analysis

PNEC

It should be noted that an assessment factor of 2 has been included in the PNEC derivation due to remaining uncertainty.

The inclusion or exclusion of the assessment factor of 2 does not influence the conclusions.

Using measured regional values:

Aforementioned exposure estimations and risk assessment are based on calculated PEC reg (i.e. 0.11 µg L^{-1}). Preference should, however, be given to measured values when available. However in the absence of reliable and representative regional measured data in the vicinity of the individual sites the RCR values have also been calculated (results not shown) using the average of the measured P90 values for different countries (i.e. 0.12 µg L^{-1}) and also using the median of the measured P90 values (i.e. 0.07 µg L^{-1}). The use of the measured regional PEC does not influence the conclusion of the risk characterisation.

3.3.3.2.5 Sediment (assessment without bioavailability correction)

For all future scenarios a risk is predicted for sediment organisms. Based only on local emissions (i.e. without the regional background contribution), no risk is predicted for the scenario with 10-75% collection when a DF of 1,000 is applicable. A potential risk is still apparent for the 10-75% collection when a DF of 100 is applied.

Table 3.260 Local risk characterisation incinerators for sediments for a generic MSW incineration plant in the EU. Future scenarios: collection rate: 10 and 75% (at dilution factor 100 and 1,000). The factor risk = PEC/PNEC. The $PNEC_{sediment}$ is 2.3 mg kg^{-1} $_{dry\ wt.}$ The factor risk is calculated for the concentration of added Cd ($Clocal_{sediment}$) and for the added and regional Cd (total Cd, i.e. $PEC_{sediment}$) without correction for bioavailability. Total cadmium concentrations

Scenario	PEC local sediment DF = 100	Factor risk sediment DF = 100 Total	Factor risk sediment DF = 100 Added	PEC local sediment DF = 1,000	Factor risk sediment DF = 1,000 Total	Factor risk sediment DF = 1,000 Added
	mg kg^{-1} $_{dry\ wt.}$	-	-	mg kg^{-1} $_{dry\ wt.}$	-	
MSW Incineration plant (10% collection; total cadmium)	8.6	3.7	2.3	3.3	1.4	0.26
MSW Incineration plant (75% collection; total cadmium)	6.8	2.95	1.8	3.0	1.3	0.13

These results are based, however, on no correction for the bioavailability of cadmium in sediments (SEM/AVS method). A **conclusion (i)** program is ongoing (see separate document).

Removing all NiCd batteries resembles the current scenario as presented in **Table 3.258** (i.e. assumption at start that 10% of the Cd load is due to NiCd batteries).

3.3.3.2.6 Sensitivity analysis

Table 3.261 Local risk characterisation incinerator for water and STP (at dilution factor 100 and 1,000). Sensitivity analysis: effluent = 0.009 mg L^{-1}. The factor risk = PEC/PNEC. The $PNEC_{water}$ is 0.19 µg Cd/L. The PNEC for micro-organisms is 20 µg L^{-1}(Table 3.245). Total cadmium concentrations

Scenario	PEC local water DF = 100	Factor risk water DF = 100	PEC local water DF = 1,000	Factor risk water DF = 1,000	Ceffluent	Factor risk STP
	µg L^{-1}	-	µg L^{-1}	-	mg L^{-1}	
MSW Incineration plant (10%; total cadmium)	0.14	0.68	0.13	0.68	0.009	0.45

Table 3.261 indicates no risks (both scenarios) for the aquatic compartment for a maximal measured effluent concentration of 0.009 mg L^{-1}

Table 3.262 Local risk characterisation incinerators for sediments for a generic MSW incineration plant in the EU. Sensitivity analysis: effluent = 0.009 mg L^{-1}(at dilution factor 100 and 1,000). The factor risk = PEC/PNEC. The $PNEC_{sediment}$ is 2.3 mg kg^{-1} dry wt. The factor risk is calculated for the concentration of added Cd ($Clocal_{sediment}$) and for the added and regional Cd (total Cd, i.e. $PEC_{sediment}$) without correction for bioavailability. Total cadmium concentrations

Scenario	PEC local sediment DF = 100	Factor risk sediment DF = 100 Total	Factor risk sediment DF = 100 Added	PEC local sediment DF = 1,000	Factor risk sediment DF = 1,000 Total	Factor risk sediment DF = 1,000 Added
	mg kg^{-1} dry wt.	-	-	mg kg^{-1} dry wt.	-	
MSW Incineration plant (10%; total cadmium)	6.6	2.86	1.71	3.05	1.7	0.56

For all scenarios a risk is predicted for sediment organisms. Based only on local emissions (i.e. without the regional background contribution), no risk is predicted when a dilution factor of 1,000 is applicable. These results are based, however, on no correction for the bioavailability of cadmium in sediments (SEM/AVS method). A **conclusion (i)** program is ongoing (see separate document).

3.3.3.2.7 Risk characterisation for MSW landfills

Since cadmium emissions from landfills reflect always all cadmium sources a comparative risk assessment has been made. First the risk associated with the total cadmium emissions is given. This analysis is followed by the calculation of the risks associated with the total cadmium without NiCd batteries.

Table 3.263 Local risk characterisation landfills (leachate concentration 5 µg L^{-1}) for water, sediment and STP. Scenario 1 = direct discharge to surface water. Scenario 2 = indirect discharge to surface water (STP). The factor risk = PEC/PNEC. The $PNEC_{water}$ is 0.19 µg Cd/L. The $PNEC_{sediment}$ is 2.3 mg kg^{-1} $_{dry\ wt.}$. The factor risk is calculated for the concentration of added Cd ($Clocal_{sediment}$) and for the added and regional Cd (total Cd, i.e. $PEC_{sediment}$) without correction for bioavailability. The PNEC for micro-organisms is 20 µg L^{-1} (Table 3.245). Total cadmium concentrations

Use-category	N°	PEClocal water	Factor risk water	PEClocal sediment	Factor risk sediment Total	Factor risk sediment Added	$C_{effluent}$	Factor risk STP
		µg /L		mg kg^{-1} dry wt.			mg L^{-1}	
MSW landfill (total cadmium)	1	0.12	0.63	3.8	1.6	0.5	0.005	n.r.
MSW landfill (total cadmium)	2	0.12	0.63	3.1	1.3	0.2	0.00024[a]	0.012

n.r. Not relevant
a) 5 µg L^{-1}/ 21 (21 being the dilution factor in STP see Table 3.95)

No risks to the aquatic environment are observed for landfills emitting a leachate with total cadmium content of 5 µg L^{-1}.

A risk is observed for all scenarios for the sediment compartment. However, based only on local emissions (i.e. without the background contribution) no risk is predicted at landfills with a leachate concentration of 5 µg L^{-1}.

In **Table 3.264** the RCR values for the scenario where all NiCd batteries would be removed from the MSW stream is given. The influence on the RCR values is negligible.

Table 3.264 Local risk characterisation landfills (leachate concentration 5 µg L^{-1}) for water, sediment and STP. Scenario 1 = direct discharge to surface water. Scenario 2 = indirect discharge to surface water (STP). The factor risk = PEC/PNEC. The $PNEC_{water}$ is 0.19 µg Cd/L. The $PNEC_{sediment}$ is 2.3 mg kg^{-1} $_{dry\ wt.}$. The factor risk is calculated for the concentration of added Cd ($Clocal_{sediment}$) and for the added and regional Cd (total Cd, i.e. $PEC_{sediment}$) without correction for bioavailability.The PNEC for micro-organisms is 20 µg L^{-1}(Table 3.245). All cadmium without NiCd batteries

Use-category	N°	PEClocal water	Factor risk water	PEClocal sediment	Factor risk sediment Total	Factor risk sediment Added
		µg /L		mg kg^{-1} dry wt.		
MSW Landfill (NiCd batteries contributed for 10%)	1	0.12	0.63	3.7	1.6	0.4
MSW Landfill (NiCd batteries contributed for 50%)		0.12	0.63	3.3	1.4	0.6
MSW Landfill (NiCd batteries contributed for 10%)	2	0.12	0.63	3.1	1.3	0.3
MSW Landfill (NiCd batteries contributed for 50%)		0.12	0.63	2.9	1.3	0.3

n.r. Not relevant;
a) 5 µg L^{-1}/ 21 (21 being the dilution factor in STP see Table 3.95).

Sensitivity analysis

Table 3.265 Local risk characterisation landfills (leachate concentration 50 µg L^{-1}) for water, sediment and STP. Scenario 1 = direct discharge to surface water. Scenario 2 = indirect discharge to surface water (STP). The factor risk = PEC/PNEC. The $PNEC_{water}$ is 0.19 µg Cd/L. The $PNEC_{sediment}$ is 2.3 mg kg^{-1} dry wt. The factor risk is calculated for the concentration of added Cd ($Clocal_{sediment}$) and for the added and regional Cd (total Cd, i.e. $PEC_{sediment}$) without correction for bioavailability. The PNEC for micro-organisms is 20 µg L^{-1}(Table 3.245). Total cadmium concentrations

Use-category	N°	PEClocal water	Factor risk water	PEClocal sediment	Factor risk sediment Total	Factor risk sediment Added	$C_{effluent}$	Factor risk STP
		µg L^{-1}		mg kg^{-1} dry wt			mg L^{-1}	
MSW landfill (total cadmium)	1	0.21	1.1	14.9	6.5	5.3	0.050	n.r.
MSW landfill (total cadmium)	2	0.15	0.79	6.8	3	1.8	0.0024[a]	0.12

n.r. Not relevant;

a) 50 µg L^{-1}/ 21 (21 being the dilution factor in STP see Table 3.95).

No risks to the aquatic environment are observed for landfills emitting a leachate with a total cadmium content of 50 µg $L^{-1}$to a STP. If this leachate concentration is discharged immediately to the surface water a risk is predicted for the scenario 'all cadmium in MSW'. Based on PEC and PNEC values not corrected for bioavailability, a risk is observed for all scenarios for the sediment compartment. These results are based, however, on no correction for the bioavailability of cadmium in sediments (SEM/AVS method). A **conclusion (i)** program is ongoing. Furthermore, an uncertainty analysis regards the impact of an EU-wide variability in PEC reg (as a default approach in the absence of site-specific data) on the risk characterisation at local level, is not yet included. Both aspects, bioavailability and variability impact, will be implemented in an update of the risk assessment report once the results of the **conclusion (i)** program are agreed at TC NES level (see separate document).

No risks are expected for the off-site STP.

Uncertainty analysis

It should be noted that an assessment factor of 2 has been included in the PNEC derivation due to remaining uncertainty.

The uncertainty surrounding the PNEC water influences the risk conclusion for the landfill discharging a landfill leachate with a cadmium concentration of 50 µg L^{-1}directly in a river. If no assessment factor is applied this scenario would not have a local risk anymore (RCR = 0.55) for the water compartment.

Using measured regional values

Aforementioned exposure estimations and risk assessment are based on calculated PEC reg (i.e. 0.11 µg L^{-1}). Preference should, however, be given to measured values when available. However in the absence of reliable and representative regional measured data in the vicinity of the individual sites the RCR values have also been calculated (results not shown) using the average of the measured P90 values for different countries (i.e. 0.12 µg L^{-1}) and also using the median of the measured P90 values (i.e. 0.07 µg L^{-1}).

The use of the average measured regional PEC concentration (0.12 µg L^{-1}) or the median regional PEC concentration (0.07 µg L^{-1}) does not change the risk conclusions.

In **Table 3.266** the RCR values for the scenario where all NiCd batteries would be removed from the MSW stream is given. The influence on the RCR values is negligible at the exception of the case where NiCd batteries for their Cd content contribute to 50% of the MSW and the landfill leachate is directly discharged to surface water. In the latter case, a reduction of the factor risk water of 23.6% is obtained, resulting in a 'no risk' situation.

Table 3.266 Local risk characterisation landfills (leachate concentration 50 µg L^{-1}) for water and sediment. Scenario 1 = direct discharge to surface water. Scenario 2 = indirect discharge to surface water (STP). The factor risk = PEC/PNEC. The $PNEC_{water}$ is 0.19 µg Cd/L. The $PNEC_{sediment}$ is 2.3 mg kg^{-1} $_{dry\ wt.}$. The factor risk is calculated for the concentration of added Cd ($Clocal_{sediment}$) and for the added and regional Cd (total Cd, i.e. $PEC_{sediment}$) without correction for bioavailability.The PNEC for micro-organisms is 20 µg L^{-1}(Table 3.245). Total cadmium without NiCd batteries

Use-category	N°	PEClocal Water	Factor risk water	PEClocal sediment	Factor risk sediment Total	Factor risk sediment Added
		µg /L		mg kg^{-1} $_{dry\ wt.}$		
MSW Landfill (NiCd batteries contributed for 10%)	1	0.20	1.1	13.7	6.0	4.8
MSW Landfill (NiCd batteries contributed for 50%)		0.16	0.84	8.8	3.8	2.7
MSW Landfill (NiCd batteries contributed for 10%)	2	0.14	0.7	6.3	2.7	1.6
MSW Landfill (NiCd batteries contributed for 50%)		0.13	0.68	4.7	2.0	0.9

n.r. Not relevant;
a) 50 µg L^{-1}/ 21 (21being the dilution factor in STP see Table 3.95).

3.3.3.3 The atmospheric compartment

No risk characterisation can be made since no data were found on Cd toxicity for organisms in the atmospheric compartment[61].

Calculated local PEC values range from 0.561 to 22.6 ng/m^3 for NiCd batteries producers and from 0.561 to 1.91 ng/m^3 for Cd recycling plants.

The PEClocal in air at a distance of 100 m from a generic MSW incineration plant is 7.5 ng/m^3 (average EU situation). Taking into account the contribution from batteries to the MSW (10%-50%), PEC local in air varies between 1.3 and 4.1 ng/m^3.

In the worst case situation (France) a PEClocal in air of 28.5 ng/m^3 can be calculated (all MSW). Taking into account the contribution from batteries to the MSW (10%-50%), PEC local in air varies between 3.4 and 14.5 ng/m^3.

[61] For health risk evaluation reference is made to the 'global' RAR on Cd/CdO (see Section 4 of this report in separate document as well as to Section 2.3 (legislative) control measures).

3.3.3.4 The terrestrial compartment

3.3.3.4.1 NiCd producing/recycling plants

The ratio PEC/PNEC for local soil risk assessment is given in **Table 3.267**. The $PNEC_{soil}$ value is 0.9 mg kg^{-1} dry wt and is the lowest for local risk assessment

No risk is predicted at all sites. The risk factors for soil are 0.5. This conclusion should be treated with caution. The local soil concentrations are calculated after 10 years exposure. In Section 3.1.3.1.3 it is mentioned that for Cd producing sites having high emissions to air (> 800 kg Cd/year) risk factors are above 1 when Cd concentrations are predicted in soil after 50 years aerial deposition. Since neither NiCd batteries producers nor Cd recyclers emit these high Cd quantities to air, the 50 years exposure calculation does not seem relevant in the context of this report.

3.3.3.4.2 MSW incinerators

No risk to soil organisms (or higher food chain via secondary poisoning) is predicted at the hypothetical EU incineration plants.

Table 3.267 Local risk characterisation for soil. The factor risk = PEC/PNEC. The PNEC value = 0.9 mg $kg^{-}_{dry\ wt.}$ is equivalent to 0.79 mg $kg_{wet\ wt.}$ (standard environmental characteristics, TGD) and is the lowest for local risk assessment based on toxicity mammals through secondary poisoning (Table 3.245)

Use-category	Plant N°	$PEClocal_{soil}$ mg $kg_{wet\ wt.}$	Factor risk soil	Year
NiCd-batteries	1	0.36	0.5	1999
	2	0.36	0.5	1999
	3	0.36	0.5	2000
	4	0.37	0.5	2000
	5	0.37	0.5	2000
	6	0.36	0.5	1999
	7	0.37	0.5	1999
Cd recyclers	1	0.36	0.5	2000
	2	0.36	0.5	1999
MSW incineration (all scenarios and total cadmium)		0.36-0.3737	0.5	

No future scenarios were developed for this compartment.

3.3.4 Risk characterisation for all scenarios: update data (year 2002)

In the following subsections risk characterisation is performed for those companies/sectors that submitted new exposure data (reference year 2002). This means that the current update assessment overwrites the RCR values and conclusions derived for corresponding companies/sectors reported in the previous stand-alone documents (global RAR, TRAR).

For the use scenarios ‘alloys’ and ‘plating’ no update exposure data were provided. Therefore the values and conclusions as previously reported remain valid.

3.3.4.1 The aquatic compartment (including sediment)

The risk factors (PEC/PNEC ratio) for WWTP/STP, local water (dissolved fraction) and sediment concentrations for the freshwater environment are given in **Table 3.268**. The PNEC was not corrected for water hardness because of lack of site-specific water hardness information.

Table 3.268 Local risk characterisation of Cd/CdO production/processing sites for WWTP/STP, water and sediment (modelled data). The factor risk = PEC/PNEC. The $PNEC_{micro\text{-}organisms}$ is 20 µg L^{-1}, The $PNEC_{water}$ is 0.19 µg Cd/L and the $PNEC_{sediment}$ is 2.3 mg Cd/kg_{dw}.(Table 3.245). The factor risk for sediments is calculated for the concentration of added Cd ($Clocal_{sediment}$, Table 3.137) and for the added+regional Cd (total Cd, i.e. $PEClocal_{sediment}$, Table 3.137). The results for the sediment compartment are based on no correction for the bioavailability of cadmium in sediments (SEM/AVS method). A conclusion (i) program is ongoing

Plant N°	$PEC_{WWTP/STP}$ (dissolved fraction)	Factor risk WWTP/STP	$PEClocal_{water}$ (dissolved Cd)	Factor risk water	$PEClocal_{sediment}$	Factor risk sediment (added)	Factor risk sediment (total)	Year
	µg L^{-1}		µg L^{-1}		mg kg^{-1}_{dw}			
Cd metal production								
1	3.6[(d)]	n.r.	0.64	3.36	71.5	29.9	31.1	2002
6	0.7	n.r.	0.11	0.58	2.7	0.01	1.2	2002
7*	50*	n.r.*	0.28*	1.46 [1.25]*	24.5*	9.5*	10.7*	2002
7*	30*	n.r.	0.21*	1.13 [0.92]*	16.2*	5.9*	7.1*	2004
Cd oxide production								
12[(a)]	n.a.	n.a.	0.11	0.58	2.7	0	1.2	2002
NiCd battery production								
2*	107	n.r.	0.15	0.77	7.4	2.0	3.2	2002
3	63	n.r.	0.13	0.69	5.5	1.2	2.4	2002
4	103	n.r.	0.14	0.76	7.2	2.0	3.1	2002
6	No update data							
7	No update data							
NiCd battery recyling								
1	370	n.r.	0.24	1.24	19.0	7.1	8.2	2002
1[(e)]	240	n.r.	0.19	1.01	13.2	4.6	5.8	2004
2[(b)]	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	2002

Table 3.268 continued overleaf

Table 3.268 continued Local risk characterisation of Cd/CdO production/processing sites for WWTP/STP, water and sediment (modelled data). The factor risk = PEC/PNEC. The $PNEC_{micro\text{-}organisms}$ is 20 µg L^{-1}, The $PNEC_{water}$ is 0.19 µg Cd/L and the $PNEC_{sediment}$ is 2.3 mg Cd/kg_{dw}.(Table 3.245). The factor risk for sediments is calculated for the concentration of added Cd ($Clocal_{sediment}$, Table 3.137) and for the added+regional Cd (total Cd, i.e. $PEClocal_{sediment}$, Table 3.137). The results for the sediment compartment are based on no correction for the bioavailability of cadmium in sediments (SEM/AVS method). A conclusion (i) program is ongoing

Plant N°	$PEC_{WWTP/STP}$ (dissolved fraction)	Factor risk WWTP/STP	$PEClocal_{water}$ (dissolved Cd)	Factor risk water	$PEClocal_{sediment}$	Factor risk sediment (added)	Factor risk sediment (total)	Year
	µg L^{-1}		µg L^{-1}		mg kg^{-1}_{dw}			
Cd pigments production								
A	19	n.r.	0.38	1.98	37.4	15.1	16.2	2003
B	19	n.r.	0.12	0.61	3.5	0.4	1.5	2003
C	121	n.r.	0.25	1.32	21.0	8.0	9.1	2003
C(90P)	80	n.r.	0.25	1.34	21.3	8.1	9.3	2004
Cd stabiliser production								
X WWTP	5	0.25						
X STP©	0.4	0.02	0.11	0.58	2.7	0.02	1.2	2002
Y	<5(f)	n.r.	0.12	0.62	3.6	0.4	1.5	2002
Y	<1(g)	n.r.	0.11	0.59	2.8	0.1	1.2	2002

* Emission to the sea: risk characterisation is only indicative and based on PNEC freshwater and PECreg water for freshwater. For water, Industry (Cd metal producer site 7) proposes to use 0.07 µg L^{-1}as local (regional?) background concentration as done by NIVA (NIVA report 4606-2002) resulting in a lower RCR value of 1.25 (2002) and 0.92 (2004) respectively. However, MSR could not validate this latter value. No formal conclusions are drawn for sites emitting to the marine environment;

n.a. Not applicable;

n.r. Not relevant for the on-site WWTP (only physc-chem based);

a) No emission to water; thermal/dry process;

b) No site emission to water. Cleaning water as well as processing water are collected internal (about 100 m3/year) and send to an external waste water treatment plant;

c) Cd concentration in effluent from municipal STP; calculated from Cd concentration in effluent from on-site WWTP; taking into account removal at STP: 60%; extra dilution: 2,000 m^3/day/370 m^3/day = 5.4;

d) The biological based wastewater purification system contains fully adapted, specialised and dedicated micro-organisms. These bacteria are not at all representative for 'standard' micro-organisms communities used in municipal STPs;

e) Emissions from the site are further reduced in 2003/2004 due to efforts to conform to ISO 14000, for which the site has been certified in February 2005;

f) Effluent analysis performed by internal laboratory (two times a month) method MIP-P-PRO-101 rev 2 year 2003;

g) Effluent analysis performed by certified external laboratory (two times a year), method EPA 200.8 (1994).

From **Table 3.268** it can be concluded that risks for freshwater aquatic organisms occur at 1 Cd metal production-sites (site 1), 1 NiCd battery recycling site (site 1) and 2 Cd-pigments producing sites (site A, C). It is to be noted that Cd metal producing plant 7 and NiCd production-site 2 emit effluents to the marine environment. No risk assessment to the marine environment is done in this report. No formal conclusions are drawn for these sites. The PECs presented in **Table 3.268** are 'calculated' local concentrations.

Measured Cd concentrations in surface water – presented in **Table 3.138** - are available for Cd metal production-site 1 and 7 and NiCd battery recycling site 1 and Cd stabiliser site Y.

In conclusion:

- Locally measured data near the Cd producer site 1 (i.e. 1 µg dissolved Cd/L; downstream from the site; including background and possible other sources) point there is predicted risk (risk factor: 5.3).
- For recycling site 1, risk is predicted as well by the locally measured data (i.e. 19.8 µg dissolved CdL, downstream from the discharge point; risk factor: 104) that however include the background and possibly other sources (historical contamination due to infiltration and run-off from old metallurgical slag heaps).
- Measurements at Cd stabiliser site Y are based on not sufficiently sensitive analytical method (detection limit too high) to make a judgment about the background and added concentrations in the receiving river.

Monitoring data are not available for any CdO producing or Cd metal/CdO processing company.

Marine environment:

- The risk characterisation for the marine environment (Cd metal producer site 7 and NiCd battery producer site 2) is based on $PNEC_{freshwater}$ and $PEC_{reg\ water}$ for freshwater. Therefore the risk characterisation for this site is only indicative. No risk assessment to the marine environment is done in this report. Industry's representative for the Cd metal producer site 7 proposes to use 0.07 µg $L^{-1}L^{-1}$ as local (regional?) background concentration as done by NIVA (NIVA report 4606-2002) resulting in a lower RCR value of 1.25 (2002) and 0.92 (2004) respectively. However, MSR could not validate this latter value.

Uncertainty analysis

The uncertainty surrounding the PNEC water is related to several aspects: statistical aspects (confidence limits on the HC5 estimated from the SSD) and more general concerns such as species representativity, the inherent uncertainty about NOEC values compared to the benchmark values, mixed pollution etc. These factors have crystallised in the AF=2 which was agreed. The uncertainty around the PNEC water influences the risk conclusion for Cd recycling plant 1 and Cd pigment plants A and C. If no assessment factor is applied the sites would not have a local risk anymore (RCR = 0.6-0.99) for the water compartment.

Using measured regional values

Aforementioned exposure estimations and risk assessment are based on calculated PEC reg (i.e. 0.11 µg L^{-1}). Preference should, however, be given to measured values when available. However in the absence of reliable and representative regional measured data in the vicinity of the individual sites the RCR values have also been calculated (results not shown) using the average of the measured P90 values for different countries (i.e. 0.12 µg L^{-1}) and also using the median of the measured P90 values (i.e. 0.07 µg L^{-1}).

The use of the average measured regional concentration (0.12 µg L^{-1}) or the median of the measured P90 values (0.07 µg L^{-1}) does not change the risk conclusions (based on 2002 exposure data) for the Cd metal/CdO producing or processing sites.

On the basis of PEC and PNEC values not corrected for bioavailability, risk for benthic organisms is predicted at all sites ($PEClocal_{sediment}$). Most sites involved in Cd production and processing have a risk for benthic organisms irrespective of the regional background ($Clocal_{sediment}$ > $PNEC_{sediment}$) (Cd metal production-site 1 (risk factor: 29.9); NiCd battery production-site 2, 3, 4 (risk factor: 1.2-2.0); NiCd battery recycling site 1 (risk factor: 4.6-7.1) and Cd pigments production-site A, C (risk factor: 8.0-15.1)

Measured Cd concentrations in sediments (without correction for bioavailability) – presented in **Table 3.139** - are available for all Cd metal producing sites, NiCd battery manufacturing site 4 and Cd recycling site 1.

- For Cd metal production-site 1, the measured Cd concentration in sediment sampled upstream and downstream near the discharge point is 5 mg kg^{-1} dw and 1.6 mg kg^{-1} dw respectively. Although still resulting in a risk factor above 1 (for the upstream Cd concentration i.e. 2.2) it is obvious that measured Cd concentrations are situated a factor 14 - 45 below the predicted concentrations; hence the risk is reduced. This site also submitted information on AVS and organic carbon content of the sediments. Using these data, the risk characterisation could further be refined (see outcome of **conclusion (i)** program, see separate document).
- Cadmium metal production-site 6 provides recent upstream and downstream measurements in sediments of 0.64 mg Cd/kg dw and 1.14 mg Cd/kg dw respectively (year 2002). As for site 1, the measured Cd concentrations are below the calculated PECsediment (2.4-4.2 times lower). Risk factors on the basis of measured data are 0.27-0.50 respectively, hence the risk is removed.
- NiCd battery manufacturing site 4 provides recent upstream and downstream measurements in sediments of 3.3 mg Cd/kg dw (100 m upstream) and 4.6 mg Cd/kg dw (3 km downstream) respectively (year 2001). Measured Cd concentrations are situated 1.6-2.2 times below the modelled sediment concentrations. On the basis of these data, the risk is reduced; risk factors varying between 1.4 and 2 are calculated. Please note that the sampling downstream is performed at a location 3 km downstream of the plant; hence influence from other sources is likely.
- Cd recycling site 1 provides recent upstream and downstream measurements in sediments of 55 mg kg^{-1} dw and 133 mg kg^{-1} dw respectively (year 2002). The measured Cd concentrations are 3-7 fold the calculated PEClocal sediment of 19.0 mg kg^{-1} dw. On the basis of these data, risk is confirmed; risk factors are 24-58. Please note that the measured data are influenced by historical contamination (infiltration and run-off waters from old metallurgical slag heaps), hence data should be treated with caution.

For all these scenarios and sites, risk is also predicted based on the measured data that include background and possible other sources.

Monitoring data are not available for any CdO producing or other Cd metal/CdO processing company/sector.

These results are based, however, on no correction for the bioavailability of cadmium in sediments (SEM/AVS method). A **conclusion (i)** program is ongoing (see separate document: ‘RAR Stage II’).

Marine environment:

- For Cd metal production-site 7, discharging in a marine environment, Cd concentrations in sediment are reported near the discharge point for the sampling year 1996: 1.1 mg kg^{-1} dw and in the open sea: 2.1-3.2 mg kg^{-1} dw. The same observation is made as for the other Cd metal producing plants. Measured Cd concentrations, representative for the year 1996, are situated 7.7-22.3 times below the modelled sediment concentrations. On the basis of these ‘old’ data; a risk factor ‘near the discharge point’ of 0.48 would be calculated.

The risk characterisation for the marine environment is only indicative as no PNEC was derived for marine species and the PEC regional is calculated for freshwater. No conclusions are drawn on the sites emitting to the sea.

The risk for micro-organisms in sewage treatment plants is investigated for on-site waste water treatment plants (WWTP) as well as off-site sewage treatment plants (STP).

<u>On-site waste water treatment plants</u>

Information from the specific production and processing sites indicates that methods to remove cadmium from discharge to water are generally in place. However, in general no detailed and/or measured data are available.

Most wastewater treatment at the plants in the Cd production area is based on physical-chemical principles only (see also IPPC report on the best available techniques in the non ferrous metals industries, May 2000). Similar information was confirmed for NiCd battery producers and recyclers (see TRAR/batteries’ related sections, Industry Questionnaire 2002/2003) and Cd containing pigments producers (pers. com., 2005). One Cd metal production plant reports the use of a biological based wastewater purification system that contains fully adapted, specialised and dedicated micro-organisms. It is clear that this type of industrial on-site waste water treatment plant cannot be compared with municipal STPs based on ‘standard’ micro-organism communities. Therefore, it is decided that for the aforementioned sectors, the derivation of the risk factor for the WWTP is not relevant (n.r.) (see **Table 3.268**).

<u>Off-site waste water treatment plants (municipal sewage treatment plants)</u>

For producers of Cd metal and CdO, no discharge occurs to municipal sewage systems, as these sites do emit to surface/sea water or do not emit at all to the aquatic compartment[62]. Therefore, the risk assessment of Cd and CdO producers for off-site STP is not relevant.

Risk to off-site STP is only relevant for the processors that have actual emissions to sewer systems. One stabiliser production-site (site X) reported to discharge its waste water to a municipal STP. Taking into account Cd removal and extra dilution of the WWTP effluent at the municipal STP (discharge rate STP/discharge rate WWTP=5.4) results in an STP effluent concentration of 0.4 µg L^{-1}. Consequently a risk factor of 0.02 is calculated, resulting in a no risk situation for this site.

[62] For Cd metal producers: Industry statements, Zinc RAR; for CdO producers: no release of water effluent.

NiCd battery recycling site 2 reports that waste waters are collected and treated off-site in an external waste water treatment plant (year 2002 data: total volume of waste water: 100 m^3/year; no further data are available) (year 1996 data: 35 tonnes fluid waste per year; Cd content: 20 ppm (total Cd); effluent concentration of off-site STP: 0.2 mg L^{-1}). Although the site does not directly discharge any waste water to the receiving environment, the effluent concentration of the off-site STP is taken forward in the risk characterisation. Since the PEC_{STP} of 200 µg Cd/L exceeds the PNECmicro-organisms of 20 µg $L^{-1}L^{-1}$, a risk occurs at the off-site sewage treatment plant (risk factor = 10).

<u>Conclusions to the risk assessment for the aquatic compartment:</u>

Conclusion (iii)

This conclusion applies to the assessment of:

- the local surface water (freshwater) at 1 Cd metal production-site (site 1), 1 NiCd battery recycling site (site 1) and two Cd pigments producing sites (A, C). Local concentrations are based on modeling. Monitoring data are available for the Cd metal production-site 1 and the NiCd recycling site 1: these data indicate risk at background level but do not allow a judgment regarding potential additional risk caused by the site's operations.
- a risk is predicted for the micro-organisms of the STP for NiCd battery recycling plant 2 discharging its effluent to an off-site STP.

Conclusion (i)

This conclusion applies to the

- For the aquatic compartment, there is a need for better information regarding the toxic effects of cadmium to aquatic organisms under low water hardness conditions.
  In particular, information is required on:
  Cd toxicity testing in very soft waters (H below about 10 mg CaCO3/L). There are no data for the very soft waters and these areas may be unprotected by the proposed PNECwater for soft water (0.08 µg Cd/L).
- For sediment[63], there is a need for further information regarding the bioavailability of cadmium in order to possibly refine the assessment at regional and local level.
  In particular:
  the AVS and organic carbon normalisation should be further validated (see outcome of **conclusion (i)** study program, see separate document, 'RAR Stage II').

Conclusion (ii)

This conclusion applies to:

- the local surface water compartment for the CdO production-site and Cd recycling plant 2 because there are no emissions to water at these sites.
- the local surface water compartment for Cd metal production-site 6, the NiCd battery producing plants (2, 3, 4), Cd pigments producing site B and all Cd stabiliser production-sites (X, Y) emitting to the aquatic compartment.

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[63] After the TMIV'02 last visit discussion on cadmium in sediment a number of MSs (UK, F, DE) and Industry commented on the sediment assessment and the current conclusions drawn in line with the outcome of that last TM (for more details, see effects assessment and risk characterisation).

- no risk is predicted for the local sediment compartment for the CdO production-site and NiCd recycling plant 2 because there are no emissions to water and no additional risk arises from their operations.
- no risk is predicted for the micro-organisms of the STP for Cd stabiliser production-site X discharging its effluent to a municipal STP.

3.3.4.2 The terrestrial compartment

The ratio PEC/PNEC for local soil risk assessment is given in **Table 3.269**. The selected $PNEC_{soil}$ value is 0.9 mg $kg^{-1}{}_{dw}$, which is the lowest $PNEC_{soil}$ value and which is based on secondary poisoning to mammals (see **Table 3.245**).

Table 3.269 Local risk characterisation for soil (modelled data). The factor risk = PEC/PNEC. The PNEC value = 0.9 mg $kg^{-1}{}_{dw}$ is equivalent to 0.79 mg $kg^{-1}{}_{ww}$ (standard environmental characteristics, TGD) and is the lowest for local risk assessment based on toxicity mammals through secondary poisoning (Table 3.245)

Plant N°	$PEClocal_{soil}$	Factor risk soil	Year
	mg kg_{ww}^{-1}		
Cd metal production			
1	0.37	0.47	2002
6	0.36	0.46	2002
7	0.38 – 0.45(d)	0.48 – 0.57	2002
Cd oxide production			
12	0.36	0.46	2005
12	0.36	0.46	2004
NiCd battery production			
2(a)	0.36	0.46	2002
3(b)	n.d.	n.d.	n.d.
4	0.36	0.46	2002
6	No update data		
7	No update data		
NiCd battery recycling			
1	0.36	0.46	2002
1	0.36	0.46	2004
2	0.36	0.46	2002
2bis(c)	0.36	0.46	2002

Table 3.269 continued overleaf

Table 3.269 continued Local risk characterisation for soil (modelled data). The factor risk = PEC/PNEC. The PNEC value = 0.9 mg kg^{-1}_{dw} is equivalent to 0.79 mg kg^{-1}_{ww} (standard environmental characteristics, TGD) and is the lowest for local risk assessment based on toxicity mammals through secondary poisoning (Table 3.245)

Plant N°	PEClocal soil	Factor risk soil	Year
	mg kg_{ww}-1		
Cd pigments production			
A	0.36	0.46	2003
B	0.36	0.46	2003
C	0.36	0.46	2003
Cd stabiliser production			
X		00.46	2002
Y	0.36	0.46	2002

a) Emission from battery manufacturing only; air emissions are broken down between two plants; battery manufacturing and Cd recycling;
b) Air emissions are not monitored. No requirement in the permit since the plant runs a wet process, therefore most emissions are releases in the water;
c) Emissions from Cd recycling unit on the site of battery manufacturing plant 4;
d) PEClocal soil derived on the basis of measured aerial deposition rates;
n.d. No data available.

Calculated $PEClocal_{soil}$ values for all Cd/CdO production and processing sites are situated between 0.36 mg kg^{-1} $_{ww}$ and 0.45 mg kg^{-1} $_{ww}$. Since the modelled PEC_{soil} are situated below the $PNEC_{soil}$ - based on toxicity for mammals through secondary poisoning- none of the sites are predicted to be at risk (risk ratio: 0.6).

Comparing the modelled PEC_{soil} for the local sites with the $PNEC_{soil}$ of 1.15-2.3 mg kg^{-1} $_{dw}$ - based on ecotoxicity for soil organisms - results in the same conclusions i.e. no local risks are predicted (risk ratio: 0.2-0.4).

Conclusion (ii)

This conclusion applies to the assessment of:

- modelled local soil Cd concentrations for Cd metal/CdO production and processing plants (10 years aerial deposition) indicate no risks neither for the terrestrial ecosystem nor for mammals via secondary poisoning.

3.3.4.3 The atmospheric compartment

No risk characterisation can be made since no data were found on Cd toxicity in the atmospheric compartment.

For Cd metal producers, calculated local PEC values range from 8.2 to 41.8 ng/m^3.

For the CdO production plant the local PEC value is varying from 5.6 ng/m^3 (year 2005) to 9.4 ng/m^3.

At the Cd/CdO processing plants the PEClocal in air (at a distance of 100 m) are in the following range:

- Production of NiCd batteries[64]: 3.2 ng/m^3 and 4.4 ng/m^3
- Recycling of NiCd batteries: 0.6 ng/m^3 and 3.6 ng/m^3
- Production of Cd containing pigments: 2.5 and 4.8 ng/m^3
- Production of Cd containing stabilisers: 0.6 and 1.0 ng/m^3

Measurements for the Cd metal producers indicate that annual average Cd concentration– in air at a distance of 300 m-450 m from the site vary between 1.8 and 8.5 ng/m^3.

For NiCd battery production-site 4 an annual average Cd concentration of 0.3 ng/m^3 (50 m from the site) is reported.

For NiCd recycling site 1, the measured data lay in the range of 37 to 126 ng/m^3 (year 2002) and from 15 to 21 ng/m^3 (year 2004), a factor 20 to 35 higher than the calculated values.

However, it should be born in mind that measured data have been reported to be influenced also or very probably by other (industrial) sources. In all cases except one i.e. Cd metal production-site 7, the contribution of specific sources has not (yet) been investigated (semi)quantitatively.

3.3.4.4 Secondary poisoning

Effects of soil-borne Cd on mammals has already been included in the previous section since this pathway is more critical than direct effects on higher plants, soil fauna or soil microbial processes.

[64] Not all production-sites submitted update exposure information. No data were provided by sites 6 and 7. Previous estimates remain valid.

4 HUMAN HEALTH

(see separate document).

5 RESULTS

5.1 INTRODUCTION

Remarks on the scope, the approach and the limitations of the study are given in Section 0.1.

An overview of the batteries' disposal scenarios is depicted in **Figure 5.1**.

Additional note: the conclusions of this report which are formulated in section 3.3.2 and 3.3.3 are updated with exposure data for the reference year 2002 (Section 3.3.4).

Figure 5.1 Overview of the different regional and local scenarios for the disposal phase taken forward in this report (batteries' related sections)

Regional scenarios

100 % incineration		24.4 % incineration-75.6 % landfill	100 % landfill
Current	Future	Current	Current
Total Cd content 10 g tonne^{-1} dry wt. Cd contribution from NiCd batteries: 10-50 %	10 % collection, total Cd content: 24 g tonne^{-1} dry wt. Cd contribution from NiCd batteries: 63 % 75 % collection, total Cd content: 13.2 g tonne^{-1} dry wt. Cd contribution from NiCd batteries: 32 %	Total Cd content 10 g tonne^{-1} dry wt. Cd contribution from NiCd bat.: 10-50 % Total Cd concentration in leachate concentration : 5 µg L^{-1}	Total Cd concentration in leachate concentration : 5 µg L^{-1} Cd contribution from NiCd bat.: 10-50 %

Local scenarios

	Local scenarios future emissions incinerators (equipped with an on-site WWTP)			
	75 %	75 %	10 %	10 %
Dilution factor	100	1,000	100	1,000

	Local scenarios current emissions incinerators (equipped with an on-site WWTP)			
	90th P effluent concentration: 0.005 mg L^{-1}			
Dilution factor	100	1,000	100	1,000

	Local scenarios emissions landfills			
	5 µg L^{-1}	5 µg L^{-1}	50 µg L^{-1}	50 µg L^{-1}
Treatm.	STP	No STP	STP	No STP

5.2 LOCAL LEVEL: CURRENT SITUATION (=UPDATED WITH 2002 DATA AND ASSESSMENT)

5.2.1 Conclusions on cadmium metal

Environment: aquatic ecosystem

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) is reached because:

- there is a predicted local risk for the freshwater aquatic ecosystem at 5 Cd production (cadmium metal: 1 site) or Cd processing (pigments producing sites (A,C), plating and alloy) sites/scenarios. Both latter two are generic scenarios ('Cd plating' and 'Cd alloys'). Local concentrations are based on modelling using site-specific and/or standard default values and could possibly have been refined if substantial monitoring data would have been provided. Monitoring data are available for the Cd metal production-site 1: these data indicate risk at background level but do not allow a judgment regards potential additional risk caused by the site's operations.
- There is anticipated local risk at 1 recycling site where modelled freshwater Cd concentrations exceed the $PNEC_{water}$. This risk would be removed if no assessment factor (i.e. 2 and reflecting the uncertainty) is applied in deriving the PNEC. Monitoring data are available for this site: these data indicate risk at background level but do not allow a judgment regards potential additional risk caused by the site's operations.

Conclusion (i) There is a need for further information and/or testing

Conclusion (i) is reached because:

- the AVS and organic carbon based normalisation should be further validated to refine the risk characterisation to benthic organisms[65] (on local as well as on regional level).
- there is a need for testing the Cd toxicity in very soft waters (H below about 10 mg $CaCO_3$/L). There are no data for the very soft waters and these areas may be unprotected by the proposed $PNEC_{water}$ for soft water (0.08 µg Cd/L).

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Conclusion (ii) is reached because:

- no risk is predicted for the aquatic ecosystem at the NiCd recycling site 2 because there are no emissions to water at this site.

[65] After the TMIV'02 last visit discussion on cadmium in sediment a number of MSs (UK, F, DE) and Industry commented on the sediment assessment and the current conclusions drawn in line with the outcome of that last TM (for more details, see effects assessment and risk characterisation in the overall RAR on Cd/CdO).

- no risk is predicted for the aquatic ecosystem at Cd metal production-site 6, NiCd battery producing sites (2, 3, 4), Cd pigments producing site B and all (two) Cd stabiliser production-sites (X, Y) emitting to the aquatic compartment.
- No risk is anticipated for aquatic organisms at 2 of the 5 NiCd battery producing plants (Site 6 & 7) because they are not emitting to the aquatic compartment.
- No risk is anticipated for aquatic organisms at a hypothetical landfill currently releasing a leachate with 5 µg L^{-1} of cadmium directly or indirectly in the aquatic environment.
- No risks to aquatic organisms are anticipated for current hypothetical incinerator (equipped with an on-site WWTP) total Cd emissions discharging in a river with a dilution factor of 100 to 1,000. Removal of NiCd batteries in the MSW has a negligible influence on the calculated risk ratios.
- No risk is predicted for the local sediment compartment for the CdO production site, some NiCd battery producers (Site 6 & 7) and NiCd recycling plant 2 because there are no emissions to water and no additional risk arises from their operations.
- There is no risk for micro-organisms if the hypothetical landfill site is discharging a leachate with a cadmium concentration of 5µg L^{-1} to a STP.
- There is no risk for micro-organisms if the hypothetical incinerator plant (equipped with an on-site WWTP) is discharging to a STP.

<u>Environment: terrestrial ecosystem</u>

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) is reached because:

- there is a need for limiting the potential risks of cadmium plating and alloy production-sites.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Conclusion (ii) is reached because:

- modelled local soil Cd concentrations for Cd metal production and processing plants (10 years aerial deposition) indicate no risk.
- modelled local soil Cd concentrations for NiCd batteries producing and Cd recycling plants (10 years aerial deposition) indicate no risks neither for the terrestrial ecosystem nor for mammals via secondary poisoning.
- modelled local soil Cd concentrations for the hypothetical MSW incineration plant (equipped with an on-site WWTP) indicate no risks neither for the terrestrial ecosystem nor for mammals via secondary poisoning.

<u>Environment: assessment of secondary poisoning</u>

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Conclusion (ii) is reached because:

- modelled local soil Cd concentrations for Cd metal production and processing plants (10 years aerial deposition) indicate no risk.
- modelled local soil Cd concentrations for NiCd batteries producing and Cd recycling plants (10 years aerial deposition) indicate no risks neither for the terrestrial ecosystem nor for mammals via secondary poisoning.
- modelled local soil Cd concentrations for the hypothetical MSW incineration plant (equipped with an on-site WWTP) indicate no risks neither for the terrestrial ecosystem nor for mammals via secondary poisoning.

Environment: atmosphere

No conclusion is reached because:

No risk characterisation was done for the atmosphere.

Sewage treatment plant

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) is reached because:

- risk to on-site and off-site STP cannot be excluded for plating and alloy industry.
- risk is predicted for the micro-organisms of the STP for the NiCd battery recycling plant (site 2) discharging its effluent to an off-site STP

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Conclusion (ii) is reached because:

- no risk is predicted for the micro-organisms of the STP for Cd stabiliser production-site X discharging its effluent to a municipal STP.

5.2.2 Conclusions on cadmium oxide

Environment: aquatic ecosystem

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) is reached because:

- there is a predicted local risk for the freshwater aquatic ecosystem at 5 Cd production (cadmium metal: 1 site) or Cd processing (pigments producing sites (A,C), plating and alloy) sites/scenarios. Both latter two are generic scenarios (‘Cd plating’ and ‘Cd alloys’). Local concentrations are based on modelling using site-specific and/or standard default values and could possibly have been refined if substantial monitoring data would have been provided. Monitoring data are available for the Cd metal production-site 1: these data indicate risk at background level but do not allow a judgment regards potential additional risk caused by the site’s operations.

- There is anticipated local risk at 1 recycling site where modelled freshwater Cd concentrations exceed the $PNEC_{water}$. This risk would be removed if no assessment factor (i.e. 2 and reflecting most of the uncertainty) is applied in deriving the PNEC. Monitoring data are available for this site: these data indicate risk at background level but do not allow a judgment regards potential additional risk caused by the site's operations.

Conclusion (i) There is a need for further information and/or testing

Conclusion (i) is reached because:

- the AVS and organic carbon based normalisation should be further validated to refine the risk characterisation to benthic organisms[66] (on local as well as on regional level).
- there is a need for testing the Cd toxicity in very soft waters (H below about 10 mg $CaCO_3$/L). There are no data for the very soft waters and these areas may be unprotected by the proposed $PNEC_{water}$ for soft water (0.08 µg Cd L^{-1})

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Conclusion (ii) is reached because:

- no risk is predicted for the aquatic ecosystem at the NiCd recycling site 2 because there are no emissions to water at this site.
- no risk is predicted for the aquatic ecosystem at Cd metal production-site 6, NiCd battery producing sites (2, 3, 4), Cd pigments producing site B and all (two) Cd stabiliser production-sites (X, Y) emitting to the aquatic compartment.
- No risk is anticipated for aquatic organisms at 2 of the 5 NiCd battery producing plants (Site 6 & 7) because they are not emitting to the aquatic compartment.
- No risk is anticipated for aquatic organisms at a hypothetical landfill currently releasing a leachate with 5 µg $L^{-1}$of cadmium directly or indirectly in the aquatic environment
- No risks to aquatic organisms are anticipated for current hypothetical incinerator (equipped with an on-site WWTP) total Cd emissions discharging in a river with a dilution factor of 100 to 1,000. Removal of NiCd batteries in the MSW has a negligible influence on the calculated risk ratios.
- No risk is predicted for the local sediment compartment for the CdO production-site, some NiCd battery producers (Site 6 & 7) and NiCd recycling plant 2 because there are no emissions to water and no additional risk arises from their operations.
- There is no risk for micro-organisms if the hypothetical landfill site is discharging a leachate with a cadmium concentration of 5µg $L^{-1}$to a STP.
- There is no risk for micro-organisms if the hypothetical incinerator plant (equipped with an on-site WWTP) is discharging to a STP.

[66] After the TMIV'02 last visit discussion on cadmium in sediment a number of MSs (UK, F, DE) and Industry commented on the sediment assessment and the current conclusions drawn in line with the outcome of that last TM (for more details, see effects assessment and risk characterisation in the overall RAR on Cd/CdO).

Environment: terrestrial ecosystem

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) is reached because:

- there is a need for limiting the potential risks of cadmium plating and alloy production-sites.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Conclusion (ii) is reached because:

- modelled local soil Cd concentrations for Cd metal production and processing plants (10 years aerial deposition) indicate no risk.
- modelled local soil Cd concentrations for NiCd batteries producing and Cd recycling plants (10 years aerial deposition) indicate no risks neither for the terrestrial ecosystem nor for mammals via secondary poisoning.
- modelled local soil Cd concentrations for the hypothetical MSW incineration plant (equipped with an on-site WWTP) indicate no risks neither for the terrestrial ecosystem nor for mammals via secondary poisoning.

Environment: assessment of secondary poisoning

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Conclusion (ii) is reached because:

- modelled local soil Cd concentrations for Cd metal production and processing plants (10 years aerial deposition) indicate no risk.
- modelled local soil Cd concentrations for NiCd batteries producing and Cd recycling plants (10 years aerial deposition) indicate no risks neither for the terrestrial ecosystem nor for mammals via secondary poisoning.
- modelled local soil Cd concentrations for the hypothetical MSW incineration plant (equipped with an on-site WWTP) indicate no risks neither for the terrestrial ecosystem nor for mammals via secondary poisoning.

Environment: atmosphere

No conclusion is reached because:

No environmental risk characterisation was done for the atmosphere.

Sewage treatment plant

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) is reached because:

- risk to on-site and off-site STP cannot be excluded for plating and alloy industry.

- risk is predicted for the micro-organisms of the STP for the NiCd battery recycling plant (site 2) discharging its effluent to an off-site STP

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Conclusion (ii) is reached because:

- no risk is predicted for the micro-organisms of the STP for Cd stabiliser production-site X discharging its effluent to a municipal STP.

5.3 LOCAL LEVEL: DISPOSAL STEP - FUTURE SITUATION AND/OR SENSITIVITY ANALYSIS

5.3.1 Conclusions on cadmium metal and cadmium oxide

Environment: aquatic ecosystem

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) is reached because:

- There is a potential risk if a hypothetical landfill site discharges a leachate with a cadmium concentration of 50 µg L^{-1}directly to surface water. Removal of NiCd batteries (if contributing to 50% of the Cd content in MSW) will remove the risk.

Conclusion (i) There is a need for further information and/or testing

Conclusion (i) is reached because:

- the AVS and organic carbon based normalisation should be further validated to refine the risk characterisation to benthic organisms[1] (on local as well as on regional level).
- there is a need for testing the Cd toxicity in very soft waters (H below about 10 mg $CaCO_3$/L). There are no data for the very soft waters and these areas may be unprotected by the proposed $PNEC_{water}$ for soft water (0.08 µg Cd L^{-1}).

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Conclusion (ii) is reached because:

- If a hypothetical landfill site discharges a leachate with a cadmium concentration of 50 µg L^{-1}indirectly to surface water (i.e. via STP) no risk to aquatic organisms is expected.
- If only the NiCd battery contribution is taken into account there is also no risk to aquatic organisms predicted for landfills emitting directly to the surface water.

[1] After the TMIV'02 last visit discussion on cadmium in sediment a number of MSs (UK, F, DE) and Industry commented on the sediment assessment and the current conclusions drawn in line with the outcome of that last TM (for more details, see effects assessment and risk characterisation in the overall RAR Cd/CdO).

- No risk is anticipated to the micro-organisms in case a hypothetical incinerator equipped with an on-site WWTP, discharges to a STP under the 75% or 10% collection scenario and landfill emitting a leachate at 50 µg Cd/L to an STP.
- No risks to aquatic organisms are anticipated for the future hypothetical incinerator, equipped with an on-site WWTP, (both scenarios: 10-75% collection) discharging in a river with a dilution factor of 100 to 1,000.
- No risks to aquatic organisms are anticipated for a hypothetical incinerator, equipped with an on-site WWTP, discharging a maximum effluent concentration of 0.007-0.0135 mg L^{-1}in a river with a dilution factor of 100 to 1,000.

Environment: terrestrial ecosystem/secondary poisoning

No conclusion is reached:

There was no future situation and/or sensitivity analysis performed for the terrestrial compartment or for secondary poisoning.

Environment: atmosphere

No environmental risk characterisation was done for the atmosphere.

5.4 REGIONAL LEVEL

5.4.1 Conclusions on cadmium metal and cadmium oxide

Environment: aquatic ecosystem

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) is reached because:

- the *modelled* regional PEC of surface water has a risk factor of 0.6 using a mean K_p value for EU while the risk factor is 1.7 using a K_p value that is distinctly smaller than average. This suggests potential regional risk. However, it is proposed to use measured values for the risk characterisation because of the uncertainties in the choice of the natural background (which is combined with the added concentration to derive the regional PEC) and in the coverage of the surface water with small K_p values. Monitoring data were collected for 13 EU countries (of the EU-16 surveyed) but limitation in data quality (detection limit, geographical coverage etc.) reduced this information to 7 countries (as proxy for regions) for which conclusions can be derived. The regional averages of the 90th percentiles of measured Cd concentrations of European rivers and lakes in these regions range from 0.0395 to 0.31 µg L^{-1}. The majority of regional averaged 90th percentiles have a risk factor < 1 whereas these values are > 1 in the UK (based on a limited dataset of 1996) and the Walloon region of Belgium. Outliers have a large impact on the risk factors as, for example, 20 sites of the 728 investigated in the largest database of UK (data of 2003) determine risk in UK. The PNEC for water was derived with an assessment factor of 2 reflecting most of the uncertainties in the effects assessment. The conclusions about risk in the 2 regions mentioned are not affected by either in- or excluding this assessment factor. During the development of the RRS, decision about (possible) reduction measures has to take into account the information on potential cadmium emission sources in these regions. In order to better characterise the regional risks to surface water in part of the EU which have not been covered in this assessment (i.e. eastern and southern Europe are underrepresented in the entire dataset, because detection limits are often too high and because fractionation is often not reported) it might be useful to obtain more information for these regions. It may be that the foreseen monitoring actions under for example the Water Framework Directive will provide this information in the future.

Environment: terrestrial ecosystem

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) is reached because:

- the 90^{th} percentiles of measured Cd concentrations of European soils have risk factors 0.43-1.56 (mean: 0.86; data from 6 EU countries). Regional risk for the terrestrial ecosystem cannot be excluded in one region (UK). However, it should be noted that the 90^{th} percentile for the UK falls (1.4 mg Cd/kg_{dw}) within the range of the proposed $PNEC_{soil}$ values based on ecotoxicity to soil microbial processes (1.15 – 3.2 mg Cd/kg_{dw}). Hence, risk cannot be excluded but will depend on the magnitude of the assessment factor chosen (either 1 or 2, see 3.2.3.6.2) in the derivation of the $PNEC_{soil}$.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Conclusion (ii) is reached because:

- modelled regional soil Cd concentrations that include natural soil, industrial soil and 8 different agricultural scenarios are all below the $PNEC_{soil}$. All these modelled values are total concentrations that are expected after 60 years (agricultural soils) or far beyond that (natural and industrial soils) with current regional emissions to soil. The starting concentrations are EU average values for the ambient concentrations. If 90^{th} percentiles of measured concentrations would have been used in such calculations, then risk cannot be excluded.

Environment: assessment of secondary poisoning

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) is reached because:

- measured soil Cd concentrations of European soils have risk factors 0.4-1.6 for poisoning to mammals (mean: 0.86; data from 6 EU countries). Regional risk for the terrestrial ecosystem cannot be excluded in one region (UK). The uncertainty surrounding the effects assessment, however, suggests that this is a borderline situation: the available information shows that literature data on Cd uptake in mammals dwelling in acid soils sensitively influences the effects assessment. If data on acid soils (pH <4.2) are excluded from the effects assessment, a larger PNEC is obtained and risk in the UK would be excluded. That conclusion would only remove concern provided that the P90 value in UK does not refer to acid soils, which is unknown. This analysis is, moreover, qualitative because there is no validated model to estimate risk to mammals along the entire range of soil pH.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Conclusion (ii) is reached because

- field data (body burden: kidney and liver Cd data) of birds (excluding pelagic birds) do not indicate Cd poisoning, even in top predators. No risk to mammals is predicted from modelled regional soil Cd concentrations.

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ABBREVIATIONS

,	Comma is used to indicate thousands
.	Point is used to indicate decimals
AC	Active Carbon
AF	assessment factor
Ann.	Annex
Ann.	annual
Avg.	average
AVS	Acid Volatile Sulphides
BCF	bioconcentration factor
BDS	Biological DeSulfurisation
BOD5	Biological oxygen demand (to complete….)
bw	body weight / *Bw*, *b.w.*
°C	degrees Celsius (centigrade)
C_{50}	median immobilisation concentration or median inhibitory concentration 1 / *explained by a footnote if necessary*
CAS	Chemical Abstract System
Cd	Cadmium (metal)
CdO	cadmium oxide
CEC	Commission of the European Communities
CEN	European Committee for Normalisation
CEPE	European Council of the Paint, Printing Ink and Artists' Colours Industry
COD	Chemical oxygen demand
CPT	Cordless power tools
d	day(s)
dl	Detection limit
DF	Dilution factor
DG	Directorate General
DRY	Dry flue air cleaning technique
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{50lab}	period required for 50 percent dissipation under laboratory conditions (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
$DT_{90field}$	period required for 90 percent dissipation under field conditions

	(define method of estimation)
dry wt.	dry weight / $_{dw}$ / DW / d.wt
EC	European Communities
EC	European Commission
EC_{50}	median effective concentration
EEC	European Economic Community
EEE	Electrical and Electronic Equipment
EEIG	Abbreviation for former 'Industry's Interest Group' working on NiCd batteries
EINECS	European Inventory of Existing Commercial Chemical Substances
ELU	Emergency Lighting Units
EPA	Environmental Protection Agency
EU	European Union
EU-16	Member states of the EU AND Norway
EUSES	European Union System for the Evaluation of Substances
ESP	Electrostatic precipitator (air cleaning technique)
FF	Fabric Filter (air cleainign technique)
FGCS	Flue Gas Cleaning System
F_{ww}	Release factor to wastewater
f_{oc}	Fraction of organic carbon
g	gram(s)
Global RAR	EU RAR on cadmium metal and cadmium oxide / overall RAR on Cd/CdO
GLP	Good Laboratory Practice
h	hour(s)
ha	Hectares / *h*
HDPE	
HELP	Hydrologic Evaluation of Landfill Production (US-EPA model see Schroeder)
HPLC	High Pressure Liquid Chromatography
IARC	International Agency for Research on Cancer
ICP	Inductively Coupled Plasma
IC_{50}	median immobilisation concentration or median inhibitory concentration 1 / *explained by a footnote if necessary*
ICdA	International Cadmium Association
IND	Industry
IPPC	Integrated Pollution Prevention and Control
ISO	International Standards Organisation
IUPAC	International Union for Pure Applied Chemistry
IUTA	Institut für Energie- und Umwelttechnik

IZA	International Zinc Association
J	Joule
kg	kilogram(s)
kPa	kilo Pascals
K_{oc}	organic carbon adsorption coefficient
K_{ow}	octanol-water partition coefficient
Kp	Solids water partition coefficient
kt	Kilotonnes / ktonnes
L	litre(s) / l
log	logarithm to the basis 10
$L(E)C_{50}$	Lethal Concentration, Median
LEV	Local Exhaust Ventilation
m	Meter
µg	microgram(s)
mg	milligram(s)
MAC	Maximum Acceptable Concentration
Model I (soil)	Standard EUSES model calculation
Model II (soil)	The alternative model to calculate regional and continental concentrations in agricultural soil is based on the Cd mass balance in the plough layer (cfr section 3.1.2.4.2 of the 'global' RAR on Cd/CdO)
MOS	Margins of Safety
MS	Member States
MSR	Member State Rapporteur / RMS
MSW	Municipal Solid Waste
N/A	Not applicable / n.a.
n.d.	No data available
ng	Nanograms (to complete with conversion factor to grams)
Ni	Nickel
NiCd	Nickel-cadmium batteries / NiCd
NIVA	Norwegian Institute for Water Research
NOAEL	No Observed Adverse Effect Level
NOEC	No Observed Effect Concentration
NOEL	No Observed Effect Level
oc	Organic carbon
OECD	Organisation for Economic Co-operation and Development
OEL	Occupational Exposure Limit
OEM	Original Equipment Manufacturer
OJ	Official Journal

OPS model	Operational Priority Substances model
Pa	Pascal unit(s)
P90	90-percentile of a dataset (result of statistical analysis: 90% of the values in the dataset are situated below the P90)
PBE	Plastic Bonded Electrode
PEC	Predicted Environmental Concentration
pH	potential hydrogen -*logarithm* (to the base 10) of the hydrogen ion concentration $\{H^+\}$
pKa	-*logarithm* (to the base 10) of the acid dissociation constant
pKb	-*logarithm* (to the base 10) of the base dissociation constant
PM10	Fine particulate matter (<10 µm)
PNEC(s)	Predicted No Effect Concentration(s)
$PNEC_{water}$	Predicted No Effect Concentration in Water
(Q)SAR	Quantitative Structure Activity Relationship
Questionnaire	To collect the needed information different types of questionnaires were used dependent on the aim and the target group: Industry questionnaire: for the collection of site-specific exposure data of batteries' producers and recyclers. The initial questionnaire was sent out by Industry in 1998, updates by the rapporteur in 2000 and 2001. The Questionnaire on Batteries : was designed by the rapporteur to obtain information related to the amounts of batteries (i.e. NiCds) put on the market, collection, recycling etc on a country basis. Three subtypes were made depending on the responder: a) Member state (competent authority for the implementation of the Battery Directive); b) Collection organisation (per country) and c) EPBA. This questionnaire was sent out in 2000.
RAR	Risk assessment report
RCR	Risk Characterisation Ratio
SCTEE	Scientific Committe on Toxicity, Ecotoxicity and the Environment / CSTEE
SEM	Simultaneously extracted metal
SRB	Sulphate Reducing Bacteria
STP	Sewage Treatment Plant
St. dev.	Standard deviation
t	Metric tonnes / tonnes / T
TGD	Technical Guidance Document[67]
Revised TGD	Technical Guidance Document[68]

[67] Commission of the European Communities, 1996. Technical Guidance Documents in Support of the Commission Directive 93/67/EEC on risk assessment for new substances and the Commission Regulation (EC) No 1488/94 on risk assessment for existing substances. Commission of the European Communities, Brussels, Belgium.
ISBN 92-827-801[1234]

[68] Commission of the European Communities, 2003. Technical Guidance Document on risk assessment in Support of the Commission Directive 93/67/EEC on risk assessment for new notified substances, Commission Regulation (EC) No 1488/94 on risk assessment for existing substances and Directive 98/8/EC of the European Parliament and the Council concerning the placing of biocidal products on the market. Office for Official Publications of the European Communities, Luxembourg.

TMT	Trimercaptotriazine (flocculans used in wastewater purification)
TOC	Total organic carbon
TRAR	Targeted Risk Assessment Report (this report)
UASB	Upflow Anaerobic Sludge Blanket
UV	Ultraviolet Region of Spectrum
UVCB	Unknown or Variable composition, Complex reaction products or Biological material
v/v	volume per volume ratio
VDI	Verein Deutscher Ingenieure
w/w	weight per weight ratio
w	gram weight
WET	Wet scrubbing (air cleaning technique)
WWTP	Wastewater Treatment Plant
wet wt.	Wet weight / WW / $_{ww}$
y	Year

Annex A The Nordberg-Kjellström kinetic model

The Nordberg-Kjellström model (Kjellström and Nordberg, 1978; Kjellström and Nordberg, 1985) is a linear eight-compartment kinetic model of cadmium metabolism which has the advantage of being able to calculate not only accumulation in the kidney, but in other tissues as well. It is the most detailed and commonly used model for cadmium risk assessment and is discussed in the ATSDR (1999).

The model is based on a number of approximate assumptions, but it appears to be able to calculate the long term accumulation of tissue levels under a number of different exposure situations with reasonable accuracy.

The coefficients C1 - C19 determine the transfer between compartments. In most cases, the daily transfer is assumed to be a fixed proportion of the accumulated amount in the compartment.

It describes the disposition of cadmium via the oral and inhalation routes of exposure. Dermal exposure and skin absorption were assumed to be negligible.

Description of the model by Nordberg and Kjellström (1985):

Absorption and uptake

For inhalation exposure, the model takes into account the different deposition patterns for different size particles in nasopharyngeal, tracheobronchial, and alveolar regions of the respiratory tract. Cadmium compounds are inhaled as particulate matter, either as fumes with very small particle size or as dust. The general principles for deposition and absorption of particulate matter described by the Task Group on Lung Dynamics * and by the Task group on Metal Accumulation ** were taken to be valid for cadmium and were used in this model. Particles with MMAD (mass median aerodynamic diameter) of 5 µm were assumed to distribute mainly to the nasopharyngeal region (75%) with lesser amounts depositing in the alveolar (20%) and tracheobronchial (5%) regions. Particles of 0.05 µm MMAD (i.e., cigarette smoke) were assumed to deposit 55% in the alveolar compartment, 10% in the tracheobronchial compartment and none in the nasopharyngeal compartment. The remaining amounts are exhaled. The respiratory Cd intake (A) can be diverted to the gastro-intestinal tract (C · A) due to the clearance of Cd deposited on the mucosa of nasopharynx, trachea, or bronchi. It can also be deposited in the alveoli (C2 · A) and from there be absorbed into the blood (C3 · E1). The remainder of the respiratory intake is exhaled. Some of the Cd in the alveoli is transported via alveolar clearance back to the bronchi (C4 · E1) and eventually to the gastro-intestinal tract after swallowing. Based on data given by the Task Group on Lung Dynamics, C1 was estimated at 0.1 to 0.2 for Cd fumes and at 0.4 to 0.9 for Cd dust. Calculations with different values were carried out and a best fit between calculated and empirical values was found for C1 = 0.1 (fume) and 0.7 (dust). In accordance with the difference in the distribution of small (fume) and large (dust) particles, C2 was estimated to be 0.4 to .06 for fume and 0.1 to 0.3 for dust. The best fit values for all coefficients are listed in **Table A1**. The alveolar clearance is likely to be small in comparison with the rest of the lung clearance and C4 was assumed to be 0.1 · C3.

Cadmium intake via the gastro-intestinal tract consists of food cadmium (G) and Cd cleared from alveoli (C4 · E1) and respiratory tract (C1 · A). Most of Cd in the intestinal lumen will pass unabsorbed and the retention C5 was assumed to be in the range 0.03 to 0.1. The Cd retained in the intestinal wall will accumulate to a certain extent before being absorbed into blood. C6 was assumed to be 0.05/day, but available data are insufficient to estimate this coefficient with accuracy. The total amount of Cd absorbed into blood each day (C3 · E1 + C6 · E2) is called daily uptake (I µg/day).

Transport and distribution

The blood was divided into three compartments: the albumin-bound Cd (B1), the cell-bound Cd (B2), and the metallothionein-bound Cd (B3). The turn-over of Cd in B1 and B3 is very rapid and all Cd input into these compartments is assumed to have continued to other compartments within less than a day. Thus the contribution of B1 and B3 to whole blood Cd concentration is less than the calculated amounts in these compartments. This fraction (C20) was assumed to be in range 0.05 to 0.5. The part of Cd uptake (C7 · I) which is bound to metallothionein (B3) will continue mainly to kidney and urine. As about a third of the body burden after long-term exposure is in the kidneys, C7 was assumed to be 0.2 to 0.4. The B3 compartment has a limited number of binding sites and therefore, the daily flow from I to B3 was maximised by C8 (0.5 to 5 µg/day).

Accumulation in B2 is determined by the turn-over rate of red blood cells. The mean life of erythrocytes is 120 days which implies a half-time of 83 days and C16 would be 0.008/day. For the modelling, it was assumed that C16 would be in the range of 0.004 to 0.015/day. From B1, Cd is transferred to red blood cells (B2), liver (L), and other tissues (T), and via intestinal wall cells to faeces (F). The proportions of B1 distributed to L and T were assumed to agree approximately with their proportion of whole body burden of Cd (16% for L, 50% for T). Thus, C12 was assumed to be 0.1 to 0.4 and C9 was set at 0.4 to 0.8. The liver is a main organ for metallothionein production and it was assumed that most of the cadmium in B3 came from the liver (C14 · L). From B2, metallothionein-bound Cd will add to the B3 compartment and the B3-Cd is cleared through the kidney glomeruli. Some Cd is reabsorbed in the proximal tubuli (C17 · B3) and adds to kidney accumulation (K) and the rest is excreted via urine (U). About 95% of the glomerular filtrate of Cd-metallothionein is reabsorbed in the renal tubuli of mice, hence C17 was assumed to be in the range 0.8 to 0.98. Tubular reabsorptive capacity decreases with age. Between 30 and 80 years, it decreased 33%. In the model a similar decrease was assumed. Cd is transported back from liver, kidney, and other tissues to the blood. This is assumed to occur mainly to the B compartment (C10 · T, C13 · L, and C18 · K), but the liver also contributes to B3 (C14 · L).

Excretion

Almost all Cd in the body is excreted via faeces and urine. Faecal Cd consists mainly of the non-absorbed part of ingested Cd. “True” faecal excretion originates from blood via the intestinal wall (C11 · B1) and from bile (C15 · L). The main part of biliary cadmium is correlated with the amount of cadmium in liver. C15 was assumed to be in the range 0 to 0.0001/day. With long-term low level exposure faecal and urinary excretion are about the same. Urinary excretion is mainly a function of the body burden, but a part of this excretion is directly dependent on blood Cd. This has been taken into consideration by splitting urinary excretion into two parts: (1-C17) · B3 coming from blood and C19 · K coming from kidney. At steady state, the total daily excretion would be the same as total daily uptake. In Sweden, the average adult daily Cd intake via food is about 16 µg and the average body burden of non-smokers is about 5 mg at 50 years. With a gastro-intestinal absorption rate of 5%, the daily uptake (0.8 µg) would be 0.016% of body burden.

Average adult (30-60 years) urinary excretion is approximately 0.35 µg/day. Thus, the daily excretion rate for urine would be 0.007% of body burden and, by subtraction from the estimated total excretion; the faecal excretion would be 0.009% of body burden.

Retention and accumulation

The main part of body burden will be found in the liver (L), the kidneys (K) and other tissues (T) (muscles, skin, and bones). C13 was set at 0 to 0.0001/ay and C14 at 0.001 to 0.003/day which in combination with C15 gave a half-time in liver between 4 and 19 years. C19 was estimated to be in the range 0.00002 to 0.0002/day, and C18 in the range 0 to 0.0001/day. The corresponding range of kidney half-times would be 6 to 38 years. It was also assumed that C19 increases linearly after age 30 with C21 each year. Initially, C21 was set at 0 to 0.000002/day. Very little data are available regarding half-times in other tissues. It was found that age-dependent accumulation curves for Cd in muscle indicate an even longer half-time than for kidney. With long-term low level exposure about half of the body burden is in other tissues, indicating that a major accumulation occurs there as well as in liver and kidneys. C10 was assumed to be in the range 0.00004 to 0.0002/day corresponding to half-times between 9 and 47 years.

Table A.1 Assumed and modelled values of coefficients (Kjellström and Nordberg, 1985)

Coefficients	Initially assumed ranges [a]	Unit	Values fitting to empirical data
C1	0.1- 0.2 (cigarette smoke) 0.4 - 0.9 (factory dust)		0.1 0.7
C2	0.4- 0.6 (cigarette smoke) 0.1 - 0.3 (factory dust)		0.4 0.13
C3	0.01 - 1	day^{-1}	0.05
C4	0.1 · C3 = 0.001 - 0.1	day^{-1}	0.005
C5	0.03 - 0.1		0.048
C6	0.05	day^{-1}	0.05
C7	0.2 - 0.4		0.25
C8	0.5 - 5	µg	1
C9	0.4 - 0.8		0.44
C10	0.00004 - 0.0002	day^{-1}	0.00014
C11	0.05 - 0.5		0.27
C12	0.1 - 0.4		0.25
C13	0 - 0.0001	day^{-1}	0.00003
C14	0.0001 - 0.0003	day^{-1}	0.00016
C15	0 - 0.0001	day^{-1}	0.00005
C16	0.004 - 0.015	day^{-1}	0.012
C17b	0.8 - 0.989		0.95
C18	0 - 0.0001	day^{-1}	0.00001
C19cadmium	0.00002 - 0.0002	day^{-1}	0.00014
CXd	0.01 - 0.05		0.04

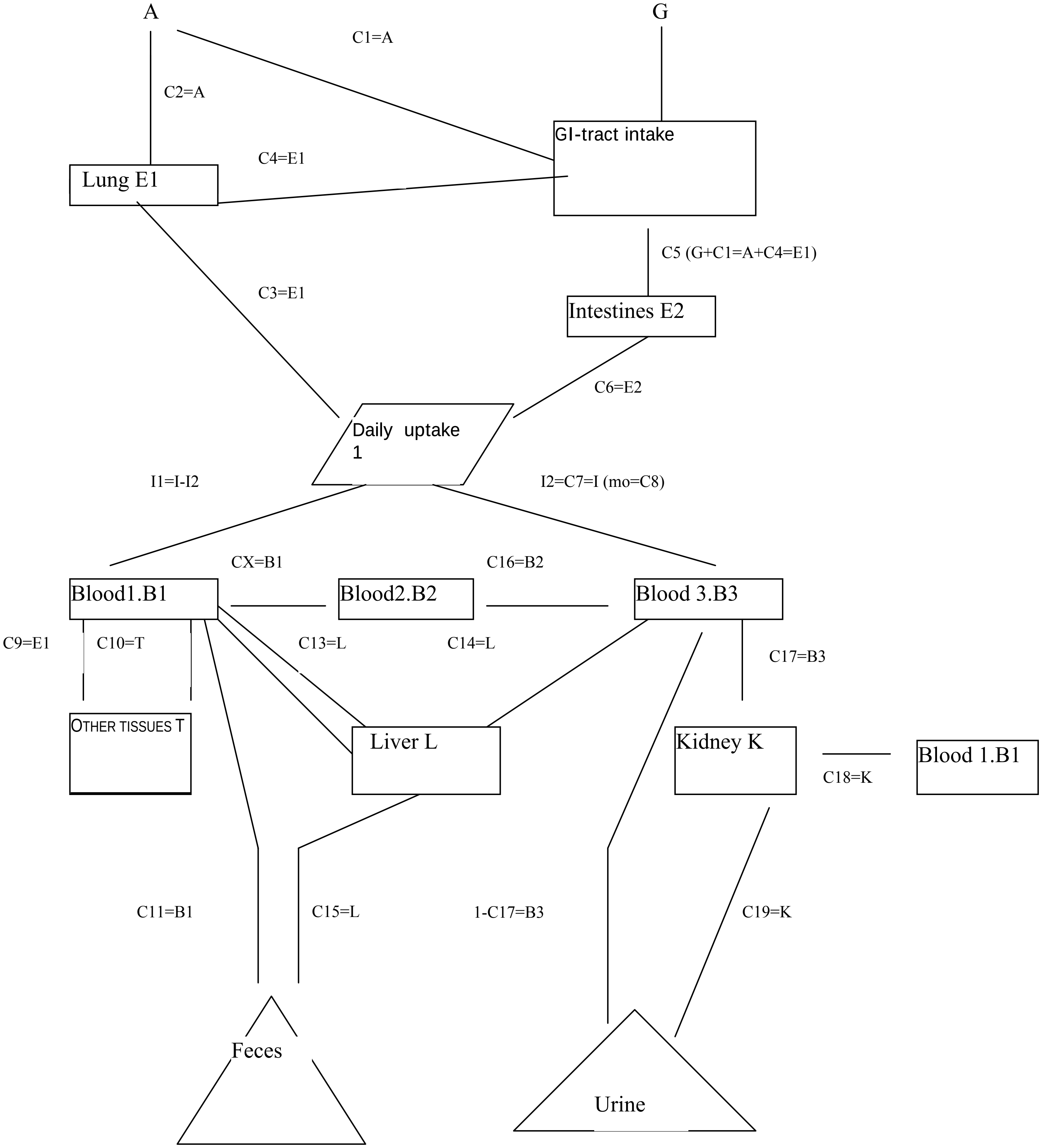
Table A.1 continued overleaf

Table A.1 continued Assumed and modelled values of coefficients (Kjellström and Nordberg, 1985)

Coefficients	Initially assumed ranges a	Unit	values fitting to empirical data
C20	0.05 - 0.5		0.1
C21	0 – 0.000002	day^{-1}	0.0000011

a If no unit is given, this means that the coefficient is a unitless proportion
b C17 decreases from age 30 to age 80 by 33%
c C19 increases from age 30 with C21 each year
d Cx = 1 - C9 - C11 - C12
* Task Group on Lung Dynamics, Deposition and retention models for internal dosimetry of the human respiratory tract. Health Phys, 12, 173-208, 1966
** Task Group on Metal Accumulation, Accumulation of toxic metals with special reference to their absorption, excretion and biological half-times. Environ Physiol Biochem, 3, 65-107, 1973

Figure A.1 Flow scheme of the Nordberg-Kjellström kinetic model of cadmium metabolism



Annex B Metallothionein

Metallothionein

In tissues, the majority of cadmium is bound to metallothionein, a low molecular weight protein (approximately 6,600 kDa) rich in cysteinyl thiol groups but deficient in aromatic amino acids. Metallothionein has been detected in human kidney, liver, heart, brain, testis, skin epithelial cells and in human embryonic fibroblasts from skin, muscles and lung. In animals, the protein has also been found in placenta, spleen and intestinal mucosa.

Separation techniques based on the charge properties of metallothionein, such as ion-exchange chromatography and iso-electric focusing, have shown that different forms of metallothionein often exist in the same organ. Usually two main forms of metallothionein are found: MT-I and MT-II. As a rule the total amount of metal ions bound to each metallothionein molecule is constant, but the types of metal ions might differ. Apart from having a different molar ratio of metals, the two different forms of metallothionein from the same species and tissues have also been shown to have slightly different amino acid composition (CRC, 1986). Transgenic mice deficient for MT-I and MT-II have been produced (Michalska and Choo; 1993)

Metallothionein is normally present in animal tissues in only trace amounts. Induction of its synthesis is under the control of a large group of genes and is stimulated by glucocorticoids and the essential metals Zn and Cu. Exposure to certain metals such as Cd, Hg, Zn, Ag, Cu, Mg can increase the concentration of MT in the liver and/or kidney, and possibly other tissues. It has also been observed that metallothionein can be induced by formaldehyde, carbon tetrachloride, hormones, drugs, alkylating agents, alcohol, infection, inflammation, food deprivation, irradiation (UV-X), cold, strenuous exercises. Certain metals appear to show organ specificity in regard to their ability to increase concentration of MT. For example, Hg and Zn induce the synthesis of MT in the kidney and the liver, respectively, whereas Cd induces synthesis in both the liver and the kidney (Waalkes and Goering, 1990; Kotsonis and Klaassen, 1978).

The exact physiologic functions of metallothionein are not known but it is thought to play an important role in the biological detoxification of metals, including Cd. It has been shown that following Cd exposure, Cd is predominantly associated with metallothionein and pretreatment with metals known to stimulate the synthesis of metallothionein prevents the toxicity of subsequent Cd exposure (Leber and Miya, 1976; Yoshikawa, 1973; Jin et al., 1986). A deficiency in metallothionein appears to occur in several mammalian tissues that are highly susceptible to the toxic effects of Cd. Rat, mouse, monkey testes, rat ventral prostate, hamster ovary are known to be susceptible to either the acute or/and chronic carcinogenic effects of Cd and appear to be deficient in metallothionein as assessed by biochemical analysis of Cd-binding protein (Waalkes and Goering, 1990).

The observed correlation between cellular Cd and MT is the result of the cell's responding to increased intracellular Cd levels by increasing the synthesis of MT. Experiment carried out on MT I and MT II null mice also support the conclusion that the persistence of Cd in the body is at least partially due to Cd binding to metallothionein in tissues (Liu et al., 1996). More than 60-80% of the Cd in the kidneys and liver is bound to MT. MT is , however, also found in other tissues, usually in amounts proportional to the Cd or Zn content. The biological half-time of Cd-MT appears to be in the order of days; this is considerably shorter than the biological half-life of Cd. Thus a constant synthesis of MT must take place in order to sequester the Cd ions which have been released from the degraded MT (Elinder and Nordberg, 1985, CRC).

The low molecular weight of metallothionein enables the protein to be filtered through the kidney glomerular membrane; it is subsequently reabsorbed by the proximal tubule cells where it can compete with other proteins for the reabsorption site. The Cd-metallothionein complex is degraded in lysosomes with release of Cd, which may induce metallothionein synthesis in the proximal tubule. This process continues until the capacity of the cell to synthesise metallothionein is exceeded. The renal toxicity of Cd is associated with Cd not bound to metallothionein. However, brush-border membranes of the renal tubule may be damaged by cadmium that is bound to metallothionein (Suzuki and Cherian, 1987; Cherian and Goyer, 1976).

The synthesis of MT in the kidney cells is considerably slower than in the liver cells. The tissue MT level is mainly related to the tissue deposition of the inducing metal.

In rats, the concentrations of MT and Cd in both kidney and liver increase with dose and time. However, the rates of increase of MT and Cd are not the same in the liver and the kidney. In the kidney , the ratio of Cd to MT increases with time; in the liver, however, the ratio reaches a plateau. This phenomenon may explain why in rats the liver apparently has a tolerance to Cd during prolonged exposure that is the synthesis of MT in the liver appears to keep abreast with continually increasing concentration of Cd and thus limits the concentration of the non-MT-bound-Cd. However, in the kidney the ratio continues to increase with time that may explain why renal injury is observed during prolonged Cd exposure. In other words, the amount of Cd taken up by the kidney increases at a faster rate than does the amount of MT (Elinder and Nordberg, 1985).

LD_{50} of $CdCl_2$ by the intraperitoneal route are not different in wild type and MT-deficient animals and the distribution of Cd in tissues (24 hour post-treatment) was not different between the two strains, indicating that the basal level of MT does apparently not protect against acute Cd toxicity. Pretreatement with Zn (MT induction) protected however wildtype but not MT-deficient mice (Conrad et al., 1997). Using a similar dosing regimen (single administration of radiolabeled Cd, ip). Liu et al. (1996) confirmed that the initial distribution of Cd was not affected by the presence of MT. However, the elimination of Cd was found much faster in MT-null mice, with a 2-fold reduction of the Cd dose retained in the liver after 24 hours and later. Cd concentration in kidney continued to increase with time in control but not in MT-null mice, indicating that an important source of Cd in the kidney is the uptake of CdMT.

Alveolar macrophages were recovered by BAL from 10 healthy nonsmokers and 10 cigarette smokers to determine whether increased concentrations of Cd were present in the macrophages of cigarette smokers and whether metallothionein accumulated in response to the presence of cadmium. Cd was detected in the alveolar macrophages of all subjects, with a higher mean in cigarette smokers (3.4 ± 0.5 versus. 1.3 ± 0.2 ng/10^6 cells; $p < 0.005$). There was a correlation between current smoking history (cigarettes per day) and the alveolar macrophage content of cadmium. The mean metallothionein content was similar in both groups, despite the higher Cd content in the alveolar macrophages of smokers. This could be due, according to the authors, either to the fact that Cd concentrations in cigarette smoke are insufficient to induce metallothionein synthesis or to a greater saturation of this protein (Grasseschi et al., 2003).

MT and nephrotoxicity

Results from experimental studies carried out mainly with $CdCl_2$ suggest that the Cd-metallothionein complex is a nephrotoxin when injected but when it is synthesised within the cell it may protect from cadmium toxicity temporarily.

The distribution of Cd from a nephrotoxic dose of radiolabeled Cd-MT was compared in subcellular fractions of kidney cortex of rats with pre-induced MT synthesis (by $CdCl_2$) and of controls. In the pretreated rats, Cd in the plasma membrane and microsome fractions of renal cortex cells was mainly bound to MT and other low molecular weight proteins. In nonpretreated rats, the major part of Cd was bound to high molecular weight proteins. The animals with pre-induced MT synthesis were protected against the toxic effects of Cd-MT, whereas the control animals later developed nephrotoxic effects (Nordberg et al., 1994).

The prevalence of nephrotoxicity rather than hepatotoxicity in chronic Cd exposure may be due to several factors (WHO, 1992):

- the release of hepatic Cd-MT or its presence in the blood can result in preferential accumulation of Cd in kidneys;
- the kidney can accumulate MT mRNA in response to Cd exposure to only about half the level of the liver (Koropatnick and Cherian, 1988)

Thus the kidney may not be able to synthesise MT as efficiently as the liver in response to Cd exposure, resulting in an accumulation of non MT-Cd in the kidney but not in the liver.

Pretreatment with Cd entails increased tolerance to subsequent exposure to Cd.

Parenterally administered Cd-MT is highly nephrotoxic. The distribution of a single dose of Cd salts differs considerably from that of Cd-MT. A couple of hours after Cd salt was administered, about 50% of the dose was found in the liver and only about 10%, or less, in the kidney. However, when Cd-MT was administered, up to 90% was found in the kidneys 2 hours later (Elinder and Nordberg, 1985).

When Cd is given in the form of Cd-MT the LD_{50} is only about one tenth of that for inorganic Cd salts. It has been suggested that the mechanism underlying this phenomenon is, probably, glomerular filtration of Cd-MT and a subsequent efficient uptake from the tubular fluid into the tubular cells by pinocytosis followed by a rapid degradation in lysosomes and release of Cd from its protein ligand in the cytoplasm. Tubular cells have a certain capacity for producing their own metallothionein which can bind Cd and thereby prevent the toxic effects of Cd ions. Following large doses of Cd-MT, the cells cannot cope with all the Cd being released and cell damage occurs. The occurrence of non MT-bound-Cd ions in the tubular cells produces the toxic effects.

The free Cd pool is sufficiently large to gives rise to interact with membrane targets to block calcium transport routes, and there is deficient uptake and transport of calcium through the cell.

When injected parenterally, a high influx of Cd-MT occurring in the tubules can overload the sequestration mechanism of the de novo cellular synthesis of MT. Such acute toxicity does not occur in human exposure that takes place by oral or inhalation routes, which can only provide a limited flow of Cd-MT (Elinder and Nordberg, 1985; Vahter, 1996).

In a further experiment using a single dose of Cd intraperitoneally (25 µmole/kg as $CdCl_2$ or as Cd-MT complex), Liu et al. (1996) compared the heptoxic and nephrotoxic responses to $CdCl_2$ and Cd-MT, respectively. They concluded that MT plays less of a protective role in protecting against CdMT-induced nephrotoxicity than CdCl2-induced hepatotoxicity, and that Zn-induced protection against CdMT-induced nephrotoxicity does not appear to be mediated through MT.

Table B.1 Comparison of the heptoxic and nephrotoxic responses to $CdCl_2$ and Cd-MT

	Liver toxicity ($CdCl_2$)	Renal toxicity (Cd-MT)
MT +/+ mice	+++	+++
MT-/- mice	+	+++
effect of Zn pretreatment	protects +/+ only	protects +/+ and -/-

Chronic toxic effects of Cd in the kidney are likely to occur when tubular cell capacity for producing MT is insufficient to sequester all the Cd ions in the cell cytoplasm.

Chronic Cd administration of $CdCl_2$ produces renal injury in MT-null mice, indicating that Cd-induced nephrotoxicity is not necessarily mediated through the CdMT complex (Liu et al., 1998; Liu et al., 2000). However, MT protects against chronic $CdC1_2$ nephropathy, suggesting that intracellular MT is an important adaptive mechanism decreasing $CdC1_2$ nephrotoxicity (Liu et al., 1999), and that a single injection of CdMT may not be a good model to study chronic Cd nephropathy (Klaassen and Liu, 1998).

There are likely species differences with regard to the capacity of different animals to produce MT in the renal cortex. Therefore, signs of renal toxicity may occur at different total concentrations of Cd. In the case of human exposure, constitutional factors as well as age and simultaneous exposure to other nephrotoxic agents may influence renal MT in production capacity and thus the susceptibility of the kidneys to Cd (CRC, 1986). The exact impact of these possible variations in humans is however not clearly identified.

Zn pretreatment protects against the nephrotoxicity of Cd-MT. Several mechanisms have been suggested (Tang et al., 1998):

- the induction of the synthesis of MT by Zn and sequestration of Cd^{++} released from the lysosomial degradation of exogenous Cd-MT by the newly synthesised renal MT. However even MT-null mice are protected by Zn (Liu et al., 1996);
- plasma Zn seems to displace some of the Cd from Cd-MT and thus decreases renal Cd accumulation
- it appears to reduce the pinocytic uptake of Cd-MT complex by affectng the stability of the renal brush border membrane (Chvapil, 1973)
- more recently, GSH has been proposed as an important factor in regulating Cd-MT nephrotoxicity. Exogenous GSH can reduce Cd-MT nephrotoxicity in MT-null mice, while depletion of GSH severely enhanced the nephrotoxicity of Cd-MT. Although Zn does not require elevation of renal cortex GSH levels for protection against Cd-MT nephrotoxicity, the protection depends on the maintenance of normal intracellular GSH levels. While Zn reduces both Cd and MT accumulation, it does not alter the subcellular distribution of Cd. Zn protection in the MT-null mice appears to be through the reduction of Cd accumulation in the renal cortical epithelial cells to a level where the normal GSH levels are sufficient to prevent toxic interactions of Cd^{++} with sensitive intracellular sites (Tang et al., 1998).

Habeebu et al. (2000) have shown that MT also protects against the bone toxicity of Cd. Upon repeated sc injections of $CdCl_2$ over a wide range of doses for 10 weeks, they found no difference in bone Cd content between wild-type and MT-null mice. Repeated Cd injections produced, however, a dose-dependent loss of bone mass (up to 25%), as shown by analysis of the femur, tibia, and lumbar vertebrae. The loss of bone mass was more marked in MT-null mice than in wild-type mice, as shown by dry bone weight, defatted bone weight, bone ash weight, and total calcium content. X-ray photography showed decreasing bone density along the entire bone length with increasing dose and time of Cd exposure.

Annex C Cadmium exposure and End-Stage Renal Disease (ESRD)

Critical original studies

a) Retrospective mortality studies

Studies from Japan: Jinzu River basin, Toyama Prefecture

Nakagawa et al. (1990) examined the mortality (20-year follow-up) of Itai-Itai disease patients, patients suspected of having Itai-Itai disease, and control subjects matched for age, gender, and place of residence. Most cases were women (186 out of 190). Control subjects had neither proteinuria nor glucosuria (sulfosalicylic acid method and Benedict's reaction, respectively). Briefly summarised, Itai-Itai patients had the highest mortality and patients suspected of having Itai-Itai disease had a higher mortality than the control subjects. The increased mortality of patients with and suspected of Itai-Itai became statistically significant after three and 18 years of follow-up, respectively. However, some questions remain open. Firstly, the Cd body burden and the values of the renal parameters are not given and it is not known whether there was a relationship between these variables and mortality. Secondly, it is not clear whether the cause of death was due to end-stage renal disease or to another cause. This is an important issue because some observations suggest that the relationship between cadmium exposure and Itai-Itai disease is not univocal as several factors may have influenced cadmium toxicity in humans including nutritional deficiencies in calcium, protein, vitamin D, and iron, or zinc intake (ATSDR, 1999). As most of these factors may reflect unfavourable living conditions (low socio-economic level), it cannot be excluded that they were to some extent responsible for the increased mortality. Thirdly, regarding renal function it would be extremely important to know whether the patients diagnosed with Itai-Itai disease used non-steroidal anti-inflammatory drugs. Indeed, some authors have stressed the potential role of these agents in the progression to chronic renal disease (De Broe and Elseviers, 1998), the use of analgesic therapy for relief of pain due to osteomalacia has been reported in Itai-Itai patients (Kagamimori et al., 1986), and an interaction between acetaminophen and Cd effects has been described in experimental animals (Bernard et al., 1988). In human studies conducted in Belgium also, the use of analgesics was found to significantly influence tubular parameters alone or in interaction with the Cd body burden (Buchet al., 1990; Hotz et al., 1999).

A last issue is the possible publication bias. Indeed, two other surveys dealing with the mortality of the population from the Jinzu River basin found no increased mortality and were published in Japanese only (abstracts unavailable on Medline), one of them reported that the mortality was low especially in the highly polluted area (Shigematsu et al., 1982; Shigematsu et al., 1980). Similarly, the publication dealing with the possible confounding factors is available in Japanese only (Kawano et al., 1981). Thus, no overall assessment of all these studies can be made. Furthermore, the study by Nakagawa et al. (1990) extends the findings reported by Kawano et al. (1986); both reports can, therefore, not be considered as independent with which consistency can be examined.

To summarise, the aforementioned study (Nakagawa et al., 1990) concludes to an association between Itai-Itai disease and increased "all causes" mortality. However, both the causal role of Cd and its association with end-stage renal disease remain unclear. In particular, it would be interesting to know whether men with a similar Cd body burden had an increased mortality as well. Moreover, the fact that results showing an increased mortality were published in English and in international journals (Nakagawa et al., 1990; Kawano et al., 1986) unlike the results of the negative study (Shigematsu et al., 1982; Shigematsu et al., 1980) or those of the report on the comparability of the control group (Kawano et al., 1981), may suggest a publication bias.

Studies from Japan: Kosaka Town, Akita Prefecture

Iwata et al. (1992) found an increased "all causes" mortality in women (but not in men) with increased urinary β2M and/or total amino nitrogen concentration which was attributed to exposure to Cd in the environment. These results were published in English in an international journal whereas a negative study (Ono and Saito, 1985) from the same region is available in Japanese only (a very short abstract could be found in Nakagawa et al., 1990).

Again, only the "all causes" mortality is known, there is no specific data on ESRD, and the publication of the negative study in Japanese only makes an overall evaluation of the results extremely difficult and suggests a publication bias.

Studies from Japan: Kakehashi River basin, Ishikawa Prefecture

Nishijo et al. (1995) reported an increased mortality from "nephritis and nephrosis" in persons with tubular dysfunction diagnosed in 1974-1975 (15 year follow-up, 930 deaths or 38.6% of the subjects having participated in the 1974-1975 survey, tubular dysfunction assessed by semi-quantitative urinary RBP concentration) thought to be due to environmental cadmium exposure in the Kakehashi River basin. However, a diagnostic suspicion bias is possible. Indeed, all cases of "urinary tract diseases" were recorded in the group without increased RBP whereas no case with this diagnosis was found in the group with increased RBP. That some persons with "urinary tract diseases" and increased RBP were diagnosed erroneously with "nephritis and nephrosis" is likely because diagnoses were apparently not confirmed objectively. Furthermore, the authors noted that the quality of the death certificates was not very satisfactory (Nishijo et al., 1995).

More importantly, Nishijo et al. (1994) examined the mortality in the population from the same region using β2M instead of RBP as an indicator of tubular dysfunction. Although they found an increased mortality in subjects with increased β2M "most deaths were due to non-specific cardiac disease such as heart failure and cerebro-vascular diseases". A further important fact was that cases with increased total urinary protein were overrepresented and total urinary protein concentrations higher in the group with increased β2M concentrations (Nakagawa et al., 1993). Further analysis of the results presented by these authors (Nishijo et al., 1994) suggests that the group of subjects with increased β2M was not homogenous and included a subgroup of subjects with cardiovascular risk factor (as indicated by increased urinary protein) (Ruggenenti et al., 1998; Grimm et al., 1997) but without increased urinary β2M. Therefore, increased cardiovascular risk factors could be considered as associated with but not due to the cadmium exposure. Finally, an association between individual cadmium body burden and mortality from renal disease was not reported. Taken together, these results suggest that patients with cardiovascular risk factors as indicated by an increased urinary protein concentration could have been overrepresented in the subgroup with increased β2M and that this finding may not have been associated with cadmium exposure. Indeed, others have found that it is unlikely that Cd exposure could be associated with the risk of cardiovascular diseases in a causal way (Staessen et al., 1991 and 2000). It should also be borne in mind that the association between age and β2M excretion has been suggested as a possible source of error (Park, 1991).

In 1999, the same authors published a 15 year follow-up of 3,119 inhabitants living in the same Cd polluted areas of the Kakehashi River bassin (1,403 men, and 1,716 women) (Nishijo et al., 1999). The age-specific cumulative survival curves were lower with increasing Cd-U measured in 1981-82 (< 5, 5-9.9, 10-19.9 and > 20 µg/g creatinine), suggesting a dose-response relationship between Cd exposure and mortality. As this study is an extension of the previous follow-up published by Nakagawa et al. (1993), the same comments hold for the present report.

To summarise, these studies from the Kakehashi River basin are compatible with Cd causing ESRD but other explanations seem plausible as well.

Studies from Japan: Sasu, Nagasaki Prefecture

In their historical cohort study, Iwata et al. (1991) examined the mortality of 256 subjects (participation rate over 80%) living in a Cd-polluted area. After a 10-year follow-up, 65 subjects (25.4%) had died. In a subgroup of residents (with a urinary β2M concentration greater than 1,000 µg/g creat in 1979), observed deaths were greater than expected. Using a Cox's proportional hazard model, the influence of age, mean blood pressure, Cd-U, and β2M on all causes mortality was examined. β2M proved to be a predictor of mortality in men (but not in women) whereas Cd-U was not ($p > 0.4$). The association between β2M and mortality in men only is surprising because both β2M and Cd-U concentrations were higher in women than in men. Cause-specific mortality was not calculated because of "uncertainty of the diagnosis". It is reported that the serum creatinine concentration of the most severe case was 3.2 mg/100 ml (no further details on serum creatinine or GFR measurements).

To summarise, no straightforward relationship between Cd body burden and uraemia was demonstrated in this study.

Mortality studies conducted outside Japan

The village of Shipham (UK) was contaminated by considerable quantities of toxic metal cadmium from nearby extinct calamine workings. Harvey et al. (1979) have conducted a limited study on 21 adults living in the most heavily polluted areas of the village to measure their liver-cadmium concentration. Their mean age was 53 years (40-62) and they had lived there on the average for more than 20 years, 3 were light smokers and 50% of the vegetables they consumed were of local origin. The mean liver-cadmium concentration in these villagers was 11.0±2.0 ppm which was significantly higher than that of 10 non-Shipham controls (2.2±2.0 ppm) of similar age (Harvey et al., 1979). The results of the survey conducted later in Shipham (Inskip et al., 1982) do neither refute nor support an association between renal diseases and environmental cadmium exposure because of small sample size, crude exposure assessment, and lack of dose-response relationship. A follow-up of the mortality in this cohort has been reported by Elliot et al. (2000). There was an excess mortality from cerebro-vascular disease, hypertension, nephritis and nephrosis (for the latter SMR 128, 95% CI: 99-162). However, it was not possible to separate the diagnoses included in the latter category, so that it remains unclear whether the effect is associated with nephritis or nephrosis (Elliot et al., 2000).

Lauwerys and De Wals (1981) wrote a letter drawing attention to a possible relationship between Cd exposure (environmental) and nephritis and nephrosis. Owing to the limitations of this type of publication, definitive conclusions relative to a causal relationship between Cd exposure and ESRD are not possible.

b) Longitudinal morbidity studies

Besides retrospective mortality studies, there are also publications dealing with the renal function in Cd-exposed subjects followed-up for some years.

Kido et al. (1990) assessed the course of glomerular function in members of the same population as Nishijo et al. (1995). These authors concluded that Cd exposure is capable of causing progressive glomerular damage. Although it cannot be excluded on the basis of the available data that long-term and high-level exposure to Cd in the environment causes glomerular dysfunction, several potential sources of error should also be considered. Indeed, although the renal parameters were non-specific for the effects of Cd, other causes of renal dysfunction were not systematically ruled out. Moreover, there was no clear dose-effect relationship, latency time did not show a consistent trend, it seems possible that the definition of the groups was based on criteria defined a posteriori, and it is not clear whether the study population was a representative sample of the whole exposed population.

In the longitudinal study by Kido et al. (1988) only tubular markers were considered and it is not known whether the subjects examined are the same as those included in the publication of 1990.

The frequently cited study of Nogawa et al. (1984) included glomerular markers but was a cross-sectional study, a design that is not very suitable to establish a causal relationship.

c) Case reports and case series

A case series including four persons exposed to cadmium and diagnosed with uremia is discussed by Tsuchiya (1992) and Kido et al. (1990) reported one case of renal insufficiency attributed to environmental exposure. Nagakawa et al. (1990) described briefly an autopsy series but it is unclear whether Cd-induced renal failure was the main cause of death (original report is available in Japanese only). Although case reports and case series are useful for drawing attention to some problem, they are weak study designs to demonstrate the existence of a causal relationship.

Annex D Kidney effects

Buchet et al. (1990). Renal effects of cadmium body burden of the general population. Lancet 336:699-702 – Detailed calculations.

In the logistic model, the probability of “elevated” value is:

$P=1/1+\exp-(a+ß_1X+ß_2Y)$

Table D.1 Parameters of the logistic model

	ß coefficient	SE on ß	p value
Constant	-1.5793	0.3906	< 0.001
Age	-0.0303	0.0088	< 0.001
U-Cd*	1.6093	0.4087	< 0.001

SE Standard error
* Cd-U is expressed as log µmol Cd-U/24h centered on the mean of the group (0.837 µg/24h)

Therefore, at age 47 years and Cd-U=2 µg/24 hours (centered log = 0.378)

$P=1/1+\exp-(-1.5793+1.6093 \cdot 0.378-0.0303 \cdot 47)$

= 0.084 or about 10% probability of elevated Ca-U

Probability of elevated Ca-U

Table D.2 Probability of elevated Cd-U

	Age 40 years	Age 50 years
Cd-U (µg/24hours)		
0	0.058	0.045
1	0.065	0.049
2	0.101	0.076

Järup et al. (2000). Low level exposure to cadmium and early kidney damage: the OSCAR study Occup Environ Med 57:668-672 - Detailed recalculations based on the raw data provided by the authors.

1) Total population

In a logistic regression analysis the estimated probability (p) can also be expressed as:

$p = [\exp(a + ß_1X + ß_2Y)]/[1 + \exp(a + ß_1X + ß_2Y)]$

Table D.3 Parameters of the logistic model

	ß coefficient	SE on ß	95% CI	p value
Constant	-5.07	0.428	-5.908 to -4.227	< 0.001
Age	0.056	0.007	0.0425 to 0.070	< 0.001
U-Cd	0.295	0.086	0.125 to 0.464	0.001

CI Confidence intervals

Therefore, at age 53 years and Cd-U=1.2 µg/g creat,

$$p = \exp(-5.07 + 0.056 \cdot 53 + 0.295 \cdot 1.2)/(1 + \exp(-5.07 + 0.056 \cdot 53 + 0.295 \cdot 1.2))$$

= 0.147 or about 15% probability of elevated HC values.

Probability of HC proteinuria

Table D.4 Probability of HC proteinuria

	Age 40 years	Age 53 years
Cd-U (µg/g creatinine)		
0	0.056	0.10
1.2	0.078	0.15
2.62	0.113	0.20

2) Subgroup after exclusion of individuals with occupational exposure

Table D.5 Parameters of the logistic model

	ß coefficient	SE on ß	p value
constant	-5.02	0.476	< 0.001
Age	0.045	0.007	< 0.001
U-Cd	1.535	0.297	0.0001

Probability of HC proteinuria

Table D.6 Probability of HC proteinuria

	Age 52-y
Cd-U (µg/g creatinine)	
0	0.06
0.5	0.13
1.0	0.24

Annex E *In vitro* studies

Some *in vitro* studies were conducted in an attempt to elucidate about the mechanism of the developmental and reproductive effects associated with an exposure to cadmium (generic). These studies were performed with water-soluble cadmium compounds.

No study specifically using cadmium oxide was located. One study using cadmium metal is reported here.

Studies have suggested that Cd accumulates in the placenta and exerts its toxicity either directly by creating placental damage or through perturbation of placental transport of nutrients such as calcium and zinc.

Wier et al. (1990) perfused lobes of placenta from normal-term deliveries of non-smoking women with cadmium (as cadmium chloride) at 0-11 mg/l for up to 12 hours. Cadmium content in the perfused tissue was dose-dependent. Alterations of circulatory parameters appeared at doses of 2.2 and 11 mg/l and were correlated with ultra structural alterations (between 5 and 8 hour perfusion): stromal oedema appeared with microvesicular changes in the endoplasmic reticulum, mitochondrial swelling in the syncitiotrophoblast; followed by subsyncitiotrophoblastic vesiculation and finally necrosis of the trophoblast (occurring between 5 and 8 hours of perfusion). There were no effects reported on glucose consumption or lactate production. However, cadmium (at 1.1 mg/l) reduced the placental transfer of zinc into the foetal circuit (Wier et al., 1990). Page et al. (1992) reported that cadmium at 5-50 µM inhibited zinc uptake by placental microvillous membranes (Page et al., 1992 cited in Lin et al., 1997).

Cadmium may also perturb the placental transport of calcium. To investigate the involved mechanism, Lin et al. (1997) used a human choriocarcinoma cell line, which exhibits trophoblastic properties. Culture medium contained low concentrations (0.04, 0.16, 0.64 µM) of cadmium as $CdCl_2$. Cadmium treatment at low, physiological doses (0.04 µM), for 24 hours did not compromise cellular integrity but decreased cellular calcium uptake and transport, calcium ion binding and modified intracellular Ca^{2+} profile. Higher doses (≥ 16µM) affected cell integrity (as assessed by lactate dehydrogenase release). The 24-hour treatment resulted also in a reduced expression of the trophoblast-specific cytosolic Ca^{2+}-binding protein (HcaBP). These results suggested that cadmium exposure compromised the calcium handling ability of trophoblastic cells as a consequence of alterations in subcellular, cytosolic Ca^{2+} binding activities (Lin et al.,1997).

Wier et al. (1990) also reported that the perfusion of cadmium (as cadmium chloride) in lobes of placenta decreased the synthesis and the release of human chorionic gonadotropin at all experimental concentrations (0-11 mg/l). This was confirmed by the study of Eisenmann and Miller (1994) that compared the toxicity of cadmium (2.2 mg/l) and selenium in a similar experimental system.

Cadmium induces the synthesis of metallothionein which may exert a protective effect against the toxicity of several heavy metal ions. To illustrate this and also the competition with other elements such as zinc, Lehman and Poisner (1984) used an *in vitro* system and studied the induction of metallothionein in human tissues exposed to Cd or Zn. Human chorionic trophoblast cells were exposed to different concentrations of cadmium (compound not specified): for dose-response experiments, Cd (1-32 µM) or Zn (5-20 µM) was added and incubation was continued for 24 hours. For time-course experiments, doses of 0.5-2 µM Cd were applied in medium and incubation was continued for 8, 24 or 48 hours. To determine the effect of simultaneous addition of Cd and Zn, an experiment was done in which Cd (0.5, 1µM) and Zn (2.5, 5µM) were added separately or together to the cells and incubation was continued for 24 hours.

Concentrations of cadmium as low as 0.5 µM significantly increased MT synthesis. Higher concentrations of zinc were required to obtain the same phenomenon (2.5 µM). When the cells were exposed to the metals for 24 hours, the increased MT levels remained elevated at least 48 hours after removing Cd or Zn. When Cd and Zn were applied simultaneously to the trophoblasts, the resulting increase in the concentration of MT was similar to the increase in MT found in cells exposed to Cd alone (data reported on histogram).

Cd has been reported to bind MT approximately 3,000 times more strongly than Zn (see Section 4 of this report in a separate document). It has been reported that Cd may displace zinc, by competing for the same binding site. The results of this study demonstrated the ability of cultured human trophoblasts to synthesise MT in response to Cd or Zn and that lower concentrations of cadmium than zinc are required for this synthesis.

Considering this, authors concluded that MT synthesised in foetal membranes may play a role in protecting the foetus from cadmium-toxicity (Lehman and Poisner, 1984).

In relation to a possible role of cadmium in mechanisms of preterm labour, effects of cadmium on the activity of myometrial strips from term pregnant women were examined by Sipowicz et al. (1995). Cadmium (Cd^{2+}) in a concentration of 10^{-9} M inhibited spontaneous contractile activity. Responses to Ca^{2+} and oxytocin were significantly increased by exposure to cadmium in low concentrations (10^{-9} M), whereas higher concentrations (10^{-3} M) had inhibitory action. These results suggest that cadmium not only blocks Ca^{2+} channels in the human myometrium, but also interferes with intracellular mechanisms involved in excitation-contraction coupling. The increased responses to Ca^{2+} and oxytocin in the presence of low amounts of Cd^{2+} support a role of cadmium in mechanisms of preterm labour (Sipowicz et al., 1995).

Clough et al. (1990) reported that cultured rat Sertoli cells were more sensitive to cadmium chloride than interstitial (primary Leydig) cells. Different cell populations within a same tissue differed markedly in susceptibility to the toxicant: the 72-hour LC_{50} for Sertoli and interstitial cells were 4.1 and 19.6 µM, respectively. Because the Sertoli cell provides support for the seminiferous epithelium, the differential sensitivity of this cell may in part explain cadmium-induced testicular dysfunction, particularly at doses that leave intact the vascular epithelium (Clough et al., 1990).

Laskey and Phelps (1991) also showed a reduction of rat Leydig cell function following *in vitro* exposure to cadmium chloride at concentrations of 1 to 5,000 µM for 3 hours (Laskey and Phelps, 1991, cited in IARC 1993).

The toxicity to the human spermatozoa of cadmium metal (200 mm^2 in a flask) was already tested by Holland and White in 1979. Human ejaculates were obtained and motility of the spermatozoa was estimated before to be incubated with the metal for 3 hours under constant shaking. Oxygen uptake, glucose utilisation and oxidation, lactate accumulation were also measured. Cadmium reduced significantly the percentage of motile spermatozoa (73.0 ± 2.5% and 43.0 ± 2.0% at 0 and 3 hours respectively) and decreased the quantity of glucose used by the spermatozoa. As cadmium had a detrimental effect on the motility of the spermatozoa but only moderately depressed glycolysis and had even less effect on oxidative metabolism, authors suggested that cadmium may specifically inhibit the motility apparatus of the spermatozoa (Holland and White, 1979).

Fertility of ejaculates of rabbit sperm after *in vitro* exposure to $CdCl_2$ (0.02-0.05-0.1 mM) was tested by Foote (1999). Semen was washed to remove seminal plasma and minimise possible bindings of the metal by proteins. Exposure of the sperm was followed by insemination of superovulated does. The concentrations used to treat the sperm *in vitro* were, as reported by the authors, higher than the concentrations found in semen and/or blood of men exposed to heavy metals in occupational studies. The tested concentrations of Cd^{2+} did not reduce hyperactivity of the sperm. The fertility tests also resulted in little or no difference, consistent with the findings that Cd did not affect the proportion of hyperactive sperm , a variable often associated with capacitation (required for fertilisation) (Foote, 1999).

Conclusions: in vitro studies

Most of the located studies have used water-soluble cadmium compounds and not cadmium metal or cadmium oxide.

Different mechanisms, which may account for reprotoxic effects of cadmium, have been suggested, involving a direct placental damage, an indirect action via a perturbation of the placental transport of other nutrients or an effect on the synthesis or release of human chorionic gonadotropin.

Some cell populations (Sertoli cells) were reported to be more susceptible than others to a toxic effect of cadmium compounds, which could explain the rather specific action of cadmium compounds on the testes in experimental animals when injected.

Cadmium metal appeared to reduce motility of human spermatozoa *in vitro* after 3 hours of incubation. This was not observed with rabbit sperm exposed to cadmium chloride.

Although, some mechanistic explanations are suggested, no definite conclusion can be drawn from these *in vitro* studies about the toxicity of cadmium oxide/metal.

Annex F The occurrence of cadmium (metal) in products according to the Swedish product register

Trades that use products containing metallic cadmium and product functions.

Trade	Product functions
Paint industry	Activators* Dyestuffs, pigments Fillers (plastic, paint,...)
Industry for rubber products	Activators* Dyestuffs, pigments Fillers (plastic, paint,...)
Industry for ceramic tiles and flags	Activators* Dyestuffs, pigments Fillers (plastic, paint,...)
Treatment and coating of metals; workshops for gen. mech. engin.	Activators* Degreasing agents* Dyestuffs, pigments Fillers (plastic, paint,...)
Retail trade; repair shops	Adhesives, glues* Cast compounds*
Fabricated metal products, except machinery and equipment	Alloy metals* Fillers (plastics, paint, etc)
Soap and detergents, cleaning and polishing preparations	Corrosion inhibitors* pH-regulating agents*
Textile	Dyestuffs, pigments
Pulp, paper and paper products	Dyestuffs, pigments
Other organic basic chemicals	Dyestuffs, pigments
Agricultural establishment and related	Feedstuff/feedstuff additives*
Basic metals industry	Metal surface coating agents*
Glass and glass products industry	Other paints and varnishes, solvent-based*
Whole sale and retail	Paints, varnishes*
Pharmaceutical preparations	Skin protection agents*

* Less than three products in the product category

In total 35 products (total volume less than 1 ton per year) whereof two consumer products with a cadmium concentration lesser or equal at 10% of the product (Swedish Product Register for the year 1996, 15/09/97). No further details could be identified related to these latter products (KEMI, pers. com 2000/2001)

Annex G The occurrence of cadmium oxide in products according to the Swedish product register

Trades that use products containing cadmium oxide and product functions.

Trade	Product functions
Industry for radio, television and communication apparatus	Contact agents*
Treatment and coating of metals; workshops for gen. mech. engine.	Electrolytes*
Industry for glass and glass products	Enamels, glazes Paints, varnishes*
Industry for ceramic products, other than non-refractory for construction purposes	Enamels, glazes
Industry for plastic products	Intermediates (plastic manufacture)*
Manufacture of chemicals and chemical products	Metal surface treatment agents*

* Less than three products in the product category

In total 45 products whereof 37 with a cadmium concentration less than or equal at 10% of the product. Mainly in the Industry for glass and glass products and Industry for ceramic products with the following use/function: enamels, glazes. The Register further mentions seven products with a substance concentration in the range 10-20% and 1 product with a high (80-100%) content. No consumer products have been registered. The overall total volume accounts for less than 1 ton per year. (Swedish Product Register for the year 1996, 15/09/97).

Annex H Check-list for evaluating epidemiological studies

(check-list established by Professor Philippe Hotz from the Institut für Sozial- und Präventivmedizin der Universität Zürich)

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ABTEILUNG FÜR ARBEITS-
UND UMWELTMEDIZIN

CROSS-SECTIONAL STUDIES.

1. Other publications on the same population.

Consider possible overlapping with other studies by quite different authors which included part of the same study population.
If relevant : on the first page indications about possible redundancy (part of the same authors have already published results on part of this study population). Indicate references for easy retrieval of publications. Briefly comment on differences / similarities between former and latter pubications and justify the exclusion of the study not considered.

2. Location.

Country / region / institution (selection bias !).

3. Purpose

precisely defined ?

4. Study population

4.1. and 4.2. Exposed and nonexposed.

- size of study population, men /women, age. If possible : socioeconomic class, smoking, alcohol, and other relevant factors in that context.
- is the study population young ?
- definition of the study population :
a) beginning of work at...

b) end of work at ...; b) if sequential cross-sectional study or inclusion of retired workers
c) minimal duration;

d) all workers presently working and exposed ? Retired and currently nonexposed workers ? Time since last exposure ?

Are workers previously diagnosed with poisoning included ?

4.3. Final study population.

- initial vs final study population (as a summary showing the lost cases and controls at each step of constitution of study population with the most important data on age, sex, employability, and other important variables in that context).
- comparability of cases and controls as for : age, sex, socioeconomic group, education, and other important variables in that context.
Are workers previously diagnosed with poisoning included ?
IMPORTANT : considerable differences may be found between initial and final study population. A presentation of the results (for example in tables) should take this issue into account.

5. Selection, participation rate, representativeness.

- selection of the study population
- selection of the study sample
- participation rate
- representative sample ?

If sequential cross-sectional study : are the samples comparable ?

6. Exposure.

6.1. Specific aspects : exposed workers

Is the word "exposed" clearly defined (with respect to type, minimal intensity, duration, frequency ?). Observational period (if not mentioned under 4.; important because of time-related changes of exposure intensity) ? Previous poisonings ?

- type :
== general population or industry ?
== type of industry (for example Cd exposure : cadmium production, alloys, soldering and/or cutting, Cd-Ni battery, etc.) ?
== is "exposure" defined by occupation and/or industry, group of agents, agent ? Are the groups specific or very broad (= how specific if this definition ?) ? Are concomitant exposures possible (for example : heavy metals vs Cd + As inorg or Pb or Ni vs Cd only ? Benzene in garages, oil refineries, printing plants represent three quite different exposure conditions).

- information on exposure frequency, duration, and intensity :
== yes/no
== only present exposure (strictly cross-sectional) or information on previous exposure (in this plant, in the same occupation but in other plants, in all occupations for the lifetime)
== minimal intensity, duration, frequency : based on exposure reconstruction or objective measures ?
== if exposure reconstruction : type of variable (dichotomous if exposed vs nonexposed, ordinal, exposure score, etc.) ?
== if dichotomous classifications : is the cut-off clearly described, credible, arbitrary ? Are minimal intensity, duration, frequency taken into account to define the word "exposed" ?
== if ordinal categories or of exposure score : is the classification / score credible, consistent ? Is there any indication of the validity of the classification / score ?
== objective measures available ? air sampling (area vs. personal, total vs respirable dust); biol.monitoring (blood/urine/neutron activation analysis/x-ray fluorescence, etc.)

samples from controls and exposed workers examined in the same series ?
quality control (exposure assessment) ?

<u>**6.2. Specific aspects : control workers**</u>

<u>**6.3. Summary**</u>

<u>**7. Diagnosis.**</u>

Is the endpoint clinically relevant (predictive value) ? Methods ? Quality control ?

If relevant :
Classification scheme
Are there objective criteria required for ascertaining diagnosis (example : FAB, SLE) ?
Blind review of medical records, slides, if any ?
Panel review ?
Other important methodologic aspects (example : biopsy for kidney diseases, immunofluorescence for glomerulonephritis, histolological confirmation for cancer).

<u>**8. Bias.**</u>

- preplacement examination
- healthy worker effect
- is it clear that the endpoint is really an effect of the exposure (cross-sectional design !)

<u>**9. Interview and coding, laboratory.**</u>

Blind interview / interview procedure / structure and content of the interview.
Blind coding of the answers / coding according to .... (are criteria mentioned, credible, arbitrary).

samples from controls and exposed workers examined in the same series and quality control (exposure assessment : see exposure). Are these units adequate and do they consider age- or sex-relaed differences (mg/l, mg/g, mg/24h for metabolite; ml/mn or ml/mn/1.76m2 for clearance)

10. Design and statistics.

- design
- control population : regional, other industrial workers, office workers, low vs high exposure (definition of control group : see 4.2.; exposure assessment in the control group : see 6.2.)
- statistical methods

11. Confounding factors

Age, sex, hospital, smoking, alcohol ?
If relevant : socioeconomic group, residence, genetic / familial factors, ethnicity, race. Are these factors clearly defined (nationality may change after wedding) ? If subgroups are used are these subgroups relevant ?

Considerable sources of misclassification ? (for exposure and disease see 6. and 7., respectively)

IMPORTANT : were the confounding factors taken into account in the analysis or were they only mentioned as items in the interview and not considered in the statistical analysis ?

12. Results.
12.1. Results
12.2. What about power ?

13. Identification, latency, DRC.

Identification : of a specific causal agent, specific causal occupation ?
Latency time (lagging of some years) : yes / no ? biologically credible ?
Dose - response curve : was it examined ?

14. Physiopathology.

Physiopathologial mechanisms

15. Miscellaneous.

26.9.1997

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ABTEILUNG FÜR ARBEITS-
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RETROSPECTIVE COHORT STUDIES, MORTALITY.

1. Other publications on the same population.

. Consider possible overlapping with other studies by quite different authors which included part of the same study population. If relevant : on the first page indications about possible redundancy (part of the same authors have already published results on part of this study population). Indicate references for easy retrieval of publications. Briefly comment on differences / similarities between former and latter pubications and justify the exclusion of the study not considered.

2. Location.

Country / region / institution.

3. Purpose

precisely defined / hypotheses - generating

4. Study population

4.1. and 4.2. Exposed and nonexposed.

- cohort size, men /women, age, number / percentage of deaths (obs. /exp. numbers of deaths). If possible : socioeconomic class, smoking, alcohol, and other relevant factors in that context.
- is the percentage of deaths higher than 10 % ?
- is the cohort young ?
- definition of the cohort :
a) begin of work at...
b) end of work at ...
c) minimal duration
d) other characteristics

Definition of follow - up : begin / end of follow - up
Are workers previously diagnosed with poisoning included ?

4.3. Final study population.

- initial vs final study population (as a summary showing the lost cases and controls at each step of constitution of study population with the most important data on age, sex, employablity, and other important variables in that context).
- comparability of cases and controls as for : age, sex, socioeconomic group, education, and other important variables in that context.
Are workers previously diagnosed with poisoning included ?
IMPORTANT : considerable differences may be found between initial and final study population. A presentation of the results (for example in tables) should take this issue into account.

5. Selection, participation rate, representativeness.

- selection
- participation rate
- representative sample
If register : is the coverage good ?
If morbidity / mortality statistics : data quality ?

6. Exposure.

6.1. Specific aspects.

Is the word "exposed" clearly defined (with respect to type, minimal intensity, duration, frequency ?). Observational period (if not mentioned under 2.; important because of time-related changes of exposure intensity) ? Previous poisonings ?

- type :
== general population or industry ?
== type of industry (for example : exposure to heavy metals/to Cd + As inorg or Pb or Ni/or to Cd only ? Benzene in garages, oil refineries, printing plants represents three quite different exposure situations).

== is "exposure" defined by occupation and/or industry, group of agents, agent ? Are the groups specific or very broad (= how specific if this definition ?) ? Are concomitant exposures possible (for example : heavy metals vs Cd + As inorg or Pb or Ni vs Cd only ? Benzene in garages, oil refineries, printing plants represent three quite different exposure conditions).
== if coding of occupations : clearly standardized ? Based on which coding system (for example : Dictionary of Occupational Titles of the Census) ? Blind ?

- information on exposure frequency, duration, and intensity :
== yes/no
== minimal intensity, duration, frequency : based on exposure reconstruction or objective measures ?
== if exposure reconstruction : type of variable (dichotomous if exposed vs nonexposed, ordinal, exposure score, etc.) ?
== if dichotomous and based on death certificates, registers, or similar sources of information : longest, usual, current, last occupation or occupation at diagnosis ?
== if other dichotomous classifications : is the cut-off clearly described, credible, arbitrary ? Are minimal intensity, duration, frequency taken into account to define the word "exposed" ?
== if ordinal categories or of exposure score : is the classification / score credible, consistent ? Is there any indication of the validity of the classification / score ?
== objective measures available ? air sampling (area vs. personal, total vs respirable dust); biol.monitoring (blood/urine/neutron activation analysis/x-ray fluorescence, etc.)

7. Diagnosis.

Classification scheme (ICD, ICD - O, etc.)
Are there objective criteria required for ascertaining diagnosis (example : FAB, SLE) ?
Blind review of medical records, slides, if any ?
Panel review ?
Other important methodologic aspects (example : biopsy for kidney diseases, immunofluorescence for glomerulonephritis, histolological confirmation for cancer).
If death certificates : underlying vs. contributing cause of death.
- high / low mortality rate ?

8. Bias.

- surveillance bias
- changes in the course of the study (for example : job changes in comparison to the job used as exposure surrogate)
- diagnostic access bias
- diagnostic suspicion bias

9. Interview and coding.

Blind interview / interview procedure / structure and content of the interview.
Blind coding of the answers / coding according to .... (are criteria mentioned, credible, arbitrary).

10. Design and statistics.

- design
- SIR, SMR, PMR
- reference population : national, regional, other industrial workers, low vs high exposure
- statistical methods

11. Confounding factors

Age, sex, hospital, smoking, alcohol ?
If relevant : socioeconomic group, residence, genetic / familial factors, race, ethnicity

Considerable sources of misclassification ? (for exposure and disease see 6. and 7., respectively)

Sensitivity analysis ?

IMPORTANT : were the confounding factors taken into account in the analysis or were they only mentioned as items in the interview and not considered in the statistical analysis ? Are these factors clearly defined (nationality may change after wedding) ? If subgroups are used are these subgroups relevant ?

12. Results.
12.1. Results
12.2. What about power ?

13. Identification, latency, DRC.

Identification : of a specific causal agent, specific causal occupation ?
Latency time (lagging of some years) : yes / no ? biologically credible ?
Dose - response curve : was it examined ?

14. Physiopathology.

Physiopathologial mechanisms (plausibility)

15. Miscellaneous.

26.9.1997

Annex I EUSES output related to the calculations of regional and continental PECs

EUSES Full report	Single substance		
Printed on	21/02/2003 12:20		
Study	Cd RAR 2003		
Substance	Cd		
Defaults	Standard		
Assessment types	1A, 1B, 2, 3A, 3B		
Base set complete	No		
Explanation status column	'O' = Output; 'D' = Default; 'S' = Set; 'I' = Imported		
Name	Value	Units	Status
STUDY			
STUDY IDENTIFICATION			
Study name	Cd RAR 2003		S
Study description	version 2003, Kp 130000		S
Author			D
Institute			D
Address			D
Zip code			D
City			D
Country			D
Telephone			D
Telefax			D
Email			D
Calculations checksum	CB01FB79		SUSES

EUSES Full report	Single substance		
Printed on	21/02/2003 12:20		
Study	Cd RAR 2003		
Substance	Cd		
Defaults	Standard		
Assessment types	1A, 1B, 2, 3A, 3B		
Base set complete	No		

Name	Value	Units	Status
DEFAULTS			
DEFAULT IDENTIFICATION			
General name	Standard		D
Description	According to TGDs		D
RELEASE ESTIMATION			
Fraction of EU production volume for region	0.1	[-]	D
Fraction connected to sewer systems	0.7	[-]	D
CHARACTERISTICS OF COMPARTMENTS			
GENERAL			
Density of solid phase	2.5	[kg.l-1]	D
Density of water phase	1	[kg.l-1]	D
Density of air phase	1.3E-03	[kg.l-1]	D
Environmental temperature	12	[oC]	D
Constant of Junge equation	0.01	[Pa.m]	D
Surface area of aerosol particles	0.01	[m2.m-3]	D
Gas constant (8.314)	8.314	[Pa.m3.mol-1.K-1]	D
SUSPENDED MATTER			
Volume fraction solids in suspended matter	0.1	[m3.m-3]	D
Volume fraction water in suspended matter	0.9	[m3.m-3]	D
Weight fraction of organic carbon in suspended matter	0.1	[kg.kg-1]	D
Wet bulk density of suspended matter	1.15E+03	[kg.m-3]	O
SEDIMENT			
Volume fraction solids in sediment	0.2	[m3.m-3]	D
Volume fraction water in sediment	0.8	[m3.m-3]	D
Weight fraction of organic carbon in sediment	0.05	[kg.kg-1]	D
Bulk density of sediment	1.3E+03	[kgwwt.m-3]	O
Conversion factor wet-dry sediment	2.6	[kgwwt.kgdwt-1]	O
SOIL			
Volume fraction solids in soil	0.6	[m3.m-3]	D
Volume fraction water in soil	0.2	[m3.m-3]	D
Volume fraction air in soil	0.2	[m3.m-3]	D
Weight fraction of organic carbon in soil	0.02	[kg.kg-1]	D
Bulk density of soil	1.7E+03	[kgwwt.m-3]	O
Conversion factor wet-dry soil	1.13	[kgwwt.kgdwt-1]	O
STP SLUDGE			
Fraction of organic carbon in raw sewage sludge	0.3	[kg.kg-1]	D
Fraction of organic carbon in settled sewage sludge	0.3	[kg.kg-1]	D
Fraction of organic carbon in activated sewage sludge	0.37	[kg.kg-1]	D
Fraction of organic carbon in effluent sewage sludge	0.37	[kg.kg-1]	DUSES

EUSES Full report Single substance

Printed on		21/02/2003 12:20	
Study	Cd RAR 2003		
Substance	Cd		
Defaults	Standard		
Assessment types	1A, 1B, 2, 3A, 3B		
Base set complete	No		

Name	Value	Units	Status
DEGRADATION AND TRANSFORMATION RATES			
Concentration of OH-radicals in atmosphere	5,00E+05	[molec.cm-3]	D
Rate constant for abiotic degradation in STP	0	[d-1]	D
Rate constant for abiotic degradation in bulk soil	0	[d-1]	D
Rate constant for abiotic degradation in bulk sediment	0	[d-1]	D
Rate constant for anaerobic biodegradation in sediment	0	[d-1]	D
Fraction of sediment compartment that is aerated	0.1	[m3.m-3]	D
SEWAGE TREATMENT			
GENERAL			
Number of inhabitants feeding one STP	1,00E+04	[eq]	D
Sewage flow	200	[l.eq-1.d-1]	D
Effluent discharge rate of local STP	2,00E+06	[l.d-1]	O
Temperature dependency correction	No		D
Temperature of air above aeration tank	15	[oC]	D
Temperature of water in aeration tank	15	[oC]	D
Height of air column above STP	10	[m]	D
Number of inhabitants of region	2,00E+07	[eq]	D
Number of inhabitants of continental system	3.5E+08	[eq]	O
Windspeed in the system	3	[m.s-1]	D
RAW SEWAGE			
Mass of O2 binding material per person per day	54	[g.eq-1.d-1]	D
Dry weight solids produced per person per day	0.09	[kg.eq-1.d-1]	D
Density solids in raw sewage	1.5	[kg.l-1]	D
Fraction of organic carbon in raw sewage sludge	0.3	[kg.kg-1]	D
PRIMARY SETTLER			
Depth of primary settler	4	[m]	D
Hydraulic retention time of primary settler	2	[hr]	D
Density suspended and settled solids in primary settler	1.5	[kg.l-1]	D
Fraction of organic carbon in settled sewage sludge	0.3	[kg.kg-1]	D
ACTIVATED SLUDGE TANK			
Depth of aeration tank	3	[m]	D
Density solids of activated sludge	1.3	[kg.l-1]	D
Concentration solids of activated sludge	4	[kg.m-3]	D
Steady state O2 concentration in activated sludge	2,00E-03	[kg.m-3]	D
Mode of aeration	Surface		D
Aeration rate of bubble aeration	1.31E-05	[m3.s-1.eq-1]	D
Fraction of organic carbon in activated sewage sludge	0.37	[kg.kg-1]	D
Sludge loading rate	0.15	[kg.kg-1.d-1]	D
Hydraulic retention time in aerator (9-box STP)	6.9	[hr]	O
Hydraulic retention time in aerator (6-box STP)	10.8	[hr]	O
Sludge retention time of aeration tank	9.2	[d]	OSES

EUSES Full report Single substance

Printed on		21/02/2003 12:20	
Study	Cd RAR 2003		
Substance	Cd		
Defaults	Standard		
Assessment types	1A, 1B, 2, 3A, 3B		
Base set complete	No		

Name	Value	Units	Status
SOLIDS-LIQUIDS SEPARATOR			
Depth of solids-liquid separator		3 [m]	D
Density suspended and settled solids in solids-liquid separator	1.3	[kg.l-1]	D
Concentration solids in effluent		30 [mg.l-1]	D
Hydraulic retention time of solids-liquid separator		6 [hr]	D
Fraction of organic carbon in effluent sewage sludge	0.37	[kg.kg-1]	D
REGIONAL AND CONTINENTAL DISTRIBUTION			
CONTINENTAL			
Area of EU	3.56E+06	[km2]	D
Area of continental system	3.52E+08	[km2]	O
Number of inhabitants in the EU	3.7E+08	[eq]	D
Number of inhabitants of continental system	3.5E+08	[eq]	O
Area fraction of water of the continental system	0.03	[-]	D
Area fraction of natural soil	0.6	[-]	D
Area fraction of agricultural soil	0.27	[-]	D
Area fraction of industrial/urban soil	0.1	[-]	D
Fraction of water flow from global scale to continent		0 [-]	D
Water depth of system		3 [m]	D
Suspended solids concentration of continental system		15 [mg.l-1]	S
Residence time of water in system		166 [d]	O
Residence time of air in system	6.41	[d]	O
Net sedimentation rate	2.72	[mm.yr-1]	O
REGIONAL			
Area of regional system		4,00E+04 [km2]	D
Number of inhabitants of region		2,00E+07 [eq]	D
Area fraction of water of the regional system	0.03	[-]	D
Area fraction of natural soil	0.6	[-]	D
Area fraction of agricultural soil	0.27	[-]	D
Area fraction of industrial/urban soil	0.1	[-]	D
Fraction of water flow from continental scale to region	0.034	[-]	D
Water depth of system		3 [m]	D
Suspended solids concentration of regional system		15 [mg.l-1]	D
Residence time of water in system	40.1	[d]	O
Residence time of air in system	0.684	[d]	O
Net sedimentation rate	2.73	[mm.yr-1]	O
AIR			
Atmospheric mixing height		1000 [m]	D
Windspeed in the system		3 [m.s-1]	D
Aerosol deposition velocity		1,00E-03 [m.s-1]	D
Aerosol collection efficiency		2,00E+05 [-]	D
Average annual precipitation		700 [mm.yr-1]	D
WATER AND SEDIMENT			
Concentration biota		1 [mg.l-1]	DES

Printed on	21/02/2003 12:20		
Study	Cd RAR 2003		
Substance	Cd		
Defaults	Standard		
Assessment types	1A, 1B, 2, 3A, 3B		
Base set complete	No		

Name	Value	Units	Status
WATER AND SEDIMENT (Continued)			
Sediment mixing depth	0.03	[m]	D
Settling velocity of suspended solids	2.5	[m.d-1]	D
(biogenic) production of suspended solids in water	0	[kg.d-1]	D
Sewage flow	200	[l.eq-1.d-1]	D
Concentration solids in effluent	30	[mg.l-1]	D
Fraction connected to sewer systems	0.7	[-]	D
SOIL			
Mixing depth natural soil	0.05	[m]	D
Mixing depth agricultural soil	0.2	[m]	D
Mixing depth industrial/urban soil	0.05	[m]	D
Fraction of rain water infiltrating soil	0.25	[-]	D
Fraction of rain water running off soil	0.25	[-]	D
Soil erosion rate of regional system	0.03	[mm.yr-1]	D
MASS TRANSFER			
Air-film PMTC (air-water interface)	1.39E-03	[m.s-1]	D
Water-film PMTC (air-water interface)	1.39E-05	[m.s-1]	D
Air-film PMTC (air-soil interface)	1.39E-03	[m.s-1]	D
Soil-air PMTC (air-soil interface)	5.56E-06	[m.s-1]	D
Soil-water film PMTC (air-soil interface)	5.56E-10	[m.s-1]	D
Water-film PMTC (sediment-water interface)	2.78E-06	[m.s-1]	D
Pore water PMTC (sediment-water interface)	2.78E-08	[m.s-1]	D
LOCAL DISTRIBUTION			
AIR AND SURFACE WATER			
Concentration in air at source strength 1 [kg.d-1]	2.78E-04	[mg.m-3]	D
Standard deposition flux of aerosol-bound compounds	0.01	[mg.m-2.d-1]	D
Standard deposition flux of gaseous compounds	??	[mg.m-2.d-1]	D
Suspended solids concentration of regional system	15	[mg.l-1]	D
Dilution factor	10	[-]	D
Flow rate of the river	1.8E+04	[m3.d-1]	D
Calculate dilution from river flow rate	No		D
SOIL			
Mixing depth of grassland soil	0.1	[m]	D
Dry sludge application rate on agricultural soil	5,00E+03	[kg.ha-1.yr-1]	D
Dry sludge application rate on grassland	1000	[kg.ha-1.yr-1]	D
Averaging time soil (for terrestrial ecosystem)	30	[d]	D
Averaging time agricultural soil	180	[d]	D
Averaging time grassland	180	[d]	D
Air-film PMTC (air-soil interface)	1.39E-03	[m.s-1]	D
Soil-air PMTC (air-soil interface)	5.56E-06	[m.s-1]	D
Soil-water film PMTC (air-soil interface)	5.56E-10	[m.s-1]	D
Mixing depth agricultural soil	0.2	[m]	D
Fraction of rain water infiltrating soil	0.25	[-]	DUSES

Printed on	21/02/2003 12:20
Study	Cd RAR 2003
Substance	Cd
Defaults	Standard
Assessment types	1A, 1B, 2, 3A, 3B
Base set complete	No

Name	Value	Units	Status
SOIL (Continued)			
Average annual precipitation	700	[mm.yr-1]	D
CHARACTERISTICS OF PLANTS AND CATTLE			
PLANTS			
Volume fraction of water in plant tissue	0.65	[m3.m-3]	D
Volume fraction of lipids in plant tissue	0.01	[m3.m-3]	D
Volume fraction of air in plant tissue	0.3	[m3.m-3]	D
Correction for differences between plant lipids and octanol	0.95	[-]	D
Bulk density of plant tissue (wet weight)	0.7	[kg.l-1]	D
Rate constant for metabolism in plants	0	[d-1]	D
Rate constant for photolysis in plants	0	[d-1]	D
Leaf surface area	5	[m2]	D
Conductance	1,00E-03	[m.s-1]	D
Shoot volume	2	[l]	D
Rate constant for dilution by growth	0.035	[d-1]	D
Transpiration stream	1	[l.d-1]	D
CATTLE			
Daily intake for cattle of grass (dryweight)	16.9	[kg.d-1]	D
Conversion factor grass from dryweight to wetweight	4	[kg.kg-1]	D
Daily intake of soil (dryweight)	0.41	[kg.d-1]	D
Daily inhalation rate for cattle	122	[m3.d-1]	D
Daily intake of drinking water for cattle	55	[l.d-1]	D
CHARACTERISTICS OF HUMANS			
Daily intake of drinking water	2	[l.d-1]	D
Daily intake of fish	0.115	[kg.d-1]	D
Daily intake of leaf crops (incl. fruit and cereals)	1.2	[kg.d-1]	D
Daily intake of root crops	0.384	[kg.d-1]	D
Daily intake of meat	0.301	[kg.d-1]	D
Daily intake of dairy products	0.561	[kg.d-1]	D
Inhalation rate for humans	20	[m3.d-1]	D
Bioavailability for oral uptake	1	[-]	D
Bioavailability for inhalation	0.75	[-]	D
Bioavailability for dermal uptake	1	[-]	D
Bodyweight of the human considered	70	[kg]	D
Oral to inhalatory extrapolation	Using adsorption rates		

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Name	Value	Units	Status
SUBSTANCE			
SUBSTANCE IDENTIFICATION			
General name	Cd		S
Description			D
CAS-No			D
EC-notification no.			D
EINECS no.			D
PHYSICO-CHEMICAL PROPERTIES			
Molecular weight	112	[g.mol-1]	S
Melting point	??	[oC]	D
Boiling point	??	[oC]	D
Vapour pressure at 25 [oC]	1,00E-10	[Pa]	S
Octanol-water partition coefficient.	-1	[log10]	S
Water solubility	5,00E-03	[mg.l-1]	SSES

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Base set complete	No		

Name	Value	Units	Status
RELEASE ESTIMATION			
CHARACTERIZATION AND TONNAGE			
High Production Volume Chemical	No		D
Production volume of chemical in EU		0 [tonnes.yr-1]	D
Volume of chemical imported to EU		0 [tonnes.yr-1]	D
Volume of chemical exported from EU		0 [tonnes.yr-1]	D
Intermittent release	No		D
INTERMEDIATE RESULTS PRODUCTION VOLUMES			
Tonnage of substance in Europe		0 [tonnes.yr-1]	O
Regional production volume of substance		0 [tonnes.yr-1]	O
Continental production volume of substance		0 [tonnes.yr-1]	O
USE PATTERNS			
EMISSION INPUT DATA			
Industry category	15/0 Others		D
Use category	55/0 Others		D
Emission scenario document available	No		O
Extra details on use category	No extra details necessary		D
Extra details on use category	No extra details necessary		D
Fraction of tonnage for application		1 [-]	O
Fraction of chemical in formulation		1 [-]	D
Production	Yes		D
Formulation	Yes		D
Processing	Yes		D
Private use	Yes		D
Recovery	Yes		D
Main category production	III Multi-purpose equipment		D
Main category formulation	III Multi-purpose equipment		D
Main category processing	III Non-dispersive use		D
INTERMEDIATE RESULTS			
USE PATTERN 1			
INTERMEDIATE RESULTS TONNAGES PER USE PATTERN			
Relevant tonnage for application		0 [tonnes.yr-1]	O
Regional tonnage of substance		0 [tonnes.yr-1]	O
Continental tonnage of substance		0 [tonnes.yr-1]	O
RELEASE FRACTIONS AND EMISSION DAYS [PRODUCTION]			
Fraction of tonnage released to air		1,00E-05 [-]	O
Fraction of tonnage released to waste water	0.02	[-]	O
Fraction of tonnage released to surfacewater		0 [-]	O
Fraction of tonnage released to industrial soil		1,00E-04 [-]	O
Source of A-table data	General table		OUSES

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Name	Value	Units	Status
RELEASE FRACTIONS AND EMISSION DAYS (Continued)			
[PRODUCTION]			
Fraction of the main local source	1	[-]	O
Number of emission days per year	1	[-]	O
Source of B-table data	General table		O
[FORMULATION]			
Fraction of tonnage released to air	2.5E-03	[-]	O
Fraction of tonnage released to waste water	0.02	[-]	O
Fraction of tonnage released to surfacewater	0	[-]	O
Fraction of tonnage released to industrial soil	1,00E-04	[-]	O
Source of A-table data	General table		O
Fraction of the main local source	1	[-]	O
Number of emission days per year	20	[-]	O
Source of B-table data	General table		O
[PROCESSING]			
Fraction of tonnage released to air	1,00E-03	[-]	O
Fraction of tonnage released to waste water	0.1	[-]	O
Fraction of tonnage released to surfacewater	0	[-]	O
Fraction of tonnage released to industrial soil	1,00E-02	[-]	O
Source of A-table data	General table		O
Fraction of the main local source	1	[-]	O
Number of emission days per year	1	[-]	O
Source of B-table data	General table		O
[PRIVATE USE]			
Fraction of tonnage released to air	0	[-]	O
Fraction of tonnage released to waste water	0	[-]	O
Fraction of tonnage released to surfacewater	0	[-]	O
Fraction of tonnage released to industrial soil	0	[-]	O
Source of A-table data	No applicable data found		O
Fraction of the main local source	0	[-]	O
Number of emission days per year	1	[-]	O
Source of B-table data	General table		O
[RECOVERY]			
Fraction of tonnage released to air	0	[-]	O
Fraction of tonnage released to waste water	0	[-]	O
Fraction of tonnage released to surfacewater	0	[-]	O
Fraction of tonnage released to industrial soil	0	[-]	O
Source of A-table data	No applicable data found		O
Fraction of the main local source	0.5	[-]	O
Number of emission days per year	150	[-]	O
Source of B-table data	General table		OUSES

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Base set complete	No		

Name	Value	Units	Status
CONTINENTAL			
[PRODUCTION]			
Continental release to air	0	[kg.d-1]	O
Continental release to waste water	0	[kg.d-1]	O
Continental release to surface water	0	[kg.d-1]	O
Continental release to industrial soil	0	[kg.d-1]	O
[FORMULATION]			
Continental release to air	0	[kg.d-1]	O
Continental release to waste water	0	[kg.d-1]	O
Continental release to surface water	0	[kg.d-1]	O
Continental release to industrial soil	0	[kg.d-1]	O
[PROCESSING]			
Continental release to air	0	[kg.d-1]	O
Continental release to waste water	0	[kg.d-1]	O
Continental release to surface water	0	[kg.d-1]	O
Continental release to industrial soil	0	[kg.d-1]	O
[PRIVATE USE]			
Continental release to air	0	[kg.d-1]	O
Continental release to waste water	0	[kg.d-1]	O
Continental release to surface water	0	[kg.d-1]	O
Continental release to industrial soil	0	[kg.d-1]	O
[RECOVERY]			
Continental release to air	0	[kg.d-1]	O
Continental release to waste water	0	[kg.d-1]	O
Continental release to surface water	0	[kg.d-1]	O
Continental release to industrial soil	0	[kg.d-1]	O
REGIONAL			
[PRODUCTION]			
Regional release to air	0	[kg.d-1]	O
Regional release to waste water	0	[kg.d-1]	O
Regional release to surface water	0	[kg.d-1]	O
Regional release to industrial soil	0	[kg.d-1]	O
[FORMULATION]			
Regional release to air	0	[kg.d-1]	O
Regional release to waste water	0	[kg.d-1]	O
Regional release to surface water	0	[kg.d-1]	O
Regional release to industrial soil	0	[kg.d-1]	O
[PROCESSING]			
Regional release to air	0	[kg.d-1]	O
Regional release to waste water	0	[kg.d-1]	OUSES

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Name	Value	Units	Status
[PROCESSING] (Continued)			
Regional release to surface water	0	[kg.d-1]	O
Regional release to industrial soil	0	[kg.d-1]	O
[PRIVATE USE]			
Regional release to air	0	[kg.d-1]	O
Regional release to waste water	0	[kg.d-1]	O
Regional release to surface water	0	[kg.d-1]	O
Regional release to industrial soil	0	[kg.d-1]	O
[RECOVERY]			
Regional release to air	0	[kg.d-1]	O
Regional release to waste water	0	[kg.d-1]	O
Regional release to surface water	0	[kg.d-1]	O
Regional release to industrial soil	0	[kg.d-1]	O
CONTINENTAL			
Total continental emission to air	113.1	[tonnes.yr-1]	S
Total continental emission to wastewater	0	[kg.d-1]	O
Total continental emission to surface water	35.2	[tonnes.yr-1]	S
Total continental emission to industrial soil	0	[tonnes.yr-1]	S
Total continental emission to agricultural soil	220.1	[tonnes.yr-1]	S
REGIONAL			
Total regional emission to air	12.6	[tonnes.yr-1]	S
Total regional emission to wastewater	0	[kg.d-1]	O
Total regional emission to surface water	3.9	[tonnes.yr-1]	S
Total regional emission to industrial soil	0	[tonnes.yr-1]	S
Total regional emission to agricultural soil	24.5	[tonnes.yr-1]	S
LOCAL			
[PRODUCTION]			
Local emission to air during episode	0	[kg.d-1]	O
Local emission to wastewater during episode	0	[kg.d-1]	O
Show this step in further calculations	No		O
Intermittent release	No		D
[FORMULATION]			
Local emission to air during episode	0	[kg.d-1]	O
Local emission to wastewater during episode	0	[kg.d-1]	O
Show this step in further calculations	No		O
Intermittent release	No		D
[PROCESSING]			
Local emission to air during episode	0	[kg.d-1]	O
Local emission to wastewater during episode	0	[kg.d-1]	O
Show this step in further calculations	No		OUSES

Study	Cd RAR 2003
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Base set complete	No

Name	Value	Units	Status
[PROCESSING] (Continued)			
Intermittent release	No		D
[PRIVATE USE]			
Local emission to air during episode		0 [kg.d-1]	O
Local emission to wastewater during episode		0 [kg.d-1]	O
Show this step in further calculations	No		O
Intermittent release	No		D
[RECOVERY]			
Local emission to air during episode		0 [kg.d-1]	O
Local emission to wastewater during episode		0 [kg.d-1]	O
Show this step in further calculations	No		O
Intermittent release	No		DUSES

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Name	Value	Units	Status
DISTRIBUTION			
PARTITION COEFFICIENTS			
SOLIDS WATER PARTITIONING			
Organic carbon-water partition coefficient	0.195	[l.kg-1]	O
Solids-water partition coefficient in soil		280 [l.kg-1]	S
Solids-water partition coefficient in sediment	1.3E+05	[l.kg-1]	S
Solids-water partition coefficient suspended matter	1.3E+05	[l.kg-1]	S
Solids-water partition coefficient in raw sewage sludge	0.0585	[l.kg-1]	O
Solids-water partition coefficient in settled sewage sludge	0.0585	[l.kg-1]	O
Solids-water partition coefficient in activated sewage sludge	0.0722	[l.kg-1]	O
Solids-water partition coefficient in effluent sewage sludge	0.0722	[l.kg-1]	O
Suspended matter-water partition coefficient	3.25E+04	[m3.m-3]	O
Soil-water partition coefficient		420 [m3.m-3]	O
Sediment-water partition coefficient	6.5E+04	[m3.m-3]	O
AIR-WATER PARTITIONING AND ADSORPTION TO AEROSOL PARTICLES			
Sub-cooled liquid vapour pressure		1,00E-10 [Pa]	O
Fraction of chemical associated with aerosol particles		1 [-]	O
Henry's law constant		0 [Pa.m3.mol-1]	S
Air-water partitioning coefficient		0 [m3.m-3]	O
BIOTA-WATER			
Bioconcentration factor for aquatic biota	1.41	[l.kg-1]	O
DEGRADATION AND TRANSFORMATION RATES			
CHARACTERIZATION AND STP			
Characterization of biodegradability	Not biodegradable		D
Degradation calculation method in STP	First order, standard OECD/EU tests		D
Rate constant for biodegradation in STP		0 [d-1]	O
Total rate constant for degradation in STP		0 [d-1]	O
Maximum growth rate of specific microorganisms		2 [d-1]	D
Half saturation concentration	0.5	[g.m-3]	D
ENVIRONMENTAL			
Specific degradation rate constant with OH-radicals		0 [cm3.molec-1.s-1]	D
Rate constant for degradation in air		0 [d-1]	O
Rate constant for hydrolysis in surface water		0 [d-1]	S
Rate constant for photolysis in surface water		0 [d-1]	S
Rate constant for biodegradation in surface water		0 [d-1]	O
Total rate constant for degradation in bulk surface water		0 [d-1]	O
Rate constant for biodegradation in bulk soil		0 [d-1]	S
Total rate constant for degradation in bulk soil		0 [d-1]	O
Rate constant for biodegradation in aerated sediment		0 [d-1]	S
Total rate constant for degradation in bulk sediment		0 [d-1]	OUSES

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Name	Value	Units	Status
SEWAGE TREATMENT			
CONTINENTAL			
Fraction of emission directed to air		0 [-]	O
Fraction of emission directed to water		0 [-]	O
Fraction of emission directed to sludge		0 [-]	O
Fraction of the emission degraded		0 [-]	O
Total of fractions		0 [-]	O
Indirect emission to air		0 [kg.d-1]	O
Indirect emission to surface water		0 [kg.d-1]	O
Indirect emission to agricultural soil		0 [kg.d-1]	O
REGIONAL			
Fraction of emission directed to air		0 [-]	O
Fraction of emission directed to water		0 [-]	O
Fraction of emission directed to sludge		0 [-]	O
Fraction of the emission degraded		0 [-]	O
Total of fractions		0 [-]	O
Indirect emission to air		0 [kg.d-1]	O
Indirect emission to surface water		0 [kg.d-1]	O
Indirect emission to agricultural soil		0 [kg.d-1]	O
CONTINENTAL AND REGIONAL			
CONTINENTAL			
Continental PEC in surface water (total)	0.0281	[ug.l-1]	O
Continental PEC in surface water (dissolved)	9.53E-03	[ug.l-1]	O
Continental PEC in air (total)	1.52E-04	[ug.m-3]	O
Continental PEC in agricultural soil (total)	0.176	[mg.kgwwt-1]	O
Continental PEC in pore water of agricultural soils	7.1E-04	[mg.l-1]	O
Continental PEC in natural soil (total)	0.0177	[mg.kgwwt-1]	O
Continental PEC in industrial soil (total)	0.0177	[mg.kgwwt-1]	O
Continental PEC in sediment (total)	0.477	[mg.kgwwt-1]	O
REGIONAL			
Regional PEC in surface water (total)	1.84E-04	[mg.l-1]	O
Regional PEC in surface water (dissolved)	0.0622	[ug.l-1]	O
Regional PEC in air (total)	5.61E-04	[ug.m-3]	O
Regional PEC in agricultural soil (total)	1.61	[mg.kgwwt-1]	O
Regional PEC in pore water of agricultural soils	6.52E-03	[mg.l-1]	O
Regional PEC in natural soil (total)	0.0656	[mg.kgwwt-1]	O
Regional PEC in industrial soil (total)	0.0656	[mg.kgwwt-1]	O
Regional PEC in sediment (total)	3.11	[mg.kgwwt-1]	OSES

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Name	Value	Units	Status
EXPOSURE			
BIOCONCENTRATION FACTORS			
Partition coefficient worm-porewater	0.4	[l.kg-1]	O
Bioconcentration factor for earthworms	1.62E-03	[kg.kg-1]	O
Bioconcentration factor for fish	1.41	[l.kg-1]	O
Partition coefficient between plant tissue and water	0.651	[m3.m-3]	O
Partition coefficient between leaves and air	??	[m3.m-3]	O
Transpiration-stream concentration factor	0.033	[-]	O
Bioaccumulation factor for meat	7.94E-07	[d.kg-1]	O
Bioaccumulation factor for milk	7.94E-06	[d.kg-1]	O
Purification factor for surface water	1	[-]	O
HUMANS EXPOSED TO OR VIA THE ENVIRONMENT			
REGIONAL			
CONCENTRATIONS IN FISH, PLANTS AND DRINKING WATER			
Regional concentration in wet fish	8.79E-05	[mg.kg-1]	O
Regional concentration in root tissue of plant	6.07E-03	[mg.kg-1]	O
Regional concentration in leaves of plant	??	[mg.kg-1]	O
Regional concentration in grass (wet weight)	??	[mg.kg-1]	O
Fraction of total uptake by crops from pore water	1	[-]	O
Fraction of total uptake by crops from air	1.13E-06	[-]	O
Fraction of total uptake by grass from pore water	1	[-]	O
Fraction of total uptake by grass from air	1.13E-06	[-]	O
Regional concentration in drinking water	6.52E-03	[mg.l-1]	O
CONCENTRATIONS IN MEAT AND MILK			
Regional concentration in meat (wet weight)	??	[mg.kg-1]	O
Regional concentration in milk (wet weight)	??	[mg.kg-1]	O
Fraction of total intake by cattle through grass	??	[-]	O
Fraction of total intake by cattle through drinking water	??	[-]	O
Fraction of total intake by cattle through air	??	[-]	O
Fraction of total intake by cattle through soil	??	[-]	O
DAILY HUMAN DOSES			
Daily dose through intake of drinking water	1.86E-04	[mg.kg-1.d-1]	O
Fraction of total dose through intake of drinking water	??	[-]	O
Daily dose through intake of fish	1.44E-07	[mg.kg-1.d-1]	O
Fraction of total dose through intake of fish	??	[-]	O
Daily dose through intake of leaf crops	??	[mg.kg-1.d-1]	O
Fraction of total dose through intake of leaf crops	??	[-]	O
Daily dose through intake of root crops	3.33E-05	[mg.kg-1.d-1]	O
Fraction of total dose through intake of root crops	??	[-]	O
Daily dose through intake of meat	??	[mg.kg-1.d-1]	O
Fraction of total dose through intake of meat	??	[-]	O
Daily dose through intake of milk	??	[mg.kg-1.d-1]	O
Fraction of total dose through intake of milk	??	[-]	O
Daily dose through intake of air	1.2E-07	[mg.kg-1.d-1]	OUSES

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Name	Value	Units	Status
DAILY HUMAN DOSES (Continued)			
Fraction of total dose through intake of air	??	[-]	O
Regional total daily intake for humans	??	[mg.kg-1.d-1]	O1/02/2003

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Base set complete	No		

Name	Value	Units	Status
EFFECTS			
INPUT OF EFFECTS DATA			
MICRO-ORGANISMS			
EC50 for micro-organisms in a STP	??	[mg.l-1]	D
Specific bacterial population?	No		D
EC10 for micro-organisms in a STP	??	[mg.l-1]	D
Specific bacterial population?	No		D
NOEC for micro-organisms in a STP	??	[mg.l-1]	D
Specific bacterial population?	No		D
AQUATIC ORGANISMS			
LC50 for fish	??	[mg.l-1]	D
L(E)C50 for Daphnia	??	[mg.l-1]	D
EC50 for algae	??	[mg.l-1]	D
LC50 for other aquatic species	??	[mg.l-1]	D
Species	other		D
NOEC for fish	??	[mg.l-1]	D
NOEC for Daphnia	??	[mg.l-1]	D
NOEC for algae	??	[mg.l-1]	D
NOEC for other aquatic species	??	[mg.l-1]	D
Additional aquatic NOEC	??	[mg.l-1]	D
Additional aquatic NOEC	??	[mg.l-1]	D
Additional aquatic NOEC	??	[mg.l-1]	D
Additional aquatic NOEC	??	[mg.l-1]	D
Additional aquatic NOEC	??	[mg.l-1]	D
Additional aquatic NOEC	??	[mg.l-1]	D
TERRESTRIAL ORGANISMS			
LC50 for plants	??	[mg.kgwwt-1]	D
LC50 for earthworms	??	[mg.kgwwt-1]	D
EC50 for microorganisms	??	[mg.kgwwt-1]	D
LC50 for other terrestrial species	??	[mg.kgwwt-1]	D
Species	other		D
NOEC for plants	??	[mg.kgwwt-1]	D
NOEC for earthworms	??	[mg.kgwwt-1]	D
NOEC for microorganisms	??	[mg.kgwwt-1]	D
NOEC for other terrestrial species	??	[mg.kgwwt-1]	D
NOEC for other terrestrial species	??	[mg.kgwwt-1]	D
Additional terrestrial NOEC	??	[mg.kgwwt-1]	D
Additional terrestrial NOEC	??	[mg.kgwwt-1]	D
Additional terrestrial NOEC	??	[mg.kgwwt-1]	D
Additional terrestrial NOEC	??	[mg.kgwwt-1]	D
Additional terrestrial NOEC	??	[mg.kgwwt-1]	D
Additional terrestrial NOEC	??	[mg.kgwwt-1]	D
BIRDS			
LC50 in avian dietary study (5 days)	??	[mg.kg-1]	DES

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Name	Value	Units	Status
BIRDS (Continued)			
NOAEL	??	[mg.kg-1.d-1]	D
NOEC via food	??	[mg.kg-1]	O
Duration of (sub-)chronic oral test	Chronic		D
Conversion factor NOAEL to NOEC	8	[kg.d.kg-1]	D
MAMMALS			
ACUTE			
Oral LD50	??	[mg.kg-1]	D
Oral Discriminatory Dose	??	[mg.kg-1]	D
Dermal LD50	??	[mg.kg-1]	O
Inhalatory LC50	??	[mg.m-3]	O
(SUB)CHRONIC			
Oral NOAEL	??	[mg.kg-1.d-1]	O
Oral LOAEL	??	[mg.kg-1.d-1]	O
Inhalatory NOAEL	??	[mg.m-3]	O
Inhalatory LOAEL	??	[mg.m-3]	O
Dermal NOAEL	??	[mg.kg-1.d-1]	O
Dermal LOAEL	??	[mg.kg-1.d-1]	O
NOEC via food	??	[mg.kg-1]	O
LOEC via food	??	[mg.kg-1]	D
Duration of (sub-)chronic oral test	28 days		D
Species for conversion of NOAEL to NOEC	Rattus norvegicus (<6 weeks)		D
Conversion factor NOAEL to NOEC	10	[kg.d.kg-1]	O
HUMANS			
(SUB)CHRONIC			
Oral NOAEL	??	[mg.kg-1.d-1]	D
Oral LOAEL	??	[mg.kg-1.d-1]	D
Dermal NOEC in a medium	??	[mg.cm-3]	D
Dermal LOEC in a medium	??	[mg.cm-3]	D
Inhalatory (fibre) NOAEL	??	[fibres.m-3]	D
Inhalatory (fibre) LOAEL	??	[fibres.m-3]	D
Dermal LOAEL	??	[mg.kg-1.d-1]	O
Dermal NOAEL	??	[mg.kg-1.d-1]	O
Inhalatory LOAEL	??	[mg.m-3]	O
Inhalatory NOAEL	??	[mg.m-3]	O
CURRENT CLASSIFICATION			
Corrosive (C, R34 or R35)	No		D
Irritating to skin (Xi, R38)	No		D
Irritating to eyes (Xi, R36)	No		D
Risk of serious damage to eyes (Xi, R41)	No		D
Irritating to respiratory system (Xi, R37)	No		D
May cause sensitisation by inhalation (Xn, R42)	No		DES

Printed on		21/02/2003 12:20	
Study	Cd RAR 2003		
Substance	Cd		
Defaults	Standard		
Assessment types	1A, 1B, 2, 3A, 3B		
Base set complete	No		

Name	Value	Units	Status
CURRENT CLASSIFICATION (Continued)			
May cause sensitisation by skin contact (Xi, R43)	No		D
May cause cancer (T, R45)	No		D
May cause cancer by inhalation (T, R49)	No		D
Possible risk of irreversible effects (Xn, R40)	No		D
ENVIRONMENTAL EFFECTS ASSESSMENT			
INTERMEDIATE RESULTS AQUATIC ORGANISMS, MICRO-ORGANISMS AND PREDATORS			
Toxicological data used for extrapolation to PNEC Aqua	??	[mg.l-1]	O
Assessment factor applied in extrapolation to PNEC Aqua	??	[-]	O
Toxicological data used for extrapolation to PNEC Aqua	??	[mg.l-1]	O
Assessment factor applied in extrapolation to PNEC Aqua	??	[-]	O
Toxicological data used for extrapolation to PNEC micro	??	[mg.l-1]	O
Assessment factor applied in extrapolation to PNEC micro	??	[-]	O
Toxicological data used for extrapolation to PNEC oral	??	[mg.kg-1]	O
Assessment factor applied in extrapolation to PNEC oral	??	[-]	O
INTERMEDIATE RESULTS TERRESTRIAL AND SEDIMENT ORGANISMS			
Toxicological data used for extrapolation to PNEC Terr	??	[mg.kgwwt-1]	O
Assessment factor applied in extrapolation to PNEC Terr	??	[-]	O
Equilibrium partitioning used for PNEC in soil?	Yes		O
Equilibrium partitioning used for PNEC in sediment?	Yes		O
PNECS FOR AQUATIC ORGANISMS, MICRO-ORGANISMS AND PREDATORS			
PNEC for aquatic organisms	??	[mg.l-1]	O
PNEC for aquatic organisms, intermittent releases	??	[mg.l-1]	O
PNEC for micro-organisms in a STP	??	[mg.l-1]	O
PNEC for secondary poisoning of birds and mammals	??	[mg.kg-1]	O
PNEC for aquatic organisms with statistical method	??	[mg.l-1]	O
PNECS FOR TERRESTRIAL AND SEDIMENT ORGANISMS			
PNEC for terrestrial organisms	??	[mg.kgwwt-1]	O
PNEC for terrestrial organisms with statistical method	??	[mg.kgwwt-1]	O
PNEC for sediment-dwelling organisms	??	[mg.kgwwt-1]	OES

EUSES Full report	Single substance		
Printed on	21/02/2003 12:20		
Study	Cd RAR 2003		
Substance	Cd		
Defaults	Standard		
Assessment types	1A, 1B, 2, 3A, 3B		
Base set complete	No		

Name	Value	Units	Status
RISK CHARACTERIZATION			
ENVIRONMENTAL EXPOSURE			
REGIONAL			
ENVIRONMENT			
RCR for the regional water compartment	??	[-]	O
RCR for the regional soil compartment	??	[-]	O
Extra factor 10 applied to PEC	No		O
RCR for the regional sediment compartment	??	[-]	O
Extra factor 10 applied to PEC	No		O
HUMANS			
MOS regional, total exposure via all media	??	[-]	O
MOS regional, exposure via air	??	[-]	OS

Annex J Temporal trends in measured Cd concentrations in the environment

Table A Temporal trends in measured local Cd concentrations in the effluent receiving water and ambient air for Cd-producing and –processing plants in the EU-16

Use category	Plant n°	Annual average Cd concentrations in water (µg L^{-1})			Annual average Cd concentrations in ambient air (ng m^{-3})					
		1994	1995	1996	1993	1994	1995	1996	1997	1998
Cd-producers	1	1.9	0.9	1.0						
	2					75	84	78		
	4				4.85	3.95				
	5				30	30	30	30		
	6					1	1	1		
	8					8.4		10.7		
	10					<40	<40	<40		
CdOproducers	12				7.6	5.4				

Table B Temporal trends in regional measured cadmium concentrations in Dutch freshwaters (total concentrations; 90 percentile; source: Milieucompendium, 2001)

	Total Cd concentrations (µg L^{-1})					
	1985	1990	1995	1998	1999	2000
The Netherlands: Rhine	0.42	0.18	0.24	0.15	0.13	0.09
The Netherlands: Schelde	2.80	0.76	0.71	7.95*	1.25	0.50
The Netherlands: IJsselmeer	0.16	0.17	0.08	0.12	0.09	0.10
The Netherlands: Rijkswateren	0.47	0.36	0.30	0.86	0.29	0.17
The Netherlands: Regionale wateren	0.56	0.57	0.37	0.31	0.69	-

* This value is misquoted in Milieucompendium 2001 and should read 0.79 (Vlaamse Milieu Maatschappij personal communication)

Table C Temporal trends in regional measured Cd concentrations in suspended matter of Dutch freshwaters source: Milieucompendium, 2001)

	Cd concentrations in suspended matter (mg kg^{-1} dw)					
	1988	1990	1995	1998	1999	2000
The Netherlands: Rhine	9.2	5.3	3.8	3.5	3.0	7.5
The Netherlands: Maas	649	57	37	12.3	11.9	19.1
The Netherlands: Schelde	20.4	12.2	9.7	7.4	7.8	8.1
The Netherlands: IJsselmeer	2.2	3.2	2.4	1.2	1.5	1.9
The Netherlands: Rijkswateren	117	12.2	11.3	5.6	5.5	8.5

Table D Temporal trends in regional measured Cd concentrations in air (source: Milieucompendium, 2001)

	Cd concentrations in air (ng m^{-3})					
	1990	1992	1994	1996	1998	2000
The Netherlands	0.5	0.6	0.5	0.4	0.3	0.2

European Commission
Joint Research Centre
Institute of Health and Consumer Protection (IHCP)
Toxicology and Chemical Substances (TCS)
European Chemicals Bureau (ECB)

EU 22919 EN **European Union Risk Assessment Report**

Cadmium oxide and cadmium metal, Part I – Environment, Volume 72

Editors: S.J. Munn, K. Aschberger, O. Cosgrove, W. de Coen, S. Pakalin, A. Paya-Perez, B. Schwarz-Schulz, S. Vegro.

Luxembourg: Office for Official Publications of the European Communities

2007 – VIII pp., 638 pp. – 17.0 x 24.0 cm

Environment and quality of life series

The report provides the comprehensive risk assessment of the substance cadmium metal and cadmium oxide. It has been prepared by Belgium in the frame of Council Regulation (EEC) No. 793/93 on the evaluation and control of the risks of existing substances, following the principles for assessment of the risks to humans and the environment, laid down in Commission Regulation (EC) No. 1488/94.

Part I - Environment

This part of the evaluation considers the emissions and the resulting exposure to the environment in the production of cadmium metal and cadmium oxide, the use of these substances in the production of stabilisers, pigments, alloys and plated products. Further down-stream uses are not or only limitedly included. Following the exposure assessment, the environmental risk characterisation for each protection goal in the aquatic and terrestrial compartment has been determined. No risk assessment was performed for the atmosphere or the marine environment.

The environmental risk assessment concludes that there is concern for the aquatic ecosystem at certain metal production, processing and NiCd batteries recycling sites. For the terrestrial compartment a risk is identified at cadmium plating and alloy production sites. A borderline risk is found for soil cadmium concentrations leading to secondary poisoning. Furthermore, there is concern for micro-organisms of the wastewater treatment plants of certain NiCd battery recycling plants. In addition, a need for better information regarding the toxic effects of cadmium to aquatic organisms under low water hardness conditions is identified. Furthermore, for sediments there is a need for further information regarding the bioavailability of cadmium in order to possibly refine the assessment.

Part II - Human Health

This part of the evaluation is published in a separate document.

The conclusions of this report will lead to risk reduction measures to be proposed by the Commission's committee on risk reduction strategies set up in support of Council Regulation (EEC) N. 793/93.

The mission of the JRC is to provide customer-driven scientific and technical support for the conception, development, implementation and monitoring of EU policies. As a service of the European Commission, the JRC functions as a reference centre of science and technology for the Union. Close to the policy-making process, it serves the common interest of the Member States, while being independent of special interests, private or national.

European Commission – Joint Research Centre
Institute for Health and Consumer Protection (IHCP)
Toxicology and Chemical Substances (TCS)
European Chemicals Bureau (ECB)

European Union Risk Assessment Report

cadmium oxide and cadmium metal
Part I - environment

CAS No: 1306-06-19 EINECS No: 215-146-2
7440-43-9 231-152-8

Series: 3rd Priority List Volume: 72

European Chemicals Bureau

European Union Risk Assessment Report
cadmium oxide

CAS: 1306-19-0
EC: 215-146-2

PL-3
75

Institute for Health and Consumer Protection

European Chemicals Bureau

Existing Substances

European Union Risk Assessment Report

CAS No: 1306-19-0

EINECS No: 215-146-2

cadmium oxide
Part II – human health

CdO

3rd Priority List

Volume: 75

EUR 22766 EN

The mission of the IHCP is to provide scientific support to the development and implementation of EU polices related to health and consumer protection. The IHCP carries out research to improve the understanding of potential health risks posed by chemical, physical and biological agents from various sources to which consumers are exposed.

The Toxicology and Chemical Substances Unit (TCS), commonly known as the European Chemicals Bureau (ECB), provides scientific and technical input and know-how to the conception, development, implementation and monitoring of EU policies on dangerous chemicals including the co-ordination of EU Risk Assessments. The aim of the legislative activity of the ECB is to ensure a high level of protection for workers, consumers and the environment against dangerous chemicals and to ensure the efficient functioning of the internal market on chemicals under the current Community legislation. It plays a major role in the implementation of REACH through development of technical guidance for industry and new chemicals agency and tools for chemical dossier registration (IUCLID5). The TCS Unit ensures the development of methodologies and software tools to support a systematic and harmonised assessment of chemicals addressed in a number of European directives and regulation on chemicals. The research and support activities of the TCS are executed in close co-operation with the relevant authorities of the EU Member States, Commission services (such as DG Environment and DG Enterprise), the chemical industry, the OECD and other international organisations.

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European Union Risk Assessment Report

CADMIUM OXIDE

Part II – Human Health

CAS No: 1306-19-0

EINECS No: 215-146-2

RISK ASSESSMENT

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CADMIUM OXIDE

Part II – Human Health

CAS No: 1306-19-0

EINECS No: 215-146-2

RISK ASSESSMENT

Final Report, 2007

Belgium

This document has been prepared by the Belgium rapporteur on behalf of the European Union.

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Review of report by MS Technical Experts finalised:	**September 2002**
Final report:	**2007**

Foreword

We are pleased to present this Risk Assessment Report which is the result of in-depth work carried out by experts in one Member State, working in co-operation with their counterparts in the other Member States, the Commission Services, Industry and public interest groups.

The Risk Assessment was carried out in accordance with Council Regulation (EEC) 793/93[1] on the evaluation and control of the risks of "existing" substances. "Existing" substances are chemical substances in use within the European Community before September 1981 and listed in the European Inventory of Existing Commercial Chemical Substances. Regulation 793/93 provides a systematic framework for the evaluation of the risks to human health and the environment of these substances if they are produced or imported into the Community in volumes above 10 tonnes per year.

There are four overall stages in the Regulation for reducing the risks: data collection, priority setting, risk assessment and risk reduction. Data provided by Industry are used by Member States and the Commission services to determine the priority of the substances which need to be assessed. For each substance on a priority list, a Member State volunteers to act as "Rapporteur", undertaking the in-depth Risk Assessment and recommending a strategy to limit the risks of exposure to the substance, if necessary.

The methods for carrying out an in-depth Risk Assessment at Community level are laid down in Commission Regulation (EC) 1488/94[2], which is supported by a technical guidance document[3]. Normally, the "Rapporteur" and individual companies producing, importing and/or using the chemicals work closely together to develop a draft Risk Assessment Report, which is then presented at a meeting of Member State technical experts for endorsement. The Risk Assessment Report is then peer-reviewed by the Scientific Committee on Health and Environmental Risks (SCHER) which gives its opinion to the European Commission on the quality of the risk assessment.

If a Risk Assessment Report concludes that measures to reduce the risks of exposure to the substances are needed, beyond any measures which may already be in place, the next step in the process is for the "Rapporteur" to develop a proposal for a strategy to limit those risks.

The Risk Assessment Report is also presented to the Organisation for Economic Co-operation and Development as a contribution to the Chapter 19, Agenda 21 goals for evaluating chemicals, agreed at the United Nations Conference on Environment and Development, held in Rio de Janeiro in 1992 and confirmed in the Johannesburg Declaration on Sustainable Development at the World Summit on Sustainable Development, held in Johannesburg, South Africa in 2002.

This Risk Assessment improves our knowledge about the risks to human health and the environment from exposure to chemicals. We hope you will agree that the results of this in-depth study and intensive co-operation will make a worthwhile contribution to the Community objective of reducing the overall risks from exposure to chemicals.

Roland Schenkel	**Mogens Peter Carl**
Director General	Director General
DG Joint Research Centre	DG Environment

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[1] O.J. No L 084, 05/04/199 p.0001 – 0075

[2] O.J. No L 161, 29/06/1994 p. 0003 – 0011

[3] Technical Guidance Document, Part I – V, ISBN 92-827-801 [1234]

0 OVERALL RESULTS OF THE RISK ASSESSMENT

CAS Number: 1306-19-0

EINECS Number: 215-146-2

IUPAC Name: Cadmium oxide

Environment

(see separate document)

Human health

Human health (toxicity)

Workers

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) is reached because at the mentioned exposure levels, health risks (acute toxicity; respiratory irritation; kidney and bone repeated dose toxicity; genotoxicity; carcinogenicity, effects on fertility and reproductive organs) cannot be excluded upon inhalation exposure.

Conclusion (i) There is a need for further information and/or testing.

Conclusion (i) is reached because further information is needed to better document the possible neurotoxic effects of CdO suggested in experimental animals, especially on the developing brain. The collection of this additional information should, however, not delay the implementation of appropriate control measures needed to address the concerns expressed for several other health endpoints including repeated dose toxicity and carcinogenicity.

Conclusion (i) "on hold".

Consumers

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) is reached because among the examined scenarios, CdO is only involved for the manufacture of Ni-Cd batteries and, in this case, consumer exposure is considered to be non-existent or negligible.

Humans exposed via the environment

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) is reached because at the mentioned exposure levels, health risks (kidney and bone (all scenarios except adult non-smokers with sufficient iron stores) and lung (scenario 3) repeated dose toxicity, carcinogenicity/genotoxicity for all scenarios) cannot be excluded upon environmental exposure.

Related to the Scenario 3 ('near point sources'): the conclusion iii) for kidney & bone repeated dose toxicity is based on RWC calculated estimates derived from the highest exposure data per life-cycle step i.e. data from 1996 (three Cd metal producers) or 1999 (one NiCd battery producer) and in the absence of more recent emission and/or reliable measured data from Industry. To date, some of the plants for which these values were reported may have ceased activity or changed their production process.

For the same scenario, the conclusion (iii) for lung repeated dose toxicity is applicable to Cd metal producers only (RWC calculated estimate based on emission data of 1996 at three sites and in the absence of more recent emission and/or reliable measured data from Industry: to date, some of the plants for which these values were reported may have ceased activity or changed the production process).

Conclusion (i) There is a need for further information and/or testing.

Conclusion (i) is reached because further information is needed to better document the possible neurotoxic effects of CdO suggested in experimental animals, especially on the developing brain. The collection of this additional information should, however, not delay the implementation of appropriate control measures needed to address the concerns expressed for several other health effects including repeated dose toxicity and carcinogenicity.

Conclusion (i) "on hold".

Human health (risks from physico-chemical properties)

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Given the level of control in manufacture and use, the risks from physicochemical properties are small (see Section 5 for more details).

CONTENTS

TABLES

1 GENERAL SUBSTANCE INFORMATION

As much of the (eco)toxicological information on Cadmium metal is derived from Cadmium oxide (and other cadmium compounds), and as a close relationship exists between both priority substances (see mass-balance) it was proposed that both RARs should be merged for the sections 1 to 4 with exception of the risk characterisation in the Human Health part where for each substance a separate section on risk characterisation and conclusions should be developed.

Primary source of information for this section and more particularly Sections 1.1, 1.2 and 1.3, was the 'IUCLID' document provided by Industry (Lead-company) in 1997 as a background document and complement to the HEDSETs.

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS-n°:	7440-43-9	1306-19-0
EINECS-n°:	231-152-8	215-146-2
IUPAC name:	Cadmium metal	Cadmium oxide
Synonyms:	Not applicable	Not applicable
Molecular formula:	Cd	CdO
Atomic/Molecular weight:	112.41 (several naturally-occurring isotopes ranging from 106-116 (Lexicon, 1972; WHO, 1992)	128.41
Colour	blue-white (Sax and Lewis, in: ATSDR, 1998)	varies from greenish-yellow through brown to nearly black, depending on the thermal history (due to lattice defects) and on the particle size

1.2 PURITY/IMPURITIES, ADDITIVES

	Cadmium metal	Cadmium oxide
Purity (powder):	Min. 99.9%	min. 99.999% (IUCLID, 1997)
Purity (massive):	Min. 99.99%	
Impurities (max.):	for 99.99% Cd metal: Fe: 10 ppm; Cu: 20 ppm; Ni: 10 ppm; Pb: 100 ppm; Zn: 30 ppm, Th: 35 ppm. Other levels are specified for other purity grades. (ASTM B440-00)	n.a. powder reagent grade: max. chloride 0,002%; nitrate 0,01%; sulphate 0,20%; copper 0,005%; iron 0,002%; lead 0,01% (JT Baker chemical Co, 1984)
Additives:	none	none

Remark: It is stated that the purity levels and chemical analyses indicated here are purely arbitrary as many grades of both cadmium metal and cadmium oxide exist. It is recommended that the ranges or specifications should be listed using the appropriate ISO or EN standards (ICdA, com. 2003). However, only the ASTM standard was provided for Cd metal grades 99.95, 99.99 and 99.995%.

1.3 PHYSICO-CHEMICAL PROPERTIES

Table 1.1 Summary of physico-chemical properties

Property	Cadmium metal	Cadmium oxide
Physical state:	solid (massive or powder)	solid (powder)
Crystal structure:	distorted hexagonal close-packed	cubic structure with each ion surrounded by six ions of opposite electric charge, octahedrally arranged. Also an amorphous form exists: stable at lower temperatures, forming crystals of the cubic type at red heat
Melting point:	320,9°C (Lexicon, 1972, Sax and Lewis: in ATSDR, 1998;CRC: in IUCLID, 1997)	Decomposes at 900-1000 °C (CRC, 1985; IUCLID, 1997)
Boiling point:	765°C (idem); 767°C (Sax and Lewis: in ATSDR, 1998)	CdO is non-fusible but volatilises at high temperature. Sublimation at 1559°C
Relative density:	8.64 g/cm^3 (Lexicon, 1972, Sax and Lewis: in ATSDR, 1998: analysis by WIAUX S.A., in LISEC, 1998e).	8.15 g/cm^3 (cubic form); 6.95 g/cm^3 (amorphous) (EPA 1985).
Vapour pressure:	1 mmHg at 394°C (Sax and Lewis: in ATSDR, 1998 133 hPa at 394°C (CRC, in: IUCLID, 1997)	1 mmHg at 1000°C (Sax, N.I., 1984)
Water solubility:	quoted as 'insoluble' (The Merck index; in: ATSDR, 1998; CRC, in: IUCLID, 1997). However it was mentioned: 0,05 mg/1 at pH 10,5 a curve in function of pH and hardness: at pH 7: solubility is 10 to 100 times higher than at pH 8.5 dependent on the total carbonate concentration (M. Farnsworth, 1980). Measured dissolved cadmium concentrations after 7 days transformation/dissolution test with cadmium metal powder at loading 1 – 100 mg/l, were in the range 0.192 – 0.135 mg/l (at pH +/- 8) (LISEC, 1998e).	quoted as 'insoluble' However measured dissolved cadmium concentrations after 7 days transformation/dissolution test with cadmium oxide powder at loading 1 – 100 mg/l were in the range 0.095 – 0.227 mg/l (at pH +/- 8) (LISEC, 1998f). Soluble in acids and solutions of ammonium salts (Farnsworth, 1980).
Partition coefficient:	No data	No data

Table 1.1 continued overleaf

Table 1.1 continued Summary of physico-chemical properties

Property	Cadmium metal	Cadmium oxide
n-octanol/water(log-value):	Not applicable	Not applicable
Flammability:	Slight fire hazard. The finely divided metal may be pyrophoric in air (MSDS, 1992; IUCLID, 1997)* GLP testing conform EC Testing methods A.10, A.12 and A.13 (BAM, 2002): Cadmium metal 'powder' [particle size distribution (in volume-%): d(0.1): 3.462µm; d(0.5): 7.154 µm; d(0.9): 14.117 µm; mean water content: 0.03] and cadmium 'fine billes' [particle size distribution (in volume-%): d(0.1): 2.485µm; d(0.5): 7.040µm; d(0.9): 15.753µm; mean water content: 0.05] are not flammable and do not have pyrophoric properties in sense of the EC-methods, Dir. 92/69/EEC.	Not flammable
Explosive properties:	Dust/air mixture may be explosive. Even as fine powder, cadmium is hardly explosive (MSDS, 1992; INRS, 1987)	
Self-ignition:	Not applicable	Not applicable
Oxidising properties:	Not applicable	Not applicable
Granulometry:	The average spherical diameter of cadmium powder prepared by distillation is about 18 µm +/- 13.3 µm (S.D.) (inhalable fraction) and the specific surface area : 580.4 cm2/g (analysis by WIAUX S.A., in: LISEC, 1998e). Particle size and surface area depend very much upon the specific process and specific application. For example, INMETCO produces a cadmium metal shot which is many times larger than the aforementioned cadmium metal powder (ICdA, com. 2003). See also remark related to flammability testing.	The average spherical diameter of CdO powder prepared by oxidation of Cd metal is about 0.55 µm (respirable fraction) (La Floridienne, 1997). Particle size and surface area depend very much upon the specific process and specific application (ICdA, com. 2003).

Table 1.1 continued overleaf

Table 1.1 continued Summary of physico-chemical properties

Property	Cadmium metal	Cadmium oxide
Odour threshold:	No data	No data
Ionisation potential:	E°Cd/Cd2+ = 0.4025 eV (= fairly reactive)	
Caloric value	0.16 Cal/g	

GLP testing on flammability and pyrophoric properties of the products, Cadmium metal powder and Cadmium 'fine billes' according to the EC Methods A.10, A.12 and A.13 was performed by Industry (ICdA) on a voluntary basis (final report of BAM, October 2002). The substances are not flammable and do not have pyrophoric properties in sense of the EC-methods, Dir. 92/69/EEC and are thus not to be classified (and labelled) related to these properties.
The grade Cadmium 'fines billes' is stated as being the finest grade of Cadmium 'powder' from current EU manufacturing that is put on the market (since 2001). However, other qualities may be manufactured elsewhere e.g. in Japan and China (ICdA, pers. com. 2003).
The physical, thermal, electrical, magnetic, optical, and nuclear properties of cadmium metal are summarised by Morrow (2001), however without indication of testing specifications or the primary source. Where available, this source confirms the aforementioned entries for physico-chemical properties.

1.4 CLASSIFICATION

According to Annex I of Directive 67/548/EEC (29th ATP) of 16/06/2004.

Cadmium metal and oxide

Carc. Cat. 2; R45	Category 2 Carcinogen; May cause cancer
Muta. Cat. 3; R68	Category 3 Mutagen; Possible risks of irreversible effects.
Repr. Cat. 3; R62-63	Category 3 Toxic to Reproduction; Possible risk of impaired fertility, and of harm to the unborn child
T; R48/23/25	Toxic: danger of serious damage to health by prolonged exposure through inhalation and if swallowed
T+; R26	Very toxic by inhalation
N; R50-53	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Note on Environmental classification and labelling

A general introduction and description of the methodology on classification and labelling of insoluble and sparingly soluble metals, including the dissolution test and the criteria for classification is given in the RAR on zinc metal[4][5]. The results of Dissolution and Short-term toxicity tests will be discussed in detail in Part I (Environment) of the present Risk Assessment Report, due to be published separately.

[4] http://ecb.jrc.it/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/zincmetalHHreport072.pdf

[5] It should be noted that the 'critical surface approach' as suggested in OECD context is not considered in the reports for neither cadmium metal nor cadmium oxide.

2 GENERAL INFORMATION ON EXPOSURE

2.1 PRODUCTION

Cadmium metal

Cadmium is a naturally occurring element with ubiquitous distribution. Although cadmium ores also exist (greenockite) these are not commercially important. Zinc (sulphide) ores are the primary source for cadmium production. Smaller amounts of cadmium are produced during the production of other non-ferrous metals such as lead. In the refining of these ores cadmium is obtained as a by-product (Technical notes on cadmium, 1991).

Whereas the extraction and refining of the primary non-ferrous metal from the ores can be obtained either by pyrometallurgical or electrolytic processes, the final step of cadmium production is done by fractional distillation or electrolysis.

Cadmium oxide

Although cadmium oxide is an important commercial compound it is not manufactured from the zinc or mixed non-ferrous metal ores, phosphate rock, coal or other rock forms, as cadmium oxide but indirectly from the cadmium produced as a by-product in the manufacture of zinc and lead. The substance is important commercially for itself and also because of its extensive use in the preparation of other cadmium compounds.

2.1.1 Production processes

Cadmium metal

The primary non-ferrous metal can be produced via two distinct types of production.

The formerly used pyrometallurgical processes. Here the residual sintered concentrate (calcine) containing oxidised zinc and cadmium materials is heated to about 1,100 to 1 350°C, reduced by carbonaceous material and the zinc and cadmium volatilised. The metal vapours are condensed and collected as metal dust. Most of the cadmium collects with the zinc metal and may be removed in the refining of zinc by fractional distillation (refluxing). In this process the boiling points of the metals present (cadmium 767°C, zinc 906°C and lead 1,750°C) are well separated and the cadmium can be concentrated in a cadmium-zinc alloy. Further repeating the distillation process under reducing conditions will result in cadmium metal with increasing purity.

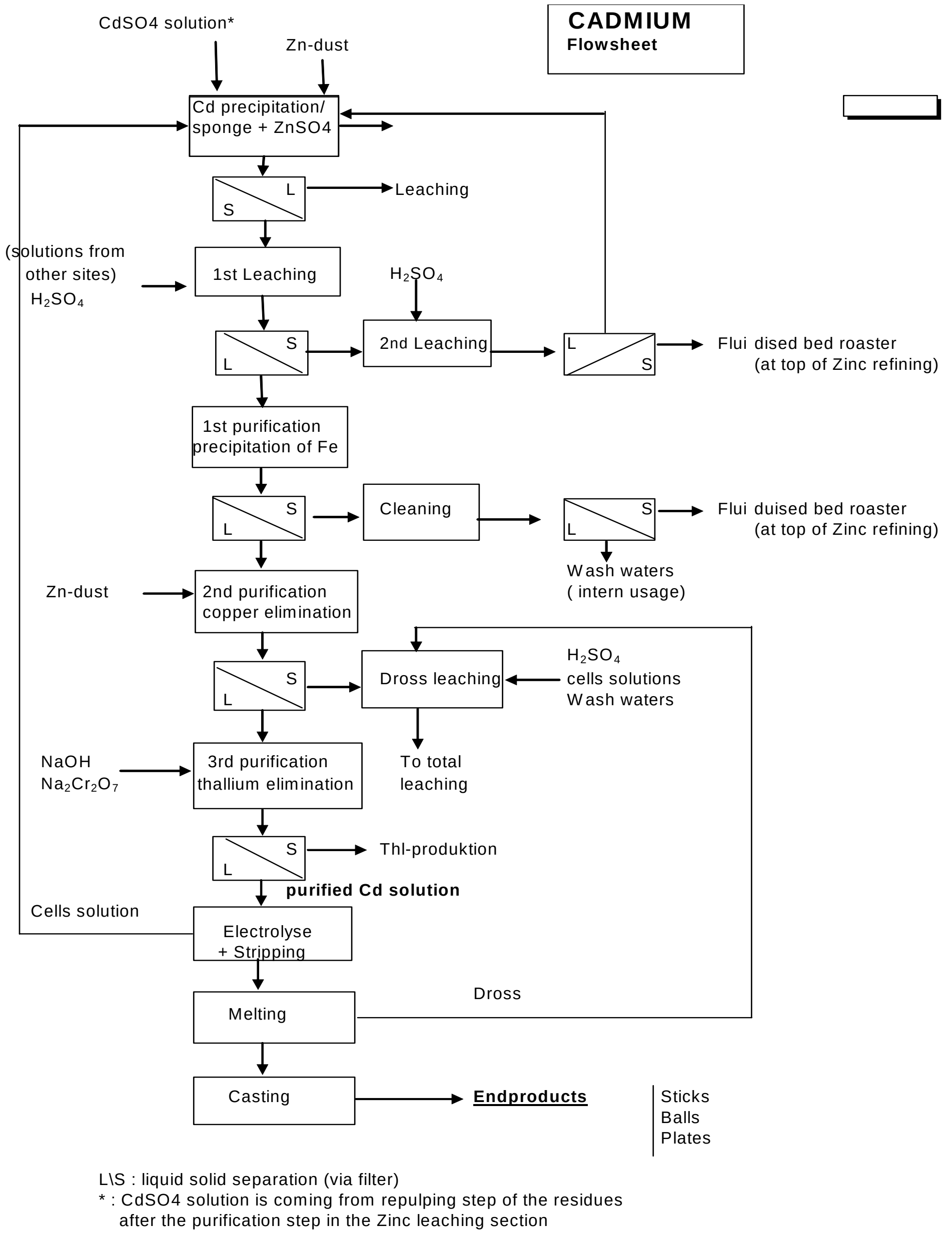
The present-day electrolytic process has the following main features. During the production of zinc, at the purification of the solutions of zinc sulphate, before the electrolysis, cadmium is present in dissolved impurities ($CdSO_4$). Cadmium is precipitated herein by adding zinc (as zinc powder or dust). The resulting impure cadmium residue (cadmium sponge) is purified and leached with aqueous sulphuric acid solution. A reasonably pure cadmium sponge is produced after two additional acid solution/zinc dust precipitation stages. The sponge is again dissolved in sulphuric acid and the solution, if sufficiently pure, is passed into electrolytic cells where the cadmium is deposited on cathodes (see **Figure 2.1**).

After deposition, the cathodes are stripped and the cadmium melted and cast into the required shapes (sticks and balls). The metal is typically either 99.95 or 99.99% pure. Higher purity grades for special purposes can be obtained by further vacuum distillation (Lexicon, 1971; Technical notes on cadmium, 1991).

Variations in the production flow-sheet exist from one production site to the other. These may be due to differences in the type of the ores (zinc, lead), origin, form and content, the purity of the end-product that is aimed at, legal environmental criteria and the extent of (auto) recycling activities (scraps, flue dust etc.).

In the EU cadmium metal is produced mainly as a by-product of zinc production via electrolytic processes (approximately 77.5% of the total volume). The rest is obtained in association with pyrometallurgical refining processes (Industry Questionnaire, 1997).

Figure 2.1 Cadmium production flow-sheet: an example of electrolytic process in a closed production system (Union Minière, 1998)



Cadmium oxide

In the commercial production process, cadmium oxide is prepared by the reaction of cadmium metal vapour with air. For the production of cadmium as part of the refining of zinc ores, we refer to the aforementioned paragraph. Other production possibilities are thermal decomposition of the carbonate, nitrate, sulphate or hydroxide but these are stated not to be in use for current industrial production (IcdA, com., 2003).

Cadmium oxide is available on the market in powder form. Its average particle size (spherical diameter) is 0,5 to 0,55µm (IUCLID, 1997).

It is packaged in metal drums, big bags, flo bins or containers (IUCLID, 1997).

Figure 2.2 Cadmium oxide production: flow-sheet

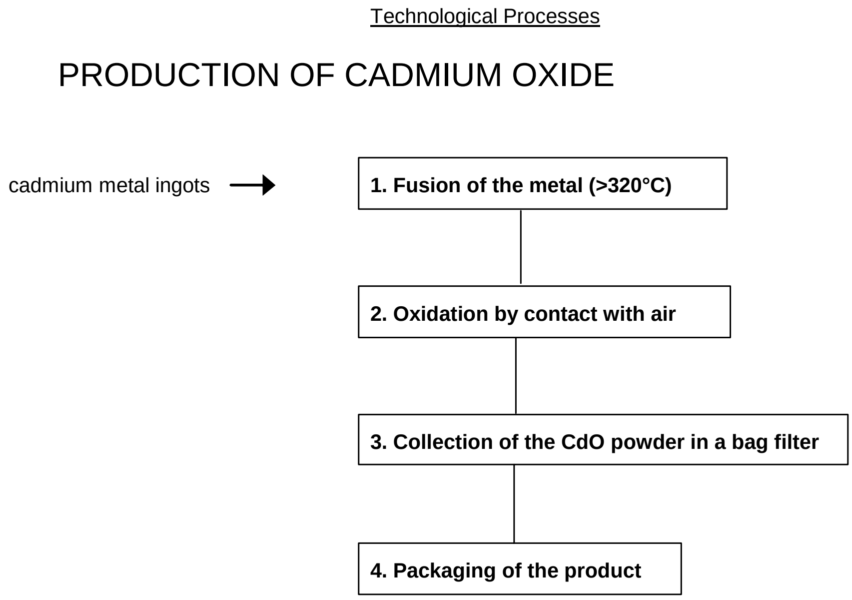
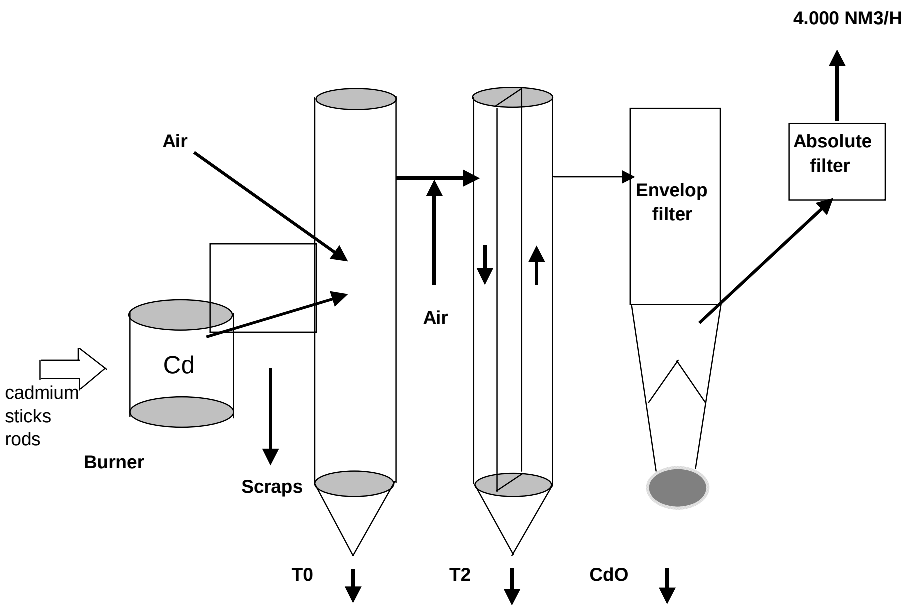


Figure 2.3 Production of cadmium oxide (PC WIAUX company information, 1998)



The manufacturing process for cadmium oxide is partly enclosed. Cadmium metal in ingots is manually placed in furnaces heated at 320°C. Emitted fumes are oxidised by contact with air in a closed system. The produced CdO powder is filtered and collected in bags, flo bins and metal drums or directly into silo. The packaging station has local exhaust ventilation at the discharge point. Workers have to place and adjust the bag or drum under the discharge and to set the process in motion (semi-automated process). Filled bags and drums are subsequently closed and carried to the storage area.

2.1.2 Production volumes

2.1.2.1 Data for the reference year 1996

Cadmium metal

The world primary cadmium production is estimated at 14,000 to 16,000 tonnes/year, the corresponding figure for Europe was approximately 5,000 tonnes/year (1994) – 5,800 tonnes/year (1996) (Industry, 1997), produced at 12 sites all over the EU territorial surface with, in these years, a major site localised in Belgium.

The amount imported in Europe in the same period is estimated at 1,500 tonnes/year – 960 tonnes/year (figure representative for January-July '96) (Eurostat, 1997; in: IUCLID, 1997). Export out of Europe is estimated at 2,200 tonnes/year (1996). This latter figure is obtained by subtracting the total EU consumption from the total EU production (IZA, personal comm., 1997).

Table 2.1 Cadmium production plant size distribution for 1996

Tonnes	Number of cooperating companies
< 300 tonnes	5
300-600 tonnes	4
> 600 tonnes	3

Table 2.2 Production sites of metallic Cadmium in the EU (in the range 10 to >1,000 tonnes/year, EUREX), IUCLID 1997

Company (and plant)	Country
Produits Chimiques Wiaux SA*	Belgium
Asturiana de Zinc	Spain
Britannia Zinc Limited	UK
Budel Zink BV	The Netherlands
Enirisorse	Italy
Espanola Del Zinc S.A.**	Spain
Metaleurop Nord S.A.S.	France
Metaleurop Weser Zink GmbH	Germany
Norzink	Norway

Table 2.2 continued overleaf

Table 2.2 continued Production sites of metallic Cadmium in the EU (in the range 10 to >1,000 tonnes/year, EUREX), IUCLID 1997

Company (and plant)	Country
Outokumpu Zinc OY	Finland
Ruhr-Zink GmbH	Germany
Union Miniere Balen***	Belgium

* Production/conversion stopped in 2001 (plant is closed down; Ind., pers. Comm., 2002)
** Last cadmium production in 1991; since: zinc refinery without cadmium production
*** Company's name became UMICORE (2001) and production stopped in 2002

Remark: one company identified by the EUREX CD ROM is not included in the risk assessment process (phase 3 company with a production/import volume between 10 and 1,000 tonnes/year). Apparently it concerns a German pigment manufacturer presumably importing/using cadmium metal for further processing only.

An update provided by Industry (IcdA, com., 2003) reveals that Asturiana de Zinc in Spain no longer produces cadmium. Britannia Zinc and Metaleurope (France) have both recently closed down. Española del Zinc and Ruhr-Zink have not produced for many years. Outokumpu and Umicore exited the cadmium production business more recently. The **Table 2.2** needs thus some serious revision. It gives the impression that there are 12 active cadmium production plants in Europe when in fact there are now only three, possibly four: Budel (now known as Pasminco Budel), Norzink (now known as Norzinc Outokumpu), Enirisorse (now known as Porto Vesme, owned by Glencore) and possibly Metaleurop Weser Zink (recently taken over by Glencore). No more details were submitted.

Table 2.3 Raw EU production, import, export and consumption data of cadmium metal in metric tonnes (Industry site specific questionnaire, 1997)

Year	EU production	EU import	EU export	EU consumption
1994	5,000	1,582	n.d.	n.d.
1995	5,648	2,822	4,953	3,517
1996	5,808	960 (until July)	2,200 (derived)	n.d.

n.d. No data

The available figure for 1996 has been derived from the production figure and the consumption figure of 1995 (assuming that this remained roughly the same in 1996); IZA, personal comm., 1997). The consumption figure for 1995 has been roughly derived from the information on production volumes used downstream in plating, pigments, stabilisers and batteries production facilities (IcdA, 1997).

Cadmium oxide

The world production of cadmium (metallic) is estimated at 14,000 to 16,000 tonnes/year. The production of cadmium oxide for Europe was approximately 3,070 tonnes/year (1994) – 2,536 tonnes/year (1996) (Industry Questionnaire, 1997), produced at 2 major sites in the EU (Belgium).

Table 2.4 Production sites of cadmium oxide in the EU (EUREX), IUCLID 1997

Company (and plant)	Country
Floridienne Chimie S.A., Ath	Belgium
Produits Chimiques Wiaux SA*	Belgium

* Production was taken over by Floridienne in 2000, and was definitively stopped in 2001 (Ind., pers. Comm., 2002)

Remark: one company identified by the EUREX CD ROM is not included in the risk assessment process (the concerned company has a production volume in the range: 10 – 1,000 tonnes/year). It concerns a pigment manufacturer presumably importing/using cadmium metal for further processing – via an in-house production of cadmium oxide - to pigments only.

The amount of cadmium oxide imported in Europe is unknown with the exception of the first half of 1996 (January to July) for which 23 tonnes was reported (IUCLID, 1997). The latter document does not cite information on export. The site-specific information however mentions an important export activity taking place every year (approximately 1,000 tonnes/year leave the EU).

Table 2.5 Raw EU production, import, export and consumption data of cadmium oxide in metric tonnes (IUCLID, 1997; Industry site specific questionnaire, 1998)

Year	Production	Import	Export	Consumption
1994	3,069	n.d.	≥ 1,050	n.d.
1995	2,757	n.d.	≥ 1,350	n.d.
1996	2,536	23 (until July)	1,000	n.d.

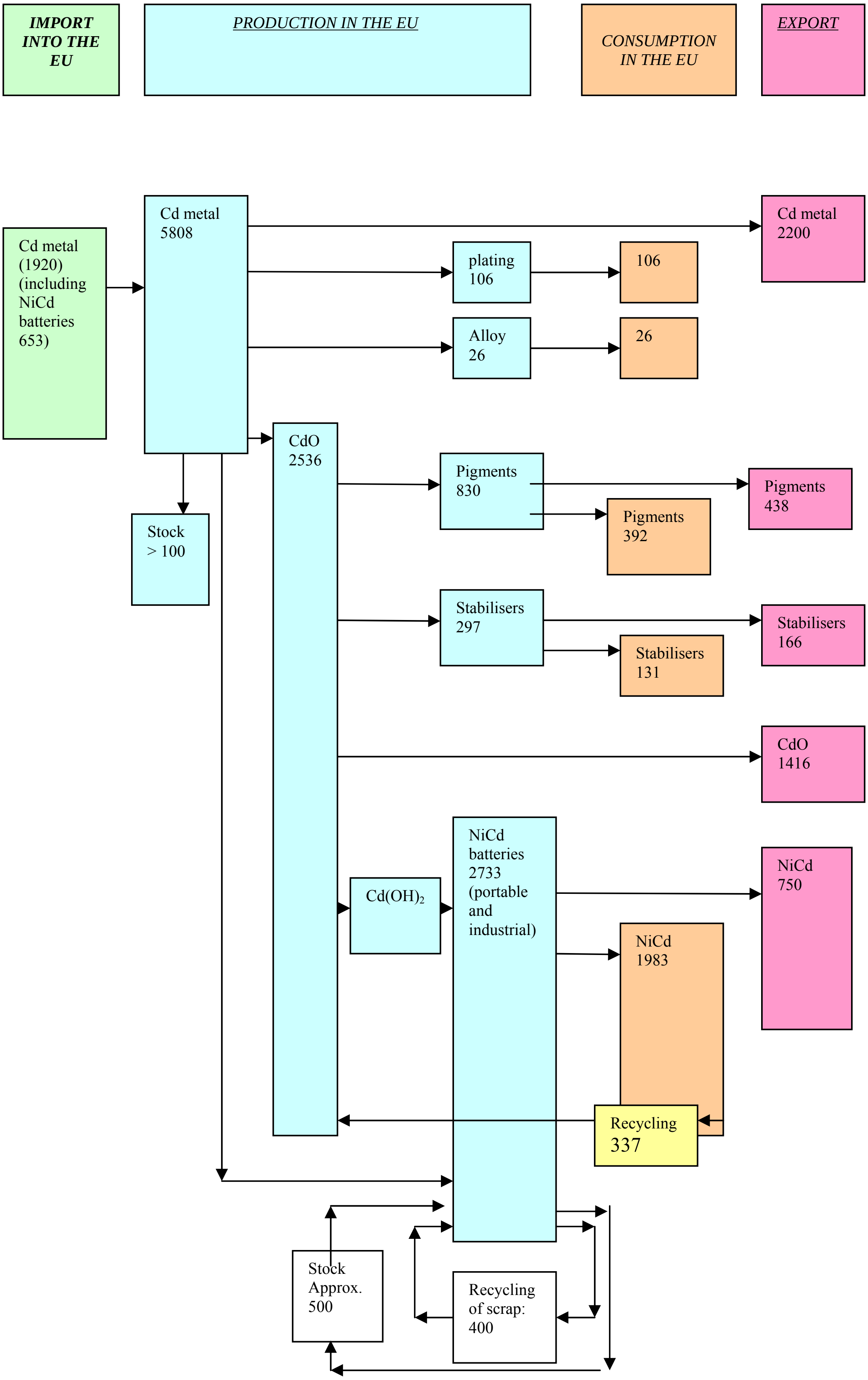
Production, import, export and consumption figures for both priority substances, cadmium metal and cadmium oxide, submitted by Industry are fragmentary.

In 2000, Industry provided a mass-balance for the reference year 1996, accompanied by an explanatory note (see **Figure 2.4** and further), reflecting the best possible estimate at the moment.

An update for the year 2000 was provided in the context of the batteries' targeted risk assessment (see **Figures 2.9** and **2.10** in Section 2.2.2.3.2) and estimates for the year 2002 in the context of the update site-specific assessment (see **Figure 2.11** in Section 2.2.3.1).

Two important confounding factors make it difficult to establish accurate cadmium consumption figures: 1) the conversion of cadmium metal into cadmium oxide and other cadmium compounds and 2) shipments of cadmium-containing residues to zinc smelters from recycling operations (Morrow, 2001).

Figure 2.4 Cadmium mass flow sheet (metric tonnes)- reference year 1996 (Source: IZA-Europe, IcdA, UM and CollectNiCd, 2000 and 2001)



Explanatory note to the mass-flow of cadmium (as provided by Industry)

The mass balance reveals that 5,808 tonnes of cadmium were produced in Europe in the reference year (1996). The imports were estimated to 1,920 tonnes including the contribution of the metal present in imported consumer/sealed portable nickel-cadmium batteries. Cd metal stocks exists in Rotterdam which may influence the trading balance but the data reported hereafter have been mainly obtained from use at the industrial level for the various applications.

It can be observed that a large industrial activity consists in the transformation of cadmium metal in the oxide: the equivalent of 2,536 tonnes of cadmium are used in the production of cadmium oxide.

The EU regional use of metal reaches the value of 2,638 tonnes, which are distributed for 75.2% to Ni-Cd batteries, 14.9% to pigments, 5% to stabilisers and 5% into alloys and plating.

Portable Nickel-Cadmium batteries are introduced on the market as a power source incorporated in Electrical and Electronic equipment in more than 90% of the cases. This is the origin of a significant export ratio for batteries. This ratio has been estimated between 33% to 50% (according to applications and countries) for the consumer/sealed portable batteries produced in Europe on the basis of the Import- Export balance.

Industrial Ni-Cd batteries are not imported in significant quantities (less than 5%). They are manufactured in European countries and are exported in a significant proportion, estimated to 35% for the global European market. The net export of cadmium from batteries reaches the estimated volume of 750 tonnes.

The largest export quantity is found in the cadmium metal produced by European companies in order to satisfy the demand in USA, Asia and South America. A significant fraction of the cadmium oxide produced in Europe is exported to non-European battery manufacturers which demonstrates the competitiveness of this European industry involved in the transformation of Cadmium into the oxide. When the battery is marketed, the cadmium content is present as cadmium hydroxide (discharged battery) or as cadmium metal (charged battery).

It has been estimated that cadmium from recycling operations reached approximately 337 tonnes from used batteries collected from the market and industrial sources. In addition, there are two types of stocks to be considered. First, the manufacturing rejects and secondly, a cadmium stock for the work in progress. Those have been presented in a closed loop independently of the total inlet and outlet of the primary cadmium. Indeed recycling operations leads to a 99% recovery of the cadmium content of the battery. The metal has a purity higher than 99.9% and is re-used in new battery manufacture. The battery manufacturing capacity will produce a new volume of waste equivalent to the treated one, which is re-introduced in the circuit. At the same time, the management of a stock required for the "work in progress" is considered.

Mass-balances are available for several EU countries, and years (e.g. Denmark for 1996 (Danish EPA, 1994 and 2000), Germany for 1990, 1991, 1992, 1993 and 1994 (UBA, 1996), the Netherlands for 1980 (VROM, 1991), France for 1995/1996 (l'Académie des Sciences Rapport N° 42, 1998) and Greece for 1993 and 1997 (EUPHEMET, 2000). From these documents, the overall consumption patterns and trends are roughly confirmed, with a largely predominant flow of cadmium in batteries that dramatically increased since the eigthies and continued during the nineties while most other uses have been declining.

2.1.2.2 Update date (reference year 2002)

In 1997, from the companies liable to the Regulation 793/93/EEC, there were 12 companies producing cadmium metal and 2 producers of cadmium oxide. Regards the import of the substances, one company for cadmium metal and one company for cadmium oxide were active in the field and were subject to the existing substances regulation.

In 2005, this picture has significantly changed. An overview is given here below.

Cadmium metal

The companies that stopped the production of cadmium metal/cadmium oxide and the approximate date are listed in **Table 2.6**.

Table 2.6 Production sites of metallic cadmium/CdO in the EU in the range 10 to > 1,000 t/y that stopped production

Company (and plant)	Country	Date/year of production stop
Asturiana de Zinc (now: Xstrata Zinc)	Spain	1998
Britannia Zinc Limited (in liquidation: 2003)	UK	2003
Espanola del Zinc S.A.	Spain	1991/1992
Metaleurop Nord S.A.S.	France	2003
Outokumpu Zinc OY (now: Boliden Kokkola)	Finland	2002
Ruhr-Zink GmbH	Germany	1998-1999
Union Minière Balen (now : Umicore)	Belgium	2002
Produits Chimiques Wiaux S.A.	Belgium	2000/2001

Former activities at Produits Chimiques Wiaux S.A.: limited to the conversion of massive cadmium metal into cadmium metal powder

The companies still manufacturing cadmium metal in 2005 are reported in **Table 2.7**. All companies produce the substance in massive form (e.g. plates, sticks, balls).

Table 2.7 Current producers of cadmium metal liable to the Regulation 793/93/EEC

Company (and site)	Country
Budel Zink (now: Zinifex Budel)	The Netherlands
Norzink (now: Boliden Odda A.S.)	Norway
Metal Europ Weser Zink (now: Xstrata Zinc GmbH)	Germany

Updated data on EU-16 production data are given in **Table 2.8**. No data are available on the situation in the EU-25.

Table 2.8 EU production, import, export and consumption data on primary cadmium metal in metric tonnes (Industry site specific questionnaire, 2004/2005)

Year	EU production	EU import	EU export	EU consumption
2002	1,114	n.d.	n.d.	n.d.
2003	1,207	n.d.	n.d.	n.d.

n.d. No data available

Based on the data of one producer 85% of the production volume is exported outside the EU-25. A second company mentions 100% export but it is not clear if this is meant as outside the EU or outside country where production is located.

The amount of secondary cadmium produced by recycling is given under Section 2.2.3.2.

The total volume of cadmium consumed within the old EU-16 (including Norway) and the new EU-25 territory is unknown.

Cadmium oxide

Update information regards the producers of cadmium oxide is given in the **Table 2.9** and **Table 2.10**.

Table 2.9 Production sites of metallic cadmium in the EU in the range 10 to > 1,000 t/y that stopped production

Company (and plant)	Country	Date/year of production stop
Produits Chimiques Wiaux S.A.	Belgium	2000/2001

Former activities at Produits Chimiques Wiaux S.A.: limited to the conversion of massive cadmium metal into cadmium oxide

Table 2.10 Production sites of cadmium oxide in the EU with volume > 1,000 tonnes/year (reference year: 2002)

Company (and site)	Country
La Floridienne	Belgium

Information on the total production of cadmium oxide by La Floridienne was submitted for the reference year 2002. Since 1996 there is an increase of the production volume.

2.2 USES

2.2.1 General overview

Cadmium metal

Metallic cadmium is mainly used in the production of batteries, cadmium compounds (cadmium oxide and to a lesser extent cadmium hydroxide). Further also in coatings, alloys and other miscellaneous uses (see **Table 2.11** showing the industrial and use categories of cadmium). The two types of ‘Main categories’ for cadmium are characterised as non-dispersive use and use resulting into or onto a matrix.

Metallic cadmium is commercialised in different forms: powder, balls (3-5 cm diameter), plates (10-200-200 to 1.000mm) or sticks (200 to 240-10 to12 mm) (IUCLID, 1997).

CdO production

An important proportion of the cadmium metal produced is subsequently used in the production of cadmium oxide powder. This substance has several applications and constitutes the (principal) raw material in the production of other cadmium compounds.

The CdO produced has a high purity (at least 99% CdO) resulting in a cadmium wt% of 87.25 to 87.5.

A short description of the uses of respectively cadmium metal and cadmium oxide and processes involved is given below (source: IcdA, 1997, unless specified otherwise).

Cadmium metal

Batteries

See the batteries' related sections (see Section 2.2.2).

Plating

By plating of metals or alloys a coating is provided that is resistant to corrosion by alkalis, salt water and atmosphere. Furthermore these coatings are highly ductile and easily soldered.

Cadmium coatings have low coefficients of friction and maintain high electrical conductivity, and hence are used mainly in applications where both corrosion resistance and lubricity or good electrical conductivity are required (IcdA, com., 2003). Cd-Ti and Cd-Sn electroplated coatings are used to resist hydrogen embrittlement in high strength steel fasteners.

The coating can be realised by electrochemical reaction: cadmium is the anode in the cell formed with an iron substrate in water. Other technologies for coating are vacuum deposition (mainly cyanide baths), dipping or spraying[6] , or mechanical plating[7] with cadmium powder, where glass shot is used. Cadmium ion vapour deposition is another technique also used. For further details on the processes see Section 4.1.1.

Electrodeposition of cadmium on a metal substrate accounts for 90% of the cadmium used in plating. The remaining 10% is applied by vacuum deposition, metal spraying[2] or mechanical[3] plating.

Cadmium plating by electrodeposition uses an alkaline cyanide solution of the metal as starting material. The plating solutions can be purchased direct from chemical manufactures; alternatively they can be prepared on-site from cadmium metal or oxide. The plating solution normally contains 18-22 g/l Cd. Baths usually have cadmium bars or ball anodes, placed in steel anode baskets with a surface area of cadmium equal to the plating load. Barrel plating usually uses and electrolytes with less cadmium (15 g/l). After electroplating, and heat treatment if required, a chromate conversion coating is usually applied on a subsequent bath (IcdA, 1997).

Plating contains 99,95% cadmium (IUCLID, 1997).

Alloys

Cadmium has been a common component of many alloys which uses are related to their melting temperatures, e.g. tin-lead-bismuth-cadmium alloy joining metal parts which may be heat sensitive; silver-cadmium-copper-zinc-nickel alloy for joining tungsten carbide to steel tools. The EU use of cadmium as a constituent of alloys (mainly Cu-Cd and Ag-CdO) has

[6] dipping and spraying are no longer used (ICdA, com., 2003)

[7] mechanical coating has declined significantly (ICdA, com., 2003)

declined in importance in the recent years (4% of total use in 1985, about 0.6% in 1996) as these have been substituted by cadmium free alloys with comparable characteristics of ductility and strength in the majority of uses.

Cu-Cd alloys are prepared by re-melting high conductivity copper in suitable furnaces and adding the necessary cadmium in the form of a copper-cadmium master alloy, or by ‘side-casting’ from holding furnaces fed by the large reverberatories of refineries.

During the manufacturing of the master alloys, drosses containing Cd are released. Usually, they are recycled internally or in other metal plants.

The normal form of the casting is a wire bar, which is hot rolled before drawing to wire. Normal practise is followed in drawing the rod to wire, using dies of suitable shape in the case of trolley wire. Limited quantities of sheet and strip are produced by rolling and of rod by extrusion and drawing (IcdA, 1997).

Cu-Cd alloys contain usually 0.2-0.8% cadmium. The production of these alloys occurs via pre-alloys (containing 49-51% cadmium) which are further processed by other industries to prepare the final Cu-Cd alloys (IUCLID, 1997).

Ag-CdO electrical contact alloys are produced by internally oxidising an Ag-Cd alloy. The percentage of Cd in Ag-CdO alloys is generally in the range of 5% to 15% (IcdA, pers. Com., 2003).

Other uses

Applications as reported by Farnsworth (1980): deoxidiser in nickel plating, in process engraving, in electrodes for cadmium vapour lamps, in photoelectric cells and in the photometry of ultraviolet sunlamps, in selenium rectifiers and Jones reductors and application of cadmium powder as an amalgam (1Cd:4Hg) in dentistry, are stated by Industry as no longer in use (IcdA, pers. Com., 2003).

<u>Cadmium oxide</u>

Cadmium oxide is used as starting material for a wide variety of other cadmium compounds (PVC heat stabilisers, pigments). Cadmium oxide has been used as a stabiliser for the cadmium sulphide and sulpho-selenide forms in glass[8]. In nitrile rubbers the substance improves heat resistance; in plastics, it improves high temperature properties.

Another field of (minor) applications is based on the catalytic properties of cadmium oxide. It catalyses reactions between inorganic compounds, as well as organic reactions such as oxidation-reduction, dehydrogenation, cleavage and polymerisation (use as vulcaniser). It sensitises photochemical reactions.

Other (former) uses included phosphors, semi-conductors, manufacture of silver alloys, and as nematocide-anthelmintic in swine and poultry.

A short description of the uses and processes involved is given below (source: IcdA, 1997, unless specified otherwise).

[8] This use is not known by Industry (ICdA, pers. com., 2003)

Batteries

Although cadmium metal is one of the principle raw materials, cadmium oxide is used in the manufacture of certain types of cadmium electrodes (IcdA, 1997). See the batteries' related sections (see Section 2.2.2).

Stabilisers

Barium cadmium stabilisers can be manufactured in a number of ways. The starting materials are usually the metals or the metal oxide. They are combined with various organic compounds. Three general processes can prepare the salts:

- Direct dissolution of finely divided metal oxides in heated organic acids
- Precipitation from aqueous solution of metal salts (chlorides or nitrates) and alkali soaps
- Fusion of metal oxides with organic acids.

For liquid barium/cadmium stabilisers the production starts from metal oxides which are dissolved directly in the heated organic acids in the presence of solvents. The reaction water is removed and the finished product filtered.

Solid stabilisers are prepared by the precipitation process through the method of preparing metal soaps of natural fatty acids to give for example, cadmium laurate. Following precipitation the resultant slurry is filtered and dried (IcdA, 1997).

Pigments

There is a number of proprietary manufacturing processes, which use either cadmium metal, or cadmium oxide as the essential raw material. In general the manufacturing process involves the preparation of a cadmium sulphate or nitrate solution; filtration to remove recoverable solids; addition of sodium sulphide and precipitation of cadmium sulphide, with simultaneous additions of other salts to alter colour characteristics; filtration to define precipitate and drying; calcination to convert crystal structure to more stable form; further rinsing, milling and blending followed by packaging (IcdA: compilation of Industry data, 1997).

Table 2.11 Industrial and use categories of cadmium in the EU (HEDSET, 1994)

Industrial category	**EC No.**	**Use category**	**EC No.**
Chemical industry: basic chemical	2		
Chemical industry: chemicals used in synthesis	3	Intermediates Laboratory chemicals	33 34
Electrical/electronic engineering industry	4	Conductive agents Batteries and cells...	12
Personal domestic	5	see Product Register	
Metal extraction, refining and processing industry	8	Electroplating agents Others: Alloys	17 55
Paint, lacquers and varnishes	14	Reprographic agents	45
Others: Basic metal used in metal industry	15	Corrosion inhibitors	14

Table 2.12 Industrial and use categories of cadmium oxide in the EU (HEDSET, 1995; Product Registers, 1997 and 1998)

Industrial category	EC No.	Use category	EC No.
Chemical industry: basic chemical	2		
Chemical industry: chemicals used in synthesis	3	Intermediates Laboratory chemicals Raw material for the production of other cadmium chemicals	33 34 55
Electrical/electronic engineering industry	4	Conductive agents Electroplating agent	12 17
Polymers industry	11	Stabilisers	49
Paints, lacquers and varnishes industry	14	Colouring agents Fillers Reprographic agents	10 20 45
Others: Industrial : other = colours/frits Other : Ceramic industry Other: Glass and related industry	- 15 15	- Colouring agents Colouring agents	- 10 10

This table reflects the information as reported by Industry falling under the HEDSET obligation and was further completed by information contained in the Product Registers.

<u>Other data on uses of the substances: Product Registers</u>

Cadmium metal

The Danish Product Register (1997) reports under the CAS number of metallic cadmium, in descending order of involved amount: construction industry and chemical industry (private household insignificant). In the same way, product types are listed: paints, lacquers and varnishes, construction materials and laboratory chemicals. With 31 out of 49 products containing 0-1% cadmium and 3 products with 80-100% cadmium content the total quantity used in products in 1997 was lower than 1 tonne for Denmark.

The register of 1998 gives a similar picture. The additional information concerns the content in the different product types: paints, lacquers and varnishes: 12 of the 26 products contain lesser than 1% of the substance; construction materials: all products contain maximum 1% cadmium; laboratory chemicals: two of the three products have a content of 80-100% cadmium; colouring agents: eight products of the twelve contain maximum 1% cadmium. The quantity for each major product type is smaller than 10kg and the overall quantity is less than 1 tonne/year.

The Swedish product register (15/09/97) reflects the presence of the substance - albeit at low concentration (< or = 10%) – in a range of products and trades. The largest number of products and highest volume are used in dyestuffs (pigments) and in fillers plastic, paints etc. The total volume in products did not exceed 1 tonne in 1996 (More details of the industrial and use categories can be found in **Annex F**).

When over viewing the information contained in the product registers it could be questioned if the entry with CAS-N° of cadmium metal (i.e. 7440-43-9) is not used also to report on cadmium in a (more) generic way.

Cadmium oxide

The Danish Product Register (April 1997) reports 14 of the 25 products containing 1-10% cadmium oxide and two products with 80-100% of the substance. The major Industry implicated is the manufacturing of electronic equipment. Product types (in descending order of used substance's quantity): Laboratory chemicals and conductive agents. The total quantity in products is less than 1 tonne/year. For 1998 the Register is very similar. Nevertheless, here reprographic agents seem quantitatively most important, followed by conductive agents (11 products) and laboratory chemicals. The total quantity of the substance used in products is less than 1 tonne/year.

Details of the Swedish Register (1997: figures of 1996) are annexed (see **Annex G**).

The consumption pattern of cadmium (oxide and other cadmium compounds):

The world wide overall consumption pattern of cadmium (and its compounds) has been estimated by the International Cadmium Association (cited in Pearse, 1996) as follows: batteries (61%), pigments (20%), stabilisers (10%), plating (8%), alloys (3%) and other uses (4%).

For the Western World, Morrow came for the year 1996 to the following figures: batteries (69%), pigments (13%), stabilsers (8%), coatings (8%) and alloys and other (2%) (cited in: Morrow, 1998). In the context of the ESR Programme, Industry estimated the consumption pattern of cadmium (oxide) in Western Europe for the year 1996 as follows: batteries (60%), stabilisers (20%) and pigments (20%). Other uses are considered insignificant (IUCLID, 1997) and estimated to be less than 0.1% (IcdA, CollectNiCad, pers. Com., 2002). The figures were reviewed by Industry, refined and reported in the mass-balance (see **Figure 2.4**).

Use of Production, Consumption and Import/Export data

The data from the HEDSET/IUCLID, 1997 and the site specific Questionnaire (producers/importers of Cd (O)) provide the basis for the exposure assessment of these industrial sources.

The data from WS Atkins and underlying completed Questionnaires were used for the exposure assessment of pigments as well as stabiliser producers and users.

For plating an EU generic scenario is used (by lack of any site-specific exposure data) and based on the amount of cadmium estimated to be consumed in this application in the EU as a whole (estimation from IcdA, 1997).

Site-specific data (collated by the Questionnaires 1998, 2000 and 2001) are used for the exposure assessment of the batteries' producing and cadmium recycling companies.

Data on the cadmium flow related to batteries and recyclers (see the mass-balance updated for the year 2000) are used in the targeted risk assessment of cadmium (oxide) used in batteries, and in particular for estimating the emissions from waste disposal (see batteries' related section 2.2.2).

Site-specific data collected via the Questionnaires (2004) are used to update the local assessment for all scenarios related to production and use of the priority substances for which new data were submitted (see Section 2.2.3). The reference year for the latter update was set at the year 2002.

2.2.2 Batteries

2.2.2.1 Used terminology on Nickel-Cadmium batteries

Electrochemical cells and batteries are identified as primary (non-rechargeable) or secondary (rechargeable), depending on their capability of being electrically recharged[9]. Within this classification different types of battery formats exist.

A battery can consist of only one cell or can be put together of several cells, which are connected among each other. There are cylindrical cells, button cells, prismatic batteries and battery packs available on the market (see **Table 2.13**) depending on application type, use, equipment.

Table 2.13 Overview of the different battery formats and chemistry

Product Group	Sub-groups		
	Rechargeability	Format	System
Batteries type and geometry	Primary[10] (non-rechargeable)	Button	Lithium: $LiMnO_2$, $Li(CF_x)_n$
			Others: AM, ZnO_2, ZnAgO, ZnHgO
		Cylindrical	Lithium: $LiMnO_2$, $Li(CF_x)_n$, $LiSOCl_2$, ZnO_2
			Others: ZN, AM
		Prismatics Packs	Lithium: $LiMnO_2$, $Li(CF_x)_n$
			Others: ZN (E-Block 9V, normal 4,5 V), AM (E-Block 9V)
	Secondary (rechargeable)	Buttons	NiCd, NiMH
		Cylindrical	NiCd, NiMH, AM, Pb-acid, Lithium: Li-ion
		Prismatics Packs	NiCd, NiMH
			Pb-acid
			Lithium: Li-ion

$LiMnO_2$	Lithium manganese dioxide	ZnO_2	Zinc-air
$Li(CF_x)_n$	Lithium polycarbonmonofluoride	ZnAgO	Zinc silver oxide
$LiSOCl_2$	Lithium thionyl chloride		
AM	Alkali-manganese	ZnHgO	Zinc mercury oxide
ZN	Zinc-carbon	NiCd	Nickel-cadmium
NiMH	Nickel-metal-hydride	Pb-acid	lead-acid

Source: IOW, 1997

[9] Rechargeable batteries can be charged many times. After a certain amount of charge cycles they are no more rechargeable and must also be disposed of.
For information: the definition as set by the EC Battery Directive reads: Battery: any source of electrical energy generated by direct conversion of chemical energy and consisting of one or more primary battery cells (non rechargeable). Accumulator: any secondary battery cell or set of secondary battery cells (rechargeable).

[10] Cadmium has been used in some primary batteries in the past. There is no current application of cadmium in primary batteries (ICdA, pers. comm., 2000)

Ni-Cd batteries are generally viewed as high performance battery chemistries with good energy density and power density, especially suitable for high drain rate applications. Included in their best performance characteristics are their long useful life, wide temperature operating range, resistance to electrical/mechanical abuse and rapid charge/discharge characteristics. Disadvantages are low energy density, the so-called 'memory effect' and higher costs than lead-acid batteries. Nickel-cadmium batteries may readily be formulated into many different types, shapes and sizes of batteries designed to meet the specific requirements of many different applications.

The pocket-plate battery is the oldest and most mature of the various designs of nickel-cadmium batteries available and is manufactured in a wide capacity range, 5 to more than 1200 Ah and is used in a number of applications. Developmental work has been conducted continuously since the introduction of the pocket-plate nickel-cadmium battery to improve the performance characteristics and reduce battery weight. These innovations have resulted in the sintered-plate, fiber-structured and plastic-bonded or pressed-plate technologies (Evjes and Catotti, 2002). The sintered plate battery consists of a perforated mechanical substrate (e.g. nickel-plated steel or nickel-clad steel wire) coated with a highly porous sintered nickel matrix which is impregnated with nickel hydroxide (positive electrode) or cadmium hydroxide (negative electrode). The fiber (foam) structure technology uses a three-dimensional nickel-plated fiber matrix, which is highly porous.

Within these technologies a further distinction can be made between vented (open) and sealed cells. A functional vented battery generates a stoichiometric mixture of hydrogen and oxygen gases during overcharge and expels them normally from the cell into the battery container. Most often vented batteries have been used in industrial applications.

Sealed nickel-cadmium batteries incorporate specific battery design features to prevent a build-up of pressure in the battery caused by gassing during overcharge. As a result, batteries can be sealed and require no servicing or maintenance other than recharging.

Since both the term sealed and portable can be applied to some industrial batteries the term consumer batteries was initially used in the questionnaire sent to the Member States to indicate batteries with mainly domestic application. However, in general sealed, portable batteries not exceeding a weight limit (e.g. < 3 kg) irrespective of some other uses are referred to under this terminology.[11] Furthermore since household applications represent to date less than 20% of the market by weight (see **Table 2.27**) it is deemed more appropriate to use the term portable batteries in order to indicate that the figures presented in this report may include professional applications next to household applications.

A battery is made of cells assembled in series. Roughly Ni-Cd batteries can be divided into the following weight categories. Sealed cells: cell weight between 10 and 150 grams (maximum 500 g), usually assembled by 3 to 10 to make packs for portable applications. The most common are 3 and 4 cell packs. Larger batteries do exist for stationary industrial applications. Vented cells: cell weight between 1 and 70 kg (typically 3 to 10), usually assembled by at least 10 cells but up to several hundred. (CollectNiCad, personal communication, October 2002). A compilation of some of the different subtypes of Ni-Cd batteries and their specific characteristics is given in **Table 2.14**.

[11] Definitions may differ within, between MSs, IND, OECD, etc; e.g. the weight limit by industry is/can be different from those applicable elsewhere e.g. by Member States

Table 2.14 Format, size and characteristics of Ni-Cd batteries

Product group	Subgroup					
	Format and size	**IEC n° (US-Standard)**	**Weight (in g)**	**Nominal Voltage (in V)**	**Capacity (in Ah)**	**Cadmium content (in g per 100 g battery)**
Portable batteries [12]	Button			1.2	up to 1 Ah	11-15 typical/average content = 13.8
	Cylindrical	R 20 (D)	145	1.2		
		R 14 (C)	75	1.2		
		R 6 (AA)	22	1.2		
		R 03 (AAA)	12	1.2		
		KR6	26	1.2	0.75	
	Prismatics	9 V E-block		9.6 V		
	Packs		20-450			
Industrial/ professional use [13]	Automotive vehicles Safety and back-up systems Aviation		200 kg 200 g to 1,000 kg 20 kg (per battery) > 1 kg (per cell)			8

Sources: Individual producers/recyclers (via Questionnaire 1998, 2000/2001)

2.2.2.2 Ni-Cd chemistry and composition

The nickel-cadmium (Ni-Cd) battery is a rechargeable battery system based on the reversible electrochemical reactions of nickel and cadmium in an alkaline potassium hydroxide electrolyte. The chemical compositions of Ni-Cd batteries can vary widely depending on the type and its specific application. For industrial batteries cadmium content may vary between 3 and 11%. For portable batteries values between 11 and 15% have been reported (battery questionnaire 2000). In addition, most Ni-Cd batteries contain significant amounts of nickel, iron, plastics and electrolytes and small amounts of metals such as cobalt and copper (Morrow and Keating, 1997).

Ni-Cd cells use a reversible electrochemical reaction between nickel and cadmium electrodes packed in an alkaline electrolyte (potassium hydroxide or sodium hydroxide and lithium hydroxide as an additive). The active materials are insoluble in the electrolyte, whose ions act only as a charge carrier and do not take part in the electrochemical charge/discharge reactions (Cornu, 1995). At the cadmium electrode during discharge, cadmium is oxidised by combining with two OH^- ions to form cadmium hydroxide [$Cd(OH)_2$] and releasing two

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[12] Since household applications represent to date less than 20% of the market by weight (see Table 2.27) it is deemed more appropriate to use the term portable batteries (instead of consumer batteries) in order to indicate that the figures presented in this TRAR may include professional applications next to household applications.

[13] For information: the definition as set by the draft EC Battery Directive ‘industrial and automotive batteries and accumulators’: any battery or accumulator use for industrial purposes, for instance as standby or traction power, emergency lighting, or for automotive starting power for vehicles. Remark: definitions may differ within and between MSs, IND, OECD, etc

electrons (US EPA, 1993, Gross, 1995). During charging the reverse happens. Hydrated nickel (III) oxide is reduced to nickel (II) hydroxide at the other electrode (US EPA, 1993). The charge-discharge equation is as follows (Cornu, 1995):

$$2\ Ni(OH)_2 + Cd(OH)_2 + 2\ e \xrightarrow{\text{Charge}} 2\ NiOOH + Cd + 2H_20$$

$$2\ Ni(OH)_2 + Cd(OH)_2 \xleftarrow[\text{Discharge}]{} 2\ NiOOH + Cd + 2H_20 - 2e$$

The principal difference between the various types of Ni-Cd cells is the nature of the cell electrodes. The three primary types of positive electrodes used are pocket plate, sintered plate, and fiber plate. The hydrated nickel oxide electrode is usually in powder form and is held in pocket plates or suspended in a gel or paste and placed in sintered (perforated mechanical support) or fiber electrodes (US EPA, 1993).

The negative electrodes use pocket plate, sintered plate, fiber plate, foam or plastic banded supports to hold the cadmium (hydroxide) in place. Graphite or iron oxide is commonly added to improve the conductivity of both the nickel and cadmium hydroxide. Since the individual cells are recycled before assembling into batteries, it is not important whether the negative electrodes are originally impregnated with $Cd(OH)_2$ (the product of discharge reactions) or Cd metal (the product of charging reactions) (US EPA, 1993).

A typical chemical composition for a Ni-Cd cell is given in **Table 2.15**.

Table 2.15 Average chemical composition for a Ni-Cd battery

Material	Weight %	
	Portable[a] Ni-Cd battery	Industrial[b] Ni-Cd battery
Iron	35	48
Nickel	22	8
Cadmium[c]	13.8[c]	8[c]
Plastic	10	10
$(OH)_2$	9	5
Water	5	16
Potassium hydroxide	2	5
Others	3.2	0
Total	100	100

Source of the figures: EPBA and EUROBAT product information (1997) in ERM (1997)

a) Portable Ni-Cd battery, are batteries weighing between 10 g and 3 kg. Since household applications represent to date less than 20% of the market by weight it is deemed more appropriate to use the term portable batteries in order to indicate that the figures presented in this report may include professional applications next to household applications.

b) Industrial Ni-Cd battery: large size batteries weighing over 3 kg in weight

c) Latest update of information from industry i.e. manufacturers/recyclers (CollectNiCad,,2000)

Large, industrial-size batteries contain on average approximately 8% cadmium. Small, portable-type batteries contain approximately 13.8% cadmium. These figures refer to actual manufacturing and production data and have been confirmed by the information collected from individual battery producers via the Battery Questionnaire 2000 and will be used in this report as representative for industrial batteries and portable batteries respectively.

2.2.2.3 Production, recycling and use

2.2.2.3.1 Ni-Cd batteries manufacturing processes

Nickel-Cadmium batteries are widely used in many different applications where an autonomous energy source is required. Each application demands a different battery design, adapted to its performance requirements. For industrial applications different battery technologies are available: pocket plate cells, sintered plate cells, nickel fiber plate cells, plastic bonded plate cells.

Pocket plate batteries represent the conventional battery technology. Pocket plate electrodes contain the active materials in perforated steel pockets. This type of plates is mechanically very strong and the steel strip retains the active material during cycling, minimising swelling. In each cell a number of positive and negative electrodes are paralleled to form the plate group. Nickel-plated steel is used for connecting the elements and the terminals. The electrodes and separators are immersed in the alkaline electrolyte and the cell has a vented design.

A process flow diagram for the pocket plate batteries process is shown in **Figure 2.5**.

The reported emission/waste data represent site specific data (local worst case) from a pocket plate Ni-Cd batteries manufacturing plant (Industry Questionnaire, 2000/2001). The emission factors for air and water were calculated using the used Cd amount for the manufacturing of Ni-Cd batteries and the emissions to air/water. The sludge factor for cadmium in the WWTP sludge was calculated from plant supplied data (Cd content of sludge, amount of sludge, Cd used during manufacturing).

The emissions/wastes from the production of this type of battery include the following:

a) Wastewaters containing cadmium. The sources of these wastewaters are the manufacturing of active materials, nickel strip manufacturing and the cell formation process. This wastewater is estimated to amount to 0.124 kg/tonne of Cd used in the battery manufacturing process (F_{WW}=1.24 · 10^{-4}).

b) Air emissions occur during manufacturing of pocket plates and during assembling. For this specific plant no air emission data were reported. However for another pocket plate manufacturing plant, recycling its emissions to water, an air emission factor of 0.464 kg/tonne Cd used was reported.

c) Sludges recovered from treatment of wastewaters (manufacturing of active materials, nickel strip manufacturing, cell formation process). These are estimated to contain 17.7 kg cadmium per tonne of Cd used. The sludge from the wastewater treatment plant is sent to an external recycling plant.

d) Rejected battery cells from the test and package step: 118.8 tonnes/year. This waste is treated at a recycling plant.

e) Other waste: raw material bags, substituted filters, cleaning materials and tools: 1.15 tonnes/year.

Nickel fiber batteries are characterised by the use of a nickel fiber mat as electrode support. The active materials are impregnated by mechanical or electrochemical methods. Average diameter of the nickel fibers is around 20 µm. Porosity, pore size and electrode thickness can be adjusted as required for every application: lower porosity, smaller pores and thinner plates are adequate for high rate applications, while higher porosity, bigger pores and thicker plates are the choice for medium rate batteries. Thickness, porosity, pore size and the impregnation method are then adjusted to each specific application, in order to achieve the best electrical performance/battery cost ratio.

A process flow diagram for the nickel fiber plate process is shown in **Figure 2.6**.

The reported emission/waste data represent site specific data (local worst case) from a fiber plate Ni-Cd batteries manufacturing plant. The emission factors for air and water were calculated using the used Cd amount for the manufacturing of Ni-Cd batteries and the emissions to air/water. The emission factor for cadmium in the filter cake was calculated from plant supplied data (Cd content of filter cake, amount of filter cake, Cd used during manufacturing).

The emissions/wastes from the production of this type of battery include the following:

a) Wastewaters containing cadmium. The source of this waste is the impregnation step. This wastewater is estimated to amount to 0.769 kg/tonne of Cd used in the battery manufacturing process. This wastewater is collected and recycled in an external recycling plant.

b) Emissions to air occur during assembling are very small; 0.00027 g/tonne of Cd used.

c) Filter cake recovered from formation process. This is estimated to contain 10.5 kg Cd/tonne of Cd used. The filter cake is recycled.

d) Rejected batteries (no information)

Sintered plate batteries contain a cadmium anode, a potassium hydroxide electrolyte, and a nickel oxide cathode. For the electrodes, sintered plates containing the active materials are used. In one operation, the plates are made by impregnating sintered nickel substrates with nickel and cadmium nitrate salts. The nickel and cadmium nitrates are converted to hydroxides in sodium hydroxide solution. The plates are then washed thoroughly and dried in a hot oven. The impregnation cycle is repeated to deposit the desired amount of active material. The plates then go through a formation treatment, which removes impurities and brings the active materials to a condition similar to that existing in working electrodes. The cell is assembled into final form using an absorbent plastic separator and a nickel-plated steel case. With the addition of the alkaline electrolyte, they are ready for electrical testing, packing, and shipping.

There are currently three distinct manufacturing processes used for preparing the electrodes of the electrodes of the sintered plate batteries. The preceding paragraph described the worst case from an environmental standpoint of the three, due to the high concentration of cadmium and nickel compounds contained in the wash water. The other processes in use are:

- An electrolytic deposition process which deposits active materials directly on the sintered plates – this process produces wastewater containing nickel and cadmium compounds, though the amount is not as large as in the impregnation process described above; and
- A pressed powder process involving active materials mixed with binders in a dry powder form. The powder mix is pressed onto a wire mesh or expanded metal grid in a mold. This is a dry process and no wastewater is involved.

A process flow diagram for the impregnation-sintered plate process is shown in **Figure 2.7**.

The reported emission/waste data represent site specific data (local worst case) from a sintered-plate Ni-Cd batteries manufacturing plant. The emission factors for air and water were calculated using the used Cd amount for the manufacturing of Ni-Cd batteries and the emissions to air/water. The sludge factor for cadmium in the WWTP sludge was calculated from plant supplied data (Cd content of sludge, amount of sludge, Cd used during manufacturing).

The emissions/wastes from the production of this type of battery include the following:

a) Wastewaters containing cadmium and nickel salts together with sodium hydroxide. The source of this waste is the washing step. This wastewater is estimated to amount to 0.048 kg) per tonne of Cd used in the battery manufacturing process.

b) Atmospheric emissions are stated not to occur since the process is merely wet.

c) Sludges recovered from treatment of wastewater. These are estimated to contain cadmium (6.3 kg per tonne of Cd used) and nickel hydroxide. The WWTP sludges are land-filled (special landfill class I).

d) Rejected batteries from the test and package step, together with other scrap, are externally recycled for cadmium.

Figure 2.5 Flowsheet manufacturing process pocket plate Ni-Cd batteries

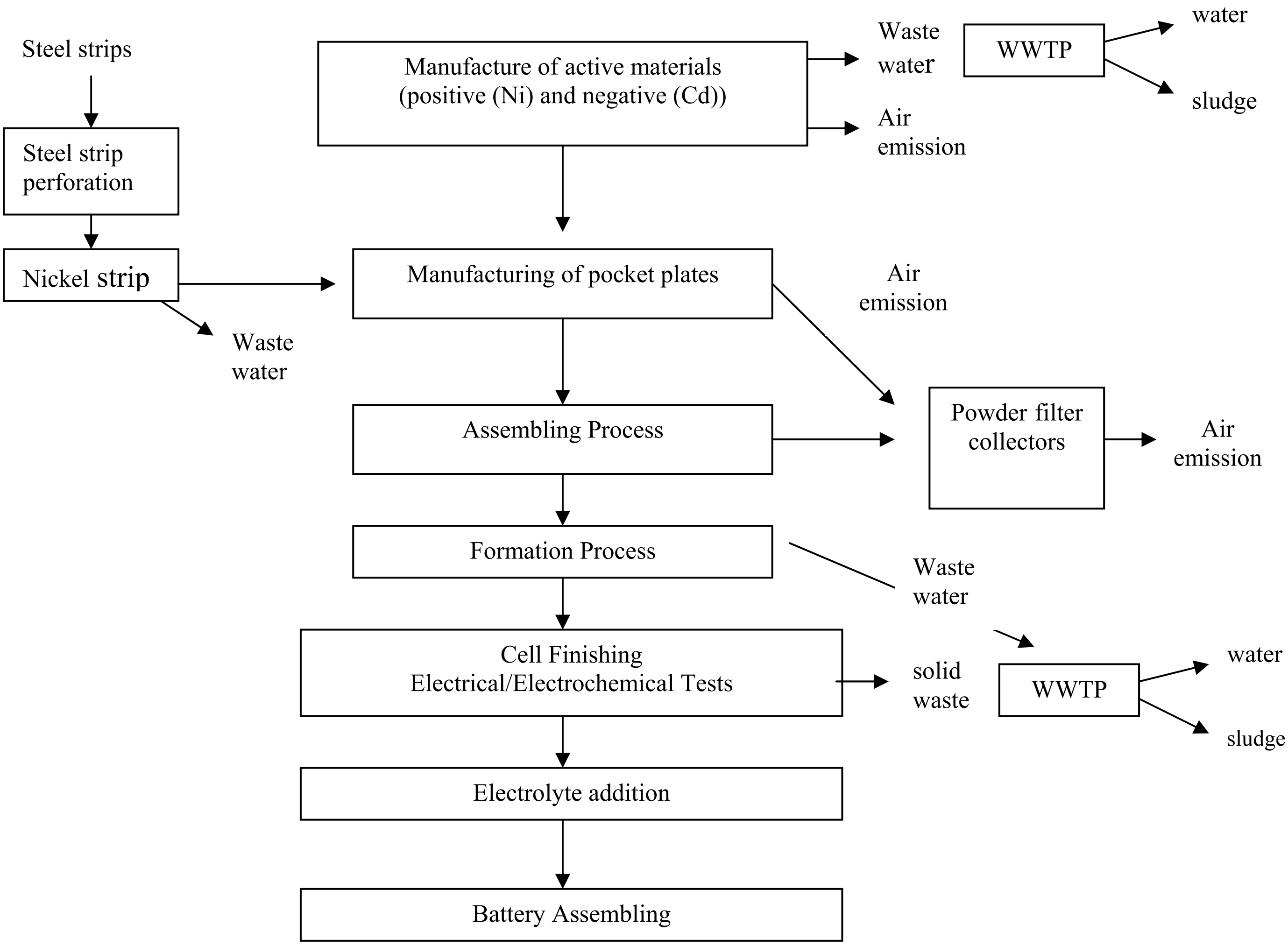


Figure 2.6 Flowsheet production process Nickel fiber plate Ni-Cd batteries

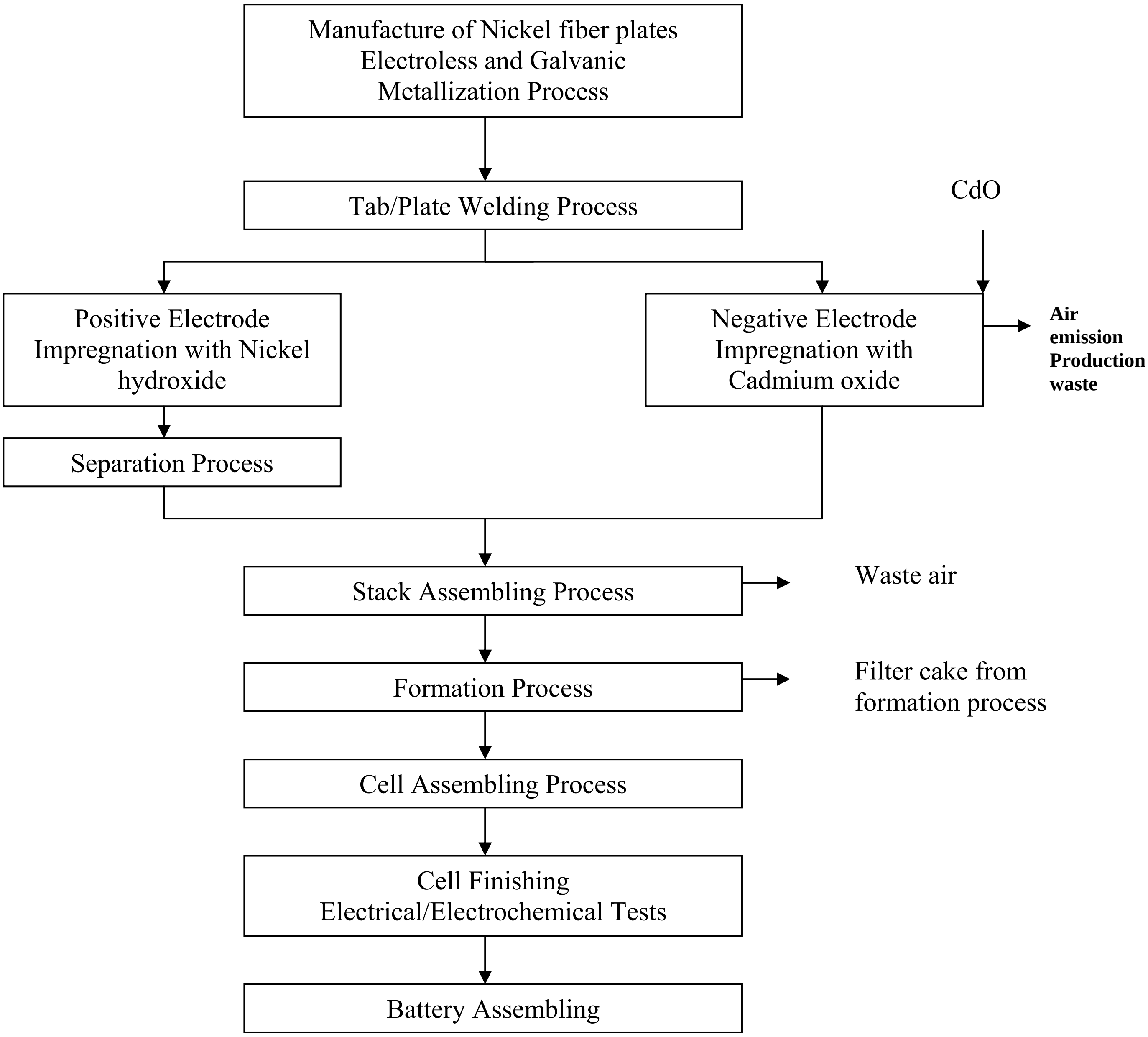
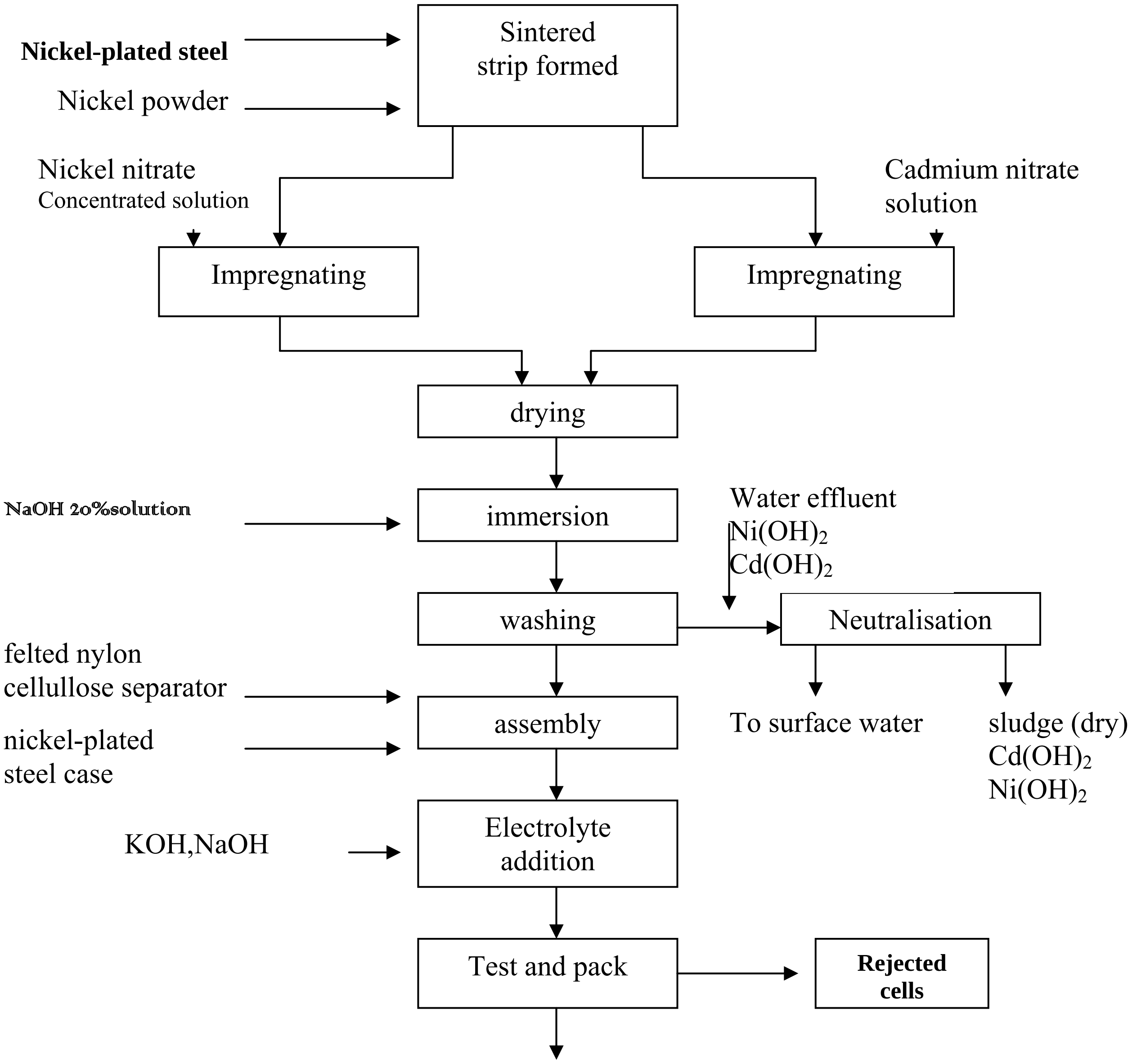


Figure 2.7 Flowsheet of major operations in sintered plate Ni-Cd batteries manufacture



Recycling processes

Ni-Cd batteries might be recycled either pyrometallurgical (high-temperature) or hydrometallurgical (wet chemical) processes. Today, commercial Ni-Cd battery and manufacturing scrap-recycling systems are usually based upon pyrometallurgical (high temperature) processes. Hydrometallurgical (wet chemical) systems have also been designed and have reached the pilot plant stage, but no purely hydrometallurgical systems are utilised today to recycle Ni-Cd batteries. Some recycling systems may have elements of both pyrometallurgical and hydrometallurgical processes in their overall system. (Morrow, 1997).

In pyrometallurgical recycling processes, cadmium-containing wastes or used batteries are heated at a low temperature to drive off moisture and organic compounds, and then heated to above 800°C to volatilise the cadmium. The vapour is then condensed, either as cadmium oxide or metal, and collected for final processing into high purity material (> 99.99%) suitable for any re-use in industrial applications. In hydrometallurgical processes the cadmium containing wastes are dissolved in a suitable reagent, usually a strong acid, and then subjected to a series of wet chemical reactions designed to successively remove impurities. The final cadmium product is normally a cadmium sulphate, chloride or nitrate solution from which high purity cadmium may be electrochemically obtained. Ion exchange techniques have been utilised in some hydrometallurgical recycling schemes, depending on the nature of other impurities present. (OECD, 1996).

A schematic presentation of the recycling processes for industrial and portable Ni-Cd batteries is supplied in **Figure 2.8**.

The reported emission/waste data represent site specific data from a Ni-Cd batteries recycling plant. The emission factors for air and water were calculated using the recycled Cd amount from Ni-Cd batteries only and the emissions to air/water. The emission factor for cadmium in waste was calculated from plant supplied data (Cd content of waste, amount of waste, Cd recycled (from batteries only).

The emissions/waste from the recycling of Ni-Cd batteries include the following:

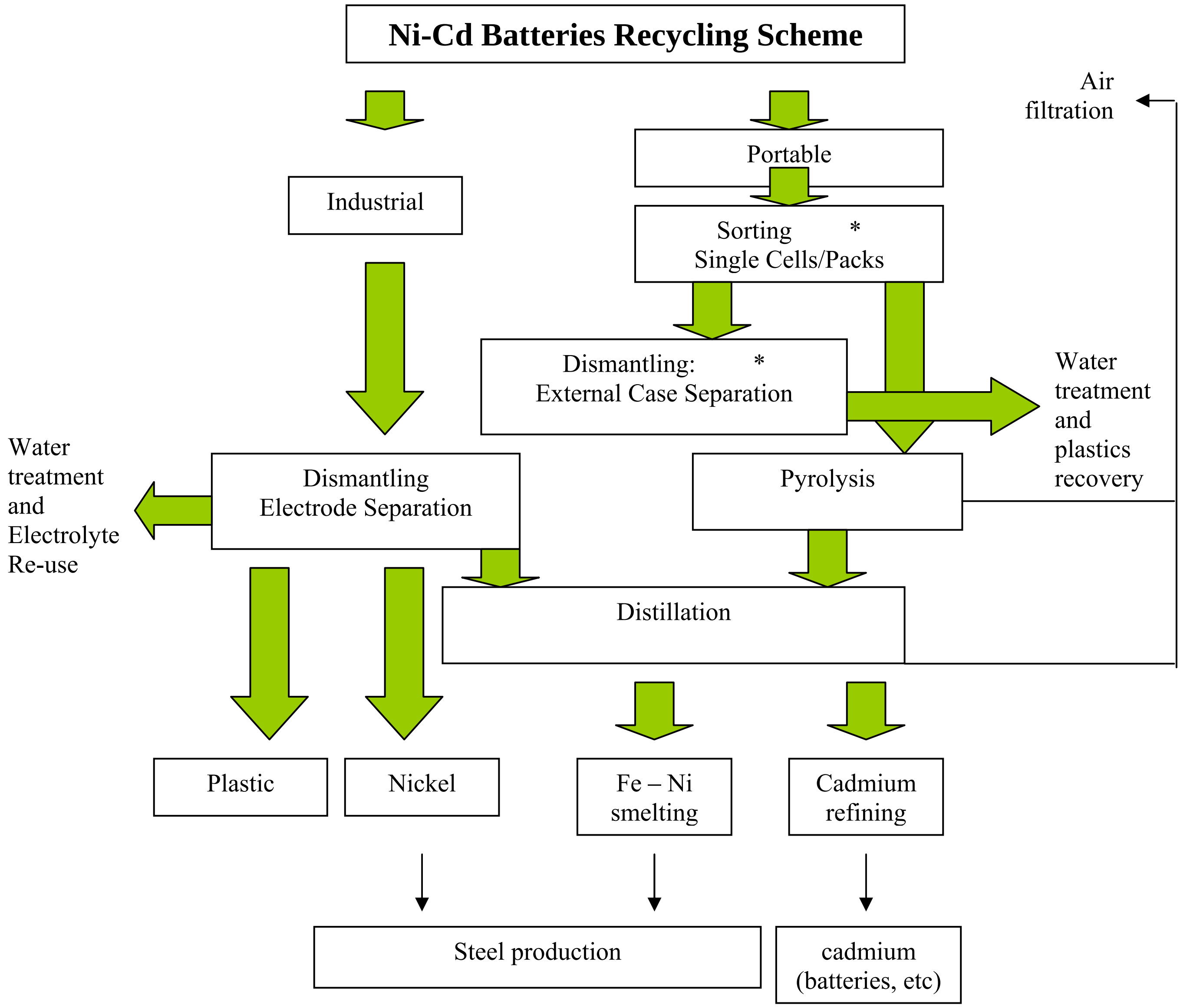
a) Wastewaters containing cadmium. The source of this waste is the dismantling step. This wastewater is estimated to amount to 0.32 g/tonne of Cd recycled (from batteries only).

b) Emissions to air occur during pyrolysis and distillation; 4.7 g/tonne of Cd recycled (from batteries only).

c) Waste:

- plastic boxes from batteries: 0.0011 kg/tonne Cd recycled (batteries) (landfilled)
- metallic boxes from batteries: 1.23 kg/tonne Cd recycled (batteries) (externally recycled)
- Fe/Cd electrodes after treatment: 1,2 kg/tonne Cd recycled (batteries) (ext. recycled)
- Conc. electrolytes: 5,7 kg/tonne Cd recycled (batteries) (ext. scrap treatment)
- Process slag: 154 kg CdO/tonne Cd recycled (batteries) (internal treatment)
- Air treatment dust: 61kg CdO/tonne Cd recycled (batteries) (internal treatment)
- Used filters: 0.138 kg/tonne Cd recycled (batteries) (internal treatment)
- Rainwater sludges: 0.0016 kg/tonne Cd recycled (batteries) (internal treatment)

Figure 2.8 Ni-Cd Battery Recycling (CollectNiCad, 2000b adapted)



* Facultative step(s)

In **Table 2.16** a summary is given of the Cd processing facilities in the world along with their location, type and estimated processing capacity (Morrow, 1999).

Table 2.16 Worldwide Cd processing facilities

Company	Location	Type	Capacity (tonnes of Ni-Cd/year)
Accurec Gmbh	Germany	NiCd Recycler	1,000
INMETCO	USA	Stainless steel	3,000
Japan Recycle Center	Japan/Korea	NiCd recycler	3,000
Kansai Catalist	Japan	Zinc refinery	500
Mitsui Mining and Smelting	Japan	Zinc Refinery	1,800
SAFT AB	Sweden	NiCd Recycler	1,500
SNAM	France	NiCd Recycler	5,400*
Toho Zinc Co, Ltd	Japan	Zinc Refinery	1,700

* SNAM St. Quentin stopped its recycling activities (2001), it has now become a battery sorting plant, all recycling capacity is transferred to the Viviez site

The present capacities of the world's Ni-Cd battery recycling plants vary from 500 tonnes to 5,400 tonnes with a present total effective capacity of approximately 15,000 tonnes (Morrow and Keating, 1999). The total EU capacity is estimated at 7,900 tonnes.

The facilities located in the EU i.e. SAFT AB (Sweden), SNAM (France), and ACCUREC (Germany) are being considered in this report.

2.2.2.3.2 Mass balance

A complete overview of the mass balance for cadmium in the EU for the reference year 1996 is given in **Figure 2.4** (see Section 2.1.2.1). The production volume of cadmium in the EU in 1996 is estimated to be 5,808 tonnes/year. Corrected for import/export 5,528 tonnes/year is available for different applications. Approximately 2,733 tonnes/year is used for battery manufacturing which equals approximately 47% of the cadmium being produced in Europe. The EU regional consumption of cadmium reaches the value of 2,638 tonnes, which are distributed for 75.2% to Ni-Cd batteries, 14.9% to pigments, 5% to stabilisers and 5% into alloys and plating.

Table 2.17 Cadmium consumption in the Western World (1990 and 1994) or EU (1996) by application

Application	% of total consumption		
	1990[a]	1994[a]	1996[b]
Ni-Cd batteries	55	60	75.2
Cadmium pigments	20	16	14.9
Stabilisers for PVC	10	12	5
Protective coatings	8	7	4
Cadmium containing alloys	3	2	0.9

Table 2.17 continued overleaf

Table 2.17 continued Cadmium consumption in the Western World (1990 and 1994) or EU (1996) by application

Application	**% of total consumption**		
	1990[a]	**1994[a]**	**1996[b]**
Miscellaneous	4	3	< 0.1
Total	100	100	100
Total production in the Western world (in tonnes)	15,900[c]	16,500[c]	13, 840[c]

a) Source: Cadmium Association, OECD Risk Reduction Monograph N° 5 (1994);
b) Source: mass balance (see Section: 2.1.2.1), EU consumption only;
c) Source: World Bureau of Metal Statistics (2000), production in the Western world (does not include Central and Eastern European countries)

Updated (year 2000) and detailed mass balances for industrial and sealed/portable Ni-Cd batteries (Cd content) are presented in **Figure 2.9** and **Figure 2.10**.

Figure 2.9 Industrial Ni-Cd batteries mass balance (EU-16 + Switzerland, Year 2000) (Cadmium content) (CollectNiCad, 2002a, revised July 2002)

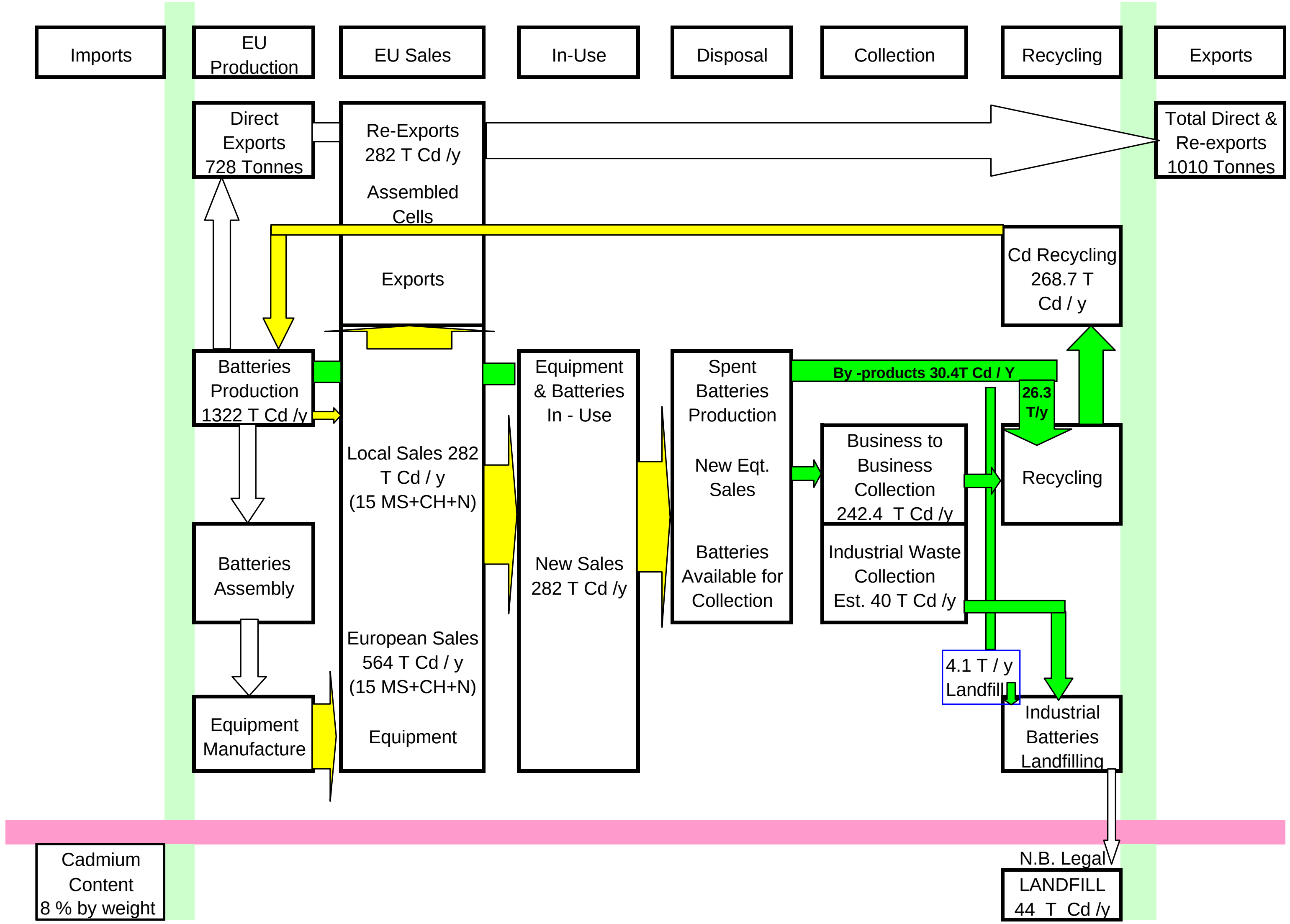
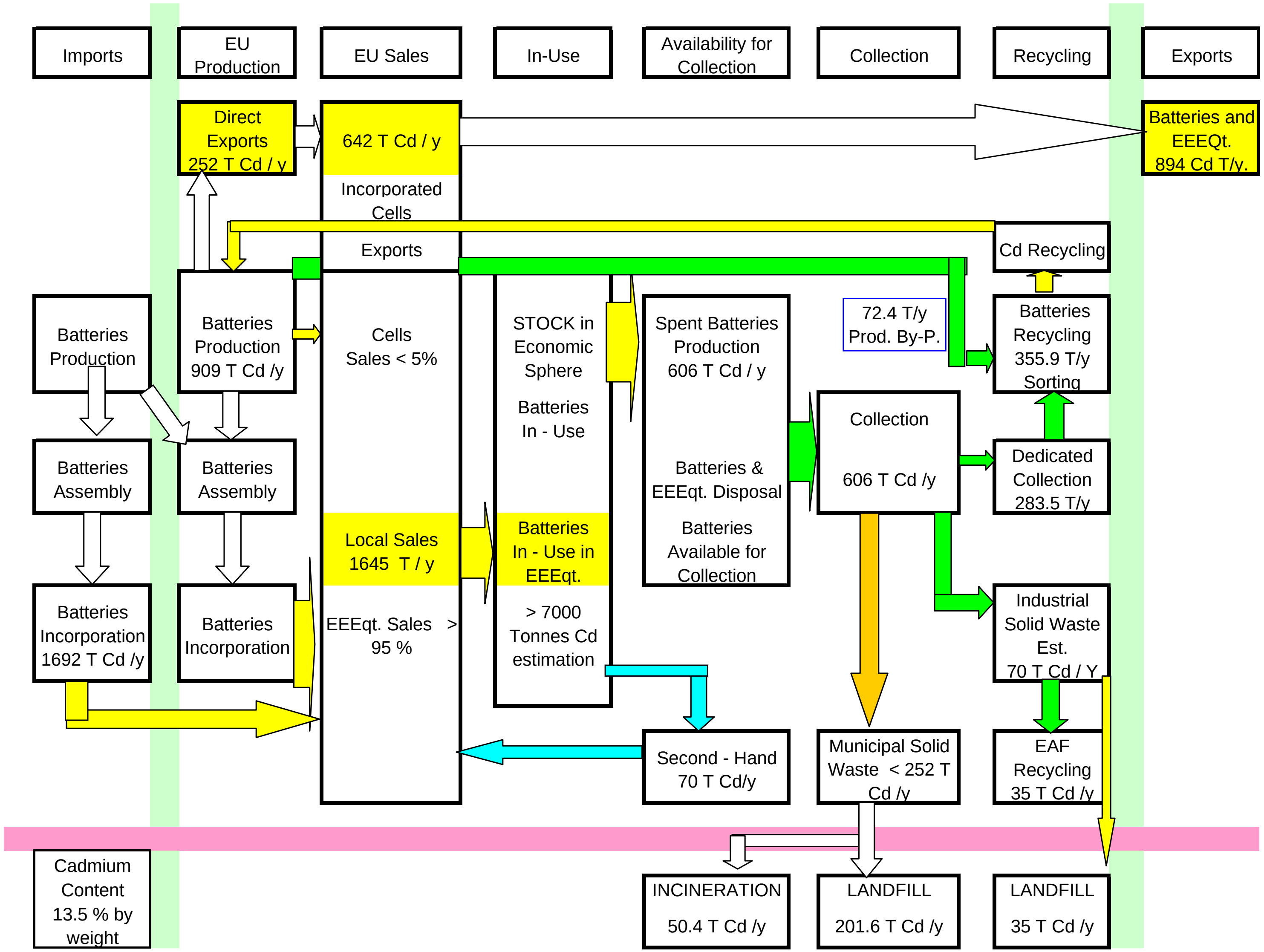


Figure 2.10 Portable Ni-Cd batteries mass balance (EU-16 + Switzerland, Year 2000) (Cadmium content) (CollectNiCad, 2002a, revised July 2002)



2.2.2.3.3 Ni-Cd batteries producing/recycling companies

In the current Risk Assessment Report the exposure data were generated by a number of companies that collaborated voluntarily in the data collection (Industry Questionnaire, 1998 and update questionnaire 2000/2001). The list of companies given in **Table 2.18** is considered as giving a complete overview of the Ni-Cd batteries producing/recycling companies.

Table 2.18 Companies producing/recycling Ni-Cd batteries in EU

Ni-Cd producers		
Country	**Location**	**Company**
France	Roullet St. Estephe	SAFT Nersac
	Bordeaux	SAFT Bordeaux
Germany	Duisburg	Friwo (EXIDE-group)[c]
	Brilon	Hoppecke
	Zwickau	GAZ (Zwickau)
Spain	Torrejon De Ardoz/ Madrid	EMISA (EXIDE- group)[b]
Sweden	Oskarhamn	SAFT-AB[a]
Ni-Cd recyclers		
Country	**Location**	**Company**
France	Viviez	SNAM
Germany	Mülheim	ACCUREC
Sweden	Oskarhamn	SAFT-AB[a]

a) Production and recycling at the same site
b) EMISA stopped the manufacturing of Ni-Cd batteries in 2003, SAFT, May 2003.
c) FRIWO, production stopped (year?), ICdA, pers.com. 2005.
SNAM St. Quentin stopped recycling (2001) with transfer of recycling capacity to the site of Viviez; VARTA stopped production (end 2000); SANYO: no production of battery cells in the EU, only assembly of imported constituents, therefore not included under manufacturers (pers. comm. 2001); PHILIPS stopped manufacturing cells and shifted to assembly (of non-EU manufactured cells into packs) only since June 2001, Panasonic (former Philips), letter 30.09.02.

At world scale other major manufacturers are Sanyo, Panasonic, GP Batteries, BYD and many of them are importers of batteries incorporated in OEMs equipment[14].

2.2.2.4 Market and sales data

2.2.2.4.1 General

Portable rechargeable batteries are utilised for a wide variety of products and applications. The most important application fields are Cordless Power Tools (CPT), Emergency Lighting Units (ELU) and applications in various Electrical and Electronic Equipment (EEE). Industrial

[14] OEM= Original Equipment Manufacturer

applications of rechargeable batteries include military and space applications, transportation applications, power systems such as reserve power supply for industrial processes.

The nickel-cadmium portable battery market has been analysed in several different ways, in some cases according to geography, in others according to millions of cells sold, and yet in others in terms of the total sales value. In compiling these data, in particular those related to the historical market, EURAS has relied heavily on work done by Industry (e.g. CollectNiCad, 2000c).

2.2.2.4.2 Portable Nickel-Cadmium batteries[15]

General

A compilation of the available data from different data sources on Ni-Cd battery sales in the EU is given in **Table 2.19**.

Table 2.19 Summary of the market data (million units) available on portable Ni-Cd batteries in the EU

Year	Market study						
	ERM[a]	EPBA[b]	Nomura[c]	SANYO[d]	SAFT[e]	CollectNiCad1[f]	CollectNiCd2[f]
1970					12.5		
1975					21		
1980					42		
1985	66	66					
1986							
1987					143		
1988					177		
1989			201				
1990	203	203	226.5				
1991		286	276				
1992			287				
1993			315	310			
1994		244	343	350			
1995	620	564	356	360			
1996		213	334	290			

Table 2.19 continued

[15] Since household applications represent to date less than 20% of the market by weight it is deemed more appropriate to use the term portable batteries (instead of consumer batteries) in order to indicate that the figures presented in this RAR may include professional applications next to household applications.

Table 2.19 continued Summary of the market data (million units) available on portable Ni-Cd batteries in the EU

Year	Market study						
	ERM[a]	EPBA[b]	Nomura[c]	SANYO[d]	SAFT[e]	CollectNiCad1[f]	CollectNiCd2[f]
1997		233	356	260			
1998		236	353	250			
1999			352	250		338	343

a) ERM (1997)
b) EPBA production sheets
c) Nomura (1994) in CollectNiCad (2000c)
d) Carcone (1998) in CollectNiCad (2000c)
e) Eloy in CollectNiCad (2000c)
f) CollectNiCad (2000c)

The results of the ERM study have been based on data provided by EPBA (European Portable Battery Association). While the presented results for the years 1985 and 1990 are in concordance with the results of the other studies the figure of 1995 is clearly out of scope. The main reason for this discrepancy is the assumption taken in the other market studies in deducing the EU share from the world market data. The EU market share in the ERM study mounts up to 40% of the world market in 1995, while the EU world market share in the other studies have been assumed to be respectively 25% in the Nomura and SANYO study and 20% for the SAFT study. The latest survey conducted by CollectNiCad (CollectNiCad, 2000c) supports these latter suppositions and will be discussed in more detail here below.

The European sales volume for the year 1999 for portable Ni-Cd batteries has been established) on the basis of data obtained from battery manufacturers and original equipment manufacturers O'EM's. Two different and independent methodologies have been used.

The first method (CollectNiCad. 1) calculates the total sales of Ni-Cd batteries from the number of cells used in the three major application areas: cordless power tools, emergency lighting**,** household equipment (shavers, dust busters, dental care etc.), telecommunications and the sales of single cells. In order to translate the number of cells into a weight estimate an average weight of 38.0 g of one cell has been assumed, calculated from the total number of cells introduced on the EU Countries market.

The second method (CollectNiCad 2) is based on production data (in number of cells and in tonnes of batteries) of all Ni-Cd battery manufacturers active in Europe and corrected for import/export ratios of cells and packs as well as of batteries incorporated in electrical and electronic equipment.

Data for portable Ni-Cd Batteries by market segments/applications (CollectNiCad. 1)

For the breakdown of the market data by application an in depth analysis was performed of the European sales of portable Ni-Cd batteries in the three major applications areas: cordless power tools, emergency lighting and household and 'electrical and electronic equipment' (EEE).

Table 2.20 provides a summary of the market data by application. Those data show a total annual market of 12,700 tonnes in 1999.

Table 2.20 Portable Ni-Cd batteries EU market, sales by application (million cells/year) reference year 1999

Electrical and Electronic Equipment (EEE)		
Application	**Average weight/cell (g)**	**Sales (million cells/year)**
Household equipment	22	28
Dust buster	48	12
Toys	55	5
Audio-Video	26	10
Single cells and others	22	54
Cordless phones	14	50
Emergency lighting		
Application	**Average weight/cell (g)**	**Sales (million cells/year)**
Emergency light	120	26
Power tools		
Application	Average weight/cell (g)	Sales (million cells/year)
Cordless tool	41	138
Others		
Application	**Average weight/cell (g)**	**Sales (million cells/year)**
Medical	20	10
Military	40	5
Average weight/unit	37.8	
Total sales		**338**

Source: CollectNiCad (2000d)

The average weight of approximately 38 g for a portable Ni-Cd battery is used in the further calculations

<u>Data for portable Ni-Cd Batteries based on production data (CollectNiCad 2)</u>

The data obtained by the second method are presented in **Table 2.21**.

Table 2.21 Overview EU market corrected for import and export in 1999

	Local annual sales (millions of cells)	Domestic sales (%)	Export sales (%)	Import Europe (%)	Net EU market (millions of cells)
Japan	158	n.d.	50	30	23.7
Europe	324	65	35		210.6
North America	457	n.d.	15	50	34.3
Asia	530	n.d.	70	20	74.2
Total	1,469	n.d.	n.d.	n.d.	342.8

n.d. No data available

Those data indicate that a total market of approximately 1,4 billion of Ni-Cd cells have been reached in 1998 and 1999. To evaluate the market in the E.U. countries the import-export of Ni-Cd cells assembled into packs and of packs incorporated in EEE were taken into account (see

Table 2.21). The net EU market contribution for each country/continent was calculated with the following formula:

Net EU market contribution = Local annual sales X export (%) X import Europe (%)

According to **Table 2.21**, 342.8 millions of cells have been sold in 1999 within the 15 EU. Member States corresponding to approximately 23.3% of the world market. The assumption of the EU market share of 20-25% is therefore confirmed and will be used to select data to build a historical market curve. In this respect the high ERM figure for 1995 is being rejected.

Historical market development

In order to make any predictions on the amounts of batteries available for collection and/or disposal it is imperative to have a good picture of the historical market development. In **Table 2.22** the selected data for the portable consumer/sealed portable market are summarised. To express these market figures in tonnes/year these values have been multiplied with the estimated average unit weight of 38 grams. Missing values were extracted by interpolation.

Table 2.22 Overview of the historical reference data for portable Ni-Cd batteries

Year	Millions/cells	Tonnes/year	Year	Millions/cells	Tonnes/year
1980	42	1,596	1991	276	10,488
1981	n.d	*1,778*	1992	287	10,906
1982	n.d	*1,960*	1993	315	11,970
1983	n.d	*2,142*	1994	343	13,034
1984	n.d	*2,324*	1995	356	13,528
1985	66	2,508	1996	334	12,692
1986	n.d	*3,971*	1997	356	13,528
1987	143	5,434	1998	353	13,414
1988	177	6,726	1999	352	13,376
1989	201	7,638	2000	314	11,930
1990	226.5	8,607	2001	275	10,995

n.d. No data available
Figures denoted in italics are interpolated

2.2.2.4.3 Industrial Ni-Cd batteries (CollectNiCad 2000c)

The European market for industrial batteries can be split into a number of well-defined sectors as follows:

- Standby, or stationary, applications - safety, and back-up systems at airports, hospitals, power stations, offshore installations etc.
- Transportation - railways, metro cars, etc.
- Aviation - starting of engines, oil board safety systems, etc.
- Electric vehicles (EV)

The batteries within the two largest segments - standby and transportation - are used within a country's infrastructure. The need for batteries for new installations is the largest during this infrastructure development phase. Batteries for standby applications are often purchased by equipment manufacturer (OEM) and delivered together with the equipment to the user. Many of these OEM's are situated in Western Europe while the users are situated in e.g. the Middle East and Far East. Thus, the batteries are purchased by and invoiced to a European customer, but they are very often re-exported to other parts of the world. In some of the Member states with important OEM'S, the re-export factor of standby batteries can be as high as 50%.

Batteries for transportation and aviation purposes are to a higher extent delivered directly to the end user and the re-export factor is lower (15%). The EV (Electric Vehicles) market is still at a low level. Main part of the EV nickel-cadmium is produced in EU and is used within EU.

The volumes of the different industrial Ni-Cd batteries for use within the EU market has been estimated from data of the three major suppliers (representing more than 95% of the market supply) with addition for an estimated volume of imported batteries and are listed in **Table 2.23**.

Table 2.23 Industrial Ni-Cd batteries EU market sales (tonnes/year)

Year	Industrial Ni-Cd battery (tonnes/year)
1995	3,242
1996	3,608
1997	3,625
1998	3,964
1999	3,697
2000	3,566

Sources Original references Saft, Exide and Hoppecke in CollectNiCad (2000c,2002)

From this table it is clear that the industrial batteries' market has reached a stable level of 3,500 to 4,000 tonnes/year. Cross-validation with the ERM study shows the same magnitude (4,000 tonnes in 1995).

2.2.2.4.4 Country by country data

The data presented in this section are obtained mainly by two ways. The first was through the Questionnaire on Batteries sent out in 2000 by the MSR to the national authorities of the EU and Norway, the collector organisations as well as the EU associations of manufacturers (i.e. EPBA). The second series of data was compiled via the efforts run in parallel by Industry (CollectNiCad 2000d).

It needs to be mentioned that to date the information in this document is rather limited and no attempt was made to verify the correctness of each figure. Another remark concerns the fact that figures obtained via different sources are not necessarily independently generated (e.g. the data provided by the national collector organisations may be the only data available at the authority level). Finally the data obtained via different ways may in some case be 'complementary' to each other (e.g. the data on collection as provided by the collection organisation versus Industry's data obtained from the recyclers) and thus allowing for at least some approximate direct check by comparison.

Data sources

Responders to the Questionnaire are indicated by a figure between brackets in the last column of the tables and accompanied by details in a footnote, if needed. The figure (1) is used when data were obtained from the MS (national authority). The indication (1C) is used when Collection organisation(s) replied. The main primary generators of data in so far as these are known, are indicated under the corresponding subsections. Data compiled and submitted by CollectNiCad are indicated by the figure (2).

Data errors and deviations

Besides the well known sources of errors e.g. reporting, (de)coding, transcription, etc deviation of data generated by different types of sources may be due to (a different degree of taking into account) stockpiling, as well as import and/or export of new, spent or recycled material or appliances containing batteries. On the other hand, differences in used definitions of e.g. ‘portable’, ‘consumer’ and ‘industrial’ but also ‘marketing’ and the specific sorting or not of Ni-Cds may cause divergences between figures generated by different MS, collector organisations and Industry. Finally, difficulties may arise due to the different units in which marketing figures versus collection amounts are expressed. The former are generally in units (or mAh) while the latter are reported in weight units. Together with the variation in battery weight, this may cause deviations.

Portable Ni-Cd batteries

A summary of the available data is given in **Table 2.24** for consumer/sealed portable Ni-Cd batteries.

Table 2.24 Portable Ni-Cd battery market data (tonnes/year) for EU countries

Country	1994	1995	1996	1997	1998	1999	2000	2001	Reference
Austria				62	98	97 309	286	247	(1C)* (2)
Belgium			381	388	368	327	302	261	(1) (2)
Denmark	214[b]	233[b]	218-328[b]	291	242	210 137	127	110	(1C) (2)
Finland[a]			250			134	124	107	(1) (2)
France						130 2,212	2,046	1,768	(1)* (2)
Germany	3,095	2,642	2,334	2,214	2,050	3,210 2,261	2,091	2,880 1,808	(1C) (2)
Greece						404	374	323	(2)
Ireland						233	216	186	(2)

Table 2.24 continued overleaf

Table 2.24 continued Portable Ni-Cd battery market data (tonnes/year) for EU countries

Country	1994	1995	1996	1997	1998	1999	2000	2001	Reference
Italy						1,567	1,449	1,253	(2)
Luxembourg						25	23	20	(2)
The Netherlands						652	603	521	(2)
Portugal						241	223	193	(2)
Spain						1,168	1,080	934	(2)
Sweden	486	338	333	328	190	175 249	 230	 199	(1) (2)
UK[a]	2,001	1,766	1,958	2,167	2,652	2,983 2,706	 2,503	 2,163	(1) (2)
Norway		199	187	124	175	215 125	 116	 100	(1) (2)
Total EU-16[a]						**14,005**	**11,793**	**11,265**	
Switzerland						274	253		(2)
Total[a]						**14,279**	**12,046**		

1) Questionnaire Member States (2000). Primary sources: (B): BEBAT, (F): only SCRA members, (UK): ERM, (S): based on information from importers and manufacturers, updated '02: Ni-Cd batteries that have been put on the Swedish market, as reported to the Swedish EPA, (NO): sealed cells, separate or in appliances, in this table: with the assumption that all cells in appliances are totally attributed to consumer application.
1C) Questionnaire (2000) Collection organisations. (A) : only data via UFB (Incl. some industrial uses, DK: Danish Battery Association, (DE): Data provided by ARGE Batterien, data for 2001 submitted by UBA, 2002.
* Incomplete data-set(2): Industry Country by country data (CollectNiCad 2000d)
a) Upper limit used and assuming average battery cadmium content of 13.8%
b) Miljoprojekt (2000)

For the data submitted by the authorities, the way the data are obtained/generated and the surrounding uncertainties are in general not explicitly specified. Industry (CollectNiCad) compiled data mainly through the information given by manufacturers and their commercial network (no primary data are available).

Six Member States have submitted their figures on the sales of portable[16] Ni-Cd batteries. Additional data for 17 countries were provided by CollectNiCad (2000f) for the year 1999. In general the latter figures are in concordance with the figures reported by the Member States. However, the market figures provided for France collated from the Member State Questionnaire are incomplete (130 versus. 2,212 tonnes/year). In comparison with countries of a similar population size (UK, Italy) the industry's estimate seems a more realistic one. The industry's estimates for Denmark, Norway and Germany are approximately 30-40% lower than the figures provided by these countries. According to Industry the differences in the market data for Germany are mainly related to exports. A considerable amount is claimed to represent exported batteries, amount which is said by Industry to be neglected as such in the German data provided by the DE MS (neither primary data nor details from Arge Batterien were submitted to the Rapporteur).

Overall it can be concluded that approximately a maximum of 14,000 tonnes of portable Ni-Cd batteries is put on the EU-16 market (including Norway) for the reference year 1999.

[16] Those MSs replied to the Questionnaire under the section 'Consumer batteries'. Some MSs gave details related to the types and applications of batteries while others did not.

Recent data given by industry indicate a decrease in the weight volume introduced on the market with respectively 11,930 and 10,995 tonnes/year for the years 2000 and 2001.

Industrial batteries

Very few countries replied on the Questionnaire 2000. The primary data sources for Industry's submitted data are in the first place the manufacturers. An overview of the present available data is given in **Table 2.25** for industrial Ni-Cd batteries.

Table 2.25 Industrial Ni-Cd battery market data (tonnes/year) for the EU member states

Country	1994	1995	1996	1997	1998	1999	Reference
Austria						144	(2)
Belgium						97	(2)
Denmark				48-54[c]		20	(2)
Finland[a]			23	121	104	68 87	(1) (2)
France						1,097	(2)
Germany						213? 251	(1*) (2)
Greece						230	(2)
Ireland							
Italy						243	(2)
Luxembourg						1	(2)
The Netherlands						80	(2)
Portugal						13	(2)
Spain						758	(2)
Sweden	250	200	200	200	150	150 142	(1) (2)
UK[a]	853	858	862	907	958	1,008 404[b]	(1) (2)
Norway		95	104	119	84	57 1	(1) (2)
Total EU-16[a]						**3,632**	
Switzerland						93	(2)
Total[a]						**3,725**	

1) Questionnaire Member States (2000) Primary sources: (B): BEBAT, (F): only SCRA members, (UK): ERM, (S): SAFT
1C) Questionnaire (2000) Collection organisations (DE) : only data from VfW-REBAT (consumer/sealed portable + industrial): data from ZVEI not available
2) Industry Country by country data (CollectNiCad, 2000f)
* Incomplete data-set on country basis
a) Upper limit used except for UK figure(s) that were corrected cfr text
b) UK + Ireland
c) Miljoproject (2000)

Four Member States have submitted market data on industrial Ni-Cd batteries. Additional data for 17 countries were provided for the year 1999 by industry. For the few cases where comparison is possible, the figures are in concordance with the figures provided by the Member States. Industry's estimate for the UK is much lower then the figure submitted by the UK-MS (DTI). ERM (on behalf of UK) provided this estimate based on sales information from SAFT and Exide ranging from 600-1000 tonnes. It was acknowledged by ERM that they did not correct for export that is estimated to be 50% (ERM, Pers. com., 2000). Applying the export rate gives an estimated figure for the UK market ranging from 400 to 670 tonnes (the figure '404' is used for calculating the totals for the year 1999).

Overall approximately 3,700 tonnes of industrial Ni-Cd batteries is put on the EU-16 market (EU including Norway) for the reference year 1999.

Market trends

Most of the data related to market evolution come from Industry. The data submitted by CollectNiCad relate to the past and to semi-quantitative information on the application's market shares (see paragraph below). No precise information is (made) available on how the Ni-Cd battery market is likely to evolve in the future.

Ni-Cd batteries can be classified into four lines of products according to their market applications: industrial batteries, Emergency Lighting units (ELU), Cordless Power Tools (CPT) and applications in numerous Electrical and Electronic Equipment (EEE).

The largest application field for Ni-Cd batteries and a growing market have become the CPT applications (separated between the Professionals and Consumer market). The ELU market is under a slight growth rate with higher market shares in countries like France, United Kingdom, Italy and Spain, by opposition to Germany where centralised units powered by lead-acid batteries are used. The EEE market, which has been the largest market segment for Ni-Cd batteries during the first half of the nineties, is declining. From 1995, Ni-Cd batteries have gradually being replaced on the market by other types of batteries like the Nickel-Metal Hydride, the Lithium-Ion and the Lithium-Polymer batteries. Industrial Ni-Cd batteries are continuously in competition with lead-acid batteries but forms a stable market. A summary of the market shares for the different applications for the years 1999 and 2000 is given in **Table 2.26** and **Table 2.27**.

Table 2.26 Weight distribution in percent of the market share of Ni-Cd batteries by applications-reference year 1999

Industrial	**Portable CPT**
22% (Stable)	35% (growing)
Portable ELU	**Portable EEE**
18% (Stable)	25% (Declining)

Source CollectNiCad (2000e)

Table 2.27 Weight distribution in percent of the market share of Ni-Cd batteries by applications (reference year 2000)

Industrial	**Portable CPT**
24% (Stable)	35% (growing)
Portable ELU	**Portable EEE**
19% (Stable)	16% (Declining)
Specialities (Aviation, Industrial Comm. and Computing)	
6% and growing	

Source CollectNiCad (2002b)

From the information available it can be concluded that the Ni-Cd market has increased significantly in the 80's to reach a more or less stable level in the late 1990's of around 13,500 tonnes/year for consumer/sealed portable nickel-cadmium batteries and 3,500 to 4,000 tonnes/year for the industrial nickel-cadmium battery market.

To date, no market projections are available for the amount of portable Ni-Cd batteries, which will be put on the market in the future. A study by ERM (2000) employed a positive common growth rate for all types of portable secondary batteries. However, since the market evolution is stated to be mainly technology driven and, as there is confidential business implication, it is difficult to get any good specific estimate for the growth rate of Ni-Cd chemistry applications.

Between 1996 and 1999 the portable Ni-Cd battery market in the EU seems to be oscillating around 13,000 -14,000 tonnes[17]. Although recent figures for 2000 and 2001 indicate a decrease in sales, the figure of 13,500 tonnes has been chosen as a worst case scenario to forecast future battery waste arising. The industrial batteries remain at the level of 3,600 tonnes.

2.2.2.5 COLLECTION/RECYCLING DATA

2.2.2.5.1 Country by country data

Portable Nickel-cadmium batteries

Data on the Ni-Cd battery collection/recycling efforts for individual EU countries were collated from the Questionnaire 2000. In addition Industry (CollectNiCad) provided a second series of data for the year 1999 and 2000. The latter represent the amount collected and processed for recycling. An overview of the available data is given in **Table 2.28** for portable Ni-Cd batteries.

[17] The reference year 1999 has been chosen because this was the most recent year for which cross validation of the data provided by industry with those provided by the Member States was possible.

Table 2.28 Total weight (tonnes/year) of collected/recycled portable Ni-Cd batteries for the individual EU countries

Country	1994	1995	1996	1997	1998	1999	2000	2001	Reference
Austria	22.5	26.7	42.5	61.8	97	97	53	84	(2) (A)
Belgium				37	79	59	177		(1)
	9	10	10	50	66	59	115	70	(2) (B)
Denmark	34	54	9	94	80				(1C)
	34	54	--	103	78	66	59	108	(2) (Dk)
Finland					91	113			(1)
		1	6		12	5	10	1	(2)
France	33	50	65	95	100				(1)
	60	35	70	105	92	140	140	182	(2)
Germany	220	206	303	440	403	596	1,001		(1)
							950	921	(2) (GRS)
Greece							1	1	(2)
Ireland						9	11	5	(2)
Italy	1			2	1	25	33	36	(2)
Luxembourg					5	5	5	5	(2)
The Netherlands	10	29	35	75	119	150	210	160	(2) (NL)
Portugal							1	1	(2)
Spain		4				38	30	66	(2)
Sweden	111	112	113	141	144	170	142	167	(1)
		108	110	142	143	169	147	167	(2)
UK					50	106			(1)
	18	63	72	94	46	75	78	93	(2)
Norway				66	63	53			(1)
		2	10			12	10	43	(2)
Total EU-16[a]	**459**	**539**	**663**	**1,106**	**1,125**	**1,446**	**1,852**	**1,943**	
Switzerland	34	96	46	21	114	48	194	198	(2)
Total[a]						**1,494**	**2,046**	**2,141**	**(2)**

1) Questionnaire (2000) Member States. Sources: (B):data from BEBAT figure of 2000 is still provisional: lower figure: amount of sorted batteries, upper figure: amount of recycled batteries during the year 2000, (F): Ministere de l'amenagement du territoire et de l'environment, (UK): data as from SNAM, (S):data as from SAFT, (DE): data from UBA, comments 2002.

1C) Questionnaire (2000) Collection organisation. DK: Danish Battery Association: figure of '95 includes collection till 31 March'96

2) Industry Country by country data (CollectNiCad, 2000f and 2001a) (A) Rumpold AG, (B) BEBAT, (Dk) Battery Association Denmark, (GRS) Gemeinsames Rücknamesystem Batterien, (NL) STIBAT

a) Lower limit used

The primary data source for Member states is data on collection as obtained via governmental or private collection organisations. Additional verification procedures by external independent organisms may enhance the confidence in these figures. Industry (CollectNiCad) compiled its series of figures through information obtained via the recycling companies and/or collection organisations (primary data are not available to the Member States Rapporteur). The transboundary movement of spent Ni-Cd batteries is liable to the Basel Convention administrative rules and offers a means to trace back collected amounts on national basis.

For the few cases where comparison is possible, no large differences are observed between the data provided by industry and the Member States. Overall approximately 1,852 tonnes of portable Ni-Cd batteries has been collected in the EU-16 for the year 2000 and 1,943 tonnes for the reference year 2001. Countries for which no (or poor) data are available have most often not yet a dedicated Ni-Cd collection system in place. A short overview of the situation in the EU is given by CollectNiCad in **Table 2.29**. The information on existing Ni-Cd collection schemes and programs present in Europe gathered by the Questionnaire is limited (only DK, S, UK, F, FIN and NO) and mostly does not provide many further details than those already reported in other publications (ERM, 1997; EUPHEMET, 2000 and CollectNiCad, 2000f). More details are available in Annex I.

Table 2.29 Overview of Ni-Cd Collection programs running in various European countries

Country	Collection Ni-Cd	Collection all type (primary and rechargeables)	Start	NCRA[a]	Sorting	Financial system (€/kg)
Austria	Yes	Yes	1990	UFB	Yes	2
Belgium	Yes	Yes	1993	BEBAT	Yes	3
Denmark	Yes*		1996**	Ministry**	No*	16
Finland	Yes			Municipalities/ importers/retailers	Some	
France	Yes		1999	SCRA	Yes	2
Germany	Yes	Yes	1998	GRS	Yes	2
Greece						
Italy						
Luxembourg						
Portugal						
Spain	Yes-local	Yes-local	1999			
Sweden	Yes	Yes	1998	Municipalities	Yes	34
The Netherlands	Yes	Yes	1995	STIBAT	Yes	2
UK + Ireland	Partial		1994	REBAT		
Norway	Yes		1997	Batteriretur		
Switzerland	Yes	Yes	1990	BESO	Yes	3-5

Source CollectNiCad (2000g), adapted.
* Will change in future: all batteries (primary and rechargeable will have to be collected);
** Before that date: other in place e.g. Danish Battery Association
a) NCRA = National Collection and Recycling Association

Industrial Nickel-Cadmium batteries

Data on the Ni-Cd battery collection/recycling efforts for individual EU countries were collated from the questionnaire 2000. In addition CollectNiCad provided data for the year 1999. An overview of the available data for industrial Ni-Cd batteries is given in **Table 2.30**.

Table 2.30 Total weight (tonnes/year) of collected/recycled industrial Ni-Cd batteries for the individual EU countries[18]

Country	1994	1995	1996	1997	1998	1999	2000	2001	Reference
Austria		91	115	173		148	304	134	(2)
Belgium	14	105	71	140	112	65	91	104	(2)
Denmark		3	5 14[b]	3	1	7	11	34	(2)
Finland		 41	 47	 70	70 98	160 131	 82	 188	(1) (2)
France	158 528	153 560	251 1,100	383 560	400 618	 529	 817	 780	(1) (2)
Germany	935	1,074	987	1,124	1,295	998	799	826	(2)
Greece			3						
Ireland						20	8	8	(2)
Italy	31	103	131	151	41	125	194	190	(2)
Luxembourg				4	3		10	5	(2)
The Netherlands	83	127	261	185	172	150	146	124	(2)
Portugal									
Spain		12		41	181	160	94	154	(2)
Sweden	136	157 147	254 254	204 204	189 189	 200	 216	 295	(1) (2)
UK	 29	 21	 24	 80	52 51	112 112	 136	 112	(1) (2)
Norway		 53	 53	 57	20 34	32 67	 55	 84	(1) (2)
Total EU-16[a]						2,677	2,963	3,038	
Switzerland	39	19	18	20	23	21	160	42	(2)

1) Questionnaire Member States (2000) Primary sources: (B): BEBAT, (F): Ministere de l'amenagement du territoire et de l'environment, (UK): SNAM, (S):SAFT
2) Industry Country by country data (CollectNiCad, 2000), updated for the years 2000 and 2001 (CollectNiCad, 2002)
a) Lower limit used
b) Miljoprojekt (2000)

In the few cases where two sets of data are available, no large differences are observed between the data provided by industry and the Member States. Overall approximately 2,677 tonnes of industrial Ni-Cd batteries have been collected in 1999.

2.2.2.5.2 Collection rate/Collection efficiency

Data on the absolute amounts of Ni-Cd batteries being collected was obtained from a questionnaire submitted in 2000 to the EU Member States. In addition CollectNiCad provided country by country data for the year 1999. Collection percentages mentioned in the questionnaires are not given in the **Table 2.28** and **Table 2.30**. Any comparison of these numbers should be performed with caution since most often the rationale behind the calculation

[18] With update for 2000 and 2001, via CollectNiCad, 2002.

of collection rates are not the same for the various EU member states. Typically, collection rates are being calculated as the percentage collected batteries of a base year sale. In that case the collected amount corresponds to only a small percentage of same years' sales of portable Ni-Cd batteries (e.g. UK). However, this kind of approach is difficult to apply for long life articles[19] such as Ni-Cd batteries for which no correlation can be found between the base year sales data and the collected quantities for that same year.

So, Industry as well as Member states developed a number of alternative calculation formulas. One of the most recent is the so-called 'collection efficiency' being defined by STIBAT as the ratio between the amount of Ni-Cd batteries collected over the maximally available amount for collection (STIBAT, Deauville, 1999) with the latter equalling the sum of the collected Ni-Cd batteries and the quantity of Ni-Cd batteries disposed in the municipal waste stream.

Calculating the collection efficiency

$$\text{Collection efficiency} = Q._{Ni-CdColl} = \frac{Q._{Ni-CdColl}}{Q_{Ni-CdColl} + Q_{Ni-CdMSW}}$$

$Q._{Ni\text{-}Cd\ Coll}$ = Quantities of batteries collected separately
$Q._{Ni\text{-}Cd\ MSW}$ = Quantities of batteries eliminated with Municipal Solid Waste

Although this equation may have advantages (i.e. independent of present market volume and battery's lifetime) it needs to be mentioned that detailed studies dealing with the analysis of MSW are complex and for the moment limited to a few countries. Furthermore the amount of Ni-Cd batteries found in MSW might not be completely representative for all Ni-Cd batteries going into the waste stream. For example, replacement of batteries in emergency lighting units is not common. Therefore, the majority of end-of-life Ni-Cd batteries in emergency lighting become waste during building refurbishment and are generally disposed of as mixed industrial and some as municipal waste (ERM, 2000). For pure conceptual and mathematical reasons the use of a collection ratio, defined as a simple percentage of the total amount of used Ni-Cd batteries coming available for collection and that will effectively be collected for recycling, is preferred. By subtraction, the remaining amount of batteries arriving into the waste stream is obtained.

Since not all European countries have a (Ni-Cd) battery collection system in place two collection ratio's are considered further in this report:

- 10% collection of the Ni-Cd batteries coming available for collection: representative for a country with a collection system with low efficiency;
- 75% collection of the Ni-Cd batteries coming available for collection: considered by Industry as representing an EU-wide realistic target (CollectNiCad, Pers. com., July 2002) and chosen to be representative for a country with a collection system with a high efficiency.

The span of 10-75% is believed to cover all possible combinations in the EU (limited to waste management options). Hence, in this regard the development of country specific scenarios are not deemed necessary.

[19] Long life articles are defined in the revised TGD as articles having a service life longer than one year

2.2.3 Updated data (reference year 2002)

2.2.3.1 Introduction

Quantitative update information regards the use of the substances in the different applications is fragmentary.

Consumption volumes are updated for the uses in batteries, in pigments and in stabilisers for those companies that participated in the updating exercise (see **Table 2.31**).

Furthermore some producers provided tentative data regards the break-down of the quantities cadmium metal and cadmium oxide: the uses of cadmium oxide expressed as percentages of the production in 2002 are estimated as follows: batteries: 83.5%, stabilisers: approximately 27% pigments: 1.5% and others: 4%. This latter information is substantially different from the data provided by the processors/users of the substances.

No update consumption data are available for Cd plating, alloys and others.

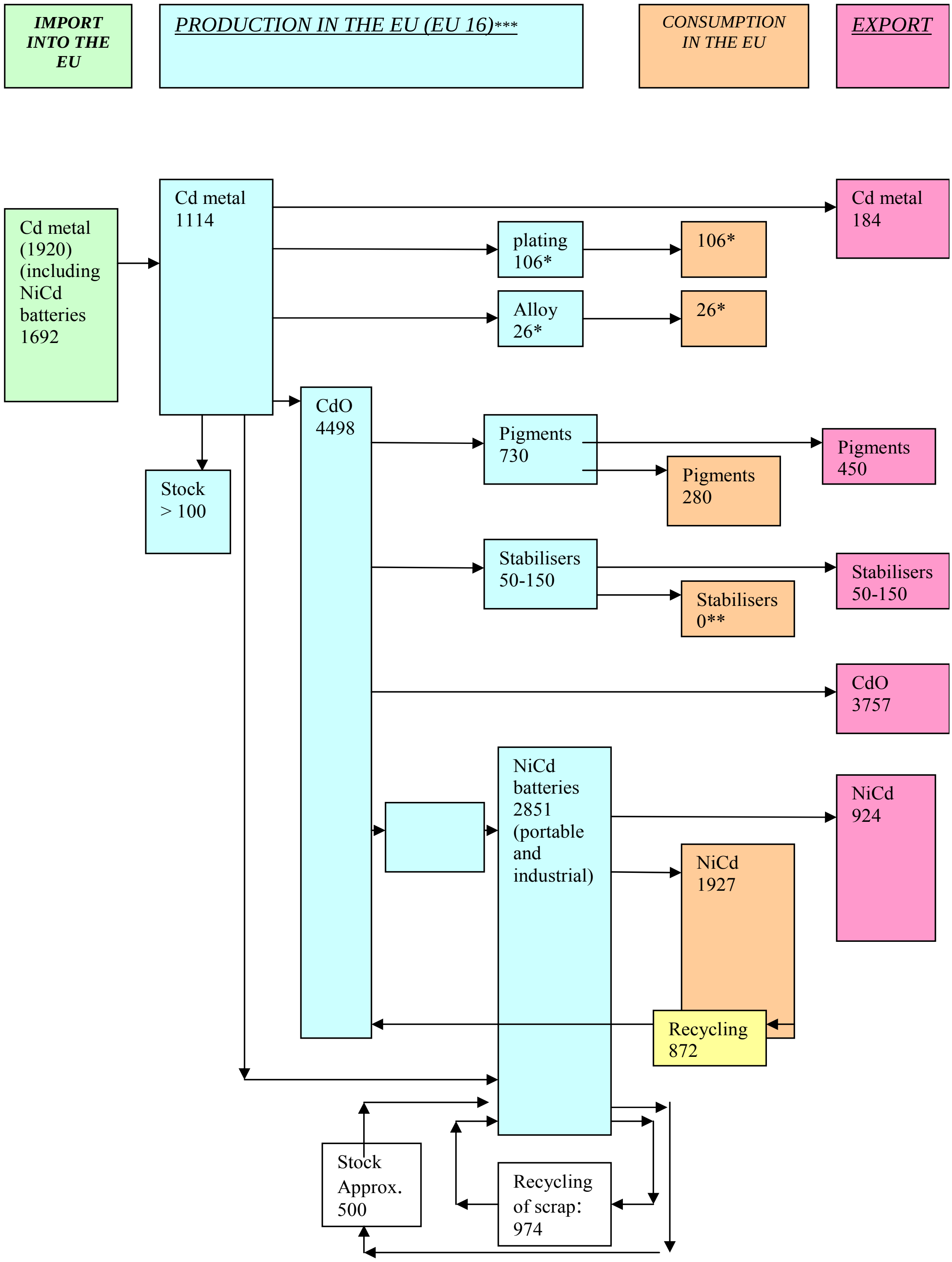
Table 2.31 Consumption data on cadmium metal and cadmium oxide for the major use applications (amounts in metric tonnes and expressed as elemental cadmium)

Year	Batteries	Pigments	Stabilisers
2002	1634.6*	n.d.	in the range 50 to 150
2003	1725*	299	in the range 50 to 120

n.d. No data available;
* Figures based on the information provided by 3 companies

Recently, an update of the mass-balance of cadmium in the EU (year 2000-2002) was provided by industry (see **Figure 2.11**). The production volume of cadmium in the EU in 2000-2002 is estimated to be 1,114 tonnes/year. Corrected for import/export 2,850 tonnes/year is available for different applications.

Figure 2.11 Cadmium mass balance flow in the EU for the reference year 2000-2002 (mass balance drawn up by ICdA, IZA-Europe and Recharge)



* Data refers to 1996. No update in figures was received

** Due to the Vinyl 2010 Commitment

*** Not included is cadmium contained in imported raw materials (zinc, copper and lead ores). For zinc ores the estimated amount of cadmium in the EU-16 is 5,000 tonnes/year. Most of this cadmium is stated to be separated in the production processes, stabilised and disposed of in authorised hazardous waste disposal sites. Estimated amount is 5,000 tonnes for EU zinc industry.

2.2.3.2 Ni-Cd Batteries

Since the previous update of information in 2002/2003, the number of companies producing Ni-Cd batteries has further decreased. **Table 2.32** mentions those companies that ceased the production of these batteries. Current producers are given in **Table 2.33**.

Table 2.32 Companies formerly producing Ni-Cd batteries and date/year of ceasing production

Company (and plant)	Country	Date/year of production stop
Friwo (EXIDE-group)	Germany	p.m. date to specify
EMISA (EXIDE- group)	Spain	2003

Table 2.33 Current producers of Ni-Cd batteries in EU*-16

Company (and location)	Country
SAFT Nersac	France
SAFT Bordeaux	France
Hoppecke	Germany
GAZ (Zwickau)	Germany
SAFT-AB	Sweden

Table 2.34 Current recyclers of Ni-Cd batteries in EU*-16

Company (and site)	Country
SNAM	France
ACCUREC	Germany
SAFT-AB	Sweden

The amount of cadmium (metal and oxide) used by three out of seven (for the year 2002) and five (for the year 2003) companies is approximately 1,635 metric tonnes for the year 2002. A slightly higher amount is reported for the year 2003 (see **Table 2.31**).

The volume of secondary cadmium produced in the EU-16 by the recycling of batteries, production scrap and other sources, was about 974 tonnes for the year (of which 56% batteries) 2002 and 10,23 tonnes for the year 2003 (of which 52% batteries). These figures are based on the information provided by 2 out of the 3 recycling companies (data of the company with highest capacity are included).

2.2.3.3 Cd containing Pigments

Compiled update information from the producers of cadmium containing pigments was submitted to the Rapporteur. Currently only three companies are producing these pigments in the EU-16. General Chimica and Degussa ceased production respectively in 2003.

Compiled data on the mass-balance of cadmium in pigments for the year 2003 was provided by the pigment producing companies and is given in **Table 2.35**.

Table 2.35 Mass-flow of cadmium within pigments for the year 2003 (in metric tonnes)

	Cd in pigments	Cd content
Production	1,216	730
Exports outside EU-16	750	450
EU-16 sales	466	280
Imports outside EU-16	33	20
EU-16 consumption	499	299

Note The calculation of the consumption figures assumes that the volumes of export and import of coloured articles are the same

2.2.3.4 Cd containing stabilisers

The production of stabilisers containing cadmium (compounds) decreased significantly since the end nineties in view of the Vinyl 2010 commitment. It should be noticed that any production of stabilisers by the companies adhering to this agreement, is destined solely for export and cannot be sold in the EU-15. The number of producers in the EU-16 dropped to only a few. Currently only 2 companies (three sites) acknowledged to the Rapporteur that some production still took place at their sites in Italy and Germany.

Only two of these use the priority substances as starting material in their process.

The consumption data of cadmium metal and cadmium oxide for this use are given as a range: between 50 and 150 tonnes in 2002. Somewhat lower values are given for the year 2003 (see **Table 2.31**).

Any EU production of stabilisers is for export and cannot be sold in the 15 original EU countries that are part of the Vinyl 2010 commitment.

2.2.3.5 Alloys, plating and other uses

No update information was submitted to the Rapporteur for these uses.

2.3 LEGISLATIVE CONTROL MEASURES

2.3.1 EU legislation

Cadmium (and its compounds) is a multi-regulated substance: in the EEC several directives have been adopted spread over the whole spectrum of risk reduction legislative instruments actually in use in the EU i.e. limitations in the marketing and use, environmental quality standards (emission and immission standards, protection of natural resources (groundwater, drinking water)), workplace (OEL's, etc) and consumer.

The directives, regulating at the source, are the Council Directive 76/769 (10^{th} amendment; 91/338/EEC) relating to the restrictions on the marketing and use (see **Table 2.36**), and the Council Directive 91/157/EEC on batteries and accumulators. The latter directive establishes a marketing ban on batteries and accumulators with high mercury content as well as an obligation for Member States to undertake steps to ensure the separate collection of batteries with a view to their recovery or separate disposal. The latter obligation concerns spent batteries and accumulators containing certain amounts of cadmium, lead or mercury.

Table 2.36 Limitations and prohibitions on the marketing and use of Cadmium and its compounds (Directive 76/769/EEC, amendment Dir. 91/338 and Dir. 99/51/CE)

Cd and its compounds 91/ 338/EEC	**1. May not be used to give colour to finished products** **1.1.Manufactured from the substances and preparations listed below:** ▪ polyvinyl chloride (PVC) [3904 10] [3904 21] [3904 22] ▪ polyurethane (PUR) [3909 50] ▪ low-density polyethylene (LDPE), [with the exception of low-density polyethylene used for the production of coloured master batch] [3901 10] ▪ cellulose acetate (CA) [3912 11] [3912 12] ▪ cellulose acetate butyrate (CAB) [3912 11] [3912 12] ▪ epoxy resins [3907 30] ▪ melamine-formaldehyde (MF) resins [3909 20] ▪ urea-formaldehyde (UF) resins [3909 10] ▪ unsaturated polyesters (UP) [3907 91] ▪ polyethylene terephtalate (PET) [3907 60] ▪ polybutylene terephthalate (PBT) ▪ transparent/general purpose polystyrene [3903 11] [3903 19] ▪ acrylonitrile methylmethacrylate (AMMA) ▪ cross-linked polyethylene (VPE) ▪ high-impact polystyrene ▪ polypropylene (PP) [3902 10] In any case, whatever their use or intended final purpose, finished products or components of products manufactured from the substances and preparations listed coloured with cadmium may not be placed on the market if their cadmium content (expressed as cadmium metal) exceeds 0.01% by mass of the plastic material. EXCEPTED for products to be coloured for safety reasons **1.2. May not be used in paints.** However if the paints have a high zinc content, their residual concentration of cadmium must be as low as possible and at all events not exceed 0.1% by mass.

Table 2.36 continued overleaf

Table 2.36 continued Limitations and prohibitions on the marketing and use of Cadmium and its compounds (Directive 76/769/EEC, amendment Dir. 91/338 and Dir. 99/51/CE)

Cd and its compounds
 	
91/ 338/EEC
	2. May not be used to stabilise:
	2.1. The finished products listed below manufactured from polymers or copolymers of vinylchloride:
	▪ packaging materials (bags, containers, bottles, lids)
	▪ office or school supplies
	▪ fittings for furniture, coachwork or the like
	▪ articles of apparel and clothing accessories (including gloves)
	▪ floor and wall coverings
	▪ impregnated, coated, covered or laminated textile fabrics
	▪ imitation leather
	▪ gramophone records
	▪ tubes and pipes and their fittings
	▪ swing doors
	▪ vehicles for road transport (interior, exterior, underbody)
	▪ coating of steel sheet used in construction or in industry
	▪ insulation for electrical wiring
	In any case, whatever their use or intended final purpose the placing on the market of the above finished (components of) products is prohibited if their cadmium content (expressed as Cd metal) exceeds 0,01% by mass of the polymer.
	EXCEPTED for products using cadmium based stabilisers for safety reasons.
	3. May not be used for cadmium plating metallic products or components of the products used in the sectors/applications listed below:
	▪ Equipment and machinery for:
	  ▪ food production
	  ▪ agriculture
	  ▪ cooling and freezing
	  ▪ printing and book-binding
	▪ Equipment and machinery for the production of:
	  ▪ household goods
	  ▪ furniture
	  ▪ sanitary ware
	  ▪ central heating and air conditioning plant
	and the manufactured products as listed in this subsection

Table 2.36 continued overleaf

Table 2.36 continued Limitations and prohibitions on the marketing and use of Cadmium and its compounds (Directive 76/769/EEC, amendment Dir. 91/338 and Dir. 99/51/CE)

Cd and its compounds 91/ 338/EEC	In any case, whatever their use or intended final purpose the placing on the market of cadmium plated products or components of such products used in the sectors/applications listed and of the products manufactured in the sectors listed is prohibited. EXCEPTED sectors: aeronautical, aerospace, mining, off shore and nuclear whose applications require high safety standards and in safety devices in road and agricultural vehicles, rolling stock and vessels. EXCEPTED electrical contacts, in any sector of use, on account of the reliability required of the apparatus on which they are installed.
99/ 51 /EC	Exemptions for Austria and Sweden, already applying stricter provisions than the aforementioned, are granted until 31 December 2002, time by which the European regulations will be reconsidered and adapted to technical progress. See in this context the study reports by WS Atkins (1999a, b) and RPA Ltd (2000), on the risks to health and the environment by cadmium contained in certain products (i.e. used as a colouring agent or as stabiliser in polymers and for metal plating), as commissioned by the EC (DG Enterprise).

In addition to Dir. 91/338/EEC, toys should also comply to Directive 88/378/EEC (‘Safety of Toys Directive’) thus fulfilling the daily limit value for cadmium for the bioavailability resulting from the use of toys i.e. 0.6 µg per day (EC, 2003). Consumer protection is further also aimed at through the establishment of regulatory standards (e.g. European Standard EN 71 part 3) in circumstances where prevention from exposure is of particular importance, i.e. in toys and articles which come into contact with food (ICdA, 1997).

Commission Regulation EC 466/2001 sets maximum levels for certain contaminants in foodstuffs.

Table 2.37 Commission Regulation (EC) 466/2001: Maximum levels of Cd in food from aquatic sources (Official Journal L 077 , 16/03/2001)

Product	**Maximum level (mg/kg wet weight)**
Muscle meat of fish, excluding fish species listed below	0.05
Muscle meat of *Dicologoglossa cunneata, Anguilla anguilla, Engraulis encrasicholus, Luvarus imperialis, Trachurus trachurus, Mugil labrosus labrosus, Diplodus vulgaris, Sardina pilchardus*	0.1
Crustaceans, excluding brown meat of crab	0.5
Bivalve molluscs	1.0
Cephalopods (without viscera)	1.0

(information extracted from EC Working document EQS for cadmium, 2003)

End of pipe EEC directives concern putting limits to discharges/emissions of cadmium in the different environmental compartments (air, water, sewage sludge for agricultural use).

Quality objectives have been adopted for the workplace as well as for different environmental compartments.

Water

Standards for surface freshwater intended for the abstraction of drinking water, and for water intended for human consumption have been fixed through the Council Directives 75/440/EEC (will be repealed in December 2007 by Dir 2000/60/EC; the Water Framework Directive) and 80/778/EEC.

Table 2.38 Directive 75/440/EEC concerning the quality required of surface water intended for the abstraction of drinking water in the Member States

Standard in mg/l	**Details**	**Source**
0.005 mg/l	Permissible level; ≥ 95% of samples Guidance levels for several water parameters pH, zinc, max. Susp. matter etc.	O.J. L 194 , 1975
Standards adopted in Member States		
n.d.	n.d.	n.d.

Table 2.39 Directive 80/778/EEC and Directive 98/83/EC on water for human consumption

Standard in µg/l	**Details**	**Source**
5µg/l	MAC; min. total hardness 60mg/l Ca (or analogous cations	O.J. N° L 229, 1981 O.J. N° L 330, 1998
Standards adopted in Member States		
n.d.	n.d.	n.d.

(MAC: max. admissible concentration, GL: Guide Levels, MRC minimum required concentration). The reference detection method in this medium is given: i.e. atomic absorption.

Council Directive 80/68/EEC for groundwater comprises cadmium compounds in List I for which MS must prohibit the direct and avoid the indirect introduction to the groundwater. The directive shall be repealed in 2013 due to 2000/60/EC. Specific measures to prevent and control groundwater pollution will be adopted within the implementation of Art. 17 of 2000/60/EC.

In Council Directive 78/659/EEC on the quality of fresh water for fish and Council Directive 79/923 on shellfish waters, no specific cadmium concentration is given. The latter Directive only stipulates that no harmful effects on shellfish and larvae should occur and aim good quality of shellfish products. Atomic absorption spectrometry preceded if needed by concentration and/or extraction, is indicated as the reference detection method.

Council Directive 76/160/EEC concerning the quality of bathing water specifies cadmium but has yet not specified a ‘Guide value’ or ‘Mandatory value’.

Council Directive 76/464/EEC on pollution by certain dangerous substances, and its daughter directive, Council Directive 83/513/EEC on the limit values and quality objectives for cadmium discharges, require Member States to set up an (prior) authorisation system for discharges of cadmium.

For most industrial discharges, with the exception of industrial plants manufacturing phosphoric acid and/or fertilisers, emission limit values are laid down. By way of alternative, Member States may base their authorisations on the quality objectives laid down for different types of waters.

Reference methods of measurement and monitoring procedures for cadmium in water, sediments and shellfish (i.e. AAS preceded by appropriate conservation and treatment of the sample) are laid down in Annexe III, of the directive including details on accuracy, precision and flow of the effluent.

Table 2.40 Directive 76/464/EEC: on pollution caused by certain dangerous substances discharged into the aquatic environment of the Community (Directive 83/513/EEC, the so-called Cadmium Discharges Directive)

Limit values* for zinc mining, refining lead and zinc and production of non-ferrous metals and metallic cadmium	**Details**	**Source**
0.2mg cadmium/l effluent	monthly mean measurements (limits for mean of daily measurements = 2-fold)	O.J. N° L 129, 1976
Limit values for the production of cadmium (compounds)	**Details**	
0.2mg cadmium/l effluent	mean of one month; total cadmium concentration	
0.5g cadmium/kg processed cadmium		
Minimum standards for the protection of aquatic life		
≤ 5 µg/l	in surface water; total cadmium conc	
≤ 5 µg/l	estuaries; dissolved cadmium	
≤ 2.5 µg/l	in marine territorial waters, coastal waters; dissolved cadmium	
Quality objective (target value)**		
≤ 1 µg/l	in surface water; total cadmium conc	
≤ 1 µg/l	estuaries; dissolved cadmium	
≤ 0.5 µg/l	in marine territorial waters, coastal waters; dissolved cadmium	
and no significant increase of concentration of cadmium in sediments or in shellfish and mollusca (e.g. Mytillus edulis)		
Standards adopted by Member States		
0.06	Nl; max. permissible conc.; dissolved	van Hout, 1994; in Pearse, 1996
0.01	Nl; target value; dissolved	van Hout, 1994; in Pearse, 1996

* To be considered as 'emission limit value' under the Dir. 2000/60/EC
** To be considered as 'environmental quality standards' under Dir. 2000/60/EC

The Water Framework Directive 2000/60/EC (O.J. L 327, 22.12.2000, p.1-73) aims at the establishing of a framework for the protection of surface, transitional, coastal waters and groundwater which prevents further deterioration and protects and enhances the status of the aquatic ecosystems and depending terrestrial ecosystems and wetlands; promotes sustainable water use; aims at enhanced protection and improvement of aquatic environment through specific measures for the progressive reduction of discharges, emissions and losses of priority substances and the cessation of phasing-out of discharges, emissions and losses of priority hazardous substances, pollution; contributes to mitigating the effects of floods and droughts. Herewith the objectives of relevant international agreements including those which aim to prevent and eliminate pollution of the marine environment with the ultimate aim of achieving concentrations of priority hazardous substances near the background values for naturally occurring substances (e.g cadmium) and close to zero for man-made synthetic substances.

The list of priority substances (Annex X of Directive 2000/60/EC) has been established by Decision N° 2455/2001/EC, as has specified cadmium as a Priority Hazardous Substance.

This implies (art. 16 of 2000/60/EC) that the European Commission has to submit proposals for progressive reduction of discharges, emissions and losses, but also, as cadmium is listed as Priority Hazardous Substance, cessation or phasing-out of discharges, emissions and losses within 20 years after adoption of the proposals.

The proposals must at least cover quality standards, for water, sediment or biota, and emission controls for point sources, and also review the Cadmium Discharges Directive (83/513/EEC). If no agreement on the proposals is reached at Community level by 2006, Member States have to establish themselves quality standards and controls on the principal sources.

As the quality standards are part of the surface water status, these would have to be reached at the latest by 2015.

Air

Waste Incineration Directives: 89/369 and 89/429 set emission limit values to air based on BAT for new and existing municipal waste incineration plants (new = exploitation permit delivered after December 1, 1990). For new installations (with a nominal capacity of at least 1 tonne waste/hour) the emission value for cadmium and mercury is fixed at 0.2 mg/Nm^3 off-gas. Old installation with minimal 6 tonnes/hour nominal capacity must apply to this value at the latest by December 1, 1996.

The hazardous waste incineration Directive (94/67) controls emissions of heavy metals by prior authorisation procedure of plants. Emission limits in flue gas for existing installations (before December 31, 1996): the sum of cadmium (compounds), expressed as cadmium and thallium(compounds) must be lower than 0.1 mg/m^3. For new installations, the corresponding limit is fixed at 0.05 mg/m^3.

In addition to Directive 75/442/EEC, Directive 2000/76/EC on the incineration of waste sets stricter emission limit values, in particular for cadmium to air (the total emission limit value of ‘Cd + Tl’ = 0.05 mg/(N)m3 as daily average value suitably standardised depending on the type of combustion; air emission limit value for cadmium and its compounds: all average values over sampling period of a minimum of 30 minutes and a maximum of 8 hours: expressed as cadmium: total: 0.05 mg/m^3; exemption until January 1, 2007 for existing plants and certain conditions, hazardous waste incinerators only), water (the emission limit value for the discharges of waste water from the cleaning of exhaust gases, mentions for cadmium and its compounds, expressed as cadmium and in mass concentration for unfiltered samples: 0.05 mg/l). These emission limit values should be met by means of stringent operational conditions and technical requirements of the installations (existing plants as from December 28, 2005; for new plants as from December 28, 2002).

Council Directive 96/62/EC of 27 September 1996 on ambient air quality assessment and management (O.J. L 296, November 11, 1996, p. 5-63) aims to define the basic principles of a common strategy to define and establish objectives for ambient air quality (AAQ i.e. related to outdoor air excluding workplaces) in the Community designed to avoid, prevent or reduce harmful effects on human health and the environment as a whole; assess the ambient air quality in the MSs on the basis of common methods and obtain adequate information on the issue and ensure its public accessibility (e.g. by means of alert thresholds) maintain AAQ where it is good and improve it in other cases. Cadmium is mentioned in the list of atmospheric pollutants to be taken into account in the assessment and management of AAQ (for cadmium, an air quality standard of 5 ng/m^3 has been proposed).

Soil

Council Directive 86/278/EEC concerns the protection of the environment and in particular of the soil when sewage sludge is used in agriculture. Limit values concentrations have been set of the substance in soil, in sludge for the agricultural use and for the maximum amounts of cadmium which may be add annually to the agricultural land.

Table 2.41 Directive 86/278/EEC: on the protection of the environment and in particular of the soil, when sewage sludge is used in agriculture (Annex IA)

Annex IA		
Limit values in soils in mg/kg	**Details**	**Source**
1 up to 3		O.J. N° 181, 1986
Standards adopted by Member States (COM(97) 23 final)		
1 up to 3	BE; Flanders: sandy soil: 1 clay soil: 3; Wallonia: 1	
1 up to 3	ES: pH < 7: 1; pH > 7: 3	
2	FR	
1 up to 4	PT: pH < 5.5: 1; pH 5.5 <7: 3; pH > 7: 4	
3	UK	

Remark: for DE: limit values: 1.5 mg/kg (or 1 mg/kg dry weight) at pH > 5 and < 6 (UBA, comments 2000).

Table 2.42 Directive 86/278/EEC: on the protection of the environment and in particular of the soil, when sewage sludge is used in agriculture (Annex IB)

Annex IB		
Limite values in sludge (mg/kg)	**Details**	**Source**
20 to 40		O.J.
Standards adopted in Member States (COM(97) 23 final)		
10 and 12	BE: Flanders: 12; Wallonia: 10	
20 up to 40	ES: pH < 7: 20; pH > 7: 40	
20 and 40	FR: reference value: 20; limit value: 40	
20	PT	

Remark: here there are no data for UK; for SE: A charge of 30 SEK per gram of cadmium exceeding 50 g/tonne P (changed to 5 g Cd/tonne P) was introduced in Sweden in 1994 and was changed to a tax in July 1995 (KEMI, comments 2000); for DE: limit value: 10 mg/kg (or 5 mg/kg dry weight) at pH >5 and < 6 (UBA, comments 2000).

Table 2.43 Directive 86/278/EEC: on the protection of the environment and in particular of the soil, when sewage sludge is used in agriculture (Annex IC)

Annex IC		
Limit values for the introduction of metals in arable soils in kg/ha/year		
0.15		
Standards adopted by Members States (representative for the p'riod '91 – '94) (COM(97) 23 final)		
0.012 and 0.024	BE: Flanders: grassland: 0.012; culture land: 0.024	
0.15	ES	
0.06	FR	
0.15	PT	
0.15	UK	

Remark: for DE: limit value: maximum 0.017 kg Cd/ha/annum (based on the limit value in sludge and the max. sludge application), maximum sludge application of 5 tonnes/ha/3 years (UBA, comments 2000).

The Fertiliser Directive (76/116/EEC) is currently under revision. In that framework, extensive work has been done by Member States in performing national risk assessment reports and by the EC (see ERM, final reports of January 2000 and June 2001, commissioned by DG Enterprise). The aim of the exercise is to review the data on the exposure of risk groups and on environmental conditions in the Member States to judge whether or not cadmium in fertlisers presents an unacceptable risk and thus to harmonise the situation within the EU (Austria, Finland and Sweden have a derogation[20] from Article 7 of the Directive in so far it concerns cadmium i.e. these MS may prohibit the marketing of fertilisers containing cadmium at concentrations in excess of those which were fixed nationally at the date of Accession) and to adopt EU-wide risk management measures related to the cadmium (content) in fertilisers, if needed so. In that context several Member States have implemented national regulations limiting the maximum cadmium concentration in fertilisers, the cadmium input in and/or the cadmium concentration in agricultural soil. A non-exhaustive overview of these figures is given in the environmental part of the Risk Assessment Report (see separate document).

Waste

Council Directive 78/319/EEC on toxic and dangerous waste determined cadmium and its compounds as requiring priority consideration in the control, prevention, recovery and recycling of any waste containing or contaminated by the substance.

The packaging and packaging waste Directive (i.e. Dir. 94/62/EC of 20 December 1994; Commission Decisions 1999/177/EC and 2001/171/EC) aims to reduce the impact of these materials (and waste arisings) by limiting the total quantity that may be put on the market, by enhancing re-use and recycling and by setting limits to hazardous substances. The sum of the concentrations of four heavy metals (lead, cadmium, mercyury and hexavalent chromium) in packaging which are not to be exceeded at different points in time, are: 600 ppm (July 1998); 250 ppm (July, 1999) and 100 ppm (July 2001). Exemptions are included in the Directive (e.g. packaging made entirely of lead crystal glass) and following COM decisions (for recycled

[20] Council Common Position (EC) No 62/98 adopted on 13 October 1998, O.J. of 14.12.98, C 388, p. 1 – 3.

material used in closed product loops and controlled chain i.e. plastic crates and pallets, and for glass packaging).

The Directive on 'End of Life Vehicles' (Dir. 2000/53/EC) aims at the prevention of waste from vehicles and at re-use, recycling and other forms of recovery of end-of life vehicles and their components so as to reduce the disposal of waste as well as at the improvement in the environmental performance of all economic operators involved and especially those directly involved in the treatment of end-of- life vehicles. Limitations of the use of hazardous substances in vehicles are encouraged and the use of heavy metals (lead, mercury, cadmium and hexavalent chromium) in materials and components of vehicles put on the market after July 2003 are prohibited, with exemptions (e.g. cadmium in batteries for electrical vehicles) foreseen in Annex II under the specified conditions (at least until 1 January 2003).

Directive 2002/95/EC on the restriction of the use of certain hazardous substances in electrical and electronic equipment (EEE) requires the substitution of various heavy metals (incl. Cadmium) and other chemicals in new EEE put on the market from 1 July 2006. Exempted is Cd plating except for applications banned by Directive 76/769/EEC. The Directive 2002/95/EC should apply without prejudice to other Community legislation in particular the Batteries Directive (91/157). Directive 2002/96/EC on waste electrical and electronic equipment aims at the prevention of the waste of EEE (EEE: including large and small household appliances, IT and telecommunications equipment, tools, toys, medical devices, etc) by promoting re-use, recycling and other forms of recovery. The list of materials and components of WEEE that should be selectively treated (i.e. removed) mentions 'batteries'.

2.3.2 National legislation

Nordic countries have been even more comprehensive in regulating cadmium and its compounds resulting in a stricter legislation than that on community level (Nordiske Seminar- og Arbejdsrapporter, 1992). Since the early eighties the use of the substance in pigments, in stabilisers (and in plating) has been banned in Denmark (since 1983) and Sweden (since 1982). All Nordic countries have strictly regulated the content of the substance in fertilisers and in sewage sludge since 1992 at the latest. Regulations on batteries did exist years before the adoption at EEC level of a directive with similar objectives.

A non-exhaustive overview of the Danish legislation focusing in particular to issues related to the environment, is given as to exemplify the extent of regulation in Nordic countries (DEPA, Pers. comm.. 2001).

Table 2.44 Danish environmental legislation on cadmium (Danish EPA, Pers. com., 2001)

Regulation	Content
No. 223 of April 5, 1989 Statutory order from the Ministry of the Environment on the content of cadmium in phosphorus-containing fertilisers	The phosphorous fertilisers are regulated on the content in phosphorous containing fertilisers sets the maximum content of cadmium relative to phosphorus in fertilisers containing ≥1% phosphorus be weight. The order does not cover manure, compost, sludge or other waste products they are added phosphorous manufactured from raw phosphate. After 01.07.1998 the maximum content of cadmium in phosphorous fertilisers are 100 mg Cd/kg P.
No. 1199 of December 23, 1992 Statutory order from the Ministry of Environment and Energy on the prohibition of sale, import and manufacture of cadmium-containing products	Importation, sale and manufacture of cadmium-containing products are prohibited. For the purpose of this Order cadmium-containing products means products in which cadmium is used either as surface treatment agent (cadmium plating), colour pigment or plastic stabiliser with more than 75 ppm in the homogeneous components of the product. Irrespective of the prohibition in subsection 1 above, manufacture, importation and sale of cadmium-containing products are permitted for the purposes specified in the Annex to this Order, within the stated deadlines.
No. 93 of February 22, 1996 Statutory order from the Ministry of Environment and Energy on collection of hermetically sealed nickel-cadmium accumulators (closed nickel-cadmium batteries) and remuneration for collection and disposal for recycling	Remuneration may be paid for environmentally sound collection and disposal for recycling of hermetically sealed nickel-cadmium accumulators (closed nickel-cadmium batteries). Remuneration may be paid to private persons and public enterprises, associations, municipalities etc. collecting and delivering or being in charge of delivery of closed nickel-cadmium batteries for recycling. In this Statutory Order recycling means recovery of the cadmium and possibly the nickel content of closed nickel-cadmium batteries.

Table 2.44 continued overleaf

Table 2.44 continued Danish environmental legislation on cadmium (Danish EPA, Pers. com., 2001)

Regulation	Content
No. 130 of February 10, 1997 Statutory order from the Ministry of Environment and Energy on provision of information by export of certain used production plants	This Order lays down rules on the duty to provide information on export of used production plants from heavily polluting enterprises (listed activ–ties - including wastewater containing cadmium), including non-complete plants, located in Denmark. The rules apply to categories of production plants which have been installed in the types of enterprises listed in Annex IA, and which meet one or more of the criteria listed in Annex IB. The duty to provide information applies no matter whether the used plant is exported for the purpose of final mounting and operation in the receiving country, or with a view to resale only. The disposer of a plant listed in Annexes IA and B of this Order shall notify the supervision authority of agreements made for export of the plant. Notification may take place before the final agreement is concluded, when the question of importing country and receiving party is decided.
No. 298 of April 30, 1997 Statutory order from the Ministry of Environment and Energy on certain requirements for packaging	This Statutory Order lays down provisions for essential requirements for the manufacture, composition, and utilisation of packaging, as well as limit values for the content of heavy metals (including cadmium) in packaging. The provisions of the Statutory Order apply to all packaging, including packaging containing products. Roads, railways, ships, and airfreight containers are outside the scope of this Statutory Order. This Statutory Order shall apply without prejudice to existing quality requirements for packaging, including requirements for health, protection of health and hygiene for the packed products, or existing requirements for the transport of hazardous goods. Between 30 June 1999 and 30 June 2001, packaging and packaging components may only be placed on the market in Denmark provided the sum of concentration levels of lead, cadmium, mercury, and hexavalent chromium does not exceed 250 ppm by weight. After 30 June 2001 packaging and packaging components may only be placed on the market in Denmark provided the sum of concentration levels of lead, cadmium, mercury, and hexavalent chromium does not exceed 100 ppm by weight.
Statutory order no. 1065 of November 30, 2000 Statutory order from the Ministry of Environment and Energy on classification, packaging, labelling, sale and storage of chemical substances and products.	This Order applies to chemical substances and products. Chemical substances means chemical elements and their compounds in the natural state or obtained by any production process, including any additive necessary to preserve the stability of the substance and any impurity deriving from the process used, but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition. Dangerous chemical substances and products shall be classified in one or more of the following danger categories: explosive, oxidising, extremely flammable, highly flammable, flammable, very toxic, toxic, harmful, corrosive, irritant, sensitising, carcinogenic, mutagenic and toxic to reproduction as well as (for substances only) dangerous for the environment. Dangerous chemical substances and products shall be assigned danger symbols and indications of danger risk indications (R-phrases),and safety advices (S-phrases).

Table 2.44 continued overleaf

Table 2.44 continued Danish environmental legislation on cadmium (Danish EPA, Pers. com., 2001)

Regulation	Content
No. 594 of June 6, 2000 Statutory order from the Ministry of Environment and Energy on cosmetic products	This Order shall apply to cosmetic products, which are marketed and to substances used in such products. According to this order cadmium and its substances may not be uses in cosmetic products.
No. 1044 of December 16, 1999 Statutory order from the Ministry of Environment and Energy on certain batteries and accumulators containing dangerous substances	Import and sale of batteries and accumulators containing: more than 0.025% cadmium by weight, shall not take place unless the battery or accumulator is marked with one of the symbols indicated in Annex I to this Order, with a view to separate collection and subsequent recovery or disposal.
No. 1042 of December 17, 1997 Statutory order from the Ministry of Environment and Energy on regulation of sale and usage of some dangerous chemicals and products to some specific purposes	Use of cadmium in paints and varnishes is forbidden. Use of cadmium in foodstuffs and stimulants is not allowed The cadmium content in glazing and decorative paintings is not allowed to be more than 0,002 percent.
No. 733 of July 31, 2000 Statutory order from the Ministry of Environment and Energy on the list of dangerous substances.	Classification of dangerous substances including cadmium compounds.

2.4 VOLUNTARY CONTROL MEASURES

On the Swedish food market, voluntary cadmium-limits are already imposed on products through initiatives taken by producer associations as well as retailing companies. These limits, which are stricter than the legally imposed criteria, have been set as a response to the perceived consumer demands. Also the tax on cadmium reduces the profitable level of cadmium in phosphorus fertiliser substantially below the allowed limit.

As an example, the co-operatives supplying the farmer with fertilisers, the Swedish Farmers Regional Selling and Purchaser Associations (sw: Lantmännen) have introduced its own limit value for soil, 0.30 mg/kg, for its most important trademark. If the top soil of a single field contains more Cd, the farmer may proceed to the second step, which consists of an analysis of the cadmium content in the wheat grains. If this level is below 0,100 mg Cd/kg, the crop can be sold under the trademark, otherwise not (KEMI, 2000, as derived from Drake and Hellstrand, 1998, The economics of the Swedish Policy to Reduce cadmium in Fertilisers, KemI PM 2/98).

The voluntary commitment of the European PVC Industry aimed – amongst other targets – to phase out the use of cadmium in all stabilisers systems placed on the EU market (i.e. by ESPA members). This target was achieved in March 2002 (Vinyl 2010, The Voluntary Commitment of the PVC Industry, Progress Report 2002).

2.5 OTHER SUPRANATIONAL INSTRUMENTS

Cadmium is included in several international declarations and programmes on reduction of micropollutants.

The OECD started in 1990 a Risk Management Programme on five chemicals, one of them cadmium, for which Risk Reduction Monographs were published. The OECD programme on

Cadmium actually recommends collection and recycling of Ni-Cd batteries as a means of reducing risk.

Cadmium falls under the UN-ECE-LRTAP Protocol for Heavy Metals, the aim of which is the reduction of heavy metal emissions due to human activity (at stationary sources) and with the potential of causing harmful affects at long distance from the source via transport trough the atmosphere.

The WHO air quality guideline value for cadmium is 5 ng/m^3 (this value was established to prevent any further increase of cadmium in agricultural soils that could increase the dietary intake of future generation, given that no reliable unit risk could be derived to estimate the excess lifetime risk for lung cancer in the general population).

In 1998, the Ministerial Meeting of the OSPAR Commission in Sintra identified Cadmium (among other substances) as a substance for priority action under its Hazardous Substances Strategy. A Background document on Cadmium was prepared and adopted in 2002.

Several PARCOM Recommendations have been adopted related to the substance i.e. Rec. 92/3 concerning New secondary steel production and rolling mills, and Rec. 92/4 relating Electroplating industry. Cadmium is one of the substances that should be substituted in the latter field of uses.

The Rhine Commission has adopted a Ministerial declaration on heavy metals (with cadmium included) that have to be banned.

In 1998, the Helsinki Commission (HELCOM) Recommendation 19/5 was adopted including cadmium on the list of substances for priority action.

Cadmium also appears on the list of candidate-substances to include in the next extension of the monitoring programme of the International Commission for Protection of the river Scheldt.

The substance is also identified within the North Sea Conference framework (1990), and is one of the substances that ‘cause a major threat to the marine environment’ for which ‘reductions between 1985 and 1995 of all inputs of the order of 70% or more - provided that the use of BAT or other low waste technology measures enable such reductions’ - should be achieved. Atmospheric emissions by 1995, or by 1999 at the latest, should be significantly reduced (by 50% or more). Within that framework, harmonised quantification and reporting procedures for chemicals were developed. One of these procedures concerns Cadmium.

3 ENVIRONMENT

(see separate document).

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

4.1.1.1 General discussion

Cadmium minerals do not occur in concentrations and quantities sufficient to justify mining them in their own right. The only cadmium mineral of importance, greenockite is found in association with zinc as a minor constituent of zinc concentrate, and in some lead or complex copper-lead-zinc ores, nearly always associated with zinc sulphide (Cadmium Association, 1991).

Cadmium is present as an impurity in other non-ferrous metal ores than that of zinc (lead, copper); in iron and steel, fossil fuels (coal, oil, gas, peat and wood), cement and phosphate fertilisers (Cook and Morrow, 1995 cited by Morrow, 1998).

Cadmium metal is obtained as a by-product of zinc refining and may also be recovered from recycled cadmium products or industrial scrap.

Cadmium oxide is produced by the reaction of cadmium metal vapour with air, by the oxidation of molten cadmium, or by the thermal decomposition of cadmium nitrate or cadmium carbonate (NTP Toxicity Report). Cadmium oxide can be generated as either a dust or fumes, depending on how it is produced.

Exposure to cadmium metal and/or cadmium oxide may occur in occupational settings where cadmium is produced or used. In occupational settings, exposure is mainly by inhalation (ATSDR 1999, CRC 1986, WHO 1992).

The main use of cadmium oxide is in the manufacture of nickel-cadmium batteries, but cadmium oxide is also used as a starting material, for the manufacture of pigments used in plastics, ceramics, window glasses, paints, paper, and inks, for PVC heat stabilisers as well as for the synthesis of other inorganic cadmium compounds. Cadmium metal has the property to protect iron against corrosion and has been used in the treatment of surfaces (plating). Cadmium metal is also a component of many alloys. However, these latter applications seem to be in notable decrease in Europe. These scenarios of occupational exposure are further considered in Section 4.1.1.2.

For the general population, non-occupationally involved in the cadmium industry, uptake of cadmium (not specifically Cd metal or CdO) occurs mainly via the ingestion of food or, to a lesser extent, drinking water contaminated by cadmium. This environmental exposure results mainly from the release of significant quantities of cadmium compounds (not specifically Cd metal or CdO) to the environment and its transfer in soil, water and air. Tobacco is an important additional source of cadmium uptake in smokers mainly by inhalation (Elinder, 1985). This is discussed in Section 4.1.1.4.

Finally, the consumer can be exposed through the use of consumption products, which may be the substance itself (in this case, cadmium and/or cadmium oxide), or a preparation, or an article containing the substance. This is considered in Section 4.1.1.3.

4.1.1.2 Occupational exposure

Table 4.1 gives an overview of the main industrial uses of cadmium metal and cadmium oxide (HEDSET, 1994)

Table 4.1 Industrial uses of cadmium metal and cadmium oxide

Industrial category	EC No.	Use category	
Chemical industry: basic chemical	2		
Chemical industry: chemicals used in synthesis	3	Intermediates Laboratory chemicals	33 34
Electrical/Electric engineering industry	4	Conductive agents Batteries and cells	12
Metal extraction, refining and processing industry	8	Electroplating agents	17
Others: Basic metals used in metal industry	15	Corrosion inhibitors	14

At the workplace, exposure to cadmium and cadmium oxide will mainly take place by inhalation. An additional exposure may occur by the oral route when workers eat with dirty hands or bite their fingernails at the workplace for example. Dermal exposure may occur when Cd powder/dust, CdO powder/dust is handled or when maintenance of the production machinery involved in the process is necessary.

Elevated levels of airborne cadmium occur in the smelting of non-ferrous metals and in the production and processing of cadmium-containing articles. The thermal operations associated with some of these processes are mainly responsible for producing CdO dusts and fumes. Because the oxidation kinetics from metal to oxide is very fast, it is very unlikely that cadmium would be present in its metallic form in the fumes.

In the past, pyrometallurgical operations with Cd have sometimes been associated with high concentrations (> 1 mg/m^3) of cadmium oxide dust or fumes. Atmospheric Cd levels were highly variable depending on working conditions, but values in the mg/m^3 range were observed regularly in the 1940s to 1960s (WHO 1992, cited in HEDSET). Since the 1960s, considerable improvements in occupational hygiene have progressively been accomplished. As a result, present day Cd concentrations at the workplace are usually of the order of 10 $\mu g/m^3$ or lower. In assessing the health risks associated with present-day working conditions, this positive trend in the actual EU member states should be taken into account (HEDSET, 1997).

Current occupational limit values for cadmium and (inorganic) cadmium compounds are reported in **Tables 4.2**, **4.3**, **4.4** and **4.5**.

Table 4.2 Occupational exposure limit values for cadmium and inorganic cadmium compounds (Cd-air)

Country/Organisation	8-hour TWA(mg/m³)	15-minute STEL(mg/m³)	References
Belgium	0.01(inhal.) 0.002 (resp.)	-	Min. Emploi et Travail, 1998
Finland	0.02	-	FIOH, 2000
Germany	0.03 (inhal.)* 0.015 (inhal.)**	-	DFG, 2001
The Netherlands	0.005 (inhal)	-	SZW, 2000
Sweden	0.02 (resp.)	-	Swedish National Board of Occupational Safety and Health, 1993
United Kingdom	0.025	0.05	HSE, 2000
France	0.05	-	INRS, 1999
USA	0.01 (inhal.) 0.002 (resp.)	-	ACGIH, 2000

* For battery production, thermal extraction of zinc, lead and copper, welding of cadmium alloys
** Other uses of cadmium

Table 4.3 Occupational exposure limit values for cadmium oxide fumes: Cd-air (CAS-number: 1306-19-0)

Country/Organisation	8-hour TWA(mg/m³)	15-minute STEL(mg/m³)	References
Finland	0.01	-	FIOH, 2000
France	-	0.05	INRS, 1999
United Kingdom	-	0.05	HSE, 2000
USA	0.01 (inhal.) 0.002 (resp.)	-	ACGIH, 2000

In general, only airborne total cadmium concentrations are monitored in the working environment; factors influencing respiratory absorption, such as speciation of cadmium are not taken into account and the size distribution of the collected particles is rarely documented (WHO 1992).

The proportion of respirable cadmium to the total amount of cadmium dust in workroom air varies from one type of industry to another. In factories where CdO fumes are generated, e.g. during smelting, most of the total cadmium content in air is respirable (Elinder 1985). However, data regarding the respirable fraction are often lacking in the studies.

In this part of the Risk Assessment, external exposure is assessed using the available information on substance, processes and work tasks. Inhalation exposure is assessed without taking account of the possible influence of personal protective equipment (PPE). Information from the industry on the effectivity of PPE in practical situations is very limited. These types of equipment reduce exposure to an extent, which depends upon the inherent efficiency of the equipment, and the skill of the wearer in achieving this efficiency in the circumstances of use. No default factors for reduction of exposure as a result of the use of PPE will be used in this Risk Assessment.

Internal dose depends on external exposure and the percentage of the substance that is absorbed (through the respiratory and the gastro-intestinal systems). Absorption through the skin is estimated to be very low when exposure is to particulate Cd and CdO (less than 1%, see Section 4.1.2.2 Toxickinetics).

When available, biological monitoring data will also be used to describe occupational exposure to cadmium oxide and/or cadmium metal. Biological monitoring of exposure to industrial chemicals assesses the health risk through the evaluation of the internal exposure of the organism (i.e. the internal dose) by a biological method. Biological monitoring of exposure offers several advantages over environmental monitoring (e.g. air monitoring) to evaluate internal dose and hence to estimate overall integrated health risks. The first advantage of biological monitoring is the fact that the biological parameter of exposure is more directly related to the adverse health effects that one attempts to prevent than any environmental measurement. Secondly, biological monitoring takes into consideration absorption by all routes (lung, skin, gastrointestinal tract) and not only the inhalation route. Because of its capability to evaluate the overall exposure, whatever the route of entry, biological monitoring presents moreover the advantage that it can be used to test the efficiency of various protective measures. Another advantage of biomonitoring is the fact that non-occupational background exposure (residence, dietary habits, smoking, leisure activity) may also be expressed at a biological level as the organism integrates this total external (environmental and occupational) exposure into one internal load (Lauwerys and Hoet, 2001). Finally, as cadmium is a cumulative toxicant, the use of a biological marker of the body burden (i.e. Cd-U) allows integrating the long-term exposure.

At low exposure conditions (i.e. general environmental exposure or moderate occupational exposure), when the total amount of cadmium absorbed has not yet saturated all the available cadmium binding sites in the body (in particular in the kidney), the cadmium concentration in urine (Cd-U) mainly reflects the cadmium level in the body and in the kidney. There is a close relationship between the cadmium concentrations in urine and kidneys. When integrated exposure has been so high as to cause a saturation of the binding sites, cadmium in urine may then be related partly to the body burden and partly to the recent exposure. When renal damage develops, a considerable increase of urinary excretion occurs (Lauwerys and Hoet, 2001).

Under occupational conditions, Cd in blood may be considered as mainly a biomarker of recent exposure. However, the relative influence of the Cd body burden may be more important or even dominant in persons with previous exposure and persons who have accumulated large amounts of Cd (Lauwerys and Hoet, 2001).

Several agencies and countries have proposed biological limit values for Cd. As with occupational exposure levels (OEL, TLV) biological limit values are defined on the assumption that occupational exposure occurs for 8 hours daily and 5 days per week. Biological limit values are usually derived from published observations on humans (most exclusively field studies for Cd). The criteria used in the setting of these limit values may differ between agencies what explains differences between recommended values (e.g. the Deutsche Forschungsgemeinschaft (DFG) proposes biological tolerance values (BAT) which are ceiling limits based primarily on a direct relationship to health effects, whereas BEI values (biological exposure indices), proposed by ACGIH are average levels expected in healthy workers with exposures equivalent to inhalation alone at the TLV) (Lauwerys and Hoet, 2001).

Table 4.4 Occupational biological limit values for cadmium: Cd-B, Cd-U

Country/Organisation		Cd-B (Cd in blood)	Cd-U (Cd in urine)
DFG	BAT	15 µg/l	15 µg/l
France	IBE	10 µg/l	10 µg/g creat
Sweden		11 µg/l	
Finland	BAL	5.6 µg/l	5.6 µg/l
ACGIH	BEI	5 µg/l	5 µg/g creat

BAT Biological tolerance values
BEI Biological exposure indices
BAL Biological action level
IBE Indicateur biologique d'exposition

Remark: Relationship between air monitoring- and biological parameters:

No well defined relationship between air and biological values can be expected as the meanings of these two types of monitoring values are different. Biological monitoring values reflect an individual's "uptake" of a chemical. Air monitoring indicates the potential inhalation "exposure" of an individual or group. The uptake within a workgroup may be different for each individual for a variety of reasons e.g. physiological and health characteristics of the workers, including age and gender; occupational exposure factors and work habits; non occupational exposure factors (e.g. smoking habits), location of the air monitoring device in relation to the workers breathing zone etc. Because of these reasons, no direct correlation can be expected between air values and biological monitoring values and some inconsistencies might be observed between these two types of values.

In addition, with regard to Cd, both biomarkers of exposure are influenced by the accumulated body burden of the metal and a straightforward relationship between Cd-B, or even less Cd-U, and current airborne levels is not expected.

The relation between external exposure (assessed by air sampling) and biomonitoring has been investigated by some authors as for example Ghezzzi et al. (1985) who examined the influence of current exposure (Cd in air) and length of exposure on Cd-U and Cd-B levels in one group of 83 subjects from an alloy factory. The behaviour of Cd-U and Cd-B in relation to the presumable total exposure over the entire working life was also investigated by using a cumulative exposure index. This index was calculated by multiplying the number of years worked in each department by the value of the mean atmospheric concentration of cadmium assigned to the department in the same period. The low correlation found between cumulative index and current exposure indicated that these two ways of expressing exposure described two different situations.

Table 4.5 Geometric mean values of biological indicators of Cd in male workers divided into subgroups according to duration of exposure, length of exposure and cumulative exposure index (Ghezzi et al., 1985, IARC 1992)

Current exposure				Duration of exposure				Cumulative exposure index			
µg/m³	N	Cd-B (µg/L)	Cd-U (µg/l)	years	N	Cd-B (µg/L)	Cd-U (µg/l)	µg/m³ years	N	Cd-B (µg/L)	Cd-U (µg/l)
0-1	27	1.6	5.0	< 5	14	2.4	3.3	< 50	23	1.5	2.5
1-10	31	2.9	5.7	6-15	44	3.0	7.2	51-250	18	2.3	4.2
10-50	16	5.9	11.2	> 15	22	2.9	10.7	251-500	17	5.1	8.9
> 50	9	6.7	10.5					501-3,000	14	4.5	11.8
								> 3,000	11	6.8	10.5

N Number of subjects

Results demonstrated the general pattern of behaviour of the two parameters of internal dose in relation to occupational exposure in this group of workers: mean Cd-B levels increased with current exposure levels but were also influenced by the elevation of the cumulative exposure index. Cd-B levels were not statistically different when different lengths of exposure were compared. Cd-U levels increased with the increase in length of service and with elevation of the cumulative exposure index.

To summarise, data used for the occupational exposure assessment are:

- exposure data from the HEDSET*;
- data regarding the production processes and use pattern of the products*;
- measured atmospheric data for cadmium oxide and for cadmium metal*;
- biological monitoring data*;
- physico-chemical data, physical appearance and vapour pressure ;
- results from exposure models (EASE – model).

* as provided by industry

Data are grouped by type of activity:

1. The production of cadmium oxide
2. The production of Cd metal
3. The production of nickel-cadmium batteries and recycling
4. The production of cadmium alloys
5. Cadmium pigments production where CdO and Cd metal are used as starting materials
6. Cadmium electroplating
7. Stabilisers where CdO and Cd metal are used as starting materials
8. Brazing, soldering, welding
9. Others

In these different activities, exposure may be to cadmium oxide and/or to cadmium metal and/or to other cadmium compounds. For clarification, **Table 4.6** summarises for each scenario which Cd compound is used or produced, to which Cd compound exposure occurs and in which risk characterisation and corresponding conclusion file (i.e. Cadmium metal or Cadmium oxide) this is respectively discussed and included.

Table 4.6 Cadmium species involved in different working scenarios

Scenario	Substance produced /used			Substance to which main exposure occurs			RC file	
	Cd metal	CdO	Remark	Cd metal	CdO	Remark	Cd metal	CdO
1. The production of cadmium oxide	+	+		-	+		-	+
2. The production of Cd metal	+	-		+	+		+	-
3. The production and recycling of Ni-Cd batteries	+	+		+	+		+	+
4. The production of Cd alloys	+	-		-	+	+ exposure to alloy fumes	+	-
5. Cd pigments production	+	+	Starting material	(+)	(+)	other Cd compounds	+	+
6. Cd plating	+	+		+	+		+	+
7. Cd stabilisers	+	+	Starting material	(+)	(+)	other Cd compounds	+	+
8. Brazing	+	-		(+)	+		+	-
9. Others	+	+		+	+	other Cd compounds	+	+

For each type of production, a general description of current exposure data will be followed by the application of a model to calculate inhalation and dermal exposure (EASE) when possible. Biological data, when available are also reported. The different data are compared using expert judgement and a choice for the best applicable estimators of exposure is made.

Main results are the estimation of a typical exposure value (mean) and of the so-called reasonable worst case value. This latter value intends to estimate the exposure level in a situation with exposure in the higher ranges of the full distribution of the exposure levels, but below the extremes. If a large number of suitable data is available, a 90^{th} percentile can be used as an estimator of the reasonable worst case value. If limited data sets are available (e.g. only measurements from one site or only small number of measurements or if measures are reported with only very little detail on tasks, working and/or sampling conditions etc.) the highest measured value is taken or the results of modelling are preferred to account for the weaknesses in the different data sets.

When insufficient data are available to carry out a specific modelling for a defined scenario of exposure, an attempt is made to reach a modelled estimate by cross-reading with other scenarios or using "worst-case" assumptions. In case of "worst-case" modelling, the relevance of the obtained estimates needs to be further assessed before reaching the conclusion that exposure (inhalation, dermal) is significant.

4.1.1.2.1 The production of cadmium oxide

Two companies were reported to produce cadmium oxide. Both were located in Belgium.

A complete process description was available for company B:

The manufacturing process for cadmium oxide is partly enclosed. Cadmium metal in ingots is manually placed in furnaces heated at 320°C. Emitted fumes are oxidised by contact with air in a closed system. The produced CdO powder is filtered and collected in bags, flo bins and metal drums or directly into silo. Exposure to CdO is likely to occur at the first step of the process at the ovens (CdO fumes) and during packaging of the product and maintenance (CdO dust).

The packaging station has local exhaust ventilation at the discharge point. Workers have to place and adjust the bag or drum under the discharge and to set the process in motion (semi-automated process). Filled bags and drums are subsequently closed and carried to the storage area. No extensive dermal contact with the cadmium oxide powder is expected to occur under normal handling conditions.

In company A, a similar process is used: Cd metal (ingots) is molten and oxidised with air in a closed oven. The resulting CdO powder is collected in a bag filter and packaged in drums, big bags, flo bins under aspiration or directly in silo. Workers add the metal ingots or package the finished CdO. However, the conditions of packaging are not well described and a skin contact with the CdO powder cannot be excluded.

Atmospheric measurements and biological monitoring have been carried out in the seventies in one of these companies (B) by Lauwerys et al. (1979). These values (no details given here) contribute to illustrate the decrease in exposure in this type of setting during the last twenty years.

Industry data

Exposure data supplied by industry are shown in **Table 4.7**. Atmospheric levels were measured by static samplers and sampling times were between 4 and 8 hours. All provided details on sampling procedures are reported and no more details are available. The aerosol fraction sampled (total, inhalable or respirable) is not known. In view of the average spherical diameter of the produced CdO (0.5 µm), the aerodynamic diameter is likely < 10 µm and it is assumed that reported figures represent the respirable fraction. Biological monitoring data are also available, reflecting body burden (Cd-U) and recent exposure (Cd-B) and are reported in **Tables 4.8** and **Table 4.9**.

Table 4.7 Exposure data: production of cadmium oxide: atmospheric level, static sampling

Companies	Workplace	Number of exposed workers	Atmospheric exposure levels (µg total*Cd/m^3)					
			1994-1996			1997		
			Mean	Range	N	Mean	Range	N
Company A	Cd production area	± 10	37	2-144	45	-	-	-
Company B[£]	Ovens	6	12.3 [§]	-	-	-	-	-
	Flo-bins	1	19.7	-	-	-	-	-
	Big bags	1	14.7	-	-	-	-	-
	Enfutage	1	7	-	-	-	-	-
	Air treatment	1	10	-	-	-	-	-
	Laboratories	1	17.7	-	-	-	-	-
	Storage 1	10	4.3	-	-	-	-	-

Table 4.7 continued overleaf

Table 4.7 continued Exposure data: production of cadmium oxide: atmospheric level, static sampling

Companies	Workplace	Number of exposed workers	Atmospheric exposure levels (µg total*Cd/m³)					
			1994-1996			1997		
			Mean	Range	N	Mean	Range	N
Company B£	Storage 2	10	6.3	-	-	-	-	-
	Overall (measurements by external advisor)	± 12	11.2	1.0-39.0**	9	9.9	2.0-35.1	3

N Number of samples
\- No information available
* It is not possible to give some indication on the chemical speciation CdO or Cd powder
** One extreme value, not considered in the derivation of the typical value: 169.0 µg/m³(at the flo-bin consecutive to a technical problem)
§ In 1996, an installation for the production of Cd metal powder was placed in the same room as where the ovens
are As this introduced some problems (such as higher Cd levels in the air), this installation was moved.
£ Workplaces correspond to the sampling points

Table 4.8 Biological monitoring data, Cd in blood (Cd-B), production of CdO

	Workplace	Number of workers exposed	Blood (µg/l)					
			1994-1996			1997		
			mean	range	N	mean	range	N
A	Cd production area	± 10	0.63	0.1-1.6	-*	0.48	-	-
B	Non-production	4-5	0.85	0.1-1.6	-	-	-	-
	Production	4	1.85	1.0-3.1	-	-	-	-

N Number of samples
\- No information available
* Reported to be 2-5 times a year

Table 4.9 Biological monitoring data, Cd in urine (Cd-U), production of CdO

	Workplace	Number of workers exposed	Urine (µg/g creatinine)					
			1994-1996			1997		
			mean	range	N	mean	range	N
A*	Cd production area	± 10	-	-	-	2.6 (1997)	0.3-9.0	-
B**	Non-production Production	4-5	6.3 18.7	0.6-16.5 6.0-67.5	- -	- -	- -	- -

N number of samples
\- no information available
* Cd-urine 1994,1995,1996: because of technical problems (external contamination), values obtained for Cd-U were considered as irrelevant by the factory and were not submitted.
** Several of the workers from Company B have been exposed to high levels of cadmium in the past and the Cd-U values may reflect these past exposure conditions. The average of the mean values is (6.3 + 18.7 + 2.6)/3: 9.2 µg/g creatinine

Other data

Data were provided by the Belgian Federal Ministry of Employment and Labour (**Table 4.10**).

Table 4.10 Exposure data, production of CdO

Companies	Workplace	Number of workers exposed	Atmospheric exposure levels (range, µg total* Cd/m³)	
			1986	1996
Static sampling				
Company	Ovens (2) Oven (1) Filters (4) Packaging Hall	- - - - -	9.5-34.9 19.2 8.8-14.6 23.6-30.6 3.6-20.8	- - - - -
Personal sampling				
Company	CdO production area	-	-	49

* It is not possible to give some indication on the chemical speciation CdO or Cd powder
\- No information available

Measured dermal exposure data for a comparable type of production (production of zinc oxide) have been reported in the RAR for ZnO (Rapporteur: NL). Although these data may not fully apply for the production of CdO, because of differences in the process (use of drums for packing CdO powder instead of sacks and bags used in the Zn facility) and in working conditions (e.g. automation of the process), a comparison between these measured Zn data and the estimates provided below by EASE modelling for the CdO might be useful:

Hughson and Cherrie (2001) studied dermal exposure to zinc in two surveys, carried out in plants producing zinc oxide or zinc dust. In the Dutch RAR, results have been clustered per job or task name with all workers performing a task called "packing", "blending", "pelletising" or "classifying" in the group "high exposure task" and all others in a group "low exposure task". This division in "high" and "low" exposure groups according to task name allows us to compare more specifically the tasks for which dermal exposure in the CdO production is relevant, i.e. the packaging of the CdO powder with the packaging of ZnO powder. However, as the division in tasks could only be made for plants B and D in the second survey conducted by Hughson and Cherrie (2001), only those measured values are presented:

Task specific dermal exposures were measured 6 times. Results for ZnO packing are reported in **Table 4.11** and **Table 4.12**.

Table 4.11 Task specific dermal exposures to zinc measured in zinc powder (ZnO/Zn dust) production facilities (Hughson and Cherrie, 2001; RAR ZnO)

Job description	Plant	Dermal exposure (µg zinc/cm²) on hands and forearms
ZnO packing (sacks)	B	389
ZnO packing (sacks)	D	49
ZnO packing (sacks)	D	27

Measurement method: repeated wet wiping of the skin at places considered representative of the skin area. Sampling occurred three times per day and might have prevented the sloping effect of dermal exposure (which is expected to slope to a maximum or ceiling at a maximum unknown level). This may have led to an overestimation of potential dermal exposure.

The measured values (expressed as µg Zn/cm^2) were recalculated into mass of zinc:

Table 4.12 Results of the measurements of zinc exposure levels (in mg zinc) in two plants producing ZnO and/or Zn dust (Hughson and Cherrie, 2001; RAR ZnO 2001)

	Results	N	Minimum	Maximum
ZnO high exposure plant B	Hands and forearms	2	448	2,216
	Whole body	2	553	2,378
Zn dust high exposure plant B	Hands and forearms	4	901	1,911
	Whole body	3	1,118	2,682
Plant D high exposure group	Hands and forearms	5	419	2,157
	Whole body	5	439	2,369

It was reported in the RAR for ZnO (2001) that six of the ten "high exposure group" workers had whole body dermal exposure levels between 1950 and 2700 mg zinc. A reasonable worst case value of 2,200 mg zinc was chosen by the Dutch rapporteur after discarding one outlier. Six of the eleven "high exposure group" workers had dermal exposure levels to Zn of hands and forearms between 1,750 and 2,250 mg zinc. Recently, new dermal exposure data became available and led to changes in the conclusions on dermal exposure estimates for zinc oxide[21] (R073_0404_hh_addendum).

Using the same methods of sampling and analysis as in the study reported above, Hughson and Cherrie (2002) measured the maximum skin surface loading after immersion , the accumulation of skin surface after hand press contact with a contaminated surface, and the accumulation of skin surface loading due to dumping bags of zinc oxide. Results are summarised in **Table 4.13**.

Table 4.13 Results of the study by Hughson and Cherrie (2002)

Parameter	Substance	Result (range in µg/cm²)
Maximum skin surface loading after immersion (hands only)	Zinc oxide	390-940
Skin surface loading after hand press contact (hands only)	Zinc oxide	88-438
Skin surface loading after dumping of 1 or 2 bags (hands and forearms)	Zinc oxide	16-70
Skin surface loading after dumping of 4 bags (hands and forearms)	Zinc oxide	14-97
Skin surface loading after dumping of 8 bags (hands and forearms)	Zinc oxide	64-184

According to the authors, the repeat contact tests suggested that the rate of dust loading tended towards a level that did not change with further activity. To account for the probable effect of the maximum adherence of zinc oxide and the possibility of overestimation due to repeat sampling, it was concluded by the Dutch Rapporteur that the maximum adherence as measured by Hughson and Cherrie (2002) will be used as the basis for the estimation of exposure in production of zinc oxide. This led to an estimated reasonable worst case dermal exposure estimate of 940 $\mu g/cm^2 \cdot 2{,}000\ cm^2$ = 1,880 mg zinc oxide/day (1,504 mg zinc/day). For the typical value, the highest "best estimate" (highest accumulated skin surface loading divided by three) was used and multiplied with the skin surface area exposed, leading to a dermal exposure estimate of 728 mg zinc oxide/day (582 mg zinc/day).

[21] http://ecb.jrc.it/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/zincoxideHHreport073.pdf

Zn values in air have also been reported in the RAR for ZnO with data grouped in categories according to workplace (EBRC 2000; RAR ZnO 2001). Median and 90th percentile values reported for the processing of finished zinc oxide (packaging, bagging) are: 1.2 mg Zn/m^3 and 4.5 mg Zn/m^3) (EBRC, 2000; RAR ZnO 2001). These values have to be compared with the Cd-air reported data for the CdO production (all workplaces):

Typical value	Worst case value
15 µg Cd/m³	150 µg Cd/m³

It should be noted that the values for Cd, reflecting workplace contamination, are hundred times less than the Zn values. Therefore, it is expected that the dermal exposure will be lower in the CdO facility.

Modelled data

Inhalation exposure to cadmium oxide takes place during melting of the ingots of cadmium metal and during the activities of packaging, cleaning and maintenance.

The vapour pressure of cadmium oxide and cadmium metal at 25°C is considered as negligible (1 mm Hg at 1,000°C). The average spherical diameter of the produced cadmium oxide is reported to be about 0.5 µm (aerodynamic diameter < 10 µm, respirable) (Annex VII, 1997).

For the packaging of the CdO powder, the most appropriate EASE scenario was dry manipulation, local exhaust ventilation (LEV) present. This results in a prediction of 2-5 mg/cubic metre.

The only potential for dermal exposure is during packaging of the CdO powder or during cleaning/maintenance. Details on packaging of the CdO powder provided by company B allowed to conclude that, under normal handling conditions, the dermal exposure to the CdO powder is expected to be low. Packaging process in company A is reported to be similar to that used in company B. However, available details on the filling of the drums, bags and flo-bins in company A are not sufficient to conclude to a lack of skin contact.

An attempt was made to estimate exposure using the EASE model. The chosen scenario for packaging of the CdO powder is non-dispersive use, direct handling, intermittent contact level. The predicted dermal exposure to cadmium oxide is 0.1-1mg/cm^2/day (42-420 mg/day for an estimated exposed skin surface of 420 cm^2). These modelled values appear very high and their interpretation should take into account the fact that the EASE model is probably not very appropriate to assess dermal exposure to such compounds. For instance, assuming a conservative value of 1% for dermal absorption, this would mean a daily systemic dose of 420-4,200 µg cadmium, which would correspond to a urinary cadmium excretion in the range of 600-6,000 µg/g creatinine. Such Cd-U values are unrealistic in occupational settings and well above the levels measured in cases of lethal poisonings (see Section 4.1.2.3). Therefore, these modelled values will not be used in the risk characterisation.

No modelling could be carried out for cleaning and maintenance as no information was available for these tasks.

Conclusions

Cadmium uptake results from inhalation and dermal exposure, the latter possibly occurring during packaging, cleaning and maintenance.

For Risk Assessment of inhalation exposure, preference is given to the measured data (instead of the modelled data) as they apply more specifically to the substance and to the type of production to be assessed. Modelled data are not in agreement with the measured data.

From the available measured data, it is concluded that a typical value for exposure is 15 µg/m^3 (≅ average of the mean values). The 90 or 95th percentile could not be calculated because of the poor precision of the data. The upper limit of the range of measured data is taken as a reasonable worst case (144 µg/m^3). However, as these values for Cd in air are derived from static sampling measurements, they have to be considered with caution because their representativity for the process and actual individual's exposure cannot be assessed. A potential bias towards lower exposure levels (as static samplers usually underestimate personal exposures) needs to be taken into account.

EASE modelling has been used to provide typical values for dermal exposure in the absence of measured data. Measured data from the ZnO production indicate that skin exposure to zinc oxide powder may reach up to 1,800 mg, for similar tasks (packaging). However, processes are not exactly similar and from data measured in air in both types of facilities, dust contamination of the workplace (and, as a consequence, potential dermal exposure) appears to be much higher in the ZnO production plant (±1 mg/m^3 vs. 10 µg/m^3 in the CdO production plant).

A typical (average) and a worst case value (upper limit of the range of data) for Cd-B and Cd-U are also derived as biological monitoring data were provided. Because of its ability to evaluate the overall exposure (whatever the route of entry: inhalation, oral and/or dermal) biological monitoring presents the advantage to bypass the uncertainties related to the ambient monitoring conditions and the dermal exposure assessment.

Values that will be used in the risk characterisation are summarised in **Table 4.14**:

Table 4.14 Values used for risk characterisation

Production of CdO		
	Typical value	**Worst case**
Cd-air	15 µg/m^3*	150 µg/m^3
Cd-U	10 µg/g creat	70 µg/g creat
Cd-B	1 µg/l	3 µg/l

* Static sampling, by default, assumed to be the respirable fraction

4.1.1.2.2 The production of cadmium metal

Massive (sticks, balls, rods, plates)

Cadmium metal production is closely associated with the refining of zinc, lead and copper.

The raw material is generally the metallic precipitate (or metallic sponge) obtained from the zinc circuit. In this circuit, zinc metal is produced by either pyrometallurgical or electrolytical processes and cadmium is recovered and refined in a number of stages (including leaching with a sulphuric acid solution, solution purification, and precipitation of metallic Cd with Zn dust).

In pyrometallurgical processes, the zinc concentrate is first roasted at 700 to 1,200°C under oxidising conditions in a sinter plant. This produces a granular sinter for the Imperial Smelting Furnace (ISF) lead-zinc blast furnace. Cadmium compounds are more volatile than those of zinc and, at these roasting temperatures, up to 70% of the cadmium content of the concentrate will volatilise and be collected as dust and fumes. The collected material, which can contain up to 20% cadmium and some lead is subsequently leached to precipitate the lead in a first step and then in a second step to precipitate cadmium as a metallic sponge by adding zinc dust to the cadmium sulphate solution. The sponge is dried and refined by distillation to cadmium metal. The residual sintered concentrate (calcine) containing oxidised zinc and cadmium materials is heated to 1,100-1,350°C, reduced by carbonaceous material and the zinc and the cadmium are volatilised. The metal vapours are condensed and collected. Most of the cadmium collects with the zinc metal and is removed by fractional distillation (this process allows a good separation of the present metals with different boiling points: cadmium 767°C, zinc 906°C, lead 1,750°C). Almost all the cadmium can be concentrated in cadmium-zinc alloy containing about 15% cadmium. The dusts, powder and alloy are repeatedly redistilled under reducing conditions to produce a pure metal. Metal is then cast into the required shapes (ingots, balls, sticks, etc.).

Information about the type of cadmium compounds encountered at the different stages of the pyrometallurgical process has been provided by one company:

- sintering: cadmium oxide dust;
- ISF furnace: cadmium/cadmium oxide dust and fumes;
- refinery and cadmium plant: cadmium oxide dust and fumes, $CdSO_4$.

Exposure to cadmium oxide (dust and/or fumes) could thus take place at the different steps of the manufacture. Exposure to cadmium metal (dust) is only possible at the end of the production process and possibly during cleaning and maintenance of the production equipment.

In electrolytic processes, the zinc concentrate is also roasted under oxidising conditions but this is usually done in fluidised bed roasters which produce a fine calcine suitable for acid leaching. The calcine is dissolved in sulphuric acid and iron and copper impurities are precipitated. Cadmium is precipitated from the sulphate solution by addition of zinc dust. The cadmium precipitate is filtered and forms a cake, redissolved in sulphuric acid. A reasonably pure cadmium sponge is produced after additional acid solution/zinc dust precipitation stages.

This can be followed by the briquetting of the obtained Cd sponge and a melting stage. The melting is done in heated furnaces at a temperature of about 400°C: NaOH is added to remove the Zn impurities and the cadmium metal underflows by gravity to a second furnace from where it is cast.

Alternatively, these first steps can be followed by further leaching/purification, and a subsequent electrolytic process (including the deposition of metallic cadmium on electrodes and the stripping from the electrodes). The obtained cadmium metal is melted and cast.

In the electrolytic process, exposure to cadmium metal/oxide (dust and/or fumes) occurs mainly during the steps of melting and casting. In the first steps of the flowsheet (cementation, leaching, purification, electrolysis) cadmium is under the form of a solution of $CdSO_4$. Maintenance workers and foremen may be exposed to a mix of Cd metal/CdO and $CdSO_4$.

One company provided details on cleaning activities: the cleaning of the filters used in the first steps of the process is performed manually and by a whole team. This activity requires one hour and up to 3 filters have to be cleaned by shift. This is also a source of exposure to a mix of substances, including cadmium compounds.

Cadmium metal powder

Cadmium metal powder was manufactured (stopped in 2001) by one company by distillation of solid cadmium metal in an inert medium. Cadmium vapours were condensed under nitrogen and cooled by water in a closed circuit. Exposure to Cd metal powder (inhalation, dermal) was likely to occur during packaging (in drums) at the end of the process (average spherical diameter is reported to be 10-13 µm) and during cleaning and maintenance. A direct handling of the powder was not expected to occur as filling of the drums of Cd metal powder was done automatically and as workers only had to set the process in motion and to close the drums. However, an incidental contact of the skin with the cadmium metal powder cannot be excluded, even under normal handling conditions. This company also produced cadmium oxide powder in the same setting and workers were involved in both types of production. Therefore, they were exposed to both compounds (oxide and metal). Data available for this company are also reported under Scenario 1 (production of cadmium oxide, company B).

In Europe, about 300 workers are still involved in the cadmium metal production process, including workers from the zinc metal industry because first steps of the process are common to both products.

Industry data

A number of cadmium metal producers provided atmospheric and biological monitoring data summarised hereafter in **Table 4.15**, **4.16**, **4.17** and **4.18**. However, most of these measured data were insufficiently supported by accompanying information or details on measurements. In particular, no information was given on the type of sampler used for airborne measurements and it is impossible to know whether figures reflect total, inhalable or respirable fractions. Additional specific information has been requested from industry (relationship working person -sample; number of samples, duration of sampling) but could not be completed. Unless otherwise specified, it is assumed that the data refer to full shift exposure. Several values were presented as single values. It is assumed that these are either averages or results of single measurements. Concentrations are usually expressed as µg Cd/m^3 or mg Cd/m^3 and precise chemical speciation is not given.

Cadmium metal (massive)

Atmospheric exposure levels measured by static sampling are reported in **Table 4.15**. ampling durations ranged from 3 to 12 hours.

Personal sampling values are reported in **Table 4.16**.

Biological monitoring data are reported in **Tables 4.17** and **4.18**.

Table 4.15 Production of cadmium metal (massive): atmospheric levels, static sampling measurements

	Companies	Workplace	Number of exposed workers	Atmospheric exposure levels (µg total*Cd/m³)							
				1994-1996				Other years			
				Mean	Range	N	Sampling duration	Mean	Range	N	Sampling duration
Electrolytic process	Company A	Headman	2	< 20	-	-	8 hours	-	-	-	-
		Cd precipitation	1	55	-	-	8 hours	-	-	-	-
		Cd pressing	1	20	-	-	8 hours	-	-	-	-
		Cd melting	3	54	-	-	8 hours	-	-	-	-
		Other	1	43	-	-	8 hours	-	-	-	-
	Company D	Storage raw material	-	14.9	10.5-19.8§	12	8 hours	-	-	-	-
		Water treatment plant	-	1.8	1.0-2.5	12	8 hours	-	-	-	-
		Electrolysis	-	2.3	1.4-3.5	12	8 hours	-	-	-	-
		Waelz kilns	-	8.3	5.3-11.8	8	8 hours	-	-	-	-
		IS plant	-	4.3	2.7-6.2	8	8 hours	-	-	-	-
		Lead production plant	-	5.2	2.2-8.9	8	8 hours	-	-	--	-
	Company G	Hydrometallurgy	10	1.1	n.d.-4	> 3	2-4 hours	-	-	-	-
		Refinery	17	10.5	8-19	> 3	2-4 hours	-	-	-	-
	Company H	Cd-Foundry	2	18	11-25	2	6 hours	-	-	-	-
		Zn leaching plant combined with Cd-process/briquetting plant	30	17	5-29	2	7.5-8.5 hours	-	-	-	-
	Company I	Roaster	7-14	50.2	1-440	13	-	3 (1993)	1-5	3	-
		Leaching/Cd process	20-35	1.8	1-5	4	-	- (1993)	-	-	-
		Melting, casting	3	1	1-2	11	-	3 (1993)	1-5	4	-
	Company K	1st site									
		Cd production	4-19	30.7	-	-	12 hours	40	-	-	12 hours
		Product preparation		21.7	-	-	12 hours	30 (1997)	-	-	12 hours
		2nd site									
		Cd production									
		Product preparation	25-31	70	-	-	12 hours	40	-	-	-
				54.7	-	-	12 hours	40	-	-	-
	Company L	Electrolysis	3	23.3	-	±9	8 hours	-	-	-	-
		Melting	4	23.3	-	±9	8 hours	-	-	-	-
		Cementation	2	23.3	-	±9	8 hours	-	-	-	-
		Filters	4	23.3	-	±9	8 hours	-	-	-	-
		Foremen	2	23.3	-	±9	8 hours	-	-	-	-
Pyrrometallul	Company F&&	Cd workshop at the Zn sintering	±6	-	3-8	-	7 hours	-	-	-	-
		Zn and Cd refining	20-40	-	3-6	-	7 hours	-	-	-	-

N Number of samples
\- No information available
* It is not possible to give some indication on the chemical speciation CdO or Cd powder
&& Due to technical problems, the zinc refinery was not in operation during 1994, 1995, and 4 months in 1996

Table 4.16 Production of cadmium metal (massive): atmospheric levels, personal sampling measurements

	Companies	Workplace	Number of exposed workers	Atmospheric exposure levels (µg total*Cd/m³)							
				1994-1996				Other years			
				Mean	Range	N	Sampling duration	Mean	Range	N	Sampling duration
Electrolytic process	Company C	Zinc plant									
		Concentrate receival	7	5	-	1-2	-	-	-	-	-
		Roasting									
		Leaching	35	10	-	1-5	-	-	-	-	-
		Sampling dpt.	5	10	-	1-5	-	-	-	-	-
			1	-	-	1	-	-	-	-	-
		Cadmium plant									
		Electrolysis									
		Casting	2	17	-	2	-	-	-	-	-
			2	13	-	2	-	-	-	-	-
	Company E[&]	Electrolysis	5	-	-	-	-	56	-	-	160 min
		Leaching	5	-	-	-	-	41 (1987)	-	-	160 min
	Company H	Cd-Foundry	2	11	< 1-28	6	6 hours	3 (1993)	2-4	2	6.8 hours
								16.8 (1997)	11-22	-	-
		Zn leaching plant combined with Cd-process/briquetting plant	30	2	< 1-5	7	7.5-8.5 hours	2 (1993)	< 1-5	3	6.4 hours
	Company I	Roaster	7-14	6.4	1-25	20	6 hours	14 (1993)	4-34	11	6 hours
		Leaching/Cd process	20-35	12.7	1-40	35	6 hours	1 (1993)	< 1-1	5	6 hours
		Melting, casting	3	3.7	1-10	13	6 hours	5 (1993)	1-12	10	6 hours

Table 4.16 continued overleaf

Table 4.16 continued Production of cadmium metal (massive): atmospheric levels, personal sampling measurements

	Companies	Workplace	Number of exposed workers	Atmospheric exposure levels (µg total*Cd/m³)							
				1994-1996				Other years			
				Mean	Range	N	Sampling duration	Mean	Range	N	Sampling duration
	Company J£	Filtration of leaching residues	5	5.5	1-17	8	-	-	-	-	-
		Leaching	15	5.5	3-8	4	-	-	-	-	-
		Zn smelting	12	0.5	-	12	-	-	-	-	-
		Cd electrolysis	3	11.7	6-24	6	-	-	-	-	-
		Roasting	5	287	29-545	2	-	-	-	-	-
		Cleaning heat exchanger (roasting installation)	4	2730	1120-4340	2	-	-	-	-	-
		Storage of Zn concentrates	3	200	15-385	2	-	-	-	-	-
	Company L	Cementation	2	-	-	-	-	2.2	2.1-2.3	2	8 hours
		Leaching/ purification	6-8	-	-	-	-	17.2	3.7-22.7	4	8 hours
		Electrolysis/ stripping	3	-	-	-	-	6.8	4.7-8.6	4	8 hours
		Melting/ casting	3-4	-	-	-	-	8.1	3.7-25.2	5	8 hours
		Maintenance	1	-	-	-	-	9.3	5.9-12.1	5	8 hours
		Foremen	2	-	-	-	-	15.4 (1997)	5.0-44.4	5	8 hours
Pyrometallurgical process	Company B	Acid plant	0	-	1-4	-	3 hours	-	-	-	-
		Sinter plant	0	-	10-60	-	3 hours	-	-	-	-
		ISF	0	-	2-7	-	3 hours	-	-	-	-
		Refinery	70	-	1-67	-	3 hours	-	-	-	-
		Cd plant	4	-	1-160	-	3 hours	-	-	-	-
		Fine Cd column	4	-	16-260	-	3 hours	-	-	-	-
		Engineering	18	-	1-560	-	3 hours	-	-	-	-
	Company F&&	Cd workshop at Zn sintering	±6	27#	10-54	-	7 hours	-	-	-	-
		Zn and Cd refining	20-40	3#	3-31	-	7 hours	-	-	-	-

N Number of samples
\- No information available
* It is not possible to give some indication on the chemical speciation CdO or Cd powder
\# Median

& Cadmium production was finished in 1991
&& Due to technical problems, the zinc refinery was not in operation during 1994, 1995, and 4 months in 1996
£ As some of the mean values reported by company J are extreme compared with the values reported by the other companies, additional information on these extreme values has been requested from the company but could not be completed.
Average of the means is calculated excluding company J.

Table 4.17 Biological monitoring data, Cd in blood (Cd-B), production of Cd metal (massive)

		Workplace	Number of workers exposed	Blood (µg/l)			
				1994-1996		Other years	
				mean	range	mean	range
Electrolytic process	A	Headman	2	2.8	-	-	-
		Cd precipitation	1	2.9	-	-	-
		Cd pressing	1	3.9	-	-	-
		Cd melting	3	8.7	-	-	-
		Other	1	5.2	-	-	-
	C	Zinc plant					
		Concentrate receival	8	1.2	-		-
		Roasting	50	-	-	1.1 (1991)	-
		Leaching	58	1.4	-	-	-
		Sampling dpt.	5	0.3	-	-	-
		Cadmium plant	8	2.4	-	-	-
	D	Leaching	9	-	-	-	-
		Roasting	18	-	-	-	-
		Maintenance	23	-	-	-	-
	E	&	-	-	-	-	-
	G	Cd hydro-metallurgy	10	-	-	-	-
		Cd refinery	17	-	-	-	-
	H	Overall	34	1.8	< 0.5-5	-	-
	I	Roaster/mel-ting/casting	7-14	0.83	0.11-3.7	0.84 (1993)	0.11-2.8
		Leaching	23-35	1.02	0.11-3.25	1.23	0.44-2.8
	J		##	##	##	##	##
	K	1st site	4-19	-	-	-	-
		2nd site	25-31	-	-	-	-
	L	Cementation/ Leaching/ Purification	10	5.7	2.3-10	5.6 (1997)	2-10.5
		Electrolysis/ stripping	3	3.8	1.4-5.3	4.8 (1997)	4-5.5
		Melting/ Casting	3-4	2.4	1.8-3.1	2.4 (1997)	1.5-2.5
		Maintenance	1	5.1	3.9-6.5	0.4 (1997)	-
		Foremen	2	8.3	6.2-10	0.8 (1997)	0.55-10

Table 4.17 continued overleaf

Table 4.17 continued Biological monitoring data, Cd in blood (Cd-B), production of Cd metal (massive)

		Workplace	Number of workers exposed	Blood (µg/l)			
				1994-1996		Other years	
				mean	range	mean	range
Pyrometallurgic process	B	Acid plant	0	1.9	?-3.2	-	-
		Sinter plant	0	1.3	?-2.9	-	-
		ISF	0	1.6	?-2.2	-	-
		Refinery	70	2.3	?-12.7	-	-
		Cd plant	4	6.7	?-14.9	-	-
		Fine Cd column	4	7.5	?-14.7	-	-
		Engineering	18	1.5	?-5.0	-	-
	F	Ingotage campaign	11	-	-	-	-
		Reconstruction Cd columns	-	-	-	-	-
		Zn sintering	62	-	-	3.3	0.9-11.4
		Zn refinery	37	&&	-	3.3 (1993)	0.5-6.8

N Number of samples
\- No information available
& Production finished in 1991
&& Not in operation
Sufficiently detailed information not available: Cd-B: mean 6 µg/L (1980)

Table 4.18 Biological monitoring data, Cd in urine (Cd-U), production of Cd metal (massive)

		Workplace	Number of workers exposed	Urine (µg/g creatinine)					
				1994-1996			Other years		
				mean	range	N	mean	range	N
Electrolytic process	A	Headman	2	2.2	-	6	-	-	
		Cd precipitation	1	2.8	-	6	-	-	
		Cd pressing	1	1.2	-	6	-	-	
		Cd melting	3	3.8	-	6	-	-	
		Other	1	2.6	-	6	-	-	
	C	Zinc plant							
		Concentrate receival	8	0.6	-	2	-	-	-
		Roasting	50	-	-	-	0.7 (1991)	-	1
		Leaching	8	1	-	3	-	-	-
		Sampling dpt.	5	0.9	-	1	-	-	-
		Cadmium plant	8	-	-	-	-	-	-
	D	Leaching	9	1.1	-	2	-	-	-
		Roasting	18	1.0	-	3	-	-	-
		Maintenance	23	1.4	-	3	-	-	-

Table 4.18 continued overleaf

Table 4.18 continued Biological monitoring data, Cd in urine (Cd-U), production of Cd metal (massive)

		Workplace	number of workers exposed	Urine (µg/g creatinine)					
				1994-1996			Other years		
				mean	range	N	mean	range	N
	E	&	-	-	-	-	-	-	-
	G	Cd hydro-metallurgy	10	2.7	-	3	1.0	0.25-2.99 (1997)	-
		Cd refinery	17	4.8	-	3	2.6	0.25-6.84 (1997)	-
	H	Overall	34	1.4	< 0.5-5.3	6	1.6	< 0.5-10.5	2
	I	Roaster/mel-ting/casting	7-14	1.0	0.22-4.6	3	1.15 (1993)	0.34-3.9	-
		Leaching	23-35	1.01	0.22-3.6	2	1.44 (1993)	0.34-3.58	-
	J		##	##	##	##	##	##	##
	K	1st site	4-19	8.1	-	3	5.7 (1997)	-	-
		2nd site	25-31	9.1	-	3	-	-	-
	L	Cementation/ Leaching/ Purification	10	3.0	0.4-9.5	30	2.9 (1997)	1.1-6.1	10
		Electrolysis/ stripping	3	3.9	1.7-5.9	6	4.8 (1997)	4.5-5.1	2
		Melting/ Casting	3-4	1.3	0.3-3.5	17	1.1 (1997)	1.0-1.5	6
		Maintenance	1	4.9	3.6-6.3	3	6.8 (1997)	-	1
		Foremen	2	5.5	4.0-8.1	6	5.36 (1997)	3.8-7.0	2
	B	Acid plant	0	-	-	-	-	-	-
		Sinter plant	0	-	-	-	-	-	-
		ISF	0	-	-	-	-	-	-
		Refinery	70	-	-	-	-	-	-
		Cd plant	4	-	-	-	-	-	-
		Fine Cd column	4	-	-	-	-	-	-
		Engineering	18	-	-	-	-	-	-
	F	Ingotage campaign	11	1.4	0.6-2.5	11	-	-	-
		Reconstruction Cd columns	-	1.2	0.2-3.3	2	-	-	-
		Zn sintering	62	5.0	1-11.9	20	5.7	0.7-18.7	-
		Zn refinery	37	£	0.4-22.7	46	4.9	0.9-11.3	-

N Number of available values (averages)
- No information available and production finished in 1991
£ Not in operation
No information available in a detailed manner: Cd-U: about 98% of the workers are between 4 and 9 µg/L, 2% higher (up to 20 µg/L).

Averages and ranges are summarised in **Table 4.19**.

Table 4.19 Cd-air, Cd-U, Cd-B (values available for the years 1987, 1991, 1993, 1994-1996,1997: mean (range)*)

Cd-air (µg Cd/m^3)	24 (1-440) (static sampling)
	12 (1-560) (personal sampling)
Cd-B (µg/L)	3.4 (0.1-14.7)
Cd-U (µg/g creat)	2.8 (0.2-23)

As some of the mean values reported by company J are extreme compared with other companies, typical value (average of the mean values) for this scenario is calculated after excluding company J. Average of the mean values for company J is: 462.9 µg total Cd/m^3 (in the range of the worst case values).

No measured data on dermal exposure are available.

Cadmium metal powder (one company)

This company also produced cadmium oxide powder and workers were involved in both processes, being exposed to both compounds (oxide and metal).

Available values for Cd (total) in air were previously reported in Scenario 1: the production of cadmium oxide (company B) and are summarised in **Table 4.20**. No personal sampling values are available. Biological monitoring values for this company are reported in **Table 4.21** and **4.22**.

Table 4.20 Production of cadmium metal powder: atmospheric levels, static sampling measurements

Companies	Workplace	Number of exposed workers	Atmospheric exposure levels (µg total*Cd/m^3)							
			1994-1996				Other year			
			mean	range	N	sampling time	mean	range	N	sampling time
M	Overall	± 12	11.2	1.0-39.0**	9	4 hours	9.9	2.0-35.1	3	4 hours

* It is not possible to give some indication on the chemical speciation CdO or Cd powder

** One extreme value, not considered in the derivation of the typical value: 169.0 µg/m^3(at the flo-bin consecutive to a technical problem)

Table 4.21 Biological monitoring data, Cd in urine, production of Cd metal powder

	Workplace	Number of workers exposed	Blood (µg/l)			
			1994-1996		Other year	
			mean	range	mean	range
M	Non production	4-5	0.9	0.1-1.6	-	-
	Production	4	1.9	1.0-3.1	-	-

Table 4.22 Biological monitoring data, Cd in urine, production of Cd metal powder

		Workplace	Number of workers exposed	Urine (µg/g creatinine)			
				1994-1996		Other year	
				mean	range	mean	range
	M	Non production	4-5	6.3	0.6-16.5	-	-
		Production	4	18.7	6.0-67.5	-	-

Other data

UK provided data (personal sampling) on non-ferrous metal manufacture relating to the year 1986. It is not known whether cadmium metal was produced or occurred only as a by-product. The aerosol fraction sampled is not given.

Atmospheric cadmium levels are summarised in **Table 4.23**.

Table 4.23 UK data, non-ferrous metal manufacture

Process	Job	Number of samples	Duration (range, minutes)	Range (µg Cd/m³)	Arithmetic mean (µg Cd/m³)
Smelting	Assistant	3	117-382	0.2-0.3	0.23
	Button man	1	224	0.3	0.3
	Chargehand	2	221-277	0.2-0.3	0.25
	Driving	3	168-365	0.2	0.2
	Furnace operator	16	120-417	0.2-0.4	0.28
	Observer	1	81	0.2	2
	General operator	1	475	0.3	0.3
	Slagman	3	162-373	2-3	0.27

Modelled data

EASE modelling is used to compare the measured data with the modelled estimates.

Massive cadmium metal production

Pyrometallurgical process:

Inhalation exposure to cadmium oxide fumes and dust may take place during roasting of the zinc concentrates, heating of the residual sintered concentrate and melting and casting of the obtained cadmium metal. Dermal exposure to cadmium is limited as the processes involve high temperatures and do not suppose direct manual handling of the cadmium. However, dermal exposure due to contamination of equipment and surfaces, after cooling of material is possible.

- EASE modelling: roasting of zinc concentrates, heating of the calcine

The name of the substance is cadmium metal
The temperature of the process is 1,200 (700-1,200-1,350-1,500)
The physical state is gas or vapour
The exposure-type is gas/vapour/liquid aerosol
The ability-airborne-vapour of the substance is high
The use-pattern is closed system

Significant breaching is false
The pattern of control is full containment

Conclusion: The predicted gas/vapour/liquid aerosol exposure to cadmium oxide is 0-0.1 ppm (about 0.6 mg/m³)

- EASE modelling: activities of melting and casting

The name of the substance is cadmium metal
The temperature of the process is 400
The physical-state is liquid (melting point: 320°C)
The exposure-type is gas/vapour/liquid aerosol
The use-pattern is Non-dispersive use
The pattern-of-control is LEV
The status-vp-value is Value measured at a different temperature
The measurement-temperature is 1,000
The vapour pressure is 1 mm Hg

Conclusion: The predicted gas/vapour/liquid aerosol exposure to cadmium is 0-0.1 ppm (about 0.6 mg/ m³)

Electrolytic process:

Exposure is mainly to $CdSO_4$ in the first steps of cementation/leaching/purification and electrolysis. Inhalation exposure to cadmium oxide fumes takes place during melting and casting of the metallic cadmium obtained by electrolysis. Dermal exposure is limited as processes involve high temperatures and preclude direct manual handling of the cadmium until it is under its massive shape.

- EASE modelling: activities of melting and casting in a not totally closed system

The name of the substance is cadmium metal
The temperature of the process is 400
The physical-state is liquid (melting point: 320°C)
The exposure-type is gas/vapour/liquid aerosol
The use-pattern is Non-dispersive use
The pattern-of-control is LEV
The status-vp-value is Value measured at a different temperature
The measurement-temperature is 1,000
The vapour pressure is 1 mm Hg

Conclusion: The predicted gas/vapour/liquid aerosol exposure to cadmium is 0-0.1 ppm (about 0.6 mg/ m³)

- One company provided some information on the cleaning and maintenance operations to allow EASE modelling of inhalation and dermal exposure during these activities (no measured data available). Cleaning of the filters used in the electrolytical process is performed manually, at room temperature and by a whole team in some companies. Cleaning may require one hour of work and several filters may have to be cleaned per shift

The name of the substance is cadmium (metal, oxide, sulphate)
The temperature of the process is 20 (room temperature)
The physical-state is solid

Dust-inhalation is true
Mobile-solid is true
Solid vp is false
The exposure-type is dust
The particle size is inhalable (respirable)
The operation is dry manipulation/ *dry crushing and grinding* (estimate because no details are available on operation)
The pattern-of-control is local exhaust ventilation present
The dust-type is non -fibrous
Aggregates is false

Conclusion: The predicted dust exposure to cadmium metal, oxide, sulphate is 2-5/2-10 mg/cubic metre

The name of the substance is cadmium metal, oxide, sulphate
The temperature of the process is 20
The physical-state is solid
dust-inhalation is true
mobile-solid is true
solid-vp is false
The exposure-type is dermal
The use-pattern is Non-dispersive use
The pattern-of-control is not direct handling (local exhaust ventilation present)
The contact-level is Intermittent (1/shift, duration 1 hour; 3 shifts/day)

Conclusion: The predicted dermal exposure to cadmium metal, oxide, sulphate is very low.

Cadmium metal powder production

- Manufacture of Cd powder by distillation (one company): exposure to cadmium metal powder is only likely to occur during packaging (in drums) of the obtained powder

The temperature of the process is 20
The physical-state is solid
Dust-inhalation is true
Mobile-solid is true
Solid-vp is false
The exposure-type is dust
The particle-size is Inhalable
The operations is Dry manipulation
The dust-type is Non-fibrous
Aggregates is false
The pattern-of-control is LEV present

Conclusion: The predicted dust exposure to cadmium metal is 2-5 mg/cubic metre

The name of the substance is cadmium metal
The temperature of the process is 20
The physical-state is solid
Dust-inhalation is true
Mobile-solid is true
Solid-vp is true
The exposure-type is dermal

The use-pattern is non-dispersive use
The pattern-of-control is direct handling (contact-level incidental)

Conclusion: The predicted dermal exposure to cadmium metal is 0-0.1 mg/cm²/day

Conclusions

Production of cadmium metal (massive):

Preference is given to the measured data (instead of modelled data) to define a typical and a worst case value because these are expected to reflect the different processes used for the manufacture of cadmium metal and appear to be closer to the reality of the workplace. Inhalation exposures to cadmium metal dust, cadmium oxide fumes and dust is likely to be the highest during roasting, melting and casting of the solid cadmium metal, cleaning and maintenance. Biological monitoring values indicate however that leaching activities also entail a significant uptake of cadmium.

From the available personal sampling data, a typical value appears to be 12 $\mu g/m^3$ (average of the mean values) and ~400 µg Cd/m³ is chosen as a reasonable worst case value. An upper limit value was taken instead of a percentile to account for the weaknesses in the different data sets (only little detailed information on tasks, working conditions supplied by several industries). In the absence of specific information on the sampled fraction and in view of the existing exposure to CdO fumes during the process, it is assumed that the provided figure reflects the respirable fraction.

Dermal exposure is expected to occur during cleaning and maintenance activities. From one company, data were available on cleaning of the filters and EASE modelling resulted in a predicted very low dermal exposure.

A typical and a worst case value for Cd-U and Cd-B are suggested (see **Table 4.23**), derived from the biological monitoring data supplied by industry. As biological monitoring evaluates the internal dose and takes into account the different routes of exposures, uncertainties related to the ambient monitoring or dermal exposure are taken into account.

Production of cadmium metal powder (one company)

Typical value for Cd-air (average of the mean values, derived from static sampling measurements) is estimated to be 10 µg Cd/m^3. A typical value for Cd-U is 12 µg/g creatinine (average from 2 mean values).

However, only one company is reported to be involved in this type of production and these values are derived from overall measurements for both cadmium oxide and cadmium metal powders production.

Dermal exposure is expected to occur only during packaging of Cd metal powder in drums and range of exposure levels is estimated to be 0-0.1 mg/cm²/day (0-42 mg/day for an estimated exposed skin area of 420 cm²). The interpretation of these exposure levels should take into account the fact that the EASE model is probably not very appropriate to assess dermal exposure to such compounds. For instance, assuming a conservative value of 1% for dermal absorption, this would mean a daily systemic dose of up to 420 µg cadmium, which would correspond to a urinary cadmium excretion up to 600 µg/g creatinine. Such elevated Cd-U values are unrealistic in occupational settings and above the levels measured in cases of lethal poisonings (see Section 4.1.2.3). Moreover, the use of biological monitoring that evaluates the internal dose allows taking into account the different routes of exposure (including the dermal route) and the uncertainties related to the ambient monitoring or dermal exposure.

Values that will be used in the risk characterisation are summarised in **Table 4.24** and are those estimated for the production of cadmium metal under its massive form as the production of Cd metal powder could not be clearly distinguished from the production of CdO.

Table 4.24 Values used for risk characterisation

Production of Cd metal		
	Typical value	**Worst case**
Cd-air	12 µg/m³*	400 µg/m³**
Cd-U	3 µg/g creatinine	23 µg/g creatinine
Cd-B	3 µg/l	15 µg/l

* Excluding company J
** Includes ~ mean of company J

4.1.1.2.3 The production and the recycling of nickel-cadmium batteries

A number of rechargeable batteries or cells incorporate cadmium as an active electrode material. The most important is the nickel-cadmium cell, which is based on the reversible electrochemical reactions of cadmium and nickel in a potassium hydroxide (alkaline) electrolyte. Cadmium (oxide) powder is used in the manufacture of these batteries.

Manufacture of Ni-Cd batteries

A nickel-cadmium battery consists of one or more cells (the basic electrochemical unit) connected in series or parallel or both. Each cell consists of three major components: a Cd anode (or negative electrode), a Ni cathode (or positive electrode) and the electrolyte which provides the medium for transfer of electrons, as ions inside the cell between the anode and the cathode. Additional basic components of a nickel-cadmium battery are the containers and lids, vent-plugs, separators, terminals and connections. Adapted to the performance requirements, different battery technologies are available what supposes different production processes. The pocket plate nickel-cadmium batteries represent the conventional battery technology: pocket plate electrodes contain the active materials (nickel hydroxide in the positive plates, cadmium oxide in the negative plates) in perforated steel pockets. Other battery technologies are available: nickel fibre plate cells (a nickel fibre mat serves as electrode support), plastic bonded electrodes. The cell itself can be built in many shapes and configurations -cylindrical, button, flat and prismatic- and the cell components are designed to accommodate the particular cell shape.

Some companies provided detailed information on the process for the production of nickel-cadmium batteries. One of these companies produces negative cadmium plastic bonded electrodes and sintered electrodes. Plastic bonded cadmium electrodes are manufactured by the application of a paste consisting of a mix of cadmium metal powder, cadmium oxide powder and a bonding agent (cellulose, styrene, etc.) on a film, subsequently dried, calibrated, cut and assembled with the other components of the cell. Exposures to the cadmium oxide/metal powders are likely to be very low because the process of mixing with the bonding agent is enclosed and because in the following steps of the process the cadmium is under the form of a paste.

Some information was also made available by other companies which produce pocket plates electrodes. The process includes a step of dosage and mixing of the cadmium oxide powder with additives, followed by the packaging of the negative active material. Exposure may take place during dosage and mixing, the filling of the pockets and the recuperation of remainders of the steel pockets. In company G, exposure to Cd/CdO dust is limited by pressing directly the CdO (produced in a closed process) to pellets. These pellets are used instead of powder and dust to fill the pocket plates. Dust exposure is also minimised by air ventilation systems. Dry pellets and pockets are only handled and stored in closed containers. Once the plates have been produced, they are arranged into electrodes. These electrodes are impregnated by electrolyte so no dust exposure is expected to occur in the following steps (assembling).

In company B, where this type of activities is no longer relevant, filling of the battery cases consisted in a winding assembly of pasted electrodes without use of dry powder. This process was automatic and the dust generated was exhausted using a local exhaust filter system. No direct handling of a powder was expected to occur.

Fibre-structure-type electrodes (FSE) manufacture was reported to include the following steps: chemical and galvanic metallisation, cutting of raw electrode structure and welding, impregnation of electrodes with nickel hydroxide (positive electrode) or cadmium oxide (negative electrode), assembling process. Other FSE share the same first steps of metallisation and welding but are followed by the mixing of negative and positive pastes (the negative paste contains CdO, the positive paste may contain Cd metal, cobalt metal and nickel hydroxide or only nickel hydroxide) and the filling of the raw structure with positive or negative paste. It has been reported that this latter process occurs under “wet conditions” and that no dust appears from the wet paste during the manufacture, handling and storage of plates (Company G).

Exposure to CdO or Cd metal powder may occur mainly during impregnation of the electrodes with CdO, Cd metal and during mixing of the pastes. Available information from several companies (A, B, C, G, H) indicate however that exposure to Cd and CdO dust has been limited by the implementation of "wet processes" or because the cadmium is under the form of a paste.

No information is available on cleaning and maintenance activities.

Recycling of Ni-Cd batteries

Some companies are involved both in the battery production and the battery recycling. Recycling of Ni-Cd batteries generates cadmium metal.

Information about the process for the recycling of the batteries was made available by one company:

Recycling of industrial nickel-cadmium accumulators

After initial checking and pre-sorting, packaging and connecting pieces are removed from the industrial accumulators. After this, electrolyte can be removed, which after filtration can be used in a process to abstract tin. Battery parts containing cadmium undergo the RVD process (Recycling by Vacuum Distillation). In the RVD construction, after water has evaporated, the charge can be heated up to an operating temperature of 750°C within about one hour. With the addition of various substances for the process, the CdO is reduced and evaporated. In a vacuum the metal vapour finds the way to the coldest area (here the water-cooled metal vapour condenser), where it forms a metallic cadmium block. The RVD process occurs in a hermetic construction (no “open” treatment steps) what decreases emissions drastically, provides maximum protection during the handling and avoids the contamination of gases by heavy metals.

The only handling of metallic cadmium occurs when the obtained metal (under its massive form) is taken out from the condenser.

Recycling of sealed nickel-cadmium accumulators

Consumer accumulators are initially sorted according to packs and single cells. The single cells can immediately begin with the RVD process without further treatment.

Industry data

At the time this scenario was worked out for the first time, 8 companies were reported to produce or to recycle nickel-cadmium batteries including one company combining the two processes (company F). Some changes in production facilities and in number of employed workers occurred with time. Industry provided some updated airborne data for some of the facilities (data are from 2001 and 2002) and those data are included in **Table 4.26** and **4.28**. No updated biological monitoring values were provided.

Exposure data supplied by industry is reported in **Tables 4.25**, **4.26**, **4.27**, **4.28**, **4.29** and **4.30** (manufacture of Ni-Cd batteries), **4.31**, **4.32** and **4.33** (recycling of (Ni)-Cd (batteries)). Additional specific information on sampling methods, working tasks and conditions was requested from industry but could not be obtained from some companies. It is assumed that the data refer to full shift exposure. Several values were presented as single values; it is assumed that these are either averages or results of single measurements.

Airborne Cd concentrations measured with static samplers are reported in **Table 4.25** and **4.31**. Cd air concentrations measured with personal samplers in the Ni-Cd battery production settings are reported in **Table 4.26**. Company F submitted one set of data for both activities of manufacture and recycling. In the absence of further information from the company allowing distinguishing between both activities, values are reported in **Table 4.25** and **4.31**.

Manufacture of Ni-Cd batteries

Table 4.25 Production of Ni-Cd batteries: atmospheric levels, static sampling measurements

	Companies	Workplace	Number of exposed workers	Atmospheric exposure levels (µg total*Cd/m³)							
				1995-1997				Other years			
				Mean	Range	N	Sampling duration	Mean	Range	N	Sampling duration
Manufacture	Company A1	Cell production	200	-	10-14	-	-	-	-	-	-
	A2	Cell production									
		Chem.	50	9.0	1-75	43	1 hour	2.8	1-8	6	1 hour
		Plaq.	20	4.0	2-6	3	1 hour	3	-	1	1 hour
		Mont.	60	1.9	1-5	15	1 hour	2.3 (1998)	1-5	7	1 hour
	A3	Cell production	360	21.7	-	-	-	23 (1998)	-	-	-

Table 4.25 continued overleaf

Table 4.25 continued Production of Ni-Cd batteries: atmospheric levels, static sampling measurements

	Companies	Workplace	Number of exposed workers	Atmospheric exposure levels (µg total*Cd/m³)							
				1995-1997				Other years			
				Mean	Range	N	Sampling duration	Mean	Range	N	Sampling duration
Manufacture	Company B	Winding zone	3	0.7	0.15-1	5	4 hours	-	-	-	-
		Assembly zone	4	5.0	1.4-10	3	4 hours	-	-	-	-
		Production hall	10	0.6	0.06-1.4	3	4 hours	-	-	-	-
	Company C	Active material process and negative plates Others	2 5 13	- - -	100-200 61-100 41-60 21-40 0-20	8 6 4 15 10 2	24 hours 24 hours 24 hours 24 hours 24 hours	- - - - -	100-200 61-100 41-60 21-40 0-20	0 2 0 1 5 1 6	24 hours 24 hours 24 hours 24 hours 24 hours
	Company D	-	150	1.7	1.4-2.1	3	-	30 (1994)	-	-	-
		others:									
		smoker cafetaria	-	< 4.5	-	1	-	-	-	-	-
		non smoker cafetaria	-	< 3.0	-	1	-	-	-	-	-
	Company F	1st site	4-19								
		Cd production		41.6	30-55	3	12 hours	-	-	-	-
		Product preparation		30	20-40	3	12 hours	-	-	-	-
		2nd site	25-31								
		Cd production		63.3	40-80	3	12 hours	-	-	-	-
		Product preparation		50	40-60	3	12 hours	-	-	-	-
	Company H	Negative electrode impregnation	4	38.3	-	3	-	31.5 (1998-1999)	-	2	-
		Stack assembling process	7	17.8	-	3	-	4.1 (1998-1999)	-	2	-

It is not possible to give some indication on the chemical speciation CdO or Cd powder

Table 4.26 Production of Ni-Cd batteries: atmospheric levels, static sampling measurements (data provided by industry on May 20, 2003)

	Companies	Workplace	Number of exposed workers	Atmospheric exposure levels (µg total*Cd/m³)			
				2001-2002			
				Mean	Range	N	Sampling duration
manufacture	Company A						
	A1	-	-	-	-	-	-
	A2	Cell production					
		Chem.	59	4	-	18	-
		Plaq.	14	5	-	2	-
		Mont.	80	1	-	16	-
	A3	Cell production	149				
		Chem.		10	-	9	-
		Plaq.		9	-	6	-
		Mont.		18	-	5	-
	Company G	Chem plant	6	4	-	6	-
		Cell assembling	9	1	-	3	-

- No information provided. Company G assets sold to company A

* It is not possible to give some indication on the chemical speciation CdO or Cd powder

Table 4.27 Production of Ni-Cd batteries: atmospheric levels, personal sampling measurements

	Companies	Workplace	Number of exposed workers	Atmospheric exposure levels (µg total*Cd/m³)							
				1995-1997				Other years			
				Mean	Range	N	Sampling duration	Mean	Range	N	Sampling duration
Manufacture	Company A										
	A1	Cell production	200	-	10-14	-	-	-	-	-	-
	A2	Cell production									
		Chem.	50	5.3	1-19	25	6 hours	4.7	1-12	3	6 hours
		Plaq.	20	1.8	1-3	9	6 hours	2.0	1-3	2	6 hours
		Mont.	60	2.7	1-8	14	6 hours	1.1 (1998)	1-2	8	6 hours
	A3	Cell production	360	-	-	-	-	-	-	-	-
	Company D	-	200	25	-	1	-	30 (1994)	-	-	-

Table 4.27 continued overleaf

Table 4.27 continued Production of Ni-Cd batteries: atmospheric levels, personal sampling measurements

	Companies	Workplace	Number of exposed workers	Atmospheric exposure levels (µg total*Cd/m³)							
				1995-1997				Other years			
				Mean	Range	N	Sampling duration	Mean	Range	N	Sampling duration
	Company G	Plate-filling	5	140	50-320	-	2 hours	-	-	-	-
		Press-welding	4	130	20-300	-	2 hours	-	-	-	-
		Set-welding machine	5	223	130-380	-	2 hours	49.5 (1998-1999)	18-120	-	2 hours
		Separation electrode sets	4	229	20-620	-	2 hours	15 (1998-1999)	7-21	-	2 hours
		1st filling	3	20	-	-	2 hours	34 (1998)	-	-	2 hours
		Mixing	3	-	-	-	-	83 (1999)	-	-	2 hours
		2nd filling	3	-	-	-	-	12 (1999)	-	-	2 hours

N Number of samples
- No information available
* It is not possible to give some indication on the chemical speciation CdO or Cd powder
§ Production started in 1997

Table 4.28 Production of Ni-Cd batteries: atmospheric levels, personal sampling measurements (data provided by industry on May 20, 2003)

	Companies	Workplace	Number of exposed workers	Atmospheric exposure levels (µg total*Cd/m³)			
				2001-2002			
				Mean	Range	N	Sampling duration
manufacture	Company A						
	A1	-	200	< 10	-	53	-
	A2	Cell production	59	20	-	17	-
		Chim.	14	22	-	11	-
		Plaq.	80	3	-	13	-
		Mont.	149				
	A3	Cell production		38	-	9	-
		Chim.		31	-	6	-
		Plaq.		19	-	4	-
		Mont.					
	Company G	Chem plant	6	16	-	9	-
		Cell assembling	9	11	-	4	-

- No information provided. Company G assets sold to company A
* It is not possible to give some indication on the chemical speciation CdO or Cd powder

Table 4.29 Biological monitoring, Cd in blood (Cd-B), production of Ni-Cd batteries

		Workplace	number of workers exposed	Blood (µg/l)			
				1995-1997		Other year (1998)	
				mean	range	mean	range
manufacture	A1	Cell production	200	2.3	-	-	-
	A2	Cell production	130	-	-	-	-
	A3	Cell production	360	-	-	-	-
	B	-	17	-	-	-	-
	C		±20	-	0-20 (35)	-	0-20 (8)
				-	20-40 (32)	-	20-40 (5)
				-	40-60 (28)	-	40-60 (7)
				-	60-80 (14)	-	60-80 (3)
				-	80-100 (11)	-	80-100 (1)
				-	100-120 (5)	-	100-120 (1)
	D		170-236	2.2	2.1-2.5	-	-
	F	1st site	4-19	-	-	-	-
		2nd site	4-19	-	-	-	-
	G		27	3.4	0-5.0	1.1	0-3.0
	H	-	-	-	-	-	-

N Number of samples
\- No information available

Table 4.30 Biological monitoring, Cd in urine (Cd-U), production of Ni-Cd batteries

		Workplace	number of workers exposed	Urine (µg/g creatinine)					
				1995-1997			Other year (1998)		
				mean	range	N	mean	range	N
Manufacture	A1	Cell production	200	1	-	-	-	-	-
	A2	Cell production	130	3.6	0.2-22.5	184	3.0	0.2-20	97
	A3	Cell production	360	-	-	-	-	-	-
	B	Winding and assembling	7	1.2	0.9-1.5	6	-	-	-
		others	22	1.0	0.9-1.2	6	-	-	-
	C		±20	-	0-2	47	-	0-2	16
					2-4	25		2-4	5
					4-6	18		4-6	5
					6-8	17		6-8	3
					8-10	13		8-10	3
					10-12	14		10-12	2
					12-14	2		12-14	0
	D		170-236	2.5	-	3	-	-	-
	F	1st site	4-19	6.1	4.5-8	3	-	-	-
		2nd site	4-19	9.8	8.7-10.8	2	-	-	-
	G		27	-	-	-	-	-	-
	H		-	-	-	-	-	-	-

N Number of samples
\- No information available

Recycling of Ni-Cd batteries

Some companies are specifically involved in the recycling of (Ni)-Cd (batteries). Other companies both produce and recycle (e.g. company A) Ni-Cd batteries but the data they provided were estimated to refer mainly to the battery production

Table 4.31 Recycling of (Ni)-Cd(batteries): atmospheric levels, static sampling measurements

	Companies	Workplace	Number of exposed workers	Atmospheric exposure levels (µg total*Cd/m³)							
				1995-1997				Other year			
				Mean	Range	N	Sampling duration	Mean	Range	N	Sampling duration
Recycling	Company E§	Dissembling	4	2.4	-	1	1 hour	2.1	-	1	1 hour
		Vacuum thermal distillation	2	3.5	-	1	1 hour	1.8 (1998)	-	1	1 hour
	Company F	1st site	4-19								
		Cd production		41.6	30-55	3	12 hours	-	-	-	-
		Product preparation		30	20-40	3	12 hours	-	-	-	-
		2nd site	25-31								
		Cd production		63.3	40-80	3	12 hours	-	-	-	-
		Product preparation		50	40-60	3	12 hours	-	-	-	-

§ Production started in 1997

Table 4.32 Biological monitoring, Cd in blood (Cd-B), Recycling of (Ni)-Cd (batteries)

		Workplace	Number of workers exposed	Blood (µg/l)			
				1995-1997		Other year (1998)	
				mean	range	mean	range
recycling	E§	Deassembling	4	-	1.2-3.0	-	-
		Vacuum thermal distillation	2	-	1.0-1.2	-	-
	F	1st site	4-19	-	-	-	-
		2nd site	4-19	-	-	-	-

§ Production started in 1997

Table 4.33 Biological monitoring, Cd in urine (Cd-U), Recycling (Ni)-Cd (batteries)

		Workplace	Number of workers exposed	Urine (µg/g creatinine)					
				1995-1997			Other year (1998)		
				mean	range	N	mean	range	N
recycling	E§		6	-	-	-	-	-	-
	F	1st site	4-19	6.1	4.5-8	3	-	-	-
		2nd site	4-19	9.8	8.7-10.8	2	-	-	-

§ Production started in 1997

No measured data on dermal exposure are available.

Other data

Sweden and UK provided Cd-air data:

Table 4.34 Data provided by Sweden, battery production, type of sampling not detailed, Cd-air (µg/m³, range)

	1990	1991
Paste preparation	12-46	13-56
Recovery	7-173	9-74
Briquette machine	7-42	5-35
Roll	9-10	6-53
Insulation	2-12	2-4
Point welding	2	2-23

Table 4.35 Data provided by UK, battery production, Cd-air (µg/m³, range, for the period 1987-1988), personal sampling measurements

Process	N samples	Duration (range, minutes)	Range (µg Cd/m³)	Arithmetic mean
Assembly	1	112	7	-
Briquetting	1	128	2	-
Cell production	19	10-135	5-150	10
Compacting	1	268	120	-
Pasting/plating	4	116-246	15-330	101
Plate preparation	7	62-176	10-1,170	272

Modelled data

EASE is used to compare measured data and estimates provided by the modelling.

Manufacture of Ni-Cd batteries

In view of the available information on work tasks and exposure, EASE modelling could only be carried out for one type of manufacturing processes: the production of the negative plastic bonded CdO electrodes. Inhalation and dermal exposure to cadmium could take place when the CdO and Cd metal powders are mixed with the bonding agent in the first step of the process:

The name of the substance is cadmium oxide, metal
The temperature of the process is 20 (room temperature)
The physical state is solid
Dust-inhalation is true
Mobile-solid is true
Solid vp is false
The exposure-type is dust
The particle size is inhalable
The operation is dry manipulation
The dust-type is non-fibrous
Aggregates is true (with the binding agent)
The pattern of control is LEV present

Conclusion: The predicted dust exposure to cadmium oxide, metal is 0.2-0.5 mg/m³

The name of the substance is cadmium oxide
The temperature of the process is 20
The physical-state is solid
Dust-inhalation is true
Mobile-solid is true
Solid-vp is false
The exposure-type is dermal
The use-pattern is Non-dispersive use
The pattern-of-control is not direct handling

Conclusion: The predicted dermal exposure to cadmium is very low

For those companies whose production process (companies D, F and H) also includes a step of mixing of powders and working conditions are not known, EASE modelling is carried out as a worst case to evaluate dermal exposure:

The temperature of the process is 20
The physical-state is solid
Dust-inhalation is true
Mobile-solid is true
Solid-vp is false
The exposure-type is dermal
The use-pattern is Non-dispersive use
The pattern-of-control is direct handling
The contact-level is Intermittent

Conclusion: The predicted dermal exposure to cadmium is 0.1-1 mg square cm/day*

* in case of worst case modelling, the relevance of the provided estimates needs to be further assessed before reaching the conclusion that dermal exposure is significant

Recycling of Ni-Cd batteries

One company provided enough information to carry out EASE modelling:

The name of the substance of the substance is cadmium oxide
The temperature of the process is 750
The physical state is gas or vapour
The exposure type is gas/vapour/liquid aerosol
The ability-airborne vapour of the substance is high
The use-pattern is closed system
Significant breaching is false
The pattern of control is full containment

Conclusion: The predicted gas/vapour/liquid aerosol exposure to cadmium oxide is 0-0.1 ppm (about 0.6 mg/m^3)

<u>Conclusions</u>

Measured data will be used for the risk characterisation and are preferred to the modelled data because they better reflect the different processes used for the manufacture of batteries and their recycling. Moreover, insufficient details were provided on the different processes to allow appropriate modelling.

Manufacture of Ni-Cd batteries

From the available data, it is concluded that in occupational settings producing the Ni-Cd batteries, a typical value for exposure is ~50 µg Cd/m³ (average of the mean values, personal sampling, and data from 3 companies). Static sampling measurements values were supplied by 5 companies and a typical value (average of the mean values) is estimated to be ~20 µg Cd/m^3. The absence of detailed information on sampling conditions does not allow concluding as to whether or not the static samples can really be considered representative for personal exposure. Consequently, the estimates derived from the personal sampling values will be used in the risk characterisation although they are "representative" for a smaller number of companies than the static sampling values would be.

A reasonable worst case value is taken in the upper limit of the range of measured data: 320 µg/m^3.

In the absence of complete specific information on the sampled fraction and because the process entails exposure to fine CdO powder, it is assumed that the provided figures reflect the respirable fraction.

Dermal exposure is expected to occur mainly during mixing, filling of pockets or impregnation of electrodes of/with Cd oxide powder. EASE modelling carried out for the production of plastic bonded, FSE, pocket plates electrodes for which information on worktasks was available, predicted a low dermal exposure level. The EASE scenario which best fits the other types of processes (little detailed information on the conditions of exposure) predicts a dermal exposure of 0.1-1 mg/square cm/day (42-420 mg/day for an estimated exposed skin surface of 420 cm²). These modelled values appear very high and their interpretation should take into account the fact that the EASE model is probably not very appropriate to assess dermal exposure to such compounds. For instance, assuming a conservative value of 1% for dermal absorption, this would mean a daily systemic dose of 420-4,200 µg cadmium, which would correspond to a urinary cadmium excretion in the range of 600-6,000 µg/g creatinine. Such Cd-U values are unrealistic in occupational settings and well above the levels measured in cases of lethal poisonings (see Section 4.1.2.3). Therefore, these modelled values will not be used in the risk characterisation. However, biological monitoring data-which evaluate the internal dose and integrate all routes of exposure (including dermal) - are available and allow deriving typical and worst case Cd-U, Cd-B values. These values will preferably be used in the risk characterisation.

Table 4.36 Values used for risk characterisation: production of batteries[22]

Production of Ni-Cd batteries		
	Typical value	**Worst case**
Cd-air	50 µg/m³	320 µg/m³
Cd-B	2.3 µg/l	80 µg/l
Cd-U	3.5 µg/g creatinine	20 µg/g creatinine

[22] The additional air monitoring data provided by Industry in May 2003 did not had an impact on the derivation of a typical (mean) and worst case value for Cd in air. No biological monitoring data were made available. Susbsequently, there was no need to change the values used for the Risk Characterisation in this scenario (agreed by Technical Meeting in June 2003).

Recycling of Ni-Cd batteries

Two companies provided information on recycling: 2 different processes were used and the different airborne Cd concentrations are difficult to average. In the absence of specific information on the sampled fraction, it is assumed that the provided value reflects the respirable fraction. Cd-U values are derived from the data provided by only one of the two companies. Cd-B values were provided by only one company and range from 1 to 3 µg/l (typical value ± 2 µg/l). No dermal exposure to Cd/CdO dust is expected in one company. In the other company, dermal exposure could not be assessed in the absence of a detailed description of the worktasks. Even in the company reporting the highest airborne Cd values (company F); the exposure levels were not higher than in the production facilities. The risk characterisation will be based on figures relating to Ni-Cd battery production activities.

4.1.1.2.4 The production of cadmium alloys

Cadmium has been a common component of many alloys which uses are related to their melting temperatures, e.g. tin-lead-bismuth-cadmium alloy joining metal parts which may be heat sensitive; silver-cadmium-copper-zinc-nickel alloy for joining tungsten carbide to steel tools. The EU use of cadmium as a constituent of alloys has declined in importance in the recent years (4% of total use in 1985, about 0.6% in 1996) as these have been substituted by cadmium free alloys with comparable characteristics of ductility and strength in the majority of uses.

Until 1999, one Belgian company used cadmium in the production of a copper-cadmium 50/50 master alloy used in the production of Cu/Cd wire/rod/cables. Production ended in 1999 because of no longer uses. One company producing and using alloys in a own wire/rod/cable factory has been identified in Sweden but cessation of this type of activities is planned. The UK copper-cadmium alloy factories studied by Bonnell (1955), Bonnell et al. (1959), Davison et al. (1988), and Sorahan et al. (1995) have ended production of cadmium alloys in 1966 and 1989. From the information submitted to the Rapporteur, no other EU setting for the production of Cd alloys could be located.

Manufacture of cadmium- alloys

Cadmium can be combined with a number of other non-ferrous metals to form alloys. Typically, massive metallic cadmium is added to the molten metal(s) with which it is to be alloyed and after thorough mixing, the resultant alloy is cast into the desired form (ingot, wire, rod) (IARC, 1993). This process has been more extensively described in the published studies on copper-cadmium alloy workers (Bonnell 1955, Holden 1980, Sorahan et al. 1995). Cu-Cd alloys are manufactured by re-melting high conductivity copper in furnaces and adding the necessary cadmium in the form of a copper-cadmium master alloy (which facilitates the mixing). The master alloy contains high levels of cadmium and is prepared first using the same procedure of melting Cd and Cu and mixing. Temperature of these processes is reported to be around 1,100°C (as the melting temperature of copper is 1,083°C). At this temperature, cadmium is present in the fumes as CdO (boiling point at 767°C). After stirring the alloy is cast and allowed to solidify. There is formation of fumes at both the mixing and the casting stages.

<u>Industry data</u>

There are no site-specific data available on the workplace exposure to cadmium for this assessment.

Modelled data

No recent information has been made available on process, work tasks, conditions of ventilation. EASE modelling is carried out based on the available literature data on the copper-cadmium manufacturing process in an attempt to predict an exposure level for this scenario.

Inhalation exposure to aerosols formed by emission of mixed alloy fumes (including volatilised cadmium) is possible. Direct unprotected handling of cadmium compounds does not occur, due to the fact that material is hot. However, dermal exposure due to dust contamination of equipment and surfaces, after cooling of material is possible.

An estimation of possible inhalation exposure to Cd aerosols is made using the EASE model with the following assumptions: handling of the cadmium occurs at temperatures above the melting point (320°C), use-pattern is non-dispersive use and local exhaust ventilation are present (direct handling does not occur because of the temperature). The predicted gas/vapour/liquid aerosol exposure to cadmium is 600-1,200 mg/m^3.

For dermal exposure it is assumed that contact with contaminated material is possible, which is assessed by assuming non-dispersive use, incidental contact. This is expected to be exposure mainly to cadmium alloy dust. This leads to an estimate of 0-0.1 mg/cm^2/day (0-42 mg/day for an estimated exposed skin area of 420 cm^2). The interpretation of these exposure levels should take into account the fact that the EASE model is probably not very appropriate to assess dermal exposure to such compounds. For instance, assuming a conservative value of 1% for dermal absorption, this would mean a daily systemic dose of up to 420 µg cadmium, which would correspond to a urinary cadmium excretion up to 600 µg/g creatinine. Such elevated Cd-U values are unrealistic in occupational settings and above the levels measured in cases of lethal poisonings (see Section 4.1.2.3). Moreover, the use of biological monitoring that evaluates the internal dose allows to take into account the different routes of exposure (including the dermal route) and the uncertainties related to the ambient monitoring or dermal exposure.

Conclusions

Only fragmentary data were available which do not allow performing a realistic exposure assessment of current work conditions in alloys producing settings. EASE modelling predicts an inhalation exposure of up to 1,200 mg/m^3. This value very probably overestimates exposure levels in settings with ventilation equipment and closed furnaces. Even in the early years of the UK copper-cadmium alloy production, estimated Cd air levels have not reached such high values (1926-1930: 600 µg/m^3; 1931-1942: 360-480 µg/m^3, 1947-1954: 240-270 µg/m^3, Davison et al., 1988). In an Italian factory of copper-cadmium alloys highest air value reported is 1,500 µg/m^3 in 1975 (measured with area sampler) (Ghezzi et al., 1985) Swedish atmospheric data from 1989 and 1991 ranged from 6 to 45 µg Cd/m^3 (static sampling) (data made available by Sweden).

From literature data (Davison et al., 1988, Ghezzi et al., 1985, Kjellström et al., 1979) and from the Swedish data, a value of 50 µg/m^3 is proposed as reasonable worst case value to take into account the possibility of small-scale productions of alloys in small settings with less favourable occupational hygiene conditions. In the absence of specific information on the sampled fraction, it is assumed that the proposed figure reflects the respirable fraction.

4.1.1.2.5 Pigments

One of the applications of cadmium oxide (powder) and cadmium metal (solid/powder) is the Cd pigments production, where these substances are used as starting material.

Cadmium pigments are insoluble colouring agents that can be produced in a wide range of brilliant colours and present the following properties: highly resistant to chemical attack, to degradation by light, to colour particle migration; high temperature stability, high opacity and good dispersion characteristics in plastics and paints. These pigments are based on cadmium sulphide, which produces a yellow colour. Partial substitution in the crystal lattice of cadmium by zinc or mercury and of sulphur by selenium forms a series of intercrystalline compounds making up the intermediate colours in the yellow to maroon range of cadmium colours. Cadmium pigments are used in plastics but also have applications in glass, ceramics, porcelain and vitreous enamels, and artists' colours (http://www.cadmium.org/, 2001).

In general, the manufacturing process of the pigments involves the preparation of a cadmium sulphate or nitrate solution followed by filtration to remove solids. Raw materials used are either cadmium metal or cadmium oxide (solid/powder). Following step is the addition of sodium sulphide and the precipitation of cadmium sulphide. Other salts (mercuric sulphide, selenium, barium sulphides) are added simultaneously to alter colour characteristics. Further filtration and washing, drying, calcination, rinsing, milling and blending are needed to finalise the production of the various cadmium pigments, ready for packaging (ICdA, 1997).

Little information has been located on specific work tasks in the production of pigments. Exposure to cadmium metal and oxide is reported to occur only during the first step before dissolving cadmium compounds in sulphuric acid. Some pigments producers use massive cadmium metal as starting material, adding a step in the process: the production of the metallic powder. No detailed data are available on the exposure conditions and specific worktasks associated with this production of the Cd metal powder.

One company provided information on the use-pattern and pattern-of- control for the overall process: the cadmium sulphate solution is prepared in a discontinuous batch process by direct dissolving of cadmium metal/oxide in acid in a closed reaction vessel. Cadmium sulphide is produced by precipitation from aqueous solutions of cadmium sulphate, zinc sulphate, selenium and sodium disulphide in a closed reaction vessel. When the precipitation is complete, soluble salts and water are removed by a filtration step and the dried material is heated at about 600°C. Then it is washed by decantation to remove soluble salts. After a second drying step, the material is blended, added barium sulphate if needed in enclosed equipment and packaged.

From the information supplied by another company, it can be derived that exposure to cadmium selenide or cadmium sulphide occurs in the steps of precipitation and washing, filling / emptying the filters and mixing of these compounds: workers take samples of the obtained products (e.g. 15 times 1 minute /shift) during washing and precipitation; they are exposed during filtration of the solution (e.g. 2 times 3 hours per shift); and exposure may also occur when filters and "drying room" are "emptied" (150 · 0.5 minutes and 1 · 30 minutes per shift respectively). In the following steps of the process, exposure is to the different cadmium compounds produced (e.g. cadmium sulphoselenide orange, cadmium sulphoselenide red, cadmium zinc sulphide yellow) and occurs while compounds are sampled (e.g. 3-5 times 2 minutes/shift), dried and mixed. Cleaning of the installation is also a source of exposure and occurs 3 times in the week (duration 30 minutes): exposure is limited to the different cadmium compounds (Cd and CdO negligible).

Industry data

A number of facilities provided data on exposure resulting from cadmium pigment manufacturing. These data are summarised in **Table 4.37**, **4.38**, **4.39** and **4.40**. Unless otherwise specified, it is assumed that the atmospheric data refer to full shift exposure. Several values were presented as single values. It is assumed that these are either averages or results of single measurements.

Some companies provided specific information on the measured fraction: for the stages of the process prior to the precipitation of cadmium sulphide, chemical compounds of cadmium have a much higher aqueous solubility than cadmium sulphide and pigments in air measured and results are for inhalable dust. For the parts of the process in which cadmium is present essentially as cadmium sulphide, or a mixed lattice of cadmium sulphide with cadmium selenide or with zinc sulphide, results are for respirable dust.

Table 4.37 Exposure levels, Cd-air, static sampling data, production of Cd pigments

Companies	Workplace	Number of exposed workers	Atmospheric exposure levels (µg total*Cd/m³)							
			1994-1996				Other years			
			Mean	Range	N	Sampling duration	Mean	Range	N	Sampling duration
E	Precipitation pre-products	2-3	14	-	2	2-2.5 hours	7 (1991)	-	2	2 hours
	Mixing, drying	3	63	24-138	5	0.5-1 hour	38.5 (1992)	37-40	2	1-1.5 hours
	Filling and blending	3-5	27	23-37	3	1-2 hours	21.5 (1991)	3-58	4	2 hours
	Mixing pigments	2	41	6-57	4	1-2 hours	-	-	-	-

* It is not possible to give some indication on the chemical speciation

Table 4.38 Exposure levels, Cd-air, personal sampling data, production of Cd pigments

Companies	Workplace	Number of exposed workers	Atmospheric exposure levels (µg total*Cd/m³)							
			1994-1996				Other years			
			Mean	Range	N	Sampling duration	Mean	Range	N	Sampling duration
A	Chemical department##	10	17.7	11-24	3	8 hours	-	-	-	-
	Pigment processing#	22	9.0	8-10	3	8 hours	-	-	-	-
B	CdO##	6	19.5	15-24	2	2 hours	-	-	-	-
	Solution making##	3	25	17-33	2	2 hours	-	-	-	-
	Presses#	6	19	-	1	2 hours	-	-	-	-
	Driers#	6	12.7	12-19	3	2 hours	-	-	-	-
	Kilns#	6	24	18-33	3	2 hours	-	-	-	-
	Wet milling#	3	13	7-19	2	2 hours	-	-	-	-
	Milling and packing#	15	30	22-35	3	2 hours	-	-	-	-
C	-	14	-	-	-	-	233*	-	1	8 hours
		14	-	-	-	-	184* (1993)	-	1	8 hours
		16	35	-**	1	8 hours	-	-	-	-
		16	41	-**	1	8 hours	-	-	-	-
		13	-	-	-	-	250£	-	1	8 hours
		13	-	-	-	-	310£ (1991)	-	1	8 hours
D	-	-	-	-	-	-	-	-	-	-

* It is not possible to give some indication on the chemical speciation
\# Respirable fraction
\## Total fraction
N Number of samples, averages
\- No information available
** No range available. Range is assumed to be within two times the typical value by analogy with the other companies.
£ No information on a change in process or new exposure conditions that could explain the reduction in Cd-air values between 1991/1993 and 1994 are available. As these 1991/1993 values are extreme and not well documented, they are excluded for the calculation of the typical value (average of the means)

Table 4.39 Biological monitoring, Cd in blood, production of Cd pigments

	Workplace	number of workers exposed	Blood (µg/l)					
			1994-1996			Other year		
			mean	range	N	mean	range	N
A	Overall#	30-34	4.2	4.0-4.6	3	-	-	-
B	Overall	94-112	- - -	0-5 5.1-10 > 10.1	256° 48° 9°	- - -	- - -	- - -
C	Overall	13-18	2.8	1.8-3.4	3	-	-	-
D	-	-	-	-	-	4.9 (2000)	-	-
E	Overall	-	-	-	-	-	-	-

N Number of samples
\- No information available
° Number of tested employees in the considered period (1994-1996)

Table 4.40 Biological monitoring, Cd in urine, production of Cd pigments

	Workplace	number of workers exposed	Urine (µg/g creatinine)					
			1994-1996			Other year		
			mean	range	N	mean	range	N
A	Overall	30-34	4.9	3.1-6.4	3	-	-	-
B	Overall	94-112	-	0-5 5.1-10 > 10.1	245° 47° 11°	- - -	- - -	- - -
C	Overall	13-18	2.3	2.0-2.5	3	-	-	-
D	-	-	-	-	-	4.9 (2000)	-	-
E	Overall	-	-	-	-	-	-	-

N Number of samples
\- No information available
° Number of tested employees in the considered period (1994-1996)

No measured data on dermal exposure are available.

<u>Other data: Cd pigments' uses (for information only)</u>

Cadmium pigments are used in plastics but they have also application in glass, ceramics and artists colours. Main sector of use is plastics (ICdA, 1997). Some data on Cd airborne concentrations occurring during processing of pigments in the plastics and paint manufacture, the ceramics and glass industry have been made available by several EU member states and are summarised in **Table 4.41**.

Table 4.41 Data provided by EU member states, processing of pigments

Industry	Process	Arithmetic mean (µg Cd*/m³)	Range (µg Cd/m³)	N	Sampling time	Type of sampling	Years	Source
Plastics	Weighing/mixing	1 (P50)	66 (P95)	64	8 hrsTWA	PS	1991-1996	BGAA
	Blending, bagging, mixing, weighing	25	0.1-310	24	62-210 minutes	PS	1987-1988	UK
Paint manufacture	Milling, mixing	2.4	0.2-20	12	21-67 minutes	PS	1985	UK
	Weighing, mixing Sieving, emptying	not detected	1 (P95) 1 (P90)	19	8 hrs.TWA	PS	1991-1996	BGAA
Ceramics/ Glass industry	Preparation, shaping, weighing, mixing, melting (Cd pigments in powder)	0.3 (P50)	30.0 (P95)	83	8 hrs.TWA	PS	1991-1996	BGAA
Further use	Glazing, spray-painting, painting by hand, screen painting (Cd pigments in solution)	0.08 (P50)	1.0 (P95)	159	8 hrs.TWA	PS	1991-1996	BGAA

P95 95th percentile
* It is not possible to give some indication on the chemical speciation
\- No information available
BGAA Berufsgenossenschaftlicher Arbeitskreis Altstoffe (Bundesrepublik Deutschland)

Modelled data

Exposure to cadmium oxide and cadmium metal occurs only during the first steps of the process while preparing the cadmium sulphate solution or generating cadmium metallic powder from massive cadmium metal. One company reported that the addition of the powders to the acid occurs in a closed vessel, preventing inhalation and dermal exposure. Moreover, local exhaust ventilation or wet scrubbing is used during all production stages involving dry powders (ICdA, 2001).

However, available data are not considered sufficient to allow adequate modelling of the potential dermal/inhalation exposure to cadmium oxide/metal dust occurring during the first part of the production process. By default, exposure can be estimated by cross-reading with Scenario 7 (manufacture of Cd stabilisers) as both productions appear to involve a first step of mixing/adding cadmium powders:

Inhalation exposure due to handling the compound at room temperature as a powder is estimated as 2-5 mg/m^3, assuming dry manipulation with LEV and dust not readily aggregating. The dermal exposure with non-dispersive use, direct handling and incidental contact is calculated as 0.1-1 mg/cm^2/day. It has been reported that the mixing occur in a closed system. However, in the absence of detailed information on work tasks and exposure conditions, "non-dispersive use and presence of LEV" are used as default variables in the model.

Conclusions

Manufacture of Cd-pigments

A typical value for Cd-air can be derived from the measured site-specific data for the manufacture of Cd pigments:

From the available personal sampling data (respirable fraction), a typical value for the years 1994-1996 appears to be 22 µg/m^3 (average of the means). ~80 µg Cd/m^3 (respirable fraction) is chosen as a reasonable worst case value. An upper limit value was taken instead of a percentile to account for the weaknesses in the different data sets (only scarce information on tasks, working conditions). One company provided static sampling data (average: 30.3 µg Cd/m^3). These values refer to total cadmium and not only CdO or Cd metal.

A typical (mean) and a worst case value for Cd-U and Cd-B are proposed.

Values reported in the literature (Kawada et al., 1989) for 1986 are more or less in agreement with the measured data.

Table 4.42 Values that will be used for risk characterisation

Production of Cd pigments		
	Typical value	**Worst case**
Cd in air	22 µg/m^3	80 µg/m^3
Cd-U	4 µg/g creatinine	10 µg/g creatinine
Cd-B	4 µg/l	10 µg/l

Dermal exposure can hardly be evaluated in the absence of detailed information on work tasks and exposure conditions. By analogy with the first step of the manufacture of stabilisers (Scenario 7), using same assumptions, dermal exposure might be estimated at 0.1-1 mg/cm^2/day (42-420 mg/day using an estimate for surface area of 420 cm^2). Again, these modelled values appear very high and their interpretation should take into account the fact that the EASE model is probably not very appropriate to assess dermal exposure to such compounds. For instance, assuming a conservative value of 1% for dermal absorption, this would mean a daily systemic dose of 420-4,200 µg cadmium, which would correspond to a urinary cadmium excretion in the range of 600-6,000 µg/g creatinine. Such Cd-U values are unrealistic in occupational settings and well above the levels measured in cases of lethal poisonings (see Section 4.1.2.3). Therefore, these modelled values will not be used in the risk characterisation.

However, biomonitoring data consider the overall exposure (including inhalation, oral and dermal routes).

Downstream users (for information only)

For the downstream users of the cadmium pigments (plastic, ceramic, glass industries, paints), atmospheric Cd values were supplied by different member states. From these data, it can be concluded that concentrations of Cd in air range widely (from under the detection limit to 310 µg Cd/m^3). Mixing powdered Cd pigments appears to entail the most important exposure. A typical value can hardly be drawn from the available data as these represent different applications and uses, different processes and tasks and consequently different types of exposure.

4.1.1.2.6 Cadmium plating

Cadmium plate is a corrosion resistant material used to protect ferrous metals (steels).

It exhibits also good soldering characteristics, low electrical resistivity, a low coefficient of friction and a good appearance for decorative applications. Electrodeposition of cadmium on a metal substrate accounts for 90% of the cadmium used in plating. The remaining 10% is applied by vacuum deposition, metal spraying or mechanical plating (ICdA, 1997).

a) Electroplating

Electroplating is the process of applying a metallic coating onto an article by passing an electric current through an electrolyte in contact with the article, thereby forming a surface having properties or dimensions different from those of the article. Any electrically conductive can be electroplated. Electroplated materials are generally used for a specific property and/or function, e.g. a material may be electroplated for decorative use as well as for corrosion resistance. The electronics industry uses cadmium plating on chassis hardware, connectors, fasteners and numerous electrical contacts.

Cadmium plating generally is performed by electrodeposition of the metal from an alkaline cyanide solution. The plating solutions may be directly purchased from chemical manufacturers; alternatively they can be prepared on-site by dissolving cadmium metal (sticks) or cadmium oxide (powders) in a sodium cyanide solution. Such a cadmium plating bath is made up once every two or three years. The plating solution typically contains 18-22 g Cd /l. Once the solution has been prepared, cadmium metal balls are used to automatically replenish the cadmium which is electroplated onto the parts being plated. No cadmium-containing aerosols are reported to be formed over the bath (UN/ECE LRTAP Protocol on Heavy Metals, 1998) and because of this no ventilation procedures are implemented to reduce cadmium exposure. Surveys of cadmium electroplating shops in the USA and Canada have all indicated exposures of less than 1 $\mu g/m^3$ (no further details available). Half the cadmium electroplating performed is barrel plating conducted in enclosed rotating barrels on small fasteners such as screws, nuts, bolts, washers, etc. The other half is on larger parts in open baths, termed “rack plating” (Morrow H, personal communication, 2001).

b) Mechanical plating:

This process uses mechanical energy to deposit metal coatings on small components by the impact of glass beads. Either cadmium or mixed-metal coatings of cadmium-tin or cadmium-zinc can be applied when glass beads, proprietary chemicals, water and metal powder are tumbled with the components in a rotating barrel. The process is suited to components such as fasteners and clips which are small enough to be plated in a barrel (http://www.cadmium.org/).

c) Vacuum and ion deposition

Conventional thermal vapour deposition involves heating of cadmium in a vacuum until it vaporises. Cadmium atoms then condense on the substrate to form a thin high quality coating of cadmium. Ion deposition in argon atmosphere adds more energy to this coating process and uses ‘sputter cleaning’ to clean the substrate surface. As a result, ion deposition is said to give improved coating adhesion, density and uniformity. Components such as undercarriage legs of transport aircraft, helicopter rotor parts and other high strength steel components have been successfully coated using this method (http://www.cadmium.org/).

Releases of cadmium metal vapours in the workplace have been reported to be low with electroplating (1.0 µg Cd/m^3 or less, in surveys conducted in the USA and Canada). The only activities in which exposures may be encountered are during the makeup of new baths (ICdA, 1997).

No other details are available on specific work tasks and exposure conditions in the electroplating industry. No cadmium-containing aerosols are reported to be formed over the bath (Morrow H, 2001, personal communication). This is not confirmed by the NIOSH which identifies the mist above cadmium-containing electroplating baths as a source of occupational exposure (NIOSH, 1985). Dermal exposure can occur when preparing the plating solution when cadmium oxide powder is added to the cyanide solution. Dermal exposure can also occur during the handling of the plated objects after their removal from the bath as well as from splashes. The extent of this depends on the level of automation used (not known).

Industry data

No site-specific data were provided by industry.

Other data

Atmospheric data were supplied by UK, relating to the period 1989 and 1990 and are reported in **Table 4.43**.

Table 4.43 Electroplating, personal sampling measurements

Process	Job	Cd-air levels , (Arithmetic mean, µg/m³)	Cd-air levels (Range)	N	Duration of sampling (range, minutes)
Electroplating	Cd and Zn plating	5	-	1	243
	Decorative chrome plater	1		1	248
	Plating	5	-	2	151-245
	Preparation plating and barrel	1	-	1	247
Treatment and coating of metals	Metals, treatment and plating	7.2	3-63*	25	90-294

* 63 µg/m³ Single value observed for metal treatment and loading, no further information available. If this value is excluded, highest reported value is 12 µg Cd/m³.

Some exposure measurements were performed in the workplace atmosphere by the German BGAA (Berufsgenossenschaftlicher Arbeitskreis Altstoffe). The measurement data were gathered during powder coating and in electroplating (32 measurement data, 17 companies, it is not known whether the figures refer to personal or static sampling, respirable or inhalable fraction): median value: 0.2 µg total Cd/m³; 90th value: 1 µg total Cd/m³ (data collected from 1991 to 1996).

Personal sampling measurements were also made available by Norway:

Table 4.44 Cd plating, personal sampling measurements

Process	Job	Cd-air levels , (Arithmetic mean, µg/m³)	Cd-air levels (Range)	N	Duration of sampling (range, minutes)	Year
Manufacture of sport goods	Cd plating	5.8	3-9	4	360-420 minutes	1991
		3.4	1.2-5.4	3	360-405 minutes	1993

Modelled data

Exposure to cadmium metal or oxide during plating can hardly be modelled as no detailed data on process, work tasks and/or conditions were available. By analogy with the chrome plating scenario (see Chromates Risk Assessment, UK), one might expect that dermal exposure during metal treatments is likely to occur when bath solutions are made up and added to the treatment bath for electrolytic process. There is also the possibility of dermal exposure from handling of treated articles and splashes from drag-out.

The most appropriate EASE scenario for preparing and mixing treatment bath is non dispersive use and direct handling with incidental contact. This results in a prediction of 0-0.1 mg/cm^2/day (0-42 mg/day) dermal exposure. The most appropriate scenario for dermal exposure during drag-out is non dispersive use and direct handling with extensive contact. This results in a prediction of 1-5 mg/cm^2/day (420-2,100 mg/day for an estimated exposed skin surface of 420 cm^2). These modelled values appear very high and their interpretation should take into account the fact that the EASE model is probably not very appropriate to assess dermal exposure to such compounds. For instance, assuming a conservative value of 1% for dermal absorption, this would mean a daily systemic dose of up to 420 µg cadmium (preparing and mixing) and 4,200-21,000 µg (drag-out), which would correspond to a urinary cadmium excretion up to 600 µg/g creatinine (preparing and mixing) and 6,000-30,000 µg/g creatinine (drag-out). Such Cd-U values are unrealistic in occupational settings and well above the levels measured in cases of lethal poisonings (see Section 4.1.2.3). Therefore, these modelled values will not be used in the risk characterisation.

Additional data

Cadmium was reported to be present in bolts, rivets and nuts and handling of these products (including screwing, riveting, polishing areas, etc.) may lead to potential exposure to cadmium. In six dust samples taken in an airforce base, levels of cadmium of 48-88 mg cadmium/kg were found (Comments on the Occupational Exposure Assessment for Cadmium and Cadmium oxide, The Netherlands, April 2001)

Conclusions

Only fragmentary data were available to assess potential exposure to cadmium oxide and/or metal during plating. From these data it appears that exposure levels for inhalation range from 1 to ~12 µg Cd/m^3 (when the extreme value of 63 µg Cd/m^3 is excluded). A typical value derived from these data would be 5 µg Cd/m^3 (average) and a reasonable worst case value 10 µg Cd/m^3.

Dermal exposure is assessed by comparison of the cadmium plating process with the chrome plating scenario as no data on specific work tasks, conditions of exposure, dermal exposure was available.

No biological monitoring data are available.

Table 4.45 Values that will be used for risk characterisation

	Typical value	Worst case value
Cd-air	5 µg Cd/m^3	10 µg Cd/m^3
Cd-U	/	/
Cd-B	/	/

4.1.1.2.7 Stabilisers

Organic cadmium stabilisers are used to retard the degradation process that occur in PVC and related polymers on exposure to heat and short wavelength (UV) light which leads to discolouration and mechanical breakdown of the material. Cadmium based stabilisers are usually mixed with barium salts and fall into two categories, liquid or solid. Cadmium oxide and metal are used to produce both liquid and solid stabilisers. Manufacturing operations such as high speed calendaring and injection moulding of plasticised PVC products may require combinations of liquid and solid stabilisers. The solid stabiliser provides lubrication and is a booster to the primary liquid stabiliser (ICdA, 1997).

The use of cadmium in stabilisers has shown a considerable decline between 1970 and 1990 (at least in Europe). Industry, in the form of a “Voluntary Agreement on Sustainable PVC”, has agreed to phase out all uses within one year, based on the Council Regulation (88/C30/01) which required substitution if technically feasible (ESPA, 2000).

Today, cadmium-based stabilisers can be replaced in most cases, predominantly through the use of organic metal compounds of tin, lead, calcium/zinc and barium/zinc as substitution products. However, some production of cadmium stabilisers seems to be maintained and is used by some producers as stabilisers in PVC windows frames, where their use is still permitted by Community Legislation. In Europe the stabiliser market is currently divided as follows: cadmium stabilisers 1%; lead stabilisers 77%; tin stabilisers 8%; calcium/zinc stabilisers 13%; and organic stabilisers 1% (CEFIC, 2000). The type of stabiliser used largely depends on the application. Only solid form stabilisers involving cadmium are used in Europe; liquid forms stabilisers no longer contain cadmium (Revised WS Atkins Report, 1998).

Manufacture of Cd stabilisers

Barium/cadmium stabilisers can be manufactured in a number of ways. The starting materials are usually the metals or the metal oxide (powders). They are combined with various organic compounds. Three general processes can prepare the salts:

a) direct dissolution of the finely divided metal oxides in heated organic acids,

b) precipitation from aqueous solution of metal salts (chlorides and nitrates) and alkali soaps,

c) fusion of metal oxides with organic acids.

For liquid barium/cadmium stabilisers, the production starts from CdO which is dissolved directly in the heated organic acids in the presence of solvents. The reaction water is removed and the finished product is filtered.

Solid stabilisers are prepared by the precipitation process through the method of preparing metal soaps of natural fatty acids to give e.g. cadmium laurate plus water. This process is undertaken in a closed system and may involve the use of a high speed blender. Following precipitation the resultant flurry is washed, filtered and dried. The blends are frequently packaged into small bags to be thrown directly into the PVC mixing system (ICdA, 1997, Revised WS Atkins Report, 1998).

Industry data

Manufacture of cadmium stabilisers

Some very limited site-specific data for the manufacture of cadmium stabilisers were reported in the "Assessment of the Risks to Health and to the Environment of Cadmium Contained in Certain Products and of the Effects of Further Restrictions on their Marketing and Use" (WS Atkins, 1998). No further data were made available.

No Cd-air values are available. Data refer to biological monitoring, cadmium in blood:

Table 4.46 Table Cd-B values for employees at stabiliser preparation and mixing facilities in the EU

Stabiliser preparation facility	**Cd-B**
Preparation	
F	"All results negative"
G	Maximum result: 4.9 µg/l
H	"All results normal"
I	All results less than 1 µg/l
J	Maximum result of 0.25µg/l
Mixing	
L	Maximum result 3.3 µg/l
M	Maximum result 0.21 µg/l

Downstream users of cadmium stabilisers

In the same report, it is noted that monitoring of cadmium in blood at a window profile manufacturing facility produced a "not detected" result. Cadmium containing solid stabilisers are provided in non-dusting forms such as pellets or tablets and often in prepacked small plastic bags that could just be dropped, unopened into the plastics mixing equipment. This equipment operates in a sealed system until the stabiliser is fully incorporated into the molten plastic (ESPA, 2000).

Other data

Manufacture of Cd stabilisers

Some measured data (Cd in air, PS) were gathered and reported by BGAA (1998) during preparation, weighing, mixing in the production of minium, litharge and stabilisers containing lead and cadmium:

P50: 0.1 µg Cd/m^3, P90: 2 µg Cd/m^3 (29 measurements, 8-hour time-weighted averages, it is not known whether it concerns personal or static sampling, respirable or inhalable fraction)

Downstream users of Cd stabilisers

Sweden provided two values for Cd in air in the plastics industry (year not specified).

Profile manufacture: Cd-air: < 0.5 $\mu g/m^3$

PVC plant, compounding: 0.02 $\mu g/m^3$

Measurements of Cd in air were also carried out during the processing of stabilisers containing cadmium in manufacture of plastics: P90: 1 µg Cd/m^3 (8-hour TWA, 20 measurements, it is not known whether it concerns personal or static sampling, respirable or inhalable fraction) (BGAA, 1998).

Modelled data

Manufacture of Cd stabilisers

The first step in the manufacture of cadmium stabilisers will be the mixing of cadmium oxide/metal (starting materials) as powders with other products. Inhalation exposure due to handling the compound at room temperature as a powder is estimated as 2-5 mg/m^3, assuming dry manipulation with LEV and dust not readily aggregating. The dermal exposure with non-dispersive use, direct handling and incidental contact is calculated as 0.1-1 mg/cm^2/day. It has been reported that the blending and mixing occur in a closed system. However, in the absence of detailed information on work tasks and exposure conditions, "non-dispersive use and presence of LEV" are preferred to be put as variables in the model.

Inhalation exposure during bagging (small plastic bags) is assumed to be 2-5 mg Cd/m^3. Dermal exposure during bagging is assumed to be intermittent, with non-dispersive use and direct handling of the substance, leading to an exposure level of 0.1-1 mg/cm^2/day (42-420 mg/day, using an estimate of 420 cm² for the exposed surface area These modelled values appear very high and their interpretation should take into account the fact that the EASE model is probably not very appropriate to assess dermal exposure to such compounds. For instance, assuming a conservative value of 1% for dermal absorption, this would mean a daily systemic dose of 420-4,200 µg cadmium, which would correspond to a urinary cadmium excretion in the range of 600-6,000 µg/g creatinine. Such Cd-U values are unrealistic in occupational settings and well above the levels measured in cases of lethal poisonings (see Section 4.1.2.3). Therefore, these modelled values will not be used in the risk characterisation.

Downstream users

Solid cadmium stabilisers are reported to be provided to the down stream users as pellets, tablets or prepacked bags, limiting exposure to dust. EASE modelling carried out for dermal exposure predicts a very low exposure (inclusion of the substance into a matrix).

Conclusions

EASE modelling very probably overestimates exposure levels and was carried out assuming worst case assumptions in the absence of available measured data and/or detailed information on work tasks and exposure conditions.

From the measured data and cross-reading with Scenario 5 (production of Cd pigments, comparison of processes and Cd-B values), one may accept that the by the BGAA measured value of 2 µg Cd/m^3 could be representative (Reasonable worst case) for the stabilisers manufacturing process although this value entails a part of uncertainty to be taken as such in the risk characterisation. From the limited biological monitoring data that were provided, it can be assumed that 5 µg/l (Cd-B) corresponds to a reasonable worst case situation.

4.1.1.2.8 Brazing, soldering and welding with Cd containing material[23]

Other possible sources of occupational exposure to cadmium oxide are brazing, soldering and welding, with a solder containing cadmium or when welders are operating on material containing or plated with Cd metal. Workers are exposed by inhalation to the solder fumes (CdO).

Historically, the alloys used for silver solder (also named hard solder) contained up to 25% of cadmium and since the melting point and boiling points of Cd are lower than those of other metals within the alloy, silver solder fumes contained very high proportions of CdO (up to 85%). Cadmium metal was mainly used to allow fragile metallic structures to be soldered at lower temperature (e.g. jig soldering).

Although, according to Industry, this use of Cd has been abandoned in the last 10 years (Cd-free solder), data provided by several Member States indicate that Cd soldering or soldering with Cd containing material was still in use at some workplaces during the nineties and some measured data for cadmium concentrations in air are available. Accidental cases of significant external exposure to Cd (with atmospheric Cd concentrations reaching up to several mg/m^3) have also been reported during soldering while the presence of Cd in the soldering material was unexpected. This latter pattern of exposure will however not be considered here as being representative for typical working conditions during welding/soldering but rather as "accidental", unintentional "misuse".

Dermal exposure to cadmium is not expected to be significant during welding (brazing, soldering) as the solder material containing cadmium is heated at melting point and direct unprotected handling of the solder material is not expected to occur. Dermal exposure due to dust contamination of equipment and surfaces, after cooling of material is possible.

23 Welding: 1) joining pieces of suitable metals (or plastics), usually by raising the temperature at the joint so that the pieces may be united by fusing or by forging or under pressure. The welding temperature may be attained by external heating, by passing an electric current through the joint, or by friction. 2) joining pieces of suitable metals by striking an electric arc between an eleectrode or filler metal rod and the pieces.
Soldering: hot joining of metals by adhesion using, as a thin film between the parts to be joined, a metallic bonding alloy having a relatively low smelting point.
Brazing: the process of joining pieces of metal by fusing a layer of brass or spelter between the adjoining surfaces.
Definitions from: Chambers Science and Technology Dictionary. Eds: P.M.B. Walker, W & R Chambers Ltd and Cambridge University Press, 1988.

a) Data on brazing, soldering and welding activities with Cd containing material provided by the EU member states.

Table 4.47 UK data (HSE, 2000)

Process	Job	Type of sampling	Cd-air levels , (Arithmetic mean, µg/m³)	Cd-air levels (Range)	N	Duration of sampling (range, minutes)	Year
General mechanical engineering							
Engineering,	Brazing, soldering	PS	3.6	1-25	16	53-300	1988/1991/1994
Electrical manufacture							
Fitting, brazing	soldering	PS	320	2-1,800	7	15-247	1987-1988
Hard metal tool manufacture							
Hard metal tool production	brazing	PS	32	5-90	7	82-304	1988/1989/1990
	soldering	PS	430	-	1	105	1990
Instrument, jewellery and coin manufacture							
Assembly, hand soldering	Soldering	PS	1	-	6	188-269	1987/1990
Manufacture of machine tools, fabricated metal products, metal container, metal goods							
	Soldering, brazing, welding	PS	17.5	0.5-70	15	51-294	1986/1987/1988/ 1991
Various							
	grinding	PS	3	1-6	5	238-275	1989/1990

From additional information provided by UK, it appears that cadmium does not play a part in soldering but that it is commonly present in hand brazing consumables, in concentrations up to approximately 25%. Cadmium is used to control the melting temperature and flow properties of the alloy. Because of its high volatility, Cd is thought to concentrate into the fumes. When used at the correct temperature the fume from brazing is quite limited but often workers overheat the parent metal to encourage the braze to run and wet more easily, although this should not be necessary. This overheating results in the generation of copious fumes. Cd is not thought to be still used in any welding consumables. The only instance would be if cadmium plated materials were welded e.g. resistance welding of studs (UK, 2001).

Table 4.48 BGAA (Berufsgenossenschaftlicher Arbeitskreis Altstoffe Bundesrepublik Deutschland) data (1998)

Process	Job	Type of sampling	Cd-air levels, (P50) (µg/m³)	Cd-air levels (P95) (µg/m³)	N	Duration of sampling (range, minutes)	Year
Metal-working/mechanical engineering/electrical engineering/waste incineration							
Hard soldering/soft soldering	-	PS	2	280	11	8-hr TWA	1991-1996

Table 4.49 Norwegian data (National Institute of Occupational Health, handed over TMII'01)

Process	Job	Type of sampling	Cd-air levels , (Arithmetic mean, g/m³)	Cd-air levels (Range)	N	Duration of sampling (range, minutes)	Year
"secondary education"	Soldering	PS	24.8	0.1-49.5	2	152-333	1999
Welding		PS	0.3 (P50)	0.04-77	298	> 60 minutes	1990-1999
		PS	0.2 (P50)	0.1-12.3	21	> 60 minutes	1999-2001

Table 4.50 Other data on soldering provided by Norway

Process	Job	Type of sampling	Cd-air levels , (Arithmetic mean, µg/m³)	Cd-air levels (Range)	N	Duration of sampling (range, minutes)	Year
Manufacture of sport goods	Tinning	PS	43	17-152	11	300-420	1991/1993

Table 4.51 Swedish data (1997)

Process	Job	Type of sampling	Cd-air levels ,(Arithmetic mean, µg/m³)	Cd-air levels (Range)	N	Duration of sampling (range, minutes)	Year
Engineering industry							
	Soldering, grinding	PS	< 0.6	-	-	-	-
	Soldering	PS	4.2	0.01-9.7	3	-	-
	Surface treatment, tooling shaping	SS	2.5	2-3	5	-	-

b) Data on brazing, soldering and welding activities with Cd containing material while the presence of cadmium was unexpected (data provided by Norway):

High Cd-air values during hard soldering (almost 100 times the Norwegian occupational exposure limit set at 0.02 mg/m³ for CdO) were reported by Hetland et al. (1996) who examined workers' exposure during welding (generic) activities in relation to a project done in a tramway company in Norway. A search for clinical respiratory symptoms and an evaluation of the welders' lung function were also included in this project (results not available). According to the supplier of the solder material, it contained a core of 40% silver, 19% copper, 21% zinc and 20% cadmium, in addition to the brass surrounding it. Values for Cd-air are reported in **Table 4.48**. The work with this solder material was stopped immediately and replaced by a solder material containing 55% silver, 21% copper, 22% zinc and 2% tin.

Table 4.52 Mean exposure to Cd during hard soldering (data provided by Norway).

Date	Method	Sampling time (hours)	Exposure (mg/m^3)
20.10.1996	Hard soldering, grinding	2	1.9
23.10.1996	Hard soldering, grinding	4	1.350
24.10.1996	Hard soldering, grinding	3	1.96
15.10.1996	Hard soldering, grinding	3	0.954
26.10.1996	Hard soldering, grinding	4	1.06
		Mean	1.44
		SD	0.467

Because of the high exposure to cadmium, biological monitoring (Cd-B, Cd-U) was offered to all the workers having worked with this solder-method. 35 of 36 workers accepted the offer (January 1996). 2 of the 35 workers had slightly enhanced levels of Cd in blood compared to Germanys BAT values (44.5 nmol/l ~5 µg/l). The fact that the biological values were not different from what is found in the general population indicates that, although high atmospheric concentrations of Cd have been reported, the potential for exposure of the workers remained limited. Cd-U values also indicate that there was no evidence for increased body burden in those workers.

Approximately one year after the first examination (June 1997), the same group was called up for a second examination (participation rate: 60%, 21/35 workers). The results from the second examination showed a significant decrease in the Cd-level both in blood and urine from 1996 to 1997. The 14 workers that participated in the first examination, but not in the second, had lower median values for Cd-levels both in blood and urine compared to the 1996-values for the 21 workers that participated both in 1996 and 1997. The 14 workers that only participated in the first examination were younger, but compared to the workers that participated in both examinations had a similar duration of exposure.

Table 4.53 Median values (range) for Cd in blood and urine in 1996 and 1997

	1996		1997	
	N=21	N = 14	N = 21	N=14
Blood (nmol/l)	8.9 (1.2-61)	5.5 (< 1-25)	4.0 (1.1-20.4)	-
Urine (nmol/l)	4.8 (1-39)	4.7 (0.5-11)	1.8 (0.5-8)	-

In another study, the exposure to gases and fumes during brazing with soldering material intended for use on stainless tubes was examined (Søstrand and Daae, 1994). The exposure to Cd during brazing ranged from < 0.0006 to 6.25 mg/m^3 (mean 0.69, median 0.0163). According to the handbook from the supplier, it was guaranteed that this soldering material did not contain any cadmium. In spite of this it was found that the soldering material contained 16, 4% Cd, which was confirmed in a reply on an inquiry to the producer. According to the producer, the soldering material was produced for a supplier in Indonesia and the soldering material was sent to the supplier in Norway by a mistake.

Conclusions

Only limited data have been reported for this scenario and probably relate to different processes and/or working conditions as values for Cd in air are in a wide range (from 0.2 to 1,800 µg Cd/m^3). No more information on job description and exposure pattern is available.

Elevated Cd-air values have also been reported in accidental cases where exposure to Cd was not expected to occur. From the provided data, a reasonable worst case estimate for inhalation exposure may be derived (280 µg Cd/m³, 95th percentile of the BGAA data).

Because welding occurs at temperatures at which direct unprotected handling of cadmium containing material is not expected to occur, and because cadmium is only a part of the used solder material (up to 25%), and usually no more present in normal workplace conditions; it is concluded that the potential dermal exposure while brazing (welding, soldering) is very low.

4.1.1.2.9 Others

Due to impurities of Cd in metal, steel and derived manufactured goods, including the scrap metal used in the production of new metal products, there is also a potential for exposure of workers involved in the foundry industry.

Table 4.54 Swedish data, steelwork industries (KEMI, 2001)

Cd-air measurements (µg Cd/m³)							**Cd-blood (µg/l)**		
	1996-2000			**11-2000**			**1989-2001**		
Type of sampling	Mean	Range	N	Mean	Range	N	Mean	Range	N
-	2	1-27	47	0.5	0.02-2	7	1.0	0.4-3.0	755

Table 4.55 BGAA data (1998)

Process	**Job**	**Type of sampling**	**Cd-air levels ,(P50) (µg/m³)**	**Cd-air levels (P95) (µg/m³)**	**N**	**Duration of sampling (range, minutes)**	**Year**
Metal/heavy metal smelting plants and foundries							
	-	-	2	20	75	8-hr TWA	1991-1996
Metal-working/mechanical engineering/electrical engineering/waste incineration							
Mechanical processing methods	-	-	Not detected	4	49	8-hour TWA	1991-1996
Electrical engineering	-	-	Not detected	7	29	8-hour TWA	1991-1996
Waste incineration	-	-	Not detected	1	23	8-hour TWA	1991-1996

Table 4.56 Increased exposure associated with the recycling of electronic waste material (BAA, 1997)

Process	Job	Cd-air		Cd-U
		Type of sampling	µg/m³ (mean)	µg/l, mean
Recycling electrical materials	-	-	2.5	1.2

No further details available

Table 4.57 Norwegian data, other uses (National Institute of Occupational Health, handed over TMII'01)

Process	Job	Type of sampling	Cd-air levels , (Arithmetic mean, µg/m³)	Cd-air levels (Range)	N	Duration of sampling (range, minutes)	Year
Manufacture of aircraft and spacecraft	Cleaning, blowing	PS	58.6	0.6-196	4	375-440	2000
Manufacture of sport goods	Vibropolishing	PS	9.4	4.8-14	2	360	1993

Table 4.58 Swedish data (1997)

Process	Job	Type of sampling	Cd-air levels (arithmetic mean, µg/m³)	Cd-air levels, range	N	Duration of sampling (range, minutes)	Year
Metal foundry	-	PS	-	1-5	-	-	1988
	-	PS	-	< 10-20	-	-	1991
Engineering industry	Grinding	PS SS	2.4 0.5	0.09-4 -	3 -	42-? 37	- -

Conclusions

Several activities may generate exposure to cadmium and cadmium compounds. From the data supplied by the member states, it can be derived that exposure levels range from < 1 µg Cd/m³ to about 200 µg Cd/m³. No average value for risk characterisation for this particular scenario (other uses) can be proposed as activities, processes and type industries vary widely. A value of 2 µg/m³ can however be derived from the available data as a reasonable worst case estimate for inhalation exposure. Dermal exposure can hardly be assessed in the absence of detailed data on working conditions. However, in foundries, in regard to the used temperatures it can be assumed that skin exposure to cadmium occurs when there is direct contact with contaminated, cooled material or equipment. By cross-reading with Scenario 4, dermal exposure estimates (EASE modelling) range from 0-0.1 mg Cd/cm²/day (0-42 mg/day for an estimated exposed surface area of 420 cm²). The interpretation of these exposure levels should take into account the fact that the EASE model is probably not very appropriate to assess dermal exposure to such compounds. For instance, assuming a conservative value of 1% for dermal absorption, this would mean a daily systemic dose of up to 420 µg cadmium, which would correspond to a urinary cadmium excretion up to 600 µg/g creatinine. Such elevated Cd-U values are unrealistic in occupational settings and above the levels measured in cases of lethal poisonings (see Section 4.1.2.3).

Table 4.59 Overall results

Scenario	External dose						Internal dose			
	Inhalation exposure: Cd-air (µg Cd/m³)				Dermal exposure (mg Cd/cm²/day) Daily dose skin exposure (mg Cd/day)		Biological monitoring			
							Cd-U (µg/g creatinine)		Cd-B (µg/l)	
	Typical Value	Method	Reasonable Worst Case	Method	Value	Method	Typical Value	Reasonable Worst Case	Typical Value	Reasonable Worst Case
1. production of CdO	15	measured	150	measured	0.1-1 (42-420)**	EASE	10	70	1	3
2 Production of Cd metal -packing powder -cleaning	12	measured	400	measured	0-0.1 (0-42)** very low	 EASE EASE	3	23	3	15
3. Production and recycling of Ni-Cd batteries -manufacture mixing*recycling	 50 35	 measured measured	 320 80	 measured measured	 very low 0.1-1* (42-420)** -	 EASE EASE -	 3.5 8	 20 12	 2.3 2	 80 -
4. Production of Cd alloys	-	-	50	literature data, data supplied by other MS	0-0.1 (0-42)**	EASE	-	-	-	-
5. Cd pigments -mixing	22	measured	80	measured	 0.1-1 (42-420)**	 EASE	4	10	5	10
6. Cd plating -mixing -drag out and handling	5	data supplied by other MS	10	data supplied by other MS	 0-0.1 (0-42)** 1-5 (420-2100)**	 EASE EASE	-	-	-	-

Table 4.59 continued overleaf

Table 4.59 continued Overall Results

Scenario	External dose						Internal dose			
	Inhalation exposure: Cd-air (µg Cd/m³)				Dermal exposure (mg Cd/cm²/day) Daily dose skin exposure (mg Cd/day)		Biological monitoring			
							Cd-U (µg/g creatinine)		Cd-B (µg/l)	
	Typical value	Method	Reasonable worst case	Method	Value	Method	Typical value	Reasonable worst case	Typical value	Reasonable worst case
7. Cd stabilisers	-	-	2	data supplied by other MS			-	-	-	5
-handling, mixing					0-0.1 (0-42)**	EASE				
-bagging					0.1-1 (42-420)**	EASE				
8. Brazing, soldering and welding	-	-	280	measured	very low	-	-	-	-	-
9. Other uses	-	-	2	data supplied by other MS	-0-0.1 (0-42)**	EASE	-	-	-	-

* Worst case modelling in the absence of details provided on the activities of mixing of the powders.
** See discussion of these values in each scenario

Since Cd-U is a marker of long-term exposure, it might reflect past heavy exposure rather than current working conditions. In occupationally exposed workers, Cd-B reflects recent exposure. With the exception of the first scenario, a comparison of the fold increases in blood and in urine (reflecting cumulative body burden) indicates a relative consistency in the reported values. For the CdO production scenario, the higher increase in Cd-U than in Cd-B values might suggest that the body burden of those workers has mainly been accumulated in the past and that a risk characterisation based on Cd-U values might need to take into account the recent improvements of working conditions.

Table 4.60 Fold increase above normal in the different scenarios.

	Urine(normal < 2 µg/g creatinine)		Blood(normal < 1 µg/L)	
	Fold increase above normal			
	Typical value	Worst case	Typical value	Worst case
CdO production	5	35	1	3
Cd metal production	1.5	11	3	15
Ni Cd batteries	1.75	10	2.3	80
Pigments	2	5	4	10

4.1.1.3 Consumer exposure

Cadmium, its compounds and its alloys have been used in a variety of consumer materials. The principal uses of cadmium oxide, metal (and compounds) fall into five categories (IARC 1993, IZA 1999, ATSDR 1999) corresponding to at least 5 scenarios of exposure:

Scenario 1: active electrode material in nickel-cadmium batteries,

Scenario 2: pigments used mainly in plastics, glasses and ceramics, enamels and artist's paints,

Scenario 3: use of cadmium as stabilisers for plastics or polymers,

Scenario 4: metal plating (steel and some non-ferrous metals),

Scenario 5: component of alloys,

A few data on other uses of cadmium metal/oxide in consumers' products, not included in these five scenarios, are available in consumer products registers and have been provided by two member states. These data are too fragmentary to discuss and/or assess a potential exposure to cadmium for the consumer of these products. However, they indicate for the type of consumers' products that still contain cadmium and are reported in **Annex F** and **Annex G**.

According to industry, the cadmium compounds are in general, physically and/or chemically contained in a stable matrix, or present in massive metallic form, and as such not available for exposure of the consumer (IZA, 1999). However, several reports indicate that significant amounts of cadmium (not specifically Cd metal or CdO) still occur in some products marketed in the EU: most of them are imported PVC goods from Eastern countries where alternatives for Cd stabilisers and/or pigments are not implemented yet. The possibility that some release of cadmium from these products might occur has been investigated for some of them. Available information on this potential risk for the consumer is discussed under Scenarios 2, 3, and 5. When Cd values are presented, they refer to total cadmium as no data on the speciation of cadmium are available. It is not possible to estimate the exposure of the consumer to individual compounds.

4.1.1.3.1 Scenario 1: Nickel-cadmium batteries

Cadmium (oxide) in batteries is part of the internal structure (electrode). The outer part of batteries consists of a nickel plated steel/steel and plastic envelope. Cadmium is totally isolated within the internal structure of the battery which is not accessible during handling and manipulation and thus not available for exposure.

Moreover the type of operation a consumer may carry out includes simple handling of the battery e.g. replacement into an electrical/electronic device or reloading. The use of batteries by the consumer is also likely to be rather infrequent and of very short duration. Therefore, although no measured data on consumer exposure are available for batteries, it can be concluded that consumer exposure to cadmium (oxide) from batteries is non-existent or negligible.

No further data were submitted by Industry on this scenario.

4.1.1.3.2 Scenario 2: Use in pigments

Cadmium sulphide and cadmium sulphoselenide are used as bright yellow to deep red pigments in ceramics, glasses, enamels, plastics, and artists colours. Cadmium metal or cadmium oxide are used as starting material for the production of these pigments and, according to Industry, not present in the consumer's product.

The abilities of the cadmium pigments to withstand high processing and service temperatures explain their use in much of their colour range for glasses, ceramic glazes and vitreous and porcelain enamels. Their dispersion, non-migration and non-bleeding properties make Cd pigments also useful in plastic applications where uniform colouring is important (http://www.cadmium.org/).

The introduction of cadmium pigments into glass, ceramic-ware and plastics for the purpose of giving colour to the final product has been regulated by EU Directive 91/338:

"Cadmium may not be used to give colour to finished products manufactured from the substances and preparations listed below:

- polyvinyl chloride (PVC)
- polyurethane (PUR)
- low-density polyethylene (ld PE), with the exception of low-density polyethylene used for the production of coloured masterbatch
- cellulose acetate (CA)
- cellulose acetate butyrate
- epoxy resins

In any case, whatever their use or intended final purpose, finished products or components of products manufactured from the substances and preparations listed above coloured with cadmium may not be placed on the market if their cadmium content (expressed as Cd metal) exceeds 0,01% by mass of the plastic material. However, Sections 1.1 and 1.2 do not apply to products to be coloured for safety reasons (Dir 91/338)."

Cadmium pigments are however still in use for some of these applications when no alternative has been found. According to industry, in those polymers where Cd pigments are still used, they are contained physically and chemically in the plastic matrix and not available for the user of the product (IZA, 1999). Limited quantitative data are available to determine whether or not cadmium will be released from these matrixes.

Available data

Decorated glass and enamels, ceramics

Some data are available in a CEN Report (2000) on "Packaging-Requirements for measuring and verifying of heavy metals present in packaging and their release to the environment". To date glass containers are still decorated with enamels containing heavy metals including cadmium compounds, in order to give the decoration the required fundamental properties of resistance, durability, compatibility and fusibility. Cadmium compounds are used in small quantities to obtain red and yellow bright colours, and there is no alternative for the time being. During manufacturing of decorated glass, the enamels containing metals become part of the glass matrix and are chemically stabilised. Enamels cannot be separated from the glass and the decorated container glass is thus to be considered as a single packaging component. On an individual decorated glass container the heavy metal concentrations may exceed the limits specified in the directive with variations in the range of 40 to 4,000 ppm between decorations and containers (CEN, 2000).

Table 4.61 European practice in packaging production: uses of cadmium (CEN, 2000)

Main material or component	Functional use	Comments
Glass		
-undecorated	-	Cd not found or at very low levels
-decorated by enamels	Cd pigments for red and yellow bright colours in small quantities	Migration resulting from leaching is undetectable (not further detailed). Measures are needed to develop appropriate substitutes.

Exposure to cadmium in foods contaminated by glazed ceramic containers has been evaluated by CEPA (Canadian Environmental Protection Act) in 1994 and is considered to be minimal compared to other sources of intake (smoking, food, air, etc.) (not further detailed).

Plastics

CEN Report on packaging (2000): Due to the fact that the biggest part of plastic packaging is going into sectors in which health and security of people is essential, plastic materials used in plastic packaging (films, crates, caps, bottles, bags, pumps, tubes) have to comply with regulations for food contact packaging materials and are currently free from heavy metals. The main type of plastic packaging which has to be studied in regard to heavy metals (and cadmium) concern is transport packaging and crates and pallets which is returnable packaging. Those packaging are made of high density polyethylene or polypropylene either virgin materials or recycled ones and are not to be sold to consumers.

Tests have been made on industrial packaging manufactured between 1970 and 1996 to check the concentration limits of 100 ppm (0.1%) for four metals including cadmium in crates, pallets and reusable boxes. Cd above the limits for those manufactured before 1994 as pigments from cadmium was still introduced in those packaging for price reasons (substitutes are three times the price). In those cases Cd is between < 2 ppm for those manufactured starting 1994 and go up to 1,500 ppm for the older ones (1970's; very few of them are still in circulation).

- In some artist's paints, cadmium pigments are still used and cover a colour range between cadmium green and cadmium deep yellow. Under normal circumstances, exposure of the user is unlikely. However, it cannot be excluded that pigments can be absorbed by the painters if they get into the artist's mouth, penetrate the skin through cuts and scratches, or if the painter inhales dusts (e.g. during sandpapering for re-use of old painted canvases). Although, according to Industry, these paints are not sold as toys for children, it cannot be excluded that children use them as they are still present on the market as hobby products. No data are available to allow a quantitative assessment of exposure. However, in view of the very low bioavailability of the Cd species involved (sulphide and sulphoselenide); it is unlikely that this will lead to a significant exposure compared to the other sources of exposure.
- Inks: pigments containing cadmium are reported to be no longer used in printing inks (CEN Report 2000).

Remark: Several organisms have reported that despite the regulations on the import and production of cadmium containing products, the cadmium content in several (mostly imported goods from Eastern Countries) products exceeds the EU limit value. A number of laboratory tests into the cadmium content of products declared for import have been carried out since 1992 and "excessively high percentages" of cadmium have been regularly found (EuroCad Appendix 10, Arcadis 2001, Dutch contribution). Most of these products consist of PVC. As cadmium compounds are used in PVC as stabiliser or/and as pigment and/or as a lubricant in the processing of plasticised PVC, this is a common issue for Scenarios 2 and 3 and is further detailed and discussed under Scenario 3: Stabilisers.

4.1.1.3.3 Scenario 3: Use as stabilisers

Cadmium-based stabilisers are used to retard the degradation processes which occur in polyvinylchloride (PVC) and related polymers on exposure to heat and ultraviolet light (sunlight). These stabilisers consist of mixtures of barium, lead and cadmium organic salts, usually cadmium stearate or cadmium laurate, which are incorporated into the PVC before processing and which limit any degradation reaction. They ensure that PVC develops good initial colour and clarity and allow high processing temperatures to be employed. Cadmium oxide and cadmium metal are used as starting materials for the production of the cadmium organic salts but are not present, according to Industry, in the final consumer's product. Barium/cadmium stabilisers typically contain between 1 and 15% cadmium (salts) and usually constitute about 0.5 to 2.5% of the final PVC compound (http://www.cadmium.org/). Cadmium stabilisers introduced in PVC are encapsulated in a relatively stable matrix, preventing further exposure (not further detailed, ICdA, 1997).

The use of cadmium compounds as stabilisers is also restricted by EU legislation (Dir 91/338):

"Cadmium may not be used to stabilise the finished products listed below manufactured from polymers or copolymers of vinyl chloride:

- packaging materials (bags, containers, bottles, lids);
- office or school supplies;
- fittings for furniture, coachwork or the like;
- articles of apparel and clothing accessories (including gloves);

- floor and wall coverings;
- impregnated, coated, covered or laminated textile fabrics;
- imitation leather;
- gramophone records;
- tubes and pipes and their fittings;
- swing doors;
- vehicles for road transport;
- coating of steel sheet used in construction or in industry;
- insulation for electrical wiring.

In any case, whatever their use or intended final purpose, the placing on the market of the above finished products or components of products manufactured from polymers or copolymers of vinyl chloride, stabilised by substances containing cadmium is prohibited, if their cadmium content (expressed as Cd metal) exceeds 0,01% by mass of the polymer. However, this does not apply to finished products using cadmium-based stabilisers for safety reasons."

Considering the inclusion of cadmium in a matrix, the regulated cadmium content in the products manufactured from polymers or copolymers of vinyl chloride, and the replacement of the cadmium-based stabilisers by calcium-zinc and barium-zinc stabilisers in PVC in the last recent years, it could have been expected that potential exposure to cadmium of the consumer from this type of product is likely low.

However, several reports indicate that cadmium is still present at values above the EU limit in products marketed in the EU and the US.

In 1995, the Netherlands Inspectorate for the Environment showed that about 15 to 20% of controlled synthetic products contained too much cadmium (> 0.01% or 100 ppm). About 80% of these controlled products were imported from countries outside Europe. About 50% of the imported products were being marketed within EU countries. Because enforcement of import and production of Cd containing goods needs a European approach, The Netherlands initiated an enforcement project (EuroCad) carried out since then by representatives of enforcement organisations of several EU member states. General aims are a) to exchange information on enforcement methods, methods of analysis, sampling techniques, etc., b) collect data on Cd containing products, c) to get more insight into implementation and enforcement problems concerning Directive 91/338 in member states and recommend actions in this matter. To do this, companies are inspected and products are analysed for Cd content by/in all participating countries. From the reported analysed samples until August 2001 (N=516), 25% contained too much cadmium (methods of determination INAA, ENV 1122). Nearly 100% of the analysed products that contained too much cadmium are produced outside the EU mostly Far East (China, Hong Kong). Almost all samples consisted of PVC and were bags, footwear, clothing, toys. Cadmium values ranged from 120 to 1,480 ppm (EuroCad inspection project, 2001; personal communication Mrs Tsatsou-Dritsa, 2001). Cadmium is found in a great number of products which originate mainly from "cheaper production" countries such as China, Taiwan, South Korea, Indonesia etc., (Arcadis 2001).

Greenpeace published in 1997 a study on lead and cadmium in certain children's products made with polyvinylchloride. Greenpeace tested a variety of consumer products with uses from childcare to home furnishing. Cadmium was present in 19/54 samples tested, of which 18 were PVC. Concentrations ranged from 0.57 ppm in a bath mat from Thailand to 230 ppm in a drawer liner from the USA. The US Consumer Product Safety Commission (CPSC) analysed subsequently all products claimed by Greenpeace to contain Cd.

Where cadmium was present at concentrations exceeding 100 ppm, further testing was conducted to determine if the cadmium would be released from the product in amounts that would pose a hazard to children during reasonably foreseeable handling or use (e.g. by wiping and/or extraction studies of the plastic). Conclusions were that although some of the vinyl products identified by Greenpeace and tested by CPSC staff contained cadmium, further CPSC testing and evaluation revealed that hazardous amounts of cadmium were not released from the products. Thus, children would not be exposed to hazardous levels or cadmium when the products are handled or used in a reasonably foreseeable manner.

Table 4.62 Examples of products containing cadmium tested by CPSC in 1997

	Cd ppm	Wiping (Cd µg)*	Extraction (Cd µg/g)**
Barbie backpack: purple plastic heart	290	-	n.d.< 50 ppm
Kentucky fried chicken Brown plastic drumstick Yellow plastic Yellow paint	 510 40 40	 0.4 - -	 0.72(saline) 18.6 (HCl) - -
Barbie tent Purple plastic Pink plastic	 90 100	 - -	 - -
Totebag tweety Yellow plastic	 160	 n.d.< 50 ppm	 -
Umbrella, Shaw White paint Orange and white paint	 20 10	 - -	 - -
Minnie mouse key bag Pink bag	 40	 0.9	
Raincoat Warber Bros Yellow plastic Red composite Yellow composite Blue composite	 30 50 40 40	 5.93 - - -	
Halloween placemat White plastic Yellow composite Blue composite Orange composite	 10 10 10 10	 5.93 - - -	

* Wiping: wiping with moist filters was indicated if children were likely to handle the plastic containing Cd. Wiping analysis was done to determine the amount of accessible cadmium on the surface of the product

** The amount of Cd that can be extracted from the product was determined using saline or mild acid, according to a procedure similar to the ASTM toy safety standard F963. Extraction with saline represents mouthing behaviours and mild acid extraction serves as a surrogate for chewing/ingestion.

If a product did not have a detectable level of Cd then the foreseeable consumer exposure would be insignificant and the product would not present a Cd hazard (CPSC 1997)

The presence of Cd (as catalyst/stabiliser) in polymeric food contact materials and in textiles has also been reported by the Danish EPA (2003). It is not clear whether this information relates to the aforementioned intended uses of Cd as stabiliser or pigment and/or whether it concerns unintended exposure (e.g. via cadmium in hair, wool). As further information about the type of Cd compound, its concentration in these materials and its potential migration is not available, consumer exposure through these specific uses cannot be assessed. It cannot be excluded that this may constitute an additional source of exposure under certain circumstances, through e.g. chewing or sweating but this exposure is expected to be (very) low compared to the other sources of Cd exposure (e.g. diet and/or tobacco smoking, see Section 4.1.1.4 indirect exposure).

4.1.1.3.4 Scenario 4: Metal plating

The use of Cd in plating is restricted by EU legislation. Dir 91/338/EEC restricts in particular the use of Cd also in applications that are used by the general consumer:

"Cd plating (any deposit or coating of metallic cadmium on a metallic surface) may not be used for plating metallic products or components of the products used in the following sectors/applications:

a) equipment and machinery for:

   -food production

   -agriculture

   -cooling and freezing

   -printing and book-binding

b) equipment and machinery for the production of:

   -household goods

   -furniture

   -sanitary ware

   -central heating and air conditioning plant

In any case, whatever their use or intended final purpose, the placing on the market of cadmium-plated products or components of such products used in the sectors/applications listed in (a) and (b) above and of products manufactured in the sectors listed in (b) above is prohibited.

From June 1995, these provisions are also applicable to following sectors/applications, or products manufactured into these sectors:

(a) equipment and machinery for the production of paper and board, textile and clothing

(b) equipment and machinery for the production of road and agricultural vehicles, rolling stock and vessels".

Cd plating is nowadays only used in those applications were it is essential for technical or safety reasons e.g. in aerospace, aeronautics, mining, offshore, safety devices, not easily available for the general consumer (IZA 1999).

No data are available on these specific uses to assess consumer exposure.

However, because of its limited uses and the presence of cadmium in these latter applications under a massive metallic form not readily available for uptake, it can be concluded that for the consumer, the potential exposure to cadmium metal in plated products is very low.

4.1.1.3.5 Scenario 5: Alloys

Most of the Cd alloys are copper-cadmium alloys in which small amounts of cadmium metal are added to improve the mechanical properties e.g. contact wires in railways, overhead power lines. In the very limited other applications cadmium alloys are used basically in the industrial environment (as special fusible and joining alloys, in nuclear power plants). In these limited applications, it is expected that the potential for consumer exposure to cadmium in alloys is very low.

No detailed data on uses and/or consumption of alloys were located. The use of Cd alloys is currently not regulated by EU legislation.

Brazing material containing up to 20% w/w Cd can be purchased by the consumer through Do-It-Yourself shops (Belgian Federal Inspection of the Environment, pers.com., 2002). One may assume that consumer uses of brazing material are likely to be infrequent and duration of exposure is expected to be shorter than in an industrial setting. In case of use by the consumer of such brazing sticks, inhalation and dermal exposure should be considered. However, the contribution of the latter route of exposure is expected to be negligible because brazing occurs at temperatures at which direct unprotected handling of cadmium containing material is not expected to occur. Detailed exposure information is currently not available and this issue may require additional investigation to better document the possible exposure of the consumer.

Recent investigations in Denmark have shown that significant concentrations of cadmium (conceivably cadmium metal) were encountered in jewels (“silver” bracelets) imported from South and South East Asia and that release of cadmium from those jewels might reach significant levels. Two samples were analysed by energy dispersive x-ray fluorescence (XRF):

Table 4.63 Cd Content of silver bracelets:

Sample	% Cd
Thick silver bracelet	24
Thick silver bracelet	7

The potential migration of cadmium from bracelets was further analysed: 18 pieces of jewellery were tested for cadmium content. Cd was not detected in 12 out of the 18 samples. In one sample, only traces of Cd were detected. The potential migration of cadmium from the 5 remaining samples was analysed in duplicates by two methods:

a) EN 71-3 1994 “Safety of toys-part 3: migration of certain elements”: samples are placed in an artificial stomach acid (HCl 0.07M/L) for 2 hours at 37 ± 2°C. The concentration of dissolved Cd is determined by flame atomic absorption spectrometry (FAAS) and expressed as mg/kg sample material.

b) According to the standardised method EN 1811 “Reference test method for release of elements from products intended to come into direct and prolonged contact with the skin”: samples are placed in an artificial sweat test solution for one week. The artificial sweat consists of deionised and aerated water containing 0.5% (m/m) sodium chloride, 0.1% lactic, 0.1% urea and 1% ammonia. The concentration of dissolved Cd were determined by FAAS and expressed as µg Cd/cm^2 (of the surface area of the sample) per week.

Table 4.64 Potential migration of Cd from silver bracelets

Sample	EN 71-3 1994 Cd migration (mg/kg, average)	EN 1811 Cd release (µg/cm²/week, average)
A	42	10
B	168	33
C	26	23
D	30-80**	10-26**
E	18	29-58**

** Both analyses' results are indicated due to large differences between the duplicates.

The migration values from two of these samples (B and D) of jewellery exceeded the limit value for migration of Cd from toys of 75 mg/kg (according to EN 71-3).

No other data on cadmium in jewels were located. It is not known how widespread this use is. It can therefore not be excluded that this might be a more general problem for these kinds of jewellery and it may be useful to further refine a potential consumer exposure to cadmium in these specific uses. Indeed, assuming a Cd release of 60 $\mu g/cm^2$/week (maximum release value observed in the EN 1811 test) from a bracelet worn continuously and corresponding to a skin surface of 10 cm^2 and a dermal absorption of 1%, the uptake could be estimated to be somewhat less than 1 µg Cd/day. Based on this conservative estimate, it can be concluded that exposure through jewels might be significant compared with food (7-32 µg/day · 5% absorption) or tobacco intake (1-2 µg/20 cigarettes · 25-50% absorption) (see Indirect exposure: summing up).

Summary and conclusions

Besides these scenarios of potential consumer exposure, it should be reminded that consumers of cigarettes and other tobacco products are exposed to cadmium contained in tobacco leaves. The cadmium content in cigarettes is variable and results from the uptake of cadmium contained in soil and water by the tobacco plant and from deposition of cadmium on the leaves. This type of exposure to cadmium is further described in Section 4.1.1.4 (Indirect exposure).

Table 4.65 Summary and conclusions

Scenario	Consumer exposure	Involved Cd species
1: Ni-Cd batteries	Considered to be very low	Cd metal/CdO
2: Pigments - Glass & enamels - Plastics - Artist's paints	 Considered to be very low Packaging not available for consumers Might occur in some specific uses or if swallowed, penetrates skin, etc.	Cd compounds (Cd sulphide and Cd sulphoselenide)
3: Stabilisers	Considered to be very low	Cd compounds (Cd laurate/stearate)
4: Metal plating	Very low	Cd metal
5: Alloys - Brazing material - Imported jewels	Very low Conservative estimate: cfr occup. scenario Conservative estimate: < 1 µg/day	Cd metal Cd metal/CdO Cd metal

Concerning the assessed cadmium compounds (Cd/CdO), 3 scenarios are relevant for consumer exposure (Ni-Cd batteries, metal plating and alloys). In both batteries and plating scenarios, consumer exposure is considered to be very low. In the scenario involving consumer uses of alloys containing cadmium metal, for brazing a conservative estimate is proposed by cross reading from the corresponding occupational scenario, for the jewels a conservative estimate of 1 µg Cd/day will be taken across to the risk characterisation.

Although in the other scenarios (which involve exposure to other Cd compounds than Cd metal or CdO), a significant consumer exposure is probably limited to very limited, it must be recognised that quantitative data to document exposure of the consumer are scarce.

4.1.1.4 Indirect exposure via the environment

4.1.1.4.1 Inhalation of ambient air

Average Cd concentrations in EU countries are found in the range < 1-5 ng/m^3 in rural areas, 5-15 ng/m^3 in urban areas and 15-50 ng/m^3 in industrial areas (see environmental part of the Risk Assessment Report). Reasonable worst case air concentrations estimates for battery production/recycling and waste management (MSW incineration: all waste) are of 22 and 28 ng/m^3, respectively (TRAR, see environmental part of the Risk Assessment Report). Extreme values up to 1 µg/m^3 have been reported near cadmium metal producing plants (exposure data from 1996; see environmental part of the Risk Assessment Report), some of which may have ceased their activity during the preparation of this report.

This cadmium is associated with particles in the respirable range and it is estimated that about 25% of the daily Cd intake from the atmosphere is absorbed for adults (IPCS, 1992a). At a daily air intake of 20 m^3, this would lead to 0.025 µg Cd uptake at a Cd concentration in air of 5 ng/m^3 and 0.075 µg Cd uptake at a Cd concentration in air of 15 ng/m^3. This daily uptake is small compared to that from food or from smoking. In houses of smokers, significantly higher Cd air levels are observed as compared to houses of non-smokers (IPCS, 1992a). Personal measurements of Cd in the breathing-zone air of individuals residing in the down-town area of Stockholm revealed very low inhalation concentrations of Cd- on average about 0.8 ng/m^3 (Vahter et al., 1991). These concentrations were considerably lower than those reported for outdoor air, which most likely can be explained by the fact that the subjects spent most of their days indoors. On the assumption of a daily respiration volume of 13 m^3, Vahter et al. (1991) estimated that, on the average, 0.01 µg Cd were inhaled per day, and that airborne Cd contributed only about 1% to the totally daily absorbed amount of Cd.

4.1.1.4.2 Soil and household dust ingestion

Ingestion of dust and/or soil by young children is known to be an important source of exposure for elements such as lead. However, this pathway is most probably not a dominating exposure route for Cd. The estimated average intake of household dust by children is 100 mg/day (IPCS, 1992a). Based on data of Cd in household dusts in UK (mean 7 mg/kg, n=4,500), it was concluded that the average daily intake of 0.7 µg is much smaller than food intake (IPCS, 1992a). At an absorption rate of 0.05, this would lead to a daily uptake of 0.035 µg/day, which is less than 10% of the total daily uptake (**Table 4.67**). Therefore, in general, the intake of soil and dust does not have to be included in the risk characterisation.

Soil/dust ingestion may, however, be an important additional source of exposure in contaminated areas. Soil or household dust Cd concentrations exceeding 100 mg/kg have been reported around former refineries or mining areas (IPCS, 1992a; Nakhone and Yound, 1993). A positive correlation was found between Cd-U or Cd-B and the average amount of Cd collected by rinsing one hand of 9-11 year-old children (Lauwerys, 1980). The amount of Cd rinsed from the hand varied between 0.4 and 15 µg Cd. The correlation was found for children living at different distances from a Cd emitting source and other factors such as air Cd concentrations may as well interfere in the exposure.

The availability of soil Cd is, however, probably smaller than food Cd or Cd salts. A feeding study was performed with eight-week-old rats that were given either a Cd contaminated soil dissolved in 5% gum acacia or an equal amount of Cd as $CdCl_2$ in solution; control rats were gavaged with an isotonic solution. Relative availability of soil Cd as compared to the solution Cd was calculated based on blood Cd levels and was 43% (Schilderman et al., 1997).

4.1.1.4.3 Tobacco smoking

Tobacco plants naturally contain high Cd concentrations in leaves and cigarettes contain 1-2 µg Cd per cigarette, the amount varying considerably with the origin of the tobacco (IPCS, 1992a). About 10% of this Cd is inhaled and it is estimated that 25-50% of the inhaled Cd is absorbed. As a result, smoking a pack of 20 cigarettes daily results in a net uptake of 0.5-2 µg. This value is large compared to the daily Cd uptake from air (0.02 µg) and in the same range of Cd uptake from food Cd (0.35-1.6 µg). The mean blood Cd in active smokers is significantly higher than in unexposed non-smokers, and it is very close to the mean Cd levels in passive smokers (Shaham et al., 1996). Smoking is directly associated with increased Cd-B (see also Section 4.1.2.2.2).

4.1.1.4.4 Drinking water

Drinking water usually contains low cadmium levels (< 1µg/l) and, consequently, Cd exposure from the intake of drinking water or water-based beverages (~2L) is relatively unimportant compared to dietary intake (IPCS, 1992a; see also Section 4.1.1.4.6.). In a survey from the Netherlands, about 99% of the drinking-water samples in 1982 contained less than 0.1 µg/l (Ros and Sloof, 1990). Some dietary Cd intake studies, cited below, included Cd from drinking water in the calculated dietary intake.

Cd concentrations in local water pits can be elevated in areas with historical Cd pollution. As an example, Cd concentration in water from such pits in the Noorderkempen exceeded 10 µg/l in 25% of the cases. In one district in the Noorderkempen, it was assumed that elevated Cd exposure might have occurred through consumption of contaminated water (Lauwerys et al., 1990). Ground water Cd may also be a significant contribution to Cd exposure in areas with acid soils. Studies in southern Sweden have shown that the concentrations of Cd in groundwater increase with decreasing pH, from a median value of 0.03 µg/l at pH 7.5 to 0.11 µg/l at pH 5.4 (Bensryd et al., 1994). The total range in the group of the most acid well waters was 0.04-1.5 µg/l.

4.1.1.4.5 Dietary intake

It is generally acknowledged that dietary intake is the major source of Cd exposure for the general population. Levels of Cd in food items are typically high in offal, organs, equine products, shellfish, crustacean, cocoa, mushrooms and some seeds (Fouassin and Fondu, 1981; Jorhem and Sundström, 1993; Tahvonen, 1996; EUR 17527, 1997). The incidence of these products in the average dietary Cd intake is low because of their low average consumption. There may be certain parts of the population, however, that have elevated intake of Cd from such food. Typical groups with high dietary Cd intake are these with preference for shellfish or mushrooms. Examples of statistical distributions of Cd intake in the total population are given below.

Dietary intake studies are based on both Cd levels in food and consumption patterns. Four methods are used to estimate the daily intake of cadmium from food. In the total diet (T) method, food items are processed for consumption and are analysed individually or combined in food groups. Cadmium intake is calculated as the product of the cadmium level in the food and the estimated amount consumed. In the market basket (M) study, individual food items are sampled from retail outlets and are analysed. Based on these levels and on estimated consumption, total Cd intake is calculated. In the duplicate meal (D) studies, duplicate samples of meals, snacks and drinks are collected and analysed. Faecal output (F) of cadmium can also be used to estimate daily intake assuming that 5% is absorbed on average (IPCS, 1992a).

Dietary Cd intake is generally estimated based on market basket or on total diet studies. These studies calculate the average dietary Cd intake using an average diet for the selected population. There are, however, variations in Cd concentrations in various foods and in the consumption of the various foods between individuals and population groups. Thus there are large individual variations in the dietary intake due to differences in dietary habits. Only few of the market basket or total diet studies include the variability of individual diets so that e.g. the frequency of groups with high Cd intake in a population can be calculated. Duplicate meal or faecal output studies offer the advantage that variability in Cd intake between individuals can be assessed. The available data from duplicate meal studies are, however, limited. It has been reported that duplicate meal studies underestimate true intake by 15-20% (Johansson et al., 1998).

Dietary Cd intake studies have been reviewed by Ryan et al. (1982), IPCS (1992a), Van Assche and Ciarletta (1993), Boisset and Narbonne (1995), Van Dokkum (1995) and Tahvonen (1996). These reviews show that the average Cd dietary intake in European countries range between 5 and 90 μg day^{-1}, but with most values ranging between 10 and 35 μg day^{-1}. As a result of improved detection limits, early data about dietary Cd intake are usually higher than more recently obtained data. As an example, the best US dietary Cd data indicated 26-51 μg Cd day^{-1} in the early 1970s. Present US diets are reported to contain about 12 μg day^{-1} (Chaney, 1999a). In addition, it has been suggested that the reduction in atmospheric cadmium deposition contributes to this decline (Van Assche and Ciarletta, 1993).

A selection of estimated dietary Cd intake values in European countries is given in **Table 4.66**. Only the most recent data are included as well as a number of duplicate meal studies. Many data are retrieved from the report of the European task force on Cd in food that started in 1994 (EUR 17527, 1997). These data are generally based on market basket studies in which average food Cd concentrations and food consumption values were collected for 16 food groups in each country. This report was chosen as the basis to compare country average Cd intake values since the methodologies were as harmonised as possible. Equine products were excluded from the meat group. Equine liver often contains Cd levels exceeding 1 mg/kg. Equine meat contains lower Cd concentrations (< 0.5 mg/kg) but these levels are generally above that of other meat. Equine meat is not consumed intensively, excluding some narrow groups. There are no data on consumption of equine products by these narrow groups.

The average dietary Cd intake for adults in European countries ranges between 7 and 44 µg/day (**Table 4.66**). The highest value is obtained for Greece and this value markedly exceeds the Cd intake values of other countries. The Greek dietary intake is not elevated due to high fish intake (only 2.5 µg Cd) but due to surprisingly high Cd intake from fruit (6 µg Cd), leafy vegetables (7 µg Cd) and meat (4.3 µg) (Tsoumbaris and Tsoukali-Papadopoulou, 1994). No information was given if the Cd analysis of the foodstuff was verified with reference samples. The average Cd concentrations were 40µg Cd/kg FW in meat and 22 µg Cd/kg FW in fruit, both values being more than twofold larger than corresponding values in other countries (EUR 17527, 1997). The elevated Cd intake via vegetables in Greece is a result of a relatively large reported average Cd concentration in leafy vegetable (75 µg Cd/kg FW, most samples in other European countries are below 50 µg Cd/kg FW) and a large estimated daily consumption. Because the reliability of these data can be questioned, it is proposed to exclude them from further analysis.

It can therefore be concluded that average dietary Cd intake values range from 7-32 µg/day with a tendency to find lowest values in Scandinavian countries and highest values in Mediterranean countries. Estimates of Cd intake by women are generally lower than those for men. This could be related to differences in energy intake. The daily energy requirement is about 9 MJ for moderately active women and 12 MJ for men (in Järup et al., 1998). The upper value of 32 µg/day represents the average of several P95 values reported in **Table 4.66** ((B:42; DK:37; UK:25; D:13 and S:40). Higher values were reported in old studies (e.g. P95 42 µg day^{-1} in Belgium; Buchet et al., 1983) but these figures will not be used for calculations in the Risk Characterisation because (1) they correspond to extreme values that are unlikely to be representative of a lifetime exposure, and (2) similar values were not reported in more recent studies performed in countries with similar dietary habits (P95 of 25 and 13 µg day^{-1} in UK and Germany, respectively; see **Table 4.66**).

Baby food based on cereals is an important source of Cd intake in infants and young children. Eklund and Oskarsson (1999) determined Cd levels in several weaning products in Sweden. Weaning diets become transitional food between a complete liquid diet and solid food. It may constitute a major source of nourishment for the child during early infancy. The study showed that the Cd levels in Swedish milk and cereal-based weaning products are low. However, the higher energy intake per kg body weight in infants and the uniform food habits make these products an important source of dietary Cd. With an intake of liquid weaning diet corresponding to the total daily energy requirement of approximately 3,500 kJ for 6-month-old infants, the Cd intake ranged from 0.30 µg/day to 3.30 µg/day i.e. 0.05-0.55 µg/kg bw/day.

The food groups that contribute largely to dietary Cd intake are cereals, potato, vegetables and fruit, with some exceptions (EUR 17527, 1997). Data from Spain show that fish consumption (including shellfish) may contribute up to 70% of the dietary Cd intake (data of Valencia, Cuadrado et al., 1995).

Table 4.66 Dietary Cd intake in European countries.

Country	Method§	Daily intake (μg Cd)	Description	year of food sampling	reference:
Belgium	M	23	mean; equine products are not included	1989-1995	EUR 17527, 1997
	D	18 (2.1-88,42)	mean (range and 95th percentile) of 124 daily meals		Buchet et al., 1983
Austria	M	10	mean; no data for meat, offal and shellfish	1990-1994	EUR 17527, 1997
	M	 3.9/3.4 6.5/6.1 7.2/6.1 7.4/6.5 8.8/6.6	school 6-18 y (boys/girls), calculated after average diet 6 years 7-9 years 10-12 years 13-14 years 15-18 years		EUR 17527, 1997
	D	24 (10-57)	mean and range of daily intake (7 days average) of 10 male adults	1988	Pfannhauser, 1991
Denmark	M	17	mean; no data for shellfish	1983-1992	EUR 17527, 1997
	M	17(37)	mean (95th percentile, dietary survey on 2,242 persons)	1983-1987	Højmark Jensen and Møller 1990
	D	15 (3-102)	mean and range of daily intake (2 days average) of 100 male adults	1988	Bro et al., 1990
Finland	M	10	mean; no data for shellfish	1985-1995	EUR 17527, 1997
	D	10	hospital diet		Kumpulainen and Tahvonen, 1989
	D	8.2 (2-25)	mean (range) of 78 duplicate meals of 40 male adults (2-hour recall)		Louekari et al., 1987
	T	14 (3-35)	mean (range) of 1348 diets (3-day recall)	< 1980	Louekari et al., 1989
France	M	20	mean	1979-1995	EUR 17527, 1997
	D	10-17	range of means of school meals for 5 regions	1990	Boudène, pers. commun.

Table 4.66 continued overleaf

Table 4.66 continued Dietary Cd intake in European countries

Country	Method§	Daily intake (µg Cd)	Description	year of food sampling	reference:
France	T	23	mean		EUR 17527, 1997
France	D/T	17	Mean of 103 meals purchased at restaurants: daily intake calculated based on Cd concentrations in food multiplied with food consumed	1998-1999	Leblanc et al., 2000
Germany	D	10 (13)/8 (11)	male/female means (90th percentile) of 320 duplicate meals	1990-1991	EUR 17527, 1997
	D T	12/10 14/11	male/female means of daily intake (7 days average) of 7 men and 7 women male/female means (dietary survey on 1,816 adults)	1990-1992 1991-1992	Müller et al., 1993
	D	7 (3.5-14., 11)	mean (range and 95th percentile) of 48 hours duplicate meals of children (5-8 years, n=47)	1988-1989	Wilhelm et al., 1995
	M	10/8	male/female means ; no data for shellfish	1988-1994	EUR 17527, 1997
Greece	M	44	mean (dietary survey on 114 households in Thessaloniki)		Tsoumbaris and Tsoukali-Papadopoulou, 1994
Ireland	M	23	mean; no data for meat, offal, vegetables and shellfish	1980-1994	EUR 17527, 1997
Italy	M	23	mean; no data for shellfish	1988-1995	EUR 17527, 1997
	T	32(19-46)	mean and range based on an average diet and the range of Cd in complete meals and foodstuffs		Coni et al., 1992
	D	12-25	range of average daily Cd intake values for five locations where 132 complete meals were sampled	1987-1988	Melchiorri et al., 1989

Table 4.66 continued overleaf

Table 4.66 continued Dietary Cd intake in European countries

Country	Method§	Daily intake (μg Cd)	Description	year of food sampling	reference:
The Netherlands			male/female means, calculated after average diet	1988-1989	Van Dokkum, 1995
			1-4 years		
	T	5.9/5.5	4-7 years		
		8.0/7.3	7-10 years		
		10/8.8	10-13 years		
		12/10	13-16 years		
		14/11	16-19 years		
		17/12	19-22 years		
		17/11	22-50 years		
		16/12	50-65 years		
		15/10	> 65 years		
		14/10	pregnant women		
		12			
	D	10(3-55)	mean and range of 24-hour daily intake of 110 adults	1984-1985	Ellen et al., 1990
Norway	M	10	mean; no data for fruit	1985-1994	EUR 17527, 1997
Portugal	M	17	mean; no data for fruit, shellfish or meat	1989-1995	EUR 17527, 1997
	M	25	mean for general population		EUR 17527, 1997
		11	mean for urban population		
		18	mean for rural population		
Sweden	D F	8.5 (5.7-14) 8.9 (5.5-12)	mean and range of one-week average daily intake of 15 non-smoking women (age 27-46 years)	1988	Vahter et al., 1991
	D F	11 (5.7-26) 11 (4.8-26)	mean and range of daily intake (4 days average) of 34 non-smoking women with mixed diet	1991-1992	Berglund et al., 1994
	D F	16 (5.5-38) 14 (4.4-38)	mean and range of daily intake (4 days average) f 23 non-smoking women with high fibre diet		

Table 4.66 continued overleaf

Table 4.66 continued Dietary Cd intake in European countries

Country	Method§	Daily intake (μg Cd)	Description	year of food sampling	reference:
	D D	11 (5.7-26) 28 (9-70))	mean and range of daily intake (4 days average) of 34 non-smoking women with mixed diet mean and range of daily intake (4 days average) of 17 non-smoking women with shellfish diet		Vahter et al., 1996
Sweden	M	9/7	mean of male/female	1982-1995	EUR 17527, 1997
	M	12	mean	1987	Becker and Kumpulainen, 1991
Sweden	T	 2.45-3.30 0.30 0.70 0.40 0.53 0.90	daily mean intake in 6-month-old infant, from the recommended amount of weaning products: wheat, oat and milk base corn and milk base rice and milk base porridge, rice and milk base porridge, cereal and milk base soy formula	1997-1998	Eklund and Oskarsson, 1999
Spain	M	18	mean	1988-1995	EUR 17527, 1997
	M	16 29 23 29	mean; Madrid region mean; Valencia region mean; Galicia region mean; Andalucia region		Cuadrado et al., 1995
United Kingdom	M	14(25)	mean(97.5th percentile)	1994	MAFF, 1997
	M	14(24)	mean (97.5th percentile)	1997	MAFF, 1999

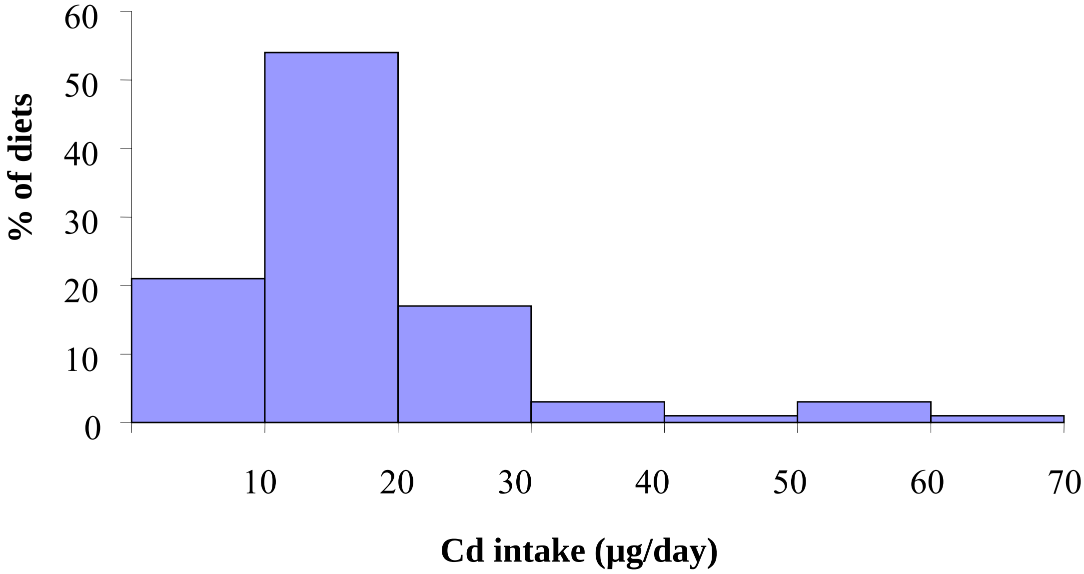
§ M Market basket,
D Duplicate meal,
T Total diet;
F Faecal output (i.e. total output of Cd)

Groups with high dietary Cd intake

Selected groups with high dietary intake Cd deserve special attention, as they are more exposed to Cd than the average population. Some of the total diet studies given in **Table 4.66** are based on an extended survey of dietary habits and report upper percentiles of dietary Cd intake. The 95th percentile of dietary Cd intake is about 37 µg Cd in Denmark (Højmark et al., 1990) and is about 24 µg Cd in Finland (Louekari et al., 1989). The British food surveillance reports that the 97.5th percentile in dietary Cd intake is 24-25 µg Cd (MAFF, 1997; MAFF, 1999). These upper percentiles are, however, calculated from the variability in food intake and the variability in consumption of certain food items or food groups (i.e. fish, cereals), using an average Cd content for the food items or the food groups. Therefore, some variability is still excluded (e.g. locally sampled products containing elevated Cd).

Duplicate meal studies offer the advantage that the variability of dietary Cd intake can be more correctly quantified. In **Figure 4.1**, the frequency distribution of dietary Cd intake is shown for 74 adult women from Sweden (Berglund et al., 1994 and Vahter et al., 1996). The frequency distribution is clearly skewed because small groups have an elevated Cd intake due to the preference for products that are naturally high in Cd such as shellfish. The distribution of the Swedish duplicate meal studies (including shellfish eaters) shows that in about 5% of the diets, 40 µg Cd or more was taken in daily (see **Figure 4.1**). It must be stressed, however, that the 74 test persons do not represent a random sample of the population. In the Danish 48-hour duplicate meal study, 2 diets out of the 100 contained more than 70 µg day^{-1} (Bro et al., 1990). The mean dietary Cd intake in Italy increases from 32 µg Cd to 54 µg Cd for the population eating at least once a week certain kinds of seafood such as calamari (Coni et al., 1992). Cuadrado et al. (1995) showed that the higher seafood consumption (including shellfish and crustacea) is the reason for higher dietary Cd intake in Valencia (29 µg Cd) compared with Madrid (16 µg Cd).

Figure 4.1 The frequency distribution of duplicate diets, collected during 4 consecutive days, of 74 Swedish women (20-50 years). Redrawn after Berglund et al. (1994) and Vahter et al. (1996)



Foods differ in bioavailability of Cd and some of the products containing elevated total Cd are lower in available Cd. As a result, elevated dietary Cd intake due to preference of these products may not necessarily induce a higher health risk for the consumers. There is evidence that higher Cd intake due to a higher consumption of shellfish and mushrooms are not reflected in a proportional increase in systemic dose of Cd. In the duplicate meal study of Vahter et al. (1996), a group of 17 non-smoking women, consuming shellfish at least once a week, was compared with a group of 34 non-smoking women with a mixed diet low in shellfish. The average dietary Cd intake in the shellfish group was 28 µg Cd while it was 11 µg Cd for the mixed diet group. The Cd-B was not significantly different between both groups (0.28 µg/l and 0.24 µg/l respectively). The Cd-concentration in the blood was strongly influenced by the body iron stores of the test persons and increased sharply when serum ferritin was below about 20 µg/l. For the subgroups with serum ferritin concentrations $\geq$ 20 µg/l, Cd-B was significantly higher ($P < 0.002$) in the shellfish group than in the mixed diet group (0.26 µg/l N=16 and 0.16 µg/l N=15). This difference in Cd-B was, however, smaller than the 2.4 fold higher dietary Cd intake in the shellfish subgroup than in the mixed diet subgroup. It was concluded that Cd ingested with shellfish gives rise to elevated Cd-B, although not to the same extent as Cd ingested with mixed food. A study from New Zealand on oyster consumers showed that, in spite of very high Cd intake via oysters (group averages 15-233 µg/day), Cd-B and Cd-U were significantly elevated, however, not to the same extent as the dietary intake (Sharma et al., 1983, McKenzie-Parnell et al., 1988). Smoking had a more pronounced effect on Cd-B than intake of Cd via oysters. In the non-smoking group, mean Cd-B increased from 1.9 µg/l to 3.7 µg/l compared with a 12-fold increase in Cd intake per day while mean faecal Cd elimination increased at least tenfold. The Cd-B of the control population (no regular oyster consumers) was 0.9 µg/l. Low bioavailability of oyster-Cd has been demonstrated in mice feeding studies. Mice fed 0.4 µg of oyster bound Cd per g of diet retained only 0.83% of the dietary Cd consumed (Hardy et al., 1984).

The gastrointestinal availability of Cd from mushrooms is most probably also low. The Cd concentrations in blood, urine and faeces was monitored daily for eight adults (5 male and 3 female, 2 moderate smokers) that consumed 290-500 g wild mushrooms (*Agaricus* species) daily during three consecutive days (Schellman et al., 1984). Monitoring started 2-3 days before the mushroom consumption and was continued for 4 days after the last mushroom meal. The extra

Cd intake due to the mushroom consumption varied between 315 and 908 µg Cd/day. The faecal excretion of Cd sharply increased on the first day of mushroom consumption and, although it decreased progressively the following days, it was still elevated up to four days after the last mushroom meal. In contrast, Cd-B did not show any trend during the whole experimental period for any individual. The Cd-B varied between 0.2 and 2.9 µg/l and the Cd-B variance among individuals was larger than that within individuals. No increase in Cd-U was found during or after mushroom consumption.

In the duplicate meal study of Berglund et al. (1994), the test persons were classified as those consuming a mixed diet and those consuming a high fibre diet (no meat consumption and high consumption of unrefined cereal products). Median dietary Cd intake in the mixed diet group (N=34) was 10 µg Cd while it was 13 µg Cd for the high fibre group (N=23). No significant differences in blood Cd could be detected between the two groups (0.24 µg/l versus 0.32 µg/l). Overall, Cd-B significantly increased with reduced serum ferritin concentrations and there was a tendency, although not significantly, of higher Cd-B with increased intake of fibre when standardised for serum ferritin. It was concluded that fibre inhibits the gastrointestinal absorption of Cd, although it does not completely compensate for the increased total Cd intake (Berglund et al., 1994). These data were re-analysed by Åkesson (2000). The dietary fibre intake in the Berglund study appeared to be overestimated in the dietary record by about 20%. This conclusion is based on a comparison of the calculated fibre intake from the dietary records, and the faecal weight. Subjects were reclassified by Åkesson (2000), three women with low iron stores, previously classified in the high fibre diet group, are now classified in the mixed diet group, and two extra women with adequate iron stores are included in the mixed diet group. The revised analysis showed that both iron status ($P \leq 0.05$) and fibre intake ($P \leq 0.03$) independently affected Cd-B. Higher fibre intake resulted in significantly higher Cd-B (0.37 versus 0.23 µg/l, low Fe group; 0.18 versus 0.11 µg/l, high Fe group). There was no interaction between iron status and fibre intake. It can be concluded that higher fibre intake results in higher Cd body burden. However, no data on dietary Cd intake of the reclassified groups are known, therefore relative availability of dietary Cd cannot be calculated for the reclassified groups, etc.

The brown meat of crab (the hepatopancreas) naturally contains high Cd concentrations. Human feeding studies in which the crab meat Cd was intrinsically labelled with ^{115m}Cd (crabs fed with shrimp pellets that were labelled with ^{115m}Cd) showed whole body retention of the label of 2.7% (±0.9%SE) at 26 days or more after the meal (Newton et al., 1984). The seven male test persons had normal body iron stores. The body retention of 2.7% is in line with toxicokinetic data obtained in other feeding studies with other food or with extrinsic labelling (see Section 4.1.2.2.1). This suggests that Cd in crab brown meat is not less available than Cd in the mixed diet.

Young children have a larger food intake per kg body weight than adults. Furthermore, infants have a diet with high milk and cereal contents. This might lead to larger Cd intake and higher tissue Cd levels. Eklund et al. (2001) studied the bioavailability of ^{109}Cd from weaning food in rat pups. Pups receiving Cd in a cow's milk formula had the highest mean whole-body retention, while the retention of Cd in cereal-based formulas was significantly lower than in the other diet groups. This can be explained by Cd binding to dietary fibre and phytic acid in the latter formulas. Cadmium levels are, on the other hand, higher in weaning formulas based on wheat, oat or rye flour than in formulas based on cow's milk (Eklund and Oskarsson, 1999).

In conclusion, the limited data from UK, Finland, Denmark and Sweden show that upper percentiles (95th or higher) of dietary Cd intake range between 24 and 40 µg/day. Average individual diets exceeding 70 µg/day are rarely found. Most studies show that shellfish Cd has lower availability than Cd from the mixed diet. Therefore, the risks of elevated Cd intake from high consumption of shellfish should not be based on total dietary Cd only. There is, however, no information on relative availability of Cd in other products that contribute to elevated Cd diets, e.g. offal, equine meat or seafood such as calamari. In addition to food properties, the nutritional status of the consumer strongly affects the net absorption rate of food Cd. This factor is discussed separately in Section 4.1.2.2.1.

4.1.1.4.6 Indirect exposure via the environment: summing up

The sum of all exposure routes in areas at ambient Cd concentrations is summarised in **Table 4.67**. This table is based on average values for ambient environmental Cd levels and for three groups of the general population, children, adults with sufficient body iron stores and adults with depleted body iron stores. An additional scenario is included representing a local scenario where Cd concentrations in soil, air and diet are all elevated.

Air Cd concentration in the local scenario is the PECair value for 3 Cd/CdO production sites with largest emissions (see environmental part of the Risk Assessment Report). Soil Cd concentration is 1 mg Cd/kg and is slightly above the largest PECsoil near point sources (see environmental part of the Risk Assessment Report). Dietary Cd that is associated with soil Cd=1 mg/kg is calculated in **Table 4.71**.

The concentration of Cd in soil and dust that is ingested is 7 mg/kg and is a mean of values measured in UK (see Section 4.1.1.4.2). The ambient scenarios are furthermore split in smokers and non-smokers. Individuals with low iron stores may absorb much more Cd via the GI route, on average 2 times more (Berglund et al., 1994). In Sweden, 10 to 40% of women at childbearing age have depleted iron stores. Furthermore, children may absorb relatively more Cd than adults because of increased absorption from the gastro-intestinal tract, a higher food intake per kg body weight and a diet of high milk and cereal contents. No data were found, however, on the relative GI absorption rate in children compared with adults. The proposed absorption rate is 0.03 for both adults with sufficient body iron stores and for children. This absorption rate is a best fit parameter based on a validation exercise where urinary Cd concentration data are compared with dietary Cd intake values (see Section 4.1.2.2.5).

The data show that smoking and dietary Cd are the main pathways of Cd exposure in uncontaminated areas. It can also be derived from these data that Cd intake through smoking 20 cigarettes per day increases the Cd systemic dose 1.2 to 7 fold above that in non-smoking individuals with equivalent Cd intake through other sources. The importance of smoking as a source of Cd is well documented in literature. The Cd concentrations in the kidney cortex of residents (40-60 years old) of an unpolluted area in Belgium were about twofold higher in smokers than in non-smokers (Lauwerys et al., 1984). Swedish data show that smokers have about 4-5 times higher blood Cd concentrations and twice as high kidney cortex cadmium concentrations as non-smokers (Järup et al., 1998).

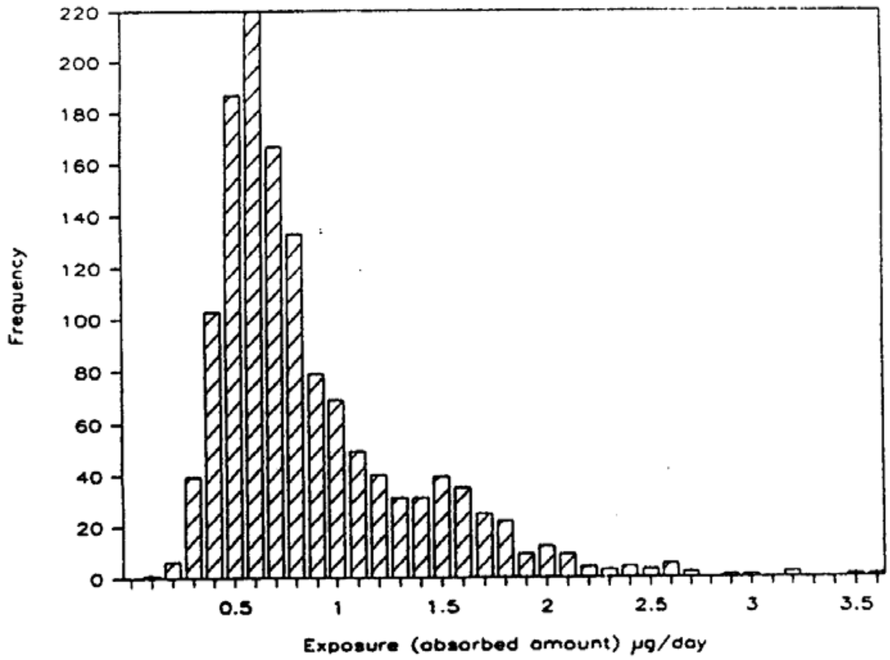
The Cd uptake near point sources is dominated by inhalation with given assumptions of estimating dietary Cd. The contribution of air Cd to dietary Cd has neglected the Cd deposition on locally produced food. There is indirect evidence that this might largely contribute to crop Cd concentrations (see Section 4.1.1.4.8) but there are no data to estimate this contribution correctly. On the other hand, restrictions on food production near point sources are often in place but there is no information to generalise the current situation in EU. Therefore, Scenario 4 should be considered as indicative only.

Table 4.67 Estimated daily Cd up take in children and adults through environmental exposure in areas at ambient Cd concentrations (Scenario's 0-2) and near point sources with largest atmospheric Cd emissions in EU (Scenario 3). (See Sections 4.1.1.4.1 to 4.1.1.4.5 for more details)

Scenario 0: children (4-7 years old)		
Source	**Cd uptake (µg day^{-1})**	**Assumptions**
Air	0.012 -0.037	Air Cd 5-15 ng/m; daily inhalation 10 m^3; absorption rate = 0.25
Soil and dust	0.04	Dust or soil Cd 7 mg/kg;100 mg intake absorption rate = 0.05
Drinking water	< 0.05	Cd water < 1 µg/l; absorption rate = 0.05; 1l/day consumption
Dietary intake	0.4	Dietary Cd 8 µg/day absorption/intake ratio = 0.05
Sum	0.5 µg/day (0.025 µg/kg_{bw}/day)	
Scenario 1: adults with sufficient body iron stores		
Source	Cd uptake (µg day^{-1})	Assumptions
Air	0.025 -0.075	Air Cd 5-15 ng/m; daily inhalation 20 m^3; absorption rate = 0.25
Soil and dust	0.02	Dust or soil Cd 7 mg/kg; absorption rate = 0.03
Smoking	0.5-2.0	Smoking of 20 cigarettes; 1-2 µg Cd per cigarette; absorbed fraction 0.025-0.05
Drinking water	< 0.06	Cd water < 1 µg/l; absorption rate = 0.03 2l/day consumption
Dietary intake	0.21-0.96	dietary Cd 7-32 µg/day, absorption rate = 0.03
Sum	Non smokers: 0.33-1.12 Smokers: 0.82-3.12	
Scenario 2: adults with depleted body iron stores		
Source	Cd uptake (µg/day)	Assumptions
		As above, but absorption rate of 0.06 for dietary Cd, soil/dust/water Cd
Sum	Non smokers: 0.53-2.08 Smokers: 1.03-4.08	
Scenario 3: near point sources (adults with sufficient body iron stores)		
Source	Cd uptake (µg day^{-1})	Assumptions
		As Scenario 2 but air Cd is 22-1000 ng/m, soil Cd 70 mg/kg and dietary Cd 17-34 µg/day
Sum	non-smokers : 0.89 – 1.40 (22 ng/m^3) non smokers: 5.9-6.4 (1000 ng/m^3)	

Table 4.67 continued overleaf

Figure 4.2 Distribution of Cd exposure to 1348 adult individuals in Finland (25-64 years). The Cd exposure includes intake from food (with 5% absorption from dietary Cd) and smoking habits (0.05 µg Cd absorption per cigarette). Redrawn from Louekari et al. (1989)



The exposure calculation presented in **Table 4.67** reflects average exposure in areas at ambient Cd concentrations and, therefore, does neither indicate Cd absorption for critical groups (heavy smokers or people with a high Cd diet) nor Cd exposure in contaminated areas. Individuals with low iron stores may absorb much more Cd, on average 2 to 3 times more (Berglund et al., 1994). In Sweden, 10 to 40% of women at childbearing age have depleted iron stores.

An attempt to calculate the frequency of critical groups in the general population was made by Louekari et al. (1989). The distribution of Cd exposure for the population of Finland was calculated using dietary habits and smoking habits (see **Figure 4.2**). The contribution of air and water was excluded. It can be inferred from the **Table 4.67** that, even at 50 ng Cd/m air (which is at the upper range in Europe), Cd absorption increases only by 0.2 µg/day. Concentrations of Cd in drinking water exceeding 1 µg/l are rarely found (see above). The survey was based on 1,348 adults (25-64 years). It was assumed that 5% of dietary Cd is absorbed and that 0.05 µg Cd is absorbed from each cigarette. The food Cd concentrations were average values for food items that were sampled before 1980. The distribution is skewed and slightly bimodal. The bimodal distribution is due to the Cd contribution of smoking. About 5% of the 653 adult men smoked > 25 cigarettes per day. The average dietary Cd intake in the population was 14 µg Cd/day, which is equivalent to a daily Cd absorption of 0.7 µg Cd/day. The most probable Cd absorption with given assumptions is 0.6 µg Cd/day but for about 2% of the population, the Cd absorption is 2.5 µg Cd/day or more (maximum 3.6 µg Cd/day).

4.1.1.4.7 Current trends in exposure of the general population

An overview of factors indicating trends in Cd exposure in Europe is given in **Table 4.68**. No trends in dietary Cd intake are included. Long-term trends in food Cd are rarely reported. Declining trends in dietary intake have been reported (Van Assche and Ciarletta, 1993) but, as discussed in Section 4.1.1.4.5, such trends may be influenced by improved analytical techniques or altered models to calculate average diets.

The trends listed in **Table 4.68** show that Cd concentrations have reduced in air and in rivers during the last two decades, whereas soil Cd concentrations generally increased during the last century. The reduction in air Cd and river Cd reflects reductions in emissions that occurred over the last two decades (North Sea Conference, 1995; see environmental part of the Risk Assessment Report). The trends of Cd concentrations in human blood (longitudinal and cross sectional studies) or children teeth indicate a declining Cd exposure in Belgium and Germany in the 1970's and 1980's. Decreasing trends in blood Cd (Cd-B) concentrations can be influenced by improved analytical techniques. The trends such as found in the German monitoring (0.4-0.3 μg/l) may, to some extent, be influenced by analytical effects since Cd concentrations below 0.5 μg/l are more difficult to analyse. However, the trends found in the Belgian studies are based on geometric means above 0.5 μg/l. The sharp decreases in blood Cd in the 1980's (Ducoffre et al., 1993) were identified in the area of Liège where smelter activities ceased in 1982. The decreasing trend in Cd-B in the Noorderkempen is ascribed to the effect of preventive measures that have been adopted in the area affected by former smelter activities (Staessen et al., 1999).

The decreasing trend in kidney Cd found in Sweden between 1970's and 1996 could reflect a trend in lifetime exposure (Friis et al., 1998). This trend can hardly be influenced by analytical effects since kidney Cd concentrations are well above 1 mg Cd/kgww. The data from the 1970's were obtained from forensic autopsies and the 1996 data were obtained from autopsies of victims of sudden and accidental deaths (n=171). Since kidney Cd increases with age, the data were sorted by age class. A significant decrease trend in Cd ($P < 0.05$) was found for all age classes up to 50 years and the decreasing trends were more pronounced in the younger age groups than among older people. In the age groups under 40 years, geometric mean kidney Cd decreased by about 60% over about 20 years. However, even in the non-smokers, kidney Cd has reduced in time. Due to a limited number of data for the population < 40 years (n=18 in 1996), statistics could only be made for the age group 20-29 years for which the mean kidney Cd halved between 1976 and 1996. In all other age groups of the non-smokers, the reduction in kidney Cd was also found. This reduction was ascribed to changing dietary habits and reduced Cd contamination from Swedish industries (Friis et al., 1998). The selection of samples in 1995 differed from that in 1970's (accidents or sudden deaths versus samples from forensic studies). Since lifestyle, and Cd exposure, may be different for these selected groups, this factor should not be ignored. It must also be noted that there were more smokers in the 1976 study (Elinder et al., 1976), and that the non-smoking group had a higher percentage women in the 1976 study than in that of 1998. This can have influenced the results since smokers have higher kidney Cd than non-smokers and women have higher kidney Cd than men. In the UK, the data published by Scott et al. (1987) have been substantially extended with a total of nearly 2700 kidney cortex samples analysed for their Cd content over a 16 year period (1978-1993) (Lyon et al., 1999). Interestingly, the authors did not detect any apparent trend in the temporal variation of corticular Cd content over the study period. It must therefore be concluded that kidney Cd data do not equivocally suggest that there is evidence for a decrease of the Cd body burden in the general population (see Section 4.1.2.2.2)

The Cd concentrations in pig kidneys from Sweden were found to increase significantly by 2% per year (1984-1992, n=1051, Petersson Grawé et al., 1997). Pig kidneys from fattening pigs (5-7 months) were collected from 31 abattoirs. Significant differences in Cd concentrations were found between individual abattoirs. Increasing trends were found in 2 abattoirs (n= 289 and n=175) and a decreasing trend was found in 1 abattoir (n=16). No trends were found in the 29 other abattoirs. A significant increasing trend was found in the combined data set. There was no information if there was a trend in the frequency of samples from selected abattoirs in the combined data set. Data from The Netherlands show sharp decreases in kidney Cd, but these decreases were only evident before 1983 (CCRX, 1991).

Since dietary intake is probably the most important pathway of Cd exposure to the general population, it is important to analyse long-term trends in food Cd or crop Cd in more detail. Plant Cd concentrations increase at a low rate, decrease in two cases or show no trend (**Table 4.68**). Increasing trends in plant Cd concentrations most probably mirror increasing trends in soil Cd or in soil acidity (Nicholson et al., 1994). The increase in soil Cd in rural areas is found in almost all long-term (> 40 years) field trials. These trends are confirmed by mass balance modelling (e.g. Jensen and Bro-Rasmussen, 1992). Current trends in soil Cd are unknown. Mass balance modelling with current Cd inputs shows that the historical increasing trends in soil Cd is unlikely to continue at the same rate (see environmental part of the Risk Assessment Report). In the context of the continued review, under the Fertilisers Directive (76/116/EEC) of risks posed to human health and the environment by cadmium in fertilisers, Member States were encouraged to perform national risk assessments (Hutton et al., 2000). Based on current fertiliser input levels, cadmium in soil tends to accumulate relatively slowly in these countries where fertiliser cadmium concentrations are below 15 mg Cd/kg P_2O_5 (34 mg Cd/kg P) or decreases after 100 years of application due to net removal rates (leaching, crop uptake) exceeding inputs. In countries where current fertilisers Cd concentrations are 25 mg Cd/kg P_2O_5 (57 mg/kg P) and above, accumulation in agricultural soils over 100 years varies between 17 and 43%. The predicted future trends are generally smaller than the historic trends reported in **Table 4.68**. It is difficult to predict if increasing soil Cd will also result in long-term increase in dietary Cd intake. Soil Cd typically explains a minor part of the variance in crop Cd. As an example: Swedish field data show that soil Cd only explains 3-19% of the variability of crop Cd concentrations (Eriksson et al., 1996). Gradual changes in soil pH, soil organic matter content or yield can obscure trends in soil Cd. The annual variations in crop Cd concentrations are large (Kjellström et al., 1975). Therefore, trends in crop Cd (i.e. Cd in grain) only become clear in long term (at least 10 years) studies. A British wheat grain survey suggests a decreasing trend in grain Cd between 1982 and 1993 (Chaudri et al., 1995, **Table 4.68**).

Ageing of Cd in soil may reduce availability with time, thereby counteracting increasing total Cd concentrations in soil. However, isotope dilutions studies have shown that the indigenous soil Cd is, for most soils, equally available to plants as freshly added Cd (Smolders et al., 1999). The same technique has been applied with soils collected from an Australian long-term field trial (Hamon et al., 1998). Fractions of Cd that were fixed were compared between soils that have received continuous P fertiliser for a long time with soils where P fertilisation has stopped 20 years prior to sampling. The P fertiliser was the major source of Cd in these soils as indicated by a positive correlation between the cumulative application of P fertiliser and the background corrected Cd concentration in soil. The fraction of radiolabile Cd was significantly higher in the soils that received P fertiliser (and Cd) continuously than in the soils where P fertilisation was stopped. A model was developed which estimated that 1-1.5% of labile Cd is fixed each year, i.e. an effective half-life of labile Cd of about 46-69 years. It is yet unclear which soil factors could explain the discrepancy between the results obtained on the Australian soils and these obtained by Smolders et al. (1999).

Barley grain samples from the Rothamsted archives did not show an increasing Cd content over the last 100 years in plots treated with phosphate or farmyard manure. The Cd content in wheat grain samples increased with time in the P treated plots but almost halved in manure treated plots (Jones and Johnson, 1989). The decrease in the manure treated plots is attributed to increasing soil organic matter content. In the arable soils (0-22.5 cm) of Rothamsted, Cd content only increased by 1.3 to 1.6 fold over the same period with no evidence of higher accumulation rates on P treated plots (Rothbaum, 1986). Wheat grain Cd increased significantly in Sweden but the trends are only significant for the longest time series assessed (62 years, old Swedish provincial variety, Andersson and Bingefors, 1985). In the park grass trials at Rothamsted (U.K.), herbage Cd content increased about 2.5 fold between 1866 and 1992 in unlimed P treated plots. In unlimed plots not fertilised with super phosphate a twofold increase of herbage Cd was found (Nicholson et al., 1994). The soil pH dropped from pH 5.3 to pH 4.9 (P treated) or to 4.8 (control) over that period. In limed plots which were started in 1903, herbage Cd was 1.5- to 5-fold lower than in unlimed plots. Herbage Cd increased about twofold in the limed plots and differences of herbage Cd between P-treated and control plots were marginal. The Cd content in the surface (0-22.5 cm) soil was analysed for the unlimed plots and increased about 1.5 fold (control) or 2.6 fold (P treated) between 1876 and 1976 (Rothbaum, 1986). These results indicate that, at least in unlimed plots, long term usage of P fertilisers increases both herbage and soil Cd (Nicholson et al., 1994).

In conclusion, soil Cd has increased in the 20th century. Increasing trends in plant Cd are less pronounced than trends in soil Cd and are not consistently found. Concentrations of Cd in water and air show decreasing trends over the last two decades in the countries for which data were found. Trends in blood Cd, as a biological indicator of human exposure to Cd, are insignificant in the general population of areas at ambient Cd concentrations. Kidney Cd concentrations, as an indication of lifetime exposure, decreased in Sweden between 1976 and 1996, but those data may be confounded by different sampling strategy between 1976 and 1996. Moreover, no such trend has been identified in U.K. over a 16 year study period.

Table 4.68 An overview of factors indicating trends in Cd exposure in Europe

Compartment	Description	Period	Ttrend	Reference
Soil Cd	Rothamsted, UK			
	Broadbalk plots: control	1846-1980	Increase from 0.51 to 0.77 $\mu g\ g^{-1}$	Jones et al., 1987
	P-fertilised	1881-1983	Increase from 0.33 to 0.42 $\mu g\ g^{-1}$	Rothbaum et al., 1986
	Hoosefield: control	1882-1982	Iincrease from 0.27 to 0.42 $\mu g\ g^{-1}$	Jones et al., 1987
	P-fertilised	1882-1982	Iincrease from 0.33 to 0.47 $\mu g\ g^{-1}$	Jones et al., 1987
	Park grass: control	1876-1984	Increase from 0.19 to 0.27 $\mu g\ g^{-1}$	Jones et al., 1987
	P-fertilised	1881-1983	Increase from 0.17 to 0.44 $\mu g\ g^{-1}$	Rothbaum et al., 1986
	Denmark			
	32 field series, 4 locations	1923-1980 (not all series)	Increasing trends in 22 series,, approx. 0.001 $\mu g\ g^{-1} year^{-1}$ No trend in 8 series Decreasing trend in 1 series	Tjell and Christensen, 1985
	Versailles, France			
	control	1930-1984	Increase from 0.19-0.27 $\mu g\ g^{-1}$	Juste and Tauzin, 1986
	P fertilised	1930-1984	Increase from 0.15-0.35 $\mu g\ g^{-1}$	Juste and Tauzin, 1986

Table 4.68 continued overleaf

Table 4.68 continued An overview of factors indicating trends in Cd exposure in Europe

Compartment	Description	Period	Trend	Reference
Plant Cd	Sweden			
	Winter wheat	1918-1980	Increase from 0.025 to 0.052 µg g^{-1} Annual variations in grain Cd > 5-fold	Andersson and Bingefors, 1985
	Spring wheat		No significant trend	
	Cd in tree rings of oak (*Quercus robur* L.) in south-eastern Sweden, n=21	1916-1972 1850-1990	Significant increase, decrease in 9 trees in the last decade	Kjellström et al., 1975 Jonsson et al., 1997
	U.K.			
	Wheat grain mean (median) of n=242 (1982) and N=393 (1993) samples collected nation-wide	1982-1993	Decrease from 0.052 (0.045) to 0.038 (0.034) µg g^{-1}	Chaudri et al., 1995
	U.K. Rothamsted			
	Winter wheat (Broadbalk): FYM applied	1877-1984	Decrease from 0.061 to 0.033 µg g^{-1}	Jones and Johnston, 1989
	NPK-fertilised	1877-1984	Increase from 0.050 to 0.076µg g^{-1}	Jones and Johnston, 1989
	Barley grain (Hoosefield): FYM applied	1877-1983	No trend	Jones and Johnston, 1989
	NPK-fertilised	1877-1983	No trend	Jones and Johnston, 1989
	herbage (Park grass): unlimed/control	1866-1992	Increase from 0.12 to 0.22 µg g^{-1}	Nicholson et al., 1994
	Unlimed/P fertilised	1866-1992	Increase from 0.15 to 0.35 µg g^{-1}	Nicholson et al., 1994
	Limed/control	1916-1992	Increase from 0.07 to 0.14 µg g^{-1}	Nicholson et al., 1994
	Limed/P fertilised	1916-1992	Increase from 0.09 to 0.18 µg g^{-1}	Nicholson et al., 1994
	Germany			
	Wheat grain, yearly averages (n=2000)	1975-1984	No trend (averages 0.05-0.06 µg g^{-1})	Lorentz et al., 1986
	Bordeaux, France			
	Maize grain	1976-1992	No trend (averages 0.04-0.06 µg g^{-1})	Mench, 1998

Table 4.68 continued overleaf

Table 4.68 continued An overview of factors indicating trends in Cd exposure in Europe

Compartment	Description	Period	Trend	Reference
Food Cd	Sweden			
	Kidneys of 5-7 months-old pigs, sampled in 31 abattoirs, n=1051	1984-1992	Increase by 2 % per year	Petersson Grawé et al., 1997
	The Netherlands			
	Median Cd content in pig kidney	1978-1992	Fourfold decrease until 1983, no further trend. Median values 0.1-0.2 mg kg^{-1}	CCRX, 1991/CCRX 1994
	Cd in mussels from the Oosterschelde (for consumption)	1981-1992	Fivefold decrease until 1986, no trend beyond 1986 (0.05 mg kg_{ww}^{-1})	CCRX, 1994
Air Cd	The Netherlands			
	Wet deposition, averages of 14 sampling points	1984-1992	Decrease from 1.8 to 1.3g ha^{-1} y^{-1}	CCRX, 1994
	Norway			
	Moss (*Hylocomium splendens*);median Cd moss concentrations in three regions	1977-1985	1.5-1.7 fold decrease	Steinnes et al., 1994
	Belgium			
	Air Cd (suspended particles)			
	Polluted area	1983-1989	Decrease from 120 to 70 ng m^{-3}	Thiessen et al., 1990
	Urban area	1983-1989	Decrease from 50 to 20 ng m^{-3}	Thiessen et al., 1990
	Rural area	1983-1989	Decrease from 40 to 10 ng m^{-3}	Thiessen et al., 1990
	24 points in Flanders (industrial-urban-rural)	1985-1995	No trend	VMM, 1997
River Cd	The Netherlands			
	Maas (Eijsden), averages of total conc.	1981-1990	No trend	CCRX, 1991
	Rhine (Lobith): averages of total conc.	1981-1990	Decrease until 1986, further no trend	CCRX, 1991
	Belgium			
	Schelde median total Cd	1982-1992	Decrease from 1.5 to 0.5 µg/L, no trend beyond 1988	VIBNA, 1994

Table 4.68 continued overleaf

Table 4.68 continued An overview of factors indicating trends in Cd exposure in Europe

Compartment	Description	Period	Trend	Reference
Biological indicators in humans:				
Blood Cd	Belgium			
	Geometric mean blood Cd for 31 males (24-58y) non-occupationally exposed in urban area	1984-1988	Decrease from 2.2 to 1.0 μg L^{-1}	Ducoffre et al., 1992
	Geometric mean blood Cd in rural area, (n=149,1985 and n=263,1988) adults (cross sectional)	1985-1988	Decrease with 45 % (non-smokers) and 25 % (smokers)	Ducoffre et al., 1992
	Geometric mean blood Cd in metal polluted area (N. Kempen) 336 men and 356 women	1985-1989 (baseline)/1991-1995 (follow-up	Significant decrease from 1.2 to 0.9 μg L^{-1} in both men and women	Staessen et al., 1999
	Germany			
	Average blood Cd in West-Germany (n=2731, 1985/1986; n=2484, 1990/1991)	1985-1991	Insignificant decrease from 0.4 to 0.3 μg L^{-1}	Umweltbundesamt, 1993
	Percentage exceeding 5 μg L^{-1}	1985-1991	Decrease from 2.3 to 0.8 %	Umweltbundesamt, 1993
Teeth Cd	Germany			
	Duisberg and Gummersbach (F.R.G.), deciduous teeth of children (incisors only), n=199	1976-1988 (sampling years)	Decrease with 45 %	Ewers et al., 1990
	Stolberg (polluted area), Cd in deciduous teeth of children (incisors only), n=206	1968/1973-1982/1983 (birth years)	Decrease with 60 %	Ewers et al., 1996
kidney Cd	Sweden			
	Geometric mean Cd in subjects < 40 years	1976-1995	Reduction with 60 %	Friis et al., 1998

4.1.1.4.8 Biotransfer of Cd from soil and air to plants

Since dietary Cd intake and smoking are the most important pathways of Cd exposure to the general population, it is mandatory to consider the factors that affect crop Cd concentrations in more detail. The crop Cd is mainly derived from soil, although atmospheric Cd can contaminate crops through direct interception by plants.

The relative contribution of root uptake and atmospheric deposition on Cd in crops

Even washed crops may contain Cd that was deposited from air on the plants during plant growth. The contribution of air-borne Cd to crop Cd may be one of the factors obscuring the relationship between soil Cd and crop Cd. There are, however, little studies on the contribution of air-borne metal to plant Cd in agricultural crops. Harrison and Chirgawi (1989) estimated the atmospheric contribution to plant Cd from the differences in Cd concentrations in plants grown in growth cabinets with either filtered or unfiltered air. The 4 soils that were used have background Cd concentrations (0.12-0.28 µg Cd/g) and air Cd concentrations were either maximal 0.2 ng/m (filtered) or 1.9-2.1 ng/m (unfiltered). The air Cd concentration in the unfiltered compartment is representative for rural areas. The atmospheric contributions to different plants (radish, turnip, peas, spinach, carrots and lettuce) varied from 0-48% (average 20%) between plant organs, crop type and soil (**Table 4.69**). The atmospheric contribution to Cd in the unexposed plant parts (e.g. carrot roots, peas) was lower than 10% except for radish roots. No information was given if plants were washed prior to analysis and if yields were similar in the two growth cabinets.

Hovmand et al. (1983) report a field experiment in Denmark in which the soil-borne contribution to crop Cd was estimated based on the isotope dilution of radioactively ^{109}Cd that was incorporated in soil. The crops grown were grass, carrots, kale, barley, wheat and rye. The air Cd concentrations (1.3 ng/m) and atmospheric Cd deposition during plant growth (1.4-3.1 g/ha/year) are representative for a rural area. Two uncontaminated agricultural soils (0.08-0.11 µg Cd/g) and one sludge amended soil (0.26 µg Cd/g) were potted in 16 litres containers and placed in existing fields. The assumption was made that the soil-borne Cd in the crop has the same ^{109}Cd/Cd ratio (the specific activity, SA) as that in the total soil or in the soil extract. The SA's in soil extracts were however, 20-40% higher than in the total soil. The uncertainty on the SA of the root absorbed Cd was included in the calculations by using the range of SA's among soil extracts, yielding a range in estimated atmospheric contributions to soil Cd. The results show that the atmospheric contribution to crop Cd varied between 10 and 60% (mean 39%) depending on crops, soils or the SA of the root absorbed Cd (**Table 4.69**). This contribution is large, taking the low air Cd concentrations in these conditions into account. The crops were not washed prior to analysis (except for carrot roots), therefore the atmospheric contribution may be somewhat overestimated for e.g. kale or carrot leaves. It is surprising to note that the atmospheric contribution to Cd carrot leaves (36-51%) is similar as to carrot roots (37-52%) or that the contribution to grain Cd sometimes exceeded that to straw Cd. Almost no airborne Cd was detected in the carrot roots by Harrison and Chirgawi (1989). It is possible that the data of Hovmand et al. (1983) are influenced by the analytical uncertainties in estimating small differences in SA's between plants and soil.

Dalenberg and Van Driel (1990) measured the relative contribution of air Cd to the Cd concentration in different field crops grown in a rural area of in the north of The Netherlands. The fraction soil-borne Cd was calculated based on the isotope dilution principle but the SA of soil-borne Cd was measured in a separate experiment where plants were grown in a dust-free cabinet on the same ^{109}Cd labelled soil. This study is probably more reliable than the preceding two studies since it does not rely on an assumption about the SA of soil-borne Cd. In addition, differences in yield between plant grown in a cabinet and in the field are not critical for the calculation of the fraction airborne Cd. The air-borne fraction of Cd varied from insignificant (grass, spinach, carrot roots and shoots) to a maximum of 21% in wheat flour and 48% in wheat straw (**Table 4.69**). The higher contribution in wheat was ascribed to the longer growing period of that crop. These plants were grown in field conditions where the Cd deposition rate was 1.6-2.1 g Cd/ha/year, a value typical for rural areas in central Europe. Soils contained background Cd (0.16-0.29 mg Cd/kg).

These three studies show that crop Cd is primarily derived from soil, especially if the data of the third study are considered as the most reliable. It can be anticipated from these data that the fraction air-borne Cd can be neglected in crops grown in contaminated soils and if the atmospheric Cd deposition is low (e.g. soils contaminated by high metal sludge). However, these data can also be used to predict that air-borne Cd may be a significant source of Cd for crops grown in areas where atmospheric Cd is at least tenfold higher and where soil Cd is not high (or not available). As an example, based on the wheat grain data of Dalenberg and Van Driel (21% airborne Cd at about 2 g Cd/ha/year) it is predicted that grain Cd would double at an atmospheric Cd deposition of only 12 g Cd/ha/year and at which the fraction airborne Cd would be 60% (assuming similar uptake from soil). It can be demonstrated that the historic build-up of soil Cd around old metal smelters from background (~0.5 mg Cd/kg) to current concentrations of e.g. 5 mg/kg should have been associated with an average Cd deposition rate exceeding 100 g Cd/ha/year during 100 years. This deposition rate is more than 30 fold higher than the actual values for rural areas. There are no known studies of Cd concentrations in crops at these deposition rates. If the airborne Cd in crops is proportional to the atmospheric deposition rate, then it is obvious that crop Cd concentration should be dominated by airborne Cd and should be well above background concentrations at Cd deposition rates 30-fold above those at which the 3 studies were performed. The air-crop foodchain pathway may therefore dominate Cd exposure in the general population at high atmospheric Cd deposition (e.g. > 10 g Cd/ha/y). This situation may have occurred around smelters with high Cd emissions and where health effects in the general population have been described.

Table 4.69 The fraction airborne Cd in different crops. Selected data from three studies

Crop	Method$	% Airborne	Air Cd ng Cd/m^3	Soil Cd mg/kg	Reference*
barley grain	ID	41-58	1.3	0.08	1
carrot root	ID	37-52	1.3	0.08	1
wheat grain	ID	21	1.3	0.08	1
rye grain	ID	17-28	1.3	0.26	1
pea leaves	F-UF	38-48	2.1(UF)/0.2(F)	0.12-0.28	2
pea (peas)	F-UF	0	2.1(UF)/0.2(F)	0.12-0.28	2
carrot root	F-UF	4-8	2.1(UF)/0.2(F)	0.12-0.28	2
spinach	F-UF	23	2.1(UF)/0.2(F)	0.12-0.28	2
spinach	ID+F-UF	n.s.	0.3-0.5	0.3	3

Table 4.69 continued overleaf

Table 4.69 continued fraction airborne Cd in different crops. Selected data from three studies

Crop	Method$	% Airborne	Air Cd ng Cd/m³	Soil Cd mg/kg	Reference*
carrot root	ID+F-UF	n.s.	0.3-0.5	0.3	3
wheat flour	ID+F-UF	21	0.3-0.5	0.3	3

$ ID Isotope dilution
F-UF Filtered - unfiltered air comparison
* 1 Harrison and Chirgawi (1989)
2 Hovmand et al. (1983)
3 Dalenberg and van Driel (1990)

F-UF Filtered - unfiltered air comparison;

Soil factors affecting crop Cd concentrations

It is generally thought that plants absorb Cd from soil as the free Cd^{2+} ion in soil solution. Therefore, any soil factors that affect this concentration may have an effect on Cd uptake from soil. The soil Cd concentration and the soil pH are considered as the major factors controlling the plant Cd concentrations. The phytoavailability of Cd increases with increased soil acidity. Extensive reviews of the effects of soil properties or agronomic practices on Cd uptake by plants can be found elsewhere (Chaney and Hornick, 1978, Tiller et al., 1994, Grant et al., 1999). **Table 4.70**. summarises the most important factors.

Table 4.70 Factors affecting Cd concentrations in plants (after Chaney and Hornick, 1978)

Soil factors	1. pH
	2. amount of Cd present
	3. metal sorption capacity (soil organic matter content, cation exchange capacity, clay, Fe and Mn oxides)
	4. microelements: Zn, Cu and Mn
	5. macronutrients: NH_4, PO_4, K
	6. temperature; moisture content, compaction
	7. aeration, flooding=CdS
	8. recurrent *v*. single application
Plant factors	1. species and cultivar
	2. plant tissue: leaf > grain fruit and edible root
	3. leaf age: older > younger
	4. metal interactions

Soil-plant transfer factors for selected crops

The risk of increased soil Cd on elevated Cd concentrations in crops can be assessed using appropriate slopes of the dose-response curves. The plant Cd concentrations increase linearly with increasing soil Cd if the Cd is added to the soil as a Cd^{2+} salt (Haghiri, 1973; Mahler et al., 1978; Reber, 1989; Mench et al., 1989; Kádár, 1995; Brown et al., 1998). This linear trend is maintained within the environmentally relevant range (up to about 20 mg kg-1) above which curvilinear trends are found (e.g. Haghiri 1973). It is evident that soil variables, such a soil pH, influence the slope of the response curve. It is often observed in these experiments that plant Cd increases slightly more than proportionally to soil Cd (see **Figure 4.3**). This means that the Cd added to the soil is somewhat more available than Cd present in soil (e.g. Mench et al., 1989;

Brown et al., 1998). When Cd is added to the soil through diffuse sources such as P-fertiliser or atmospheric deposition, increasing crop Cd concentrations are likely to occur. Since the annual Cd addition rates from these sources are generally small (typically about 1% of the amount present in soil, see environmental part of the Risk Assessment Report) these slopes can only be assessed from long-term observations. It is, however, generally impossible to reconstruct exact dose-response curves from the historic data. Therefore, it is *hypothesised* that increasing soil Cd from these diffuse sources will lead to a *proportional* increase in plant Cd (assuming constant soil, pH, plant etc.). The slope of that proportional increase equals the so-called Cd Transfer Factor (TF), the ratio of Cd concentration in crops to that in soil. This value can be found from paired observations of soil and plant Cd concentrations in soils at background Cd concentration (see **Figure 4.3**).

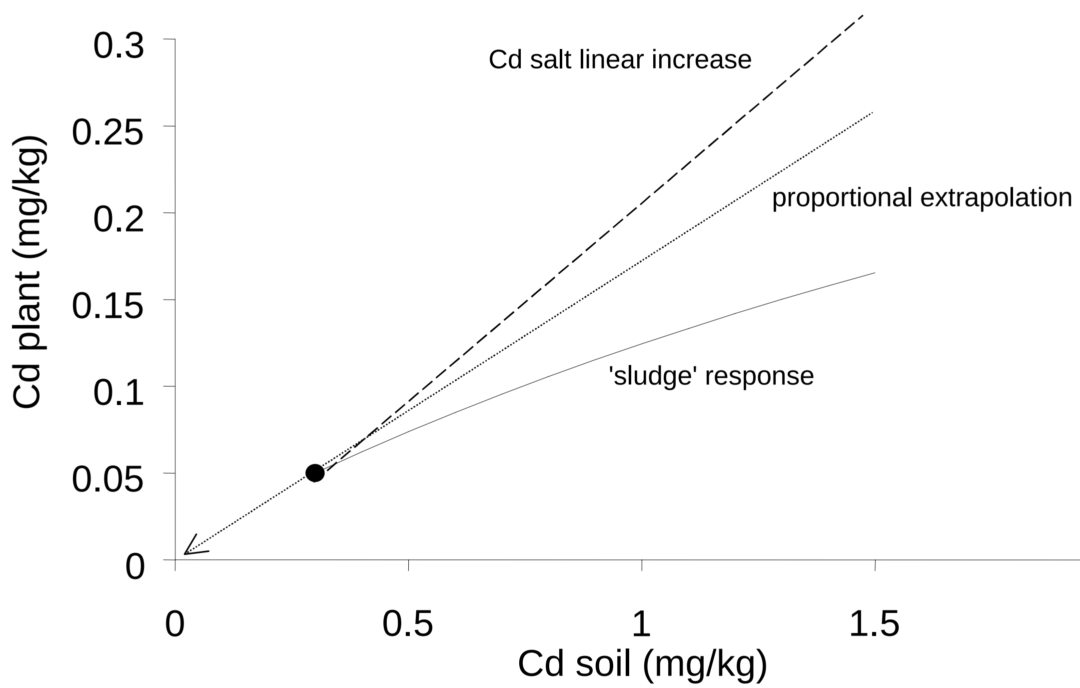
If the TF's of soils at background Cd concentrations are used for risk assessment of diffuse sources of Cd, it is ignored that recently added Cd may be more available to plants than Cd present in the soil. This is in conflict with the above-mentioned observations where Cd salts are found to be slightly more phytoavailable than the indigenous soil Cd (e.g. up to twofold difference, Mench et al., 1989). This aspect has been studied recently in detail using the isotope dilution technique. In this technique, soils are homogeneously mixed with very small quantities of Cd salt, labelled with ^{109}Cd. After equilibration, the soils are cropped in pot trials and the relative uptake of Cd from the indigenous source (soil Cd) and the recently added Cd source (^{109}Cd salt) is calculated from the $^{109}Cd/Cd$ ratio in the plants. Most of these studies confirm that the soil Cd is less available than the recently added Cd, but the differences are only small. The whole range of relative availability of ‘old’ to ‘new’ Cd is 55%-109% (mean: 79%) for 12 different soil types (Smolders et al., 1999 and references therein). Effectively, this means that recently added Cd is maximal about two times more available than soil Cd. In one soil, however, Hamon et al. (1997) found only 20-36 % relative availability of soil Cd to recently added Cd.

Studies on the relative availability of fertiliser Cd to soil Cd also confirm similar availability. Lettuce was grown in five different soils supplied with a ^{109}Cd labelled fertiliser (Jensen and Mosbaek, 1990). Two soils were sampled inside a 200-year-old barn, i.e. soils with only aged Cd, and three soils were sampled just outside these buildings, i.e. soils with aged and more recent Cd. Based on the specific activities of Cd in plants it was concluded that fertiliser Cd was equally available to plants as soil Cd and that all soil Cd was equally available to lettuce. In field trials where potato soils were fertilised with high and low Cd fertiliser P source there was only little effect on tuber Cd concentrations (Sparrow et al., 1993; McLaughlin et al., 1995). This indicates that the residual Cd in the soil is a major source of Cd to the crop during growth.

We hypothesise that the risk assessment based on actual Cd Transfer Factors in soils at background Cd levels is not underestimating plant Cd concentrations in soils that are contaminated with diffuse sources of Cd (fertilisers, atmospheric deposition, alluvial deposits). Cadmium contamination of soil from diffuse sources typically enriches soil Cd at a very low rate (see environmental part of the Risk Assessment Report). This slow increase in soil Cd warrants sufficient equilibration time with the total amount of Cd in soil.

The Cd TF's should not be used for assessing the risks of sludge-born Cd on food-chain contamination with Cd. When Cd is added to the soil through sludge application, a curvilinear increase is often found (Brown et al., 1998). Increasing sludge levels in soil increase the metal sorption capacity of the soil, and therefore, availability is reduced compared with Cd added as Cd^{2+} salt (see **Figure 4.3**). The lower bioavailability of sludge born metals soil is conserved on the long-term, even if most of the sludge organic carbon has decayed (Brown et al., 1998 and references therein). The US-EPA 503 Rule for land application of municipal sewage sludge has been calculated using linear regression on the dose-response curves of sludge trials, despite the curvilinear trend that is often observed in long-term trials (Chaney et al., 1999b). There is a wealth of information on transfer of Cd from sludge amended soils to plants. We did not find, however, a review of European long-term sludge field trials that allows identifying TF's or regression lines of Cd in plants versus soil Cd. Since such a review is beyond the scope of this risk assessment, we refer to the US-EPA risk assessment (US-EPA, 1989) that was made for the US-EPA 503 Rule for land application of municipal sewage sludge (US-EPA, 1993). Sludge of Cd and CdO producing plants is not used in agriculture but is landfilled or incinerated (see environmental part of the Risk Assessment Report). The estimated total amount of Cd that is applied onto agricultural soils through sludge is lower than that applied from P-fertiliser and atmospheric deposition (see environmental part of the Risk Assessment Report).

Figure 4.3 Schematic representation of the increase in plant Cd upon adding Cd to the soil as Cd salt or as sludge containing Cd. The proportional extrapolation is based on soil and plant Cd concentrations in soils with background Cd levels (black dot)



The Cd Transfer Factors (TF’s) should preferably be calculated from paired observations of soil and plant Cd concentrations. The TF's are no unique crop characteristics since phytoavailability of Cd is strongly dependent on soil type (see previous section). As an example, a Dutch field survey in floodplains of the Rive Meuse showed that the TF’s of endive and lettuce decrease about two orders of magnitude between pH 5 and pH 7. Paired soil-plant data of field crops are not widely available. Most surveys on crop Cd concentrations do not express their data as TF's but rather show means of soil and plant Cd concentrations. Some studies present empirical regressions that predict crop Cd concentrations based on soil factors such as soil pH, soil Cd concentrations and soil organic matter content. The TF’s are derived from these surveys by dividing mean or predicted crop Cd concentrations by corresponding mean or median soil Cd concentrations (**Table 4.70** and **4.71**). If corresponding soil Cd concentrations were not given, they were estimated from country means or medians. It was attempted to pair regional means of soil and plant Cd as good as possible rather than pairing the data of the whole survey. Only wheat grain, potatoes and some vegetables are included because of their importance in dietary Cd intake.

Surveys on crop Cd content were only found for central and northern European countries. The mean TF's for each crop vary about fourfold between the data sets (**Table 4.71**). The range in local or regional TF's is obviously wider than the range in mean TF's. As an example, mean wheat grain TF's range between 0.11-0.20. The French data show a regional TF for wheat grain of 0.02 in an area with naturally high Cd in soil (2 mg/kg) but with a high soil pH of about 8. In contrast, the TF is 0.30 in an area where plant tissue analysis suggests marginal Cu and Zn deficiency (Mench et al., 1997). The regression models predict that crop Cd concentrations are 1.2-2.4 folds higher on soils with pH 5.8 than on soils with pH 6.8 (**Table 4.72**).

Table 4.71 The Cd Transfer Factor (TF, plant to soil Cd concentration ratio) in selected agricultural crops calculated from mean or median values of soil and plant Cd concentrations in areas at ambient Cd concentrations. The TF's are not valid for sludge amended soils

Crop	Crop Cd† μg kg^{-1} fresh weight	Soil Cd μg kg^{-1}	TF (dimensionless)	Comments	Reference
Wheat grain	38 (M, dry weight based)	700(m)	0.055	UK, n=393 for grain and n=5,692 for soils. Soils and crop do not correspond	Chaudri et al., 1995(grain) McGrath and Loveland, 1992 (soils)
	58-M- (15-150)	435-m-(170-3,500)	0.11-M-(0.02-0.3)	France, mean (or median) and range, n=16; soils with elevated Cd of geological origin; TF's calculated based on means of five districts	Mench et al., 1997
	60 (m)	400 (m)	0.15	The Netherlands, n=84 for grain and n=708 for soils	Wiersma et al., 1986
	40-69 (M)	270-420(M)	0.14-0.20	Sweden, n=354, range of averages from three data sets; TF's calculated based on means in the three data sets	Eriksson et al., 1996
	56 (M)	440(M)	0.13	Germany, n=886 for grain. Soils and crops do not correspond.	Weigert et al.,1984 (grain) Crössman and Wüstermann, 1992 (soil)
Potato tuber	10.2 (M)	270(M)	0.038	Sweden, n=69	Eriksson et al., 1996
	30 (m)	400(m)	0.08	The Netherlands, n=94 (crops) and n=708 (soils)	Wiersma et al., 1986
	30 (m)	440(M)	0.07	Germany, n=133. Soils and crops do not correspond.	Weigert et al.,1984 (tuber) Crössman and Wüstermann, 1992 (soil)
Carrots	30(m)	400(m)	0.08	The Netherlands, n=100 (crops) and n=708 (soils)	Wiersma et al., 1986
	27(7-90)	300(110-830)	0.11(0.03-0.33)	Sweden, median and range, n=72; TF's (median and range) calculated based on 7 county medians for 2 subsequent years	Jansson and Öborn, 1997
Lettuce	40(m)	400(m)	0.10	The Netherlands, n=75 and n=708 (soils)	Wiersma et al., 1986

Table 4.71 continued overleaf

Table 4.71 continued The Cd Transfer Factor (TF, plant to soil Cd concentration ratio) in selected agricultural crops calculated from mean or median values of soil and plant Cd concentrations in areas at ambient Cd concentrations. The TF's are not valid for sludge amended soils.

Crop	Crop Cd† µg kg^{-1} fresh weight	Soil Cd µg kg-1	TF (dimensionless)	Comments	Reference
Spinach	60(m)	400(m)	0.15	The Netherlands, n=82 and n=708 (soils)	Wiersma et al., 1986
Leek			0.28 (pH_{KCl} < 5) 0.032 (pH_{KCl} > 5.5)	Belgium, survey in home gardens of smelter affected sandy soils	Ide, 1988
Cabbage	4(m)	400(m)	0.01	The Netherlands, n=86 and n=708 (soils)	Wiersma et al., 1986
Cauliflower	6(m)	400(m)	0.015	The Netherlands, n=84 and n=708 (soils)	Wiersma et al., 1986
Tomato	10(m)	400(m)	0.025	The Netherlands, n=40 and n=708 (soils)	Wiersma et al., 1986
Onion	13(m)	400(m)	0.032	The Netherlands, n=83 and n=708 (soils)	Wiersma et al., 1986

Table 4.72 The Cd Transfer Factor (TF, plant to soil Cd concentration ratio) in selected agricultural crops calculated from predicted crop Cd concentrations (empirical models) and mean or median Cd concentrations in corresponding soils. All Cd concentrations in µg/kg. The TF's are not valid for sludge amended soils

Crop	TF	Predicted TF		Comments	Reference
	(Predicted Cd crop concentration)/soil Cd; (µg kg^{-1} fresh weight/µg kg^{-1})	pH 5.8	pH 6.8		
Wheat grain	TF=(92-10.3pH+0.10 Cdsoil - 0.26Znsoil)/290	0.17	0.14	Sweden, n=192. Soil Cd concentration is mean of corresponding soils. Mean soil Zn concentration (Znsoil) is 42 mg kg^{-1}	Eriksson et al., 1996
	TF=(181-27pH)/100 (pH 5-6.2) TF=0.1 (pH > 6.2)	0.24	0.10	US data from 7 long-term wheat experiments (n=93). Soil Cd ranges between 30-160 µg kg-1 and most samples contain about 100 µg kg^{-1}	Gavi et al., 1997
Carrots	TF=10(3.39-0.29pH-0.01(%C)+3.5 E-4Cdsoil)/300	0.18	0.09	Sweden, n=72. Soil Cd concentration is mean of corresponding soils. Median % C is 7% in these soils.	Jansson and Öborn, 1997
Potatoes	TF=(193-24pH-0.94(%OM)+0.039Cdsoil)/270	0.18	0.09	Sweden, =69. Soil Cd concentration is mean of corresponding soils. Median % OM is 17% in these soils.	Eriksson et al., 1996

† M Mean,
m Median.

Transfer of Cd from soils to crops that are not included in the **Table 4.71** and **4.72** can be calculated using the 'relative uptake index', i.e. the Cd uptake in that crop compared with that in a reference crop when grown in the same soil. The relative uptake index (RUI) of 6 crops was assessed using lettuce as the reference crop (Brown et al., 1996, **Table 4.73**). The plants were grown in field plots that were amended with varying rates and types of biosolids and with Cd salt. The selected plots contained elevated Cd content (1-7 mg Cd/kg) in order to quantify the RUI more reliably. Small differences in the relative uptake index were found between the different plots. The dry weight based TF's of the 6 plants can be found by multiplying the dry weigh based TF of lettuce with the RUI. The Dutch data show a mean Cd TF of lettuce of 0.1 (fresh weigh basis) or 2.0 (dry weigh basis, assuming 5% dry matter). The calculated dry weight based Cd TF of lettuce in the control plots are about 2-3 (Brown et al., 1996).

Table 4.73 The relative uptake index (RUI) of 7 crops. The RUI is the ratio of Cd content in the crop to that in the reference crop (lettuce) when grown in the same plot. All data refer to dry weigh based concentrations of the edible portions. The RUI was identified from a range of sludge amended or Cd salt amended plots. Data after Brown et al. (1996)

Plant	RUI (mg kg^{-1} dry weight/mg kg^{-1} dry weight)
Bean	0.026
Cabbage	0.14
Carrot	0.29
Corn	0.34
Lettuce	1.00
Potato	0.11
Tomato	0.11

4.1.1.5 Combined exposure

For occupationally exposed people, all or not living nearby an emitting plant and possibly also exposed via consumer goods, the dominant exposure route is presumably the inhalation route especially when the occupational exposure is high.

In case the occupational exposure is low, the oral route may become predominant as this is the case in people indirectly exposed to the substance (generic) via the environment. Parameters used to assess exposure in occupational settings reflect the cadmium body burden (Cd-U) which integrates all sources and routes of exposure (occupational/inhalation + environmental/oral). The issue of combined exposure is therefore covered in Section 4.1.1.2.

4.1.2 Effect assessment

4.1.2.1 General discussion

4.1.2.1.1 Introduction

The first cases of (acute) poisoning by cadmium were reported in 1858 by the Belgian physician Sovet who described symptoms of pulmonary and gastrointestinal irritation in three individuals who had polished silverware with cadmium carbonate. Stephen (1920) and Hardy and Skinner

(1947) were among the first to suggest that serious disease(s) might occur in industrial workers undergoing chronic exposure to Cd. Prodan (1932) reported studies in which cats were exposed by inhalation to cadmium oxide fumes and dust and developed lung, liver and kidney disorders However, this intoxication was first recognised as a clinical entity only in 1948 following the biochemical and toxicological studies of Friberg in workers exposed to cadmium iron oxide dust in a Swedish accumulator battery factory (Friberg, 1948, 1950). The most striking effects of cadmium noted by Friberg were pulmonary emphysema and renal dysfunction with proteinuria.

Great concern was triggered in the late sixties by the demonstration that chronic cadmium poisoning may not be restricted to industrial workers, but might also constitute a health hazard to the general population. Reports of extensive non-occupational exposure to cadmium emerged such as the one from Japan where residents in the Fuchu area where exposed to relatively high levels of Cd for several years as a result of contamination of river water and crops by a mine discharging cadmium-laden wastewater in that polluted area (Tsuchiya, 1969). Tsuchiya described the Itai-Itai disease in 1969, the main features of which included severe pain in the bones and pathological fractures, aminoaciduria, glycosuria, altered pancreatic function and severe osteomalacia.

In 1965, Schroeder incriminated cadmium as a possible factor in the etiology of hypertension in humans. At the same time, prostatic cancers were reported to occur in workers employed in a plant manufacturing nickel-cadmium batteries in the United Kingdom. Several cohort studies were undertaken following this report, which did not confirm the excess mortality by prostatic cancer but detected an increase in mortality rates from lung cancer.

Increased prevalence’s of chromosomal aberrations were reported in Itai-Itai patients by Shiraishi and Yosida in 1972.

Studies on the chronic effects of cadmium conducted in several countries have confirmed that the kidney is the critical target organ following moderate chronic exposure to cadmium. Recent studies indicate that bone damage might also be considered as a critical effect of cadmium exposure both in workers and in the general population.

Finally, as cadmium appeared to be reprotoxic in animals, the possibility that occupational or/and environmental exposure to this substance would result in deleterious reproductive effects in humans has also been considered by several authors.

As a consequence of these diverse health effects associated with cadmium exposure, an extensive scientific literature is available, including several authoritative reviews. For this RAR, it was tried to develop a methodology to perform a useful and relevant literature search and evaluation.

Methodology

The HEDSET made available by industry was first considered as a starting point. In order to complete this data-set, conclusions of four literature reviews with an international credit (CRC 1985-1986, IARC 1992-1993, WHO 1992, ATSDR 1992-1999) have been used in a first attempt for summarising the information published before 1992, assuming that the authors did an exhaustive and well-evaluated review work. A complete, well-defined literature search has then been performed to identify all relevant publications on cadmium toxicity since 1992 and these studies have been evaluated. This was expected to be done in the time period allowed for the RAR.

However, although the four reviews provided a lot of information, it became rapidly evident that a thorough evaluation of the data was not systematically performed and a simple overwriting of their statements was not satisfying for the purpose of this RAR. Another obstacle to the use of these reviews for the effects assessment of cadmium oxide and cadmium metal was that these reviews mostly considered cadmium as an element and did not make a distinction in their evaluation of the toxicity between the different cadmium compounds. So, it was necessary for at least some effects (e.g. genotoxicity) for which most of the human studies were published before 1992 to go back to the original reports to evaluate them and to specify when possible the involved cadmium compound(s).

In industrial settings, workers may be exposed by inhalation to cadmium (oxide) fumes and/or dust. Studies (cohort, cross-sectional, case reports, etc.) on the health effects in workers occupationally exposed to cadmium oxide/metal were considered in the effects assessment. The general population is exposed to cadmium (not necessarily CdO/Cd metal) mainly by the oral route via food or water. Tobacco is an additional source of cadmium intake. In addition to data specifically dealing with CdO/Cd metal, data on cadmium compounds are included when no (not enough) information on the effects of CdO/Cd metal is available and when the studies using cadmium compounds are mechanistically relevant. Information obtained with other Cd compounds is reported with another letter type and size in the text.

Experimental data using CdO or Cd metal and critical experimental studies using cadmium compounds were described at large and included in the IUCLID.

Data quality

A) Experimental data (validated in IUCLID)

Experimental studies included in the IUCLID were validated using a reliability index (see **Table 4.74**).

Table 4.74 Reliability index and usefulness of information (within the framework of Council Reg. 793/93/CEE and ComReg. 1488/94 (Klimisch H.J., Andreae M., Tillmann U.(1996), adapted by TNO/RIVM (1997) and modified

Reliability index	Description reliability
1. Reliable without restrictions: 1	The method and description are in accordance with test guidelines [1]
2. Reliable with restrictions: 2	The method and/or description are less in accordance with test guidelines [2]
3 .Not reliable: 3	The method and/or description are not in accordance with test guidelines [3]
4. Not assignable: 4	The original data are not available [4]

1 Complete test report available: GLP, Annex V, OECD, EU etc.
Publications are not included
2 Validity of data cannot be fully established
Some modifications or omissions in method and description
Acceptable publication (e.g. according to EU- or OECD guidelines)
3 Method unknown and/or critical pieces of information are not available (e.g. identity of the substance)
Documentation not sufficient for unequivocal assessment
Do not meet important criteria of today standard test methods
4 Only abstract available
Secondary literature (reviews, tables, etc)
Further information is available in the IUCLID.

B)Epidemiological

All selected studies were evaluated with a check-list relating to population, exposure, endpoints, biases and confounders. Used check-list is reported here (see **Annex H**) and was established by Professor Philippe Hotz from the Institut für Sozial und Präventivmedizin der Universität Zürich.

4.1.2.1.2 Others

To convert from ppm to mg/m^3: (ppm) · (molecular weight of the compound)/(24.45). For cadmium: 1 ppm = 4.6 mg/m^3

To convert mg CdO to mg Cd: (·) mg/ (molecular weight of CdO) · (molecular weight of Cd)

Cd-U 1 µg/g creatinine ≅ 1 nmol/mmol creatinine

4.1.2.2 Toxicokinetics and metabolism

4.1.2.2.1 Introduction

Uptake of cadmium occurs in humans via the inhalation of air and the ingestion of food and drinking water. The major route of exposure to cadmium for the non-smoking general population is via food; the contribution from other pathways to total uptake is small. Tobacco is an important source of cadmium uptake in smokers.

In exposed workers, lung absorption of cadmium following inhalation of workplace air is the major route of exposure. Increased uptake can also occur as a consequence of contamination of food and tobacco (mainly in workers who eat or smoke at the workplace) (WHO, 1992).

Toxicokinetic studies specifically dealing with CdO are limited in number. No study specifically dealing with Cd metal was located. Since, following absorption, the biodisposition of cadmium (Cd^{+2}) is assumed to be independent of the chemical form to which exposure occurred, information obtained with other Cd compounds is considered relevant and is included in this section under "other data".

A toxicokinetic model (the Nordberg-Kjellström model) is described in **Annex A**.

Metallothionein is a metal-binding protein of low molecular weight, which has a key role in the metabolism of cadmium. Its role in the transport, distribution, and toxicity of cadmium is summarised in **Annex B**.

4.1.2.2.2 Absorption

Oral route

Studies in animals

No study regarding the oral absorption of Cd metal was identified. Only one study regarding the absorption of CdO via the gastrointestinal route has been located.

Weigel et al. (1984) exposed weanling rats to dietary CdO (0.14 in controls, 2.80 or 7.15 ppm) for up to 60 days (the form of Cd in the control group diet was probably not CdO). After 40 and 60 days of exposure, Cd content in selected organs and tissues and excreta were measured by atomic absorption spectroscopy in groups of 10 rats each. This approach gives only an estimate of the exact absorption rate. Compared to the control animals, Cd levels in hair, bone (femur), blood, and testes did not increase. Soft tissues (liver, kidney, lung and spleen) displayed significantly elevated Cd concentrations after 40 and 60 days in both dosage groups. Maximum Cd levels were 11.6 ppm in liver and 9.75 ppm in kidney on a dry weight basis, reflecting a 68 and 50 fold accumulation of the metal compared to the controls. Liver and kidney showed a dose-dependent accumulation of Cd, as the Cd organ levels were significantly higher either in the higher dosage group compared to the lower dosage group or after prolonged Cd exposure at the same dietary concentration (compared to the shorter Cd period exposure). In none of the treated groups was there a significant rise in Cd blood levels. No significant increase in the Cd urine level was recorded. The measurement of Cd concentrations in the faeces indicated that the absorption rate of Cd from orally supplied low dose was much greater than that of the higher doses. Cd retention in the body (µg Cd/g body dry weight) was not linear with the applied dose. Therefore it was assumed that Cd absorption and retention from such relatively low levels of supply follow a mechanism of saturation for this metal.

Table 4.75 Cd accumulation in rats after 40 days of exposure to CdO (mean values from 3 animals) (Weigel et al., 1984)

Cadmium accumulation	Treatment group		
	Control (0.14 ppm)	**Control (0.14 ppm)**	**7.15 ppm**
Total Cd intake (µg)	85.90	1,351.90	3,563.8
Cd retention			
µg Cd/g dry weight[a]	0.23	0.43	0.48
µg Cd/whole body [a,b]	22.40	35.30	37.00
	-(26)*	12.9	14.6
			< 0.5
Cd absorption (% of total intake)		< 1	

a For whole body analysis, rats were killed and immediately frozen in liquid nitrogen. Single rats were pulverised in liquid nitrogen and resulting powders were dried and subjected to Cd analysis
b Obtained from µg Cd/g dry weight x whole body dry weight (mean of three animals)
* The form of Cd in the low dose diet was probably not CdO, it was assumed that Cd in this diet was also in an inorganic form, which may explain the different absorption rate. This value is probably an overestimation of the absorption rate because it does assume that the Cd body content is the sole result of the 60 days feeding period.

Iijima (1972) and Wada et al. (1972) (cited in Tsuchiya, 1978) performed an experiment on the solubility of various cadmium compounds in artificial gastric and intestinal juices. The solubility of CdO was estimated to be 94% in the artificial gastric juice and 0.15% in artificial intestinal juice. Therefore, it should be considered that, although the water solubility of Cd-salts used in most experimental studies is probably substantially higher than that of CdO, differences in oral bioavailability may be less marked because of the almost complete solubilisation of CdO in gastric juice.

No data regarding the solubility of Cd metal in gastric juice was located but it is reasonable to assume that it is not greatly different from CdO.

Considering data derived from solubilisation studies in artificial analogues of digestive fluids, it must be recognised that it is likely, at least for other elements such as Pb and As, that these methods may overestimate the *in vivo* bioavailability (Ellickson et al., 2001).

Other data

Digestive absorption rates varying between 0.5 and 12% (on the average 2%) have been reported according to the animal species and the chemical form of cadmium. The higher values have been reported for monkeys and large animals compared to rodents. In small animals, absorption in the range of 1 to 2% is commonly reported (CEC, 1978; Nordberg, 1985).

Little is known about the mechanism of uptake of the various forms of Cd and the transport across the epithelial cells in the intestine.

Ingested Cd may be sequestered in the intestinal mucosal cells bound to metallothionein after which the Cd-metallothionein complex may be eliminated in faeces several days later by desquamation of the mucosal cells (Nordberg, 1985).

Andersen et al. (1992) have summarised the available knowledge as follows. "The molecular mechanism of intestinal uptake of ionic Cd has been studied mainly with high doses of Cd perfused through jejunal loops without the normal intestinal contents. The major site of uptake under more natural conditions may be elsewhere. The duodenal preference for intestinal uptake of ionic Cd suggested by some studies may be explained by the low pH of the gastric contents emptying into the duodenum. Distal to the pancreatic duct, the pH increases, and Cd will rapidly be chelated by various dietary components and thus be less available for intestinal uptake. However, during dietary Cd exposure, Cd may be absorbed as complexes with MT or other dietary constituents. If these complexes are stable at low pH, they need not preferentially be absorbed in the duodenum. Experimental data on the absorption site of "food" Cd are lacking. While the effect of MT induction on intestinal Cd uptake has been mainly studied at very high Cd doses, its effect at Cd levels relevant for dietary exposure is unknown. Intestinal MT binds Cd and reduces the rate of systemic uptake. The availability of CdMT for intestinal uptake is far lower than that of ionic Cd."

Several factors seem to have an influence on the bioavailability and the absorption after ingestion of cadmium:

- <u>Age</u>: Young animals absorb Cd to a much greater extent than adult animals (e.g. Engström et Nordberg, 1979; Kello et Kostial, 1977; Matsusaka et al., 1972 cited in CRC, 1986). The neonatal period is a time of enhanced uptake and retention of orally administered Cd. Absorption rate decreasing from 12 to 5 and 0.5% at respectively 2 hours, 24 hours and 6 weeks after birth have been measured in rats (Sasser and Jarboe, 1977). Pregnant and lactating mice absorb and retain substantially more Cd from their diets than non-pregnant mice.
- <u>Trace elements in diet</u>: A number of studies of trace element interactions have shown that a low calcium diet, iron, zinc, copper and protein deficiency increased the gastrointestinal absorption of Cd (on average by a factor of 2) (see e.g. Reeves and Chaney 2001). On the other hand, a high Cd ingestion may reduce the gastrointestinal absorption of calcium, copper, and iron.
- <u>Form of cadmium present and composition of the diet</u>: According to Andersen et al. (1992): "The bioavailability of cadmium incorporated into dietary components does not seem to differ from that of ionic cadmium. However, diet composition may markedly affect the bioavailability of ionic cadmium for intestinal uptake. Rats and mice fed human dietary items absorbed 5-8 times more cadmium than animals fed ordinary rodent pellets". Contradictory results have been reported on the bioavailability of plant Cd compared to inorganic Cd (McKenna et al., 1992). Experimental data indicate that the relative oral

bioavailability of soil-absorbed Cd, calculated on basis of the blood level, appears to be reduced more than 2-fold as compared to pure-form Cd (Cd chloride). This result indicates that the soil matrix may significantly reduce the absorption of Cd in the gastrointestinal tract (Schilderman et al., 1997).

Experimental studies indicate that ingested **Cd-MT** may be absorbed intact by the intestine, but data on the rate of absorption are contradictory. Studies on animal given a single oral dose of Cd in the form of Cd-MT, shellfish-Cd, or $CdCl_2$ have indicated similar absorption of all three forms of Cd, although differences were observed in the tissue distribution, with Cd-MT and shellfish-Cd being distributed preferentially to the kidneys. On the other hand, when animals were given Cd-MT or shellfish-Cd with the diet or via gastric tube for several weeks, the concentrations of Cd in liver and kidney were consistently lower than in animals exposed to similar doses of $CdCl_2$, indicating a lower absorption of Cd-MT (data summarised by Vahter et al., 1996). It has also been demonstrated in experimental studies that the bioavailability of Cd from boiled crab hepatopancreas is slightly lower than that of Cd from mushroom and inorganic Cd ($CdCl_2$). Cd in crab hepatopancreas is mainly associated with denaturated proteins of low solubility, whereas a large fraction of Cd in dried mushrooms is associated with soluble ligands (Lind et al., 1995).

Zn-Cd interaction: The most common sources of Cd pollution also carry high inputs of Zn into the environment (e.g. smelter emissions and sewage sludge have contaminated agricultural land with both Cd and Zn in industrialised countries). Effects of plant Zn on plant Cd bioavailability have been investigated by McKenna et al. (1992) because of this coexistence of high levels of both metals in most Cd-polluted environments and because of the importance of the nutrient Zn on Cd metabolism and toxicity in animals. Results of this study demonstrated that a) increased plant Zn lowered Cd retention in kidney, liver and jejuno-ileum of animals; b) a lower bioavailability of Cd from crops grown in Zn-Cd contaminated sites compared with Cd-only polluted sites if both metals were absorbed readily in edible plant tissues; c) plant species differed in Cd availability for identical concentrations of Zn and Cd in edible tissues because of differences in plant speciation or plant components that may interfere with absorption in the animal gut (McKenna et al., 1992; McKenna et Chaney, 1995, Reeves and Chaney, 2001).

Studies in humans

Human toxicokinetic studies carried out with CdO/Cd metal

No experimental data specifically regarding the uptake of CdO/ Cd metal by ingestion in humans has been located.

Other data

Depending on the dietary intake and on the iron status, it has been estimated that European or American adults absorb cadmium orally at average rates varying between 1.4-25 µg/day (Elinder, 1985; Lauwerys, 1982). In Japan, in Cd-polluted regions, the intake is somewhat higher, 35-50 µg per day (Oberdörster, 1992; Ikeda, 1992). Higher intakes may also be consequent to the consumption of kidney, certain mushrooms, shellfish, oysters or seal (e.g. Vahter et al., 1996; Hansen et al., 1985). Dietary Cd contributes to 99% of the total Cd absorbed in non-smokers in the general population, at least in Sweden (Vahter et al., 1991).

Data reviewed by several authors (Nordberg, 1985; WHO 1992; CRC 1986; ATSDR 1999; CEC 1978; Oberdörster, 1992; Bernard and Lauwerys, 1989) and based on limited observations in humans given radioactive cadmium compounds and comparisons of whole body burden of Cd in non-smokers with estimated daily intakes from the diet, indicate that the average gastrointestinal absorption is about 3 to 7% or even lower (see below, Vahter et al., 1996; Berglund et al., 1994) when no specific modifying factors are present (calcium, iron or protein deficiency).

As suggested by Nordberg (1985), in addition to the evident influence of iron intake, the quality of protein intake may also be of importance. There is some evidence that the type of protein to which cadmium is bound might also influences the gastro-intestinal absorption rate.

In oyster consumers (oyster species containing on average 5 µg/g wet weight, some consumers eating as high as 30 oysters /day) or seal meat eaters with, in some cases, an extremely high Cd intake (up to 500 µg/day) levels, the blood and or urine cadmium levels were increased but not greatly in proportion to the intake and disproportionately low compared to those of Japanese farmers with similar intakes from polluted rice (McKenzie et al., 1982; Sharma et al., 1983; Kjellström et al., 1977; Nogawa et al.,1989). This may be explained by a lower gastrointestinal absorption of Cd bound to the protein in these oysters or seal meat than in polluted rice. This suggests that in humans, as in other animal species (see above), metallothionein-bound Cd in food may be dealt with in a different way from other Cd compounds (Nordberg 1985; WHO 1992; ATSDR 1999). However, it is also possible that the lower bioavailability of Cd from oysters than from rice (as reflected by differences in blood and urinary Cd levels between oysters and Japanese rice consumers) might also partly depend on the differences in intake/status of iron and zinc. The higher absorption of Cd from contaminated rice has in particular been attributed to the fact that rice excludes soil Zn from its grain, which allowed increased Cd exposures without any counteracting increase in food Zn. Cultures and crops grown in Western countries such as wheat, lettuce or others do not seem to exclude Zn as rice does. An additional element which may explain the high bioavaialability of Cd from rice is the relatively low bioavailablility of Fe remaining in polished rice compared to other foods (Reeves and Chaney, 2001).

Vahter et al. (1992) found a significant but relatively weak ($p < 0.05$, $r=0.6$) correlation between cadmium concentration in blood (median 0.3 µg/l) and average daily cadmium intake (8.5 µg per day) but blood levels could vary by a factor of four for the same average intake. The authors suggested that this might be due to variations in the bioavailability and/or tissue distribution of cadmium from various foods or to dietary factors, e.g., fibres influencing the gastrointestinal absorption of cadmium.

A study in volunteers who consumed wild mushrooms (see Section 4.1.1.4.5) indicated that cadmium from mushrooms is not absorbed through the intestine in significant amounts; authors suggested that it might be due to the chitinous nature of fungi (Schellmann et al., 1984).

Seven male volunteers with normal iron stores ate the brown meat from crabs whose diet had contained radioactive ^{115m}Cd. The amount ingested by each subject varied from 24 to 166 µg. The whole body retention of the ^{115m}Cd was assessed at intervals for up to 87 days by external gamma-ray counting. Four subjects provided several days output of urine and faeces at times later than 23 days after intake for measurement of their ^{115m}Cd content. Systemic uptake of Cd derived from measurements of their residual body radioactivity several weeks after intake, averaged 2.7 ± 0.9 (SE)% (Newton et al., 1984).

In male human subjects eating a single serving of crab meat containing ^{115m}Cd (crabs fed chopped shrimps mixed with $^{115m}CdCl_2$) the whole-body retention was the same as in subjects with similarly normal iron stores ingesting $^{115m}CdCl_2$ mixed with cereals and milk (cited by Vahter et al., 1996).

Vahter et al. (1996) compared the dietary intake and uptake of Cd in non-smoking women (20-50 years) consuming a mixed diet low in shellfish (n=34) or with shellfish once a week or more (n=17). The shellfish diet (median 22.3 µg Cd/day) contained twice as much Cd as the mixed diets (median 10.5 µg Cd/day) ($p < 0.0001$), respectively. Cd in faeces corresponded to 100 and 99% of that in shellfish and mixed diets, respectively, indicating a low average absorption of the dietary Cd (< 1%). In spite of the differences in the daily intake of Cd, there was no statistically significant difference in the concentrations of Cd in blood or urine suggesting either a lower absorption of Cd in the shellfish, or a difference in the kinetics. A higher gastrointestinal absorption in the mixed diets group could also be explained partly by lower body iron stores measured by the concentrations of serum ferritin (mixed diet: median 18 µg/l, mean 31 µg/l, SD30, range 3-124; shellfish group: median 31 µg/l, mean 53, SD 55, range 17-233). When women with S-fer exceeding 20 micrograms/l were compared, the higher dietary intake of Cd in the shellfish group compared to the mixed diet group (24 versus 10µg/day) resulted in higher B-Cd (0.26 versus 0.16 µg/l), although not in proportion to the difference in Cd intake. In the mixed diet group, serum ferritin was negatively correlated with Cd-B and the main determining factor for Cd-B besides Cd-U.

Berglund et al. (1994), in a carefully designed and performed study (quality control), compared the intestinal absorption of dietary Cd in a vegetarian/high fibre diet group and a mixed-diet group (57 non-smoking women, 20-50 years). Faecal Cd corresponded to 98% in the mixed diet group and 100% in the high-fibre diet group. No differences in blood Cd or urinary Cd could be detected. The median serum ferritin concentrations were low in both groups: 18 µg/l in the mixed diet group (mean 31 µg/l, SD 30, range 3-124) and 13 µg/l in the high fibre group (mean 26 µg/l, SD 26, range 3-83). A significant negative correlation between Cd-B and serum ferritin was noted. The results also indicated that Cd absorption and/or body burden (as measured by Cd-B) were significantly and positively influenced by a depleted iron store status (serum ferritin < 20 µg/l), irrespective of the consumption of dietary fibres; a depleted iron store status was associated with, at most, a doubling of Cd oral absorption (**Table 4.76**).

Table 4.76 Median Cd-B according to serum ferritin and fibre intake (Berglund et al. 1994)

		Fibre intake (g/MJ/day)	
serum ferritin (µg/l)		< 2.6	> 2.6
< 20	Cd-B	0.27	0.31
(n=32)	Cd intake	10	12
	serum ferritin	14	8
> 30 and < 85			
(n=17)	Cd-B	0.11	0.22
	Cd intake	10	13
	serum ferritin	53	52

A frequently cited study is that of Flanagan et al. (1978), who sought to determine in a group of 22 subjects whether iron deficiency enhances the absorption of low levels of dietary cadmium. Included subjects were given a breakfast containing around 25 µg labelled cadmium chloride (range: 22-29 µg). Absorbed cadmium was determined from body cadmium counts. With the exception of 1 male with mild iron deficiency anaemia, the haemoglobin concentration, serum iron, and iron-binding capacity were reported to be within normal limits. Sixty six percent of the included female subjects had a low ferritin ranging from 0-20 µg/l. Cadmium retention curves were reported for 3 subjects from the low-ferritin group (with 3,4,19 µg/l ferritin respectively) and body retention (% dose) values were estimated to vary between 8 and 22% after ± 40 days. All results taken together, authors reported that the average absorption was 8.9 ± 2% in 10 individuals with low body iron stores (< 20 µg/l) and 2.3 ± 0.3% in 12 subjects with normal iron stores (> 20 µg/l).

Andersen (1992) stated that the human studies, although limited in number, indicate that, depending on the source of dietary cadmium, the bioavailability of cadmium incorporated in the diet may or may not be the same order as that of ionic cadmium. In this context, it is important to discriminate between the mere mixing of cadmium with the dietary component and the incorporation of Cd during the growth of the dietary component. Large inter-individual differences in fractional intestinal uptake, only partially explainable on the basis of difference of iron status, suggest the need for relatively conservative risk estimates. The combined variation due to individual factors, health, vitamins and trace element status and composition of the diet with which diet is ingested is essentially unknown at the present time (Andersen, 1992).

<u>Inhalation route</u>

Studies in animals

Studies carried out with CdO fumes

Yoshikawa and Homma (1974, cited in Tsuchiya, 1978) exposed male rats (Sprague-Dawley, body weight 250-300 g) to 20 mg/m^3 CdO fumes (median: 0.2 µm diameter) for 30 minutes and sacrificed them immediately after exposure. The deposition rate in the lungs was about 30%.

In a study by Barrett et al. (1947, cited by Nordberg et al., 1985), several animal species were exposed to CdO fumes for 10 to 30 minutes. The total doses varied up to above 15,000 min · mg CdO/m^3. The percentage retention of the inhaled dose varied between 5 and 20% as measured at autopsy.

Boisset et al. (1978) treated young male rats with five consecutive 30-minutes exposures to CdO fumes (280 min · mg/m^3). They calculated that 12% of the inhaled dose was deposited in the lungs. The estimated half-life of lung-deposited Cd was 56 days. At the end of the post exposure period (84 days), about 53% of the amount cleared from the lung could be recovered in liver and kidneys. Assuming that Cd content in the liver and kidneys represents 50% of the whole body burden, the author stated that approximately 60% of the Cd deposited in the lungs is absorbed. The absorption in this study is calculated to be 7.2% (12% of the inhaled dose is deposited; 60% of the Cd deposited is absorbed). It must however be emphasised that the severe lung damage caused by CdO might have disturbed the normal absorption process. In a further study they showed a close relationship between CdO deposited in lung (Cd Total Lung Burden) determined 72 hours following a single 30-min exposure to CdO fumes and the exposure level ($r = 0.883$, $p < 0.05$). The increase of deposited Cd was linear in the range of air Cd concentration selected (1.45, 4.50, 8.60 mg/m^3). For the authors, this could mean that a rather constant percentage of particulate CdO reached the deep lung compartment at the studied exposure levels (Boisset and Boudène, 1981).

In a thirty-day inhalation study, Glaser et al. (1986) exposed male Wistar rats continuously to submicron aerosols of $CdCl_2$, CdO (0.1 mg/m^3) and CdS (1 mg/m^3). For $CdCl_2$ and CdO, most of the cadmium was found in the lung cytosolic compartment: this was observed both at the end of the inhalation and also after an additional 2-month period in fresh air. After 1 month of Cd inhalation and also after the observation period, the lung cadmium retention was twice lower for the $CdCl_2$ exposed rats than for the CdO group. The cadmium content of the lung homogenates, cytosols, and the lung cytosolic metallothionein were found to be twice as much in case of exposure to CdO than in case of exposure to $CdCl_2$. These results were confirmed by results from alveolar lavage analysis indicating that inhaled CdO is more available to lung tissue than the very soluble $CdCl_2$. In comparison to the controls, the mean urinary cadmium content showed a slight but statistically significant increase for the CdS group at the end of the inhalation period as well as in the CdO group at the end of the observation period. It should be noted that the CdS data have been questioned due to probable oxidation to the sulfate as a function of the aerosol generating system used.

Grose et al. (1987) exposed rats and rabbits to aerosols of $CdCl_2$ and CdO (0.25, 0.45, 4.5 mg/m^3) for two hours to compare their pulmonary biochemical effects. Both compounds showed a deposition response that was linearly related to the chamber concentration. This study also indicates a greater clearance of $CdCl_2$ (58%) than of CdO (46%) at 4.5 mg/m^3 although both compounds had similar total deposition rates.

Studies carried out with Cd dusts

No study specifically using Cd metal was located.

Friberg (1950, cited by Boisset et al., 1978) exposed rabbits during 8 months to a mixture of CdO and iron oxide dusts (daily exposure level = 900 min · mg/m^3): they reported in this experiment that 30% of inhaled Cd was absorbed, suggesting that absorption of Cd from deposited CdO may be quite high.

In order to examine the translocation of CdO from the respiratory surface, Hadley et al. (1980) gave rats an intratracheal instillation of CdO tagged with ^{109}Cd (primary particle size < 1 μ). The half-life of Cd in the lung was about 4 hours at which time nearly 40% of the body burden was in the liver. These data suggest that inhaled CdO is highly soluble in the lung but the cadmium is slowly excreted from the body resulting in a long-term dose commitment to several tissues.

An aerosol of ^{115m}CdO dust (and other Cd compounds: $CdCl_2$, CdS) was administered by a single inhalation through endotracheal tubes in anaesthetised monkeys (Macaca fascicularis) and rats. Pulmonary retention was determined over a period of up to 240 days (rats) and 600 days (monkeys) by external counting of the radioactivity in the lungs with a collimated detection system (Oberdörster and Cox, 1989; Oberdörster, 1992).

CdO dust showed a very rapid decrease during day 1 to about 75% of initial lung cadmium in the two monkeys. The subsequent long-term pulmonary retention half time was 431 days with wide inter-individual variations: 302 and 637 days. Pulmonary retention of CdO dust in rats could be described by a two exponential expression: a part with a fast retention half time of 9 days, and the rest (most of the compound) cleared with a slow retention half time of 217 days.

It seems that CdO dust exhibits a much longer pulmonary retention in the rat than CdO fumes (about 70 days) although it is also solubilised in lungs. According to the authors, an explanation for this difference might be that the CdO fumes particles are smaller than the CdO dust particles and thus their solubilisation rate is faster than that for CdO dust. Note that CdS and $CdCl_2$ were cleared from the lungs of rats about three times as fast as CdO dust (half time: about 70 days). Accumulation of Cd in the kidney, as determined by *in vivo* counting, showed a continuous increase in the two monkeys. The transfer of Cd from the lungs to the kidneys and to the liver was confirmed at autopsy 240 days after exposure: 41.6% of inhaled cadmium was found in the kidney and 16.3% in the liver. In the rat, CdO dust led to an accumulation in the left kidney of about 30% of the initially deposited lung Cd.

In a further study, Oberdörster (1992) exposed rats by intratracheal instillation to 2 µg ^{115}CdO dust (geometric particle size: ≈ 1 µm), 1 µg $^{109}CdCl_2$ and 5 µg ^{115}CdS (geometric particle size: ≈ 1.4 µm). On days 1, 2, 4, 10 and 30 after instillation, rats were killed and the Cd content in lavaged lung, lung lavage fluid (separately for cellular pellet and supernatant), in kidney and in liver was determined. After exposure to CdO, about 40-60% of the total lung Cd could be lavaged (for CdS > 90%, for $CdCl_2$ < 20%); about 30-50% could be found in the pellet (for CdS about 90%, for $CdCl_2$ about 10%) and 4-8% (for CdS no detectable solubilised Cd, for $CdCl_2$ (4-8%) was found in the supernatant. These results confirm that CdO is readily solubilised in the lungs and that this solubilisation probably occurs to a large degree in alveolar macrophages. The kinetics of cadmium accumulation in liver and kidney was quite similar in the chloride and oxide groups, confirming the solubilisation of CdO in the lung and the subsequent transport to other body organs. The instilled oxide dust particles are cleared from the lung by alveolar macrophage-mediated processes, i.e. initial solubilisation with subsequent transfer to lung tissue of the solubilised fraction (major fraction) and elimination via alveolar macrophages (minor fraction) as solubilised cadmium or particulate oxide. The soluble fraction of cadmium in the lavage supernatant was interpreted as the probable result of the binding of Cd to proteins of the alveolar surface fluid (Oberdörster, 1992).

Male rats were exposed to 0.10 (MMAD 1.2 µm), 0.25 (MMAD 1.4 µm), 1 (MMAD 1.6 µm) mg CdO mg/m^3 for approximately 6 hours/day, 5 days/week, for 13 weeks (Dill et al., 1994). The lung burdens of Cd, the concentration of Cd in whole blood and the concentration of Cd in the kidneys were determined at study days 3, 9, 30 and 93.

Table 4.77 Cd concentrations from rats exposed to CdO (Dill et al., 1994)

mg CdO/ m³	Cd in rat lungs at each time point							
	Day 3		Day 9		Day 30		Day 93	
	µg Cd/g*	µg Cd**	µg Cd/g*	µg Cd**	µg Cd/g*	µg Cd**	µg Cd/g*	µg Cd**
0	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1
0.1	1.7 ± 0.3	± 0.1	4.4 ± 0.9	3.9 ± 0.6	7.3 ± 1.9	7.6 ± 0.4	16.7 ± 3.3	25.6 ± 3.0
0.25	3.2 ± 0.5	2.2 ± 0.2	6.2 ± 1.5	5.9 ± 0.5	13.1 ± 1.3	13.7 ± 1.0	25.7 ± 2.7	45.7 ± 2.3
1.0	4.9 ± 0.6	3.7 ± 0.4	10.8 ± 1.6	10.5 ± 0.6	19.3 ± 1.6	27.2 ± 2.6	34.6 ± 5.2	75.1 ± 8.5

* Lung burdens are reported as the mean total µg Cd/g of lung tissue (±SD, n = 4 or 5)

** Lung burdens are reported as the mean total µg Cd in the lungs (±SD, n = 4 or 5)

Table 4.78 Deposition rate, clearance half-life, expected steady state lung burden (Dill et al., 1994)

Exposure concentration	Deposition rate[b]	Clearance rate constant[c]	Clearance half-life[d]	Steady-state lung burden[e]
0.1	0.37	0.0073	96	52
0.25	0.74	0.0099	70	75
1.0	1.24	0.0102	68	121

b Deposition rate estimated as one-third of the 3-day lung burdens in µg Cd/day

c Clearance rate constant: b estimated from linear least squares fit (days^{-1}).

d Values of t1/2 calculated as (ln2)/b in days

e Steady-state lung burdens calculated as a/b in µg Cd

Lung burdens and deposition rates did not increase in direct proportion to increasing exposure concentration but became progressively less than expected when exposure concentrations were increased. The authors explain this behaviour by differences in deposition or clearance rate between the different exposure groups. Lung clearance half-lives did not change significantly with exposure concentration. Estimation of the deposition rate and the clearance rate constant allowed calculation of the equilibrium lung burdens expected in each of the exposure groups after long-term exposure.

Studies in humans

Studies carried out with CdO/Cd metal

No experimental data in humans have been located.

No direct data are available on CdO/Cd metal deposition, retention or absorption in the human lung. Indirect data come largely from comparisons between smokers and non-smokers.

Other data

Studies of the particle size distributions of cadmium in urban aerosols generally show that the metal is associated with particulate matter in the respirable range (WHO, 1992).

A CEC-working group (1978) has estimated that about 64% of the amount of Cd deposited in the lung can be absorbed. As in the general environment, 20-30% of the inhaled Cd is probably deposited in the pulmonary compartment. 13-19% of the total amount inhaled should effectively be absorbed.

In 1973, the Task Group on Metal Accumulation made estimates of the respiratory absorption of an aerosol of metal compounds. Estimates of the respiratory and total absorption of Cd (expressed in inhaled amount) after inhalation of an aerosol of a compound with relatively low solubility such as CdO are reported in **Table 4.79**. It is assumed that ventilation is moderate and that the Cd aerosol is deposited and cleared from the respiratory tract, as are particles in general. It is also assumed that since the Cd compound is of relatively low solubility, the particles deposited on the ciliated epithelium will be entirely transferred to the gastrointestinal tract. It can be seen from **Table 4.79** that under these assumptions, respiratory absorption will vary between 2.5 to 50% depending on particle size and alveolar deposition. The corresponding total absorption of inhaled cadmium would be 7 to 50% based on the assumption of a 5% gastro-intestinal absorption. For humans breathing at a moderate work rate (20 l/minute), the deposition in the alveolar compartment is estimated to vary from about 5% for particles with a MMAD of 10 µm to about 50% for particles with a MMAD of 0.1 µm (Nordberg et al., 1985; Nordberg 1992).

Table 4.79 Absorption after inhalation of an aerosol of Cd compounds: calculation of respiratory (r) and total (t) absorption into the body as a function of two different rates of alveolar absorption and different particle sizes for a specific deposition and clearance model (Task Group, 1973)

Particle size (MMAD) (µm)	Alveolar deposition (%)	Tracheo-bronchial-nasopharyngeal deposition (%)	Absorption (%) into body when alveolar absorption is			
			100%		50%	
			r	t	r	t
0.1	50	9	50	50.4	25	26.7
1.5	30	16	30	30.8	15	16.6
2.0	20	43	20	22.2	10	12.6

Table 4.79 continued overleaf

Table 4.79 continued Absorption after inhalation of an aerosol of Cd compounds: calculation of respiratory (r) and total (t) absorption into the body as a function of two different rates of alveolar absorption and different particle sizes for a specific deposition and clearance model (Task Group, 1973)

Particle size (MMAD) (µm)	Alveolar deposition (%)	Tracheo-bronchial-nasopharyngeal deposition (%)	Absorption (%) into body when alveolar absorption is			
5.0	10	68	10	13.4	5	8.6
10.0	5	83	5	9.2	2.5	

Gastro-intestinal absorption is assumed to be 5%
MMAD = mass median aerodynamic diameter

The amount of Cd absorbed by the pulmonary route in non-smokers from the general population does not exceed 0.02 - 0.2 µg/day (Oberdörster, 1992; Bernard and Lauwerys, 1989). However, in some circumstances, such as at specific workplaces in cadmium industries or living near a cadmium emission source, air concentration can be rather high so that Cd uptake by inhalation in those cases can exceed that from ingestion (1.4-25 µg/day).

Kjellström and Nordberg (1978, 1985) described an eight-compartment kinetic model of cadmium metabolism. The respiratory cadmium intake (A) can be diverted to the gastrointestinal tract (C1 X A) due to clearance of cadmium deposited on the mucosa of nasopharynx, trachea, or bronchi. It can be deposited in the alveoli (C2 X A) and from there be absorbed into the blood. Based on data given by the Task Group on Lung Dynamics, they estimated C1 at 0.1 to 0.2 for cadmium fumes (e.g. cigarette smoke) and at 0.4 to 0.9 for cadmium dust. Calculations with different values were carried out and a best fit between calculated and empirical values was found for C1 = 0.1 (fumes) and 0.7 (dust). In accordance with the difference in distribution of small (fumes) and large (dust) particles, C2 was estimated to be 0.4 to 0.6 for fume and 0.1 to 0.3 for dust; the best fit values being 0.4 (fumes) and 0.13 (dust) (See **Annex A**).

Indirect data obtained from comparisons between smokers and non-smokers

According to Krajncin (1987), since cadmium in ambient air is associated to particles of ca. 1-2 µm, a deposition of 20-30% is assumed and as particles of cigarette smoke are much smaller a deposition of 50% is assumed for these particles. Based on data from autopsies it was calculated that 67% of the deposited amount in the lung due to smoking is being absorbed and the same rate is assumed for ambient air. Hence, it has been calculated 14% of the inhaled amount of cadmium from ambient air and 40% from cigarettes is being absorbed.

The cadmium concentration measured in 26 brands of cigarettes purchased in eight different countries ranged from 0.19 to 3.0 µg Cd/g dry weight. The amount of cadmium inhaled from smoking one cigarette containing about 1.7 µg Cd was estimated to be 0.14 to 0.19 µg, corresponding to about 10% of the total Cd content of the cigarette (Elinder et al., 1983). According to Ellis et al. (1979), cigarette smoking results in the absorption of 1.9 µg/pack. In their comprehensive model Kjellström and Nordberg (1985) estimated that smoking 20 cigarettes per day gives rise to a cadmium intake of 3 µg/day.

Based on the comparison of Cd body burdens in human smokers and non-smokers, cadmium absorption from cigarettes appears to be higher than absorption of Cd aerosols measured in animals (Nordberg et al., 1985). The chemical form of cadmium in cigarette smoke is likely to be similar to that produced by other combustion processes, primarily CdO. The greater absorption of Cd smoke is likely due to the very small size of particles in cigarette smoke and the consequent very high alveolar deposition; the MMAD of Cd aerosol in cigarette smoke would be ≤ 0.1 µm (Norberg et al., 1985).

Elinder et al. (1976) analysed Cd in kidney cortex, liver and pancreas from 292 autopsied Swedish subjects. Based on the proportion of total Cd in the body that is accumulated in kidneys, on the biological half-time of Cd in the body and on the total amount of Cd assumed to be inhaled from 2 to 5 years of smoking; the authors estimated the respiratory absorption rate of Cd from tobacco smoke to be approximately 45-50%.

Lewis et al. (1972) have found that in non-smokers (± 60 years old, autopsy data), the mean total content of Cd in kidney (4.16 ± 0.51 mg), liver (2.28 ± 0.25 mg) and lung (0.36 ± 0.053 mg) was 6.6 mg while in persons who have smoked the equivalent of 1 packet of cigarettes per day for 40 years it amounted to 14 mg (kidney: 10.28 ± 0.57 mg; liver: 3.06 ± 0.16 mg; lung: 0.81 ± 0.053 mg).

Table 4.80 Cadmium concentration (µg/g) in wet tissues related to smoking history (Lewis et al., 1972)

Smoking category	Kidney		Liver		Lung	
	n	mean (SEM)	n	mean (SEM)	n	mean (SEM)
Non-smokers						
Male	23	13.2 (2.33)	23	1.06 (0.11)	21	0.30 (0.05)
Female	11	18.0 (2.83)	11	2.06 (0.29)	9	0.41 (0.10)
Total	34	14.8 (1.86)	34	1.38 (0.24)	30	0.33 (0.04)
Cigarette smokers						
< 1pk/day	11	24.3 (3.00)	11	1.79 (0.32)	11	0.51 (0.11)
> 1- < 2pks/day	57	32.5 (2.49)	57	2.02 (0.17)	56	0.59 (0.04)
> 2pks/day	37	30.9 (2.38)	38	2.16 (0.22)	36	0.52 (0.04)
Total	105	31.1 (1.63)	106	2.05 (0.12)	103	0.56 (0.03)
Ex-cigarette smokers	21	21.6 (2.49)	21	1.69 (0.18)	19	0.70 (0.13)
Cigar and/or pipe smokers	11	16.4 (2.23)	11	1.33 (0.25)	10	0.42 (0.06)
Total males	160	26.2 (1.30)	161	1.81 (0.09)	153	0.53 (0.03)

Using the figures from this study, and assuming that the Cd content of kidney + liver + lung represents 50% of the total body burden, this means that smokers have accumulated ± 14 mg more than non-smokers [$2 \cdot (14-6.6)$µg]. The amount retained per day due to smoking would then be 14,000 µg/($40 \cdot 365$) = 0.96 µg. Neglecting the excretion (which is a small fraction of the amount absorbed) and assuming that the cigarette smoke inhaled each day contains 3 µg Cd (Kjellström and Nordberg, 1985), the fraction absorbed would then be $0.96/3 \cdot 100 = 32\%$. If the amount deposited in the alveolar compartment is 50% of the amount inhaled (particle size < 0.3 µ), one can conclude that approximately 64% of the amount deposited is absorbed. The true absorption rate is probably higher since excretion was not taken into consideration. If one makes the same calculation but assuming that approximately 2 µg Cd are inhaled per packet, then one arrives at about 96% absorption of the amount deposited (CEC, 1978).

Moreover, since large differences exist in blood cadmium levels between smokers and non-smokers (Friberg and Vahter, 1983; Elinder et al., 1983), it is likely that the respiratory absorption may be even greater.

<u>Dermal route</u>

Studies in animals

No data on dermal absorption of CdO/Cd metal in animals were located.

Other data

Application of a 1% solution of $CdCl_2$ or of a 2% ointment of the same compound to the shaved skin of rabbits for 5 weeks or to hairless mice for 2 weeks indicated substantial percutaneous absorption of Cd which accumulated, two weeks after the end of exposure, in kidney and liver at 0.4-0.6 and 0.2-0.8% of the dose in rabbits and mice, respectively (Kimura and Otaki, 1972). $CdCl_2$ was also applied to the shaved skin of the dorsum of rats and mice during 10 days at concentrations of 1, 0.1 and 0.01%. Cd accumulated in the skin and caused local dose-dependent toxicity (hyperkeratosis, acanthosis and ulcerations). Percutaneous absorption of Cd was substantiated by measurements in blood, kidney and liver at the end of the administration period. Cd also accumulated in the skin as evidenced directly by the measurement of the element itself but also by the increased concentration of Zn in the skin, which probably reflects the local induction of metallothionein (Lansdown and Sampson, 1996). The relevance of these studies for estimating percutaneous absorption rate in the present RA of CdO is limited because (1) of the relatively high concentration of $CdCl_2$ used which caused local skin toxicity and hence influenced the degree of absorption of the element, (2) absorption rate was estimated from the concentrations measured in liver and kidney, which most probably represents an underestimation, and finally (3) because the biodisposition of CdO, which is less water soluble, is likely to vary substantially as compared to $CdCl_2$.

Studies in humans

No data on dermal absorption of CdO/Cd metal in humans were located.

Other data

The percutaneous absorption of Cd from $CdCl_2$ in water and soil has been measured *in vitro* using human cadaver skin dermatomed to 500 µm and placed in a glass diffusion cell with human serum as the receptor fluid (16 h application time) (Wester et al. 1992). The bioavailability of ^{109}Cd mixed as the chloride salt with a sample of soil (26% sand, 26% clay, 48% silt, 0.9% organic content, 80 mesh) at a dose of 13 ppb (13 µg ^{109}Cd/kg) and applied on the skin (0.04 g soil/cm²) was low; skin penetration was between 0.6 and 0.13% of the applied dose and amounts absorbed into plasma were 0.01-0.07%. These results indicate that *in vitro* soil has a relatively higher affinity for Cd than the stratum corneum; moreover, it is likely that the bioavailability of soil-bound cadmium will be even lower than from $CdCl_2$ simply mixed with the soil sample in the laboratory. Application of a water solution of ^{109}Cd at 116 ppb (116 µg ^{109}Cd/l) resulted in the penetration after 16 hours of about 10% of the applied dose into the skin fragment and about 0.5% absorption in the plasma. To simulate exposure which would be comparable with a swim or bathing, an additional experiment was performed where human skin was exposed to $CdCl_2$ in water during 30 minutes only followed by skin surface wash with soap and water. After 30 minutes, about 2% of the applied dose was measured in the skin and no cadmium was found in the plasma receptor fluid. Another set of skin samples exposed during 30 minutes and washed were perfused for an additional 48 hours; while the Cd skin content was not significantly different, 0.6% of the dose had diffused into plasma. The authors of this study conclude therefore that Cd has the ability to be absorbed into the body through human skin after a short exposure in water. These conclusions cannot be directly extrapolated to CdO, which is markedly less water soluble than $CdCl_2$.

Summary: absorption

In non-smokers, the diet provides 99% of the cadmium intake, probably not as CdO and certainly not as Cd metal. Although accurate data are lacking, it is reasonable to assume that gastrointestinal absorption of CdO is not significantly different from that of other Cd compounds, mainly because of the high solubility of CdO (and probably Cd metal) in gastric juice (94%). Therefore, data from studies conducted with other Cd compounds are judged relevant for assessing the gastro-intestinal absorption of CdO/Cd metal in this RAR.

Overall, it is considered that a large proportion of ingested Cd (including from CdO) is eliminated in the faeces and that only a few percent (maximum 5%) is absorbed via the gastrointestinal tract. This rate is, however, subject to variations according to:

- age: studies in animals indicate that absorption rate is markedly higher during the first weeks of life,
- composition of the diet: low Ca, Fe, Zn and protein contents tend to increase Cd absorption,
- source of Cd: the bioavailability of soil-absorbed and seafood Cd is lower than that of ionic Cd; that of rice-associated Cd (Japanese studies) is reported to be higher than for other sources,
- the concomitant presence of Zn in contaminated food reduces the absorption rate of Cd in studies in animals,
- depleted iron status (mainly women) increases Cd absorption rate by a factor of 2.

Therefore it is concluded that the gastro-intestinal absorption rate of CdO/Cd metal is generally below 5% when iron stores are adequate but may increase up to 5-10% when iron stores are depleted (mainly women).

After inhalation, the alveolar absorption rate of Cd from CdO varies depending on the type of exposure (fumes > dust; intra-tracheal > inhalation). It is a slow process that continues for many weeks after a single inhalation exposure (Norberg et al., 1985). Absorption rates after inhalation of CdO derived from the studies in animals range from 50% (fumes) to 30% (dust, depending on particle size, see human studies).In humans, figures of 10-30% of absorption rate according to particle size are derived for CdO dust (Task Group 1973). For CdO fumes, based on cigarette smoke studies, it can be calculated that the respiratory absorption of CdO is between 25% and 50% (Lewis et al., 1972; Friberg and Kjellström, 1974; Elinder et al., 1976). Although specific data for Cd metal dust are not available, it is reasonable to assume that it does not differ greatly from CdO.

No specific data on the dermal absorption of CdO and Cd metal were identified. However, from studies performed with soluble Cd salts, it can be deduced that their percutaneous absorption is likely to be significantly less than 1%.

Table 4.81 Summary of figures for absorption

Exposure route		CdO	Cd
oral		generally < 5% max 5-10%	generally < 5% max 5-10%
inhalation	fumes	25-50%	-
	dust	10-30%	10-30%
percutaneous		< 1%	< 1%

4.1.2.2.3 Transport and distribution

Oral route

Studies in animals

Studies carried out with CdO

Weigel et al. (1984) who exposed rats to dietary CdO (2.80 ppm and 7.15 ppm) for 60 days observed that the metal concentration was the highest in kidney and liver and increased in a dose dependent manner. The highest Cd levels were found in the kidneys. However, the ratio between the Cd concentration in kidneys and in liver decreased with increasing doses i.e. the higher the Cd dose, the more was found in the liver.

Other data

The overall retention and tissue specific distribution of Cd following a *single oral* administration is dependent on the dosage. Oral administration of low dosages of Cd (^{109}Cd mixed with $CdCl_2$; 1-10 µg/kg) resulted 7 days later in less than 1% retention and higher concentrations of Cd in kidneys than in liver. However, as the dosage of Cd increased (1-10.000 µg/kg), more Cd was retained and accumulated in the liver; the ratio of the concentration of Cd in the kidney to the liver decreased (Lehman et Klaassen, 1986).

The distribution of cadmium was also examined in rats fed diets containing either cadmium-metallothionein (Cd-MT) or cadmium chloride for 4 weeks (*subchronic* administration). Feeding with Cd-MT resulted in a dose- and time-dependent increase of the Cd concentration in liver, kidneys, and intestinal mucosa. Rats fed with high dose level Cd-MT (30 ppm) consistently showed less Cd accumulation in liver and intestinal mucosa than did rats fed with 30 ppm $CdCl_2$. Metallothionein levels in both liver and kidneys increased after $CdCl_2$ or Cd-MT exposure during the course of the study. Although metallothionein levels in liver were higher after $CdCl_2$ intake than after Cd-MT intake, renal metallothionein concentrations were the same for both groups. Authors concluded that after oral exposure to Cd-MT in the diet, there was a relatively higher cadmium accumulation in the kidneys but that the indirect renal accumulation via redistribution of Cd from the liver might be lower than after $CdCl_2$ exposure (Groten et al., 1991).

Many studies in animals have shown that in *chronic* exposure experiments, the greatest amounts of Cd are found in the liver and the kidneys. According to these experiments, 50 to about 75% of the body burden were found in these organs. Single exposure experiments in various species by the oral or parenteral routes have shown that, initially, a very high proportion of the dose is found in the liver and that with time, there is redistribution from the liver to other tissues, particularly the kidneys. In case of repeated exposure, liver cadmium levels increase rapidly and a redistribution of cadmium to the kidney occurs over a period of time. The higher the intensity of exposure, the higher the initial liver-to-kidney concentration ratio (WHO, 1992; CRC, 1986).

In contrast when administered parenterally, distribution of Cd to the liver increased from 40 to 75% of the dose, whereas distribution to kidney decreased from 30 to 7% of the dose as administered doses increased (Liu and Klaassen, 1996). There is also evidence from animal experiments that the physical form of Cd may affect its distribution. Cd administered orally as Cd-MT is distributed proportionally more to the kidneys whereas ionic Cd or Cd as chloride administered by the same route distributes primarily to the liver (Cherian et al.,1978; Cherian 1983; Maitani et al., 1984).

It should be noted that under certain circumstances, e.g. when Cd-MT is given orally, it is possible that a proportion of the absorbed Cd enters the plasma as Cd-MT. It is thereafter selectively taken up by the kidney. In long-term exposure there is a slow release of Cd-MT from the liver to blood. The observation of nephrotoxicity in rats following liver transplantation from Cd-exposed rats suggests that the major source of renal Cd in chronic exposure may be derived from hepatic Cd which is transported in the form of Cd-MT in blood plasma (Chan et al., 1993).

Studies in humans

Human toxicokinetic studies carried out with CdO/ Cd metal

No data on transport or distribution of Cd after specific exposure to CdO/Cd metal have been located.

Other data

Data concerning the transport and distribution of Cd in humans have been summarised in Nordberg and Nordberg (1988), Nordberg et al. (1985), CRC (1986), WHO (1992), CEC (1978), Bernard and Lauwerys (1986), ATSDR (1999).

<u>a) Cd in blood</u>

A great number of studies have determined reference values for cadmium in blood in the general population. However, it must be emphasised that reports on blood Cd levels in the general population have in the past often been unreliable owing largely to the difficulties encountered in the analysis of this element in blood (Lauwerys et al., 1975). In 1974, Friberg stated that there was at that time no accurate study available and that the normal range of cadmium concentration in blood could not be determined (Friberg, 1974).

Accurate determination of Cd is not a simple task, especially in low level samples. No ideal, exact, or absolute method exists. Atomic absorption spectrophotometry (AAS) has become the most commonly used method of analysis. Facilities equipped with electrothermal atomisation (ETA) and automatic compensation for non-specific atomic absorption are able to measure Cd in biological fluids at concentrations as low as 0.1 to 0.3 µg/l (CRC, 1986). The WHO (1996) has suggested the graphite furnace atomic absorption spectrometry (GFAAS) as the method of choice for the determination of Cd in blood and urine. In recent years, a new powerful analytical method, inductively coupled plasma mass spectrometry (ICP-MS), has been developed for the measurement of trace and ultra-trace elements in biological materials. This method appears to be precise, accurate, fast and allows simultaneous multi-elemental determinations of samples (Zhang et al., 1997).

In blood, most cadmium is found in the erythrocytes (about 90%). In humans with long term high exposure, whole blood Cd may be about 30 times higher than plasma Cd (Honda et al., 1982 cited in Friberg et al., 1985).

Cigarette smoking adds to Cd exposure via inhalation and this is reflected in the increased (2-5 times) blood Cd level in smokers.

According to Elinder (1985) in countries with "background" dietary Cd intakes via food of 10 to 20 µg/day, the median concentration in whole blood of adults' non-smokers, not occupationally exposed to Cd is about 0.4 to 1.0 µg/l whereas smokers have a median concentration of 1.4 to 4.5 µg/l. In a previous study, he also observed a very strong association between smoking habits and average blood Cd levels. The median blood cadmium level was 0.2 and 0.3 µg/l blood for non smoking Swedish males and females, respectively. About 90% of all non-smokers had Cd concentration in blood below 0.6 µg/l, whereas about 90% of the current male and female smokers had Cd concentration in blood of 0.6 µg/l or more. Those who smoked 20 cigarettes/day had Cd blood levels on average about 2 µg/l. Wibowo et al. (1982) have calculated that for each cigarette smoked per day, Cd-B increases by 1.6%.

A UNEP/WHO project on the assessment of human exposure to lead and cadmium through analysis of blood (and kidneys) revealed geometric means for cadmium in blood ranging from 0.5 µg/l in Stockholm and Jerusalem to 1.2 in Brussels and Tokyo. This study compared blood Cd concentrations in major cities of 10 countries (Belgium, China, India, Iran, Israel, Japan, Mexico, Peru, USA and Yugoslavia) using similar protocols and strict quality controls (Friberg and Vahter, 1983). The study has also shown the close correlation between cadmium concentration in blood and the smoking habits. Smokers had in general considerably higher concentrations than non-smokers while former smokers had values close to those of non-smokers. The differences in blood cadmium levels among the areas studied were obvious for smokers, indicating that the type of tobacco used and/or the tobacco consumption is of great importance for the exposure to cadmium. Smokers in Mexico City and Zagreb had for example about 4 times higher values than smokers in the Indian cities. Analysis of Cd in cigarettes from different countries has shown lower levels in Indian cigarettes compared to those in most other countries (Elinder et al., 1982). This may explain why previous studies did not find differences in blood Cd levels between smokers and non-smokers in India (Vahter, 1982)

Alessio et al. (1992) have reviewed papers between 1976 and 1991 in an attempt to define blood (and urinary) cadmium concentrations normally occurring in the general population ("reference values"). Because of the strong evidence in favour of the log-normality of the distribution of Cd-B values, they considered only those studies containing estimated values of GM (geometric means) and GSD (geometric standard deviations). After evaluation, they considered that only three studies were found to be suitable for the establishment of tentative reference values for cadmium in blood (Elinder et al. 1983, Friberg and Vahter 1983, Kowal et al. 1979). The results are presented in **Table 4.82**.

Table 4.82 Results of Cd-B (µg/l) data (Alessio et al., 1992)

Non-smokers (n=1502)	GM	0.56
	GSD	1.75
	75th percentile	0.84
	90th percentile	1.19
Smokers (n=785)	GM	1.50
	GSD	1.97
	75th percentile	2.47
	90th percentile	3.78

In an additional study (Watanabe et al. 1983), clearly greater Cd-B values were found in subgroups living in Japan (non-smokers: n=1,539, GM=3.42 µg/l, GSD=1.50; smokers: n=470, GM=4.19, GSD=1.48). This is in accordance with the geometric mean values observed by Ikeda (1992) in over 2,000 blood samples collected in 49 non-polluted areas in Japan (GM 3.2 µg/l in men, 3.7 µg/l in women).

In the Cadmibel study (n=2,086), Staessen et al. (1991) also observed higher blood levels in combined groups of past and current smokers than in never smokers (geometric mean: 1.4 µg/l versus 0.8 µg/l). According to Järup et al. (1998), in Sweden, the blood cadmium concentrations are 4 - 5 times higher in smokers (1 - 4 µg/l) than in non-smokers (0.1 - 0.8 µg/l). In the Netherlands, Zielhuis et al. (1977) measured blood levels (geometric means) of 0.41 µg/l (range: < 0.2-2.5) in 84 non-smokers, 0.62 µg/l (range: < 0.2-2.4) in 61 light smokers (1-9 cigarettes/day) and 0.70 µg/l (< 0.2-4.4) in 77 heavy smokers (≥ 10 cigarettes/day). The influence of smoking habits on blood Cd level has been confirmed in several more recent studies in Germany (Hoffmann et al., 2000), Sweden (Baecklund et al., 1999), Italy (dell'Omo et al., 1999) or Croatia (Telisman et al., 1997).

According to Shaham et al. (1996), exposure to cigarette smoke increases blood Cd by an average of 0.01 µg% over the background (unexposed non-smoker). This was derived from a study conducted in a population of 158 workers non-occupationally exposed to cadmium, including 47 active smokers, 46 passive smokers, and 65 unexposed non-smokers. Cd-B levels were used as biomarkers of Cd exposure and cotinine levels in urine as biomarkers of cigarette smoke exposure. The mean cadmium level in active smokers was significantly higher than in unexposed non-smokers and was very close to the mean Cd levels in passive smokers (0.097, 0.085, 0.093 µg/100 ml whole blood for active smokers, unexposed non-smokers and passive smokers respectively).

The Cd-B levels in pregnant women has been found significantly lower (mean Cd-B 0.38 µg/l, range 0.10 – 1.15) than in a control group (mean Cd-B 0.77 µg/l, range 0.10 – 2.7) living in the same area. The difference has been ascribed to the physiological hemodilution that takes place in pregnancy. Cd-U levels were however comparable in the two groups (mean Cd-U 0.52 µg/l, range 0.10 – 1.71) suggesting that no mobilisation of the metal from tissue deposits occurred during pregnancy (Alessio et al., 1984). Jakobsson et al. (1993) report a reduction of Cd-B during pregnancy in smoking women, probably ascribed to reduced smoking during pregnancy. On the other hand, the same authors report an increasing Cd-B in non-smoking women from week 32 to delivery, possibly explained by an increase in gastrointestinal absorption caused by reduced iron stores (Järup et al., 1998).

Staessen et al. (1990) measured blood cadmium in 466 randomly selected London civil servants (without occupational exposure to metals) to examine the determinants of blood cadmium. Age and employment grade were used to stratify the sample. Subjects completed a detailed health questionnaire including questions about their smoking habits and their alcohol intake. The alcohol intake was also assessed by a three-day dietary recall. Blood pressure was measured and blood sampling performed.

Table 4.83 Blood cadmium determinants in a population of London civil servants (Staessen et al., 1990)

Determinant (N)	Cd-B (µg/l)geom. means	Statistical significance
Gender*		
Females	1.06	p < 0.01
Males	0.88	
Smoking habits		
Smokers	1.51	p < 0.01
Non-smokers	0.72	
Never smokers	0.72	NS
Past smokers	0.72	
Alcohol intake*		
Regular drinkers	0.93	NS
Non-drinkers	0.9	
Menstrual status*		
Post-menopausal	1.19	p=0.05
Pre-menopausal	0.95	
Body weight		NS

* Unadjusted for age or smoking

In men, authors reported an inverse relationship between blood cadmium and employment grade ($r=-0.21$, $p < 0.001$) (Staessen et al., 1990).

The maximum value of Cd-B is generally below 3 µg/l in European subjects not occupationally exposed to cadmium. Concentrations in the order of 5-10 µg/l are extremely rare, unless in heavily contaminated areas. Much higher levels have been reported in Japanese women living in Cd polluted area (e.g. Nishijo et al., 1995; Nogawa et al., 1989). As tobacco smoking is an additional source of cadmium intake in the general population, values for Cd-B are 2-5 fold higher in smokers than in non-smokers. A recent study in a group of monozygotic and dizygotic twin pairs has recently indicated that Cd-B is not only determined by recent exposure, but also by genetic factors (Björkman et al., 2000).

Cd-B values measured in European subjects from different countries are reported in **Table 4.84**. Values for smokers and non-smokers, when available, are reported separately.

Table 4.84 Cd concentrations in blood in European subjects not occupationally exposed to Cd

Country	Study population	Cd-B (µg/l)				Reference
		Smokers		Non-smokers		
		Mean	Range or SD	Mean	Range or SD	
Belgium	M/F age: 7 - 10			0.5 - 0.8	0.1 - 3.1	Buchet et al. (1980)
	60 F 70 F 45 F age: > 60			1.2 1.6* 0.6	0.2 - 4.5 0.5 - 5.5 0.1 - 2.8	Roels et al. (1981) * : Cd-polluted area
	M (29 S, 50 NS) F (15 S, 39 NS)	2 2	1.76 P90: 5.5 1.62 P90: 5.3	1.1 0.9	0.48 P90: 1.8 0.60 P90: 1.8	Vahter (1982)
	603 M + 920 F age: 18 - 88	smokers + non-smokers M: 1.0 (0.09 - 7.9) F: 0.8 (0.09 - 9)				Sartor et al. (1992)
	1985: 64 M, age: 20-83 85 F, age: 20-82 1988 117 M,age:20-83 146 F, age: 21-90	 1.9 2.5 1.5 1.7	 0.9 - 5.08 1.1 - 4.6 0.4 - 5.08 0.07 - 4.3	 1.3 1.5 0.6 0.8	 0.7 - 2.6 0.5 - 4.5 0.2 - 2.1 0.1 - 7.7	Ducoffre et al. (1992)
	83 M/147 F age: 20 - 83	smokers + non-smokers M: 1.22 (0.2 - 4.5) F: 1.34 (0.2 - 4.6)				Staessen et al. (1992)

Table 4.84 continued overleaf

Table 4.84 continued Cd concentrations in blood in European subjects not occupationally exposed to Cd

Country	Study population	Cd-B (µg/l)				Reference
		Smokers		Non-smokers		
		Mean	Range or SD	Mean	Range or SD	
Belgium	331*/372, M/F age: 20 - 87 *vicinity of Zn smelter	smokers + non-smokers 1.14 (0.2 - 7.23)* 1.2 (0.1 - 5.08)				Staessen et al. (1994)
	600 M/F age: 20 - 65	1.3	P5: 1.17 P95: 1.4	0.6	P5: 0.56 P95: 0.63	Quataert and Claeys (1997)
Finland	42 F			< 0.1		Louekari et al. (1991)
France	440 M (age 25-55) 140 NS 86 Ex-S 214 S	 0.57 1.3	 0.37 0.95	 0.4	 0.24	Moreau et al. (1983)
Germany	M - adults	2.5	0.5 - 6.4	0.4	0.1 - 0.7	Manthey et al. (1981)
	F/M (age: 60 – 65)	LS: 1.16 HS: 1.85		0.4		Brockhaus et al. (1983)
	3864 F/M (age: 4 – 11)			0.1 - 0.2	P95 : < 0.4	Brockhaus et al. (1988)
	229 F/M (age: 6 – 9) Stolberg			0.14	< 0.1 - 0.5	Hofstetter et al. (1990)
	60 (age: 6-7) Stolberg			0.14	< 0.1-0.4	Ewers et al. (1996)
Italy	40 F (age: 18 – 39) pregnant 40 F (age: 18 – 40)	smokers + non-smokers 0.38 (0.10 - 1.15) smokers + non-smokers 0.77 (0.10 - 2.7)				Alessio et al. (1984)
	M/F: 900	smokers + non-smokers 0.6 (0.3) (0.1 - 1.7)				Minoia et al. (1990)

Table 4.84 continued overleaf

Table 4.84 continued Cd concentrations in blood in European subjects not occupationally exposed to Cd

Country	Study population	Cd-B (µg/l)				Reference
		Smokers		Non-smokers		
		Mean	Range or SD	Mean	Range or SD	
Italy	141 F/130 M (age: 18–64)	1.03	P5: 0.3 P95: 2.3	0.44	P5: < 0.1 P95: 1.4	Dell'Omo et al. (1999)
Netherlands	F (age: 20-50) 84 NS 61 LS 77 HS	 0.6 0.7	 0.2 - 2.4 < 0.2 - 2.4	 0.4	0.2 - 2.5	Zielhuis et al. (1977)
	69, age: 2- 3 vicinity of secondary Pb smelter (≤2 km)			0.76	0.4 – 1.3	Zielhuis et al. (1979)
Sweden	M (25 S, 19 NS) age: 20 - 55 F (20 S, 25 NS) age: 20 - 55	2.3 2.0	0.6 - 6.1 0.5 - 7.6	0.6 0.5	0.3 - 1.2 0.2 - 1.0	Ulander and Axelson (1974)
	473 F/M M (age: 18 – 72) F (age: 20 - 71)	 1.5 1.3	 0.2 - 7.3 0.3 - 3.9	 0.2 0.3	 0.2 - 1.2 0.2 - 1.2	Elinder et al. (1983)
	M/F:105 age: 4 - 11 vicinity of Pb smelter			F: 0.14 M: 0.13	0.06 - 0.61 0.05 - 0.42	Willers et al. (1988)
	15 F age: 23 - 53			0.3	0.16 (0.1 - 0.8)	Vahter et al. (1991)

Table 4.84 continued overleaf

Table 4.84 continued Cd concentrations in blood in European subjects not occupationally exposed to Cd

Country	Study population	Cd-B (µg/l)				Reference
		Smokers		Non-smokers		
		Mean	Range or SD	Mean	Range or SD	
Sweden	M/F: 107 , age: 26 - 52 M/F: 77, age: 7 - 10	F: 1.7 (NSH) F: 1.5 (SH) M: 2.0 (NSW) M: 1.7 (SW)	0.73 - 3.4 0.19 - 3.6 1.4 - 2.4 0.99 - 3.7	F: 0.19 (NSH) F: 0.21 (SH) M:0.19(NSW) M: 0.15 (SW) 0.08	0.09 - 0.43 0.08 - 0.56 0.07 - 0.42 0.09 - 0.33 0.04 - 0.2	Willers et al. (1992)
	F, pregnant, smelter area non-smelter area	 1.1 1.0	 0.4 0.4	 0.8 0.8	 0.3 0.3	Jakobsson Lagerkvist et al. (1993)
	F, age: 20 – 50 mixed diet (34) high fibre (23) shellfish (17)			 0.24 0.32 0.28	 0.13 (0.09-0.68) 0.23 (0.09 - 0.96) 0.14 (0.13 - 0.74)	Berglund et al., 1994;Vahter et al. (1996)
	176 M + 248 F : 49-92 y (mean 68 years)	1.3*	0.11-6.8	0.32	0.05-2.2	Baecklund et al. (1999)
UK	M/ F (53 S, 87 NS) age: 45 – 64	3.3	2.0	1.8	0.9	Beevers et al. (1980) (cited in CRC)
	M + F age: 16 – 51	4.5	2.0	2.2	0.7	Ward et al. (1978) (cited in CRC)

Table 4.84 continued overleaf

Table 4.84 continued Cd concentrations in blood in European subjects not occupationally exposed to Cd

Country	Study population	Cd-B (µg/l)				Reference
		Smokers		Non-smokers		
		Mean	Range or SD	Mean	Range or SD	
UK	Adults -A (n = 414) -B (n = 428)	Smokers + non-smokers 0.68 (P95% 2.7) 0.97 (P95% 3.4)				
	Adults -A -B	1.3 1.6		0.5 0.7		
	M/F: 466 civil servants age: 37 – 58	1.5		0.7		Staessen et al. (1990)
		smokers + non-smokers M: 1.1 (0.9) (0.4 - 5.8) F: 1.4 (1.3) (0.4 - 8.4)				
	M/F: 210 age: 16 – 70	0.61	0.2 - 3.2	0.37	0.16 – 0.8	White et Sabbioni (1998)

M Males
F Females
S Smokers
NS Non-smokers
P5 Percentile 5
P90 Percentile 90
P95 Percentile 95
SH Smoking husband
NSH Non-smoking husband
SW Smoking wife
NSW Non-smoking wife
* Excluding former smokers (n= 23)
DL Detection limit

b) Body burden

Most of the measurements have been done on tissues samples obtained at autopsy or by biopsy but more recently *in vivo* neutron activation analysis has been used to measure kidney and liver Cd concentration, mainly in Cd workers (Ellis et al., 1980, 1985; McLellan et al., 1975; Roels et al., 1981; Thomas et al., 1979; Nilsson et al., 1995; Christoffersson et al., 1987). Such measurements have clear advantages over predictions of kidney levels and risks of adverse effects obtained through monitoring blood and urine concentrations of Cd (see below). Determination of Cd concentration in the kidney cortex provides a measure of lifetime accumulation of Cd. However, *in vivo* measurements of kidney and liver concentrations of Cd require costly equipment that is not easily mobile and qualified personnel for handling. These methods are subject to greater errors than chemical determinations mainly because of difficulties in standardising the geometry of *in vivo* measurements. According to Nilsson et al. (1995), except in the presence of very deeply situated kidneys, where the minimum detectable concentration becomes high, non invasive *in vivo* XRF analysis of kidney Cd should be a useful tool for evaluating the effects of long term low level exposure to Cd and the risk of kidney damage.

Cd is retained in the organism and accumulates throughout life. Hence, the body burden increases due to the continuous exposure and the long biological half-life of about 20 years. At age 50, the average total body burden has been estimated to range from 5 to 30 mg:

The newborn baby has a total body burden of less than 1 µg of Cd (CEC, 1978; WHO, 1992).

Cadmium concentrations of 0.004 to 9.3 and < 0.002 to 1.2 µg/g wet weight of tissue were found in kidney and liver, respectively, of 41 children and juveniles by means of neutron activation analysis. The tissue cadmium concentration increases 200-fold during the 3 first years of life (Henke et al., 1970). Schroeder and Balassa (1961 cited by Flick et al., 1971) reported data suggesting that cadmium was "virtually absent" in the foetus at term. Fox (1969, personal communication, cited by Flick et al., 1971) cited an average value of 0.05 µg/g body weight in human foetus. In a recent study on metal concentrations in tissue in second trimester foetuses and infants (deceased before 3 months of age) median kidney concentration was about 0.002 µg/g wet weight in both age groups (Lutz et al., 1996). Tiran et al. (1995) examined 60 autopsy samples obtained from fœtal life to adulthood in a moderately industrialised region of Austria. Tissue Cd concentrations were very low during gestation and accumulation in the kidney and liver started immediately after birth; in adults (25-87 years) no age dependency was found (medians liver 0.85 µg/g; kidney 6.72 µg/g).

Lewis et al. (1972) determined the Cd concentrations in kidney, liver and lung derived from 172 American adults (mean age 60 years). The mean values for total organ content of the metal in kidney, liver and lungs were respectively 4.16 mg, 2.28 mg and 0.36 mg in non-smokers; 10.28 mg, 3.06 mg and 0.81 mg in smokers. They estimated that adult American non-smokers (mean age 60 years) have on average a total body burden of about 13 mg Cd (based on assumption that composite kidney, liver and lung values constitutes 40-50% of this total). The total body burden of cigarette smokers (mean age 60) was estimated to amount to 30-40 mg.

Hammer et al. (1973) found approximately the same values in a population of 40-79 years old males (assuming 50% of the cadmium body burden is in the kidneys and the liver): about 17.8 mg for non-smokers (kidneys: 5.2 mg; liver: 3.7 mg), and 37.8 mg in smokers (kidneys: 11.4 mg; liver: 7.5 mg). Applying the same assumption to data published by Shuman et al. (1974) would lead to an average body burden for adult non smokers and smokers of 19.2 mg and 32.4 mg, respectively.

Using a body neutron activation technique to measure the absolute amounts of Cd present in the left kidney and liver of 20 adult male Americans, and assuming again that kidneys and liver contain 50% of the total cadmium body burden, the average body burden at the age of 50 years was estimated to be 19.3 mg for non-smokers and 35.5 mg for smokers (Ellis et al., 1979).

These data are thus in good agreement and the difference between non smokers and smokers suggests that more than half of the cadmium found in the latter group is due to accumulation through cigarette smoking.

Cd is widely distributed in the body. After long-term low-level exposure about half the body burden of cadmium is localised in the kidneys and liver, a third of the total being in the kidneys with the major portion located in the cortex. The distribution of Cd in the kidney is of particular importance as this organ is a critical target after long-term exposure to low concentrations of cadmium. At higher levels of exposure a greater proportion of the body burden is found in the liver. The ratio between the cadmium concentration in the kidney and that in the liver decreases with the intensity of exposure; it is for instance much lower in occupationally exposed persons than in the general population (Kjellström, 1979).

The cortex/whole kidney ratio has been estimated to be about 1.5:1 by Livingstone (1972), however a re-evaluation of these data indicated that the ratio should be 1.15 (Kjellström et al., 1984). Svartengren et al. (1986) calculated a ratio of 1.25:1 for people aged 30-59 years, which is currently considered to be more exact.

The Cd content of the renal cortex increases with age up to about 50 years after which the concentrations levels off and decreases (Lauwerys et al., 1984, WHO, 1992; Nordberg et al., 1985; ATSDR, 1999; CEC, 1978). The reason for this observation remains unclear.

In the US and Europe, the mean Cd concentration in the renal cortex at age 40-50 has been shown to range from 10 to 50 ppm (Piscator and Lind, 1972; Hammer et al., 1973; Kjellström 1979; Elinder et al., 1985; Miller et al., 1976; Chung et al., 1986; Lauwerys et al., 1984; Ryan et al., 1982; Friberg and Vahter, 1983; Svartengren et al., 1986; Thürauf et al., 1986; Vuori et al., 1979; Tiran et al., 1995), corresponding to about 10-30 mg/kg calculated for a whole kidney. The accumulation of cadmium in the cortex is more pronounced in smokers than in non-smokers. Elinder et al. (1976) measured an average Cd concentration in kidney cortex at age 50 of 11 µg/g wet weight in non-smokers. When smokers were included the average concentration amounted to 22 µg/g wet weight. Using an X-ray fluorescence technique, Nilsson et al. (1995) also observed a significantly higher cadmium concentration in the kidney cortex of smokers (median: 28 mg/kg, mean: 26 mg/kg, n=10) compared to non-smokers (median: 8 mg/kg, mean: 10 mg/kg, n= 10). According to Järup et al. (1998), in general in Sweden, the kidney cadmium concentrations are about 2-3 times higher in smokers than in non-smokers.

In normal human renal cortex there is an increase in zinc content with increasing Cd levels up to the age of 50 or at least to a Cd level of 60 ppm. After this age there is a lowering of the Cd-Zn ratio (Piscator and Lind, 1972; Elinder et al., 1977; Pandya et al., 1985; Hammer et al., 1973; Chung et al., 1986; Tsuchiya and Iwao, 1978)

The studies providing data on the cadmium concentration in the kidneys of non-occupationally subjects are summarised in **Table 4.85**; these data should be compared with great caution because some of the recruited populations may not be representative of the general population (e.g. the fraction of smokers is considerably higher in “sudden death” cases than in the general population), proportions of smokers are not always comparable, age groups are not similar, residence place (polluted or not) is varying, analytical procedures are not standardised.

As illustrated below, although some studies report a decrease over the last years, it is extremely difficult to have a clear idea of the time trend concerning the Cd kidney content in non-occupationally exposed populations in Europe.

In Sweden, a recent study (Friis et al., 1998) has shown that the mean cadmium concentration in kidney cortex in subjects 40 years of age and younger was about 40% of the concentration found in a sample taken 20 years earlier (Elinder et al., 1976), while the reduction was less pronounced among older people. Such comparison of the whole 1976 and 1996 samples must be interpreted with caution because the proportions of smokers/non-smokers and males/females were not strictly identical in the 1976 and 1996 samples. However, when stratifying the analysis according to sex or smoking habits, similar decreases were noted in men or women only and in non-smokers and smokers only. Reasons suggested by the authors for this reduction could be in part reduction in tobacco smoking and probably changes in dietary habits and reduced Cd contamination from Swedish industries (Friis et al., 1998). The picture is however obscured by the apparently higher values reported by Barregard et al. (1999) in biopsies performed on living kidney donors. Differences between these data might be explained by the fact that the collection periods were different (1986-91 and 1995-96, respectively). Another difference between both studies is that the wet weight of the samples were measured and estimated in the studies by Friis et al. (1998) and Barregard et al. (1999), respectively. The samples examined in these studies were also collected in different regions of Sweden (Göteborg and Uppsala, respectively), which might also be associated with different exposure levels. Therefore, the results of both studies should not be compared at face value.

Very recently, Nilsson et al. (2000) have reported on the kidney cortex Cd concentration in 40 non-smoking farmers in the south of Sweden; interestingly, they found an inverse relationship between the drinking water pH and the kidney cortex concentration.

The data reported in the various studies from Germany present the same drawbacks and are also difficult to interpret with regard to a possible trend in Cd kidney concentrations over the last decades (Thürauf et al., 1981, 1986, Drasch et al., 1985, Mai and Alsen-Hinrichs 1997).

In the UK, the data published by Scott et al. (1987) have been substantially extended with a total of nearly 2700 kidney cortex samples analysed for their Cd content over a 16-year period (1978-1993) (Lyon et al., 1999). Interestingly, the authors did not detect any apparent trend in the temporal variation of corticular Cd content over the study period.

Overall, it must be recognised that, based on the available studies on Cd kidney content, the evidence for a decrease of the Cd body burden in the general population, as suggested by some authors, is not robust. Other elements supporting a decrease of the Cd body burden over the last decades include the reduction observed in the Cd content in deciduous teeth in German children (Ewers et al., 1993, see below) and the reduction in Cd-U observed in the Pheecad study after implementation of risk reduction measures (Hotz et al., 1999, see repeated dose - kidney).

Table 4.85 Cd concentrations in kidneys in European subjects not occupationally exposed to Cd

Country	Study population	Cd-Kidney µg/g wet weight				Reference
		Smokers		Non-smokers		
		Mean	SD or range	Mean	SD or range	
		Smokers + Non-smokers (mean, SD or range)				
Belgium	≤ 19 years (n = 4) 20 – 29 years (n = 2) 30 – 39 years (n = 11) 40 – 49 years (n = 16) 50 – 59 years (n = 35) ≥ 60 years (n = 89) all (sudden unexpected death without renal disease)	9.0 (1.3) * 16.9 (1.8) 20.8 (1.7) 39.3 (1.7) 38.4 (1.6) 29.7 (1.7) 30.5 (1.8) *: geometric mean (SD)				Vahter (1982)
Finland	≤ 9 years (n = 3) 10 – 19 years (n = 16) 20 – 29 years (n = 23) 30 – 39 years (n = 9) 40 – 49 years (n = 13) 50 – 59 years (n = 7) 60 – 69 years (n = 4) ≥ 70 years (n = 5) (traumatic accident victims)	6.78 (1.11-17.4) 25.3 (11.4-44.6) 49.4 (2.4-197) 78.1 (33.0-150) 86.9 (17.8-239) 83.7 (49.3-178) 87.1 (48.7-123) 58.7 (21.8-143)				Vuori et al. (1979)
Germany	M/ F: 38 Age: new-born – 18 (neutron activation analysis)	0.004 - 0.009				Henke et al. (1970)
	1969 Bavaria 25 M (mean 37 years) 12 F (mean 53.5 years) 1980 Bavaria 26 M (mean 37.5 years) 13 F (mean 52 years)	8.4 whole kidney (cortex : 8.4 ・ 1.25 = 10.5) 7.9 whole kidney (cortex : 7.9 ・ 1.25 = 9.9)				Thürauf et al. (1981)

Table 4.85 continued overleaf

Table 4.85 continued Cd concentrations in kidneys in European subjects not occupationally exposed to Cd

Country	Study population	Cd-Kidney µg/g wet weight				Reference
		Smokers		Non-smokers		
		Mean	SD or range	Mean	SD or range	
		Smokers + Non-smokers (mean, SD or range)				
Germany	263 autopsy cases in Bavaria (not occupationally exposed) 125 F (mean 43.5 years) 138 M (mean 41.3 years)	17.1 (calculated) 16.25 (calculated)				Drasch et al. (1985)
	Low-pollution area (Franconia) (autopsy specimen) cortex 20 M/ (mean age : 69 years) 30 F (mean age: 67 years) high pollution area (Goslar) cortex 7M (mean age : 75 years) 21 F (mean age : 63 years)	12.2 (5.3-29.1) § 12.4 (7.1-28.9) 21.4 (5.7-41.1) 19.2 (6.2-35.9)				Thürauf et al. (1986)
	212 M/F (mean age 60) (autopsy)	Rural : 24.7 (1.8)* Urban/industrial : 23.2 (1.8) Duisburg : 21.2 (1.8)		Rural : 13.9 (1.8) Urban/industrial : 12.2 (1.8) Duisburg : 17.7 (1.6)		Hahn et al. (1987)
	0.02-87 years (forensic medicine) 22 F 40-60 years > 60 years 33 M 40-60 years > 60 years	23 (9.4-43.0) 15.1 (5.5-23.4) 31.1 (6.2-78.0) 15.3 (5.1-26.8)				Mai and Alsen-Hinrichs (1997)

Table 4.85 continued overleaf

Table 4.85 continued Cd concentrations in kidneys in European subjects not occupationally exposed to Cd

Country	Study population	Cd-Kidney µg/g wet weight				Reference
		Smokers		Non-smokers		
		Mean	SD or range	Mean	SD or range	
		Smokers + Non-smokers (mean, SD or range)				
Sweden	Cortex					Elinder et al. (1976)
	0-29 years	15.3	1.8	7.4	1.35	
	30-39 years	18	2.06	19.35	2.51	
	40-49 years	22.5	1.4	17.4	1.82	
	50-59 years	24	2.62	9.6	2	
	60-69 years	22	1.6	13.5		
	70-79 years	16.2	2.2	9.7		
	80-89 years	13				
	(victims sudden and accidental death)					
	≤9 years (n = 7)	2.4 (1.75)				
	10-19 years (n = 24)	6.4 (1.9)				
	20-29 years (n = 32)	10.6 (1.9)				
	30-39 years (n = 34)	18 (1.9)				
	40-49 years (n = 40)	21.7 (1.8)				
	50-59 years (n = 43)	18.3 (1.9)				
	60-69years (n = 39)	18.1 (2.3)				
	70-79 years (n = 41)	12.0 (2.0)				
	80-89 years (n = 25)	7.4 (2.0)				
	90-99 years (n = 6)	5.6 (1.5)				
	20 M, age: 30-59	18.4 (12.2)				Svartengren et al. (1986)
	cortex	6.9 (4.8)				
	medulla	14.4 (9.7)				
	whole kidney					
	(sudden and unexpected deaths)					
	15 M/F Age: < 3 months (termination, abortion or deceased)	0.0031 (0.0017) (0.0007 – 0.0059)				Lutz et al. (1996)
	M/F (age: 26 – 60) 10 S, 10 NS (volunteers, XRF analysis)	28	< DL – 41	8	< DL - 15	Nilsson et al. (1995)
		NB: 11/20 < DL				

Table 4.85 continued overleaf

Table 4.85 continued Cd concentrations in kidneys in European subjects not occupationally exposed to Cd

Country	Study population	Cd-Kidney µg/g wet weight				Reference
		Smokers		Non-smokers		
		Mean	SD or range	Mean	SD or range	
		Smokers + Non-smokers (mean, SD or range)				
Sweden	M/F collected from 1995-96					Friis et al. (1998)
	10-19 years			2.48	1.59	
	20-29 years			3.87	1.45	
	30-39 years	5.13	1.44	5.52	1.57	
	40-49 years	8.49	1.94	6.82	2.81	
	50-59 years	19.1	1.55	6.92	1.54	
	60-69 years	18.8	1.54	6.17	1.67	
	70-79 years	17.8	1.61	4.92	2.29	
	80-89 years	16.3	1.41	6.31	1.96	
	M/F					
	0-9 years	0.47				
	10-19 years	2.48 (1.46)				
	20-29 years	4.22 (1.47)				
	30-39 years	7.52 (1.83)				
	40-49 years	13.2 (2.24)				
	50-59 years	13.6 (1.9)				
	60-69 years	10.1 (1.98)				
	70-79 years	9.35 (2.24)				
	80-89 years	5.93 (1.80)				
	(sudden and accidental deaths)					
	M/F living donors mean 53 years (30-71) collected from 1986-91	24	(14-35)	17	(13-34)	Barregard et al. (1999)
	40 male farmers south of country	low pH drinking water (med : 5.2)	high pH drinking water (med. 7.8)	Cd-B (med. 2.6)	Cd-B (med. 1.3)	Nilsson et al. (2000)
		18*	14	15	8	
UK	Autopsy cases mainly from Scotland					Scott et al. (1987)
	15 M/11 F	geometric mean (SD)				
	50-59 y	15 (19)				

Table 4.85 continued overleaf

Table 4.85 continued Cd concentrations in kidneys in European subjects not occupationally exposed to Cd

Country	Study population	Cd-Kidney µg/g wet weight				Reference
		Smokers		Non-smokers		
		Mean	SD or range	Mean	SD or range	
		Smokers + Non-smokers (mean, SD or range)				
	Autopsy cases from various regions mainly natural death + some accidents 2,659 M/F (about equal)	Overall mean : 19 (median 16) M : geometric mean : 14.8 F : geometric mean : 14.6 Smokers : geometric mean : 16.4 Non-smokers : 12.6 increase with age				Lyon et al. (1999)

M Males
F Females
S Smokers
NS Non-smokers
DL Detection limit
§ Median (66% range)
* Geometric means and SD
* Median (n=10 in each group)

The levels of Cd in the liver of adults not exposed to cadmium at work are generally much lower than those in the renal cortex and range approximately from 0.5 to 5 ppm (mg/kg wet weight) but values as high as 25 ppm have been reported) (Kowal et al., 1979; Piscator and Lind, 1972; Hammer et al., 1973; Chung et al., 1986; Lauwerys et al., 1984; Sumino et al., 1975; Vuori et al., 1979; Elinder 1985; Tiran et al., 1995).

In tissues such as muscle, bone and fat, the cadmium concentration is usually below 1 mg/kg wet weight (Elinder, 1985).

The cadmium (and lead) content has been measured in deciduous teeth of 103 German children born in 1968/73 and 1982/83; a 60% reduction in the Cd content was reported suggesting that cadmium body burden of children and probably also of the general population of Germany has decreased during the last years (Ewers et al.,1993).

<u>Inhalation route</u>

Studies in animals

Experimental studies carried out with CdO/Cd metal.

No inhalation study specifically using Cd metal was located.

In the inhalation study by Yoshikawa (1975, cited in Tsuchiya, 1978), an accumulation of cadmium was noted in the lungs, the kidneys, followed by the liver and spleen.

In an experiment by Yoshikawa and Homma (1974, cited in Tsuchiya, 1978), Sprague Dawley rats were exposed to 20 mg/m^3 CdO fumes (0.3 µm diameter) for 30 minutes, and sacrificed immediately after exposure, after 24 hours, and after 7 days. Cd in the lungs decreased rather rapidly but Cd in the kidney continued to increase during the seven days. Other organs such as the heart, liver, and spleen showed the highest concentrations 24 hours after exposure ceased and decreased after that time.

Oberdörster et al. (1979) observed that one day after rats were exposed to a single inhalation of CdO (930 µg/m^3, aerodynamic diameter of the particles about 1µm), 5% of the initial lung burden was found in the liver and kidneys, whereas after 100 days these tissues contained 9% of this initial burden.

Table 4.86 Relative organ burden of Cd after single inhalation exposure. Lung Cd content on day 0 is set at 1, and organ burdens are expressed in relation to this (Oberdörster et al., 1979)

Time after exposure	Organ	Relative organ burden
1 day	Lung	0.85
	Liver	0.05
	Kidney	0
100 days	Lung	0.26
	Liver	0.06

In the rat study by Boisset et al. (1978), (5 consecutive daily 30-minutes exposures to a CdO aerosol of 280 min · mg/m³), about 53% of the amount cleared from the lungs could be recovered in the liver and kidneys at the end of the post-exposure period (84 days).

It was shown in a 30-day inhalation study carried out with $CdCl_2$, CdS and CdO in rats that the lung cytosolic metallothionein was twice as much after exposure to CdO than after exposure to $CdCl_2$ (Glaser et al., 1986).

Hart (1986) exposed rats from 1 to 6 weeks to a CdO aerosol (1.6 mg/m^3). Pulmonary metallothionein quantities increased significantly with repeated exposure to Cd. Both Cd and metallothionein increased as a function of exposure suggesting that metallothionein might be responsible for Cd retention within the lung. Prior exposure to Cd significantly increased the amount of Cd translocated to the kidneys but not to the liver. Liver and kidney burdens increased during the 6 weeks of exposure. Tissue metallothionein values rose but hepatic metallothionein increased faster and to a greater extent than renal metallothionein.

Male rats were exposed to 0.10 (MMAD 1.2 µm), 0.25 (MMAD 1.4 µm), 1 (MMAD 1.6 µm) mg/m^3 CdO for approximately 6 h/day, 5 days/wk, for 13 wk (Dill et al., 1994). The lung burdens of Cd, the concentration of Cd in whole blood and in the kidneys were determined at study days 3, 9, 30, and 93. The concentration of Cd in blood was found to be very low at all time points. This could be due to the slow clearance of CdO from the lungs (resulting from low solubility or protein binding) but is most likely explained by a result of rapid clearance from blood to the kidney and the liver (no measurement in liver tissue). The amount of Cd measured in the kidneys of exposed animals represented a significant fraction of the accumulated lung burden and the concentration of Cd in the kidney was linearly proportional to the accumulated lung burden.

Table 4.87 Cd concentrations in whole blood from male rats exposed to CdO (Dill et al., 1994)

Exposure concentration (mg CdO/m^3)	Concentration of Cd (ng/g) in whole blood at each time point			
	Day 3	Day 9	Day 30	Day 93
0	< 1.5	< 1.5	< 1.5	< 1.5
0.1	< 1.5	2.5 ± 2.7	2.5 ± 0.6	3.7 ± 1.4
0.25	< 1.5	3.6 ± 1.9	4.2 ± 0.8	5.0 ± 1.1
1.0	3.6 ± 0.9	3.9 ± 0.9	11.1 ± 1.7	22.5 ± 8.4

Values are reported as the mean (n = 4 or 5) concentration in whole blood (±SD)

Table 4.88 Cd concentrations in kidney from male rats exposed to CdO (Dill et al., 1994)

Exposure concentration (mg CdO/m^3)	Concentration of Cd (µg/g) in kidneys at each time point			
	Day 3	Day 9	Day 30	Day 93
0	0.013 ± 0.007	0.03 ± 0.02	0.012 ± 0.004	0.015 ± 0.005
0.1	0.03. ± 0.006	0.23 ± 0.03	0.86 ± 0.08	3.1 ± 0.4
0.25	0.057 ± 0.004	0.45 ± 0.12	8 ± 0.1	5.5 ± 0.1
1.0	0.20 ± 0.01	1.1 ± 0.2	4.6 ± 0.5	5 ± 2

Values are reported as the mean (n = 4 or 5) concentration in kidneys (±SD)

Other data

Data concerning experimental studies carried out with Cd salts have been reviewed by e.g. CEC, (1978), Nordberg (1985), Nordberg and Nordberg (1988), CRC (1986), WHO (1992), ATSDR (1999).

After absorption from the lungs, Cd is transported via blood to other parts of the body. In plasma, Cd is predominantly bound to proteins of high molecular weight (albumin or larger) a short time after exposure. To a large extent Cd bound in this form will be taken up by the liver where it accumulates. After induction of metallothionein (4-24 hours after a single exposure), Cd is present in liver mainly bound to metallothionein.

Studies in humans

Human toxicokinetic studies carried out with CdO/Cd metal.

No data on transport and/or distribution of Cd after specific inhalation exposure to CdO/Cd metal have been located.

Other data

Data concerning the transport and distribution of Cd in humans exposed via the inhalation route have been summarised in Nordberg and Nordberg (1988), Nordberg et al. (1985), CRC (1986), WHO(1992), CEC (1978), Bernard and Lauwerys (1986), ATSDR (1999).

Populations exposed to cadmium compounds by the inhalation route are essentially the working population exposed via their occupational activities (e.g. non-ferrous smelter, production of batteries) but also part of the general and the working population smoking tobacco. Most studies that examined the general population also reported values for the fraction of smokers. Therefore information about the distribution of cadmium in smokers can be found in both sections: oral route and inhalation route.

a) Cd Blood

In workers, after the start of exposure Cd concentration in blood increases linearly then levels off when equilibrium is reached (Lauwerys et al., 1979, 1980; Kjellström and Nordberg, 1978, Roels et al., 1981; Ghezzi et al., 1985). Blood Cd level is considered to be related to more recent exposure, it is a useful indicator of exposure during recent months. After long term high Cd exposure, an increasing proportion of blood Cd will be related to body burden. After long-term low-level exposure, cadmium concentration in blood might be, on a group basis, an indicator of cadmium concentration in liver (Elinder et al., 1978).

Reported Cd concentrations in the blood of exposed workers are generally between 5 and 50 µg/l but levels between 100 and 300 µg/l have resulted from extreme exposure (Roels et al., 1982; Hassler et al., 1983; Christoffersson et al., 1987). After cessation of long-term high exposure, blood Cd reflects mainly the body burden and the decrease of whole blood Cd displays an initial fast component with a half-time of 3-4 months and a slow component with a half-time of about 10 years. Järup et al. (1983) observed that workers who left Cd exposure displayed a bi-phasic elimination of cadmium in blood. The half-time in the fast component was about 100 days (75-128 days) and in the slow component ranged from 7.4 to 16 years. Hence, workers with relatively long exposure duration but whose Cd exposure has ceased have elevated blood Cd levels for several years and for some times blood cadmium level may serve as an indicator of the body burden or the concentration in the kidney.

Cigarette smoking adds to occupational Cd exposure via inhalation and this is reflected in the increased (2-5 times) blood Cd level in smokers.

Wibowo et al. (1982) have calculated that for each cigarette smoked per day, Cd-B increases by 1.6% (See also: oral route).

b) Body Burden

High body burden values have been found in cadmium-exposed workers without functional renal impairment (up to 450 or even 600 ppm) (Kjellström, 1979; Friberg et al., 1974; Roels et al., 1981; Friberg and Vahter, 1983; Ellis et al., 1981, 1985; Elinder, 1985).

In studies carried out with *in vivo* neutron activation analysis on exposed workers, the average ratio of the Cd concentration in the renal cortex to that in the liver has been reported to be about 8 (Ellis et al., 1981) or 7 (Roels et al., 1981). These values are lower than what can be estimated on the basis of the studies carried out in the general population (> 10 up to 30) reviewed by Elinder (1985). Cadmium concentration in liver is proportional to duration and intensity of Cd exposure in workers with and without renal dysfunction (Roels et al., 1981). This is in agreement with studies in animals showing a greater proportion of accumulated Cd in the liver when exposure level increases (Nordberg and Nordberg, 1988).

After the development of severe Cd-induced renal dysfunction, Cd is lost from the renal tissue. When renal dysfunction occurs, the cadmium level in the renal cortex decreases and urinary excretion increases. The reduction of renal Cd is very likely due to a release of cadmium from the kidney combined with a depressed reabsorption of circulating Cd. This phenomenon explains why in most severely poisoned workers and also in patients with Itai-Itai disease, the concentration of Cd in the renal cortex may be relatively low in contrast to the liver level.

In cases of severe renal dysfunction, the kidney cadmium concentration is generally lower and ranges between 20 and 120 mg/kg wet weight (Friberg et al., 1974). *In vivo* NAA measurements have confirmed the disproportionately low kidney levels in workers with renal dysfunction. Roels et al. (1981) showed that Cd workers with renal dysfunction (total proteinuria > 250 mg/g creatinine and/or β_2-microglobulinuria > 200 µg/g creatinine and/or albuminuria > 12 mg/g creatinine) excrete significantly more cadmium in urine than those without renal dysfunction. They also observed that the renal cortical cadmium level of Cd workers with renal dysfunction does not increase proportionally to the hepatic cadmium level whereas in the Cd workers without renal dysfunction there is a significant positive correlation. The results of this investigation suggest the existence of a range of critical Cd-renal cortex level (i.e. approximately from 160 to 285 ppm), above which the probability is very high that all persons will show sign(s) of renal dysfunction. Authors estimated also that renal dysfunction is likely to develop in workers with Cd-liver concentrations between 30 and 60 ppm (Roels et al., 1981).

This estimate has been reassessed after the depth of the left kidney was measured in each worker by echography. The correction introduced for kidney depth demonstrates that the critical level of 30 ppm in liver corresponds to a corrected critical level of cadmium in renal cortex of 216 ppm (Roels et al., 1983).

Table 4.89 Cd parameters in Cd workers without and with renal dysfunction (Roels et al., 1981)

Parameters	Without renal dysfunction n=66			With renal dysfunction n= 23		
	Mean ± SD	Median	Range	Mean ± SD	Median	range
Cd-B µg/l	14.2 ± 1.0	11.9	1.8-34.8	17 ± 1.6	15.1	7.3-31.1
Cd-U µg/g creatinine	13.8 ± 1.36	11.9	0.65-61.6	21.4 ± 2.34	22.1	4.23-46.3
Cd liver ppm	32.8 ± 1.67	32	10-61	66.5 ± 7.57	59	28-158
Cd kidney ppm	167.4 ± 8.17	155.2	51.7-310.3	175.4 ± 13.7	165.5	103.4-300
Cd total body	171.5 ± 7.33	172	64-300	284.5 ± 25.7	268	134-556
Proteinuria *	89.5 ± 5.11	80.1	16.1-237.3	288.3 ± 38.9	233.1	90.6-825.2
β_2-microglobul **	67.6 ± 6.51	49.6	5.4-199	3,826 ± 1154	1659	29.6-20465
albuminuria *	3.5 ± 0.21	3.1	0.7-10.5	19.3 ± 3.61	16.7	1.6-57.8

* mg/g creatinine
** µg/g creatinine

In the study of Ellis et al. (1980, 1985), kidney cadmium levels ranged from 0.9 to 57 mg and liver concentrations ranged from 0.8 ppm to 120 ppm in 82 industrially exposed workers. Comparison values for the control group (n=10) were 0.4 mg to 11.8 mg for the kidney and 0.6 to 7.9 ppm for the liver. A biphasic relationship between kidney and liver Cd levels was observed. The kidney and liver Cd levels increased until approximately a 40 ppm concentration was reached in the liver. Thereafter, the kidney levels decreased as the liver concentration continued to increase. The kidney Cd level at which this change occurred was approximately 31 mg for the total kidney. Further estimates of the critical level, based on years of exposure and renal dysfunction yielded estimates of 31 to 42 mg Cd (300-400 µg/g for the renal cortex, assuming the weight of the total kidney is 145 g and a ratio of 1.5 between cortex and total kidney concentration). However as mentioned above, according to Svartengren et al. (1986) a conversion factor of 1.25 might be more appropriate than 1.5 when calculating cadmium concentrations in kidney cortex from data on cadmium concentration in the whole kidney. As a result of this finding it may be necessary to recalculate the estimates of the concentration of cadmium in kidney cortex of Roels et al. (1981) and Ellis et al. (1980, 1985) based on neutron activation analyses *in vivo* of whole kidney. The use of 1.25 instead of 1.5 would result in a 17% reduction of the estimated critical cadmium concentration.

In cadmium-exposed workers Cd in liver may be up to 100 times greater than normal. Hepatic cadmium levels exceeding 150 ppm have been reported in Cd workers (median: 59 ppm, mean: 66.5, SD: ±7.57, range: 28-158 ppm) (Roels et al., 1981). Ellis et al. (1985) measured levels up to 120 ppm. Harvey et al. (1975) measured liver cadmium levels of between 35 and 200 ppm in patients or industrial workers with known or suspected Cd poisoning.

The WHO reports levels up to 300 ppm (WHO, 1992).

<u>Other routes</u>

Studies in animals

Intratracheal instillation

Hadley et al. (1980) treated rats with an intratracheal instillation of 15 µg ^{109}CdO (primary particle size < 1.0 µm) in physiological saline. The half-life of Cd in the lungs was about 4 hours, at which time nearly 40% of the Cd body burden was in the liver. At 24 hours, the distribution of Cd (expressed as % of body burden, mean ± SD) was: lung, 23.9 ± 3.0; liver, 58.4 ± 3.9; kidney 2.7 ± 1.8 and testes, 0.22 ± 0.0. Two weeks after instillation the lung, liver and kidney had 18, 57 and 8% of the body burden, respectively. Less than 10% of the instilled Cd was excreted during the first 2 weeks.

Parenteral administration

It has been shown that shortly after parenteral administration of Cd most of the Cd in the liver is bound to high molecular weight proteins in the cytosol, but that already after 8 hr more than 80% of the Cd present in the liver cell cytoplasma is bound to MT (Elinder et Nordberg, 1985). Subsequently Cd-MT appears in blood probably as a result of release from the liver. Cadmium in blood is mainly found in the red blood cells, where it is bound to a low molecular fraction protein similar to metallothionein.

In a study in transgenic mice, lacking MT-I and MT-II (MT-null mice), it was found that after one parenteral administration of $CdCl_2$ the urinary elimination of Cd was much faster than in control mice; this finding confirms the role of MT in the tissues retention of Cd. It was also observed that the renal Cd concentration continued to increase with time in control mice but not in MT-null mice, confirming that an important source of Cd in the kidney is the uptake of Cd-MT (Liu et al., 1996).

It has been shown that Cd administered IV distributes mainly to the liver (70%) and kidneys (10%) and is independent of the dose, in contrast to oral administration (Cherian et al., 1978; Cherian, 1983; Maitani et al., 1984).

Summary

Once absorbed, cadmium is distributed to most tissues of the body but tends to concentrate in the liver and the kidney. It enters the blood and most is found in the erythrocytes (about 90%). The maximum value of Cd-B is generally below 3 µg/l in European subjects not occupationally exposed to cadmium. Values for Cd-B are 2-5 fold higher in smokers than in non-smokers. Cadmium accumulates throughout life. Hence, the body burden increases due to the continuous exposure and the element has a biological half-life of about 10-20 years. After long-term low-level exposure, about half the body burden of cadmium is localised in the kidneys and liver, a third of the total being in the kidneys with the major portion located in the cortex. The distribution of Cd in the kidney is of particular importance as this organ is a critical target after exposure to cadmium. The ratio between the cadmium concentration in the kidney and that in the liver decreases with the intensity of exposure. High body burden values have been found in cadmium-exposed workers without functional renal impairment (up to 450 or even 600 ppm). In non-occupationally exposed subjects the cadmium concentration in the kidneys is generally between 10 and 50 ppm (2-5 fold increase in smokers).

4.1.2.2.4 Elimination

Oral route

Studies in animals

Experimental studies carried out with CdO/Cd metal

No study regarding the elimination of Cd after oral exposure to CdO/Cd metal has been located.

Other data

Studies on several animal species, by several routes of exposure to Cd salts have shown that urinary excretion of Cd increases slowly during the early phase of exposure. As kidney tubular dysfunction develops, a sharp increase in excretion is observed and this leads to a reduction of renal cadmium concentrations.

Before renal tubular impairment has occurred, a correlation exists on a group basis between the body burden and urinary concentration of Cd (CRC, 1986; WHO 1992, ATSDR 1999).

Studies in animals have shown that at low or moderate doses, true excretion of Cd in faeces (originating from absorbed Cd) is about the same as the urinary excretion. True faecal excretion is dose-dependent and partly proportional to body burden particularly at low doses. The faecal excretion comes mainly from the intestinal mucosa and only a smaller part originates from bile and pancreatic fluid (Nordberg et al., 1985).

Exposure of mice and rats to cadmium compounds (mainly $CdCl_2$) has shown that during lactation, mammary tissue takes up and retains Cd. Transfer of Cd to milk, however, appears to be limited (Bhattacharyya et al., 1981, 1982; Pietrzak-Flis et al., 1978; Lucis et al., 1972).

Studies in humans

Human toxicokinetic studies carried out with CdO/Cd metal

No data regarding the elimination of Cd after oral exposure to CdO/Cd metal have been located.

Other data

The considerable age-related accumulation of Cd in the body indicates that only a small part of cadmium absorbed from long term low level exposure will be excreted. Most absorbed Cd is excreted very slowly, with urinary and faecal excretion being approximately equal (Kjellstrom and Nordberg, 1978). The daily excretion which takes place via faeces and urine represents only about 0.005 - 0.02% of the total body burden of Cd, which corresponds to a biological half life of about 10 - 20 or even 40 years (Nordberg et al., 1985).

a) Urine

The mean urinary cadmium levels in individuals neither occupationally exposed to cadmium nor living in a cadmium-polluted area is generally below 1-2 µg/g creatinine. In Sweden, non-smokers have urinary cadmium concentrations of 0.02-0.7 µg/g creatinine (Järup et al., 1998). There is, however, a large variation among individuals. Several studies have shown that in the general population, urinary Cd excretion increases with age and this increase coincides with an increased body burden. Women have generally higher urinary Cd concentrations than men, probably as a reflection of higher body burden associated with increased gastro-intestinal absorption (relative iron depletion) (Sartor et al., 1992). Post-menopausal women had, in the same study (Sartor et al., 1992) a significantly higher 24-hour Cd-U than younger women, independently of age. In addition, when comparing, in men and women, Cd urinary excretion rates "normalised" for urine dilution as µg Cd/g creatinine, it is important to take into consideration that creatinine urinary excretion is significantly lower in women (lower muscular mass).

It has recently been reported that the increase of Cd-U with age was more pronounced in multiparous than in women with 1 or no child (0.020 versus 0.009 µg/l per year; p:0.046). This effect was interpreted as the consequence of increased gastro-intestinal absorption during the episodes of relative iron deficiency associated with pregnancies. In those women followed during 2 years from early pregnancy, Cd-U (and Cd-B) were correlated with iron status (ferritin, transferrin receptor) throughout the study period. In late gestation, more than 50% of the women developed exhausted iron stores (soluble transferrin receptor/serum ferritin ratio of 500) and 15% developed tissue iron deficiency (soluble transferrin receptor > 8.3 mg/l). The latter had 40-50% higher Cd-B and Cd-U during lactation than those who did not develop tissue iron deficiency (Akesson et al., 2002).

At the group level, there is a close relationship between the cadmium concentrations in urine and kidneys. If one assumes a linear relationship between cadmium in urine and kidney, which, however, may not always be totally correct (e.g. after an acute exposure to high Cd levels or after renal damage has occurred), a Cd-U of 5 µg/g creatinine corresponds to a concentration of about 100 mg/kg in the kidneys, while 2.5 µg/g in urine corresponds to about 50 mg/kg in the kidneys (Järup et al., 1998). Orlowski et al. (1998) conducted an autopsy study in 39 Polish subjects not occupationally exposed to Cd and deceased at the age 42 ± 14 years and found that the urinary cadmium level determined post mortem is strongly correlated with the renal Cd levels. Eliminating cases with high urinary proteins and extrapolating from sets of data with elevated urinary protein concentration to its normal range yielded a value of 1.7 µg/g creatinine as equivalent to the renal level of 50 µg/g ww.

The urinary excretion of Cd is influenced by smoking habits, but not to the same extent as blood Cd levels (Elinder, 1985). Sartor et al. (1992) estimated that the urinary excretion of cadmium due to smoking (20 cigarettes per day) increases by about 63% at age 45. The 24-hour Cd-U in male past-smokers was dependent on the quantity of tobacco smoked daily. This was not found in female past-smokers smoking less tobacco than men (16.6 versus 22 cigarettes per day in men past-smokers) and for a shorter time.

In subjects living in polluted area, high urinary Cd cadmium concentrations can be observed and when tubular proteinuria develops even higher urinary excretion occurs (e.g. Nishijo et al., 1995).

Most of the cadmium in urine is probably bound to metallothionein. The urinary metallothionein concentration can be measured quantitatively with a sensitive radio-immunoassay. Using this technique, a good correlation between the urinary cadmium and metallothionein concentration has been found in people exposed to Cd in the general environment as well as in workers occupationally exposed to Cd before the onset of renal dysfunction (Shaikh et al., 1990a,b; Roels et al., 1983; Tohyama et al., 1981; Chang et al., 1980).

It can be concluded from the literature data that, at low exposure level (general environmental conditions), the amount of Cd absorbed may be insufficient to saturate all the body binding sites (e.g. induced metallothionein) and that the urinary excretion increases in proportion to the amount of Cd stored in the body and not proportionally to the exposure levels. In such circumstances, there is a significant correlation between urinary Cd and Cd in kidney.

In high exposure conditions (workers, Itai-Itai), the Cd binding sites in the organism become progressively saturated and the cadmium that is still absorbed cannot be further retained in the kidney: it is rapidly excreted in the urine. In these situations, the urinary concentration could be more a reflection of current exposure levels. The relative influence of the body burden and the recent exposure on Cd-U depends on the exposure intensity.

If exposure continues and kidney damage occurs, urinary Cd excretion is much increased. Eventually, the amount of Cd that can be released from the kidney decreases progressively and the urinary Cd concentration follows the same trend.

In newly exposed subjects, a latent period may thus be observed before Cd in urine correlates with exposure.

In a comprehensive model developed for human Cd toxicokinetics, parameters for urinary excretion were derived by adjustments to empirical data from human and animal studies. Urinary excretion is mainly a function of body burden but a part of this excretion is directly dependent on blood cadmium. At steady state, the total daily excretion would be the same as total daily uptake. Using these methods and assumptions daily urinary excretion is estimated to be 0.009% of body burden (Kjellstrom and Nordberg, 1978, 1985) (see **Annex A**).

Cd-U values measured in European subjects from different countries are reported in **Table 4.90**.

Values for smokers and non-smokers, when available, are reported separately.

A recent survey conducted in the US (NHNES, 1999) conducted on 1,007 subjects aged 6 years and older found a geometric mean for Cd-U of 0.29 µg/g creatinine (P10, 0.11; P25, 0.17; P50, 0.27; P75, 0.46 and P90, 0.74), which is consistent with the most recent findings in Europe.

Table 4.90 Cadmium concentrations in urine of non-occupationally exposed Europeans (M: males F: females)

Country	Study population	Cd-U				Reference
		Smokers		Non-smokers		
		Mean	Range or SD	Mean	Range or SD	
Belgium	60 F 70 F 45 F age > 60			0.093 0.055 0.04 µg/h	0.015 – 0.365 0.012 – 0.119 0.002 – 0.156 µg/h	Roels et al. (1981)
	83M/147F age: 20-83	smokers + non-smokers M: 1.0 (0.1 – 3.8) µg/24 h F: 0.9 (0.2 – 5.3) µg/24h				Staessen et al. (1992)
	603 M + 920 F age: 18-88	smokers + non-smokers M: 0.9 (0.08 – 3.8) µg/24 h F: 0.8 (0.06-8.0) µg/24 h				Sartor et al. (1992)
Italy	40 F (age: 18 – 39) pregnant 40 F (age: 18 – 40)	smokers + non-smokers 0.52 (0.1 – 1.71) µg/l smokers + non-smokers 0.62 (0.24 – 1.34) µg/l				Alessio et al. (1984)
UK	203 M/F healthy adults (16-70 y)	Mean : 0.48 (0.05-3.4) µg/g creatinine				White et al. (1998)
Germany			0.2 – 0.8 µg/l		0.1 – 0.3 µg/l	Ewers et al. (1993)
	4728 adults (18-69 y)	GM : 0.178 µg/g creatinine p10 : 0.06 p90 : 0.55				GerES (III) (1998) in Becker et al. (2003)

Table 4.90 continued overleaf

Table 4.90 continued Cadmium concentrations in urine of non-occupationally exposed Europeans (M: males F: females)

Country	Study population	Cd-U				Reference
		Smokers		Non-smokers		
		Mean	Range or SD	Mean	Range or SD	
Czech Republic	1192 adults (816 M/ 376 F) 2008 children (1052 boys/ 956 girls)	Median : 0.36 µg/g creatinine 0.29				Benes et al. (2002)
Netherlands	290 M, F (20-65 y, mean 41 y)	Smokers + ex-smokers + non-smokers GM (SD) : 0.44 (0.43), median : 0.34 P95 : 1.35, range 0.03-2.76 µg/g creatinine				Fiolet et al. (RIVM) (1999)
Sweden	10 F 16 M (age: 40-49)			0.33 0.21 µg/g creatinine		Elinder et al. (1978)
	F M (± 40)	0.5 0.5 µg/g creatinine		0.4 0.2 µg /g creatinine		Jawaid et al. (1983)
	34 F			0.15 µg/g creatinine		Berglund et al. (1994)
	11 M living within 500m of a Ni/Cd plant			0.9 µg/g creatinine		Järup et al. (1995)
	21 F 28 M living within 1 km of a Ni/Cd plant			0.3 0.6 µg/g creatinine		Järup et al. (1995)
	35 M (age: 24 – 68)	0.2 µg/g creat (including smokers)				Järup et al. (1995)

Table 4.90 continued overleaf

Table 4.90 continued Cadmium concentrations in urine of non-occupationally exposed Europeans (M: males F: females)

Country	Study population	Cd-U				Reference
		Smokers		Non-smokers		
		Mean	Range or SD	Mean	Range or SD	
Sweden	471 M 533 F living close to a Ni-Cd battery plant in Southern Sweden	0.82 nmol/mmol (p10 : 0.18- p90 : 1.8) 0.66 (0.15-0.80)				Järup et al. (2000)
		Ex-smokers		Never smokers		Olsson et al. (2002)
	57 M	0.26 ± 0.13 nmol/mmol creatinine	0.15-0.66	0.18 ± 0.17	0.065-0.41	
	48 F non-smokers, living on farms in South Sweden	0.40 ± 0.17	0.23-0.70	0.30 ± 0.17	0.097-0.99	

Significant determinants of Cd-U were identified by stepwise multiple regression analysis in the cross-sectional study conducted by Sartor et al. (1992). Selected variables included place of residence (urban area: Liège or Charleroi; rural area: Hechtel-Eksel or NoorderKempen with different degrees of environmental exposure to cadmium), age, body mass index, social classes (low, intermediate, high), smoking habits (never, past, current smokers), current and past quantity of tobacco smoked (g per day), alcohol consumption habits (never, past, current consumer), current and past alcohol intake (g per day), serum ferritin, zinc, menopause and use of the contraceptive pill. Past alcohol consumption, current and past alcohol intake, contraceptive pill intake, serum ferritin, and zinc did not influence urine cadmium significantly after the above determinants were controlled for.

Table 4.91 Determinants of 24-h Cd-U (in µg/24h) ranked by decreasing percentage of explained variance[a] (Sartor et al., 1992)

Determinant	Men	Women
Age (linear and quadratic terms)	26.8	29.0
Place of residence	7.4	9.4
Current smoking and quantity smoked	6.3	3.3
Social class	3.3	0.7
Past quantity smoked	2.7	n s
Current alcohol consumption	0.4	1.3
Body mass index	0.4	n s
Menopause	-	0.3

a Values are percentage of variance explained by the determinant (squared partial correlation coefficient)
n s Non significant

<u>b) Faeces</u>

It is extremely difficult to distinguish between faecal Cd content representing mainly the unabsorbed part of ingested Cd and true excretion of Cd, i.e. originating from absorbed Cd. Faecal content is often a good indicator of ingested Cd as 90-95% of ingested Cd is unabsorbed and eliminated via faeces. True faecal excretion is difficult to study in humans due to the preponderance of unabsorbed Cd. The contribution from bile and pancreatic fluid is dependent on dose and body accumulation, but it is only a relatively small proportion of Cd in faeces as intestinal mucosa is a greater contributor (Nordberg et al., 1985).

Kjellström et al. (1978) collected three consecutive daily faecal specimens from 80 volunteers in the age range of 5 – 69 years in order to estimate the average daily cadmium intake via food. Average daily faecal cadmium amount was about 16 µg for non-smokers and 19 µg for smokers.

In the study conducted by Vahter et al. (1992), the average daily faecal elimination of cadmium (8.9 µg) was essentially the same as the average cadmium content of the duplicate diets (8.5 µg). Assuming that faecal excretion of cadmium, previously absorbed in the body, is about the same as the urinary excretion, they estimated that a few percent of the cadmium in faeces originated from faecal excretion of endogenous cadmium. The amount of cadmium inhaled, cleared from the airways, swallowed and eliminated in faeces was 10-20 ng per day at the most.

Berglund et al. (1994) and Vahter et al. (1996) have measured faecal cadmium in relation to diet-cadmium and blood-cadmium: 98 – 100% of the ingested Cd was found in the faeces (see Section 4.1.1.2).

In a comprehensive model developed for human Cd toxicokinetics, parameters for faecal excretion were derived by adjustments to empirical data from human and animal studies. This model assumes that faecal excretion constitutes the unabsorbed part of ingested cadmium plus "true" faecal excretion originating from blood via the intestinal wall and from bile. Using these methods and assumptions daily faecal excretion is estimated to be 0.009% of body burden. In this model biliary cadmium excretion is assumed to be in the range 0 to 0.0001 µg/day (Kjellström and Nordberg, 1978, 1985) (see **Annex A**).

c) Hair

Cd is also eliminated through hair but this route is of limited importance for total excretion and does not significantly contribute to the biological half-time. Numerous studies report measurement of Cd concentrations in the hair and, in individuals without excessive exposure to cadmium, these levels range usually between 0.5 and 2 mg/kg.

For instance, examining 50 autopsy specimens, Oleru (1975) found that Cd concentration in hair was significantly correlated with cadmium concentration in kidney (r=0.52) and in liver (r=0.36) but not with Cd concentration in lung (r=0.15). Ellis et al. (1981) found no significant correlation between the cadmium levels measured in scalp hair and the *in vivo* measurements of cadmium in kidney and liver, neither in environmentally nor in occupationally exposed subjects. Bergomi et al. (1989) also found no correlation between cadmium concentration in hair and Cd-B and Cd in teeth.

The geometric means in smokers versus non-smokers observed by Wolfsperger et al. (1994) in hair samples from 79 young adults living in Vienna and Rome were 0.075 versus 0.038 µg/g.

Concentrations of Cd in samples obtained from 474 pre-school children during summer were on the average nearly twice as high as those in samples obtained during winter (GM: 0.116 versus 0.0637 µg/g). Sex, race, hair colour and place of residence were also found to influence the Cd hair level (Wilhelm et al., 1988; Carvalho et al., 1989).

It is highly difficult to distinguish between endogenous Cd and Cd externally deposited on the hair and the interpretation of data from hair analysis is difficult.

d) Milk

Under normal conditions cadmium is found in human breast milk at concentration < 1 µg/l (Abadin et al., 1997) or even < 0.1 µg/l (Hallen et al., 1995).

Radisch et al. (1987) reported median blood and milk concentrations of 0.54 and 0.07 µg/l in 15 non-smoking mothers and 1.54 and 0.16 µg/l in 56 smoking mothers. Milk concentrations of cadmium were approximately 10% of corresponding blood concentrations.

It has been suggested that Cd levels in human milk are 5-10% of levels in blood possibly due to limited transfer from blood because of metallothionein binding of Cd in blood cells (Radish et al., 1987). It should also be considered that Cd in milk is in equilibrium with that in serum not in whole blood. As indicated above, the serum Cd concentration is very low in comparison to whole blood.

The amount of Cd excreted via skin, hair, sweat, saliva and milk is considered of minor importance in comparison with that excreted via urine and gastrointestinal tract.

Inhalation route

Studies in animals

Studies carried out with CdO/Cd metal

No study regarding elimination of Cd after inhalation exposure to CdO/Cd metal has been located.

Studies in humans

Human toxicokinetic studies carried out with CdO/Cd metal

No specific toxicokinetic studies using CdO/Cd metal by inhalation were located.

Other data

a) Urine

In cadmium exposed workers, high urinary Cd cadmium concentrations can be observed and when tubular proteinuria develops even higher urinary excretion occurs (e.g. Ghezzi et al., 1985; Verschoor et al., 1987).

As it was described for the subjects exposed to cadmium via the oral route, it can be concluded from the literature data that, at low exposure level (general environmental conditions), the amount of Cd absorbed may be insufficient to saturate all the body binding sites (e.g. induced metallothionein) and that the urinary excretion increases in proportion to the amount of Cd stored in the body and not proportionally to the exposure levels. In such circumstances, there is a significant correlation between urinary Cd and Cd in kidney. Roels et al. (1981) have compared, among other parameters, Cd-U and cortical kidney Cd concentration (neutron capture γ-ray analysis) in 309 male workers from two Belgian zinc-cadmium plants. Among those workers without renal dysfunction, they found a significant correlation (r: 0.40) between both parameters. Significant correlation between Cd-U and cortical kidney concentration measured by X-ray fluorescence in 30 workers from a Ni-Cd battery plant in Sweden (Borjesson et al., 1997)

In high exposure conditions (workers) and in the absence of renal damage, the Cd binding sites in the organism become progressively saturated and the cadmium that is still absorbed cannot be further retained in the kidney: it is rapidly excreted in the urine. In these situations, the urinary concentration could be more a reflection of current exposure levels. The relative influence of the body burden and the recent exposure on Cd-U depends on the exposure intensity.

If exposure continues and kidney damage occurs, urinary Cd excretion is much increased. Eventually, the amount of Cd that can be released from the kidney decreases progressively and the urinary Cd concentration follows the same trend.

In newly exposed persons, a latent period may thus be observed before Cd in urine correlates with exposure.

In a comprehensive model developed for human Cd toxicokinetics, parameters for urinary excretion were derived by adjustments to empirical data from human and animal studies. Urinary excretion is mainly a function of body burden but a part of this excretion is directly dependent on blood cadmium. At steady state, the total daily excretion would be the same as total daily uptake.

Using these methods and assumptions daily urinary excretion is estimated to be 0.009% of body burden (Kjellstrom and Nordberg, 1978, 1985) (see **Annex A**).

b) Faeces

Faecal excretion in workers exposed to Cd reflects mainly Cd dust swallowed from industrial air and/or incidentally ingested from contaminated hands. Adamsson et al. (1979) studied the elimination of cadmium in faeces in a group of 15 workers exposed to CdO dust in a nickel-cadmium battery factory. The cadmium content in faeces was on the average 619 (range: 97-2,577) µg/day in smokers (n=7) and 268 (range: 31-1,102) µg/day in non-smokers. It was estimated that Cd naturally occurring in food and cigarettes, Cd excreted from the gastro-intestinal tract, and Cd transported from the lungs by the mucocillary clearance to gastro-intestinal tract, only could explain up to 100 µg of the Cd found in the faeces. The much higher values measured were interpreted as being the result of absorption of Cd from contaminated hands and other body surfaces. It is emphasised that smokers inhale the Cd contained in the tobacco smoke from contaminated cigarettes but that direct oral contact with contaminated cigarettes or pipes is an additional factor.

In a comprehensive model developed for human Cd toxicokinetics, parameters for faecal excretion were derived by adjustments to empirical data from human and animal studies. This model assumes that faecal excretion constitutes the unabsorbed part of ingested cadmium plus "true" faecal excretion originating from blood via the intestinal wall and from bile. Using these methods and assumptions daily faecal excretion is estimated to be 0.009% of body burden. In this model biliary cadmium excretion is assumed to be in the range 0 to 0.0001 µg/day (Kjellstrom and Nordberg, 1978, 1985) (see **Annex A**).

Summary

Only a small part of the Cd absorbed from long-term low level exposure will be excreted. The daily excretion which takes place via faeces and urine represents only about 0.005 - 0.02% of the total body burden of Cd, which corresponds to a biological half life of about 10-20 years.

The amount of cadmium in urine of exposed workers increases with body burden, but the amount of cadmium represents only a small fraction of the total body burden unless renal damage is present: in this case, excretion increases markedly.

Cd can be excreted via skin, hair, sweat, saliva and milk, but the amount is considered of minor importance in comparison with that excreted via urine and gastrointestinal tract.

4.1.2.2.5 Transplacental transfer

Studies in animals

Studies carried out with CdO/Cd metal

No study specifically regarding the transplacental transfer of CdO/Cd metal was located.

Other data

Data concerning experimental studies carried out with Cd salts are summarised below (Webb and Samarawickrama, 1981; Christley and Webster, 1983; Pietrazk-Flis et al., 1978;

Bhattacharyya et al., 1982; Sorell and Graziano, 1990; Bhattacharyya, 1983, Whelton et al., 1993, Saltzman et al., 1989; Goyer 1991; Goyer and Cherian, 1992).

Studies carried out with Cd salts (mainly $CdCl_2$) have indicated an accumulation of Cd in the placenta during gestation, but generally no significant transfer and accumulation in the foetus. Concentrations in rats and mice foetus have been reported to be only 1% of that observed in the placenta. A cadmium/zinc/copper/iron interaction has been observed in cadmium salts-exposed pregnant animals. It has been suggested that adverse perinatal effects such as birth weight and congenital malformations reported in experimental studies are mediated through cadmium-induced maternal zinc retention. Maternal injections of cadmium or Cd given to pregnant rats in drinking water (from 50 ppm) decrease the transportation of zinc from the mother to the foetus as well as the zinc-dependent enzymes present in the foetus (e.g. Elinder 1985; Sorell and Graziano, 1990). Retention of cadmium in the placenta has been related to the synthesis of and binding to metallothionein. Several studies have demonstrated the presence of metallothionein in rodent and human placenta. Zinc and copper also bind to metallothionein in placenta. These findings raised the following question: if cadmium, zinc and copper are all bound to metallothionein, how is it that Cd is retained and copper and zinc undergo maternal to foetal transfer? The latter two are important essential metals for the foetus and foetal blood levels are similar to, or higher than those of the mother. The following hypotheses for this selective retention have been proposed:

- Zn could be released from MT and readily transferred, whereas Cd would remain tightly bound to MT (De et al., 1990);
- Cu-MT and Zn-MT have a selective affinity for proteolytic enzyme activity present in trophoblasts which facilitates their release to foetal blood, whereas Cd-MT is resistant to this effect (Goyer and Cherian, 1992; Min et al., 1992).

It has been shown that MT-null mice foetuses accumulated significantly more Cd (3-10 fold) than control foetuses but never exceeded 0.3% of administered dose. These data suggest that placental MT reduces maternal to foetal Cd transfer, however the low doses of Cd administered in this experiment resulted in high levels of Cd accumulation in liver and kidney with a low concentration of Cd reaching the placenta. Thus the role of placental MT as a barrier for Cd is inconclusive (Lau et al., 1998).

Recently an inhalation study has used pregnant guinea to examine transplacental transfer of Cd after inhalation exposure to low levels of $CdCl_2$ ($\pm$ 50 µg Cd/m^3) (Trottier et al., 2002). The choice of this test animal was dictated by two factors: their relatively long gestation period and their largely human-like hemomonochorial placental structure. Inhalation of Cd during the late gestation (50-55 days, 4-hour/day during 1 or 5 consecutive days) led to a transfer from the mother through the placenta and an important deposition of Cd was observed in the fetal brain, liver, and to a small extent, heart. These results indicate that, at least in this species, even though the placental acts as a barrier, transport and fetal distribution of Cd is not negligible at relevant exposure levels.

Studies in humans

Human toxicokinetic studies carried out with Cdo/Cd metal

No data specifically regarding the transplacental transfer of Cd after exposure to CdO/Cd metal have been located.

Other data

According to the WHO review (1992), the cadmium concentration in the human placenta is usually 5-20 µg/kg wet weight.

Gross et al. (1976) reported Cd concentrations in the liver, kidney and hair of humans of many ages from foetal through old age. Cadmium concentrations in the kidney and liver of human foetuses, and infants from 0 to 1 month old were determined and, in contrast to those in adults, were found to be "barely detectable."

In 1975 and 1976, Lauwerys et al. (Lauwerys et al., 1978; Buchet et al., 1978; Roels et al., 1978) have undertaken a survey among 472 pregnant women living in different areas of Belgium in order to evaluate the extent of exposure to heavy metals during foetal life, their possible biological effects, and the environmental factors which may influence the intensity of exposure. They observed that the median value was 50% lower in new-born blood than in mother blood. Increased Cd-B due to cigarette smoking in mothers (non-smokers n=331: mean 1.2 µg/l, median: 0.9, range: 0.1-9.7; SD: 1.2; smokers n=109: mean: 2 µg/, median: 1.8,, range: 0.2-6.1, SD: 1.2) was not associated with a similar increase of Cd-B in new-borns (non-smoking mothers n=332: mean 1 µg/l, median: 0.5; range: 0.1-10.3; SD: 1.3; smoking mothers n=109: mean: 0.7 µg/l, median: 0.5, range: 0.1-8.8, SD: 0.9). The median value of Cd in placenta was 1.08 µg/100 g wet weight, indicating that the placenta concentrates Cd about 10-fold in comparison with maternal blood. The mean concentration observed in the placenta amounted to 1.32 µg/100 g wet weight (SD: 0.87), with a mean value of 1.25 (SD: 0.86) for the non-smoking mothers and 1.57 (SD: 0.92) for the smoking mothers.

Hubermont et al. (1978) conducted a study of placental transfer of lead, mercury and cadmium in 70 women living in Libramont, a rural area in Belgium. The median Cd concentration in maternal blood taken at delivery was 1.2 µg/l (mean: 1.4; range: 0.1-6.3) whereas that in placenta at term was almost 10-fold higher: 9.3 µg/kg (mean: 11.4; range: 3.0-37.5). Blood of the new-borns, taken from the umbilical cord contained a median cadmium concentration of 0.4 µg/l (mean: 0.6; range: 0.1-4.3) or one-third of that in the mothers. The smoking habits were found to influence only Cd blood concentration in mothers but not in foetuses.

Van Hattum et al. (1981) collected, during 1978 and 1979, 61 placentas from mothers living in the Amsterdam area in The Netherlands. Mean placental cadmium levels in smokers (66 ± 33 ng/g dry weight) appeared to be slightly elevated compared to those in non-smokers (51 ± 20 ng/g dry weight).

In the study of Alessio et al. (1984), Cd-B levels in 40 pregnant women (not occupationally exposed to Cd) were significantly lower (mean Cd-B 0.38 µg/l, range: 0.10-1.15) than in a control group living in the same area (n=40, mean Cd-B: 0.77 µg/l, range: 0.10-2.7). The difference was ascribed to the hemodilution that takes place during pregnancy. The Cd-B (mean: 0.24 µg/l, range: 0.10-1.33) and Cd-U (mean: 0.21 µg/l, range: 0.10-0.96) levels in the newborns were significantly lower than those found in the mothers (mean Cd-U: 0.52 µg/l, range: 0.10-1.71).

Korpela et al. (1986) from Finland determined the Cd concentration in maternal and umbilical cord blood and in amniotic fluid in 19 parturient women at delivery. Six placental and amniotic membrane tissue specimens were also investigated. Cd concentrations in maternal blood (1.1 ± 0.9 µg/l) and amniotic fluid (1.0 ± 0.2 µg/l) were significantly higher than in umbilical cord blood (0.4 ± 0.2 µg/l) and there was no significant correlation between these values. The highest concentrations of cadmium (35.1 ± 24.2 µg/kg ww) were found in amniotic membranes.

Kuhnert et al. (1987a,b) carried out a study to determine whether zinc status would be affected in pregnant women exposed to Cd through cigarette smoke. Increased Cd-B levels in pregnant women as the result of smoking increased Cd and Zn levels and decreased cord red blood cell zinc levels. Significantly higher levels of both Cd and Zn were found in the placentas of pregnant women who smoked; moreover, whole blood Cd levels predicted placental Zn levels. A significant decrease in the red blood cells zinc level correlated with smoking habits was observed in infants. According to these authors, in smokers maternal whole blood cadmium levels are predictive not only of the placental cadmium levels but also of the placenta zinc levels. This study suggests that a cadmium/zinc interaction takes place in the maternal-foetal-placental unit of pregnant women who smoke.

Table 4.92 Indices of Zinc and Cadmium status in smoking and non-smoking mothers (Kuhnert et al., 1987)

	Smokers (n=65) Mean ± SD	Non-smokers (n=84) Mean ± SD
Mothers		
Cd-B (ng/g)	1.3 ± 0.8	0.80 ± 0.4
Zn-plasma (µg/100 ml)	57.5 ± 9.7	57.0 ± 10.0
Placenta *		
Cd (µg/kg)	12.0 ± 7.5	8.1 ± 5.0
Zn (µg/kg)	12.1 ± 2.7	11.1 ± 2.8
Infants		
Zn-plasma (µg/100 ml)	81.1 ± 14.5	83.2 ± 15.0
Zn-red cells (ng/g)	230 ± 55	250 ± 60

* Wet weight ? dry weight?

Lagerkvist et al. (1992) determined the cadmium levels in blood of mothers and new-borns from the surroundings of a copper smelter and a control area in Northern Sweden. There were no significant differences in Cd levels between exposed and control mothers, and blood levels were low, even in the industrial area. There was however a significant increase in Cd-B levels during pregnancy among non-smoking women in both groups, from 5.9 ± 4.0 nmol/l at the 12th week of pregnancy, to 7.8 ± 2.6 at delivery in exposed women and from 4.7 ± 2.2 to 7.2 ± 3.4 nmol/l in the controls. In smokers, Cd-B levels decreased significantly from 14 to 10 nmol/l in both groups. The Cd-B levels in new-borns were about 70% of those in the mothers and there was a significant correlation between mother and infant in exposed women and controls, respectively. Cd-B levels in the babies of non-smoking mothers were significantly higher in the vicinity of the smelter than in the control area. It should be noted that Cd-B in non-smoking mothers living in the non-smelter town are surprisingly high; the reason for this is unknown.

Table 4.93 Cadmium levels in whole blood at delivery (nmol/l) (means ± SD) (Lagerkvist et al., 1992)

Category	Copper smelter town		Non-smelter town	
	Mothers	Infants	Mothers	Infants
Smokers	10.0 ± 4.3 n=41	7.4 ± 2.9 n=35	9.8 ± 3.3 n=16	6.9 ± 2.0 n=14
Non-smokers	7.8 ± 2.6 n=75	6.6 ± 2.4 n=66	7.2 ± 3.4 n=50	5.4 ± 2.3 n=44

Berlin et al. (1992) analysed the placenta of female workers in a nickel-cadmium battery factory (n=27). Placental cadmium concentrations (mean: 2.1, SD: ± 2.2, range: < 0.2-9.5 µg/100 g wet weight) were positively correlated with maternal blood cadmium (values not reported).

Goyer and Cherian (1992) measured a mean Cd content in 55 human placentas of 32.3 µg/kg (± 16.1) (wet weight). All mothers were current non-smokers, but 16 (30%) acknowledged smoking in the past. They observed strongly positive correlations between zinc and metallothionein, and copper and metallothionein in the placenta but an equally significant negative relationship between cadmium and metallothionein. The zinc and copper mean (± SD) concentrations were 0.59 (± 1.8) mg/kg and 1.63 (± 0.18) mg/kg, respectively. As observed by the authors, these results suggest that zinc and copper are the primary or major determinants of metallothionein levels in the placenta and that there must be a considerably larger exposure to Cd before binding of the latter to metallothionein would be expected to have any influence on metallothionein levels.

Lutz et al. (1996) have studied the concentration of Cd in brain and kidney during foetal (second trimester terminations or abortions, n=20) and postnatal (infants deceased before three months of age, n=15) development. The concentration of Cd in brain was less than 1 µg/kg in most cases both in foetuses (mean: ≤ 0.6 µk/kg wet weight, range: ≤ 0.2-1.8) and infants (mean: ≤ 0.4 µk/kg wet weight, range: ≤ 0.2-0.8). The concentration of Cd in the kidneys amounted to a median of about 2 µg/kg (1-8 µg/kg) in both groups (foetuses: mean: 2.6 µg/kg wet weight, SD 1.8, range: 0.7-7.8; infants: mean: 3.1, SD: 1.7, range: 0.7-5.9). There was no detectable association between kidney Cd concentrations and the post-conceptional age, not even when an extreme value in the foetal group (7.8 µg/kg) was excluded.

The median kidney Cd concentration in the foetuses of non-smoking women was 1.6 µg/kg (range 1.2-7.8 µg/kg, n=7), while that in the foetuses of women smoking 3-20 cigarettes per day was 2.4 µg/kg (range 0.7-4.0 µg/kg, n=5). However, the difference was not statistically significant, not even when the extreme value of 7.8 µg/kg in the non-smoking group was excluded.

Galicia-Garcia et al. (1997) observed a significant correlation (r^2=0.578) between maternal blood cadmium (n=49, mean: 1.4 µg/l, median: 1.2; SD: 0.4, range: 0.8-2.9) and cord blood cadmium levels (mean: 1.2 µg/l, median: 1.2, SD: 0.3, range: 0.6-2.0). Cord blood was also correlated (r^2=0.499) with new-born blood cadmium (mean: 1.2 µg/l, median: 1.1, SD: 0.3, range: 0.8-2.1). Maternal blood Cd and new-born blood Cd were not correlated. Previous smoking habits of the mother increased maternal blood Cd concentrations significantly but did not modify Cd concentrations in either the cord or the new-born blood.

Recently, Osman et al. (2000) reported on the concentration of different elements including Cd in maternal (36 wk) and cord (delivery) blood in a group of 106 Swedish women. Cord blood cadmium (median of 0.19 nmol/L) was only about 10% of that in maternal blood. The concentrations of cadmium in placenta ranged from 10 to 170 nmol/kg, with the median value being 46 nmol/kg (5 µg/kg).

Summary

The placenta provides a relative barrier protecting the foetus against cadmium exposure. There is some build up of cadmium in the placenta and cadmium levels in placenta are significantly higher in smokers than in non-smokers. The mechanism involved is still unknown but the most plausible hypothesis is that Cd is retained by binding to metallothionein in the placenta. Cd can cross the placenta but at a low rate. The cadmium concentration in newborn blood is on average 40-50% lower than in maternal blood. An interaction between the essential metals zinc and copper and cadmium is suggested but its mechanism and potential consequences for toxicity to the foetus is not known.

Relationship between Cd intake and Cd-U (validation study)

The risk characterisation for man exposed via the environment will mainly consider Cd dietary intakes and a conversion of critical Cd-U concentrations (LOAEL) in Cd intakes will be required to calculate critical Cd intakes. A one compartment model derived from the toxicokinetic model of Nordberg-Kjellström (**Annex A**) can be used for that purpose.

The one compartment model calculates the whole kidney Cd content (Cd_{kidney} ,mg) after t years of Cd exposure through ingestion as

$$Cd_{kidney}(mg) = \frac{A(1-e^{-Bt})}{B}$$

A is the amount of Cd that is transferred to the kidney (mg/year) and depends on intake and distribution as

$$A = \frac{f_u f_k U}{1000} 365$$

f_u is the fraction of food Cd that is absorbed in the gastrointestinal tract (also called the absorption rate), f_k is the fraction of body burden that is transferred to the kidney and U is the daily dietary Cd intake (µg/day).

The parameter B is the first order elimination rate constant ($year^{-1}$) that can be expressed in terms of the half-time ($t_{1/2}$) of Cd in the cortex as

$$B = \frac{\ln 2}{t_{1/2}}$$

The fraction of food Cd absorbed by the GI tract (f_u) varies between 3 and 10% (**Annex A** and Section 4.1.2.1.1), largest values being associated with deficiencies of e.g. Fe, Zn or Ca. The biological half life of Cd is estimated between 10-20 and even 40 years (see Section 4.1.2.2.3) and this range of values is used here as half life in kidney cortex. The Nordberg-Kjellström model assumes a first order elimination rate constant of 0.014% per day, equivalent to a kidney Cd half life of 13.6 years (**Annex A**, **Table A.1**, C19=0.00014). At steady state (e.g. age 50), urinary Cd elimination from kidney[24] is about 0.016% of total Cd content in kidneys (half life 11.7 years) but a somewhat lower elimination rate was chosen to reflect conditions up to age 30 (**Table A.1**, **Annex A**).

The assumptions behind the model to convert urinary Cd values into dietary Cd intake values are:

1. Cd-U is proportional to kidney cortex Cd and Cd-U=2.5 µg/g creatinine is equivalent to 50 mg Cd/kg FW in kidney cortex (see Section 4.1.2.2.3),

[24] based on the steady state example given in Annex 1, section on excretion: daily absorption is 0.8 µg of which 1/3 (0.27µg) is transferred to the kidney. Urinary excretion is 0.35µg day^{-1} and faecal excretions is 0.8-0.35=0.45 µg. Urinary excretion from kidney is assumed equal to net input (0.27µg) and urinary excretion from blood is 0.35-0.27=0.08µg (i.e. 23% of urinary excretion). Daily urinary excretion from kidney is 0.016% of total Cd in kidney (0.27µg of 1/3 of 5 mg body burden = 0.016%)

2. Kidney weight is 300 g FW at body weight 70 kg and 235 g FW at body weight 55 kg,
3. Fraction of body burden Cd retained in kidney (f_k) is 1/3 (**Annex A**),
4. Cd concentration in the renal cortex is 25% higher than renal average (see Section 4.1.2.2),
5. Constant daily Cd intake during the last 53 years.

The validity of this one compartment model can be verified to some extent by comparing calculated dietary and measured Cd-U data in the general population. Two independent data sets discussed before will be used for this purpose (see **Table 4.92**). These data sets were chosen because of the quality of the data (mean Cd-U are often only 2-4 fold above limits of quantification) and data quantity: (1) Umwelt Bundes Amt, German Environmental Survey (GerESIII) and Seifert et al., 2000 (a,b) (abstract) and (2) Berglund et al., 1994 (mixed diet group). Furthermore, these surveys examined samples representative of the general European populations with exclusively environmental exposure. Other data sets dealing with specific populations leaving near point sources (e.g. Buchet et al., 1990) and/or also including people with present or past occupational exposure (e.g. Järup et al., 2000) were not considered because of the contribution of other exposure routes than the diet.

Table 4.94 Validation of the one compartment model that relates calculated Cd intakes in the general population with measured urinary Cd concentrations.

Germany: general population data			
Predicted Cd-U (µg/g creatinine) For non-smoking adults at age 43 (estimated population mean), dietary Cd intake = 9 µg/d (means of 320 duplicate meals and means of predictions at body weight 55 and 70 kg. Range (in brackets) of age 30-50 y, body weight 55-70 kg and dietary Cd intake = 7-13 µg/d (90th perc. is 11 (F) and 13 (M) µg; 10th percentile is unknown but is assumed). Assumptions 1-5 as stated above			
	estimated half life of Cd in kidney (y)		
f^*_u	10	13.6	40
0.03	0.11 (0.07-0.12)	0.14 (0.08-0.23)	0.24 (0.12-0.42)
0.05	0.18 (0.11-0.29)	0.23 (0.14-0.38)	0.39 (0.21-0.70)
0.10	0.36 (0.22-0.59)	0.45 (0.27-0.76)	0.79 (0.42-1.41)
Observed Cd-U (µg/g creatinine)			
median (10-90th perc.), n=4,728 data from 1998 smokers included age 18-69 year		0.18 (0.06-0.55)	Umwelt Bundes Amt, German Environmental Survey (GerESIII) Becker et al. (2003) and Seifert et al. (2000 a,b) (abstract)
Reference value for non-smokers		0.10-0.30	Ewers et al. (1993)

Table 4.94 continued overleaf

Table 4.94 continued Validation of the one compartment model that relates calculated Cd intakes in the general population with measured urinary Cd concentrations

Sweden: monitoring data on 34 women (Berglund et al., 1994)			
Predicted Cd-U (µg/g creatinine) for non-smoking adults with median age (38), dietary Cd intake (10 µg/d) and body weight (63 kg) range (in brackets) of age 20-50y, body weight 55-70 kg and dietary Cd intake 5.7-26 (i.e. ranges in this group) assumptions 1-5 as stated above			
	estimated half life of Cd in kidney (y)		
f^*_u	10	13.6	40
0.03	0.12(0.05-0.35)	0.15(0.05-0.46)	0.24(0.07-0.84)
0.05	0.19(0.08-0.59)	0.24(0.09-0.76)	0.40(0.12-1.41)
0.10	0.39(0.16-1.18)	0.48(0.18-1.52)	0.80(0.24-2.81)
Observed Cd-U (µg/g creatinine)			
median and range (n=34) body weight 52-82 (median 61) age 20-50 y (median 38) daily Cd intake 6-26 µg (median 10)		0.15(0.02-0.36)	Berglund et al.(1994)

* Fraction of dietary Cd that is absorbed by the GI tract

Median Cd-U data are adequately predicted using $t_{1/2}$= 13.6 year as in the Nordberg-Kjellström model (**Annex A**) and a gastrointestinal absorption rate of maximally 5% as concluded in Section 4.1.2.2.1. It should be noted that the extensive German population data (n > 4,000) includes smokers whereas the calculations are made for non-smokers only, i.e. the median Cd-U in the non-smoking German population is, therefore, most likely below the reported median Cd-U of 0.18 µg Cd/g creatinine. This suggest that an average gastro-intestinal (GI) absorption rate may be even more close to 3 than to 5% as also suggested by the calculations based on the data of Berglund et al. (1994). The predictions at $t_{1/2}$=10 years are somewhat lower than at $t_{1/2}$= 13.6 years but the latter value is used below as a conservative approximation.

The largest observed Cd-U (0.36 µg Cd/g creatinine) in the data of Berglund et al. (1994) is generally overestimated by the model when assuming a GI absorption rate of 10% at $t_{1/2}$=13.6 years. Moreover, the largest calculated Cd-U at the GI absorption rate 5% (at same $t_{1/2}$) is 0.76 µg Cd/g creatinine, which is still > 2 fold above the largest observed value. This indicates that either the 5% GI absorption rate also overestimates the body burden in this group or that groups with the largest Cd intake have a lower average GI absorption rates as often found in feeding studies. The latter suggestion effectively means that it would be inappropriate to estimate upper percentiles of Cd-U from upper percentile of dietary Cd with average toxicokinetic parameter values (see also Section 4.1.1.4.5). The Swedish group also had women with depleted iron stores (Fe-S 3-124 µg/l, median 18 µg/l; depleted iron stores is Fe-S< 15 µg/l).

The 90th percentile of Cd-U in the German data is underestimated by the model, even at an absorption rate of 5% (all data at $t_{1/2}$=13.6 years). Smoking may explain these upper percentiles rather than elevated GI absorption rates or elevated dietary Cd intake. The 90th percentile of Cd-U in the non-smoking population would be about 0.27 µg Cd/g creatinine if it is assumed that the 90th percentile in the entire population (0.55 µg/g creatinine) is mainly influenced by smoking individuals and twice as high as in a non-smoking population. This value corresponds to the reported upper range for the German non-smoking population (0.30 µg/g creatinine, Ewers et al., 1993). The largest predicted Cd-U values at 10% absorption rate (0.76 µg Cd/g creatinine) and at 5% absorption rate (0.38 µg Cd/g creatinine) both overestimate this 90th percentile in the non-smoking population.

This model validation suggests that the GI absorption rates of 5 and 10% and the kidney Cd half life of 13.6 years overestimate median and upper values of observed Cd-U in two reliable databases. The predicted/observed Cd-U ratio is 1.3-1.6 (f_u=5%) and 2.5-3.2 (f_u=10%) for the group *median* values whereas this ratio is 1.4-2.1 (f_u=5%) and 2.8-4.2 (f_u=10%) for either *largest* values or (estimated) *90th percentiles* in the German non-smoking population.

The model was also validated with the data of a second diet group described by Berglund et al., 1994. This group of 23 women has a vegetarian/high fibre diet. While there was a tendency for increased prevalence of Fe deficiency in this group compared to the mixed diet group, adequate predictions of Cd-U were also obtained with a GI absorption rate of 3% and the kidney Cd half life of 13.6 years: predicted Cd-U (µg/g creatinine, median and min-max, assumption as in **Table 4.92**) was 0.19 (0.05-0.67) while observed Cd-U was 0.14 (0.05-0.58). The largest observed Cd-U was 1.8 fold overestimated with a 5% absorption rate and 3.8-fold overestimated with a 10% absorption rate.

We note that the upper ranges are best described when selecting a 3% GI absorption rate for a kidney Cd half-life of 13.6 years (predicted/observed ratio 0.9-1.3). This might reflect the fact that, while increased GI absorption rates up to 10% may exist during certain periods of iron deficiency (e.g. late pregnancy), this status does not persist constantly during the whole life. Considering a constant f_u of 10% during 50 years would therefore be inadequate for a risk characterisation.

4.1.2.2.6 General Conclusions Toxicokinetics

The main parameters to be taken into account in the risk assessment are summarised in **Table 4.95**. These figures relate to cadmium element (generic) and are not specifically derived from studies performed with Cd metal or CdO.

Table 4.95 Most significant toxicokinetic parameters in humans (CdO)

		modifying factors
Absorption		
oral	1.4-25 µg/day	
	5 % of ingested dose; (max. 10 %) (animal and humans)	
		↑ with low iron status
		↑ with low Zn, Ca or protein diet
		↓ with presence of Zn contamination
		age (newborn >)
	toxicokinetic model : 3% best fit	including low iron status
inhalation	fumes: 25-50% (humans) dusts: 10-30% (humans)	depending on particle size
dermal	< 1% (animal)	

Table 4.95 continued overleaf

Table 4.95 continued Most significant toxicokinetic parameters in humans (CdO)

		modifying factors
Cd-B	non-smokers: < 1 µg/l smokers: < 5 µg/l	
		females > males
		↓ (hemodilution) or ↑ (relative depletion of iron stores) during pregnancy
	cord blood : 50% maternal blood	
Body burden	5-30 mg at 50 years (general population)	↑ with age
	non-smokers : 15 mg smokers : 30-40 mg	females > males
	kidney + liver = 50% kidney = 33%	ratio kidney/liver ↓ with intensity of exposure
	kidney cortex: 10-50 ppm (smokers = 2-3 · non-smokers) (newborn about 3 ppm)	
	cortex:whole kidney ratio: 1.25	
	liver : 0.5-5 ppm	
	placenta : 5-10 ppm	
Cd-U	0.01% of body burden/day	
	< 2 µg/g creatinine	↑ with age
		smokers > non-smokers
		Females > males
		↑ with kidney damage
Effects of smoking		
	inhalatory absorption: 50%	
	20 cig/d = 3 µg Cd/d	
	Cd-B : 2-5-fold increase	
	body burden : 2-3-fold increase	
	Cd-U : 1.5-fold increase	

4.1.2.3 Acute toxicity

Introduction

The isolation of cadmium in 1817 was rapidly followed by the discovery of its acute effects in humans on the lung (after inhalation) and on the gastrointestinal tract (after ingestion).

With increasing production, industrial workers became acutely exposed to high concentrations of CdO fumes.

Subjects of the general population have suffered from acute symptoms of food poisoning in cases of ingestion of food or beverages contaminated with significant amounts of cadmium. Additional acute toxic effects have been observed in experimentally exposed animals (liver effects, changes in blood pressure), but inference from such results of a possible hazard for humans remains difficult (CRC, 1986).

Currently, the major routes of exposure to cadmium in human populations are:

1) the oral route for the non-smoking general population;

2) the inhalation route for workers and smokers.

Focus will be put on these 2 relevant pathways for cadmium transfer to man.

Data are available from studies in animals and are reported in Section 4.1.2.3.1.

Human data on the acute effects of cadmium oxide and metal are available from case reports after accidents and following short-term exposure of users'; these will be reviewed in Section 4.1.2.3.2.

The term "cadmium compounds" refers to other compounds of cadmium than cadmium oxide and cadmium metal and includes cadmium chloride, cadmium acetate, cadmium sulfide, etc. Data relating to these compounds are given hereafter with another letter size and type. Data on cadmium compounds are included in the CdO/Cd metal risk assessment when no (not enough) information on the effects of CdOCd metal is available and when the studies using cadmium compounds are mechanistically relevant.

4.1.2.3.1 Studies in animals

Oral route

LD_{50} values were reported by WHO (1992) and CEC (1978) for cadmium metal and cadmium oxide. Values were derived from studies in rats and mice using CdO or Cd metal administered orally or intra-gastrically but details on the primary studies reporting these values are not available.

Table 4.96 Summary of LD_{50} values

Species	Type of compound	Route of administration	LD_{50} values (mg CdO/kg bw) (confidence limits)	LD_{50} values (mg Cd/kg bw) (confidence limits)	Reference (secondary source)
Rat	CdO	oral	72 -296*	63-259*	CEC (1978)
Mouse	CdO	intragastrically	72 (41-113)	63 (36-99)	WHO (1992)
Rat	Cd metal powder	oral	-	2330**	CEC (1978)
Mouse	Cd metal powder	intragastrically	-	890 (636-.1246)	WHO (1992)

* Range,
** No confidence limits available

No details about the specific mechanism of action of CdO and Cd metal were located.

The oral LD_{50} for various soluble compounds in rodents has been reported to be 50 to 400 mg/kg bw.

ATSDR (1999) summarised and plotted mortality data from studies investigating the effects of a single oral dose of cadmium chloride in rats:

Table 4.97 Mortality data (rats, CdCl2, single dose)

Dose (mg Cd/kg)	Rat Strain	Follow-up(days)	Mortality (Dead/total)	Remarks	Reference
15.3	Sprague-Dawley	1 day	1/10males 1/10 females		Borzelleca et al. (1989)
47 211 170	NS	8 days	LD_{50}	2-week old pups 6-week-old 18-week old	Kostial et al. (1978)
225	Sprague-Dawley	14 days	LD_{50}		Kotsonis and Klaassen (1977)
327 107	Sprague-Dawley	24 hours	LD_{50}	Fed rats Fasted rats	Shimizu and Morita (1990)

(adapted from ATSDR, 1999)
NS Not specified

Andersen (1989) listed and summarised mortality data from several studies in mice (**Table 4.98**). Dose-related mortality occurred after single administrations of increasing doses of cadmium chloride to mice.

Table 4.98 B: Effect of dose on mortality in male mice after a single dose of cadmium (oral route)

Dose		Mouse Strain	Follow-up(days)	Mortality(dead/total)	Reference
(µmol/kg)	mg Cd/kg				
140	15.9	CBA	10	0/10	Andersen et al. (1988)
270	30.7	CBA	10	2/54	Andersen et al. (1988)
500	56.8	CBA	14	3/10	Andersen (1989)
530	60.2	CBA CBA	10 21	11/60 6/10	Andersen et al. (1988) Engström (1981)
790	89.8	CBA	10	36/42	Andersen et al. (1988)
890	101.1	Swiss Webster	10	8/10	Baer and Benson (1987)
1,000	113.6	CBA ICR ICR	4	37/40 16/30 12/25	Andersen (1989) Basinger et al. (1988) Jones et al. (1988)
1,334	151.6	Swiss Webster	30	10/10	Baer and Benson (1987)
1,500	170.4	CBA	14	10/10	Andersen (1989)

(adapted from Andersen, 1989)

Andersen et al. (1988) exposed groups of 20 mice to $CdCl_2$ at doses of 0, 5, 35, 70, 140, 270, 530 and 790 µmol Cd/kg bw. (respectively, 0, 0.6, 3.9, 7.9, 15.9, 30.7, 60.2, and 89.9 mg Cd/kg bw), administered as single dose by gavage. Authors observed a dose-effect relation for tissue damage occurring among the surviving mice at 10 days after exposure. Targets were the proximal parts of the intestinal tract. Catarrhal gastro-enteritis with hyperaemia, haemorrhagic gastro-enteritis with epithelial desquamation, or even necrosis of the entire epithelium with severe haemorrhage were observed in the stomach, duodenum, and although less severe, in the small intestine. Damage to liver and kidneys was only slight but extensive testicular necrosis was found at the highest dose (Andersen, 1989).

In the same experiment, animals dying within the 10 days of the post-exposure observation period were also investigated histologically: liver damage was slightly less than in surviving animals, while slightly increased renal and much more pronounced gastrointestinal damage (also in ileum and colon) were observed. However, due to the possibility of post-mortem changes (several hours have passed between death and preparation of organs for study) histological results have to be considered with caution as acknowledged by the authors. It could not be concluded that gastrointestinal damage was the primary cause of death. Hepatic damage, contrary to what happens when cadmium is injected, appeared to be of minor importance. Andersen et al. (1988) concluded that a critical effect during acute oral cadmium intoxication seemed to be induction of intestinal atony and constipation, resulting in severe gastrointestinal necrosis and increased fractional intestinal absorption (Andersen et al., 1988).

Inhalation route

Main characteristics

No experimental data on acute effects of Cd metal powder or dust on mammals were located.

By heating of cadmium metal, as occurs at the workplace, one produces metal fumes that are instantly transformed into CdO fumes.

Several experiments using cadmium oxide dust or fumes were conducted in animals and according to most reviews, the salient characteristics of the acute intoxication with CdO are as follows:

Inhalation of cadmium oxide fumes/ dust can cause death in animals because of pulmonary oedema. Hadley et al. (1979) exposed 61 rats to cadmium oxide at a concentration of 60 µg Cd /l air for 30 minutes: 27 of the exposed rats died from acute pulmonary oedema within 3 days after exposure (Hadley et al., 1979). Pulmonary oedema was also reported to be cause of death in the experiments of Yoshikawa and Homma (1974) who exposed rats to 25 mg Cd/m^3 as CdO.

Symptoms following a single exposure to CdO fumes (128 mg/m^3, 2 hours) were reported by Rusch et al. (1986): dry rales (20 of 30 rats), moist rales (5 of 30 rats) and labourate breathing (20 of 30 rats) were observed during the four-hour post-exposure observation (Rusch et al., 1986).

Table 4.99 presents the located experimental data on the acute toxicity of cadmium oxide fumes/ dust for various animal species.

Table 4.99 Acute toxicity experiments in animals

Species	Type of compound	Duration	Tested concentrations	LOAEL	Reference
Rats (strain not specified)	CdO fumes	15 min	30 mg Cd/m^3	30 mg Cd/m^3 (LC_{50})	Barrett et al. (1947)
Rats (Sprague-Dawley)	CdO fumes	30 min	25 mg Cd/m^3	25 mg Cd/m^3 (LC_{50})	Yoshikawa and Homma (1974)
Rats (S-D)	CdO dust	15 min	10 mg Cd/m^3	10 mg Cd/m^3: increased relative lung weight, increased in death rate of exposed animals following a test infection with Salmonella enteriditis	Bouley et al. (1977)
Rats (S-D)	CdO fumes	30 min	1.45, 4.53, 8.63 mg Cd/m^3	2.3 mg Cd/m^3: decrease of lung microsomal cyt P-450 content 4.53 mg Cd/m^3: increase lung weight	Boisset and Boudène (1981)
Rats (Sprague-Dawley)	CdO fumes	2 h	112 mg Cd/m^3	112 mg Cd/m^3: 25/32 died	Rusch et al. (19860
Rats (Sprague-Dawley)	CdO dust (mmad : 1.28-1.56 µm)	2 h	0.25, 0.45, 4.5 mg Cd/m^3	0.45 mg Cd/m^3: increase in lung weight and lung-to-body weight ratio but no change in body weight, biochemical changes 4.5 mg Cd/m^3: proliferative pneumonitis	Grose et al. (1987)
Rats (Wistar)	CdO	30 min	60 mg Cd/m³	60 mg Cd/m^3: 27/61 died	Hadley et al. (1979)
Rats (Wistar)	CdO aerosol (mmad : 0.26- 0.33 µm)	3 h	0.5, 5.3 mg CdO/m^3	0.5 mg CdO/m^3(0.4 mg Cd/m^3): mild hypercellularity, increased number of cuboidal epithelial cells lining alveoli (repair by 7- days post exposure), slight increase in lung enzyme activities 5.3 mg CdO/m^3(4.6 mg Cd/m^3): sustained alveolitis, noncellular thickening of the interstitium, increases in lung enzyme activities	Buckley and Bassett (1987)
Rats (Lewis)	CdO dust	3 h	8.4 mg Cd/m^3	8.4 mg Cd/m^3: diffuse alveolitis, focal areas of haemorrhage and alveolar oedema, small sheets of mononuclear cells; biochemical alterations	Hart et al. (1989)
Mice (Charles River)	CdO fumes	15 min	9 mg Cd /m^3	9 mg Cd/m^3: infectious death rate lowered	Chaumard et al. (1983)
Rabbits (FdB)	CdO fumes	15 min	6.4, 8.8, 12.6, 22.4 mg Cd/m^3	22.4 mg Cd/m^3: decrease body weight, increase relative lung weight, reduced activity of microsomal enzymes	Fukuhara (1981)

Table 4.99 continued overleaf

Table 4.99 continued Acute toxicity experiments in animals

Species	Type of compound	Duration	Tested concentrations	LOAEL	Reference
Rabbits	CdO iron dust	4 h	N.I.	28.4 mg Cd /m³ (LC_{50})	Friberg (1950)
Rabbits (NZW)	CdO dust	2 hours	0.25, 0.45, 4.5 mg Cd/m³	0.45 mg Cd/m³: slight increase in number of alveolar macrophages, decreased lung and body weights 4.5 mg Cd/m³: multifocal, interstitial pneumonitis	Grose et al. (1987)

Regarding the identification of a lethal dose and quantitative aspects, data are contradictory. Duration of exposure and concentrations used were different in each experiment and some authors reported only approximations because of the small number of animals tested.

The lowest reported CT_{50} (concentration · time, causing the death in 50% of a defined experimental animal population) for CdO fumes (particle size and generation mode not mentioned) was for rats exposed to 450 mg · min/m^3 (Barrett et al., 1947). The validity of this figure is however questionable because this study was not performed according to the current standards. Barrett et al. (1947) suggested that the mortality rate was directly proportional to duration of exposure multiplied by cadmium concentration (Barrett et al., 1947 cited in CRC, 1986). However, different CT_{50} (concentration · time) have been reported by various authors, as shown in **Table 4.100**.

Table 4.100 Reported CT_{50} in animals (CT_{50}: concentration · time)

Species	Concen - tration (mg/m³)	Time (min)	CT_{50} (mg · min/m³)	Type of compound	Remarks	Reference
Rats (strain not specified)	30	15	450	CdO fumes	questionable validity	Barrett et al. (1947)
Rats (Sprague-Dawley)	25	30	750	CdO fumes	Only abstract	Yoshikawa and Homma (1974)
	112	120	13,440	CdO fumes		Rusch et al. (1986)
Rats (Wistar)	10.9	180	1962	CdO aerosol	No experimental details available	Buckley and Bassett (1987)
Rabbit	28.4	240	6,816	CdO dust	No experimental details available	Friberg (1950)
Mouse (strain not specified)	46.7	15	700	CdO fumes	approximations because of insufficiency in the data or small numbers of animals used	Barrett et al. (1947)
Monkey	940	14	13,160	CdO fumes		
Guinea-pig	204	15	3,060	CdO fumes		
Dog	230	15	3,450	CdO fumes		

For further details on methods, see IUCLID CdO

Differences between species are possible but are not explicitly reported as a cause of the diverging CT_{50} (Barrett et al., 1947 cited in CRC, 1986). Recently, these possible interspecies (and interstrain) susceptibility differences to cadmium-induced lung injury were investigated by McKenna et al. (1997). These authors compared pulmonary inflammatory processes (assessed by broncho-alveolar lavage fluid analyses, histopathology and immunohistochemical detection of cell proliferation) in Wistar Furth rats with those in C57 and DBA mice exposed to CdO fumes (count median diameter 0.008 µm, GSD 1.1generated from Cd shots heated at 445°C and mixed with flushed air). All animals were exposed to 1 mg Cd/m³ for 3 hours. In comparison to mice, rats responded to CdO inhalation with a more transient response in BALF and a higher degree of acute inflammatory lesions in lung tissue. The inflammatory processes also varied widely in the two mouse strains (McKenna et al., 1997).

Another explanation of observed variations might be the form of cadmium tested: CdO fumes, CdO dust or other Cd compounds.

According to Friberg (1950), the CT_{50} for cadmium oxide dust would be about three to four times the values for cadmium oxide fumes in rabbits (Friberg, 1950). This could be explained according to Oberdörster et al. (1992), by a much longer retention of CdO dust in the lung (Oberdörster et al., 1992). The retardation of the clearance of the CdO oxide particles may be due to a slower solubilisation of the particles, compared to that of the fine and very porous fume particles (Oberdörster, 1992).

Because the acute pulmonary toxicity of cadmium seems to depend on the chemical and physical form of the administered compound, the question of the validity of an extrapolation to CdO of results obtained with other compounds to potential CdO effects should be considered.

For example, Rusch et al. (1986) observed that the different Cd compounds they tested in rats were not equivalent with respect to toxicity: CdO fumes and Cd carbonate, representative of soluble compounds, appeared to be more toxic than two insoluble cadmium pigments, "cadmium red" (Cd: 69.9%, Se: 16.4%, S: 13.2%) and "cadmium yellow" (Cd: 77.4%, S: 21.7%, Zn: 0.28%, Se: 0.27%).

Table 4.101 Animal termination history after exposure to various Cd compounds (adapted from Rusch et al., 1986)

Group	Concentration (mg Cd/m^3)	Duration of exposure	Animal termination history (number of animals that died spontaneously, death was attributed to exposure)				
			0-24 hr	24-72 hr	72 hr-7 days	7-30 days	Total
Control group	0	2 hours	0	0	0	0	0
Cadmium red	97	2 hours	0	0	0	0	0
Cadmium yellow	99	2 hours	0	0	0	0	0
Cadmium carbonate	132	2 hours	0	0	1	2	3
Cadmium fumes	112	2 hours	0	19	6	0	25

For further details on methods, see IUCLID CdO

This difference in toxicity was attributed by Rusch et al. (1986) to an increased retention and greater absorption for the more soluble compounds compared to the highly insoluble cadmium pigments which have a greater mucociliary clearance.

However, some authors warned of predicting the behaviour of compounds in complex biological systems by their chemical solubility alone (Hadley et al., 1980 cited by Glaser et al., 1986). For example, based on the water solubility of CdO and CdS that are very low compared to the highly soluble $CdCl_2$, one might predict a higher bioavailability of $CdCl_2$ *in vivo*. The pulmonary effects of water insoluble cadmium oxide (dust, fumes) were compared with those induced by water-soluble cadmium chloride in groups of rats exposed by inhalation by Oberdörster et al. (1987). They observed that the small CdO particles (insoluble) and $CdCl_2$ (soluble) were equally toxic. Authors concluded that acute effects of Cd compounds in the lung cannot only be predicted from their water solubility (Oberdörster et al., 1987). The *in vivo* solubility in the lung after inhalation exposure is very high for CdO (Oberdörster and Cox, 1990).

Inhaled CdO appeared to be even more damaging to the lung than $CdCl_2$ in the experiment conducted by Grose et al. (1987) who compared the effects of aerosols of both compounds on the pulmonary biochemistry and histology in rats and rabbits. Inhalation by the rat of 0.45 mg Cd/m^3 either as $CdCl_2$ or CdO did not cause any significant treatment-related histopathological lesions. However, at this concentration, CdO had an effect on body weight, on lung weight and on homogenate and supernatant total protein. Both compounds caused multifocal, interstitial pneumonitis 72 hours after exposure to 4.5 mg/m^3, but the CdO lesions were more severe with proliferation of fibrocytic-like cells as well as pneumocytes. Authors concluded that because of the more acute response of the lung to CdO compared to $CdCl_2$, extrapolation of $CdCl_2$ effects to potential CdO effects could be scientifically vulnerable (Grose et al., 1987).

Mechanism of action

Pulmonary inflammation is generally considered as the most important cause of death after acute exposure to CdO.

The inflammatory phenomena following a single 15 minutes exposure to CdO (10 mg/m^3) caused in rats a temporary increase in lung weight (Bouley et al., 1977).

Table 4.102 shows the lowest exposure levels of cadmium oxide sufficient to produce a significant increase in lung weight in animals after 15 to 30 minutes of exposure.

Table 4.102 Levels of exposure to CdO producing an increase in lung weight (from CRC, 1986)

Species	Compound	Dose (mg Cd/m^3)	Duration of exposure	Reference
Rats	CdO	10	15	Bouley et al. (1977)
	CdO	1.5 – 8.6	30	Boisset an. (1981)
Rabbits	CdO	6.4 – 22.4	15	Fukuhara et al. (1981)

Acute inhalation exposure of rats to CdO aerosols was found to produce localised areas of pulmonary inflammation and epithelial hyperplasia in the study of Buckley and Bassett (1987). They demonstrated that CdO- induced lesions (like those produced by more soluble compounds) were localised primarily at broncho-alveolar junctions. They suggested that the broncho-alveolar junction was the site of greatest particle deposition. The observed region specificity could also be explained by the migration of injured macrophages to the broncho-alveolar junction or by the accumulation of translocated particles at this site (Buckley and Bassett, 1987)

Macrophages were counted with endo-pulmonary washings or on lung sections of sacrificed animals.

In rodents exposed to cadmium oxide microparticles (single constant 15-minutes exposure at 10 mg/m^3), the number of pulmonary macrophages in washing fluid was first lowered and then increased, by an influx of probably neo-formed macrophages, in the study of Bouley et al. (1977).

Two distinct types of macrophages were seen at histological examination following the intratracheal injection of 5 mg CdO (particulate): the first one showed a significant increase in vacuoles and size when compared to those seen in controls, some of the vacuoles contained electron dense structures and degenerated mitochondria's; the second type was smaller in size, contained large mitochondria's, more profiles of rough endoplasmic reticulum and a few vacuoles. These two types of macrophages might represent the transformational stages of a continuing pathological process: the small type of macrophage may represent an early stage of transformation while the larger macrophage may represent a later stage. The larger macrophages exhibited a decrease in the number and size of mitochondria’s (result of mitochondria's being phagocytosed by secondary lysosomes). The presence of degenerated mitochondria's in autophagosomes as seen in this study could account for decreased metabolic activity and ultimately lead to permanent lung damage (Murthy et al., 1982).

A low-dose 3-4 hour exposure at 0.5 mg CdO/m^3 of CdO fumes caused slight pulmonary damage, entirely repaired by 7-15 days post-exposure: mild hypercellularity was observed at broncho-alveolar junctions and in adjacent alveoli. The numbers of cuboidal epithelial cells lining the alveoli appeared to be slightly increased, indicative of epithelial hyperplasia. A high-dose exposure of 5.3 mg CdO/m^3 resulted in more severe injury (focal areas of interstitial thickening, presence of numerous inflammatory cells and cuboidal alveolar epithelial cells) not entirely resolved after 30 days (Buckley and Bassett, 1987).

Several biochemical changes have been shown to parallel morphological alterations. Several authors investigated the biochemical defence mechanisms of the lung by measuring time-course changes in enzyme activity.

CdO inhalation revealed a dose-related inhibitory effect on benzo(a)pyrene hydroxylase activity but this required relatively high doses. Inhibition of the enzyme occurred slowly as a function of time, reaching its maximum inhibition rate 2 days after the inhalation (68.0 ± 2.7 versus 83.9 ± 6.5 pmoles/min per mg for rabbits exposed to 12.6 ± 0.4 mg Cd/m^3 and controls, respectively) (Fukuhara et al., 1981).

Boisset and Boudène (1981) reported also a significant decrease in benzo(a)pyrene hydroxylase and ethoxycoumarin deethylase activity in rabbits exposed to cadmium oxide fumes (> 4.5 mg CdO/m^3 for 30 minutes) (Boisset and Boudène, 1981).

Another possible mechanism by which CdO may exert its toxicity in the lung is the enhancement of the production of active oxygen species which may cause lipid peroxidation and cell injury. Hirano et al. (1990) hypothesised that oxidant defence enzymes such as glutathione peroxidase, glutathione reductase, glucose-6-phosphate dehydrogenase, and superoxide dismutase might play a role in the detoxification of CdO and measured their time-course changes in male Wistar rats after intratracheal instillation of cadmium oxide (5µg). All 4 antioxidant enzymes showed significant increases in their activity when expressed as units per lung, what is consistent with the hypothesis (no reported data). Buckley and Bassett (1987) had described similar findings (Buckley and Bassett, 1987). However, when the results of Hirano et al. (1990) were expressed as units per gram of tissue, no significant changes were observed at any time in glutathione peroxidase, glutathione reductase activities. Superoxide dismutase activity in the lung decreased following CdO treatment.

GSH-reductase activity was increased 72 hours after exposure to 4.5 mg/m^3 CdO (20%) or 0.45 mg/m^3 CdO (16%) in the study by Grose et al. (1987).

A marked increase in susceptibility to bacterial infections (Salmonella enteridis, Pasteurella multocida) has been shown in rats and mice after short exposure to CdO fumes (10 mg Cd/m^3) (Bouley et al. (1977). In contrast, Chaumard et al. (1983) found a significantly lowered death rate when mice, after a single short exposure to CdO microparticles (9 mg Cd/m^3), were challenged with influenza virus (Chaumard et al., 1983). To our knowledge, such experiments or observations have not been reported for other animal species or humans exposed to cadmium oxide.

An effect of cadmium on the immune function has also been reported in mice exposed to 0.190 mg Cd/m^3 (as cadmium chloride, 2 hours) which showed suppression of the primary humoral immune response (Graham et al., 1978). The NOAEL for immunological effects from this study was 0.11 mg Cd/m^3 (ATSDR, 1999). Krzystyniak et al. (1987) observed a reduction in spleen lymphocyte viability and humoral response at 0.88 mg Cd/m^3 in mice exposed to cadmium chloride for 60 minutes (Krzystyniak et al., 1987 cited in ATSDR 1999).

Summary: inhalation route

No experimental data on acute effects of Cd metal powder or dust on mammals were located.

Inhalation exposure to high levels of cadmium oxide fumes or cadmium oxide dust can give rise to severe, potentially fatal pulmonary lesions in animals.

The lowest dose (LOAEL) reported here to cause mild pulmonary damage (hypercellularity indicative of hyperplasia) was an 3-hour exposure to 0.5 mg CdO/m^3 as CdO fumes (Buckley and Bassett, 1987) and is considered as reliable data although methods used were not totally conform with ER 67/548/EEC, Annex V and OECD guidelines.

Minimal CT_{50} reported in the identified literature and reviews was 450 mg $\cdot$ min/m^3 for CdO fumes (Barrett et al., 1947).

For CdO dust, the LOAEL is 0.45 mg CdO/m^3 for an exposure period of 2 hours (Grose et al. 1987).

As mentioned previously, there is some uncertainty about the CT_{50} of cadmium oxide and no recent review work could be identified on this issue. Some imprecision is likely due to the fact that authors reported only approximations of inhaled doses, using few animals, and especially did not indicate the physical and chemical characteristics of the dust or fumes. Recent investigations reported interspecies and interstrain differences of susceptibility to CdO-induced pulmonary inflammation that could also account for the variability of the CT_{50} results. Exposure to cadmium oxide at concentrations above 5 mg/m^3 has caused destruction of lung epithelial cells, resulting in pulmonary oedema, tracheo-bronchitis, and pneumonitis. In addition to morphological changes and increased lung weight, various types of biochemical effects have also been observed.

<u>Dermal route</u>

No studies were located regarding death or other acute effects in animals after dermal exposure to cadmium oxide or cadmium metal.

9/20 guinea pigs died several weeks (3/9 after 2 weeks, 3 deaths occurring in the 5^{th} and 6^{th} weeks) after being exposed in a skin depot to 2mL of 0.239 molar aqueous of cadmium chloride (0.14 mg/kg bw) (Wahlberg, 1965, cited in ATSDR, 1999). However, it is difficult to attribute these deaths to cadmium exposure due to the low dose compared to oral LD_{50} values and to the fact that no necropsy was done (ATSDR, 1999).

Available information in the published literature does not allow the derivation of a N(L)OAEL. However, acute toxicity effects of cadmium via the dermal route are not expected to be significant as uptake of soluble and less-soluble cadmium compounds applied on the skin of animals appears to be low (see Section 4.1.2.2 Toxicokinetics: 4.1.2.2.2 absorption, dermal route).

<u>Other routes</u>

Not relevant for human risk assessment.

<u>Conclusions: studies in animals</u>

Very few data are available about the acute effects of cadmium metal in animals. Most of the experiments have used soluble cadmium compounds or cadmium oxide.

LD_{50} values are available for the oral route (890, 2,330 mg /kg for Cd metal), but no experimental details are available. LD_{50} oral values range from 72 to 300 mg CdO/kg for CdO (63-259 mg Cd/kg) and from 50 to 400 mg Cd/kg for other water-soluble compounds. No clear dose-effect (response) relationship for CdO administered by the oral route could be determined.

Experiments using cadmium compounds gave some additional information about the target organs of ingested cadmium at acute toxicity doses: targets were the proximal parts of the intestinal tract.

No specific data are available for inhalation exposure to Cd metal. Since inhalation exposure to cadmium metal dust is very unlikely in occupational settings, this absence of information is not deemed critical.

Acute inhalation exposure of animals to cadmium oxide aerosols was found to produce pulmonary inflammation and oedema. Several biochemical changes have been shown to parallel the morphological alterations. Minimal CT_{50} reported in the identified literature and reviews was 450 mg CdO · min/m^3 for CdO fumes but the reliability of this figure may be questioned. Concentrations above 5 mg/m^3 have caused clear pulmonary damage (destruction of lung epithelial cells, resulting in pulmonary oedema, tracheo-bronchitis, and pneumonitis).

The lowest dose (LOAEL) reported to cause mild pulmonary damage (hypercellularity indicative of hyperplasia) was an 3-hour exposure to 0.5 mg/m^3 CdO fumes, and is considered as reliable data although methods used were not totally conform with ER 67/548/EEC, Annex V and OECD guidelines.

No information on skin exposure could be retrieved neither for CdO nor for Cd metal.

4.1.2.3.2 Sudies in humans

Introduction

Focus will be put on the two relevant pathways for cadmium transfer to man: the oral route and the inhalation route.

Ingestion of food or beverages contaminated with cadmium (species not specified) may give rise to acute symptoms.

Acute cadmium poisoning and, in some cases, death have been reported among workers shortly after exposure to fumes when cadmium metal or cadmium-containing materials have been heated to high temperatures. Cadmium metal fumes are reported to be instantly transformed into cadmium oxide fumes when entering in contact with air (HEDSET).

Oral route

Main characteristics

According to the main reviews, food contamination may arise when acid foods and drinks are prepared and stored in contact with cadmium metal-plated surfaces (WHO 1992).

During the period 1940-50, such cases occurred mainly due to the substitution of cadmium for scarce chromium in the plating of many cooking devices and containers. Some reports indicate that this problem has existed in other circumstances: this type of poisoning may arise as a result of food and drink contamination by cadmium from solders in water pipes, taps, cooling or heating devices or from dissolution of cadmium from pottery, usually occurring when acid juices and the like are stored in these items (CRC, 1986). A group of about 10 persons presented acute symptoms of poisoning after consumption of gherkins stored in varnished vases. Cadmium concentration measured in the fluid containing the gherkins reached 2.62 g/l (Rème and Peres, 1959). Effects occurred following the consumption of drinks (with a cadmium concentration of approximately 16 mg/l) from a cooled soft-drink machine constructed with cadmium-containing solder (Nordberg et al., 1973) or the consumption of Algerian wine stored in a cadmium-plated crock (no dose reported) (Baker and Hafner, 1961). Cadmium poisoning was also diagnosed in a family following the use of a cadmium-plated refrigerator shelf as an improvised barbecue grill. The shelf was submitted to chemical analysis which revealed that the metal contained cadmium in greater than trace amounts (Baker and Hafner, 1961).

The main symptoms of oral toxicity are nausea, vomiting, diarrhoea, abdominal cramps, headache and salivation.

Two fatal cases of self-poisoning with cadmium compounds were reported in the literature. The ingestion of about 150 g cadmium chloride caused haemorrhagic necrosis of the stomach, duodenum and jejunum. Death occurred 30 hours after admission. Necropsy showed also pulmonary oedema, pleural effusions and ascites, focal hepatic necrosis and slight pancreatic haemorrhage. Kidneys appeared normal (Buckler et al., 1986). Wisnieska-Knypl et al. (1971) reported that ingestion of 25 mg/kg cadmium iodide resulted in death 7 days later; necropsy revealed damage to the heart, liver and kidneys besides gastrointestinal damage.

Acute oral intoxication has also been observed in workers exposed to cadmium dust that ate their meals with dirty hands, smoke or bite their fingernails at the work place (Bernard and Lauwerys, 1986 cited in HEDSET).

Recovery from mild or moderate acute poisoning by the oral route appears to be rapid and complete.

However, no follow-up studies of people who have experienced acute cadmium poisoning have been reported (WHO 1992).

The emetic threshold dose for cadmium (element) has been estimated to be in the order of 15 mg/l water. The no-effect level (NOEL) of a single oral dose for humans is estimated at 3 mg elemental Cd and the lethal doses range from 350 to 8,900 mg (Bernard and Lauwerys, 1986 cited in HEDSET). These values are reported in several reviews without further evaluation. Primary studies are unavailable.

Physiopathology

No data were located about the specific physiopathology of the poisoning induced by cadmium oxide/metal in case of ingestion. Cadmium compounds taken as a means of suicide in two cases caused death due to gastrointestinal haemorrhage and fluid loss, oedema, widespread organ destruction.

In animals, oral administration of cadmium compounds induces epithelial desquamation and necrosis of the gastric and intestinal mucosa, what could suggest a similar mechanism and might explain the loss of fluid followed by a shock observed in humans.

Inhalation route

The first known case of acute cadmium poisoning with cadmium oxide/metal was reported by Legge in 1924 and occurred, as repeatedly observed in subsequent reports, when cadmium metal was heated during pyrometallurgical processes and instantly transformed into CdO-fumes (HEDSET).

Table 4.103 presents a summary of case reports which extends over more than a half century. All available data are presented. This review of acute poisoning cases with cadmium oxide and cadmium metal includes recent reports, published after 1992 and also some less recent cases which were not mentioned in the aforementioned reviews. For some of these reports, simultaneous exposure to other toxicants occurred but an effect of cadmium could not be definitively excluded.

Table 4.103 Acute human intoxications with cadmium metal and oxide fumes

Reference	Circumstances	Compound, exposure level and duration (when known)	Number exposed, age, sex, smoking (when known)	Clinical signs, outcome
Legge (1924)	Melting Cd lingots in crucible	N.I. (no information available)	3	1 death
Schwarz (1929) cited in Prodan (1932)	Melting cadmium	Room without ventilation, several hours in "thick fumes"	1	End of the day: weakness, cough Next day: nausea, shivering, pain in the sternal region, difficulties in respiration, incessant coughing Hospitalised for bronchitis and bronchopneumonia
Wahle (1932)	Producing copper-cadmium alloy	N.I.	1	intense respiratory irritation, precordial pain, severe dyspnoea (no further detailed)
Bulmer et al. (1938)	Passing 300 pounds of cadmium plated rivets in an annealing furnace	Reconstitution of exposure by Barrett et al. (1947): estimated mean in the furnace section: 2,000 min.mg/m³ (range: 1,330-2,850)	15	Intense respiratory irritation, causing precordial pain and severe dyspnea a few hours after exposure in 2 workers, both death in 5 to 8 days
Nasatir (1941)	Burning off of Cd deposits with a torch	N.I.	1	1 death (no further details)
Ross (1944)	Accidental ignition of Cd dust on floor of workroom with a Cd recovery chamber	N.I.	23	0 death (no further details)
Spolyar et al. (1944)	Heat flanging of Cd-plated pipes	N.I.	5	1 death (no further details)
Shiels and Robertson (1946)	Fire in machine shop which burned box of Cd-containing bearings in a cadmium recovery plant	Cadmium dust	14 (+ firemen fighting the fire)	1 death (no further details)

Table 4.103 continued overleaf

Table 4.103 continued Acute human intoxications with cadmium metal and oxide fumes

Reference	Circumstances	Compound, exposure level and duration (when known)	Number exposed, age, sex, smoking (when known)	Clinical signs, outcome
Huck (1947)	Cutting of Cd-plated steel with a torch	N.I.	1	0 death (no further details)
Amdur and Caputi (1953)	Melting Cd wire in oxyacetylene flame	N.I.	4	0 death (no further details)
Reinl (1953)	CdO fumes from molten Cd	N.I.	2	2 deaths (no further details)
Bauer and LeScao (1956)	Heating a Cd-plated cathode with a blow torch	N.I.	1	1 death (no further details)
Christensen and Olsen (1957)	Spot welding on a Cd-coated metal fixture for 5 hours	N.I.	1	1 death (no further details)
Kleinfeld et al. (1958)	Melting of Cd-alloy with a torch in a seam brazing operation	N.I.	1	0 death (no further details)
Evans (1960)	Cutting Cd-plated scrap metal with welder's torch	N.I.	1	0 death (no further details)
Reinl (1961)	Molten Cd wire in a metal spraying operation	N.I.	17	0 death (no further details)
Lamy et al. (1963)	Oxyacetylene torch on steel contaminated with cadmium	N.I.	2	0 death (no further details)
Kleinfeld (1965)	Melting Cd alloy with oxyacetylene torch	N.I.	1	0 death (no further details)

Table 4.103 continued overleaf

Table 4.103 continued Acute human intoxications with cadmium metal and oxide fumes

Reference	Circumstances	Compound, exposure level and duration (when known)	Number exposed, age, sex, smoking (when known)	Clinical signs, outcome
Blejer et al. (1966)	Brazing operation with Cd-silver alloy (26% Cd)	-CdO fumes, indoors, without ventilation or respiratory protective device, two and a half hours. Cd at autopsy: Cd-U: 500 µg/l, Cd-B: not detected	1, 35 year-old man	1 death after 4 days (on day of exposure, feeling ill. Next day, cough, chest pain, shortness of breath, increased malaise and fever, diagnosis of chemical bronchitis. At autopsy, massive pulmonary oedema and haemorrhagic congestion)
Beton et al. (1966)	Cutting Cd-plated bolts with an oxyacetylene torch dismantling a girder frame	-CdO fumes, calculated exposure: 8.63 mg/m^3. Cd in lung tissue (at autopsy): 2.5 µg/g ww	5	1 death after 5 days (on day of exposure, irritating cough, breathlessness. Three days later, breathlessness, cyanosis and pyrexia. Fifth day, slight improvement in the chest but haemoptysis, then deterioration and death). At autopsy, massive pulmonary oedema and cortical necrosis in the kidneys
Townshend (1968)	Welding a Cd alloy	-Single day's exposure to Cd fumes	1	0 death Acute pneumonitis

Table 4.103 continued overleaf

Table 4.103 continued Acute human intoxications with cadmium metal and oxide fumes

Reference	Circumstances	Compound, exposure level and duration (when known)	Number exposed, age, sex, smoking (when known)	Clinical signs, outcome
Zavon and Meadows (1970)	Cutting the bolts of a water meter located in an underground vault with an oxygen-propane torch	Opening of the water meter had a diameter of 24 inches. No respirator, no ventilator before completion of the job. Exposure time > 1hour15 minutes, and potential exposure determined by simulating similar conditions: 38.6 mg/m³ with Zn content of 5.17 mg/m³	4 (2 in the vault, 56 and 29 year-old men, 2 outside)	-1 worker in the vault: on day of exposure, nauseated, then following day: fever, chest pain, cough, sore throat, on admission 4 days later: cyanosis, rales, elevated temperature, autopsy revealed coronary arteriosclerosis with massive infarction and corpulmonale, emphysematous changes in the lung and acute broncho-pneumonia, death after 18 days -other worker in the vault: felt nauseated and throat irritation during exposure, complained later of chills, nausea, difficulties in breathing, not hospitalised, recovery after 3 months -2 others (outside the vault) “not affected to any great extent”
Winston (1971)	Welding with Cd-Ag solder with oxyacetylene torch	Total brazing time: 20 minutes, mouth 30 cm from the valve (alloy containing 24-26% cadmium)	1	Severe symptoms and signs began to develop one hour after exposure, diagnosed as influenza with bronchitis, death 5 days later
Patwardhan and Finckh (1976)	Welding handles onto cadmium–plated drums	Cadmium fumes No protection Cd in lung tissue (at autopsy): 1.5 µg/g ww	1	Irritation of the throat, cough, difficulty in breathing some hours after exposure. Fevers, dyspnoeic, cyanotic, unable to walk and laboured speech 3 days after exposure. Pulmonary oedema, death (3.5 days later)

Table 4.103 continued overleaf

Table 4.103 continued Acute human intoxications with cadmium metal and oxide fumes

Reference	Circumstances	Compound, exposure level and duration (when known)	Number exposed, age, sex, smoking (when known)	Clinical signs, outcome
Lucas et al. (1980)	Working with an oxyacetylene torch and silver solder (which contained over 20% cadmium)	Fumes Duration of exposure: approximately 30 minutes Large airy building with high roof, doors open but no specific ventilation system Cd in lung tissue (at autopsy): 4.7 µg/g ww	1 man, 34 years	dyspnea and persistent productive cough within hours of completing the job, death (5 days after exposure)
Taylor et al. (1984)	Lead smelting (182 kg)	Smelting for about 24 hours in an enclosed environment without wearing adequate protective protection. Cd tissue concentrations measured , Cd-U "considerably increased (11 µg/l)" (normal 1.1 µg/l)	1 man, 36 years	vomiting, water diarrhoea, abdominal pain, headache, myalgia, tightness of the chest, slightly confused, shock, increasingly dyspnoeic, pulmonary oedema, fever, anuria, cyanosis, death (± 4 days after exposure)
Barnhart and Rosenstock (1984)	Silver soldering (contained cadmium)	1 hour in a closed, unventilated small tank with an opening only large enough to admit his upper body	1	At time of exposure: diplopia Later, same evening: cough, dyspnea, myalgias, febrile 2 weeks later: persistent cough and dyspnea (resolved over 4 weeks) 4 years later: chest X-ray normal, TLC below normal (79% predicted)

Table 4.103 continued overleaf

Table 4.103 continued Acute human intoxications with cadmium metal and oxide fumes

Reference	Circumstances	Compound, exposure level and duration (when known)	Number exposed, age, sex, smoking (when known)	Clinical signs, outcome
Seidal et al. (1993)	Manufacturing an apparatus for the illegal production of alcohol , keeping metal pieces in front while another was brazing with a silver solder (containing 20-30% cadmium)	In a garage, without using any respiratory protective equipment, brazing for about 15 minutes Cd in lung tissue (at autopsy) : 1.6 µg/g ww	2 men: a 78-year old, non-smoking man keeping the pieces in front and the other, brazing, who used respiratory protection (less exposed)	Continuous cough, fever, pneumonitis 3 days after exposure Sore throat and dyspnea 5 days later, cyanotic lips. Admitted to hospital, tachypnea, inspiratory ronchi Death due to respiratory insufficiency 25 days after exposure Autopsy: lungs were large and firm with appearance of extensive bronchopneumonia
Inoue et al. (1994) (only abstract)	Welding copper water supply pipe and used silver brazing with an oxyacetylene torch	7 hours of work	1, 48 year-old man	High fever, chill, dyspnoea, hypoxemia in blood gas analysis, diffuse bilateral lung shadow with ground-glass appearance (RX), lymphocyte infiltration and fibrous changes of the alveolar walls at lung biopsy Improved with corticosteroids
Ando et al. (1995)	Soldering a large iron pot with a silver alloy containing cadmium	Outdoors, but the man inserted his head into the pot without a protective mask. Duration of soldering: 30 minutes Cd-U levels on day 7 (10 days after exposure): 86.3 µg/l, on day 22: 3.3 µg/l	1 43 year-old man, 2 packs of cigarettes a day for 20 years	Nausea, sweet taste in mouth, dyspnea, chills, and fever. Next day, progressive dyspnea, fatigue and cough. Admitted on hospitalisation 3 days after exposure with rales and fever, fatigue and dyspnea On the 5th day, the dyspnea rapidly worsened (pulmonary edema) Recovery and discharged on postexposure day 25

Table 4.103 continued overleaf

Table 4.103 continued Acute human intoxications with cadmium metal and oxide fumes

Reference	Circumstances	Compound, exposure level and duration (when known)	Number exposed, age, sex, smoking (when known)	Clinical signs, outcome
Kilburn and McKinley (1996)	Fighting a fire in a battery box (banks of nickel-cadmium cells) beneath a passenger coach in a train	Composition of the fire's fumes not measured Concomitant exposure to vinyl chloride, but perhaps also other neurotoxic substances (lead, acrylonitrile,etc.) Cd-U: 485 µg/24h for patient 1, and 25 µg/24h for patient 2 (nl < 3)	2 train conductors: patient 1:38 years, non-smoker, patient 2:43 years, ex-smoker (10 cigarettes per day during 6 years)	Chest tightness, cough, painful breathing, muscle cramps, nausea. Shortly thereafter they became anosmic, had excessive fatigue, headaches, sleep disturbances, irritability, unstable moods and hypertension. Abnormal neurobehavioral testing + anosmia when compared to referents with persistent abnormalities 6 and 12 months later
Fernandez et al. (1996)	Flame-cutting an alloy containing around 10% of cadmium	60-75 minutes Cd-B: 0.34 µg/100ml, Cd-U: 17.6 µg/g creat 15 days after the fume inhalation	1, 53 year-old man	progressive dyspnoea, hypoxemia, cough, fever, chest pain Death (19 days later) on severe chemical pneumonitis
Barbee and Prince (1999)	Cutting a galvanised steel grating with acetylene torch	Recreation of exposure: elevated air levels for Cd and Zn	1, 43 year old man	Malaise, chills, fever 12 hrs after cutting. Over the next 72 hrs, progressive shortness of breath. Patchy and interstitial infiltration (bilaterally). Biopsy: focal mild interstitial pneumonia. Discharged after 13 days

N.I No information available
Cd-U Cadmium in urine
Cd-B Cadmium on blood

Causative agent was in almost every instance cadmium oxide fumes, formed readily when the metal was heated in air. Cadmium concentrations in air were not reported in most cases.

Initial symptoms during exposure may be mild and consist only of irritation of the throat and a nasty taste in the mouth. After some hours, patients developed symptoms suggesting the onset of an acute upper respiratory tract infection: irritation and dryness of nose and throat, cough, headache, dizziness, weakness, chills, fever, chest pain and breathlessness. Nausea and vomiting may also occur. This first stage is very similar to the typical "metal fume fever" caused e.g. by zinc fumes and often confounded with the chemical pneumonitis caused by cadmium. Both diseases begin several hours after exposure and symptoms closely mimic each other. However, while metal fume fever is spontaneously resolutive (zinc fume fever subsides usually in 12 hours or less), cadmium cases develop a prolonged phase of pulmonary reaction which may progress to serious consequences such as pulmonary oedema or respiratory failure. A fatal outcome several days after acute exposure to cadmium is frequently due to pulmonary oedema (Beton et al., 1966; Barnhart and Rosenstock, 1984; Bernard and Lauwerys, 1986).

There is no apparent relationship between the latency period and the severity of symptoms.

The lung content in cadmium has been investigated in some cases that were autopsied and compared to lung cadmium concentrations of occupationally unexposed men (30-79 years of age): values ranged from 1.5 to 4.7 µg/g ww versus 0.1 to 0.7 µg/g ww (Patwardhan and Finckh (1976), Lucas et al. (1980), Seidal et al. (1993), for exposed and non-exposed, respectively.

In some cases, urinary cadmium concentrations were normal at the time of diagnosis of intoxication (Beton et al., 1966). However, other case-reports suggest that after excessive cadmium exposure, there may be temporary elevations in urinary cadmium excretion:

Lucas et al. (1980) reported a fatal case of cadmium fume inhalation with an ante mortem urine cadmium level of 2,000 nmol/l (or 225 µg/l) (normal being < 112 nmol/l or 13 µg/l). Taylor et al. (1984) reported the case of a 36-year-old man who died 4 days after having been smelting 182 kg impure lead, contaminated by cadmium, and whose urinary cadmium level reached 11 µg/l (compared with a normal level of 1.1 µg/l). Blejer et al. (1966) have reported two cases of acute cadmium poisoning with increased cadmium concentrations in the urine on post-exposure day 4 in the fatal case (500 µg/l, determined at necropsy) and post-exposure day 13 (50 µg/l) in the non-fatal case. Data from Ando et al. (1995) suggest that elevated urinary cadmium excretions may persist for longer than two weeks following exposure and authors concluded that the measurement of urinary cadmium concentrations is an effective method for verifying recent cadmium poisoning (Ando et al., 1995).

Subjects who survive the acute episode may recover without permanent damage, but it is also possible that a single acute or even subacute pneumonitis may result in delayed development of lung impairment. A 34-year-old worker exposed to cadmium fumes from soldering for 1 hour (dose not determined), had persistent impaired lung function 4 years later (Barnhart and Rosenstock, 1984). Townshend (1982) reported the case of a welder who developed acute cadmium pneumonitis after a single day's exposure to cadmium fumes (dose not determined). Follow-up of the patient for 4 years did not reveal any permanent pulmonary damage, but 17 years later the man developed evidence of progressive pulmonary fibrosis which was presumed to be a late result of the acute poisoning. However, the man was a regular smoker and this assumption has to be taken cautiously.

Based on the measured cadmium concentrations in the lung, and other factors like the weight of the lung, and on the assumption that the percentage of retention of cadmium oxide fumes in human is the same as in animals, some authors estimated the lethal levels (Barrett et al., 1947, Elinder in CRC, 1986). Barret et al. (1947) calculated a lethal concentration in the air of 2,500 min · mg/m^3, from the Cd lung content found in deaths assuming that 11% retention in human lung occurred. Using same method, Beton et al. (1966) calculated the concentration of cadmium in fumes from post-mortem findings in one steel erector exposed for five hours and came to a quantity in keeping with the findings of Barrett et al. (1947): 2,589 min · mg/m^3.

Thus, for 8 hours of exposure, a lethal concentration would be around 5 mg/m^3 (2,400 min · mg/m^3). However, this estimate, as pointed out by the authors of above calculations and reviewers (CRC, 1986), includes a number of uncertainties concerning duration of exposure and the retention of cadmium in the human lung.

Table 4.104 Values available in the published literature

Type value	Dose		Dose	Remark	Reference
	mg/m^3	duration	(mg Cd · min/m^3)		
Lethal concentration	-	-	2,500-2,900	Calculated from post-mortem findings	Barrett et al. (1947)
Lethal concentration	8.63	5 hours	2,589	Calculated from post-mortem findings	Beton et al. (1966)
Lethal concentration	± 39	± 2 hours	4,632	Reconstitution of exposure conditions	Zavon and Meadows (1970)
Lethal concentration	5	8 hours	2,400	Review	CRC (1986)

Lethal exposure values have also been proposed by several organisms and are summarised in **Table 4.105** and are in the same range, probably based on the same estimations.

Table 4.105 Lethal exposure values

Compound	Dose		Dose	Dose	Reference
	mg/m^3	duration	(min · mg/m^3)	(mg/m^3 for 8 hours)	
CdO	5.2	8 hours	2,500	5.2	EPA (1985)
CdO	9.0	5 hours	2,700	5.6	ACGIH (1986)
CdO dust	40-50	1 hour	2,400-3,000	5-6.3	EPA (1985), ACGIH (1986)
CdO fume	40-50	30 minutes	1,200-1,500	2.5-3.1	EPA (1985), ACGIH (1986)

However, it has been stressed that this lethal value of 5 mg/m^3 should not be considered as the lowest concentration that can give rise to a fatal poisoning (CRC, 1986). Animal experiments indicate that exposure to lower concentrations can give rise to acute symptoms and a significant degree of lung damage. Therefore, it has been proposed that an exposure level of about 1 mg/m^3 should be considered as directly dangerous (CRC, 1986).

Summary of the acute toxicity of cadmium fumes and dust (inhalation route)

Acute poisonings and, in some cases, deaths have been reported among workers shortly after exposure to fumes when cadmium metal or cadmium-containing materials were heated to high temperatures. At an early stage, the symptoms may be confused with those of “metal fume fever”. However, these conditions are different, with Cd-lung leading to delayed pulmonary oedema and possibly death.

Subjects who survive the acute cadmium poisoning may recover without damage, although some authors have reported delayed development of lung impairment. Cadmium concentrations in air were not reported in most case-reports. It has been estimated that an 8-hour exposure to 5 mg/m^3 may be lethal and an 8- hour exposure of 1 mg/m^3 is considered as immediately dangerous for life.

Dermal route

No data were located about the acute dermal toxicity of cadmium oxide and/or cadmium metal in humans.

Only a few data were located on the dermal toxicity of cadmium compounds. Among eczema patients patch-tested with one dose of cadmium chloride (2%), 25 out of 1,502 showed some reaction (irritation) (Wahlberg, 1977). No other effects were reported.

Available information in the published literature does not allow the derivation of a N(L)OAEL. However, acute toxicity effects of cadmium via the dermal route are not expected to be significant as uptake of soluble and less-soluble cadmium compounds applied on the skin appears to be low (see Section 4.1.2.2 Toxicokinetics and 4.1.2.2.2 Absorption dermal route).

Other routes

Not relevant for human risk assessment.

Conclusions: human studies

- Ingestion of food or beverages contaminated with significant amounts of cadmium (species not otherwise specified) gives rise to acute symptoms. The no-effect level (NOAEL) of a single oral dose is estimated at 3 mg elemental Cd.
- Brief inhalation of high concentrations of cadmium compounds can give rise to severe, potentially fatal pulmonary damage. The compound involved in such accidental, acute cases is predominantly a freshly formed fume of cadmium oxide. Information on Cd metal is not available.

General conclusions

Relevant effects are acute respiratory effects: lethality and chemical pneumonitis.

Parameter	Endpoint	Animals	Humans	Type value
LOAEL	Chemical pneumonitis	0.5 mg CdO/m^3 (180 min)	1 mg Cd/m^3 (480 minute)	Directly dangerous

Summary information related to the classification[25] as well as the judgement on the fulfilment of the base-set requirements

[25] The **classification was done for cadmium oxide** and based on specific substance data, if available, and/or data from other cadmium compounds (more soluble forms).

For metallic cadmium the same classification is extrapolated on the basis of the so-called 'ion theory' and as a 'worst case' approach related to the bio-availability of the metal.

Oral route

According to the LD_{50} values, a classification as T; R25 is considered justified.

Inhalation

A classification for acute toxicity by inhalation is warranted: T; R23.

Dermal

No classification for acute toxicity by dermal route is required.

4.1.2.4 Irritation

4.1.2.4.1 Skin

Studies in animals

No studies were located regarding irritation effects in animals after exposure to cadmium oxide and/or metal.

Studies in humans

No studies were located regarding dermal effects in humans after exposure to cadmium oxide and/or metal.

Cadmium chloride (2%) in distilled water was included in routine patch series together with about 30 well-known contact allergens. None of the patients tested had experienced any exposure to cadmium compounds. 25 out of the 1,502 (1.7%) tested patients showed some reaction (+ to ++, but no vesicular reactions (Wahlberg, 1977). In 6 of these reactive patients, a serial dilution test was performed: only one reacted down to 1.0% cadmium chloride; all others were negative to all dilutions applied. ATSDR (1999) considered that the effect observed at 2.0% $CdCl_2$ was likely direct irritation of the skin as no reaction was found at lower dilutions and 2.0% was indicated as a LOAEL value.

4.1.2.4.2 Eye

Studies in animals

No studies were located regarding eye irritation effects in animals after exposure to cadmium oxide and/or metal.

Studies in humans

No studies were located regarding ocular effects in humans after exposure to cadmium oxide and/or metal.

4.1.2.4.3 Respiratory tract

Studies in animals

No studies were located regarding respiratory irritation effects in animals after exposure to cadmium oxide. However, based on data after single (see Section 4.1.2.3) and repeated inhalation exposure (see Section 4.1.2.7), it could be appropriate to consider cadmium oxide (fumes, dust) as an irritant to the respiratory tract, after inhalation exposure. No data were located on respiratory effects of cadmium metal dust and powder.

In animals, the lowest dose reported to cause mild pulmonary damage (hypercellularity indicative of hyperplasia) after single exposure was a concentration of 0.5 mg Cd/m^3 (3 hours) as CdO fumes. Lowest dose reported to cause lung changes after repeated exposure of the respiratory tract to CdO fumes was 50µg CdO/m^3 in rats for 13 weeks (rats) and 10 µg in hamsters (for 14 months).

Studies in humans

No studies were located regarding irritant effects on the respiratory tract in humans after exposure to cadmium oxide and/or metal. However, as in animals, based on the data after single (see Section 4.1.2.3) and repeated inhalation exposure (see Section 4.1.2.7); it seems possible that cadmium oxide/metal (fumes) are irritant to the respiratory tract. No data were available to identify a threshold.

Summary

No data were located regarding the irritation potential of cadmium oxide and/or metal on skin, eye and respiratory tract in animals and in humans. Based on the data after acute and repeated exposure, it seems however possible that cadmium oxide/metal (as fumes) are irritant for the respiratory tract in animals as in humans.

Summary information related to the proposed classification[26] as well as the judgement on the fulfilment of the base-set requirements

Skin

The base-set is formally incomplete. However, given the carcinogenic properties of the substance, it is supposed that risk reduction measures are in place to prevent irritation, if any, to occur. There is therefore little benefit expected from an additional effort to clarify the need to label CdO/Cd metal for skin irritation; no classification for skin irritation is warranted.

Eye

The base-set is formally incomplete. However, given the carcinogenic properties of the substance, it is supposed that risk reduction measures are in place to prevent irritation, if any, to

[26] The **classification was done for cadmium oxide** and based on specific substance data, if available, and/or data from other cadmium compounds (more soluble forms).

For metallic cadmium the same classification is extrapolated on the basis of the so-called ‘ion theory’ and as a ‘worst case’ approach related to the bio-availability of the metal.

occur. There is therefore little benefit expected from an additional effort to clarify the need to label CdO/Cd metal for eye irritation; no classification for eye irritation is proposed.

Respiratory tract

The base-set is formally incomplete. A classification as Xi; R37 might have been indicated based on effects reported in single and repeated exposure. However, given the carcinogenic properties of the substance, it is supposed that risk reduction measures are in place to prevent irritation, if any, to occur. There is therefore little benefit expected from an additional effort to clarify the need to label CdO/Cd metal for respiratory irritation; no classification for respiratory irritation is proposed.

4.1.2.5 Corrosivity

No studies were located regarding corrosive effects on the skin, the eye and the respiratory tract in humans after exposure to cadmium oxide and/or cadmium metal.

4.1.2.6 Sensitisation

4.1.2.6.1 Skin

Studies in animals

No studies were located regarding sensitisation effects in animals after exposure to cadmium oxide/Cd metal.

Only one study could be located investigating the skin sensitisation potential of the water soluble cadmium compound $CdCl_2$. In this test Guinea pigs showed no contact sensitisation following intradermal or topical exposure to cadmium chloride at concentrations up to 0.5% (Wahlberg and Boman, 1979). The test is stated to be performed using the Guinea Pig Maximisation Test but at least some deviations from the current regulatory test protocol are noticed. Furthermore the study is only briefly reported, no justification for the used dose levels is given, observation at induction are omitted and the challenge results are provided without grading scores.

Studies in humans

No studies were located regarding a sensitisation effect of cadmium oxide/Cd metal.

Positive patch-test reactions to $CdCl_2$ and $CdSO_4$ have been summarised by Wahlberg (1977).

Table 4.106 Test reactions to cadmium compounds reported in the literature (in Wahlberg, 1977)

Reference	Total number tested	% Positive	Concentration-Compound
Borelli (1965)	6,798	1.01	2.0% $CdSO_4$
Scarpa and Ferrea (1967)	356	1.1	2.0% $CdSO_4$
Düngemann et al. (1972)	356	3.5	2.0% $CdSO_4$
Fregert and Hjorth (1969)	651	0	2.0% $CdCl_2$
Hegyi et al. (1974)	248	1.2	2.0% $CdSO_4$

According to the authors, the percentage of positive reactions may have varied with the vehicle used for the cadmium solution (ethanol or water) or with possible impurities contained in the test substance (Wahlberg, 1977). No details are available on previous exposures to cadmium compounds.

Positive patch-test reactions were also observed in 8 out of 21 denture wearing persons with burning mouth sensations during 1979 and 1980 and in 13 of 125 patients attending a Dermatological Department in 1980 and 1981. After re-testing these patients with cadmium chloride and cadmium sulphate, only 7 persons demonstrated a clear skin reaction indicative of a sensitisation reaction. In one case, the sensitisation had probably occurred during occupational exposure in a PVC plant where the subject had worked for 2 years. In the remaining 6 cases, the most likely exposure factor to cadmium were probably the smoking habits, as all the persons were heavy cigarette smokers with a daily consumption in excess of 25 cigarettes for periods or more than 10 years. The reported observations did not lend support to the pink acrylic denture base material as being a relevant cadmium exposure factor (Kaaber et al., 1982).

With regard to cadmium metal and cadmium oxide, the accumulated experience in occupational practice over several decades does not indicate a sensitising potential. Furthermore no worker compensation case related to that effect has ever been registered at least in Belgium.

Examination of the available experimental and human studies leaves the picture unclear as to whether cadmium or cadmium oxide has properties of skin sensitisation.

4.1.2.6.2 Respiratory tract

Studies in animals

No studies were located regarding respiratory sensitisation in animals after exposure to cadmium oxide/Cd metal. There exists no validated experimental method to assess the respiratory sensitising potential of inhaled particles. No alternative tests (e.g. Mouse Ear Swelling Test, Local Lymph Node Assay) which could give some indication on the respiratory sensitising potential of cadmium oxide/metal were located.

Studies in humans

No studies were located regarding sensitisation effects on the respiratory tract in humans after exposure to cadmium oxide/Cd metal.

CdO/Cd metal is apparently not respiratory sensitisers and should not be classified for this property.

Summary information related to the classification[27] as well as the judgement on the fulfilment of the base-set requirements

Skin

No test results with cadmium (oxide) as test substance were submitted. A single test with a soluble cadmium salt ($CdCl_2$) was located in animals (with negative result but insufficient information to document the test conditions). A skin sensitisation test with CdO and/or Cd metal, conform to the current regulatory standards, would be formally requested. However, given the carcinogenic properties of the substance, it is supposed that risk reduction measures are in place to prevent sensitisation, if any, to occur. In addition, the overall evidence from available data on other cadmium compounds in humans -including the fact that for cadmium (oxide) no effects are reported in occupational practice- does not warrant a classification of cadmium oxide as skin sensitiser.

Respiratory

CdO/Cd metal are apparently not respiratory sensitisers and should not be classified for this endpoint.

4.1.2.7 Repeated dose toxicity

Lower cadmium concentrations with longer periods of exposure than those described in Section 4.1.2.3 (acute toxicity) will cause chronic cadmium poisoning.

Prolonged occupational exposure to cadmium dust or fumes can give rise to chronic pulmonary disorders, characterised by obstructive changes. The kidney damage resulting from chronic cadmium intoxication has been known to exist since the early studies among alkaline battery workers in the late 1940s.

For people in the general environment, exposure occurs usually by the oral route. In advanced cases of cadmium poisoning, where the main source of cadmium was contaminated rice, manifestations including osteoporosis and osteomalacia have accompanied kidney dysfunction.

Other potential target systems have been explored: data about cardiovascular, gastro-intestinal, haematological, liver, neurological and immunological effects have been reported.

Information about the adverse effects of cadmium will be reviewed by target organ (lung, bone, kidney, liver, others), separating animal from human data and inhalation from oral exposure. This mode of presentation which departs from the classical format was used to facilitate the readability of the document.

The term “cadmium compounds” refers to other compounds of cadmium than cadmium oxide and cadmium metal and includes cadmium chloride, cadmium acetate, cadmium sulfide, etc. Data relating to these compounds are given hereafter with another letter size and type. Data on cadmium compounds are included in the CdO/Cd metal risk assessment when no (not enough)

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[27]. The **classification was done for cadmium oxide** and based on specific substance data, if available, and/or data from other cadmium compounds (more soluble forms).

For metallic cadmium the same classification is extrapolated on the basis of the so-called ‘ion theory’ and as a ‘worst case’ approach related to the bio-availability of the metal.

information on the effects of CdO/Cd metal is available and when the studies using cadmium compounds are mechanistically relevant.

4.1.2.7.1 Lung

Studies in animals

Oral route

No experiments using cadmium oxide or cadmium metal were identified.

Some experiments were conducted with cadmium chloride.

No respiratory effects were seen in Rhesus monkeys fed with 4 mg Cd/kg/day in food for 9 years (Masaoka et al., 1994 cited in ATSDR 1999). Ingestion of 2.4 mg Cd/kg/day caused lung fibrosis after 6 and 16 weeks in (Miller et al., 1974 cited in ATSDR 1999).

Petering et al. (1979) observed a reduced static compliance and lung lesions (not detailed) in male rats exposed via water to 1.2 mg Cd/kg/day for 200 days. Zinc deficient rats were more susceptible to lung lesions from exposure to $CdCl_2$. Rats exposed to 3.62 mg Cd/kg/day via water for 120 days developed emphysema (Petering et al., 1979 cited in ATSDR 1999).

Lung weight was unchanged in rats after 90 days of exposure in drinking water at 16 mg/kg/day (Prigge, 1978 cited in ATSDR 1999).

No histopathologic lesions of the lung were found in male rats after 24 weeks of exposure to cadmium chloride in drinking water at a maximum dose of 8 mg/kg/day (Kotsonis and Klaassen, 1977 cited in ATSDR 1999).

Inhalation route

No study specifically using cadmium metal dust or powder was located.

Chronic pneumonia and emphysema were found in rabbits exposed to cadmium-iron oxide dust (approximately 4 – 5.6 mg/m^3, 3 hours/day, 21 - 23 days/ month for 8 months (median aerodynamic diameter (MMAD) unreported in CRC 1986). All the rabbits showed signs of emphysema in addition to inflammatory changes (Friberg, 1950 in CRC 1986).

Yoshikawa et al. (1975) exposed rats to cadmium oxide fumes (0.1 or 1.0 mg Cd/m^3) for up to three months. Each group included 10 rats and 3/10 rats of the high-exposure group died after about 7 weeks. Lung fibrosis and the first stage of emphysema were observed at the end of the experiment in the high-dose group (Yoshikawa et al., 1975, cited in WHO 1992).

Prigge (1978) exposed female Wistar rats to concentrations of 25, 50 and 100 µg Cd/m^3 (as cadmium oxide), continuous for 90 days in the 25 and 50 µg Cd/m^3 groups, and for 63 days in the last group (MMAD: 0.19 µm, standard deviation: 1.5). No clinical signs were reported (Prigge et al., 1978).

In a thirty-day inhalation study, male Wistar rats were exposed to aerosols of cadmium oxide (100 µg Cd/m^3, 22 hours/day, 7 days a week, MMAD: 0.2-0.5 µm) (Glaser et al., 1986). No clinical signs of intoxication were reported, except elevated white blood cell counts (12.9 ± 3.6 10^6/ml for the CdO exposed rats versus 8.9 ± 1.9 10^6/ml for the controls, $p < 0.05$) and elevated serum activities of the GPT in the CdO exposed group (42 ± 6 U/l serum for exposed rats versus 29 ± 4 U/l for the controls).

In a 13-week study, F344/N rats and $B6C3F_1$ mice were exposed to 0, 25, 50, 100, 250, and 1,000 µg CdO/m³ (MMAD: 1.1-1.6 µm, standard deviation: 0.1). No effects on survival of rats or mice were observed. Clinical signs of toxicity included nasal discharge in male and female rats, the frequency of this sign increasing with exposure concentration. No clinical signs of toxicity considered to be related to cadmium oxide exposure were observed in male or female mice during the study (NTP report, 1995).

- Histological examination after inhalation of CdO fumes and/or dust has been performed in a number of studies:

In the study of Prigge et al. (1978), the histological investigation of the lungs revealed the occurrence of emphysematic areas, cell proliferation studies of the bronchi, bronchioli and alveoli, and histiocytic cell granulomas in almost all exposed animals (Prigge et al., 1978)

In rats exposed to an atmosphere of 1.6 mg Cd/m^3 for several weeks (as CdO for 80 ± 5%, 3 hours/day, 5 days/week, 1 to 6 weeks), histopathological examination performed on the lungs reported following findings: aggregates containing mononuclear cells and polymorphonuclear leukocytes were observed in the interstitium of the lung after 2 weeks of exposure and there was also some thickening in alveolar septa (Hart, 1986).

In both groups of rats of Yoshikawa et al. (1975), at examination, free macrophage cells in the alveoli were numerous, and there was an increased surface tension of the surfactants (Yoshikawa et al., 1975 cited in WHO 1992).

When Syrian Golden hamsters were exposed to aerosols of cadmium oxide (10- 90-270 µg Cd/m^3 for 16 months, 5 days a week, 8 hours a day, particle size unknown), hyperplasia in the peribronchiolar regions was observed in the two highest dosed groups (90-270 µg Cd/m^3). No proliferative activity was seen in the 10 µg Cd/m^3 group (Aufderheide et al., 1989).

Small numbers of these animals were derived for ultrastructural evaluation: inhalation of Cd-compounds caused acute damage to type-I epithelium and proliferation of type-II pneumocytes in the centro-acinar region of the alveolar duct in the hamster and in the rat. Damage was more pronounced in the rats than in the hamsters (Thiedemannn, 1989). Type-II cells proliferation initially lead to the formation of type-II cell hyperplasias in both species. These type-II cells later differentiated into Clara cells in the hamster but not in the Wistar rats. Authors considered the different composition of the interstitial matrix and/or differences in cell/matrix interactions as possible mechanisms to explain these discrepancies (Thiedemann et al., 1989).

In other experimental inhalation carcinogenicity studies, CdO induced similar toxic lesions characterised by alveolar lipoproteinosis, interstitial fibrosis, hyperplasia in mice, necrosis of type I pneumocytes, proliferation of epithelial cells and focal alveolar inflammation in rats (Heinrich et al., 1989; Glaser et al., 1990; Takenaka et al., 1990 cited in NTP Report 1995).

In the 13-week study cited in the NTP report (1995), treatment related microscopic lesions were present in all exposed rats except those in the 25 µg CdO/m³. Histopathologic findings included alveolar histiocytic infiltrates, inflammation and fibrosis. At the end of the study, necrosis of the alveolar epithelium was not apparent but a dose-related increase in hyperplasia of the type II epithelium was evident at exposure of 50 µg/m³ and greater (NTP report, 1995).

Table 4.107 Selected histopathologic lesions for male and female F344/N rats in the 13-week inhalation study of CdO (NTP Report, 1995)

		Concentration (mg/m³)					
		0	0.025	0.05	0.1	0.25	1
Lung	Cd concentration (µg/g lung)§	0.05	N.I.	N.I.	19.1*	29.4**	39.5**
	Weight (absolute and relative)	NS	NS	NS	↑	↑	↑
	Alveolar histiocytic infiltrate	-	-	+	+	+	+
	Alveolar epithelial hyperplasia	-	-	+	+	+	+
	Inflammation	-	-	-	-	+	+
	Fibrosis	-	-	-	+	+	+
Toxicity in other organs of the respiratory system	Mediastinal lymph node						
	Inflammation	-	-	-£	+	+	+
	Larynx##						
	Epithelial degeneration	-	+	+	+	+	+
	Nose###						
	Olfactory epithelium						
	Degeneration	-	-	-	-	+	+
	Resp.metaplasia	-	-	-	-	-£	+
	Squamous metaplasia	-	-	-	-	-	+
	Respiratory epithelium						
	Inflammation	-	-	-	-£	+	+
	Degeneration§	-	-	-	-	-	+

- No lesions present (histopathology)
+ Significantly different from the control group
NS Not significantly different from the control group
N.I. Not measured at this exposure level
£ Significant in females
§ Results in male rats
* Significantly different (p≤0.05) from the control group by Shirley's test
** Significantly different (p≤0.01) from the control group by Shirley's test
Larynx was considered to be a common site for lesions in rodents exposed by inhalation to chemicals with characteristic lesions including metaplasia, erosion, ulceration and inflammation (NTP Report, 1995)
Nasal toxicity was considered as being characteristic of inhalation exposure to metallic compounds (NTP Report, 1995)
↑ Increased

NOAEL rats (lung effects): 0.025 mg CdO/m³

Table 4.108 Selected histopathologic lesions for male and female B6C3F1 mice in the 13-week inhalation study of CdO (NTP Report, 1995)

		Concentration (mg/m^3)					
		0	0.025	0.05	0.1	0.25	1
Lung	Weight (absolute and relative)	NS	NS	↑	↑	↑	↑
	Alveolar histiocytic Infiltrate#	-	+	+	+	+	+
	Alveolar epithelial hyperplasia	-	-	-	+	+	+
	Inflammation	-	-	-	+	+	+
	Fibrosis	-	-	+	+	+	+
Toxicity in other organs of the respiratory system	Tracheobronchial lymph node						
	Hyperplasia						
	Larynx	-	-	+	+	+	+
	Squamous metaplasia##						
	Nose###	-	+	+	+	+	+
	Olfactory epithelium						
	Degeneration						
	Resp.metaplasia	-	-	-	+	+	+
	Squamous metaplasia	-	-	-	-	+££	+
	Respiratory epithelium	-	-	-	-	-	+££
	Hyaline droplets	-	-	-	-	+	+

- \- No lesions present (histopathology)
- \+ Significantly different from the control group
- NS Not significantly different from the control group
- N.I. Not measured at this exposure level
- ££ Not significant in females
- ## Reported to be morphologically similar to the epithelial degeneration that occurred in the larynx of the rats. Larynx was considered to be a common site for lesions in rodents exposed by inhalation to chemicals with characteristic lesions including metaplasia, erosion, ulceration and inflammation (NTP Report, 1995)
- ### Nasal toxicity was considered as being characteristic of inhalation exposure to metallic compounds (NTP Report, 1995)
- ↑ Increased

NOAEL mice: could not be determined.

- Adverse effects on lung have also been evaluated in different studies by analysis of the bronchoalveolar fluid:

In the study of Glaser et al. (1986), Wistar rats were exposed to an aerosol of cadmium oxide (100 µg/m^3, 22 hours a day, 7 days a week for 30 days), and bronchoalveolar lavage analyses demonstrated an elevation of the macrophage cell counts that amounted up to 3.3 times that of the controls. The alveolar macrophages were larger when compared to controls (size: 13.1 ± 0.3 µm versus 10.5 ± 0.2 µm, $p < 0.05$). Lavaged leukocytes were elevated (50.5 ± 8.7 $\cdot$ 10^4 for the exposed group versus 2.1 ± 0.7 $\cdot$ 10^4 for the controls, $p < 0.05$) and increased protein levels were measured in all CdO-exposed animals (10.2 ± 1.7 mg vs. 6.1 ± 1.0). High quantities of lavaged lactate dehydrogenase (3.0 ± 0.5 U vs. 1.2 ± 0.8 for exposed when compared to controls, $p < 0.05$), and β-glucoronidase (761 ± 85 mU versus 54 ± 47 mU for exposed and controls respectively) were reported (Glaser et al., 1986).

Results of bronchoalveolar lavage fluid analysis in rats exposed to an atmosphere of 1.6 mg Cd/m^3 for several weeks (as cadmium oxide for 80 ± 5%, 3 hours/day, 5 days/week, 1 to 6 weeks) showed evidence of injury: cytological alterations in lavage fluid of the exposed animals were characterised by increases in total alveolar cell population (12.5 $\cdot$ 10^6 cells for the exposed rats versus 2.5 $\cdot$ 10^6 as control value), due mostly to increases in alveolar macrophages and polymorphonuclear leukocytes. There were also significant elevations in total protein and all of the enzymes assayed after 1 or more weeks of exposure. Interesting to note was that, in spite of the continued increase in cadmium burden in the lung, the severity of the pulmonary damage did not progress after 2 weeks of Cd exposure: biochemical and cytological alterations began to resolve during the third week (Hart, 1986).

An explanation suggested by the author is the possible involvement of the synthesis of metallothionein-like proteins by the lung that could serve to sequester the cadmium and render it less toxic. This was supported by the observation of a linear increase in the total amount of metallothionein in the lung as a function of the number of weeks of exposure (from a value of 7.5 ± 0.8 nmol Cd-thionein/lung in unexposed animals to a value of 270.34 ± 31.8 nmol following 5 weeks of Cd inhalation). Authors concluded that the lung appeared more and more able to cope with the accumulating Cd as metallothionein amounts rose (Hart, 1986).

In a later paper, the same authors reported that male rats pretreated by inhalation exposure 1.6 mg Cd/m^3 for 4 weeks (3 hours per day, 5 days per week) exhibited pulmonary tolerance when challenged with a single exposure to 8.4 mg/m^3. This tolerance was suggested by the reduction in the number of inflammatory cells in the bronchoalveolar fluid, the decrease of the release of enzymes in the alveolar space and the earlier resolution (compared to controls) in the lung histopathology. Mechanisms of defence suggested were the increase in the type II alveolar cells in the pretreated animals (those cells may be responsible for increasing antioxidant enzymes in the lung) or the synthesis of metallothionein (the content in pre-exposed animals was 50-fold higher than that in untreated animals (Hart et al., 1989).

Other authors have reported a clear agreement between the levels of lung cytosolic cadmium and the metallothionein content of the lung: in the aforementioned study of Glaser et al. (1986), the MT content in the lungs had increased five times compared to the controls at the end of the inhalation period (mean: ±1.32 µg MT/mg protein for the CdO exposed rats versus 0.26 µg MT/mg protein for the controls) (Glaser et al., 1986).

Against these findings stands an early study by Princi and Geever (1950). They exposed dogs, in special inhalation exposure chambers, to cadmium oxide dust (10 dogs, 6 hours/day, 5 days/week, for 35 weeks) without finding any respiratory changes at post-mortem when compared with a control group. Average cadmium concentration in air was 4 mg/m^3. Of the particles, 98% were less than 3 µm in diameter. No evidence of pulmonary fibrosis, emphysema or alveolar wall thickening was seen. In his comments (CRC, 1986) about this study, Elinder stated that several of the dogs had to be killed because of severe injuries received while fighting among themselves and that at examination; it was observed that these animals suffered from bronchopneumonia. As emphasised by Elinder, this study appears to present several methodological drawbacks and the reported findings should not be taken as indication that cadmium does not cause lung lesions (Princi and Geever, 1950, cited in CRC 1986).

Conclusions

Studies in animals

No study specifically using cadmium metal was located. Since inhalation exposure to cadmium metal dust is very unlikely in occupational settings, this absence of information is not deemed critical.

No study reporting lung effects after oral exposure to cadmium oxide was located.

Some lung effects (weight changes, fibrosis) were seen after oral administration of cadmium compounds in rats (1.2-3.62 mg/kg for several weeks) but no effects were reported at higher doses (8-16 mg Cd/kg/day for 12-24 weeks, 4 mg/kg/day (in monkeys) for 9 years). It has been suggested that the observed lung effects would be related to liver or kidney damage and subsequent changes in cellular metabolism.

Long-term inhalation exposure to cadmium oxide in animals results in similar effects as seen upon acute exposures, i.e. pneumonia and emphysema accompanied by histopathologic alterations and changes in the cellular and enzymatic composition of the bronchoalveolar fluid. Differences in metallothionein metabolism could be noted as an explanation for differences in response.

Some tolerance to cadmium appears to develop with duration so that lung lesions developed after a few weeks of exposure do not progress, and may ever recover after longer exposure. Multiple mechanisms could explain this tolerance, including the synthesis of lung metallothionein and proliferation of type II cells (ATSDR, 1999).

Identified NOAELs are: 0.025 mg CdO/m^3 in F344/Nrats exposed for 13 weeks and 0.01 mg Cd/m^3 in hamsters exposed for 16 months.

Studies in humans

Oral route

No studies were located regarding respiratory effects in humans after oral exposure to cadmium oxide or cadmium metal.

Inhalation route

Friberg published the first study on a large number of workers on possible chronic respiratory effects of cadmium in 1950. He examined 43 male workers exposed to cadmium oxide dust (3-15 mg/m^3) with a period of employment ranging from 9 to 34 years (long exposure) and 15 male workers who had been employed for only 1-4 years (short exposure). He compared them with a group of 200 sawmill workers. He reported an increased residual quotient, estimated as the ratio between the residual volume and the total lung capacity in percent (100% x RV/TLC) for the workers exposed for a long time to cadmium. The lung function of the group with short exposure was found to be normal (Friberg, 1950 cited in CRC, in WHO 1992).

The Swedish results were later supported by the observations of several other authors (Baader, Bonell et al., Smith et al., Gill, Lauwerys, and Davison). However, there are also some studies in which authors report no evidence of effects on the respiratory system from cadmium exposure (e.g. Princi, Tsuchiya, Teculescu and Stanescu, Edling et al.) (CRC, 1986).

All the identified studies have been summarised in the tables below (**Table 4.109** and **4.110**) and are commented, grouped in two categories: A. the studies reporting lung changes and concluding to an adverse effect of cadmium on the respiratory function; and B. the studies reporting no lung changes in cadmium-exposed workers and concluding to the absence of deleterious effect of cadmium.

Table 4.109 Clinical studies reporting lung changes in workers chronically exposed to cadmium

Reference	**Main characteristics of the population**	**Exposure assessment**	**Findings**			**Considered confounders**
			Subjective symptoms	**Chest X-ray**	**Lung function test**	
Hardy and Skinner (1947)	E: 5 (M only) C: 0	Type of compound: CdO fumes Exposure duration: 4-8 years Exposure level: *Cd-air:* 100 µg/m³ *Cd-B:* N.I. *Cd-U:* 0.01-0.05 mg/L	+	-	N.I.	Smoking: N.I. Other simultaneous exposures: N.I.
Friberg (1948,1950)	E: 43 (M only) C: 200	Type of compound: Cd iron oxide dust Exposure duration: 9-34 years (mean = 20 years) Exposure level: *Cd-air:* 3,000-15,000 µg/m³ *Cd-B:* N.I. *Cd-U:* N.I.	+	+ (N=14)	+ (N=14)	Smoking: N.I. Other simultaneous exposures: N.I.
Baader (1951)	E: 8 (M only) C: N.I.	Type of compound: CdO dust Exposure duration: 8-19 years Exposure level: *Cd-air:* 1 – 270 µg/m³ *Cd-B:* N.I. *Cd-U:* N.I.	+	+ (N=6)	N.I.	Smoking: N.I. Other simultaneous exposures: N.I.

Table 4.109 continued overleaf

Table 4.109 continued Clinical studies reporting lung changes in workers chronically exposed to cadmium

Reference	Main characteristics of the population	Exposure assessment	Findings			Considered confounders
			Subjective symptoms	**Chest X-ray**	**Lung function test**	
Bonnell (1955)	E: 100 (M only) C: 104 (M only)	Type of compound: CdO fumes Exposure duration:5- > 20 years Exposure level: *Cd-air:* N.I. *Cd-B:* N.I. *Cd-U (µg/ specimen of 200 ml):* Range: 42-1,240 µg.	+ (N=19)	+ (N=9)	+	Smoking: N.I. Other simultaneous exposures: N.I.
Potts (1965)	E: 70 (M only) C: N.I.	Type of compound: CdO dust Exposure duration: > 10-40 years Exposure level: *Cd-air:* Up to 1949: 600-23,600 µg/m³ Since 1950: < 500 µg/m³ *Cd-B:* N.I. *Cd-U:* N.I.	" Emphysema and chronic bronchitis in 4 workers"	N.I.	N.I.	Smoking: N.I. Other simultaneous exposures: N.I.
Adams et al. (1969)	E: 27 (M only) of the same factory C: N.I.	Type of compound: CdO dust Exposure duration: 5-44 years Exposure level: *Cd-air:* (see above) Since 1957: 1st area:300-5,000 µg/m³, 2nd area:100-1000 µg/m³, 3rd area:50-200 µg/m³ *Cd-B:* N.I. *Cd-U:* N.I.	N.I.	N.I.	+ (N=5)	Smoking: N.I. Other simultaneous exposures: N.I.

Table 4.109 continued overleaf

Table 4.109 continued Clinical studies reporting lung changes in workers chronically exposed to cadmium

Reference	Main characteristics of the population	Exposure assessment	Findings			Considered confounders
			Subjective symptoms	Chest X-ray	Lung function test	
Materne et al. (1975)	E: 90 (M only) in two groups	Type of compound: CdO dust and Cd fumes Exposure duration: < 20 years (mean: 7.5 years) Exposure level: Cd-air: 1-88 µg/ m^3 (defined as respirable fraction) 3.7- 27,050 µg/m^3 (total concentration)	-	-	+	Smoking: yes Other simultaneous exposures: other compounds of Cd, lead: ±
		Cd-B (mean ± SD, µg/100 ml): 2.5 ± 0.3 Cd-U (mean ± SD, µg/g creat): 23.3 ± 3.3 Type of compound: CdO dust and fumes Exposure duration: > 20 years Exposure level: Cd-air: 1-88 µg/ m^3 (respirable fraction) 3.7- 27,050 µg/m^3 (total concentration) Cd-B (mean ± SD, µg/100 ml): 2.6 ± 0.3 Cd-U (mean ± SD, µg/g creat): 30.7 ± 4.5	+	-	+	Smoking: yes Other simultaneous exposures: other Cd compounds, lead: ±

Table 4.109 continued overleaf

Table 4.109 continued Clinical studies reporting lung changes in workers chronically exposed to cadmium

Reference	Main characteristics of the population	Exposure assessment	Findings			Considered confounders
			Subjective symptoms	Chest X-ray	Lung function test	
Smith et al. (1976)	E: 17 (M only), "high exposure population" C: 17	Type of compound: CdO fumes Exposure duration: mean: 26.4 years Exposure level: Cd-air: "commonly > than 200 µg/ m^3" Cd-B: N.I. Cd-U (mean ± SD, µg/L): 45.7 ± 16.9	-	-	+	Smoking: yes Other simultaneous exposures: cadmium sulfate : ±
Kossman et al. (1979)	E: 42 (M only) C: 0	Type of compound: N.I. Exposure duration:1-33 years Exposure level: N.I. Cd-air: N.I.; Cd-B: N.I.; Cd-U: N.I.	N.I.	+ (N=3)	+ (N≅ 20)	Smoking: N.I. Other simultaneous exposures: N.I.

Table 4.109 continued overleaf

Table 4.109 continued Clinical studies reporting lung changes in workers chronically exposed to cadmium

Reference	Main characteristics of the population	Exposure assessment	Findings			Considered confounders
			Subjective symptoms	Chest X-ray	Lung function test	
Sakurai et al. (1982)	E: High-exposure: 7 Low exposure: 9 C:122	Type of compound: cadmium dust and fumes Exposure duration: High-exposure (mean ± SD): 10.6 ± 5.7 years Low-exposure (mean ± SD): 7.3 ± 4.5 years Exposure level: Cd-air: High-exposure: 1970 (mean ± SD): 2340 ± 3030 µg/m³ (range): 60– 8400 µg/m³ 1974 (mean) : 53.8 µg/m³ 1977 (mean) : 38.5 µg/m³ Cd-B (µg/100 ml, mean ± SD): High-exposure: 2.08 ± 0.71 Low-exposure: 0.71 ± 0.11 Cd-U (µg/L, mean ± SD): High-exposure: 32.6 ± 12.1 Low-exposure: 2.4 ± 1.6	N.I.	N.I.	+	Smoking: yes Other simultaneous exposures: Yes High exposure: silver, zinc, copper Low-exposure: oil mists, acid mists, metal dusts

Table 4.109 continued overleaf

Table 4.109 continued Clinical studies reporting lung changes in workers chronically exposed to cadmium

Reference	Main characteristics of the population	Exposure assessment	Findings			Considered confounders
			Subjective symptoms	Chest X-ray	Lung function test	
Chan et al. (1988) cited in ATSDR (1999)	E: 44 (36F/8M) C: N.I.	Type of compound: CdO dust Exposure duration: N.I. Exposure level: Cd-air: 30-90 µg/m³ Cd-B: N.I. Cd-U: N.I.	+	N.I.	+	Smoking: N.I. Other simultaneous exposures: N.I.
Davison et al., (1988)	E: 101 (M only) C: 96 (M only)	Type of compound: Cadmium fumes Exposure duration: "for at least one year" Exposure level: Cd-air (year. µg/m³, N= 97) < 400: 34 workers 401-1,600: 37 workers > 1,600: 34 workers Cd-B: N.I. Cd-U: N.I. Cd-liver (ppm, mean ± SD) E: 26.1 ± 3.7 C: 0.6 ± 0.5	+	+	+	Smoking: yes Other simultaneous exposures: N.I.

Table 4.109 continued overleaf

Table 4.109 continued Clinical studies reporting lung changes in workers chronically exposed to cadmium

Reference	Main characteristics of the population	Exposure assessment				Findings			Considered confounders
						Subjective symptoms	Chest X-ray	Lung function test	
Cortona et al. (1992)	E: 69 (M only) C: 79 (M only)	Type of compound: Cadmium fumes Exposure duration: Exposure level: Cd-air (µg/m³)				N.I.	N.I.	+	Smoking: yes Other simultaneous exposures: N.I.
			Foundry A	Foundry B	Alloys				
		1975[a]	1530	100	-				
		1976[a]	128	70	14				
		1978[a]	207	30	12				
		1980[a]	139	22	25				
		1982[b]	67	28	3				
		1985[b]	67	12	3				
		1990[b]	30	8	3				

Table 4.109 continued overleaf

Table 4.109 continued Clinical studies reporting lung changes in workers chronically exposed to cadmium

Reference	Main characteristics of the population	Exposure assessment	Findings			Considered confounders
			Subjective symptoms	Chest X-ray	Lung function test	
		a: area sampling b: personal sampling *Cd-B (µg/L, mean ± SD):* 2.4 ± 1.9 *Cd-U (µg/L, mean ± SD)* 4.3 ± 3.9				

N.I. No information available in this publication
N number of subjects
\+ changes present
\- changes absent
E Cd exposed persons
C non-exposed persons
M males
F females
Cd-B blood cadmium
Cd-U urinary cadmium
Considered confounders (smoking, other simultaneous exposures):
yes were considered in selection of the population and in discussion
no not considered in selection of population nor in the discussion
± some attempt to consider this factor was made

Some authors had already drawn attention to the fact that cadmium might cause chronic illness before Friberg. Stephens (1920) described the case of a man who had been exposed to small quantities of cadmium (probably CdO) in a zinc smelter and who suffered from recurrent bronchitis, weakness and loss of weight (no more detailed). Mancioli (1940) described chronic rhinitis and pharyngitis in men plating metals with cadmium by an electrolytic process (authors reported by Bonnell, 1955).

Hardy and Skinner (1947), in a paper entitled "The Possibility of Chronic Cadmium Poisoning" reported observations on five men exposed to cadmium-containing dusts and fumes (probably CdO) over a period of several years. The symptoms reported by all these men were remarkably similar: fatigue, loss of appetite, coughing, substernal pain and a burning sensation in the throat were common to all. No details were available about other exposures or use of tobacco (Hardy and Skinner, 1947 cited by MacFarland, 1979).

In 1946, frequent complaints of tiredness and shortness of breath among men employed in an alkaline accumulator factory in Sweden led to an investigation by Friberg (1948, 1950). The men made small briquettes of cadmium and iron which composed the negative electrode of the accumulator. During manufacture, finely divided CdO dust passed into the working atmosphere and settled on the floor, machines and benches and on clothes, hands and faces of the workers.

Quantitative data concerning the exposure were incomplete as air analyses were carried out on only one occasion and at only five locations in the working areas. The reported concentrations of cadmium varied between 3,000 and 15,000 µg/m³.

Forty-three workers who had done this work for more than 9 years complained of dyspnoea, excessive tiredness, impairment of the sense of smell, cough and a sensation of dryness of the mouth (Friberg, 1948, 1950). The clinical studies included e.g. physical examination, X-rays and functional tests of the respiratory and cardiovascular systems. Impaired lung function was defined and demonstrated by an increased residual capacity (RC) in relation to total lung capacity (TLC). In about one third of the subjects exposed for a long time, this ratio (RC/TLC) exceeded 35%. This impairment was closely associated with poor physical working capacity evaluated by means of a standardised working test on a bicycle ergometer (Friberg, 1948, 1950 cited in CRC 1986).

Friberg and Nyström re-examined this population in 1952. Five of these 43 men had died and in two cases the death was due to emphysema. In nine of the remaining 38 men, five of them complained of increased dyspnoea, in 25 men the symptoms were unchanged and in the last four men, there was a distinct improvement in the performance of tests of respiratory function. Friberg concluded that the prognosis for men suffering from emphysema was favourable if they were removed from exposure before the symptoms became severe (Friberg and Nyström, 1952 cited by Bonnell, 1955)

Baader investigated a group of workers in an alkaline accumulator factory in Germany and eight of these were found to have emphysema, proteinuria, and loss of weight. No quantitative analysis of the exposure was reported. Emphysema was diagnosed by the author on the basis of clinical and X-rays findings but the used diagnostic criteria were not detailed. Complaints of coughing and shortness of breath were common (Baader et al., 1951 cited by Bonnell, 1955, CRC 1986). One of these workers died and autopsy findings were reported by Baader (1952): severe emphysema of the lungs was observed (Baader, 1952 cited in CRC 1986).

Lane and Campbell (1954) reported 2 fatal cases among a group of some 20 workers making copper alloys. Both men died of emphysema after working for less than 2 years. Industrial process suspected of being responsible for their condition consisted of melting copper (melting point 1083°C) and adding small quantities of cadmium (boiling point: 767°C). The workers stood on a platform above the molten mixture. The process was carried out under exhaust ventilation and workers were provided with respirators. However, at the critical moment of adding the cadmium, the mixture had to be stirred and the men pushed aside the exhaust hood to make it easier to stir. Added to the mixture, the cadmium immediately boiled and the workers were exposed to considerable quantities of fumes. Thus the workers worked under conditions of continuous exposure and determination of Cd levels in air was carried out over the period 1951-1953 (range: 0.07-0.21 mg/m^3). But an additional and different type of exposure was also considered by the authors, occurring when the exhaust ventilation was pushed aside, namely to cadmium fumes breathed in high concentrations for very short periods.

No proteinuria was found in the case where it was sought. Authors explained this by the short duration of exposure of the patient (less than 4 years) and noted that it was consistent with the findings of Friberg (1950) where no proteinuria was observed in the short-term exposure group (< 4 years of exposure).

It is not reported if the two men were smokers. One of them had worked previously in a coal-mine. However, at necropsy, the carbon pigmentation of his lungs was not sufficient to suggest a primary anthraco-emphysema (Lane and Campbell, 1954).

Bonnell (1955), King (1955), Kazantzis (1956), Smith et al. (1957) and Bonnell et al. (1959) reported observations on workers from two English factories manufacturing copper-cadmium alloys (containing 0.5 to 1% cadmium). Although the two factories used different types of furnace and differed for some details of the process, the method of manufacture was in principle the same.

In factory A, brass, bronze and copper-cadmium alloys were manufactured in the same workshop. Because the workshop was relatively small, Bonnell (1955) also included the workers engaged in the manufacture of brass and bronze in the exposed group, in addition to the 14 workers casting copper-cadmium. The control group was made up of 60 men with the same age distribution, never exposed to cadmium.

At factory B, the low-percentage copper-cadmium alloy was manufactured at one end of a large workshop. The 19 men employed casting copper-cadmium were included in the exposed group as were 23 men who had worked for a prolonged period in this process but were employed at the time of the survey in other departments. The control group was made up of 44 men in the same age distribution, who had worked in either the brass or the iron foundry for up to 30 years but who had never been exposed to cadmium. The maximum allowable concentration of cadmium in the working atmosphere had been set at 100 µg/m^3.

Bonnell identified 19 workers exposed to cadmium oxide fumes in these plants who exhibited emphysema, proteinuria or both. In addition, four men in one of the two factories (factory A) had been forced to give work up because of disabling shortness of breath. The clinical examination and chest radiographs (radiological criteria not detailed) of these last men suggested that the disability was due to emphysema. One of these four "factory A-workers" died and necropsy findings were reported by the authors: lungs were found to be oedematous with moderate diffuse but uneven emphysema, with occasional bullae measuring up to 2 by 1 cm.

Tests of the ventilatory capacity of the lungs (vital capacity, maximum ventilatory capacity at controlled rates of breathing, expiratory fast vital capacity) which were carried out at both factories showed that there was a definite impairment of respiratory function (fast vital expiratory capacity curve significantly lower in exposed group) in the groups of men exposed to cadmium when compared with control groups from the same factories (Bonnell, 1955).

King (1955) performed a thorough environmental survey of these two factories. Concentrations of cadmium in air were quite variable; ranging from as little as 1 µg/m³ to occasional peaks to about 270 µg/m³. About 90% of the particles had a size of less than 0.5 µm. From this report, it was obvious that the mean exposure must have been in fact, considerably less than 100 µg/m³. However, these last values are unlikely to be a true reflection of the working conditions at the time when the majority of the men affected started work. Indeed, these analyses were performed in the post-war period after improved controls and local exhaust ventilation had been installed. Concentrations were without doubt, fairly higher in the war-period, when to comply with blackout regulations, all windows and doors had to be closed and covered at night (King, 1955 cited by MacFarland, 1979, CRC 1986).

Kazantzis (1956) provided results of a detailed examination of the pulmonary function of all but 4 of the 100 workmen examined by Bonnell. It was found that nearly all subjects who exhibited clinical signs of emphysema performed abnormally in the pulmonary function tests. Vital capacity was not adversely affected, nor could this group be distinguished from a control group by means of differences in maximum ventilatory capacity. A reasonable degree of correlation was found between individual pulmonary function performance and the symptomatology and radiological findings of the subject (Kazantzis, 1956 cited by MacFarland, 1979).

Further studies were made on 37 of the exposed men from factory B (Buxton, 1956). Those men with more than 10 years exposure showed a significant increase in the mean value of the residual air expressed as a percentage of the total lung volume (mean 43.9%) compared with a control group (mean: 34.6%) and workers exposed less than 10 years (mean: 36.6%). There was no significant difference in the mean values for the total lung volume.

The workers from factory B with diagnosed emphysema all had been exposed from 7 to 27 years (Buxton, 1956 cited in CRC, 1986).

In 1956, a workman from the factory B died and was autopsied. This man had been exposed to cadmium oxide fumes for 9 years. Both lungs were found severely emphysematous (Smith et al., 1957, cited by MacFarland, 1979).

Bonnell et al. (1959) performed later a follow-up study in the same factories. One of the objectives of the follow-up was to ascertain if the progressive deterioration was self-limiting in the absence of further exposure. Unfortunately, the disease progressed with increasing respiratory insufficiency and unequivocal evidence of deterioration in pulmonary function was found in workers previously tested (Bonnell et al., 1959 cited by MacFarland, 1979).

From another accumulator assembly plant, Potts reported that 6 men out of 70 examined workers with more than 10 years exposure had bronchitis. In four of these cases, bronchitis was associated with emphysema. Unfortunately, diagnostic methods were not detailed (Potts, 1965 cited in CRC 1986).

Adams et al. (1969) reported the results for lung function tests carried out in the same factory. Forced expiratory volume (FEV1) was below the normal range in 5 workers out of 27 examined. Furthermore, the group as a whole showed significantly lower than normal values for FEV (Adams et al., 1969 cited in CRC 1986).

L’Epée et al. (1968) reported unspecific respiratory symptoms among 5 out of 22 workers from an alkaline accumulator industry. No data were available about the quantitative aspect of the exposure to cadmium and the pulmonary studies (L’Epée et al., 1968).

From the U.S.S.R, Vorobjeva (1957) reported "diffuse pulmonary sclerosis" among female workers in the production of alkaline accumulators (Vorobjeva, 1957 cited in CRC, 1986).

All the aforementioned studies did not consider a possible confounding effect of tobacco or other simultaneous exposures.

Materne et al. (1975) (and Lauwerys, 1974) studied workers exposed to cadmium fumes and dusts employed in different factories: an electronic workshop, a nickel-cadmium battery factory and two cadmium-producing plants. This cross-sectional study has also been reported in a later paper by Lauwerys et al. (1979).

Control group included male workers never exposed to cadmium from the same factories and were matched as carefully as possible for age, sex, socio-economic aspects, smoking habits and duration of employment. The presence of other potential respiratory irritant agents was assessed in both groups. Workers were classified into groups following the length of exposure (exposed population) or duration of work in the factory (control population): workers with duration of work less or more than 20 years constituted 2 groups.

The survey demonstrated that in workers exposed to cadmium, although exhibiting no subjective symptoms and considered in good health, the application of oriented functional and biological tests revealed that some of them presented lung disturbances. The lung lesion consisted of a slight obstructive syndrome with possibly slight beginning emphysema.

In the group including the workers with less than 20 years of work, Cd-B and Cd-U were, as expected, significantly higher in the exposed group than in the control group. However, interesting to note is that even the unexposed workers had elevated cadmium levels in comparison with the general population. This was due to the fact that although they were not working directly with cadmium, they were exposed to a certain degree of environmental pollution by cadmium in the factory.

No significant difference was found between the control and exposed workers with regard to frequency of respiratory symptoms (cough, sputum production, wheezing or shortness of breath). By comparison with the control group, the exposed group showed a very slight (but statistically) significant reduction in forced vital capacity (FVC, - 7.2%), 1-sec forced expiratory volume (FEV, -6%) and peak expiratory flow rate (PEFR, -6%). No abnormality was found in chest X-rays.

In the second group composed of workers exposed for more than 20 years, frequency of cough but not that of sputum production was greater in the exposed workers than in the controls. The three same indices of lung function were moderately reduced in the exposed workers compared to the controls: FVC (-12%), FEV (-12%), and PEFR (-9.5%). Lung X-rays were normal (Materne et al., 1975; Lauwerys et al., 1979). The lung x-rays were normal.

Smith et al. (1976) examined workers in a cadmium production plant in the Colorado. The exposed group was divided into a high- and a low-exposure group. The high-exposure group included all workers (N=17) with 6 years or more work in plant areas with airborne cadmium concentrations commonly greater than 0.2 mg/m³. The low-exposure subjects (N=12) were selected from the remainder of the plant population who had not worked in areas with airborne cadmium fume. They were matched with the high-exposure workers by age and cigarette smoking status as was also a group of persons not exposed to cadmium selected from maintenance employees outside the plant (N=17). There was no significant difference between the two cadmium-exposed groups with respect to the proportion of present or past cigarette smokers, the intensity or duration of smoking habits. The control subjects had a significantly higher exposure to cigarette smoke than the exposed workers did.

When pulmonary function findings were compared in the high- and in the low-exposure groups, a significantly lower Forced Vital Capacity (FVC) was found in the high-exposure group. Other differences were not significant. A dose-response relationship was found between forced vital capacity and urinary cadmium and with months of exposure.

No significant differences were found between these two groups with regard to data on respiratory symptoms (cough, sputum, wheezing, and dyspnoea). Five subjects with mild or moderate fibrosis on chest X-rays were identified and belonged to the high-exposure group. No such findings were observed in the low-exposure group or in the controls. The authors suggested that exposure to cadmium fumes might give rise to mild fibrotic reactions in the lung. However, exposure to other agents able to cause pulmonary fibrosis was not documented and could not be ruled out (Smith et al., 1976).

Kossman et al. (1979) examined, in Poland, the respiratory function of 42 workers from a non-ferrous metal plant, exposed to cadmium for periods ranging from 1 to 33 years. Exposure levels were not reported.

Chest X-ray examination revealed emphysema in three workers. Reduced 1-sec forced expiratory volume (FEV) and reduced peak expiratory flow rate (PEFR) were reported in 23.8 and 42.8% of the examined workers respectively. Other signs of obstructive lung disease were seen in about 50% of the exposed workers. Smoking habits were however not considered (Kossman et al., 1979, cited in CRC 1986).

Lung function tests were applied in a group of workers employed in a factory manufacturing cadmium alloys (Sakurai et al., 1982). A first group of seven workers had been exposed to considerably high levels of cadmium fumes in the melting and casting shop. The second group consisted of nine workers who had been engaged in other processes in the manufacture of the alloys, but these processes did not generate cadmium dust or fumes. However, they may have been exposed to some irritating airborne agents such as oil mists, acid mists, and/or mixed metal dusts. The reference group included 122 subjects who had worked in other factories, manufacturing petrochemical products. They had not been exposed to any chemicals to the extent that the exposure in question caused health effects.

Cadmium measurements in the air of the casting and the melting shop were performed three times during the 10 years preceding the study and demonstrated drastically reduced levels between 1970 and 1977. Although the elevated levels encountered in the years 1970, and the lack of wearing protective equipment, no history of acute respiratory distress of acute cadmium poisoning was found in the workers of this part of the plant. No data on the cadmium concentration in the air were available for the second group.

Blood and urinary cadmium values were reported for the two exposed groups. These concentrations were remarkably high for the workers of the first group (melting and casting) in spite of the fact that five out of seven workers had been transferred to “cadmium-free” jobs 5 years before. No abnormal values were found for the other exposed group.

Distribution of smokers and the mean number of cigarettes consumed per day were the same for the two exposed and the reference groups.

A comparison was made between the seven highly exposed workers and the same number of age-, height- and smoking-matched referents. No significant difference in the prevalence rates of the individual respiratory symptoms was found. However, although not significant, larger prevalence were observed for the seven exposed workers for such symptoms as cough, phlegm, breathlessness, wheezing, effect of weather on these symptoms and rhinitis. Most of the tested lung function indices (forced vital capacity, forced expiratory volume in 1 second, peak expiratory flow, and maximum expiratory flow at 75, 50 and 25% of the FVC) were significantly deteriorated in the cadmium-exposed workers:

Table 4.110 Comparison between the highly exposed workers (N=7) and their matched referents (N=7) (Sakurai et al., 1982)

	Highly exposed workers	Matched referents
Age (mean ± SD, years)	46.14 ± 7.47	47.57 ± 6.73
Height (mean ± SD, cm)	161.0 ± 5.1	161.3 ± 5.4
Smoking duration (mean ± SD, years)	23.8 ± 5.8	28.2 ± 6.4
FVC (mean ± SD, l)	3.40 ± 0.28	4.04 ± 0.41
FEV_{1s} (mean ± SD, l)	2.62 ± 0.31	3.31 ± 0.35
PEF (mean ± SD, l/s)	6.23 ± 2.00	8.19 ± 1.32
MEF_{75} (mean ± SD, l/s)	5.41 ± 2.08	7.86 ± 1.47
MEF_{50} (mean ± SD, l/s)	3.24 ± 1.25	4.20 ± 1.14
MEF_{25} (mean ± SD, l/s)	1.00 ± 0.43	1.49 ± 0.47

FVC Forced vital capacity,
FEV_{1s} Forced expiratory volume in 1 second,
PEF Peak expiratory flow,
MEF_{75}, MEF_{50}, MEF_{25}: maximum expiratory flow at 75, 50, 25% of the FVC

The workers slightly exposed to cadmium showed almost the same mean predicted values as the reference group except for FVC and FEV_{1s} but the reduction in FVC and FEV found was not attributed to cadmium because the level of exposure of these workers had been minimal, as indicated by the normal blood and urine cadmium concentrations. It was concluded that the respiratory function of the high exposed group was clearly affected by cadmium exposure and that the induced effects were of the chronic obstructive type, mainly affecting small airways (Sakurai et al., 1982).

Chan et al. (1988) studied a cohort of workers at a Singapore cadmium battery factory exposed to cadmium oxide dust. Lung function was measured using spirometry, helium dilution, tidal sampling, X-rays, and respiratory symptoms. A recovery of the lung function after reduction or cessation of occupational exposure to cadmium dusts was assessed. Total lung capacity increased following reduction of exposure and, following cessation of exposure, vital capacity, FEV, and prevalence of respiratory symptoms all improved. Blood and cadmium concentrations were considerably lower with the reduction or cessation of exposure and were consistent with a decrease in the cadmium air levels (Chan et al., 1988 cited in ATSDR 1999).

Lung function and chest radiographs of men (N=101) who had worked on the production of copper-cadmium alloy for 1 or more years in a factory located in the United Kingdom were compared by Davison et al. (1988) with those of a reference group (N= 96) matched for age, sex and employment status. Referents came from others division of the factory on the same site. The matching did not include height or smoking. So, for the lung function tests results, a linear regression analysis was used to calculate “expected” values from the referents with age, height and pack years taken into account.

Cadmium exposure was estimated by consideration of all the available measurements, changes in production techniques, ventilation and levels of production and from discussions with the occupational health physician, industrial hygienist, the management and the work force. The cumulative cadmium exposure was calculated for each worker (sum of estimated or measured mean airborne cadmium during each year worked in the factory and expressed as year. µg/m³). Liver cadmium was measured by neutron activation analysis to have an objective measurement of cadmium body burden and to complete the estimates of cumulative cadmium exposure. Liver cadmium correlated with cumulative exposure.

77 cadmium workers and 71 referents were seen at the factory medical centre. The others were seen at home. Smoking histories were available and workers were classified in smokers, past smokers or non--smokers.

41% of cadmium workers and 27% of referents reported shortness of breath at exercise, 35% of the workers and 27% of referents produced sputum on most days for as much as three months of each year. No worker claimed of past acute cadmium poisoning. 14 workers and 5 referents had radiographic emphysema of any grade (slight, moderate or severe). Only 2 workers (and none of the referents) with emphysema had never smoked. Considering lung function tests results, the difference between the cadmium workers' observed and expected values (O-E) was calculated and reported to the exposure category.

Table 4.111 Mean (O-E) for forced expiratory volume 1 second (FEV 1.0), FEV 1.0/ forced vital capacity (FVC), transfer factor (TLCO) and transfer coefficient (KCO) (Davison et al., 1988)

Cumulative exposure(year. µg/m³) (N)	FEV 1.0(ml)	FEV 1.0/FVC(%)	TLCO(mmol/min . kPa)	KCO(mmol/min. kPa. L)
< 400 (26)	- 60	- 4.7	+ 0.07	- 0.10
401-1,600 (37)	- 175	- 5.4	- 1.11	- 0.26
> 1,600 (34)	- 398	- 10.5	- 1.58	- 0.43

The difference (O-E) was greater in the workers with the highest cumulative exposure. It was also reported to be the highest in those with the highest liver cadmium level and in those exposed before 1951.

Table 4.112 Mean (O-E) for (FEV 1.0), FEV 1.0/ forced vital capacity (FVC), transfer factor (TLCO) and transfer coefficient (KCO) according to liver cadmium (Davison et al., 1988)

Liver cadmium (ppm)	FEV 1.0 (ml)	FEV 1.0/FVC(%)	TLCO(mmol/min . kPa)	KCO(mmol/min. kPa. L)
< 12.5 (28)	- 76	- 3.7	- 0.4	- 0.14
12.5-25(23)	- 120	- 6.7	- 0.7	- 0.21
> 25 (24)	- 146	- 8.7	- 1.4	- 0.40

Table 4.113 Mean (O-E)for (FEV 1.0), FEV 1.0/ forced vital capacity (FVC), transfer factor (TLCO) and transfer coefficient (KCO)according to years of beginning exposure (Davison et al., 1988)

Years started exposure	FEV 1.0(ml)	FEV 1.0/FVC(%)	TLCO(mmol/min . kPa)	KCO(mmol/min. kPa. L)
Post-1970 (28)	- 70	- 2.1	- 0.08 (N=26)	- 0.05 (N=26)
1951-1970 (25)	- 35	- 3.4	- 0.44 (N=21)	- 0.19 (N=21)
Pre 1951 (44)	- 493	- 11.1	- 1.76 (N=28)	- 0.48 (N=28)

These last workers had not only experienced the highest intensity of exposure, but had also the longest time elapsed since the onset of their exposure.

The difference in the transfer coefficient (KCO) between cadmium workers and referents increased linearly with increasing cumulative exposure without evidence for threshold. The authors estimated a mean decrement in KCO for a cadmium worker employed 5 or more years with a cumulative exposure of 2,000 year.µg/m³ (exposure to 50 µg/m³ for a working lifetime of 40 years) that lied between 0.05 and 0.3 mmol/min. kPa.l (95% confidence interval).

Davison et al. (1988) also examined 98% of a further 76 cadmium workers from the same factory who were eligible but who had died by the time of the study. High exposed workers, as these men would have been classified; have been found to have an increased mortality from "bronchitis".

It was concluded that the findings in the study were consistent with the hypothesis that inhaled cadmium fumes causes emphysema. Lung function was significantly worse in cadmium workers than in the unexposed referents and there was an excess of respiratory symptoms and of radiographic emphysema in cadmium workers which, although not reaching statistical significance, were consistent with the lung function results (Davison et al., 1988).

Sixty-nine male workers from a factory producing silver- cadmium- copper alloys for brazing, exposed to cadmium fumes, were studied by Cortona et al. (1992) and their lung function tests (forced expiratory volume in one second, forced vital capacity, residual volume, transfer factor, transfer coefficient) were compared to those of a group of controls (N=79), not occupationally exposed to cadmium fumes but of the same age and with the same smoking habits.

Cadmium levels in air were measured and available for the years 1975 to 1990, showing an important decrease of exposure over these years (from > 1,500 µg Cd/m^3 in 1975 to 30 µg Cd/m^3 in 1990). A cumulative exposure index was calculated for each worker by multiplying the number of years worked in each department by the mean value of the airborne concentration (in µg/m³) assigned to the department during the period.

Exposed subjects were divided into two subgroups depending on whether their cumulative cadmium exposure was less than or greater than 500 µg/m^3 years in order to assess the trend of the respiratory parameters studied. The subgroup with greater cumulative exposure to cadmium had a higher mean age and cumulative smoking index as compared with the other two groups (no statistical test reported):

Table 4.114 Mean values of smoking habits, Cd-B and Cd-U in controls and exposed workers (Cortona et al., 1992)

	Controls	Cadmium-exposed workers		
		Total	Cumulative exposure index (µg/m³.years)	
			< 500	> 500
N	79	69	54	51
Smoking (cigarettes/day · years)	304.4	313.0	280.8	430.0
Cd-B (µg:100 ml)	-	0.24	0.19	0.42
Cd-U (µg/l)	-	4.3	3.1	8.5

FVC, FEV1, TLCO and KCO observed in cadmium-exposed workers were not significantly different from controls:

Table 4.115 Percentage (mean ± SD) in cadmium-exposed workers as compared with controls

Parameter	Percent of controls (%)
FVC	100.2 (± 12.1)
FEV1	98.6 (± 13.8)
TLCO	99.9 (± 17.5)
KCO	96.8 (±18.6)

Mean values of residual volume were however moderately higher in exposed subjects as compared with those in the control group (+ 8.6%) and the difference was statistically significant.

Table 4.116 Percentage (mean ± SD) in RV in two subgroups of cadmium-exposed workers as compared with controls (Cortona et al., 1992)

N workers	Cumulative exposure index (µg/m³. years)	Variation in residual volume (RV)
69	-	108.6 (± 24.1)*
54	< 500	107.3 (± 24.2)*
15	> 500	110.2 (± 24.4)*

* $p < 0.05$

This effect was greater (+ 10%) in the subgroup of workers with greater cumulative exposure to cadmium. Authors concluded that their data suggested an important role of cadmium exposure in increasing residual volume in cadmium workers. In the subgroup with the highest cumulative exposure, smoking also increased the RV (Cortona et al., 1992). No details were reported on kidney function of the exposed workers.

Thirty-four workers from the Ni-Cd division of a battery plant were examined by Bar-Sela et al. (1992), and signs and symptoms were recorded. Information about working conditions in the factory and exposure control measures came for the greatest part from the workers themselves. Data on blood cadmium levels were acquired from medical records. The Ni-Cd division opened in 1973. In 1987, a major redesign and clean-up process was carried out in the factory after several acute health and safety problems occurred among the workers of the whole plant (including other types of batteries). Before this clean-up, air sampling was not performed and protective equipment was not used. After the clean-up, Cd air levels were measured and exceeded 10 µg/m³ (50 measurements). In 1989, the 8 measurements performed were all higher than this value.

Some workers in the Ni-Cd division were reported to have already developed tubular renal disease as attested by their β2M (values not given). Twenty-six Ni-Cd division workers complained of cough, phlegm production, wheezing and shortness of breath. Of these, 14 were diagnosed as having asthma and another 12 were sent for pulmonary function studies. These last tests revealed hyperreactivity in six and chronic bronchitis was diagnosed in the remaining six on the basis of their clinical history. Only four workers on the whole group were smokers.

The prevalence of bronchopulmonary symptoms in the whole studied group was increased with increased duration of Ni-Cd exposure.

Workers migrated regularly between the different production lines of the factory what meant that nearly every worker was at risk from exposure not only to Ni and Cd but also to many of the other toxic agents used in the plant (cobalt, chromates, magnesium, solvents, glues, asbestos based dusts and powders). So a definite effect can hardly be attributed to cadmium dust alone (Bar-Sela et al., 1992).

Table 4.117 Clinical studies reporting NO lung changes in workers chronically exposed to cadmium

Reference	Main characteristics of the population	Exposure assessment	Findings			Considered confounders
			Subjective symptoms	**Chest X-ray**	**Lung function tests**	
Princi (1947)	E: 20 (M only) C: N.I.	Type of compound: CdO fumes Exposure duration: 0.5-22 years (mean=8 years) Exposure level: Cd-air: 40-1440 µg/ m^3 (some areas with higher concentrations: 17 mg/m^3) Cd-B: N.I. Cd-U: N.I.	-	-	N.I.	Smoking: N.I. Other simultaneous exposures: cadmium sulphide, no
Friberg (1950)	E: 15 (M only) C: 200 (M only)	Type of compound: CdO dust Exposure duration: 1- 4 years (mean = 2 years) Exposure level: Cd-air: 3,000-15,000 µg/m^3 Cd-B: N.I. Cd-U: N.I.	-	-	-	Smoking: N.I. Other simultaneous exposures: nickel-graphite dust, ±
Tsuchiya (1967) (cited in CRC,1986)	E:13 (M only) C:13	Type of compound: Cd fumes Exposure duration: N.I. Exposure level: Cd-air: 68- 241 µg/m^3 (for 5 days) Cd-B: N.I. Cd-U: N.I.	-	-	N.I.	Smoking: N.I. Other simultaneous exposures: silver, N.I.
Teculescu and Stanescu (1970)	E: 11 (M only) C: 0	Type of compound: CdO fumes Exposure duration: 7-11 years (mean =8.4 years) Exposure level: Cd-air: 1,210-2,700 µg/m^3 Cd-B: N.I. Cd-U (µg/24h, range): 3-65	±	-	-	Smoking: ± Other simultaneous exposures: N.I.

Table 4.117 continued overleaf

Table 4.117 continued Clinical studies reporting NO lung changes in workers chronically exposed to cadmium

Reference	Main characteristics of the population	Exposure assessment	Findings			Considered confounders
			Subjective symptoms	**Chest X-ray**	**Lung function tests**	
Lauwerys et al. (1974)	E: 31 (F only) C: 29 (F only)	Type of compound: CdO dust Exposure duration: 1-12 years (mean = 4.08 years) Exposure level: Cd-air (µg/m³): 6.8-18.6 µg/m³ Cd-B (µg%, mean): 1.63 Cd-U (µg/g creat, mean): 5.32	N.I.	N.I.	-	Smoking: yes Other simultaneous exposures: Cd sulphide dust, ±
Stanescu et al. (1977)	E: 18 (M only) C: 20 (M only)	Type of compound: CdO fumes and dust Exposure duration: mean: 32 years Exposure level: Cd-air: 1972: 50-356 µg/ m³ Prior to 1970: “much higher” Cd-B (µg/100 ml, mean ± SD): 2.47 ± 1.32 Cd-U (µg/g creat, mean ± SD): 27.5 ± 12.7	±	-	-	Smoking: yes Other simultaneous exposures: Cd sulphide, Cd sulphate, ±
Gill (1978)	E: 34 (M only) C: 34 (M only)	Type of compound: Cd dust and Cd fumes Exposure duration: 3-37 years Exposure level: Cd-air: 19-31 µg/m³ Cd-B: N.I. Cd-U: N.I.	+	-	-	Smoking: yes Other simultaneous exposures: N.I.

Table 4.117 continued overleaf

Table 4.117 continued Clinical studies reporting NO lung changes in workers chronically exposed to cadmium

Reference	Main characteristics of the population	Exposure assessment	Findings			Considered confounders
			Subjective symptoms	**Chest X-ray**	**Lung function tests**	
Edling et al (1986)	E: 57 (M only) C: 31 (M only)	Type of compound: Cd Exposure duration: 5 –14 years (mean = 14 years) Exposure level: Cd-air(mean (range): 1976: 200 (60-497) µg/m^3 (stationary sampling) N.I. (95-1958) µg/m^3(personal sampling) 1977: N.I. (91-191) µg/m^3 (N.I.) Median cumulative exposure: 1,700 µg Cd/m^3 x year Cd-B: N.I. Cd-U: N.I.	-	-	-	Smoking: yes Other simultaneous exposures: Cd containing solders, N.I.

N.I. No information available in this publication,
N Number of subjects,
\+ Changes present,
\- Changes absent
ECd Exposed persons,
C Non-exposed persons,
M Males,
F Females,
Cd-B Blood cadmium,
Cd-U Urinary cadmium,
Considered confounders (smoking, other simultaneous exposures),
yes Were considered in selection of the population and in discussion,
no Not considered in selection of population nor in the discussion,
± Some attempt to consider this factor was made

Princi (1947) examined 20 workers from a cadmium smelter where they were exposed to cadmium in the form of dust or fumes of cadmium oxide and/or cadmium sulphide. Air measurements were carried out at three different occasions at 11 different areas of work. Some of the areas had considerably higher concentrations of dust than others. Since many of the men alternated between different areas of work, an accurate estimate of individual exposure was not possible. Respirators were provided but worn irregularly. Both clinical and X-ray examination were normal. Lung functions tests were not carried out (Princi, 1947).

Friberg (1950) also reported observations on 15 male workers from the same alkaline battery factory as previously mentioned, similarly exposed to cadmium (iron) oxide dust but employed for only 1 to 4 years. Lung function was normal (Friberg, 1950).

Tsuchiya (1967) examined 13 workers exposed to cadmium fumes while smelting alloys of silver and cadmium and compared them with 13 controls. Cadmium concentrations in air were reported as time-weighted averages at nose level of the workers for 5 days.

Lung function tests were not reported. No abnormalities could be detected at examination (clinical and X-rays) (Tsuchiya, 1967).

Teculescu and Stanescu (1970) examined 11 workers in Romania engaged in extracting cadmium from master alloys containing also Pb and Zn. They were exposed to cadmium oxide fumes for 7 to 11 years. Eight of the subjects were smokers and one was an ex-smoker. Seven workers had repeatedly experienced episodes of "fume fever".

Cadmium levels in air at the time of the study were measured. As stated by the authors, the intensity of exposure was difficult to ascertain because no long-term determinations of cadmium in the atmosphere were available and the determination of the concentration at one moment (at the time of the study) did not account of fluctuations. Values for urinary cadmium were reported and ranged from 3 to 65 µg/24 hours.

Five patients on seven claimed of shortness of breath. Other symptoms reported were fatigue, insomnia, headache, bone and joint pain.

None of the workers had a vascular pattern on chest X-rays examination, compatible with emphysema. No obstructive ventilatory impairment was observed when lung function tests were carried out. It was concluded that emphysema was absent in the studied group (Teculescu and Stanescu, 1970).

Pulmonary ventilatory function was also examined by Lauwerys et al. (1974) in a group of 31 female workers exposed to cadmium oxide dust and compared to that of a matched control group. Workers came from (as in the study of Materne et al., 1975, previously detailed) three different factories: an electronic workshop, a nickel cadmium storage battery factory and a cadmium producing plant. Controls were issued from the same factories and selected to match the exposed group according to sex, age, weight, height, smoking habits and socio-economic status.

The workers had been exposed on average for 4.08 years (range 1 to 12 years) to total and respirable (< 5µ) atmospheric cadmium concentrations of 31 and 1.4 µg/m³. Cadmium concentrations in blood and urine were reported. Values of cadmium in urine were significantly different when exposed and control groups were compared (5.32 versus 2.01 µg/g creatinine in exposed and controls, respectively).

Lung function tests were not significantly different in the two groups.

The comparison between smokers and non-smokers (13 smokers and 18 non-smokers) in this group indicated that cigarette smoking entailed a faster deleterious effect on maximal expiratory flow rates than did inhalation of CdO dust (Lauwerys et al., 1974).

Stanescu et al. (1977), in Belgium, examined 18 workers exposed to cadmium oxide fumes and dust for a very long time (more than 22 years) above the safe limits. A control group from the same factory was selected to match the exposed group with regard to age, weight, height, socio-economic status and smoking habits. The work of the control subjects was similar to the Cd-exposed workers but they had never been exposed to cadmium. The matching regarding the tobacco use was, however, not perfect since smokers in the control group smoked considerably more than those in the control group (22.2 pack years, 13 smokers in the exposed group versus 34.5 pack years for 12 smokers in the control group).

For each worker, a blood and urine sample was collected and X-rays and lung function tests were performed. Cadmium in blood and urine were significantly higher in the exposed group. The excretion of urinary proteins was also significantly higher in the exposed group.

The proportion of workers with grade 1 dyspnoea without other respiratory symptoms was significantly higher among exposed workers. No difference in the prevalence of other respiratory symptoms was found. Lung function tests were comparable in the two groups, except for closing capacity, significantly higher in the exposed group. Authors were reticent to explain the higher number of exposed workers with grade 1 dyspnoea. The workers were well aware of the implication of the results of the study and this was illustrated by what happened after a previous investigation in the same factory: several subjects had asked for compensation for occupational disease. The increase in closing capacity could have been attributed to a decrease in the elastic recoil of the lung in the Cd group, however no alteration of the elastic recoil was found. In fact, in both groups (exposed and control), closing capacity was above normal limits and the functional pattern (decrease in specific airways conductance, maximal expiratory flow rates) was rather suggestive of a generalised airway obstruction, due long-term smoking, as suggested by the authors. As conclusion, authors stated that their results did not support the concept of cadmium-induced emphysema (Stanescu et al., 1977).

Gill (1978) reported a study on 34 men exposed to cadmium dust and fumes in a recovery plant where cadmium is extracted from a cadmium-copper precipitate, a by-product of the purification of zinc.

65% of the exposed workers complained of dyspnoea, compared with 32% of the controls (men from an office well-removed from cadmium source in same plant). There was no significant difference between smokers and non-smokers in both groups. Most exposed workers complained of grade III dyspnoea (22/34 in exposed workers versus 11/34 in controls), but did not feel seriously inconvenienced and were able to work and to enjoy recreational activity without discomfort. No radiological abnormalities were reported in either group. Lung function tests were performed but there was no significant difference between the exposed and the control group, moreover there was no correlation between abnormal tests findings and symptoms. Authors concluded that although these workers had more respiratory symptoms than the non-exposed subjects, there were no clinical signs or changes in respiratory function that could be definitively ascribed to cadmium effect (Gill, 1978).

Edling et al. (1986) examined the lung function of workers exposed to cadmium in connection with the use of cadmium containing solders, by spirometry and single breath nitrogen washout. Workers were compared with a control group, matched for height and age, which performed similar tasks (welding and soldering) but without known exposure to cadmium.

Each individual's exposure (and occupation) was classified into 4 categories: high (welding or soldering using cadmium containing solders), medium (production hall), low (tasks only partly carried out in the production hall), and no exposure (work before 1955, after 1978). Based on the measurements carried out in 1976, it was estimated that high, medium, and low exposure was about 0.5, 0.15 and 0.05 mg/m^3 respectively. A cumulative dose estimate was then calculated for each worker as mg Cd/m^3 · years.

A self-answered questionnaire provided data about upper airways and lung symptoms and smoking habits. Lung function tests used were performed because they are considered to be particularly sensitive in identifying small airway disease.

Calculated cumulative dose estimate ranged from 340 to 9,900 µg Cd/m^3 · years (mean: 1,700 µg/m^3 · years).

No significant difference was observed between the exposed and the control group regarding the frequency of symptoms. Spirometric and single breath nitrogen washout variables were within the predicted limits (standard references) for all the subjects and not significantly different in both groups. Additional analyses were undertaken to assess the dose-response relation within the exposed group by using the cumulative years of cadmium exposure or the estimated cumulative dose. But no evidence of chronic respiratory effects associated with long term or high exposure was reported.

Analyses were also made comparing smokers and non-smokers. Smokers had some alteration in their lung function tests and this regardless of their exposure status, consistent with the known effect of tobacco smoking on the small airways. These last results supported the hypothesis that the response to occupational dust exposure may differ from the response to tobacco smoking.

Despite the elevated percentage of workers suffering from induced renal damage (42% of the exposed subjects had renal tubular dysfunction (β2M > 0.034 mg/mmol creatinine), no pulmonary adverse effects could thus be demonstrated in this study (Edling et al., 1986).

C. Other studies relating exposure to cadmium with respiratory effects

Some data are provided by retrospective mortality studies. All these studies will be more detailed in the section dealing with carcinogenicity (see Section 4.1.2.9):

Holden studied a group of 347 men employed in two factories producing cadmium copper alloys and exposed to cadmium fumes. Exposure to cadmium fumes exceeded very probably 1,000 µg/m^3, with a reported peak at 3,600 µg/m^3 before 1953, < 150 µg/m^3 from 1955 to 1957 and 50 µg/m^3 thereafter. The cumulative mortality among the exposed men up to 1978 was compared to the expected mortality estimated from death rates in England and Wales. Mortality from respiratory diseases was slightly increased in the workers exposed to cadmium (O/E: 25/20.3, SMR: 123) (Holden, 1980).

The same group of workers was further studied by Sorahan et al. (1995) for the period 1946-1992. Mortality was also assessed for a group of vicinity workers from the same factory (also exposed to arsenic) and a group of iron and brass foundry workers. An assessment of the cadmium exposure was only available for one of the factories producing the Cd-Cu alloys (see Davison et al., 1988 who reviewed measurements made between 1951 and 1983). These available values were used to estimate individual cumulative exposures and the exposure assessment in the other factory.

Increased SMRs for non-malignant diseases of the respiratory system were observed for the three groups compared with the general population.

Table 4.118 Mortality in participants (1954-1992) from diseases of the respiratory system (Sorahan et al., 1995)

	Observed	Expected	SMR (95% CI)
Alloy workers factory A	14	5.7	245 (134-411)**
Alloy workers factory B	9	2.4	368 (168-699)**
Vicinity workers	32	19.5	164 (112-231)*
Control group	2	3.7	54 (6-194)

** $p < 0.01$
* $p < 0.05$

When Poisson regression was used to investigate risks of chronic respiratory disease in relation to the level of exposure (cumulative exposure), there was a significant positive trend between cumulative exposure to cadmium and risk of mortality, after adjustment for age, year of starting alloy work, factory (A or B), and time from starting alloy work (Sorahan et al., 1995).

Table 4.119 Relative risks for chronic diseases of the respiratory system (non-malignant diseases) by level of cumulative exposure, adjusted for age, year of start alloy work, factory and time since starting alloy work (Sorahan et al.,1995)

Cumulative exposure to cadmium (µg.years/m^3)	Deaths (N)	RR (95% CI)	Likelihood ratio test §p value
< 1,600	8	1.0	
1,600-	28	4.54***(1.96-10.51)	
≥ 4,800	24	4.74** (1.81-12.43)	< 0.001
Evaluation of trend		1.96** (1.27-3.02)	0.002

** $p < 0.01$
*** $p < 0.001$

In the study of Armstrong and Kazantzis (1983), there was a statistically significant excess of deaths due to bronchitis correlated with duration and intensity of exposure. Authors examined a cohort of 6,995 men from five industries (primary production, copper-cadmium alloys, silver-cadmium alloys, pigments and oxide, and stabilisers) in the United Kingdom, exposed to cadmium for more than one year. Jobs were assessed as involving high, medium or low exposure to cadmium on basis of discussions with hygienists and others with knowledge of past working procedures, taking into account available results of biological or environmental monitoring. Workers were divided into three groups on basis of these categories and recorded job histories: “ever high”, “ever medium”, “and always low” (no more details available).

Observed number of deaths (between 1942 and 1970, ascertained with death certificates) was compared with expected number calculated from the general population of England and Wales. SMR for deaths attributed to “chronic bronchitis” in the highest-exposed group of workers was large and highly significant (observed/ expected number of deaths = 12/2.8, SMR: 434, 95% CI: 224-758). No deaths could be attributed to emphysema (O/E: 0/0.1). However, some deaths in the cohort caused by emphysema may have been coded as bronchitis because emphysema is rarely certified as underlying cause of death in Britain, as explained by the authors.

According to the authors, the relationship of mortality from bronchitis with intensity of exposure, the discrepancy between mortality from bronchitis and that from lung cancer and the implausibility that the high-exposure group smoked much more than the other groups make it unlikely that the excess mortality observed in the high-exposure group could be accounted for by cigarette smoking (Armstrong and Kazantzis, 1983, Bernard and Lauwerys, 1986).

Kazantzis et al. (1988) updated the cohort study for an additional 5 years. Over the five-year period only, there was a non-significant excess of deaths coded as bronchitis or chronic bronchitis, not related to intensity of exposure. However, over the total study period, the excess mortality from bronchitis remained significant (SMR: 132, 95% CI: 113-151) particularly in the small high-exposure group (SMR: 382, 95% CI: 203-654). There were a small but significant number of deaths from emphysema for the five-year period, but all from the low-exposure group. According to the authors, these emphysema deaths were difficult to interpret in relation to cadmium exposure (Kazantzis et al., 1988).

Several autopsy studies have indicated that persons who died of emphysema and/or chronic bronchitis had high levels of cadmium in lung, liver and kidneys (Morgan 1969, 1970; Morgan et al., 1971; Hirst et al., 1973). It was suggested that cadmium may play a role in the development of these diseases. However, as smoking also increases the cadmium body burden, it is necessary to have some information about the smoking status of the patients before to be able to draw some conclusion. In view of the known causal relationship between smoking and chronic bronchitis and emphysema, the accumulation of cadmium in these patients was probably more a secondary effect than a causal factor (Bernard and Lauwerys, 1986).

Discussion: inhalation route

Long-term occupational exposure has been reported to cause emphysema and dyspnoea in humans in several studies. Other studies, however, have not shown a cadmium-related increase in impaired respiratory function. Some of the discrepancies can be explained by both following considerations:

1) Diagnostic criteria used for detecting and diagnosing lung disease in cadmium workers have been variable, in particular in the early studies. Indeed, several of these early studies exploring “emphysema in cadmium-exposed workers” have been completed before an agreement on the term “pulmonary emphysema” was reached. All the data concerning “cadmium emphysema” are therefore to be critically reviewed with the knowledge of what the definition of lung emphysema covered in each study: clinical and/or radiological and/or lung function tests findings (Teculescu and Stanescu, 1970, CRC 1986).

Table 4.120 Diagnostic criteria used by the authors

Reference	N	Diagnosed on basis of		
		Clinical examination	Radiological criteria	Lung function tests
Friberg (1950)	43	X	X	X (RV/TLC ratio)
Baader (1951)	6	X (not detailed)	X (not detailed)	-
Bonnell (1955)	19	X	X (not detailed)	X
Potts (1965)	4	N.I.	N.I.	N.I.
Kossman (1979)	3	N.I.	X (not detailed)	-
Davison et al. (1988)	19	X	X	X

If one considers that emphysema can only be diagnosed with certainty by histological examination of sections of whole lung fixed at inflation (Harrison’s 12th edition), one can hardly draw firm conclusions from the aforementioned studies where only isolated cases have been examined: post-mortem evidence of anatomical emphysema was reported in only seven workers (Friberg 1950, Baader 1952, Bonnell, 1955, Smith et al., 1957).

2) The earlier studies did not control for the effects of cigarette smoking. The presence of chronic obstructive respiratory disease in cigarette smokers exposed to an additional potentially harmful environmental agent presents difficulties in determining the contribution made by the latter. The relative effects of smoking and occupation on chronic respiratory disease can only be assessed from meticulous epidemiological investigations where study populations include smokers and non-smokers, workers with and without the relevant occupational exposure and where full smoking histories are available to allow a quantitative measure of cumulative consumption (Hendrick, 1996).

There is some evidence that cadmium may accelerate the development of emphysema in smokers. Leduc et al. (1993) reported a case of rapidly progressive emphysema developing in a 59 year old smoker who had smoked a mean of 20 cigarettes daily since the age of 16. In 1975, he became a furnace worker in a plant producing cadmium salts and oxide and was exposed during the following 4 years to a very dusty environment. He did not use protective equipment. Airborne cadmium levels were measured in the workplace with a personal air sampler in 1979 and ranged from 164 to 1,192 μg/m³. In 1979, chest radiograph and lung function tests of the patient were consistent with pulmonary emphysema and the patient was told to stop work. Between 1979 and 1989, lung function tests declined rapidly. Values of cadmium in blood and urine were regularly monitored and remained high:

Table 4.121 Cadmium levels in blood and urine and results of lung function tests (Leduc et al., 1993)

	1979	1980	1983	1989
Cd in blood (μg/100 ml)	9. 7	5.5	2.8	1.8
Cd in urine (μg/l)	17	7.7	4.8	3.5
Lung function tests				
Vital Capacity (l)	-	3.9	3.2	2.7
FEV1 (l)	-	2.3	1.6	0.9
Residual Volume (l)	-	2.1	2.8	4.5
TLCO (ml/min/mm Hg)	-	20	22	13

The mean cadmium concentration in a removed section of lung was 580 μg/g dry weight, confirming the very high exposure. Authors concluded that cadmium was the offending agent for the development of emphysema in this patient. They hypothesised that tobacco may have had a synergistic effect, either by increasing the cadmium burden in the lung (since cadmium is a constituent of tobacco) or indirectly by reducing the lung clearance of cadmium (Leduc et al., 1993).

Lung function and Cd-U data were collected in 16024 non-occupationally exposed adults from the US, grouped according to their smoking status (current, former or never smokers). Current smokers had higher levels of urinary cadmium than former or never smokers. Higher levels of urinary cadmium were associated with significantly lower FEV1in current (-2.06%, 95%CI: -2.86 to –1.26 per 1log increase in Cd-U) and former smokers (-1.95, 95%CI –2.87 to –1.03) but not in never smokers (-0.18, 95% CI –0.60 to 0.24). Similar results were obtained for forced vital capacity (FVC and FEV1/FVC). According to the authors, these results suggest that the cigarette cadmium may be important in the development of lung disease (Mannino et al., 2004). This further confirms the importance of smoking as confounding factor when assessing the effect of an occupational exposure on the lung function.

Studies that have considered a) smoking as a confounder and b) lung function tests are summarised in **Table 4.122** in an attempt to identify a NOAEL or a LOAEL.

Table 4.122 Summary of the studies (not) reporting lung function tests changes after exposure to cadmium and that have considered smoking as a confounder

Reference	Study population (N)	Levels of exposure of concern	Statistically significant reported changes in lung function tests
Materne et al. (1975), Lauwerys et al. (1974), Lauwerys (1979)	90 M	< 20 years of exposure (average: 7.5 years) at ranges of total dust concentration: 3.7-27,050 µg/m^3	Reduction in FVC (-7.2%), FEV1.0 (-6%), PEFR (-6%)
	25 M	> 20 years of exposure (average: 27.5 years) at ranges of total dust concentration: 3.7-27,050 µg/m^3	Reduction in FVC (-12%), FEV1.0 (-12%), PEFR (-9.5%)
	26 F electronic workshop, Ni-Cd battery factory, 2 Cd-producing plants	Average duration of exposure: 4.4 years. TWA total dust: 10 µg/m^3	-
Smith et al. (1976)	E: 17 M Cd production plant	High exposure group: commonly > 200 µg/m^3 for both 6 years or more	FVC (-14.6%) lower in the high-exposure group
Stanescu et al. (1977)	18 M Cd production plant	> 22 years of exposure (average: 32 years) 1972: 50-356 µg/m^3 < 1970: much higher	Only the closing capacity was significantly different in workers compared to controls (119.9 vs. 110.2% TCL, in E and C respectively)
Sakurai et al. (1982)	7 M cadmium alloys	High-exposure group: duration: (mean ± SD): 10.6 ± 5.7 years 1,970 (mean ± SD): 2,340 ± 3,030 µg/m³ (range): 60 – 8,400 µg/m³ 1,974 (mean) : 53.8 µg/m³ 1,977 (mean) : 38.5 µg/m³	Significant deterioration of FVC (-11.6%), FEV1.0 (-19.4%), PEF (-25.6%), $MEF_{75-50-25}$(± -30%) in the high-exposure group

Table 4.122 continued overleaf

Table 4.122 continued Summary of the studies (not) reporting lung function tests changes after exposure to cadmium and that have considered smoking as a confounder

Reference	**Study population (N)**	**Levels of exposure of concern**	**Statistically significant reported changes in lung function tests**
Davison et al. (1988)	E: 101 M copper-cadmium alloys	Cumulative Cd exposure (µg/m3 · years) < 400, 401-1,600 > 1,600	Differences (observed-expected) values in all the exposed workers for FEV 1.0, FEV 1.0/FVC%, TLCO, KCO, RV, without threshold, difference was greater in workers with the highest cumulative exposure
Edling et al. (1986)	E: 57 M Cd solders	Median cumulative Cd exposure (µg/m3 x years) 1,700	-
Cortona et al. (1992)	E: 69 M Cd alloys	Cumulative exposure (µg/m3 · years) < 500 (mean Cd-U : 3.1 µg/l, N=54) > 500 (mean Cd-U : 8.5 µg/l, N=19)	RV: + 7.3% RV: + 10.2%

M	Males
F	Females
FVC	Forced vital capacity
FEV 1.0	Forced expiratory volume in 1 sec
RV	Residual volume
TLCO	Transfer factor
KCO	Transfer coefficient
RV	Residual volume
PEF(R)	Peak expiratory flow rate
MEF25-50-75	Maximal expiratory flow rate at 25, 50, 75% of the FVC
TWA	Time weighted average
TCL	Total lung capacity

Conclusion

Studies in humans

Several authors concluded that long-term inhalation exposure to cadmium (generic) leads to decreased lung function and emphysema. Chronic obstructive airway disease has been reported leading in severe cases to an increased mortality.

A moderate increase in residual volume was observed in workers exposed to cadmium fumes (CdO) at a cumulative exposure of < 500 µg Cd/m^3 · years (Cortona et al. 1992). No other significant differences were seen for the other parameters of the lung function tests at this cumulative exposure. An increased residual volume has been previously reported by authors investigating lung effects in workers at a Cd producing plant with a cumulative exposure of < 400, 400-1,600 or greater than 1,600 µg Cd/m^3 · years (Davison et al., 1988). In this study, differences in FVC, FEV1.0, TLCO and KCO values in exposed workers compared to controls were also significant. Differences were greatest in workers with the highest cumulative exposure, exposed before 1951 and with the highest liver cadmium content.

One study conducted among Cd solders did not report effect on lung function tests although median cumulative exposure was much higher (1,700 µg Cd/m^3 · years) (Edling et al. 1986).

The increase in residual volume observed in the study by Cortona et al. (1992) is considered as the critical effect. The LOAEL derived from this study is 3.1 µg Cd/l (Cd-U) and will be used in Section 4.1.3 (Risk characterisation) taking into consideration that this value is for CdO fumes but may not necessarily apply to CdO or Cd metal dust.

Table 4.123 Summary respiratory effects

	CdO		Cd metal
	fumes	dust	
oral	not relevant		
inhalation			
studies in animals		0.01 mg Cd/m³ (16 months)	-
studies in humans	Cd-U : 3.1 µg/l		-

4.1.2.7.2 Bone

Introduction

Bone metabolism is a dynamic process throughout life, where bone is continuously resorbed and formed in a finely tuned process known as remodelling. A strong and healthy skeleton results from a balanced activity between bone resorbing cells (osteoclasts) and bone forming cells (osteoblasts). The initial event in remodelling occurs when osteoclasts digest bone to form cavities and release collagen peptide fragments, pyridinium crosslinks, calcium, and phosphate which to some extent are excreted in urine and may be used as biomarkers of bone resorption. Subsequently, osteoblasts refill the cavities by synthesising and secreting bone matrix proteins of which more than 90% is type I collagen. The mechanical strength of this organic matrix is enhanced by extra cellular crosslinking and mineralisation, the latter involving osteocalcin, a non--collagenous matrix protein, whose synthesis by osteoblasts is vitamin K dependent. Osteocalcin avidly binds calcium and promotes the formation of hydroxyapatite (calcium phosphate) in the bone matrix. At this stage of the bone formation skeletal alkaline phosphatase, which is an osteoblastic ectoenzyme, is thought to play a role by setting free inorganic phosphate needed in the formation of apatite crystals. Osteocalcin and skeletal alkaline phosphatase can be measured in plasma and used as biomarkers of bone formation.

Bone (and hence calcium) metabolism is under the control of several hormones including vitamin D (1,25-$(OH)_2$-D_3), parathyroid hormone (PTH), calcitonin, oestrogens and growth factors. 1,25-$(OH)_2$-D_3 is formed in the kidney and stimulates the gastro-intestinal absorption of calcium and phosphate as well as the osteoblastic synthesis of osteocalcin. PTH increases plasma Ca levels by stimulating bone resorption, calcium tubular reabsorption and 1,25-$(OH)_2$-D_3 synthesis in the kidney. Bone growth is also affected by several non-hormonal factors, including physical activity, nutrition, smoking, alcohol consumption as well as genetic determinants. Renal diseases are often associated with bone (and hence calcium) disorders through tubular dysfunction and/or alteration of the 1,25-$(OH)_2$-D_3 formation.

During the period of skeletal growth, bone formation outweighs resorption and the skeletal mass increases. The peak bone mass is reached between 20 and 30 years and women have, on the average, 25% lower peak bone mass than men. Thereafter formation and resorption are almost balanced until 35-40 years, at which time the total bone mass decreases. This bone loss is accelerated in case of oestrogen deficiency (menopause) so that at an age of 80, women have lost about twice as much bone mass as men (40 versus 25% loss, respectively) (Berglund et al. 2000).

Osteoporosis is the term used for diseases that cause a reduction in the bone mass per unit volume. It is used to define any degree of skeletal fragility sufficient to increase the risk of fracture.

Osteomalacia is a disorder in which mineralisation of the organic matrix of the skeleton is defective, resulting from a number of conditions (e.g., inadequate dietary intake of vitamin D, renal tubular disorders, acquired and inherited disorders of vitamin D metabolism. It is also influenced by other etiological factors such as smoking, physical activity, sex, race, genetic factors, etc.) (Krane and Holick in Harrison's, 1998).

Clinical cases of severe bone disease due to environmental cadmium exposure have been described in Japan (Itai-Itai disease which comprises severe signs of osteoporosis and osteomalacia associated with renal disease in aged women) (ATSDR, 1999; WHO, 1992).

Extensive reviews on the bone effects of cadmium compounds (not specifically Cd metal/CdO) are available (see e.g. Kjellström in CRC 1986). The exact mechanism behind cadmium-induced bone changes and/or disturbances in calcium balance is not exactly known but several hypotheses have been suggested (ATSDR 1999, Berglund 2000). A direct effect of cadmium on bone metabolism (with impairment of bone formation and/or increased bone resorption) and loss of bone calcium is a first possibility. The second putative mechanism includes several factors resulting from kidney damage. Indeed, renal tubular cells reabsorb all but a small fraction of calcium filtered by the glomerulus and thus, increased calciuria may be explained by cadmium-induced tubular damage (WHO 1992). Hypercalciuria might also be responsible for the renal stones reported in cadmium-exposed workers (WHO 1992). Moreover, kidney damage may cause other changes capable of disturbing bone metabolism: loss of phosphate, reduced hydroxylation of 25-OH-vitamin D, acidosis. The increase in parathyroid hormone secretion secondary to kidney damage may further aggravate bone disease.

Based on these reviews, it is evident that the bone tissue constitutes a target organ for the general and occupational populations exposed to cadmium compounds. The hazard is relatively well identified both in experimental and epidemiological studies and there is little benefit expected from another extensive review of all the published studies.

In this section, the emphasis is mainly on human studies to evaluate the strength of this evidence (what are the limitations of the strongest studies?) and identifying critical doses (LOAEL, NOAEL). Therefore, the studies deemed essential for the definition of the critical doses are commented in detail to identify their strengths and weaknesses and how their conclusions should be taken forward in the overall risk assessment.

In vitro and studies in animals

Numerous experiments, which do not specifically refer to CdO or Cd metal, have been conducted *in vitro* and *in vivo* to study the toxicity of cadmium compounds for the bone tissue.

From *in vitro* experiments, evidence has accumulated that cadmium compounds may directly damage bone. Cadmium compounds have been reported to accelerate the differentiation of osteoclasts from their progenitor cells, to activate mature osteoclasts and induce calcium release but also to inhibit osteoblasts activities:

Normal canine bone marrow was cultured in the presence of cadmium (chloride) to study the effects of low-level Cd exposure on bone resorption (Wilson et al., 1996). Cultures were evaluated for the number of multinucleate osteoclast-like cells (MNOC) formed. Cadmium chloride at doses of 10 to 100 nM increased transiently the number of MNOCs formed and these osteoclast-like cells were functional as evidenced by pits excavated on bone wafers included in cultures. However, at day 14, the number of MNOCs in untreated cultures was no longer significantly lower than in the Cd-exposed cultures and excavated pit areas were similar. The pattern of resorption was, however, visually different as Cd-treated cultures exhibited more extensive pit complexes. Authors suggested that the used Cd^{2+} concentration not only stimulated the MNOC formation but also affected the bone-resorbing activity of the MNOCs formed in culture. These data supported previous experiments of Miyahara et al. (1991) where Cd exposure (60-90 nM) increased MNOC formation in mouse marrow cultures.

The activity of mature osteoclasts exposed to low levels of cadmium was assessed on isolated osteoclasts from long bones of rat neonates and cultured on bone slices. Exposure of these cells to 100 nM Cd (as chloride) increased the number of osteoclasts and the area excavated per osteoclast by approximately twofold and increased the number and area of pits by approximately threefold. Toxicity was observed at higher concentrations of Cd (clumped cells, cellular debris, and decrease of the number of osteoclasts).

Overall, these data demonstrated that Cd^{2+} acts directly on bone-associated cells in culture to stimulate the osteoclast formation from marrow precursors and to increase the activation or activity (or both) of mature osteoclasts for bone resorption (Wilson et al., 1996).

Effects of cadmium on bone resorption were investigated by Miyahara et al. (1992) using a neonatal mouse parietal bone culture system. Cadmium at 0.5 µM and above stimulated hydroxyproline as well as ^{45}Ca release. This was further investigated by e.g. Romare and Lundholm (1999) who observed a significant calcium release from neonatal mouse calvaria organ culture at submicromolar concentrations of Cd^{2+}. Cadmium (chloride), added in the culture medium for 48 hours of incubation at doses of 0.1-0.2-0.4-0.8 or 1.6 µM, dose-dependently increased the release of calcium. Maximal stimulatory effect occurred at Cd concentrations between 0.4 and 0.8 µM, higher concentrations had an inhibitory effect on the calcium release. Interestingly, authors noted some differences in the calcium release pattern according to the considered mouse strain and this might suggest that sensitivity to skeletal effects of Cd might vary, in animals and in humans, for as yet unidentified reasons.

An inhibiting effect of cadmium on osteoblastic activities in a culture of a clonal osteogenic cell line, (MC3T3-E1) has been reported by Miyahara et al. (1988). Cd^{2+} at 1.78 μM and above caused a significant decrease in ^{45}Ca accumulation. Decreases in mineralisation, in collagen content or alkaline phosphatase (ALP) activity were also demonstrated in the presence of Cd. Histologically, the cell density and the mineralisation degree were lower than those of the controls. Ultrastructurally, degenerated cells were observed with undifferentiated cells which had fewer rough-surfaced endoplasmic reticulum and many mitochondria. This suggested that Cd^{2+} may inhibit the differentiation into osteoblasts as well as the cell function.

An interfering effect of cadmium with DNA and matrix protein synthesis in osteoblastic cell cultures has also been shown by Iwami and Moriyama (1993) at concentrations of 1 μM and lower. Significant decreases in alkaline phosphatase activity, an osteoblastic cell marker, were observed at Cd concentrations of 100nM.

In calcifying growth plate cartilage chondrocytes (isolated from chickens), an effect of cadmium on the cellular activity and the extracellular mineralisation process was demonstrated by Litchfield et al. (1998) in the range of metal concentrations 0.1-5 μM. Cd^{2+} did not affect alkaline phosphatase activity or culture mineralisation at the tested doses but levels of total protein were significantly reduced. Cellular biosynthetic activities also appeared to be inhibited. Cadmium acted as a cytotoxic agent disrupting normal cellular activities and treatment with doses as low as 1 μM resulted in the induction of metallothionein in the cultured chondrocytes (Litchfield et al., 1998).

It has been suggested that the perturbations of osteoblastic processes might be mediated by effects on the calcium messenger system (Long et al., 1997).

Overall, levels of Cd required to stimulate osteoclast activity seem to be lower than those decreasing osteoblast activity what would suggest that Cd at low exposure would primarily affect bone resorption, causing an uncoupling between bone formation and bone resorption and yielding a bone loss.

In animals, bone damage has been described as osteoporosis, osteomalacia, osteopetrosis, or osteosclerosis at doses ranging from 2-10 mg Cd/kg/day (as Cd compounds administered for 15 to 364 days) (ATSDR, 1999; WHO, 1992). Although demonstrating the toxic potential of Cd on the bone tissue, a limitation of most of the animal studies is the doses and routes used which are not useful to select a NOAEL/LOAEL (e.g. acute intravenous administration versus long-term oral exposure in the general population).

Katsuta et al. (1994) used young, ovariectomised, growing female rats and administered cadmium chloride intravenously (1.0 or 2.0 mg$CdCl_2$/kg, 5 days a week during 13 weeks). This treatment produced severe nephropathy evidenced pathologically by tubular atrophy and interstitial fibrosis as well as clinically by enzymuria and polyuria. The skeletal changes were detected mainly in the femur and tibia where osteomalacic and osteopetrotic changes were detected. Relevant serum hormone levels were not modified by the treatment. Overall, this study demonstrates the bone toxicity of very high doses of Cd. The results do not allow discriminating whether the bone effects observed are due to a direct action of Cd on the bone tissue or are an indirect consequence of kidney damage (renal osteodystrophy).

Table 4.124 Kidney and bone effects in young ovariectomised rats treated with $CdCl_2$ (Katsuta et al. 1994)

Lesions observed after 13 weeks of treatment	Controls	1.0	2.0 mg/kg
Mean Hb (g/dl)	13.7	8.2	7.7
Kidney			
Tubulopathy (n=6 animals)	0	6	6
Interstitial fibrosis (n=6)	0	3	6
Mean urine volume (ml/15 h, n=6))	12.1	40.5	19.1
Mean γGT in urine (IU/l, n=6)	5.5	41.5	71.8
Bone			
Malacic changes in cortical bone (n=6)	0	1	6
Osteopetrotic changes in metaphysis (n=6)	0	1	6
Mean serum PTH (pmol/l, n=3)	320	307	363
Mean serum osteocalcin (ng/ml, n=3)	40.6	53.9	42.2

Li et al. (1997) have examined the bone response in female rats treated with $CdCl_2$ (0.228 mg intraperitoneally 3 times a week during 16 months). Part of the rats treated with Cd were first ovariectomised (OV-Cd, n=30) or not (Sham-Cd, n=10) and an additional group was ovariectomised but did not receive Cd (OV-NS, n=12); unfortunately the experimental design did not include a group of un-ovariectomised rats which would have allowed to differentiate the effect of Cd in both in ovariectomised and un-ovariectomised animals (i.e. the possible interaction of Cd with ovariectomy which is relevant in regard of characteristics of Itai-itai patients). Male rats receiving the same dose of Cd (M-Cd, n=16) or not (M-NS, n=6) were also examined. Cd content was measured at the end of the 16 months in several organs in a limited number of animals. Cadmium kidney content (µg/g wet weight) was very significantly increased in animals treated with Cd, with higher values in females than in males. The cadmium content in trabecular and cortical bone was elevated to a similar extent in both male and female animals treated with Cd. No significant effect of ovariectomy was found on kidney or bone tissue Cd content.

Table 4.125 Cadmium content in organs at 16 months (Li et al., 1997)

	Females			Males	
	OV-NS(n=5)	OV-Cd(n=14)	Sham-Cd(n=5)	M-NS(n=6)	M-Cd(n=8)
kidney	0.24	173.29	148.60	0.55	80.70
femur	0.32	6.38	6.22	0.02	7.43
vertebrae	0.35	8.49	7.17	0.03	7.35

Mean values (µg Cd/g wet weight, probably misprinted as g/g wet weight in the original paper).

This treatment produced severe pathological (tubular damage, interstitial fibrosis and infiltration, moderate glomerular sclerosis) and functional renal toxicity in animals treated with Cd (serum creatinine was approximately doubled at 16 months).

The bone Ca content (measured in a fraction of the original animals) was significantly affected by the Cd treatment:

Table 4.126 Calcium content in bones at 16 months (Li et al., 1997)

	Females			Males	
	OV-NS (n=5)	OV-Cd (n=10)	Sham-Cd (n=5)	M-NS (n=3)	M-Cd (n=5)
femur	138.0	98.9*	140.0	193.7	142.8
vertebrae	84.2	89.5	99.0	118.3	85.0**

mean values (mg Ca/g wet weight)
* $p < 0.05$ versus OV-NS and Sham-Cd;
** $p < 0.05$ versus Sham-Cd

The bone pathology did not reveal “abnormal skeletal lesions” in the M-NS and OV-NS rats. In rats treated with Cd, increased osteoid seam and osteolytic osteolysis were seen in the cortical bone of the femur, these lesions being more severe in M-Cd than in OV-Cd or Sham-Cd groups. The OV-Cd animals showed severe bone loss (osteopenia) accompanied with osteoid fibrosis compared to Sham-Cd rats. Bone histomorphometry revealed that bone volume of the vertebrae and femur was significantly lower in the OV-Cd rats than in the Sham-Cd.

These authors concluded that their experimental model (mainly in OV-Cd rats) produced pathological changes very similar to those seen in Itai-itai disease, although, according to their manuscript, “used doses were much higher than the estimated exposure in Itai-Itai disease” (not otherwise specified). This study indicates that severe renal toxicity produced by long-term administration of high doses of Cd is accompanied by bone damage in male and female rats. Bone lesions similar to those observed in Itai-itai disease patients were produced in ovariectomised rats treated with Cd.

Umemura (2000) also conducted several experiments to explore the pathological mechanism of Itai-Itai disease. Toxic effects of different doses of cadmium were assessed in ovariectomised and non-ovariectomised rats and in monkeys after intravenous injections of cadmium chloride.

Table 4.127 Summary of the results in the studies by Umemura et al. (2000)

	Experiment 1	Experiment 2	Experiment 3	Experiment 4
Species	Rats	Rats	Rats	Monkeys
Ovariectomy	Yes (control and Cd-treated rats) 1 group of non-ovariectomised rats	Yes (control and Cd-treated rats)	Yes (control and Cd-treated rats)	Yes (control and Cd-treated monkeys)
Cd treatment	2.0 or 3.0 mg Cd/kg/day) i.v.	1.0 or 2.0 mg Cd/kg/day i.v.	0.05 or 0.5 mg Cd/kg/day i.v.	1.0 or 2.5 mg Cd/kg/day i.v.
Duration	14 days	5 days a week, 13 weeks	5 days a week, for 50 weeks	2 or 3 days a week for 13 to 15 months
NOAEL kidney	< 2.0 mg Cd/kg/day	< 1.0 mg Cd/kg/day	≤ 0.05 mg Cd/kg/day	< 1.0 mg Cd/kg/day
NOAEL bone	3.0 mg Cd/kg/day	< 1.0 mg Cd/kg/day	0.05 mg Cd/kg/day	< 1.0 mg Cd/kg/day

The results of the first experiment suggested that ovariectomy exacerbated Cd-induced nephrotoxicity and hepatotoxicity as hepatic and renal lesions were far more severe in ovariectomised rats compared to non-ovariectomised rats (for similar liver and kidney Cd concentrations). Femur and sternum of all examined rats were unremarkable.

In the second experiment, histologic changes in the kidney of treated rats were characterised by tubular degeneration/regeneration and subsequent tubular atrophy and fibrosis. Incidence and severity of such changes were higher and more severe in rats receiving 2.0 mg/kg/day compared to those treated with 1.0 mg Cd/kg/day. The bone Cd content increased gradually with time but Ca and P concentrations in the bones of control and Cd-treated rats were not different. Bone lesions were restricted to the distal portion of the femur and proximal portion of the tibia and consisted in dilated Haversian canals surrounded by an increased amount of uncalcified matrix composed of osteoid seams. Osteoblasts and osteoclasts were not observed in the dilated canals. Cancellous bone mass increased with time in the metaphysis of Cd-treated rats. Such changes were more frequent and more severe in the 2.0 mg Cd/kg/day group than in the 1.0 mg Cd/kg/day group. Urinalysis revealed that NAG values and excretion of Ca in Cd-treated rats were increased compared to control rats.

In rats exposed to 0.5 mg Cd/kg/day for 50 weeks (third experiment), femur, tibia, sternum and vertebrae showed thickening of spongiosa at the metaphyses, dilatation of the haversian canals in the cortex and increased amounts of osteoid tissue. These changes appeared after the administration of cadmium for 50 weeks and progressed till the end of the experimental period, 20 weeks later. None of the rats exposed for 50 weeks to a ten times lower concentration of cadmium showed abnormalities of the bone. Kidney changes were observed in almost all animals from the 0.5 mg Cd/kg/day group and consisted in cortical fibrosis, dilatation of the renal tubules and glomerulosclerosis. In the 0.05 mg/kg group regeneration of the tubular epithelium was slightly observed at 50 weeks. Kidney cadmium content is not reported. Cd content in the bone increased for the first 25 weeks but abruptly decreased thereafter.

In the last experiment, interstitial fibrosis accompanied by atrophy or dilatation of the tubules and hyalin casts were observed in both Cd-treated groups of monkeys. Femur, vertebrae and sternum showed significant increases of osteoid and reduced amounts of cancellous bone, findings attributed by the authors to osteomalacic and osteoporotic Cd-induced changes. Cd content in bone or kidney was not reported. Assays for parathyroid hormone and osteocalcin were conducted only in the second experiment. Serum levels of parathyroid hormone and osteocalcin were not significantly different between Cd-treated and control groups. Overall, these experiments indicated that a disease entity assembling tubular nephropathy, anaemia (experiments 3 and 4, results not detailed) and bone changes could be induced in rats and monkeys by chronic intoxication in the absence of malnutrition, vitamin D deficiency. In all experiments reporting bone changes, renal changes consisting in tubular atrophy and interstitial fibrosis accompanied by increased enzymuria (LDH, NAG) were present as well and might have had some effect on the bone lesions induced by Cd. However, Umemura suggested that findings in experiment 2 (accumulation of Cd in the bone, osteomalacic-like changes at histology, hypercalcemia and hyperphosphatemia, similar levels of PTH and osteocalcin as compared to controls) were inconsistent with the hypothesis that osteomalacia develops by an indirect action of Cd through abnormal calcium homeostasis resulting from renal osteodystrophy, secondary hyperparathyroidism, but speak for a direct action of Cd on bone (Umemura 2000).

Another group (Uriu et al., 2000) examined the effect of Cd on bone metabolism (0.18 mg $CdCl_2$ intraperitoneally 3 times a week during 28 weeks) in ovariectomised Sprague-Dawley rats (15 rats treated with Cd and 10 controls). At 44 weeks, urinary Cd excretion was significantly increased in Cd-treated rats (4.16 versus 0.07 µg/24 h in controls) and doubled serum creatinine levels (0.7 versus 0.4 mg/dl) indicated severe renal toxicity. Bone mineral content was significantly decreased in Cd-treated rats both in the lumbar vertebral body (60.2 versus 74.3 mg/cm^2 in controls) and in the femur (117.9 versus 135.2 mg/cm^2 in controls), resulting in reduced mechanical strength. Structural changes and exacerbated uncoupling between bone formation and resorption resulting in pathological features of osteopenia were clearly induced by the chronic administration of Cd. This study confirms the bone effects of Cd in ovariectomised rats, which occur concomitantly with serious renal damage. The interpretation of urinary Cd levels associated with those effects should take into account the presence of renal damage which is known to modify urinary Cd excretion and may lead here to an inappropriate estimate the severity of the Cd poisoning. This study does not provide new insight into the mechanisms of bone effects induced by Cd and the dose-effect relationship is not clarified further.

Wilson and Bhattacharyya (1997) developed a mouse model to measure *in vivo* the early calcium release from bone. In mice under low-calcium diet conditions, whose skeletons were prelabeled with ^{45}Ca, increased faecal excretion of ^{45}Ca was interpreted as being the direct result of ^{45}Ca release from bone. 200 µg Cd (as chloride) were administered by single gavage and faecal calcium was monitored during 4 days. Approximately 94% of gavaged Cd was excreted into the faeces by the time of the end of the experiment. Blood Cd levels were significantly higher than basal levels at 8 hours and increased slowly throughout the observation period.

Exposure to Cd clearly increased faecal calcium excretion (for the 8- to 24-hour and 24-to 56-hour faecal collection periods) and corresponding mean Cd blood levels for the same time period amounted 7.9 ± 0.7 µg/l (N=6 mice). Bone response was transient and faecal calcium excretion dropped to nearly background levels during the 56- to 104-hour collection period. Blood calcium levels remained normal throughout the time course, supporting the author's hypothesis that Cd-induced bone resorption does not affect the calcium homeostasis. A strict regulation of the serum calcium had also been observed in mice on the same diet in a previous experiment by Wang and Bhattacharyya (1993).

In an attempt to reproduce the pattern of food deficiencies in Japanese women who developed the Itai-Itai disease, Whelton et al. (1994, 1997a, 1997b) administered cadmium (as cadmium chloride 0.25, 5 and 50 ppm orally) to mice and considered the confounding effect of nutrient-deficient diet, multiparity and ovariectomy; the calcium-depleting effect of each factor was evaluated by determining Ca levels in femur and lumbar vertebrae. Skeletal degeneration characteristic of the Itai-Itai syndrome was not reproduced in this mouse model suggesting that the full-blown disease required primary and profound skeletal demineralisation secondarily supported and enhanced by renal dysfunction.

In a study where skeletons of ovariectomised dogs were prelabeled with ^{45}Ca and Cd was administered in drinking water (5-15-50 ppm) for successive periods, Cd induced the release of ^{45}Ca in blood and faeces at a dose of 50 ppm. Blood Cd levels increased over time from 2 to 15 µg/l. Urinary Cd concentrations ranged from 7 to 50 µg/l in exposed dogs but were not detectable in non-exposed dogs.

No correlation was observed between serum ^{45}Ca increases and parathyroid hormone, 1,25-$(OH)_2$-vitamin D_3, or calcitonin. No effects of ovariectomy and/or Cd were observed in total serum Ca, calciotropic hormone concentrations, serum or urinary phosphorus and creatinine, creatinine clearance, or urinary specific gravity. Cd increased bone resorption in dogs without renal dysfunction or calciotropic hormone interaction (Sacco-Gibson et al., 1992).

Habeebu et al. (2000) have shown that MT protects against the bone toxicity of Cd. Upon repeated sc injections of $CdCl_2$ over a wide range of doses (0.05-0.8 and 0.0125-0.1 mg Cd/kg for wild-type (129 background) and MT-null mice, respectively) for 10 weeks, they found no difference in bone Cd content between wild-type and MT-null mice. Repeated Cd injections produced, however, a dose-dependent loss of bone mass (up to 25%), as shown by analysis of the femur, tibia, and lumbar vertebrae. The loss of bone mass was more marked in MT-null mice than in wild-type mice, as shown by dry bone weight, defatted bone weight, bone ash weight, and total calcium content. X-ray photography showed decreasing bone density along the entire bone length with increasing dose and time of Cd exposure. Histopathology showed dilatation of Haversian canals with increased osteoid seams, rounded astrocytes with expanded pericellular space and expansion of hyperplastic bone marrow into metaphyseal cortical bone. Interestingly, bone damage occurred both in male and female wild type mice at a dose level (0.1 mg/kg) which was slightly lower than that producing renal damage in the same strain of mice (Liu et al., 1998). In MT-null mice decrease in bone mass and calcium content and morphological lesions occurred at 0.0125 mg/kg, the lowest dose tested.

Summary: in vitro and studies in animals

In vitro studies have demonstrated that cadmium compounds (not specifically Cd metal or CdO) might exert a direct effect on bone affecting both bone resorption and formation, and inducing calcium release.

In animals, cadmium has been shown to affect bone metabolism. These effects have manifested themselves as osteopetrosis, osteosclerosis, osteomalacia and/or osteoporosis and have been produced experimentally in several species. Thus there are solid experimental arguments to demonstrate that Cd poisoning entails bone toxicity, generally in association with overt kidney damage.

Several authors tried to develop an animal model which would mimic the characteristics of the Itai-Itai patient’s exposure. High doses of $CdCl_2$ (intraperitoneal or intravenous administration) induced bone loss, decreased bone mineral content, increase in osteoid bone, dilatation of Haversian canals in the cortex of ovariectomised mice and rats. In mice treated subcutaneously with $CdCl_2$ loss of bone mass and calcium accompanied with histological changes was produced at a dose level that was slightly lower than that producing renal damage in the same animals. Metallothionein appeared to play a protective role in Cd-induced bone toxicity as MT-null mice were more susceptible to Cd-induced bone mass loss and bone injury than their wild-type counterparts.

While demonstrating the toxic potential of Cd on the bone tissue, a limitation of the studies in animals is that they are not useful for selecting a NOAEL/LOAEL (e.g. acute intravenous administration of relatively high doses versus long term oral exposure of lower intensity in the general European population). In most studies, bone effects were accompanied or preceded by renal damage induced by the Cd-treatment. Young age (growing bones), gestation, lactation, and ovariectomy (used as an animal model of menopause) appeared to exacerbate Cd-induced bone toxicity.

<u>Studies in Humans</u>

Oral route

Most human data come from environmentally exposed populations and do not specifically refer to cadmium oxide or cadmium metal.

The effects of ingested cadmium on human bone have been described as painful bone disorders due to osteoporosis and/or osteomalacia, spontaneous bone fractures, and loss of bone density. The extreme clinical picture is Itai-Itai disease which combines bone disorders and renal dysfunction (ATSDR, 1999). Clinically apparent cases of Itai-Itai disease showed particular characteristics: female sex, age over 40 years, exposure to cadmium for more than 30 years, risk factors such as multiple pregnancies (on average 6 children), and menopause (WHO, 1992). Several reviews of Itai-Itai disease are available (e.g. Kjellström in CRC 1986; Nogawa 1981, Kjellström 1992).

The Cooperative Research Committee on Itai-Itai disease conducted extensive epidemiological studies in Japan and concluded that Itai-Itai disease was restricted to a limited area (Fuchu area) irrigated by the Jinzu river (Toyama prefecture). The major source of pollution was a copper mine 50 km upstream from the endemic area which dumped Cd sludge into the river. The distribution of patients in this area was consistent with the levels of Cd measured in the paddy fields irrigated by the Jinzu River. In 20 samples of rice from the endemic area, the average Cd concentration (expressed per kg wet weight) was more than ten times higher (0.68 mg/kg) than in other areas (0.066 mg/kg) (Moritsugi and Kobayashi, 1964 cited in Kjellström CRC 1986).

Standard diagnostic criteria were devised by the Itai-Itai disease research group (1962-65). The patients should present the following manifestations:

- Subjective symptoms: pain (lumbago, back pain, joint pain); disturbance of gait (duck gait)
- Physical examination: pain by pressure; “dwarfism”; kyphosis, restriction of spinal movement,
- X-rays: Milkman's pseudo fractures (Looser’s zones); fractures (including callus formation); thinned bone cortex; decalcification; deformation; fishbone vertebrae; coxa vara,
- Urine analysis: coinciding positive tests for protein and glucose,
- Decreased phosphorus to calcium ratio,
- Serum analysis: increased alkaline phosphatase; decreased serum inorganic phosphate.

In 1967, about one hundred cases of Itai-Itai disease had been recorded out of a total of 6,717 subjects. The use of these diagnostic requirements was, however, reported as quite conservative and may have lead to an underestimation of the total number of cases. 200 additional cases were diagnosed by the local authorities since 1967 (Kjellström in CRC 1986).

Cases of bone disease allegedly associated with cadmium exposure were also reported in other areas (e.g. Hyogo prefecture, Tsushima area, Kakehashi River). Although the incidence of these cases is apparently lower than in the Fuchu area, a direct comparison is not possible because the same diagnostic criteria were not used (Kjellström in CRC 1986).

The relationship between cadmium exposure and Itai-Itai disease is not univocal and has been the subject of intense debate after the postulation that Cd played a role in the etiology of this disease. In 1968, however, the Japanese Ministry of Health and Welfare concluded that “Itai-Itai disease is caused by chronic cadmium poisoning, on condition of the existence of such inducing factors as pregnancy, lactation, imbalance in internal secretion, aging and deficiency of calcium”. In 1975, a WHO task group set up to prepare an Environmental Health Criteria Document for Cadmium concluded that “cadmium was a necessary factor in the development of Itai-Itai disease” (Friberg 1985).

Several other factors may also (have) influence(d) cadmium-induced bone toxicity in Itai-Itia patients : relative absence of zinc in food, low caloric intakes, nutritional deficiencies in calcium, protein, vitamin D, and iron (ATSDR, 1999). Furthermore, it should be kept in mind that, as indicated in the introduction, osteoporosis is a multifactorial disease.

The possible association between serum activity of the bone-type alkaline phosphatase (bone-type AP) and cadmium exposure was examined by Tsuritani et al. (1994).

This cross-sectional study included 7 Itai-Itai female patients, 20 cadmium-exposed women, and 44 control women, 23 cadmium-exposed men and 21 non-exposed men. Eligibility criteria and selection procedure are not known. All target persons (exposed + patients) had excessive (not detailed) urinary $ß_2$- microglobulin (ß2M-U) excretion. Urinary cadmium concentrations (geometric mean and S.D.) were 7.5 (1.8) and 8 (1.8) µg/g creatinine in men and women from the exposed group and 2.5 (1.3) and 4.4 (1.4) in non-exposed men and women, respectively. Kidney dysfunction (as assessed by ß2M-U) was more severe in exposed women than in men despite similar Cd-U concentration. Serum bone-type AP, calcium, inorganic phosphorus and ß2M-U (pH adjusted after collection), tubular reabsorption of phosphate (%TRP), and bone density of a metacarpal bone II (microdensitometry) were determined. Serum phosphorus was decreased in the cadmium-exposed subjects and Itai-Itai patients whereas bone-type AP activity was increased. Serum calcium correlated negatively and significantly with bone-type AP activity in cadmium exposed women and Itai-Itai patients but not with ß2M-U. Microdensitometry indices were negatively and significantly correlated with bone-type AP activity in women with the exception of Itai-Itai patients. No correlation was found in male subjects. Correlations with urinary cadmium were not calculated.

The results of this study indicate an association between cadmium exposures increased bone remodelling (increased bone-type AP activity) with disequilibrium in favour of bone resorption leading to a loss in bone density. The effect might be secondary to Cd-induced kidney dysfunction but other mechanisms are possible. It should be noted that the reliability of the method for bone-type AP determination (wheat-germ lectin) has been questioned, and calcium in urine was neither measured nor estimated. Some determinations were not carried out in every subject, and the possible confounding effect of several factors was not known or not considered (age, smoking, drinking, physical activity, vitamin D intake).

In a cross-sectional study, Tsuritani et al. (1996) examined 35 subjects (18 women) from the Kakehashi River basin who were environmentally exposed to cadmium (pollution due to sludge from a zinc mine) and were identified as “requiring observation” because of renal tubular dysfunction but their representativity of the general population is unknown. The control group was made of 68 “non-exposed” persons (45 women) without renal disease or diabetes. It is not known whether this study also included subjects examined in the above study (Tsuritani et al., 1994). It is not known whether physical activity was similar in patients and controls, an issue which might have distorted the results. Indeed, exercise might strongly influence bone mineral density in calcaneus (Levis and Altman, 1998). Urinary cadmium (no indication on quality control) was (geometric mean and S.D in µg/g creatinine) 7.8 (1.7) and 9.3 (1.8) in exposed men and women, respectively, and 2.4 (1.5) and 4.0 (1.5) in nonexposed men and women, respectively. Kidney dysfunction (as assessed by ß2M-U) was more severe in exposed women than in men despite fairly similar urinary cadmium concentrations. Bone density (microdensitometry of metacarpal II and ultrasonic assessment of the calcaneus), ß2M-U (pH adjusted after collection), tubular reabsorption of phosphate (%TRP) and endogenous creatinine clearance were measured (the two latter tests in cadmium-exposed subjects only). Years of residence in the area, physical activity, sun exposure, smoking, alcohol and drug consumption, zinc intake, and nutritional factors were not considered.

The highest cadmium and ß2M concentrations in urine were observed in exposed women whose bone density as assessed by speed of sound, broadband ultrasonic attenuation, and stiffness was reduced ($p < 0.01$). Taking age, height and weight into account did not alter the results (the non-exposed subjects were somewhat younger, taller, and heavier). No similar trend was found in men. Ultrasonic measurements correlated negatively with ß2M-U and %TRP ($0.41 < r < 0.62$; $n = 18$; $0.01 < p < 0.10$) but not with creatinine clearance or Cd-U. Bone density as assessed by microdensitometry did not correlate with ß2M-U, %TRP, creatinine clearance, or Cd-U. This study further indicates that Cd-exposure is associated with bone effects and that ultrasonic assessment of the calcaneus (mostly trabecular bone) might be more sensitive than microdensitometry of the metacarpal for detecting bone density changes in cadmium-exposed subjects (Tsuritani et al., 1996).

It should also be noted that control subjects in both studies conducted by Tsuritani et al. (1994 and 1996) had Cd-U values well above what is generally found in European populations (see Section 4.1.2.2) and higher than the LOAEL derived from the study by Alfvén et al. (2000) (see below).

In a cross-sectional study, Honda et al. (1997) measured at autopsy the bone (central part of the eighth right rib) content in cadmium, zinc, copper, calcium, phosphorous, and magnesium in 38 cadmium-exposed subjects (10 with Itai-Itai disease) and 17 non-exposed subjects. The purpose was to examine whether there were cadmium-induced changes in zinc and/or copper homeostasis and whether those changes could be related with the bone lesions associated with Cd exposure, osteomalacia and osteoporosis. Cadmium in bone was clearly increased in exposed subjects. Calcium to zinc ratio in rib was negatively related to Cd exposure and the severity of osteomalacia (assessed for 32 patients). Copper variations associated or not with calcium, phosphorus or magnesium changes did not show any association with osteomalacia. No result was available regarding osteoporosis (most subjects had similar pathological findings). Information on renal function was not provided and the control group was not matched to the cadmium-exposed group regarding causes of death.

In addition to the Japanese studies, some information about the effects on bone of an oral exposure to cadmium comes from other countries.

Although the aim of their study was not to assess bone effect, Inskip and Beral (1982) reported very briefly that no case of osteomalacia (diagnostic procedure not given) had been found in Shipham despite soil-cadmium levels ten times greater than those observed in the Toyama Prefecture. Although a limited number of individuals were reported to be overexposed in Shipham (Harvey et al., 1979), these findings are difficult to interpret for risk assessment because very limited information on individual exposure to Cd was available. Moreover, soil levels and cadmium intake (rice in Japan versus home grown vegetables in UK) may differ greatly (see Section 4.1.2.2.1 oral route and 4.1.2.7.3). This report is therefore not useful for the characterisation of the bone effects in the present RA.

Staessen et al. (1999) examined the relationship between cadmium exposure and bone disease in the Pheecad study, a follow-up of the Cadmibel study (Buchet et al., 1990; see Section 4.1.2.7.3). From the 1,014 Cadmibel participants asked to take part in the follow-up, 614 accepted a measurement of the forearm bone density but 101 had to be excluded because of occupational exposure to heavy metals and seven because of missing data, leaving 506 responding persons whose exposure was environmental only (199 men, 307 women, mean age (SD) of 44.1 (14.0) and 44.0 (13.1) years, respectively). Median follow-up was 6.6 years (5.3-10.5). Because subjects “with the disease” were not excluded at the beginning of the follow-up, this study is not a genuine cohort study.

Urinary 24-hour cadmium excretion (mean Cd-U of about 1 µg/g creatinine), soil, leek and celery cadmium concentration, and residence in polluted area defined exposure to cadmium.

Forearm bone density was measured and bone disease was defined as height loss and/or occurrence of fracture during the 5 years interval of follow-up.

In single regression models, proximal and distal bone densities were negatively correlated with Cd-U at baseline in women but not in men. In stepwise multiple regression models, after considering several possible confounding factors (age, physical activity, diuretics intake, socio-economic status), the interaction term between cadmium excretion and menopause was also significantly and negatively associated with forearm bone density. A positive association was found between Cd-U measured at baseline and the risk of fractures in women and possibly with a higher risk of height loss in men.

Strengths of the study are the size of the study population, the determination of a reliable exposure index, the use of clinically relevant outcomes (fractures and height loss), the consideration of numerous confounding factors, and a quality control.

Some questions remain open:

- Nothing is reported about the lost cases (not occupationally exposed to heavy metals), who represented an important part of the initial study population
- Other potential confounding factors could be considered such as neuromuscular impairment or poor visual acuity (factors that may influence accidental fall in the elderly), or use of other drugs such as psychotropic and anti-depressive medications (Levis and Altman, 1998)
- It has also been suggested that habitual salt excess may contribute to bone loss and that postmenopausal women are more sensitive to the calcium-losing effect of NaCl (Massey and Whiting, 1996). Although, on the average, no difference in sodium excretion was observed in this study between subjects from polluted and control areas in serial 24-hour urine collection, it might be worth examining the individual relationship between Na and Cd excretion, which may suggest an alternative explanation to the effects of cadmium
- Associations between exposure and outcome were often stronger with exposure surrogates (e.g. residence in polluted area) than with urinary cadmium excretion, which may suggest the possible involvement of an associated unidentified environmental factor. An alternative explanation is that Cd-U decreases with age > 60 years and also in the presence of kidney damage (though subjects with overt renal damage were not included in this study), which may contribute to reduce its association with body burden, explaining the stronger association with external exposure indexes.
- The exact definition of a fracture was not given in the paper.

In conclusion, this study strongly suggests a negative dose-effect relationship between bone density and cadmium exposure (Cd-U) and that Cd exposure may play an important role in the occurrence of bone fractures with a significant attributable risk (population-attributable risk of fracture in the six polluted districts of 35%) (Staessen et al., 1999). The exact mechanism through which cadmium exerts this effect (and hence the causality of the association) remains to be clarified.

In their cross-sectional study, Alfvén et al. (2000) examined 1064 persons (participation rate 60.7%) both occupationally and environmentally exposed to cadmium. The study population is almost the same as in the OSCAR study reported in Section 4.1.2.7.3. Age ranged from 16 to 81 years. Non participants did not differ in a systematic way with respect to age, gender, and morbidity (not specified) on the basis of a telephone survey in a random sample (n=35 out of 689 non-participants).

Exposure was defined as urinary cadmium concentration (Cd-U; nmol/mmol creatinine = µg Cd/g creatinine).

Effect was bone mineral density (g/cm² and Z-score values) measured in the forearm of the non-dominant arm with dual energy X-ray absorptiometry. Osteoporosis was defined as a Z-score less than – 1. Quality control was conducted for Cd-U and bone density measurements.

Several potential confounding factors (gender, age, weight, and smoking defined as non/ever smoker) were considered in the analyses.

The 95th percentiles for Cd-U were 0.86 and 1.3 nmol/mmol creatinine for environmentally exposed men and women, respectively. In occupationally exposed men and women the 95th percentiles were 5.9 and 4 nmol/mmol, respectively. The results indicate, especially in older men (> 60 years), an inverse association between Cd-U and bone mineral density and also between tubular proteinuria (as assessed by the concentration of HC protein) and bone mineral density. A logistic regression model, including the total population, indicated a significantly increased risk of osteoporosis (adjusted for gender) for Cd-U ≥ 3 nmol/mmol creatinine.

There was a suggestion of an increased risk of osteoporosis (Z-score) in men > 60 years with 0.5 ≤ Cd-U < 3.0 nmol/mmol creatinine (OR 2.2, CI 1.0-4.8) and a similar tendency in women > 60 years (OR 1.8, CI 0.65-5.3). This was not shown in the total population. Furthermore, the logistic regression model indicated that at this exposure level the risk of osteoporosis was not significantly increased in the total population after adjustment for gender (OR 0.98, CI 0.69-1.4).

Finally, although several non-occupational factors were recorded only smoking, age and sex were included in the statistical analysis and only two smoking categories (non- and ever-smokers) were used, which may have caused a residual bias. The consistency of these results with those of Staessen et al. (1999) is discussed below.

Main strengths of the study are power, quality control, and wide exposure range. The results support the hypothesis of a relationship between exposure to Cd and osteoporosis. Divergent opinions arise to define the LOAEL in this study:

The authors of this study contend that the LOAEL should be set at a Cd-U of 0.5 nmol/mmol creatinine. They believe that the significant effects detected in men > 60 years may reflect the possibility that it takes a long time before a Cd-induced bone lesion is manifested. They interpret the larger confidence interval seen in women as a reflection of the fact that the BMD in women is most likely dominantly affected by endocrine factors and that, thus, the influence of Cd may not be as apparent in women. This interpretation was supported during the Technical Meetings by Swedish, Finnish, Norwegian (and Danish) experts.

The rapporteurs of the present document, followed by German and UK experts, support a more cautious interpretation of the increased or [detected in men ≥ 60 years at 0.5 ≤ Cd-U< 3 nmol Cd/mmol creatinine], and this for the following reasons:

- it results from an analysis conducted after a relatively simple stratification for age (i.e. below or above 60 years). The selection of the 60-year threshold (although biologically plausible) is arbitrary; a threshold of 40 years would have been relevant also,
- the effect is not confirmed in women with the same age at the same Cd-U level (despite a larger group size, i.e. 104 women versus 55 men within the same Cd-U category),
- this specific effect in men contradicts the finding of Staessen et al. (1999) who detected an increased risk of osteoporosis (and fractures) associated with Cd exposure mainly in

women. The finding is also biologically difficult to reconcile with the well-known increased risk associated with Cd exposure in women (including Itai-Itai patients) not in men,

- one plausible explanation for this unexpected finding is that the study population examined by Alfvén et al. (2000) included occupationally exposed subjects (mainly men, 201 men versus 64 women) who were heavily exposed to Cd in the past (1955-1978 in the subgroup also examined by Järup et al. 1998). It is therefore likely that the unexpected increased or found in men ≥ 60 years was influenced by this subgroup of workers, for whom the detected bone effect may be the consequence of past heavy exposure. In that case, the dose-response/effect relationship would be significantly shifted to the left (i.e. the bone effects detected should be related to past (high) rather than present (lowered) Cd-U). According to the publication dealing with the bone effects specifically in these workers mean Cd-U in 1984 was 8.6 nmol/mmol creatinine and estimated airborne levels up to 500 µg/m³ were reported) (Jarüp et al. 1997 cited in Section 4.1.2.7.2.). The same authors (Alfvèn et al. 2002) recently reported on the relationship between kidney and bone effects and cadmium exposure, assessed this time by the measurement of Cd-B. Interestingly, in this study, 43 individuals with previous high occupational exposure were excluded and in the whole population, no significant effect of Cd exposure on BMD was detected. When the analysis was restricted to individuals > 60 years, a significant effect of Cd exposure on BMD was found in women, not in men.

The Belgian rapporteur based his assessment of the LOAEL on data presented in **Table 4.128** in the original publication, which result from a multivariate analysis adjusted for gender, age, weight and Cd-U. In this more elaborate and powerful analysis, a statistically significant or of osteoporosis was found for Cd-U≥ 3 nmol Cd/mmol creatinine (1.9, CI 1.0-3.8), not for 0.5 ≤ Cd-U < 3 nmol Cd/mmol creatinine (0.98, CI 0.69-1.4). The main justification for this choice is that the logistic regression model, by its multivariate nature, is more powerful to detect a genuine effect after integration of other factors (gender, age, and weight). This multivariate approach is also less sensitive (although not completely) to the effect of occupationally exposed subjects because age is considered here as a continuous variable.

In an attempt to reach a conclusion, both studies with the best power, the use of a quality control for exposure assessment and measurement of bone mineral density, and the consideration of at least three important confounding factors (age, gender, weight) are compared (see **Table 4.128**).

NI: Information not reported in the publication

M: Male;

F: Female;

Y: Years;

E: Exposure type;

P: Participation rate;

R: Representativeness of study population;

Exposure: U-Cd expressed as mean (range) or geometric mean (10^{th}-90^{th} percentiles); Environmental and occupational: Environmental and occupational exposure, respectively. 1 nmol/mmol creatinine = 1 µg/g creatinine;

BMD: Bone mineral density;

DXA: dual energy X-ray absorptiometry (measurements carried out with an ambulant instrument which gave results 15% lower than a hospital based instrument considered superior);

SPA: single photon absorptiometry;

DRR: Dose-effect (response) relationship;

MA: multivariate analysis.

Table 4.128 Main characteristics of the two most convincing studies

Reference Place and time Design	Study population	Exposure Indicator Exposure estimates	Endpoint(s)	Dose-effect(response) relationship in multivariate analysis	Comments
Staessen et al. (1999) Belgium 1985-1989 (baseline) 1991-1994 (follow-up) See comments	506 (M: 199; F: 307) 44 ± 14 years (20 – about 80) E: only environmental exposure P: about 70% R: NI	U-Cd; nmol/day M: 8.8; F: 8.6 (range 3.5-19.1 and 3.5-22, respectively). Mean values correspond to about 0.5 and 0.8 µg/g creatinine in men and women, respectively	BMD (forearm; mean of 6 "proximal" and mean of 4 "distal" measurements corresponding to 5 and 35% trabecular bone, respectively). SPA (forearm immersed in water; bone density in g/cm2 corrected for subcutaneous fat and bone width) Height loss Incidence of fractures	Exposure to Cd is associated with increased risk of fracture in women and, possibly, raised risk of height loss in men. The interaction term U-Cd*menopause was a significant predictor of decreased BMD (U-Cd and menopause removed from the equation) In men U-Cd was not a significant predictor of BMD. Numerous potential confounding variables were tested (age, gender, smoking, season, alcohol, Ca intake, vitamin D supplements, menopause, contraceptives, hormonal therapy, socio-economic level, body surface area, diuretics, physical activity, and calcium excretion at baseline).	U-Cd determined with a quality control. Daily calibration check of scanner. Results based on following variables: - U-Cd: as determined at baseline - height: difference between baseline and follow-up. Median follow-up: 6.6 (5.3-10.5) y. - fractures: information on fracture(s) obtained at follow-up home visits and updated when bone density was measured. Physicians were contacted to ascertain reported fractures. Fractures from major trauma were excluded. In women relation between age and BMD was curvilinear.

Table 4.128 continued overleaf

Table 4.128 continued Main characteristics of the two most convincing studies

Reference Place and time Design	Study population	Exposure Indicator Exposure estimates	Endpoint(s)	Dose-effect(response) relationship in multivariate analysis	Comments
Alfvén et al. (2000) Sweden Between 1997-2000 Cross-sectional	1,064 (M: 520; F: 544) 52 years (16 – 81) E: occupational (M: 201; F: 64) and environmental (M: 319; F: 480) P: 60.7% R: 35 out of 689 lost cases (random sample) did not differ systematically from participants regarding age, gender, morbidity	U-Cd; nmol/mmol creatinine Environmental: M: 0.38; F: 0.55 (range: 0.06-1.8 and 0.07-3.7) Occupational: M: 2.1; F: 1.5 (0.10-18 and 0.06-4.7) Previous cases of poisoning in workers: NI	BMD (forearm; nondominant arm, patient supine) DXA (bone density in g/cm2 and Z-scores)	A clear association between Cd-U and decreased BMD in older men Stratified analysis by age and gender: U-Cd increased the risk of osteoporosis (Z-score < - 1) significantly only in men = 60 y. A tendency towards a similar effect was found in women > 60 years. Logistic regression with U-Cd, age, weight, and adjustment for gender: risk of osteoporosis increased only at U-Cd ≥ 3 nmol/mmol (OR: 1.9; 1.0-3.8). Including smoking in multivariate analyses did not change the results.	U-Cd determined with a quality control. Daily calibration of scanner (phantom) Relationship age-BMD: nonlinear

M	Males
F	Females
FVC	Forced vital capacity
FEV 1.0	Forced expiratory volume in 1 sec
RV	Residual volume
TLCO	Transfer factor
KCO	Transfer coefficient
RV	Residual volume
PEF(R)	Peak expiratory flow rate
MEF25-50-75	Maximal expiratory flow rate at 25, 50, 75% of the FVC
TWA	Time weighted average
TCL	Total lung capacity

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It appears from **Table 4.128** that none of the studies have obvious flaws. Both support the existence of an association between cadmium dose (as defined by Cd-U) and osteoporosis (as defined by bone mineral density).

There are however some differences.

First, in the study by Alfvén et al. (2000), the effect is detected in men mainly. This might be explained by the fact that hormonal factors are important determinants of osteoporosis in women and therefore the effect of cadmium might become less apparent or difficult to prove in women. However, this does conflict with the results of Staessen et al. (1999) who mainly detected an effect of cadmium in women. Alfvén et al. (2000) suggest that their different result could be due to the inclusion of cadmium-exposed workers in their study. Indeed, the wider exposure range in the men included may have facilitated the detection of an association between cause and effect. As discussed above, an additional piece of explanation might be that subjects with past intense occupational exposure (201 men, 39%) do contribute more heavily to the general bone effect detected in their study. Whatever the exact explanation, both findings are somewhat surprising because the studies did not detect a clearly increased risk of Cd-induced bone effects in women, despite the theoretical increased risk associated with increased gastro-intestinal absorption and body burden in this gender (see Section 4.1.2.2).

Secondly, Staessen et al. (1999) did not report that the effect was restricted to older persons. The non significant tendency towards less osteoporosis with higher Cd-U described by Alfvén et al. (2000) in men under 60 years of age (see **Table 4.196**) is also intriguing and would have deserved a discussion. While the 60-year limit is credible, it is arbitrary and it is not known whether another age limit would have had a similar influence on the results.

A third issue is the selection of the forearm for bone density measurements. Indeed, in their survey conducted in occupationally exposed subjects (see below), Järup et al. (1998) reported a "suggested dose-response relation between cadmium dose and osteoporosis" defined as a Z-score < -2 at this site (see below, inhalation route). The study population was made of occupationally exposed workers who were also included in the study by Alfvén et al. (2000) (exposure between 1955 and 1978; Cd-U: about 0.2-7.8 nmol/mmol creat). No association was found in the study by Järup et al. (1998) between Cd dose and bone mineral density for spine, hip neck and hip trochanter. As suggested by the authors, this might be explained by the fact that cadmium-induced osteoporosis, like senile osteoporosis, predominates in cortical bone of the forearm. The reason why cadmium is acting like senile osteoporosis rather than like estrogens or cortisone which cause damage initially predominating in trabecular bone is presently unsettled. However, Staessen et al. (1999) reported loss of height in their population, which could suggest osteoporosis of trabecular bone. Alike, the increased incidence of vertebral fractures may suggest reduction of trabecular bone, a finding that cannot be explained by a higher exposure or age range in the study by Staessen et al. (1999).

Finally, methodological factors may also have influenced some results. First, the relationship between age and bone mineral density was not linear in the whole study group, and the use of a more suitable statistical model might contribute to refine the results. Secondly, a selection bias is not excluded because a lot of subjects did not participate and the characteristics of non-participants were determined in a rather small group in one study only.

Summary

Oral route

Work of the most recent years may be summarised as follows:

- Cadmium is likely to have a negative effect on bone metabolism in humans exposed via the diet. The mechanism is, however, not fully understood and the type of bone lesions associated with cadmium exposure are not clearly identified. One likely explanation is disturbance of bone metabolism but another explanation is that Cd induces kidney damage and/or hypercalciuria which might promote osteoporosis and osteoporotic fractures. The most severe form of cadmium intoxication is Itai-itai disease,
- The study by Alfvén et al. (2000) suggests a LOAEL of 3 nmol Cd/mmol creatinine for bone effects,
- Buchet et al. (1990) suggest a LOAEL of 2 µg Cd/day in urine for increased calciuria (see kidney section),
- Bone and kidney effects of cadmium are interrelated.

Inhalation route

The effects of inhaled cadmium on human bone or calcium metabolism are described as calcium deficiency, abnormalities of calcium metabolism, osteopenia, osteoporosis, or osteomalacia. Enostosis, periosteal proliferation, and sclerotic foci have also been reported (Järup et al., 1998; ATSDR, 1999; WHO, 1992). Considering the large number of workers who have been exposed to cadmium in industry, the very high exposures they sustained in the past and the high prevalence of severe renal damage, the reported number of workers with bone effects is small (summarised in **Table 4.125**). Unfortunately, as commented by Kjellström (in CRC 1986), diagnostic methods and criteria for bone damage differed between these studies, making comparisons and conclusions difficult. Cadmium exposure levels may have played a role alone or in association with nutritional habits. Indeed, the incidence of bone disorders appears to have peaked 40 to 50 years ago when exposures were high and the dietary conditions may have been deficient in the countries with reported cases (Kjellström in CRC 1986).

Table 4.129 Bone effects reported among cadmium workers

Reference	Number of workers		Exposure			Findings (method of examination)
	Examined	**Abnormal**	**Duration**	**Compound**	**Cd- air (µg/m³)**	
Nicaud et al. (1942); Valetas (19460	20	6	8–13 years	CdO dust	N.I.	Lines of pseudo fracture (X-ray)
Bonnell (1955)	N.I.	1	32 years	CdO fumes	40-50	Decalcification (Autopsy)
Blainey et al. (1955) (updated in Blainey et al., 1980)	N.I.	1	36 years	CdO dust	N.I.	Osteoporosis and osteomalacia (X-ray and clinical)
Gervais and Delpech (1963)	N.I.	8	8-30 years	CdO fumes and dust	N.I.	Pseudo fractures (X-ray)
Horstowa et al. (1966)	80	26	1-2 years.	N.I.	130 –1,170	Osteoporosis, Pseudo fracture, Sclerotic foci (X-ray)
Adams et al. (1969); Adams (1980)	38	1	N.I.	CdO dust	500	Osteomalacia (X-ray, biopsy autopsy)
Kazantzis (1978)	12	1	N.I.	CdO dust and fumes	N.I.	Osteomalacia and osteoporosis (X-ray and clinical)

N.I. No information was found in this publication

Due to the lack of more detailed data on the prevalence and/or incidence of bone effects in industry, a quantitative organ dose-response relationship cannot be established on the basis of these old data (Kjellström in CRC 1986).

In a cross-sectional study, Järup et al. (1998) investigated the relation between cadmium exposure and bone mineral density in 43 workers (41 men; 2 premenopausal women; mean age: 55 years), exposed to solders containing cadmium for more than 5 years between 1955 and 1978. The original population comprised 68 workers but 25 were lost for several reasons (six deaths, exclusion of two workers older than 80 years, refusals, and some missing values). Proceeding to an exposure reconstruction, the authors estimated the average air cadmium concentrations were 50 and 500 µg/m³ in the low and high exposure categories, respectively.

Cadmium in blood (mean: 29.3 nmol/l; range 3.5-89.4) was determined in 1996, with an external quality control. Urinary cadmium concentrations were from 1993 (mean 3.7 and range approximately 0.2-7.8 nmol/mmol creatinine; exact results not given) and much lower than in 1984 (mean 8.6 nmol/mmol creatinine) (Järup et al., 1997).

Bone mineral density of the forearm, lumbar spine, and hip (neck and trochanter) was measured with dual energy X-ray absorptiometry. Internal variation was checked by daily calibration with a phantom. Results are based either on Z scores or on g/cm². The four mean Z scores (forearm, spine, hip neck, hip trochanter) were decreased in the exposed workers. A weak but statistically significant dose-effect and dose-response relationship could be demonstrated between Cd dose estimates and forearm bone mineral density (g/cm^2 and Z score). No dose-effect relations were found for hip and spine bone density. Multivariate analyses did not disclose new determinants. Alcohol consumption, nutritional factors, and physical activity were not included in the list of potential confounding factors. Calculations of Z scores were done by comparison “with a reference material provided by the instrument supplier and to a local reference material” but no carefully matched control group was investigated. It is not known whether the study group differs from the 68 workers making up the original population.

Taken together, these results are compatible with cadmium playing a role in the genesis of osteoporosis. As the study population did not include aged individuals or women after the menopause, the dose-response relationship may be significantly different from that in the general population. It should also be stressed that the endpoint was the bone mineral density only and that the occurrence of fracture or height loss was not examined.

Finally, it should be borne in mind that the group described by Järup et al. (1998) has been included later in the study by Alfvén et al. (2000) described under “oral route” and cannot be viewed as an additional independent study showing the effect of cadmium on bone.

Chalkley et al. (1998) determined lead (blood), cadmium (blood and urine) and 1,25-dihydroxy-, 24,25-dihydroxy-, 25-hydroxycholecalciferol in 19 workers exposed to both cadmium and lead. For some calculations, these workers were subdivided into three subgroups according to their exposure to lead and cadmium. Results suggested that increased blood and urinary cadmium and blood lead caused perturbation of the conversion of $25(OH)D_3$ to $24,25\ (OH)_2D_3$ and $1,25(OH)_2D_3$. he highly significant correlation between the cadmium concentrations in blood and urine was interpreted by the authors as supporting the hypothesis that continuous long term exposure to cadmium may result in a state of equilibrium between blood and urinary cadmium and that cadmium concentrations in blood could be predicted from the cadmium concentration in urine. The interpretation of these results is not straightforward because few information is available on the study population and on modifying factors, and because some results may be chance findings (the size of the subgroups is very small (n=5-7) and about 30 probability levels were calculated) (Chalkley et al., 1998).

Summary: inhalation route

Results of studies in workers exposed to cadmium oxide or cadmium fumes by inhalation are compatible with cadmium playing a role in the genesis of osteoporosis. However, nutritional factors and physical activity were, however, not systematically considered as potential confounders. In the oldest studies, exposure levels are not always characterised with precision. Mechanisms of action have been postulated: the cadmium-induced bone changes and the disturbances in the calcium balance may be a direct effect of cadmium on the bone or the consequence of the cadmium-induced kidney damage. The available studies do not allow deriving a precise critical cadmium dose at which these effects occurs (LOAEL or NOAEL). By default, the value extracted from studies performed in environmentally exposed populations (3 nmol Cd/mol creatinine) will be taken forward in the Risk Characterisation section.

Conclusions

The specific contribution of CdO/Cd metal could not be assessed specifically.

In vitro and studies in animals indicate that cadmium compounds (not specifically Cd metal or CdO) exert toxic effects on the bone tissue and hence support the causality of the association between cadmium exposure and bone effects reported in human studies. Experimental studies have also suggested that Cd-induced bone effects can be caused either by a direct effect on the bone tissue or indirectly via Cd-induced renal damage (tubular dysfunction, hypercalciuria, impaired hydroxylation of vitamin D).

Results in the general population reported by Alfvén et al. (2000) suggest a LOAEL of 3 nmol Cd/mmol creatinine or 3 µg/g creatinine (not specifically Cd metal or CdO). This threshold would be in line with the idea that bone effects follow or are accompanied by kidney dysfunction and is compatible with the results of Buchet et al. (1990) who suggested that when Cd-U was below 2 µg/24 hours (roughly equivalent to 2 µg/g creatinine, the risk of occurrence of renal tubular effects (as assessed by five renal effect variables, including urinary calcium excretion) remained low (see Section 4.1.2.7.3). This interpretation is supported by the rapporteur and other MSs (Germany, UK). Other MS (Sweden, Finland, Norway and Denmark) supported a LOAEL at 0.5 nmol Cd/mmol creatinine based on the finding of a significantly increased risk in men > 60 years; but this effect should be interpreted with caution mainly because of the presence in this subgroup of occupationally exposed subjects with previous high Cd-U values.

It must be acknowledged that it is very difficult to define critical values based on the available epidemiological data because of the complexities of the relationship between current measurements of urinary Cd, past exposure (via whatever route) and the relationship between these and any changes in BMD that may be observed. Therefore, it might be appropriate to consider the uncertainties that exist rather than to try to be too exact about a critical dose (BE, UK, SE, DK and NL viewpoint).

In workers exposed to cadmium compounds (not specifically Cd metal or CdO), clinical bone disease has been described but the number of cases is limited. One cross-sectional study reported results compatible with a role of cadmium in the genesis of osteoporosis (Järup et al., 1998) but no critical Cd dose could be derived. By default, the value extracted from studies performed in environmentally exposed populations (3 nmol Cd/mol creatinine) will be taken forward in the Risk Characterisation section.

Suggestion for further research

Further epidemiological studies are strongly encouraged because of the serious public health implications of the effect of Cd on bone metabolism and, if available, the results will be evaluated before the risk reduction strategy for CdO and Cd metal are approved.

Cohort studies with clinically relevant endpoints represent the most useful approach. Care should be taken to insure that the study population is representative, that diagnostic access bias, diagnostic suspicion bias, or misclassifications due to changes in exposure, lifestyle or health are avoided. Owing to the information already available in the Oscar, Cadmibel and Pheecad studies further long-term follow-up of these populations in the frame of a cohort study ought to be considered. Such studies would certainly be expensive. However, if there is an effect of Cd on the bone at lower levels of exposure, this may have a very significant impact on a large population and preventive measures could have a major financial impact.

4.1.2.7.3 Kidney

<u>Introduction</u>

The kidney is reported as the critical target organ for cadmium (generic) toxicity following repeated exposure by the inhalation and oral routes:

- Friberg (1950) was the first to describe renal effects in workers exposed to cadmium oxide dust in a Swedish accumulator factory. In this group of workers with very long exposure (9 to 34 years), he demonstrated “proteinuria” in 65 or 81% of the workers, depending on the test used (nitric acid or trichloroacetic test, respectively). Several investigators have subsequently provided further evidence of proteinuria (tubular and/or glomerular) in cadmium workers,
- Signs of renal dysfunction very similar to those reported in cadmium-exposed workers have been found and repeatedly investigated in residents of cadmium-polluted areas in Japan; the etiological factor was supposed to be the ingestion of cadmium-contaminated rice, which is not specifically related to Cd or CdO. The renal effects of cadmium (generic) in the general population have been further investigated in epidemiological studies conducted in Belgium**,** Scandinavia**,** and China.
- In addition, experimental studies have confirmed the nephrotoxic effects of various Cd compounds.

Because of the extensive literature on the nephrotoxicity of cadmium[28] which precludes an exhaustive review of all publications, a selective approach was needed for this RA. As already mentioned, there is ample and robust evidence of the nephrotoxic potential of cadmium. The main issue for this RA remains therefore to define the dose-effect/response relationships for this endpoint as well as the health relevance of the endpoints used to establish these relationships. In the following sections, emphasis is mainly put on the abundant human data that contribute to clarify these quantitative relationships, rather than on studies in animals. An attempt was made to thoroughly analyse the strengths and weaknesses of studies that are deemed with the strongest impact, critical and useful for the definition of the dose- effect/response relationships. A special attention was given to studies that used biomarkers (mainly Cd-U) to characterise exposure

[28] A Medline search "cadmium" and "kidney or renal" yielded 2554 articles published between 1966 and June 2000.

because similar parameters are used in the Exposure Assessment section, which allows a direct and valid confrontation in the Risk Characterisation section.

The conclusions emitted by recent reviews were used as starting points (WHO 1992; Staessen and Lauwerys, 1993; Järup et al., 1998; ATSDR, 1999). As the conclusions reached by these different authors are not always convergent, a detailed analysis of the original publications that appeared critical to the authors follows. Special consideration is given to exposure assessment, possible biases and potential confounding factors that might have to be considered in an overall assessment.

Kidney physiology

In the kidneys, a fluid that resembles plasma is filtered through the glomeruli into the renal tubules (glomerular filtration). As this glomerular filtrate passes down the tubules, its volume is reduced and its composition altered by the processes of tubular reabsorption (reabsorption of water and solutes from the tubular fluid) and secretion (secretion of solutes into the tubular fluid) to form the urine that enters the post-renal urinary tract.

The kidneys play thus an essential role in the regulation of the fluid and electrolyte balance in the body. They have also important endocrine functions: they produce hormones regulating blood pressure (renin), the production of red blood cells in the bone marrow (erythropoietin), the absorption of calcium from the intestinal tract and bone mineralisation (1,25-$(OH)_2$-vitamin D) (see e.g. Bone).

Finally, kidneys are also important actors in the elimination of several potentially toxic substances, both exogenous and endogenous.

The glomerular function is usually assessed by measuring the glomerular filtration rate (GFR). The GFR can be assessed in intact animals and humans by measuring the urinary excretion and plasma level of a substance "x" that is freely filtered through the glomeruli and neither secreted nor reabsorbed by the tubules.

GFR= Clearance $_x$ = U_x. V/P_x

Where U_x: concentration of the substance x in the urine

V: urine flow per unit of time

P_x: arterial plasma level of the substance x (in practice substituted by the venous plasma level).

Different substances are suitable for measuring the GFR: inulin, a polymer of fructose, is extensively used; but radioisotopes such as ^{51}Cr EDTA may also be used.

The clearance of endogenous creatinine is also frequently used in clinical practice as a worthwhile index of renal function although creatinine does not strictly meet all the criteria to be suitable for the measurement of the GFR. Indeed, creatinine is slightly secreted by the tubules and some may be reabsorbed. However, the clearance of endogenous creatinine is easy to measure and sufficient for a rough estimation of the GFR in clinical settings. For the purpose of epidemiological studies aiming at detecting slight alterations of the kidney function, the limitations of the use of creatinine should, however, be kept in mind.

The GFR in an average sized normal man is approximately 125 ml/min. Its magnitude correlates fairly well with body surface area, and values in women are 10% lower than those in men even after correction for body surface area.

The normal serum concentration of creatinine (70-120 µmol/l or 7.9-13.6 mg/l) varies between persons, and is affected by, among other factors, the muscle mass and diet of the subject. In renal insufficiency, the excretion via the urine is decreased and the concentration of creatinine in the blood increases. Usually this does not happen until the GFR has been reduced to approximately half its normal value (renal reserve capacity). Thus an elevation of serum creatinine is a sign of relatively advanced renal impairment (Järup et al., 1998; Ganong, 1997, Harrison's 12th edition).

Various disease processes in the kidneys may alter the glomerular filtration leading to excessive protein leakage in the urine. Normally only plasma substances with a molecular weight less than 50,000 are filtered through the glomerulus to form primary urine. Heavy proteinuria, with the appearance of large plasma molecules such as albumin and immunoglobulins in the urine reveals a glomerular lesion with increased permeability. However, proteinuria may also be found in asymptomatic individuals (with, for instance, orthostatic proteinuria or after a violent exercise).

Analysis of low-molecular weight proteins (LMW) in urine, such as β2-microglobulin (β2M), Retinol-Binding Protein (RBP), α1-microglobulin (α-1M, also termed protein HC) or intracellular enzymes (e.g. N-acetyl-β-D-glucosaminidase; NAG) is used to detect *tubular effects*. Under physiologic conditions, proteins in glomerular filtrate are actively reabsorbed by proximal tubular cells and catabolised in the lysosomal subcellular compartment. The preferential uptake of LMW proteins by the proximal tubule (99.97 versus 90-99% for LMW and HMW proteins, respectively) explains their higher relative increase in urine in case of tubular injury (tubular proteinuria).

Three mechanisms can explain the presence of an elevated concentration of LMW in urine:

(1) Damage to the proximal tubular cells which leads to a reduction of the reabsorption capacity,
(2) Increased production as seen in certain conditions such as cancers and autoimmune disorders,
(3) Competition and/or saturation of reabsorption sites.

Although the determination of ß2M has been widely used for the screening of proximal tubular effects, this test presents a major pitfall arising from the instability of this protein in acid urine (pH < 5.5-6.0). This degradation is very rapid at 37°C and can therefore occur in the bladder, necessitating neutralising urine by the ingestion of sodium bicarbonate several hours before collection of the urinary specimen. Since this complicated procedure was not applied in most epidemiological studies that used ß2M, it should be considered that some of them may have underestimated the urinary ß2M levels in subjects with acid urine. Proteins such as RBP and α1-M are more resistant to degradation and are now preferred to ß2M (Bernard and Lauwerys, 1991).

Increased NAG activity is interpreted as reflecting damage to the lysosomal compartment of the proximal tubular cells. The association between increased urinary excretion of NAG and renal damage has not been fully determined and may reflect normal increased lysosomal activity. It is also possible that such association reflects the natural turnover rate and exfoliation of tubular cells (which contain both Cd and NAG).

NAG is present in kidney and urine as two major isoenzymes : the isoenzyme A (acidic) which is part of the soluble intralysosomal compartment and secreted in urine by exocytosis; and the isoenzyme B (basic), also intralysosomal, but membrane-bound and released in urine associated with disrupted lysosomal membranes. The urinary activity of NAG-A (the predominant form in normal urine) reflects the secretory activity of tubular cells (functional enzymuria) whereas that of NAG-B is an index of the rate of tubular cell breakdown (lesional type enzymuria) (Bernard et al., 1995).

When these tubular markers are analysed it is important to remember, particularly in the context of this Risk Assessment, that increased levels of LMW proteins or enzymes are not *diagnostic* of a renal damage specifically induced by cadmium and that a differential diagnosis should be considered. Moreover, it should be kept in mind that tubular proteinuria does not give rise to any subjective symptoms or disease (Järup et al., 1998) and in itself should not be considered as an adverse effect. Tubular proteinuria is to be considered as an adverse event (early biomarker) when it has been demonstrated that such changes are predictive of subsequent renal damage (e.g. accelerated reduction of GFR with age, end stage renal disease).

Several other renal parameters have been investigated such as urinary excretion of calcium, sodium, potassium, enzymes, phosphate, glucose, or amino acids.

Several terms have been used to describe the effects of cadmium (generic) on the kidney, but their meaning has sometimes been different depending on the authors and from paper to paper, which has introduced confusion in the literature. Therefore, we report hereafter some definitions useful for the interpretation of this Risk Assessment (Lazarus and Brenner, in Harrisson's 12th Ed.):

Azotemia, uremia, chronic renal failure:

Azotemia occurs when the glomerular filtration rate (GFR) is reduced to about 20 to 35% of normal. Although patients are still relatively asymptomatic at this stage, renal reserve is diminished sufficiently so that any sudden stress such as an intercurrent infection, nephrotoxic drugs, etc. are capable of compromising renal function further leading to signs and symptoms of overt renal failure.

Overt renal failure occurs with further loss of the nephron mass (GFR below about 20% of normal). Uraemia may be viewed as the final stage, when many or all of the clinical and biochemical manifestations of chronic renal failure become evident. Thus, uraemia refers to the constellation of signs and symptoms associated with chronic renal failure, irrespective of their cause (Lazarus and Brenner, 1998).

Nephrotoxic agents:

This general term refers to substances such as drugs or occupational agents capable of damaging the kidney.

Nephrotoxic effect:

The general term “nephrotoxic effect” refers to the effect of nephrotoxic agents and is not precisely defined. It includes effects ranging from a slight subclinical tubular dysfunction to chronic renal failure.

Glomerular damage, glomerular dysfunction:

These terms refer to morphological and/or functional disturbances at the glomerular level. GFR, total proteinuria and urinary albumin are clinically important markers of glomerular damage. However, urinary protein and albumin are probably not specific for renal diseases; there also seems to be a relation between urinary protein or albumin excretion and cardiovascular risk factors (hypertension, physical exercise).

Tubular damage, subclinical tubular dysfunction:

These terms refer to morphological and/or functional disturbances at the tubular level. Health relevance depends on the clinical context (see below). ß2M, RBP, protein HC and NAG are four markers of Cd-induced subclinical tubular dysfunction that have frequently been used.

Studies in animals

Oral route

Numerous studies in rats, mice, rhesus monkeys and rabbits have indicated that exposure to cadmium compounds administered orally causes kidney damage (e.g. Andersen et al., 1988; Bernard et al., 1980,1988, 1992; Bomhard et al., 1984; Borzelleca et al., 1989; Cardenas et al., 1992; Cha, 1987; Fingerle et al., 1982; Gatta et al., 1989;Gill et al., 1989; Itokawa et al., 1974; Kawamura et al., 1978, Masaoka et al. 1994 cited in ATSDR 1999). ATSDR also noted that other studies showed no effect on renal function (Basinger et al., 1988, Borzelleca et al., 1989, Boscolo and Carmignani, 1986; Groten et al., 1990; Jamall et al., 1989; Loeser and Lorke, 1977). The absence of renal effect in the latter studies does, however, not question the reality of the nephrotoxic potential of cadmium but illustrates the existence of a critical cumulative dose (renal cortex concentration) to produce these effects (see below). For instance, in the study by Loeser and Lorke (1977) the maximum Cd kidney concentrations after 3 months of oral administration of 30 ppm $CdCl_2$ were 11-13 and 15-17 µg/g renal tissue in rats and dogs, respectively, which is likely below the critical renal level.

ATSDR (1999) concludes that oral cadmium (generic) exposure in animals may increase or decrease relative kidney weight, and may cause histological (necrosis of the proximal tubules, interstitial renal fibrosis) and functional (reduced glomerular filtration rate, proteinuria) changes but does not mention renal effects that would be specific for cadmium metal or cadmium oxide.

There is no good agreement about the cadmium (generic) dose necessary to bring about these renal effects in experimental animals (even in the same species). Critical tissue concentrations reported in the literature vary between 50 and 300 µg Cd/g renal cortex. Most authors agree however that a mean critical concentration of about 200 µg Cd/ g renal cortex (200 ppm) must be reached to observe tubular proteinuria, which is the most sensitive indicator of cadmium-induced renal toxicity.

The health significance of tubular proteinuria and its predictive value for the development of end-stage renal failure (see below) is not answered by the experimental data.

Inhalation route

The renal effects of inhalation exposure to cadmium are, in general, similar to those occurring after oral exposure (ATSDR, 1999).

The first experimental study of proteinuria was reported by Friberg in 1950 who exposed rabbits to cadmium oxide dust for 3 hours a day during 8 months (8 mg Cd/m³). After 4 months of exposure, moderate proteinuria was detected. Animals were killed after 7 to 9 months of exposure and histopathological examination of the kidneys revealed interstitial infiltration of leukocytes in the majority of the exposed rabbits. Similar changes were not found in the control group.

Princi and Geever (1950) could not find evidence of morphological renal changes in the kidney of dogs after prolonged exposure to cadmium oxide dust (4 mg/m³) but neither their methods nor their results were described (WHO, 1992).

Most subsequent experimental studies using inhalation exposure have not found proteinuria (Glaser et al., 1986; Kutzman et al., 1986; Prigge 1978). However, these studies have been limited by the serious respiratory disturbances brought about by the used cadmium exposure levels (ATSDR, 1999).

Studies in humans

As already mentioned, the first scientific evidence of the nephrotoxic potential of cadmium compounds was derived from populations occupationally exposed (mainly by inhalation). The biomonitoring concepts developed to assess exposure and early renal effects were first developed in occupational settings where exposure was relatively high and reasonably well characterised. These biomarkers were later applied to the general population exposed via the environment (mainly by the oral route). For this section, it was therefore deemed more logical and appropriate to address inhalation exposure first.

Inhalation route: occupationally exposed populations

Main reviews

According to ATSDR (1999), WHO (1992), Staessen and Lauwerys (1993) and Järup et al. (1998), the kidney is the main target organ after inhalation exposure to cadmium (generic) but these reviews do not mention renal effects which would be specific for cadmium metal or cadmium oxide.

As indicated by the most recent epidemiological studies, the first manifestation of cadmium nephrotoxicity in occupationally exposed subjects is usually a tubular dysfunction associated with an increased urinary excretion of LMW proteins such as ß2M and RBP (Lauwerys et al., 1979; Elinder et al., 1985; Smith et al., 1986; Jakubowski et al., 1987; Shaikh et al., 1987; Verschoor et al., 1987; Mason et al., 1988; Järup et al., 1988; Thun et al. 1989; Chia et al., 1989; Bernard et al., 1990; Roels et al., 1991; Jakubowski et al., 1992; Roels et al., 1993). An effect on the glomerulus may also be observed in cadmium-exposed workers, as indicated by increased urinary excretion of HMW proteins including albumin, immunoglobulins G or transferrin (Mason et al., 1988; Thun et al., 1989; Bernard et al., 1990; Roels et al., 1993). (see **Table 4.130**).

Definition of the critical dose (LOEL).

WHO (1992) concludes that an increased prevalence of LMW proteinuria occurred in workers after 10-20 years exposure to airborne Cd levels of 20-50 µg/m³ (Cd species not specified).

Studies that have used Cd-U as an index of cumulative occupational exposure have reported thresholds of 5-10 µg/g creatinine or equivalent at and above which renal effects were observed in excess (LOEL).

Table 4.130 Thresholds for renal effects in recent studies in occupational settings (inhalation exposure).

	Type of industry	n	Glomerular effect	Tubular effect	Threshold
Lauwerys et al. (1979)	Electronic workshop Ni-Cd storage battery factory Cd-producing plants	-	HMW proteins ß2M-S creatinine-S	ß2M-U	Cd-U : 10 µg/g creatinine (G and T)
Elinder et al. (1985)	Cd soldering	60		ß2M	3 year.mg/m³
Jakubowski et al. (1987)	alkaline battery factory	102		ß2M, RBP	Cd-U : 10-15 µg/g creat
Shaikh et al. (1987)	Cd smelter	53		ß2M	Cd-U : 13.3 µg/g creat
Verschoor et al. (1987)	secondary Cd users	26		ß2M, RBP, NAG	Cd-U : 5.6 µg/L
Mason et al. (1988)	CuCd alloy manufacture	75	albumin, GFR	ß2M, RBP,NAG, Ca, P, urate	1,100 year µg Cd/m³[a] (T*) less clear (G)
Järup et al. (1988)	battery factory	440		ß2M	500 year µg Cd/m³[a]
Thun et al. (1989)	Cd recovery plant	45	serum creatinine	ß2M, RBP, Ca, P	300 days mg/m³[a] (G and T)
Chia et al. (1989)	NiCd battery factory	65		ß2M, NAG	Cd-B : 5-10 µg/L
Kawada et al. (1989)	Cd pigment factory	29		ß2M, NAG	Cd-U : < 10 µg/g creat (NAG)
Bernard et al. (1990)	non-ferrous smelter	58	albumin, transferrin, serum ß2M	ß2M, RBP, protein-1, NAG	Cd-U : 10 µg/g creat
Roels et al. (1991)	Zn-Cd smelter	108	GFR decline		Cd-U : 10 µg/g creat
Jakubowski et al. (1992)	alkaline battery factory	141		ß2M, RBP	Cd-B : 300 year µg/L
Toffoletto et al. (1992)	Cd alloy factory	105		ß2M	Cd-U : 10 µg/g creat
Roels et al. (1993)	Zn-Cd smelter	37	albumin, transferrin	ß2M, RBP and other markers	Cd-U : 4 µg/g creat (G) Cd-U : 10 µg/g creat (T)
van Sittert et al. (1993)	Zn-Cd refinery	14		ß2M	Cd-U : 7 µg/g creat
Järup and Elinder (1994)	battery factory	561		ß2M	Cd-U : 3 µg/g creat (> 60 y) Cd-U : 5 µg/g creat (< 60 y)

G Glomerular effects
T Tubular effects
a Cumulated exposure: number of years (days) of exposure times airborne concentration(s) in mg or µg/m³

The critical concentration of cadmium in the renal cortex associated with increased incidence of renal dysfunction in an occupational setting (mainly LMW proteinuria) is estimated to be about 200 ppm, equivalent to an urinary Cd excretion of about 5-10 µg Cd/g creatinine (Friberg et al., 1974; Kjellström et al., 1977; Roels et al., 1983).

Health relevance (LOEL or LOAEL)

This threshold has been considered as clinically relevant because several studies have indicated that when Cd-U > 10 µg/g creatinine renal changes are *irreversible* and may lead to an *exacerbation of the age related decline* in the glomerular filtration rate. Roels et al. (1989) have followed during five years 23 workers (58.6 ± 1.38 years at baseline) removed since 6.0 ± 0.86 years from Cd exposure because of increased urinary excretion of ß2M and/or RBP (> 300 µg/l). The most significant finding was that serum creatinine and ß2M in these workers increased with time indicating a progressive reduction of GFR (overall reduction estimated to 31 ml/min/1.73 m² during the 5 year follow-up). The average reduction of the estimated GFR was about five times greater than expected when taking aging into account, and was more pronounced in workers with impaired renal function at baseline. Limitations of the study are that GFR was estimated on the basis of serum β2M and that the groups of age-matched control subjects examined at the beginning and the end of the study were not the same. This investigation was otherwise very carefully designed and several sources of errors could be excluded (quality control, examination of age-matched control groups, absence of primary or secondary renal diseases, examination of individual data and subgroup analyses).

Table 4.131 Biological parameters in 23 workers removed from Cd exposure (Roels et al., 1989)

	Year 1	Year 2	Year 3	Year 4	Year 5
Cd-U (µg/L)	22.2 ± 2.93	16.0 ± 2.28	15.5 ± 1.60	15.6 ± 2.08	18.0 ± 2.98
ß2M-U (µg/L)	1,770 (31-48,900)	1,550 (24-129,000)	2,560 (48-165,000)	2,570 (43-170,000)	2,580 (66-123,000)
RBP-U (µg/L)	1,570 (171-66,000)	985 (95-88,000)	1,260 (28-96,000)	1,870 (41-106,000)	2,000 (59-100,000)
creatinine-S (mg/L)	12.0 ± 1.1	13.5 ± 1.3	13.9 ± 1.4	15.3 ± 1.6	15.1 ± 2.2
ß2M-S (mg/L)	1.89 ± 0.19	2.07 ± 0.18	2.35 ± 0.26	2.63 ± 0.32	3.00 ± 0.42

Roels et al. (1991) have also reported that a reduction of the filtration reserve capacity of the kidney (creatinine clearance measured before and after an oral load of protein) was only observed in cadmium workers with increased LMW proteinuria (geometric mean Cd-U 11.1 µg/g creatinine), which was interpreted as a further validation of the clinical significance of this 10 µg/g creatinine threshold for Cd-U.

Järup et al. (1993) followed 16 workers (mean 59.9.years, 42-84 at baseline) previously exposed to Cd in soldering procedure who had been shown 5 years earlier to have marked tubular proteinuria (> 60 µg/mmol creatinine or 531 µg/g creatinine). Urinary parameters and GFR (^{51}CrEDTA method) were measured in 1984 and 1989 with the same techniques. The reduction in GFR over the 5-year period was 2 ml/min/1.73m² more than expected from aging only.

Table 4.132 Biological parameters in 16 workers previously exposed to Cd (Järup et al., 1993)

	1984	1989
Cd-U (µg/g creat)	16.6 ± 8.2*	13.5 ± 6.3
ß2M-U (µg/g creat)	11,828 ± 18,132	10,991 ± 13,601
GFR (ml/min/1.73 m²)	77.3 ± 20.2	71.7 ± 16.9

* Mean ± SD

In conclusion, the value of 5-10 µg/g creatinine is to be considered as a LOAEL in workers, mainly exposed by inhalation of Cd-containing dust.

Reversibility

Several studies conducted in workers with heavy exposure to Cd (Cd-U > 10 µg/g creatinine) and severe tubular dysfunction have shown that, under those circumstances, tubular proteinuria is almost always irreversible (Roels et al., 1984; Piscator 1984; Elinder et al., 1985a; Elinder et al., 1985b; Roels et al., 1989; Järup et al., 1993, see also reviews in WHO 1992; Järup et al., 1998; Mason et al., 1999).

Tsuchiya (1976), who followed up some cadmium workers with proteinuria over a period of 10 years already suggested the reversibility of incipient tubular dysfunction. However, this study suffers from several methodological problems (e.g. small group of subjects, semi-quantitative methods for proteinuria detection).

Later, in a 9 year follow-up of 14 workers in a zinc ore refinery with Cd-U ranging from 4.5-9.6 µg/g creatinine at the beginning of the study, Van Sittert et al. (1992) reported results that, according to the authors, suggested that under these conditions ß2-microglobinuria (mainly in group A, see **Table 4.133**) was not progressive. None of the other renal tests showed a positive trend over the observation period. The major limitations of this study are, however, the low number of subjects observed and the quasi absence of proximal tubular dysfunction in most of the subjects examined (only one subject with ß2M-U > 200 µg/g creatinine in group A). Another limitation of this study is the main reliance on ß2M measurements to detect early proximal tubular dysfunction because of the rapid degradation of this protein in acid urine. The absence of NAG and RBP alteration support, however, the integrity of the tubular function. Overall, this study does not provide adequate evidence to support the hypothesis of the reversibility of incipient microproteinuria in Cd-exposed workers.

Table 4.133 Biomarkers of renal effects in the study of Van Sittert et al. (1992)

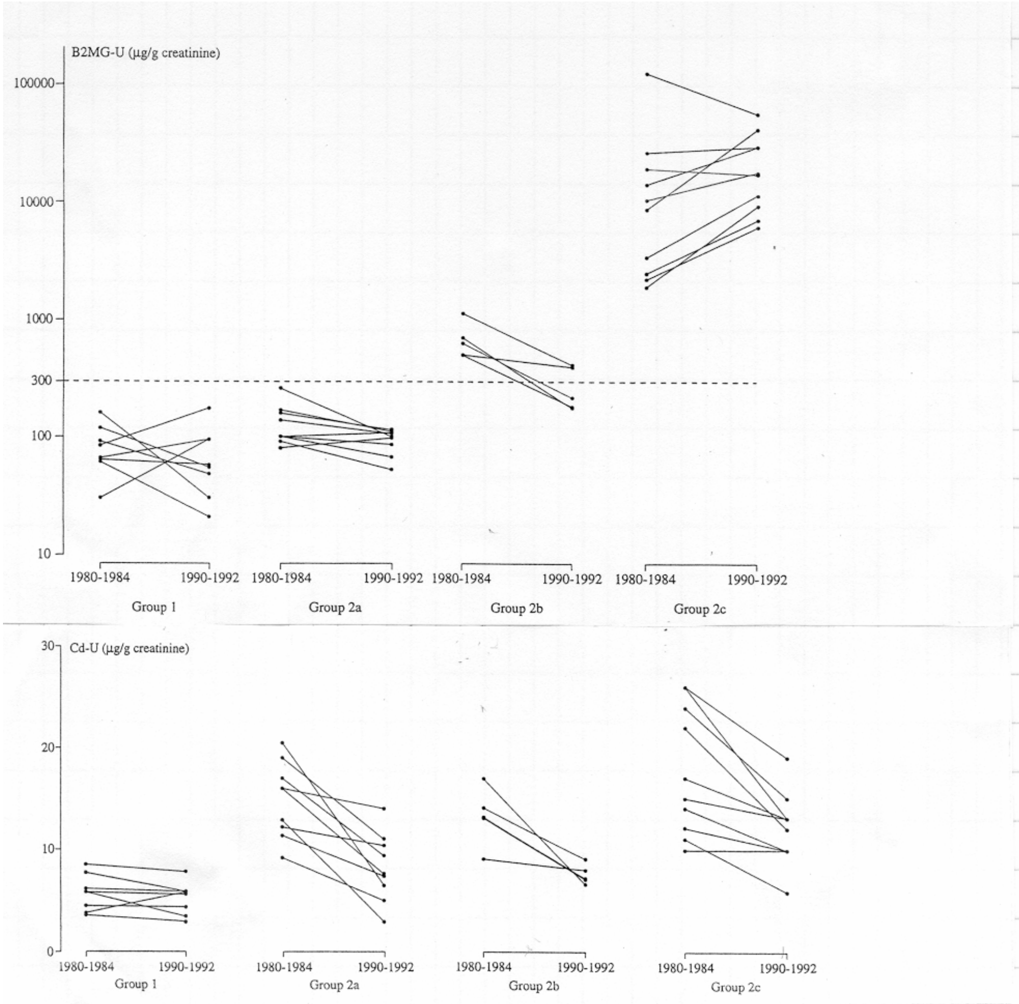
	Group A (n=4)		Group B (n=11)	
	1980	1989	1980	1989
age	43.2 (7.1)*		35.2 (9.1)	
Cd-U (µg/g creatinine)	7.4 (5.8-9.6)§	8.0 (4.5-8.9)	2.8 (0.4-7.5)	1.8 (0.6-7.5)
ß2M-U (µg/g creatinine)	150 (100-400)	184 (150-506)	58 (34-75)	73 (34-104)
RBP-U (µg/g creatinine)	-	77 (14-122)	-	54 (31-86)
NAG-U (U/g creatinine)	4.4 (2.0-7.7) §	6.7 (3.9-8.2)	2.6 (1.6-5.4)	3.8 (1.5-6.3)
creatinine-S (µmolL)	103 (95-109)	97 (88-108)	91 (88-109)	89 (81-103)

* Mean (SD) (range)
§ 1981

The possible reversibility of cadmium-induced tubular dysfunction has been further investigated by Roels et al. (1997) in 32 male workers employed in the cadmium production industry whose formerly high exposure had markedly decreased and for whom relevant medical data were available. When reduction of Cd exposure took place while ß2M did not exceed 300 µg/g (and historical Cd-U never exceeded 20 µg/g creatinine), the risk of subsequent development of tubular dysfunction was almost absent (0/9 workers). When LMW proteinuria was mild (300 < ß2M < 1,500 µg/g creatinine) at the time exposure was reduced (and the historical Cd-U had never exceeded 20 µg/g creatinine) there was indication of reversible tubulotoxic effects of cadmium. In case of severely increased LMW proteinuria (ß2M > 1,500 µg/g creatinine together with Cd-U > 20 µg/g creatinine) tubular dysfunction progressed in spite of reduction of exposure. The reversibility of mild proteinuria observed in the group with (300 < β2M < 1,500 µg/g creatinine, and Cd-U < 20 µg/g creatinine) was reported to be in line with the findings of Harada (1987) who showed in Cd-exposed workers a marked reduction of β2M-U values that coincided with a substantial reduction of their exposure after mildly elevated β2M-U had been detected (publication in Japanese, cited by Roels et al., 1997). The same remark concerning the reliability of ß2M measurements applies to this study, but this was most probably of limited impact because the same trend was observed with RBP-U also. The most significant data of this study are presented in the figure below.

Figure 4.4 Most significant data of the Roels et al. (1997) study

From Roels et al. 1997



Group 1 Cd-U never > 10 µg/g creat
Group 2 Cd-U at least once > 10 µg/g creat
Group 2a ß2M or RBP never > 300 µg/ g creat
Group 2b at least once 300 < ß2M-U < 1,500 µg/g creat
Group 2c at least once > 1,500 µg:g creat

Overall, the data presented by Roels et al. (1997) appear convincing to support the hypothesis of a reversibility of incipient microproteinuria in Cd-exposed workers.

A recent study carried out in Polish workers previously exposed to Cd in a nickel-cadmium battery factory and removed from exposure confirms these findings (Trzcinka-Ochocka et al., 2001). Reversibility of ß2M and RBP elevation in urine was observed after cessation of exposure:

Table 4.134 Evolution of microproteinuria in Polish workers removed from exposure (Trzcinka-Ochocka et al., 2001)

	ß2M (µg/g creat)			RBP (µg/g creat)		
	< 300	300-1,500	> 1,500	< 300	300-1,500	> 1,500
1986-88 (n)	38	12	7	28	24	7
1999 (% < 300 µg/g creat)	81	50	28	92	58	42

A multivariate analysis indicated that the main determinants of the reversibility were the severity of the microproteinuria in 1986-88, Cd-U and duration since removal from exposure.

Bernard et al. (1997) recommended the following guidelines for interpreting ß2M and RBP measurements in workers exposed to Cd:

- < 300 µg/g creatinine: normal values
- 300-1,000 µg/g creatinine: incipient cadmium tubulopathy with possibility of reversibility after removal from exposure. No change in GFR.
- 1,000-10,000 µg/g creatinine: irreversible tubular proteinuria which may lead to accelarated decline of the GFR with age. GFR normal or slightly altered.
- 10,000 µg/g creatinine: overt cadmium nephropathy usually associated with decreased GFR.

Overall, it should be concluded that, while there is ample evidence of the irreversibility of the renal damage above 5-10 µg/g creatinine in Cd-exposed workers, incipient proximal tubular effect can be reversible when exposure is reduced or ceases. These conclusions contribute to strengthen the health significance of the LOAEL previously defined in workers.

Glomerular dysfunction

As already mentioned above, Roels et al. (1989) described an accelerated decline in GFR in Cd-exposed workers followed up over 5 years after removal from exposure because of enhanced urinary excretion of β2M and/or RBP and/or albumin.

Another European study examined the dose-effect/response relationship for renal effects in cadmium workers using a series of biomarkers (Roels et al., 1993). Three main groups of thresholds were identified: one around 2 µg Cd/g creatinine mainly associated with biochemical alterations of uncertain clinical significance (prostanoids, sialic acid); a second around 4 µg Cd/g creatinine for HMW proteins (albumin and transferrin, which might reflect an early manifestation of glomerular involvement) as well as increased urinary excretion of tubular antigens or enzymes (e. g. brush border antigen, NAG), and a third one around 10 µg Cd/g creatinine for increased urinary excretion of LMW proteins (ß2M, RBP and other indicators) corresponding to the onset of proximal tubular dysfunction. While the clinical significance of the effects noted around 2 and 4 µg/g creatinine is not well documented, this study points to the possibility of a glomerular effect of occupational exposure to Cd.

Bernard et al. (1990) already suggested that in some subjects subtle defects in glomerular barrier may precede the onset of proximal tubular impairment after chronic exposure to Cd (58 workers from a zinc smelter, Cd-U 0.9-165 µg/g creatinine, average duration of exposure 10.4 years). While the prevalence of LMW proteinuria (RBP, ß2M, protein-1) increased when Cd-U was > 10 µg/g creatinine, in some subjects the markers of glomerular function (increased urinary excretion of albumin and/or transferrin, ß2M in serum) were found elevated at lower Cd-U values (not further specified), irrespective of age.

The exact significance of these observations (Roels et al., 1993, Bernard et al., 1990) is, however, not clear. It has been suggested that the HMW proteinuria observed in Cd-exposed workers reflects the loss of polyanionic charges at the surface of the glomerular membrane (Bernard et al., 1988). Further studies are needed to understand whether, as in diabetic patients, this isolated increased excretion of HMW proteins in urine is predictive of an increased risk of renal insufficiency in Cd-exposed workers.

In a cross-sectional study, Järup et al. (1995) measured the glomerular filtration rate (^{51}Cr-EDTA method) in 42 out of the 68 workers exposed to Cd for more than 5 years (refusal of 14 workers). The subgroup with highly decreased tubular function was about 60 years of age with a Cd-U and a Cd-B of about 7 µg/g creatinine and 8 µg/L, respectively (duration of exposure at least 5 years). The age-adjusted GFR values correlated inversely with Cd-B, used by the authors as an index of cumulative exposure, as well as with ß2M-U. Thus, the study suggests that occupational exposure to cadmium induces a glomerular damage. In the absence of a control group, the results are based on a comparison between measured and expected values (as defined by Granerus and Aurell, 1981). Since in the population used for calculating the reference values there is a lack of data in the 60-70-year age range (which was the age range of the Cd-exposed workers with the lowest GFR) the comparison may, however, not be completely appropriate. It is also surprising that no significant change was found in a subgroup of 12 workers with “notable tubular proteinuria” followed up from 1984 to 1993, which would further support the possibility that irreversible progression is not the absolute rule in Cd-exposed workers (see above). A limitation of this study is that the possible influence of conditions such as hypertension, cardiovascular disease or diet (protein intake) (Epstein, 1996) was not taken into account.

Overall, it can be concluded that further research would be needed to verify the possibility of an early glomerular damage in Cd-exposed workers.

Occupational cadmium exposure and end-stage renal disease

It has also been reported that occupational exposure to cadmium (generic), not specifically Cd metal or CdO, is associated with an excess mortality by end-stage renal disease (Järup et al., 1998a).

In an historical cohort study, Järup et al. (1998b) examined the SMR due to “nephritis and nephrosis” in battery workers exposed to Cd and nickel. The power of the study was increased relative to a first survey conducted by Kjellström in this cohort (1979), because additional employment records had been discovered so that the cohort could be extended with almost 400 additional workers. The SMR was 150 (95% CI: 31-439, based on three cases). This result might be interpreted either as an underreporting of the ESRD as cause of death in Cd workers or as an actual lack of association between Cd exposure and ESRD. Cardiovascular diseases which are a major cause of death in ESRD patients receiving hemodialysis, were, however not found in excess in this cohort (SMR for ischaemic heart diseases or cerebro-vascular diseases were 116 and 78, respectively) suggesting that ESRD were not over-represented.

Thun et al. (1985) also found no increase of the SMR due to non-malignant renal diseases (1 observed, 1.35 expected cases) in a group of workers exposed to Cd. One limitation of this study is that only the underlying cause of death was considered. An update of this study using the new exposure reconstruction proposed by Sorahan and Lancashire (1997) in this cohort is, unfortunately, not available.

Similar findings were reported by Armstrong and Kazantzis (1983), Kazantzis et al. (1988) (no excess of death due to renal diseases) and further publications could be cited as examples.

To summarise, these findings would indicate that the GFR of workers heavily exposed to Cd declines more rapidly than that of non-exposed subjects but there is no evidence (from mortality studies) of a progression to ESRD. A lack of power due to the few ESRD cases and/or the use of the underlying cause of death for analysis are a possible explanation for the apparent absence of increased death from ESRD in Cd-exposed workers. It should also be taken into account that in developed countries patients rarely die from ESRD but from complications of the disease.

In addition to mortality studies, an epidemiological study was recently conducted to assess the incidence of renal replacement therapy (dialysis or transplantation) during the period 1978-1995 in a Swedish population living in the vicinity of Cd-battery plants, including a subgroup occupationally exposed (Hellström et al., 2001). The age-standardised rate ratio calculated in the subgroup of men with occupational exposure (at least 1 year employment in one of the factory) was 2.1 (95CI 0.6-5.3) for the group of persons aged 20-79 years in 1995 and 2.5 (0.7-6.5) for those aged 40-79 years, which is consistent with an increased risk of ESRD in this population occupationally exposed to Cd and supports the view that mortality studies are probably not sensitive enough to detect the renal impact of occupational Cd exposure. This study is detailed further under the next section dealing with oral exposure and environmentally exposed populations.

Conclusion occupational exposure

For workers occupationally exposed to cadmium (mainly by inhalation), a Cd body burden corresponding to a Cd-U of 5 µg/g creatinine constitutes a LOAEL based on the occurrence of LMW proteinuria. There is consensus in the literature concerning the health significance of this threshold because of the frequent observation of irreversible tubular changes above this threshold and in view of its association with further renal alteration. Although mortality studies were not able to detect an excess of end-stage renal disease in populations occupationally exposed to cadmium compounds, a recent epidemiological study shows that the incidence of renal replacement therapy is increased in a population with occupational exposure to Cd.

Oral route: environmentally exposed populations

According to ATSDR (1999) and Järup et al. (1998), the renal effects of oral exposure to cadmium (generic) are of the same nature as those occurring after inhalation exposure. These reviews do not mention renal effects that would be specific for ingested cadmium metal or cadmium oxide. The reported renal effects of cadmium in environmentally exposed populations mainly consist in tubular proteinuria that may be accompanied by other signs of tubular dysfunction such as enzyme leakage and depressed tubular resorption of amino acids, glucose, calcium, copper, and inorganic phosphate (ATSDR, 1999).

Associations between tubular proteinuria (ß2M, RBP or protein HC) and Cd exposure have been found in several epidemiologic studies of residents of cadmium (generic)-polluted areas in Europe (Roels et al.,. 1981; Buchet et al., 1990; Hotz et al., 1999; Järup et al., 2000), Japan (Nogawa et al., 1980, 1989) and China (Cai et al., 1998; Shiwen et al., 1990, Jin et al., 1999) at Cd-U levels that are lower than those found in occupationally exposed populations. The clinical significance of these findings is, however, not completely elucidated. A number of studies have also indicated that changes in NAG (or NAG-B) activity occur at low Cd-U levels (Bernard et al., 1995, Järup et al., 1995, Noonan et al., 2002) but the clinical significance of these changes is even more difficult to discern (see introduction above under 'Kidney physiology').

While the existence of these effects is well established, difficulties arise to define (1) the critical level at which such changes are observed and (2) the clinical significance of these early alterations.

In 1992, WHO concluded that an association between cadmium exposure (not otherwise specified) and increased urinary excretion of LMW proteins has been noted in humans with a life-long daily intake of 140-260 µg Cd, or a cumulative intake of about 2,000 mg or more. Based on their experience in the Cadmibel study conducted in Belgium (see below), Lauwerys et al. (1991) concluded that several markers of renal tubular function (urinary excretion of RBP, NAG, ß2M and aminoacids) were significantly and positively associated with Cd-U. However, these authors indicated that the morbidity associated with the functional changes, observed in the Cadmibel Study, remained at that time unknown and required further investigation, preferably in longitudinal population studies. Since then, several studies have contributed to refine these assessments.

For the purpose of this RA, it has been deemed appropriate to focus on the main epidemiological studies which have the best design and would help to answer the uncertainties expressed above. Studies conducted in Europe and in Asia will be considered separately because (1) exposure levels were substantially different, (2) the gastro-intestinal absorption of Cd from contaminated rice in Asian studies may significantly differ from other crops and foods in Europe (Reeves and Chaney 2001; see also Section 4.1.2.2.1), and (3) because of possible ethnic differences in susceptibility.

Main European studies

Cadmium exposure and renal effects have been studied in the population living in Shipham, a village in the United Kingdom located on the slag heaps of an old zinc mine with high levels of Cd in the soil and dust, and hence in leafy vegetables. The daily Cd intake estimated for the population in Shipham (35 µg/day) was about twice the national average. Some individuals living in the most polluted area of the village were examined by *in vivo* neutron activation analysis (Harvey et al., 1979). The mean liver concentration was 11.0 ± 2.0 mg/kg and 2.2 ± 2.0 in 21 local volunteers (40-62 years) and 20 age-matched controls, respectively. Health effects were, unfortunately, not investigated in these individuals. The mean 24-hour urinary Cd concentration measured on a larger sample of Shipham residents was, however, only slightly increased showing 0.68 and 0.60 µg/g creatinine in Shipham and a nearby control village, respectively (n=543 age- and sex-matched individuals for a total of about 1,000 residents) (Barltrop and Strehlow, 1982a). No difference in the distribution of ß2M urinary excretion was found and all laboratory data were in the normal ranges (Barltrop and Strehlow, 1982b). The absence of significant increase in Cd body burden and renal effect in Shipham residents is most likely attributable to the only partial reliance of residents on locally grown vegetables as well as to the low Cd uptake in the presence of Zn in the vegetables (Morgan and Simms, 1988). A study of the long term health outcome of people who were resident in Shipham in 1939 was carried out, and compared with similar follow-up of residents of the nearby village of Hutton. An analysis of 40-year follow-up of mortality was reported in 1982 (Inskip and Beral, 1982). A report of a further 18 years of mortality follow-up of the original 1939 cohort, together with follow-up of cancer incidence from 1971-1992, and a geographical study of mortality and cancer incidence, has recently been published (Elliott et al., 2000). Overall, mortality for Shipham was found to be lower than expected, and, although there was an excess of mortality from hypertension, aminoacids disease, and nephritis and nephrosis, of borderline significance (SMR 128, 95% CI 99 to 162), no clear evidence of health effects from possible exposure to cadmium in Shipham was found.

In the Netherlands, a group of individuals living in a quarter contaminated by cadmium (but also Cr, Cu, Pb, Zn and Ni) in Stadskanaal have been examined for potential impact on their health (Sangster et al., 1984). The Cd concentration in leafy vegetables was high for Cd (up to 1.8 mg/kg) whereas the concentrations of other metals were within normal range. A total of 286 inhabitants older than 4 years were included in the study (response rate 70%) together with 300 controls living in an environment with no known pollution by Cd. A spot urine sample was obtained from each participant for the determination of Cd, total proteins, ß2M (acidic urine excluded), glucose and creatinine. Individuals with renal disease and/or diabetes were excluded for further analysis. While, overall, Cd-U was found to increase with age and smoking habits, and was higher in women than in men, higher Cd-U values (range 0.10-2.46 µg/g creat) were only found in non-smoking exposed men (as compared to non-smoking control men; range 0.16-1.14 µg/g creat). The increase in Cd-U between non-smoking exposed and controls was, as reported by the authors, of the same amplitude as the difference between control smokers and non-smokers. No difference in Cd-U concentration was found between exposed and control women (0.17-2.98 µg/g creat). This study does not help to define the relationship between Cd body burden and renal function because the statistical analysis was limited to paired comparisons between stratified exposed and control subgroups. In male non-smokers and smokers, protein and glucose excretion was higher than in corresponding controls. Glucose excretion was also higher in female non-smoking inhabitants than in corresponding controls. The authors of the study concluded, however, that the observed differences were of no clinical significance. It should, however, be noted that there was very little difference in exposure (Cd-U) between exposed and controls, which did probably not allow to detect an adverse health effect.

In a study conducted in aged (> 60 years) women in Belgium (Roels et al., 1981), those women having spent the major part of their life in a cadmium-polluted area (Liège, n=60), but without occupational exposure, had significantly higher Cd-U levels (median 2.02 µg/24 hours) than those living in two less polluted areas (Charleroi and Brussels, n=70 and 45) (medians 1.32 and 0.79 µg/24 hours, respectively (recalculated from data expressed as µg/h)). Urinary parameters selected to assess renal effects (total protein, amino acids, ß2M and albumin) followed the same trend.

Epidemiological studies conducted later in Belgium (Cadmibel, 1699 subjects, both genders, 20 < age < 80 years) have examined the relationships between a large array of renal biomarkers and Cd body burden or exposure as assessed by Cd-U or Cd-B, respectively (Buchet et al., 1990). After normalisation of the data and centering to avoid collinearity, multivariate analysis indicated significant but relatively weak associations between Cd-U and RBP, NAG, ß2M, aminoacids and calciuria (partial r^2: 0.0210, 0.0684, 0.0036, 0.0160 and 0.0168, respectively). After adjustment for age, gender, smoking, use of medications and urinary tract disease, it was found that tubular effects (increased Ca-U) occurred in the general population at Cd-U levels ≥ 2 µg/24 hours (roughly equivalent to 2 µg/g creatinine). “Elevated” (> 95th percentile in the same cohort after exclusion of individuals with renal disease, analgesic abuse and diabetes) urinary excretion of Ca, NAG, RBP, ß2M and amino acids was predicted with a probability of 10% when the urinary excretion of cadmium reached 1.9, 2.7, 2.9, 3.1 and 4.3 µg/24 hours, respectively (Buchet et al., 1990). The weak association between renal parameters and cadmium exposure has been further confirmed in a follow-up study in the most exposed subgroup of the Cadmibel study (Pheecad study) despite the use of different regression models and a narrower exposure range (partial $r^2 < 0.010$). The causal nature of the association was also supported by the reversibility of the renal effects after reduction of exposure (Hotz et al., 1999).

Järup et al. (2000) have examined a population of individuals aged between 16 and 80 years who had lived for a minimum of 5 years and were still living in the south of Sweden in a region with past substantial environmental pollution by cadmium from nickel-cadmium battery plants (OSCAR study). This cohort is almost the same as that examined with respect to osteoporosis (Alfvén et al., 2000) and includes individuals occupationally exposed already examined in previous publications (Järup et al., 1994; Järup et al., 1995, see above inhalation exposure). The final study population was made of 799 environmentally and 222 occupationally exposed subjects (479 men and 542[29] women; mean age 54 and 52 years, respectively). Exposure was

[29] correction in Occup Envrion Med 59:497 (2002)

defined as Cd-U corrected for creatinine and effect was urinary concentration of protein HC (α1 microglobulin). No transformation of the data was performed (arithmetic means) and statistical analyses took into account age, gender, and exposure type. The potential influence of other factors such as smoking, analgesic consumption, or hypertension which has been reported by others (Buchet et al., 1990, Hotz et al., 1999) was not considered. No adjustment was made to avoid collinearity. Cd-U was slightly higher in men than in women (arithmetic mean: 0.82 versus 0.66 µg/g creatinine; 10-90th percentiles: 0.18 and 1.8 versus 0.21 and 1.3). Excretion of protein HC was found associated with Cd-U but Cd explained less than 10% of the variance (partial r^2 for Cd-U: 0.054 and 0.016 for men and women, respectively, Järup personal communication 2003). The prevalence of values above the 95th percentile defined in a Swedish reference population (HC-U > 0.8 and 0.6 mg/mmol creat or 7.1 and 5.3 mg/ g creat for men and women, respectively) increased with Cd-U (OR increasing from 1 to about 6[30] for Cd-U concentrations increasing from less than 0.3 to about 7.5 µg/g creatinine after adjustment for age and sex). These published data tend to confirm the existence of a tubular dysfunction in subjects exposed to cadmium in the environment and the small explained variance agrees well with the results reported by Buchet et al. (1990) and Hotz et al. (1999). In the original publication, logistic regression analysis including age and Cd-U as independent variables indicated that an excess prevalence of elevated HC protein values of 10% (15% calculated-5% background) corresponded with a Cd-U of 1.0 µg/g creatinine[31]. The cut-off values selected to conduct this logistic regression analysis were the 95th percentiles determined in a population with a mean age of 40 years (maximum 63 years) whereas the study population had a mean age of 53 years (maximum 80 years). In view of the positive relationship between protein HC and age reported by the authors, it was likely that the prevalence of elevated protein HC be slightly higher in the study population, simply because of age differences and the calculation of the Cd-U threshold leading to a 10% increased risk might have been influenced by a left-handed shift of the dose-response relationship. Based on these cut-offs, the prevalence of elevated HC proteinuria was 17 and 19.5% in the total population and in subjects with environmental exposure only, respectively.

Because this study was of such a critical importance for the risk assessment, both the rapporteur and the Swedish CA have made requests to the research group to obtain the detailed calculations leading to these values (agreed at the Technical Meeting of September, 2002). These details have been submitted in February/March and April 2003 and it appears that the published figures needed slight re-consideration.

Indeed, according to the equation communicated to the rapporteur (see **Annex D**), the actual threshold at which 15% HC proteinuria (10% excess) was predicted at age 53 years in the total population (environmentally + occupationally exposed) should be at 1.2, not 1.0 µg/ g creatinine.

In addition, the equation allowed calculating the theoretical prevalence of HC proteinuria in the study population in the absence of cadmium (i.e. for zero Cd-U). At age 40 (the mean age in the reference population) or 53-year (the mean age in the Oscar population), this prevalence is 5% or 10%; respectively (**Annex D**). This supports the idea that age alone significantly affected the prevalence of elevated values in the Oscar population. The Cd-U that would produce a 10% excess of elevated values (i.e. a doubling) in this population is therefore the level that would be associated with a probability of 20% (compared to 15% as originally assumed). Based on the same equation (**Annex D**), this Cd-U level is 2.6 nmol/mmol creatinine when considering the total cohort. When the same calculation is done on the group of subjects with environmental

[30] The exact figures may need to be recalculated
[31] Correction in Occup Envion Med 59 :497 (2002)

exposure to Cd only, the Cd-U level that is associated with a doubling of the prevalence of elevated HC proteinuria is 0.5 nmol/mol (the 65th percentile in this subgroup).

The two largest studies conducted in Belgium and Sweden share several characteristics but also differ on a number of points:

Table 4.135 Comparison of the characteristics of the two most relevant human studies in Europe

	Buchet et al. (1990)	**Järup et al. (2000)**
N (participation rate %)	1,699 (70)	1,021 (60)
age (years)	20-80	16-80
Population exposure	Exclusively environmental	Environmental and occupational
Cd-U (µg/g creat)	24-hr urinary samples Geometric mean 0.84/24 hours	Morning urinary samples Mean (10-90th percentile) : 0.82 (0.18-1.8) in men 0.66 (0.21-1.3) in women
tubular parameters examined	ß2M, RBP, NAG, amino acids, calcium	HC protein
Statistical procedures	Log-normalised data Centering (collinearity)	No normalisation No centering
reference population to determine cut-off values for "abnormality" of LMW proteinuria	95th percentile in the same cohort after exclusion of individuals with renal disease, analgesic abuse or diabetes	95th percentile in the general Swedish population (mean age 39y compared to 54y in the examined cohort)
Association between tubular parameter and Cd-U	Partial r^2 : 0.0684-0.0160	Partial r^2 : 0.075-0.036
Independent variables considered in logistical regression model (other than Cd-U)	Sex, age, renal disease, diabetes, medications, BMI, urinary tract disease	Age, sex
critical Cd-U	2 µg/24 hours Doubling of elevated values	2.6 µg/g creatinine in the total population, 0.5 after exclusion of individuals with occupational exposure doubling of elevated values

Despite their respective strengths, significant differences between these studies limit the possibility to directly compare their conclusions. Both proposed critical U-Cd values appear, however, very close.

It is also important to emphasise that, because of their cross-sectional nature, in both the Belgian (Buchet et al., 1990; Hotz et al., 1999) and the Swedish (Järup et al., 2000) studies, associations between renal effects and Cd-U are based on current measured Cd-U levels. It can therefore not be excluded that some of the tubular effects observed in these cohorts are the results of previously much higher exposures (particularly in occupationally exposed subjects in the Swedish study), which may also have shifted the current dose-effect/response relationship to the left.

The sensitivity of protein HC to detect early tubular effects in population environmentally exposed to cadmium has been examined in another survey conducted in Europe. Pless-Mulloli et al. (1998) examined the relationship between Cd-U and α1-M (HC protein) in 24-hour urine collections of 841 people 2-87 years old from a German population residentially exposed to cadmium (4.2 mg Cd/kg soil) and from two control populations matched for socioeconomic status. The excretion of α1-M ranged from 0.1 mg to 176.3 mg/24 hours (44% of samples showed concentrations near the detection limit, fixed value of 0.1 mg/24 hours assigned for people with a measurement < LOD). Cd-U was not different in exposed and control populations (median, interquartile range, 0.39, 0.42 versus 0.36, 0.44 µg/24 hours, respectively). Ordinal logistic regression analyses were conducted to calculate the likelihood of crossing several cut-off values of α1-M (2.05, 5, 8.5 and 15 mg/24 hours). In people of all ages the analysis identified an effect of gender (OR for males 2.14; 95% CI 1.56-2.94), age, and duration of living on contaminated soil (OR 1.03/year; 95% CI 1.02-1.04), but not of Cd-U (OR 1.30; 95% CI 0.96-1.77). For people ≤ 50 years of age a weaker effect of gender (OR 1.76; 95% CI 1.13-2.73) and age and an effect of similar magnitude for the duration of soil exposure (OR 1.03; 95% CI 1.01 to 1.04) were found. Also, the urinary cadmium excretion (OR 2.26; 95% CI 1.38 to 3.70) and occupational exposure (OR 1.71; 95% CI 1.03 to 2.83) were found to be significant predictors in this younger age group. The authors concluded that α1-M is a suitable marker for early tubular changes only for people < 50 years.

Main Asian studies

As indicated above (see Section 4.1.2.7.2), cases of Itai-Itai disease associating severe bone and kidney lesions (tubular dysfunction with proteinuria and glucosuria in most cases) in aged women were reported in Japan in the 1950s and 1960s. The pollution was attributed to the contamination of the locally cultured rice which represented almost 50% of the daily cadmium intake for the local populations. Following the recognition of those cases, several surveys have been performed to assess the health effect of this environmental pollution (exposure was often indirectly estimated on the basis of figures reflecting rice contamination). The main studies are reported below.

An assessment of renal effects was reported in a Japanese study conducted in environmentally exposed populations (1,850 exposed + 294 non-exposed subjects, both genders, age > 50 years; Kakehashi River, Ishikawa prefecture, Nogawa et al., 1989). Analysis of the prevalence of "elevated" urinary ß2M (defined as ≥ 1,000 µg/l or 1,000 µg/g creatinine, which is much higher than in European surveys) as a function of estimated cadmium ingestion calculated from the Cd content in rice indicated that after a total intake of approximately 2,000 mg cadmium (for a 53-kg person), renal damage will occur. This figure was calculated from the regression equations obtained between total Cd intake and prevalence of "elevated" urinary ß2M both in males and females; a total intake of 2000 mg corresponded with the prevalence observed in controls (3-6 %). This intake would correspond to a 50-year dose of approximately 2.1 µg Cd/kg/day. The relationship between the concentration of Cd in rice and the development of renal dysfunction (proteinuria, glycosuria) has been further examined in this Kido et al., 1993, Kido and Nogawa 1993, Hochi 1995) and other regions (Jinzu River, Toyama prefecture) with similar results (Osawa et al., 2001). Recently, however, the validity of rice Cd content as an index of exposure has been questioned (Izuno et al., 2000), in part because year to year variations in these measurements were reported to be very large even in the same rice field (Masui et al., 1971). Measurements of Cd in urine or in blood were not available in the studies by Nogawa et al. (1989) and Osawa et al. (2001).

Monzawa et al. (1998) examined the urinary Na and K excretion in 3,164 Cd-exposed persons from the Kakehashi River basin and those of 294 controls. The study was cross-sectional, restricted to measurements of Cd, β2M, Na, and K, and possible confounding and modifying factors (e.g. diet, diuretics, and blood pressure) were not considered. Data on β2M and Cd were taken from previous publications. The authors concluded that "increased K excretion was a more sensitive effect of cadmium exposure than increased Na excretion".

Yamanaka et al. (1998) examined 1,301 subjects (558 men, 743 women; 50-99 years of age) from a “Cd-nonpolluted town”. In this target group Cd-U geometric mean ranged between 0.5 and 1.4 µg/g creatinine according to sex and age. These authors found correlations (0.06 to 0.46) between renal endpoints (total protein, β2M, and NAG) and Cd-U in these non-exposed subjects. Furthermore, the probability of having “abnormal values” as defined by the 84th percentile of a “reference group” of 2,778 non-exposed” persons (non-exposed not defined more precisely and characteristics of the reference group unknown; total protein: 113.8 and 96.8 mg/l, ß2M: 378 and 275 µg/l, NAG: 8.0 and 7.2 µg/l in males and females, respectively) increased with Cd-U. These results are difficult to interpret. Indeed, both the target and reference groups were considered as non-exposed to Cdbut Cd-U was measured in the target group only. The same population from this nonpolluted area was further examined in a subsequent study which led to similar conclusions (Suwazono et al. 2000). The population examined included 2,753 subjects (1,105 men and 1,648 women). Cd-U values (µg/g creatinine) reported in this population were relatively high compared to the populations examined in European studies (e.g. Hotz et al., 1999, population living in a polluted area): geometric mean Cd-U (GSD) were 1.8 (2.5) versus 0.6 (1.9) in men, and 2.4 (2.7) versus 0.9 (2.0) in women, respectively.

Overall, these authors reported results consistent with the most recent European studies (Buchet et al., 1990; Hotz et al. (1999); Järup et al. (2000)). They found weak (r^2 generally of a few percent) and not always consistent associations between Cd-U (or Cd-B) and urinary parameters of kidney dysfunction (total protein, ß2M and NAG). In some instances they detected negative or no significant association between the examined parameters. A LOAEL cannot be derived from the published data.

Oo et al. (2000) have also examined a population of individuals ≥ 50 years living in a “nonpolluted” area of Japan (Noto Peninsula of Ishikawa Prefecture). The target group comprised 875 subjects (346 males, 529 females; area A; participation rate 70%) and 635 subjects (222 males, 413 females; area B; participation rate 72%); subjects with occupational exposure to heavy metals were excluded. They examined the relationship between urinary Cd concentration (exposure parameter) and renal dysfunction markers (urinary total protein, ß2M concentration and NAG activity). The main descriptive results are summarised in **Table 4.136**:

Table 4.136 Cd-U and urinary renal parameters in a Japanese population from a non-polluted area (Oo et al. 2000)

	Cd-U (µg/l)*	protein (mg/l)	ß2M (µg/l)	NAG (U/l)
Males				
Area A	2.2 (2.4)	43.1 (3.3)	140 (3.0)	3.2 (2.6)
Area B	3.4 (2.3)	55.6 (2.2)	125 (3.1)	4.5 (2.0)
Females				
Area A	2.8 (2.5)	37.2 (3.2)	112 (2.4)	2.6 (2.4)
Area B	3.9 (2.3)	55.1 (2.3)	122 (2.9)	4.3 (1.9)

* Geometric mean (GSD)

In multiple regression analyses, total proteinuria, ß2M-U and NAG-U were significantly and positively correlated with age and Cd-U in men and women from both areas. Partial determination coefficients (r^2) were, however, not reported, which does not allow assessing the consistency with European findings as to the relative influence of these independent variables. An additional logistic regression analysis indicated that the probability of having “elevated” urinary renal parameters (as defined in the above study by the 84th percentile in a control population, Yamanaka et al. 1998) was significantly related to Cd-U for total protein and NAG in men and women of both areas. The odds ratio for ß2M-U was significant only in females in area A. Those results were interpreted as a further indication of renal dysfunction induced by Cd exposure in non-polluted areas.

Ikeda et al. (2000) have also examined the relationship between environmental Cd exposure and kidney effects in a population of non-smoking healthy women (19-78 years) living in 30 different sites in Japan with no known environmental heavy metal pollution. 607 women were examined between 1991 and 1997; the exposure parameters included Cd-intake as assessed by 24-hour food duplicate samples (Cd-F), Cd-U and Cd-B and the renal parameters were protein HC-U, ß2M-U and RBP-U. All the biological parameters were assumed to be distributed log-normally and log-transformed before statistical calculations. The overall distribution of the exposure and effect parameters is summarised in **Table 4.137**. Significant differences were observed between regions.

Table 4.137 Exposure and effect parameters in 607 women living in non-polluted Japan areas (Ikeda et al. 2000)

Cd-F (µg/day)	Cd-B (µg/l)	Cd-U (µg/g creat)	protein HC-U (mg/g creat)	ß2M-U (µg/g creat)	RBP-U (µg/g creat)
24.7 (2.23)*	1.76 (1.98)	3.94 (2.11)	3.07 (2.22)	222 (1.86)	83 (2.31)

* Geometric mean (standard deviation)

Multiple regression analyses including age and Cd-U or Cd-B as independent variables indicated that renal parameters were significantly and positively associated with biological exposure parameters (partial $r^2 < 0.27$), age being more influential than Cd-U or Cd-B. An analysis restricted to 367 women aged 41-60 years indicated that Cd-B or Cd-U explained only a minor portion of the variance of renal parameters (partial $r^2 < 0.15$) with age being non significantly associated. A similar individual analysis was not conducted for Cd-F and the influence of this parameter was only investigated at the group level; when restricted to the group of 367 women with similar age, a significant dose-dependency was found for protein-HC but not ß2M-U or RBP-U (**Table 4.138**).

Table 4.138 Cadmium intake in 367 Japanese women and renal effect parameters (Ikeda et al. 2000)

	low Cd-F (< 18 µg/day)	intermediate Cd-F (18-30 µg/day)	High Cd-F (> 30 µg/day)	ANOVA
N	113	131	123	
Age	51 ± 5.5	51.1 ± 5.5	50.6 ± 5.0	NS
Cd-F (µg/day)	16.0 (2.07)	25.3 (1.88)	47.4 (1.85)	
Cd-B (µg/l)	1.65 (1.75)	1.87 (1.52)	2.84 (1.75)	**
Cd-U (µg/g creat)	3.92 (1.69)	4.14 (1.72)	6.00 (2.30)	**
protein-HC (mg/g creat)	3.18 (2.18)	3.14 (1.90)	3.99 (1.92)	*
ß2M-U (µg/ g creat)	221 (1.73)	259 (1.65)	258 (1.86)	*
RBP-U (µg/g creat)	81 (2.32)	82 (2.36)	107 (2.05)	NS

* and ** p < 0.05 and 0.01, respectively,
NS Non significant

A dose-response analysis was also performed in a Chinese population exposed to Cd via contaminated irrigation water (342 subjects, both genders, > 25 years old) (Cai et al. 1998). An increased prevalence of LMW proteinuria (ß2M only) occurred for an estimated absorbed dose

≥ 150 mg. According to the authors, these observations were in agreement with the dose-response relationship reported by Nogawa et al. (1989), since a total oral intake of 2,000 mg would correspond to an absorbed dose of 100 mg if a fractional gastro-intestinal absorption rate of 5% is considered (Cai et al., 1998). In this study again, an exposure index calculated from the lifetime estimated consumption of contaminated rice and smoking habits was used for calculations rather than objective measurements of Cd in blood or urine. A significant correlation was, however, reported at the group level between Cd-U and Cd-B and exposure index.

ß2M-U, Alb-U and urinary NAG isoenzymes have been studied in a population group residing in a polluted area in China (Nordberg et al., 1997; Jin et al., 1999). The area (Zhejiang province) studied was contaminated by industrial wastewater from a nearby smelter that discharged cadmium-polluted waste into the Tang River used for the irrigation of rice fields. Cadmium concentrations in rice were 3.70, 0.51, and 0.07 mg/kg for the highly and moderately polluted areas and the control area, respectively. Cd-U exceeded 5 µg/litre in the majority of subjects in the most highly polluted area (< 2 µg/litre in controls).

The 3 biomarkers of tubular effects were significantly increased with Cd exposure (**Table 4.138**). There was a marked dose-dependent increase in total NAG and NAG-B content of urine (but not NAG-A) related both to Cd-U and to the calculated cadmium uptake (linear trend test).

Table 4.139 Urinary ß2M-U, Alb-U and NAG in Chinese populations living in Cd polluted areas (Jin et al., 1999)

	Controls	Moderate exposure	High exposure
ß2M-U (µg/ g creat)	130	159	531*
Alb-U (mg/g creat	4.498	6.592	8.594*
NAG total (µmol/creat.hr)	29.99	54.33*	74.13**

Means, * and ** reflect p < 0.05 and 0.01

Overall, it can be concluded that studies conducted in Asia confirm the association between environmental Cd exposure and the occurrence of renal effects detected in the main European studies. The definition of the critical exposure level at which these effects occur and the possible comparison with European data is, however, hampered by the fact that objective measurements of Cd exposure were not always available, exposure was apparently high in some control groups, different cut-off values were used to define an effect, and also because of the difference in bioavailability of Cd from rice.

Reversibility of the renal effects in the general population

Some controversy exists as to the reversibility of renal effects of cadmium both in the general population and in workers.

Järup et al. (1998a) mentioned that "cadmium-induced tubular proteinuria is not reversible in almost all cases". There is however evidence demonstrating that, both in the general population as in workers (see above inhalation exposure), the (ir) reversibility of tubular proteinuria after reduction or cessation of exposure depends on the intensity of exposure and/or the severity of the tubular damage. Japanese studies have shown that while renal tubular dysfunction caused by cadmium is irreversible and slowly progressive when ß2M levels in urine are ≥ 1,000 µg/g creatinine, it appears that these effects are reversible when ß2M levels in urine are < 1,000 µg/g creatinine (Kido et al., 1988, Kasuya et al., 1991, Tsuchiya 1992).

The follow-up of the Pheecad cohort in Belgium also indicates that early renal effects associated with low-level environmental exposure to cadmium are reversible when the cadmium body burden/exposure decreases (Hotz et al., 1999). The Pheecad study was conducted as a follow-up (1991-1995) of the Cadmibel study (1985-1989). Industrial reconversion, improvements and local preventive measures were implemented at the end of the 1990s by the industry, the government and the inhabitants of the polluted region, which resulted in a reduction of Cd-B by 29.6% and of Cd-U by 15.2% (Staessen et al., 2000).

Table 4.140 Reversibility of renal parameters in the Pheecad Study (Hotz et al., 1999)

	Men		Women	
	Baseline	Follow-up	Baseline	Follow-up
Cd-U (nmol/mmol creat)	0.6 (1.9)	0.5 (1.9)*	0.9 (2.0)	0.8 (2.0)*
ß2M-U (nmol/mmol creat)	0.7 (2.4)	0.6 (0.01)*	0.7 (1.9)	0.6 (2.4)
RBP-U (µg/24h)	164 (1.7)	89 (1.9)*	107 (1.8)	59 (2.0)*
NAG-U (U/24h)	1.7 (1.7)	1.0 (1.9)*	1.4 (1.8)	0.7 (2.1)*
calcium-U(mmol/24h)	4.4 (1.9)	3.9 (1.8)*	3.5 (1.8)	3.3 (1.9)

means (SD); * : significantly different (paired t-test)

These findings are also supported by studies in occupational settings (Roels et al., 1997; Trzcinka-Ochocka et al., 2001) discussed in the previous section. It can therefore be concluded that, as for inhalation exposure, incipient tubular effects associated with low Cd exposure in the general population are reversible if exposure is substantially decreased. Severe tubular damage (RBP or ß2M > 1,000-1,500 µg/g creat) are generally irreversible.

Environmental Cd exposure and glomerular effects

In the extensive Belgian study on the renal effects induced by Cd in the environment (Cadmibel study), no glomerular dysfunction as assessed by 24-hour urinary total protein, 24-hour urinary albumin excretion or endogenous creatinine clearance was found (Buchet et al., 1990). However, in a further statistical analysis restricted to the "rural" subgroup of this population which comprised the most heavily exposed subjects (geometric mean and standard deviation: 8 and 2 nmol/24 hours, respectively), a small negative effect of Cd-U on creatinine clearance was described (Staessen et al., 1994). In this second publication both the calculated and the measured creatinine clearance were used as endpoints. However, it should be emphasised that the design was cross-sectional and that the differences between the low and high exposure groups were clearly smaller than the difference between measured and calculated creatinine clearance (4-5 ml/min vs. 13-14 ml/min). Moreover, the authors themselves drew attention to the fact that a (non-identified) confounding factor could not be excluded. Finally, it should also be borne in mind that the inevitable constraints of this large study did not allow for a very precise measurement of the clearance (blood sampling was performed within 2 weeks of the urine collection) and that the value of calculated creatinine clearance for precise assessments has been challenged (Sokoll et al., 1994; Malmrose et al., 1993). It should also be emphasised that there is some indication of a publication bias here also: indeed, whereas the possible effect of Cd on the clearance in the rural subgroup is analysed and reported in depth in the second publication (Staessen et al., 1994) the lack of effect of Cd on the same parameter in the whole population is only briefly mentioned (one short sentence) in the discussion section of the first publication (Buchet et al., 1990).

In the 5-year follow-up of this same “rural population” (Pheecad study; Hotz et al., 1999) detailed analyses of all available data (baseline, follow-up, and changes between both examinations) showed that urinary Cd excretion was associated with creatinine clearance but the association was positive and, thus, contradicted the hypothesis of a toxic impact of low-level Cd exposure on the GFR. No consistent association was found between 24-hour urinary Cd excretion and 24-hour urinary albumin excretion. In addition, this recent survey demonstrated that elevated urinary RBP (> 338 µg/24 hours) or NAG (> 3.6 IU/24 hours) at baseline were not predictive of a subsequent deterioration of the glomerular function after reduction of exposure.

Overall, it can be concluded that the clues for a glomerular dysfunction in populations exposed to low-level of Cd in the environment are weak.

Susceptible groups in the general population

Because of the larger heterogeneity in the general population than in occupationally exposed cohorts (age, gender, disease), it can easily be conceived that variations in individual susceptibility may significantly determine the occurrence of disturbed renal function in environmentally exposed populations. This interindividual variation could occur at various levels (IARC, 1992):

- higher intake (people with certain dietary preferences, people living in Cd-polluted areas, smokers),
- the fractional intestinal uptake may vary depending on gender, individual and nutritional factors, the contribution of pulmonary exposure to the internal dose mainly depending on smoking habits,
- kinetics of cadmium after systemic uptake: unidentified interindividual variations could also play a role in the proportion of cadmium accumulating in the kidney,
- sensitivity of the critical organ,
- presence of pre-existing or intercurrent renal disease (e.g. glomerulonephritis or secondary to diabetes, analgesic nephropathy, hypertension or other cardio-vascular diseases).

Variations of Cd uptake upon oral exposure are discussed in Section 4.1.2.2. However, when the definition of the dose-effect/relationship is based on the body burden (Cd-U in the present case), toxicokinetic factors do not need to be further considered for the risk characterisation.

While the Cadmibel study confirmed the higher Cd body burden in women than in men, it also identified an interaction between Cd-U and the presence of diabetes as a significant determinant of renal effects, indicating that these patients might be at increased risk of renal damage. A similar interaction with the regular use of analgesic drugs was found. Subsequent studies in animals have shown that the symptoms of diabetic renal complications or induced by acetominophen are exacerbated by Cd exposure (Jin et al., 1994; Jin and Frankel 1996; Bernard et al., 1988; Bernard et al., 1991).

Children constitute another group which deserves special attention for possible increased susceptibility. Most studies that are useful for the characterisation of the quantitative relationships between Cd exposure and renal effects included people residing in Cd polluted areas and therefore with a lifelong exposure (including their childhood). If any, the possible increased susceptibility of children is therefore included in the present assessment and does not need additional consideration.

No further published information on individual susceptibility factors in the general population exposed to cadmium could be located. Potentially sensitive subgroups of the general population remain to be clearly identified and examined.

Environmental Cd exposure, health significance of early renal changes and ESRD

ATSDR (1999) concluded that the health significance of the early kidney effects is difficult to assess because the decreased resorption of LMW proteins is not adverse in and of itself, but may be indicative of increased excretion of other solutes (e.g. calcium). Deaths from renal failure due to cadmium exposure are rare, but even after cadmium exposure ceases, the renal damage may continue to progress (ATSDR, 1999).

Järup et al. (1998) believe that the LMW protein effects observed in populations environmentally exposed to cadmium are the "forerunners of clinical disease leading to ESRD". They wrote, "uraemia was a common cause of death among Japanese farmers suffering from Itai-Itai disease" but there is no systematic and critical discussion to support this view. Publications that are cited in this review and seem crucial in this context were examined more in depth in order to examine the association between environmental exposure to cadmium and ESRD (see **Annex C**). It can certainly not be concluded from these studies that "uraemia was a common cause of death among Japanese farmers suffering from Itai-Itai disease (...)". It should, however, be considered that measuring mortality may not be the most appropriate method to detect the health impact of Cd exposure. Indeed, in developed countries where renal replacement therapy is available, ESRD may not be noted as the underlying cause of death, which may distort the results of mortality studies. It should also be borne in mind that some studies considered overall mortality only and that it remains to understand whether the association found in several studies between increased overall mortality and Cd exposure is causal.

It is fair to recognise that, in the recent literature; the health significance of the early renal changes observed in populations exposed to low-level environmental Cd via the oral route has been appreciated and interpreted by experts with some contrasted opinions. These sometimes different interpretations were largely reflected during the discussion of the successive drafts presented at TMs by the rapporteurs. Two views were essentially defended:

1) Some scientists (including the rapporteurs of the present document) express the view that early renal effects associated with low levels of environmental exposure (Cd-U < 5 µg/g creatinine) most likely reflect benign, non-adverse responses (Hotz et al., 1999). Arguments offered to support this interpretation and developed above are as follows:

- variations of tubular parameters observed below this Cd-U level remain within a physiological range (e.g. < 300 µg/g creatinine for RBP or ß2M),
- associations with Cd body burden remain weak (fraction of explained variance < 10%)
- human studies in environmentally exposed populations (but also in workers) have shown that variations of this amplitude are reversible when exposure decreases timely,
- recent observations have found that such changes are not predictive of an alteration of the renal function,
- other interpretations than Cd-induced toxicity are plausible. It is indeed possible that the association observed between low-level cadmiuria and LMW proteinuria reflects a competition between Cd-loaded MT and LMW proteins at tubular reabsorption sites and/or the binding of a fraction of Cd-U to excreted LMW proteins.

2) Other experts (mainly Swedish scientists) indicate that elevated concentrations of LMW in urine is widely accepted, as such, as an indicator of kidney damage. Even if they do not necessarily progress to severe or clinically relevant renal disease, the early dysfunctions of the renal tubular cells are to be considered as an adverse effect because it should be aimed at detecting the earliest effects of Cd, at a stage where it is possible to prevent health effects, also in the most sensitive groups of the population. While it might be possible that some of the lesions are reversible, they also consider these early renal changes in populations exposed to low-environmental levels of Cd as adverse, especially because the half-life of Cd in the environment and in the kidney is very long. In addition they insisted on the fact that the sources of Cd in the environment are rather unclear and difficult to decrease making that, as long as the exposure levels remain unchanged, the effect cannot be reversed but may become more serious.

Recently, Hellström et al. (2001) have examined the relationship between environmental (and occupational, see above inhalation route) exposure to Cd and the occurrence of ESRD, as assessed by renal replacement therapy (RRT, dialysis or transplantation) in a Swedish population living near a Cd battery production facility in the southeast of Sweden (Kalmar County). Comprehensive data were available for all individuals undergoing RRT (384 cases between 1978 and 1995, 250 men and 134 women). Based on the distance between the dwelling place, and to some extent environmental monitoring data, it was possible to identify groups with high (occupational), moderate (living within a 2 km radius of the point source), or low exposure (between 2 and 10 km) as well as a control group with no exposure (rest of the residents in the county). The incidence of RRT (number of cases per million person-years between 20 and 79 years) was higher in the exposed groups than in the controls (201.4 versus 118.4 for both genders cumulated, Mantel-Haenszel rate ratio, 1.8; 95% CI, 1.3-2.3). The age and sex adjusted rate ratio increased from 1.4 in the low exposure group to 2.3 in the high exposure group (**Table 4.141**):

Table 4.141 Incidence rate ratio of renal replacement therapy (RRT) in populations (20-79 years) with environmental and occupational exposure to Cd (Hellström et al., 2001)

	Men	Women	All
Unexposed	1.0	1.0	1.0
Low	1.4 (0.6-2.2)	1.2 (0.2-2.2)	1.4 (0.8-2.0)
Moderate	1.3 (0.7-2.0)	3.0 (1.7-4.4)	1.9 (1.3-2.5)
high (occupational)	2.1 (0.6-5.3)	-	2.3 (0.6-6.0)

Trend test, all categories, $p < 0.001$.

Interestingly, there was no remarkable difference in diagnostically labelled causes of ESRD in the Cd exposed groups compared with the unexposed population (not further detailed), suggesting that (even in the occupationally exposed group) Cd did not seem to be the primary cause of ESRD but rather contributed to accelerate the progression of non specific renal diseases such as chronic glomerulonephritis or renal diabetes. This observation is reminiscent of the findings of Buchet et al. (1990) and Hotz et al. (1999) who reported that interaction terms of Cd-U with the existence of a condition such as the abuse of analgesics, diabetes or urinary tract disease were significant determinants of the tubular dysfunction parameters (sometimes stronger determinants than Cd-U alone). This observation is potentially important because it may contribute to understand why early renal changes observed in individuals with environmental exposure to Cd are not predictive of a degradation of renal function (Hotz et al., 1999) although Cd exposure might be associated with an increased incidence of ESRD through the exacerbation of pre-existing or intercurrent renal diseases (not necessarily associated with early renal changes).

Kidney stones

An additional effect on the kidney seen in workers after high levels of exposure is an increased frequency of kidney stone formation (ATSDR, 1999). This has been reported by several investigators (Friberg et al. (1950), Falck et al. (1983), Thun et al. (1989), Elinder et al. (1985), Kazantzis (1979), Scott et al. (1978)).

The early study of Friberg (1950) suggested a correlation between exposure to cadmium and the prevalence of kidney stones. Further investigations in the same factory revealed that 44% of a group of workers exposed to cadmium oxide dust for more than 15 years had a history of renal stones (CRC, 1986).

Falck et al. (1983) studied the prevalence of renal dysfunction among 33 male subjects exposed to cadmium fumes in a plant producing refrigeration compressors with silver brazed copper fittings (silver brazing wire contained 18-24% cadmium). For each participant, blood (Cd-B, β2M, creatinine) and urine (creatinine, pH, osmolality, glucose, protein, β2M) analyses were performed and a questionnaire was administered to document medical history and personal habits. Two subjects reported a history of nephrolithiasis. Their blood and urine characteristics and their cumulative time-weighted exposure estimation are reported in **Table 4.142**.

Table 4.142 Quantitative urinalysis results and time-weighted exposure data, cadmium-exposed group (Falck et al., 1983)

Subject	Cumulative exposure (µg/m³xyear)	Cadmium/creatinine *(µg/g)	Creatinine (g/24 hr)	Protein(mg/24 hr)	β2M(µg/24 hr)	Glucose (mg/24 hr)
15	1,591	12	1.40	247	210	131
22	356	21	1.53	360	1,610	207

Reference limits are as follows: Creatinine: 1-2 g/24hr, β-2M 400 µg/L, Protein < 188 mg/24 hr, Glucose < 250 mg/24 hr
* Spot urine

No further comment is given in the paper about these two cases. Exposure to other nephrotoxins at the plant or analgesic abuse was excluded (Falck et al., 1983).

Thun et al. (1989) examined 45 workers employed at a plant that recovers cadmium from industrial waste to assess the quantitative relation between exposure to cadmium and various markers of renal function. Cumulative external exposure to airborne cadmium was estimated from historical air sampling data, adjusted for respirator use. The studied population included finally 17 current workers, 18 highly exposed former workers, 2 salaried workers and 8 former short-term production workers. The last 10 workers took part although they were not in the target population. Cumulative exposure in the exposed group ranged from 0 to 5383 mg/m³.days. A control group consisted of 32 male workers employed at a local hospital. Blood and urine cadmium concentrations were significantly higher in the exposed workers than in the unexposed (Cd-B (GM ± SD): 7.9 ± 2.0 µg/L vs. 1.2 ± 2.0 µg/L, Cd-U (mean ± SD): 9.3 ± 6.9 vs.0.7 ± 0.7 µg/g creatinine for exposed and controls respectively).

Kidney stones were reported more commonly by the cadmium workers than by the unexposed in the questionnaire (8/45 (18%) versus 1/32 (3%)). Authors noted that several mechanisms could link stone formation to renal tubular disease, including hypercalciuria, phosphaturia, uricaciduria, reduced urinary citrate or renal tubular acidosis. Differences in calcium and phosphorous excretion, associated with the cadmium workers were demonstrated at the group level. However, no individual data were available for the eight reported cases with kidney stones (Thun et al., 1989). No validation of the data collected by the questionnaires was performed by consulting the clinical records.

Other reports in occupational settings described cases of renal stone formation: Adams et al. (1969) in British accumulator factory workers, Scott et al. (1978) in 5/27 coppersmiths exposed to cadmium; Kazantzis (1979) in 3/12 workers with more than 25 years exposure to cadmium.

Järup and Elinder (1993) explored the incidence of renal stones in relation to exposure to cadmium in a cohort of Swedish battery workers and examined dose-response relations. A questionnaire was sent to all the workers who were employed for at least one year in the battery factory between 1931 and 1982. This questionnaire included questions of exposure to hazardous substances, past and present health state and smoking habits. 12% of the workers (N=74/619) stated in the questionnaire that they had a history of kidney stones. For 48 workers, stones were confirmed in hospital records. Authors assumed that specificity of self reported kidney stones is high because of the typical clinical picture and that it was thus unlikely that a reported kidney stone has been mistaken for some other disease. The authors included all the reported cases of kidney stones in the further analyses.

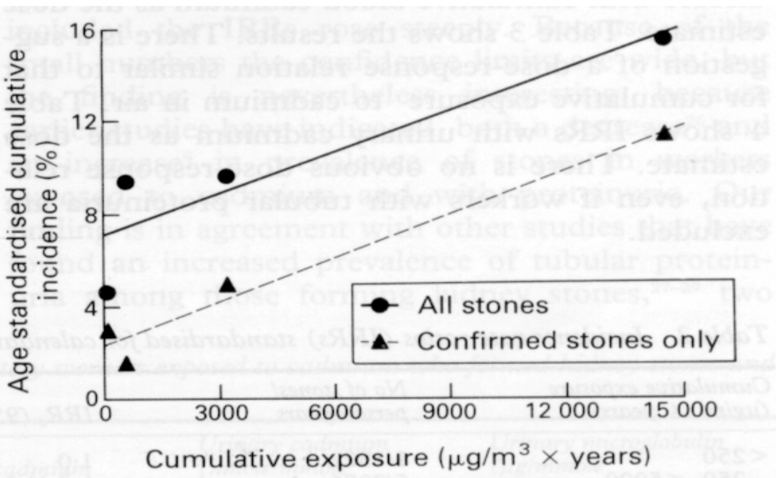
The employment period for each member of the study group was combined with the measurements of Cd in air for different periods giving a cumulative exposure estimate (4 categories: < 250, 250-< 1,500, 1,500-< 5,000, ≥ 5,000 µg/m³ · year). A subgroup with cumulative exposure of less than 250 µg/m³ · year was used as internal control group. Results are given in **Table 4.143**.

Table 4.143 Kidney stones incidence rate ratios for Swedish male battery workers exposed to cadmium (Järup and Elinder, 1993)

Cumulative exposure (µg/m³ · year)	N° of stones/person-years	Incidence rate ratio (95% CI)
< 250	10/3201	1.0
250 -< 5,000	29/7377	1.3 (0.6-2.6)
≥ 5,000	34/5501	2.0 (1.0-4.0)

Järup et al. (1998) reported the dose-response relation between cumulative cadmium exposure and the age-adjusted cumulative incidence of renal calculi in the group of workers.

Figure 4.5 Age Standadised cumulative incidence of urolithiasis in Swedish male battery workers exposed to cadmium



Age standardised cumulative incidence of urolithiasis in Swedish male battery workers exposed to cadmium. The solid line represents all workers with kidney stones; the dotted line includes only workers whose stones were confirmed in hospital records.

This was also reported in the original publication in another type of figure.

β2M measurements were available for 33 stone formers: 13 of these workers had tubular proteinuria (β2M ≥ 34 µg/mmole creatinine, about 300 µg/g creatinine). The authors emphasised that their findings were in agreement with other studies that found an increased prevalence of tubular proteinuria among the workers forming kidney stones. Measured biological parameters (Cd-U, Cd-B, β2M-U) in the study showed differences between those forming kidney stones and workers without kidney stones.

Table 4.144 Comparisons of medians for biological parameters between battery workers exposed to cadmium who formed kidney stones and those who did not ((Järup and Elinder, 1993)

	N°	Age	Cd-B(nmol/l)	Cd-U(nmol/mmol creatinine)	β2M(µg/mmol creatinine)
Those forming stones	73	67 (61-69)	63.5 (51.6-95.3)	3.7 (2.4-6.4)	17.6 (9.3-140)
Those not forming stones	532	64 (62-66)	50.5 (44.5-55.6)	2.0 (1.5-2.5)	6.9 (6.4-7.6)
p Value		0.21	0.02	0.008	0.0007

The authors concluded that this indicated both higher internal cadmium doses and a greater degree of tubular damage among those forming stones (Järup and Elinder, 1993). No other measurements which could give some information on the mechanism of stone formation were performed (e.g. Ca-U). No information (as in most of the previously cited studies) was made available about nutritional habits, heredity, etc.

Summary and conclusions

For the reasons indicated above, it is presently not possible to determine precisely at which Cd body burden a health relevant alteration of the renal function appears. In a conservative approach, the TM considered, however, that small changes of very sensitive, early biomarkers of renal/bone effects of uncertain clinical significance represent adverse health effects that could be used for the risk characterisation.

For workers occupationally exposed to cadmium (mainly by inhalation), a LOAEL of 5 µg Cd/g creatinine constitutes a reasonable estimate. The health significance of this threshold is justified by the frequent observation of irreversibility of tubular changes above this value and its association with further renal alteration.

On the basis of the most recent studies conducted in Europe (Buchet et al., 1990, Hotz et al., 1999, Järup et al., 2000), it appears that renal effects can be detected in the general population (mainly exposed by the oral route) for Cd body burdens below 5 µg/g creatinine: 2 µg/g creatinine (Buchet et al., 1990), 0.5, 1.2 or 2.6 µg/g creatinine depending on the mode of calculation (Järup et al., 2000). When discussing these figures during TMs, Member States insisted on the fact that it is very difficult to define values such as LOAELs based on the data from these types of studies, because of the complexities of the relationship examined. They also indicated that it is important to express uncertainties that exist rather than trying to be too exact about a LOAEL.

Although increased calciuria might be linked with the concomitant bone changes detected at low level exposure to Cd (LOAEL 3 µg/g creatinine; see Section 4.1.2.7.2), it should be considered that there is uncertainty about the exact clinical significance of these changes and that the scientific debate is not settled on this issue. In addition, it is also important to keep in mind that in all the above mentioned epidemiological studies, the influence of Cd on kidney parameters was low (fraction of explained variance < 10%). These uncertainties, a refined assessment of exposure and a better characterisation of the dose-response relationship could be achieved through a large (preferably pan-European) epidemiological study that should be iniated.

Trying to aggregate all these data, a LOAEL of 2 µg Cd/g creatinine is proposed. This figure should be understood as a composite level, based on the association between Cd and not only LMW proteins but also calcium excretion in urine and its possible relationship with bone effects.

The most significant difference between occupational and environmental exposure is that the populations at risk are different (generally healthy young male workers versus general population). As indicated above, it is plausible that the lower LOAEL in the general population exposed by the oral route is the consequence of an interaction of Cd exposure with pre-existing or concurrent renal disease. As workers exposed to Cd may also suffer from such disease during or after their occupational career, it appears prudent to recommend that they should be offered the same degree of health protection than individuals from the general population. For this reason, a single LOAEL of 2 µg/g creatinine will be used in Section 4.1.3 (Risk characterisation), both for oral and inhalation exposures. The interpretation of this LOAEL and of the margin of safety that will be calculated should also take into account the long half life of cadmium and the uncertainties regarding the present hazard assessment.

Those LOAELs were determined for exposure to cadmium in general and, in the absence of specific data, it can be assumed that they also apply to cadmium metal and cadmium oxide.

The possible relationship between kidney and bone effects induced by Cd exposure is discussed in Section 4.1.2.7.2.

4.1.2.7.4 Cardiovascular system

Studies in animals

Oral route

No experiment specifically using cadmium oxide and/or cadmium metal has been located.

Some experiments using other cadmium compounds were reported and are briefly summarised here:

Oral exposure of rats, rabbits, and monkeys to cadmium compounds over intermediate and chronic duration has been found to increase blood pressure in some studies. They are summarised in **Table 4.145**.

Table 4.145 Oral exposure of to cadmium compounds and effects on blood pressure

Species	Type of compound	Dose (mg/kg/day)	Route	Duration	Results	Reference
L.E. rats	Cd acetate	0.01	W	18 m.	20% increase in blood arterial pressure	Kopp et al. (1982)
S.D. rats	Cd acetate	1.4	W	190 d.	20% increase in blood arterial pressure	Carmignani and Boscolo (1984)
L.E. rats	Cd chloride	0.0081	W	5 m.	15mm Hg increase in blood arterial pressure	Perry and Elanger. (1989)

Table 4.145 continued overleaf

Table 4.145 continued Oral exposure of to cadmium compounds and effects on blood pressure

Species	Type of compound	Dose (mg/kg/day)	Route	Duration	Results	Reference
Rabbits (New Zealand)	Cd chloride	1.6	W	200 d.	Increased aortic resistance	Boscolo and Carmignani (1986)
Rabbits (New Zealand)	Cd acetate	0.07	W	34 d	Increased arterial pressure	Tomera and Harakal (1988)
Monkey (Rhesus)	Cd chloride	0.53	F	9 y.	Increased arterial blood pressure (first 1.5 year)	Akahori et al. (1994)

W Water
F Food
M Months
D Days
Y Years

This was not reported in other studies in animals where administered doses ranged from 2.3 to 8.0 mg/kg/day. ATSDR (1999) commented the studies and stated that those showing an effect on blood pressure had control groups with lower blood pressure than studies showing no effect and that observed increases in blood pressure were generally small.

In the study conducted by Kopp et al. (1982), where cadmium acetate was administered in L.E. rats, the effect on blood pressure appeared to be biphasic, reaching a maximum effect (an increase of 12-14 mm Hg in average systolic pressure) at intakes of 0.07 mg/kg/day but decreasing to normal or even below normal at intakes 10-100 times higher (Kopp et al., 1982).

According to CRC (1986), several factors appear to influence the degree of hypertensive response. Experiments on rats have shown that apart from species and/ or strain, sex and diet are also of importance. Hypertension has mainly been seen when rats have been given a rye-based or a high-salt content diet but not when fed other types of chow (Whanger, 1979; Ohanian and Iwai, 1980; Perry et al., 1983, cited in CRC 1986). Content of the diet in other trace elements influences also the hypertensive response in rats: Perry et al. (1974, 1976) showed that the pressure effect from 2.5 and 10 mg cadmium per litre in drinking water was inhibited by the simultaneous addition to water of either 3.5 mg/L of selenium, 20 mg/L of copper, or 100 to 200 mg/L of zinc. The addition of 1 mg/L of lead enhanced the hypertensive response.

Several mechanisms have been postulated to explain the effects of chronic cadmium exposure on the cardiovascular system. Oral administration of cadmium doses that induce hypertension was shown to increase circulatory renin activity (Perry and Erlanger, 1973 cited in WHO 1992). Nishiyama et al. (1986) postulated that cadmium exposure increases sodium and water retention, which are important factors controlling the development of hypertension (Nishiyama et al., 1986 cited in WHO1992). By morphometric methods, Fowler et al. (1975) demonstrated effects on the blood renal vessels of rats exposed to various concentrations of cadmium (up to 200 mg/L in drinking water) for several weeks. Significantly smaller arteriolar diameters were found in the exposed animals than in the controls (Fowler et al., 1975 cited in WHO 1992).

Histopathologic lesions of heart tissue (congestion, separation of muscle fibres) and decreased activity of antioxidant enzymes, but no increase in peroxidation were found among rats given 2.5 mg/kg/day of cadmium in the diet for 7 weeks (Jamall et al., 1989, cited in ATSDR 1999).

Inhalation route

No experiment specifically using cadmium metal was located.

Some experiments have been conducted with cadmium oxide.

However, opposite to the findings of studies using cadmium compounds administered orally, the inhalation exposure of rats to cadmium oxide (at 0.02, 0.16 and 1.0 mg/m³ for up to 27 weeks) did not result in arterial hypertension. According to the authors, the difference may be due not only to different routes of exposure but to some of several factors modifying the hypertensive effect of cadmium, as previously mentioned (Baranski et al., 1983).

Kutzman et al. (1986) reported a significant increase in relative heart weight in rats exposed to 1.06 mg Cd/m³ as cadmium chloride for 62 days (6 hours a day, 5 days a week). Body weights were also significantly reduced from this exposure, and absolute organ weights were not reported, so the significance of this toxic effect on the heart is unclear (Kutzman et al., 1986 cited in ATSDR 1999).

One study was undertaken to evaluate the ultra structure of the cardiac muscle in rats exposed by inhalation to cadmium oxide fumes (0.16, 1.0 mg/m³ 5 hours daily, 5 days a week for 3 and 6, 3 and 4 months). The structure of muscle cells, arterioles and capillaries remained unchanged in the two exposed groups and in the control group. Examination of cardiac papillary muscle showed distinct differences in the ultra structure of intercalated discs between control rats and those exposed to CdO. The severity of the structural changes depended on the duration of exposure and Cd concentration. According to the authors, the increased width of intercalated discs induced by cadmium may significantly alter heart functions such as conducibility and the intercellular transport of ions and low molecular cellular components (Kolakowski et al., 1983)

No effects considered as biologically significant were observed in rats exposed for 13 weeks to 0.1, 0.25, or 1 mg/m³ CdO (NTP technical report, 1995).

Conclusions: studies in animals

Contradictory findings have been reported in studies investigating effects on blood pressure after oral administration of cadmium compounds in animals. Inhalation exposure to cadmium oxide was not associated with an increase in blood pressure. In one study, exposure was reported to have induced ultra structural changes in the cardiac papillary muscle of rats (at a concentration of 0.16 mg Cd/m^3).

No conclusion can be drawn for cadmium metal. Overall, evidence for cardiovascular toxicity resulting from oral and inhalation exposure to cadmium oxide and compounds in animals is suggestive of a slight effect

Studies in humans

Oral route: environmentally exposed populations

Studies regarding cardiovascular effects in humans after oral exposure to cadmium have primarily investigated relationships between blood pressure and biomarkers of cadmium exposure such as cadmium levels in blood, urine or other tissues.

Schroeder (1965, 1967) observed that people in the general population dying from hypertensive and/or cardiovascular disease had somewhat higher cadmium concentrations in liver and kidney tissues than people dying from other causes. He suggested that cadmium could be a causative factor for these diseases (Schroeder, 1965, 1967 cited in WHO 1992).

Smoking is an important confounding factor because of the higher blood, urine and tissue levels of cadmium in smokers and the known cardiovascular toxicity of cigarette smoking.

Case-control and cohort epidemiological studies that controlled for smoking have typically found no association between body cadmium levels (primarily reflecting dietary exposure) and hypertension (Beevers et al., 1980; Cummins et al., 1980; Ewers et al., 1985; Lazebnik et al., 1989; Shiwen et al., 1990). However, some studies found positive (Geiger et al., 1989; Tulley and Lehmann, 1982) or negative correlations (Kagamimori et al., 1986; Staessen et al., 1984) (ATSDR 1999).

The cross-sectional Cadmibel study (1985 to 1989) failed to demonstrate an independent positive correlation between blood pressure and environmental exposure to cadmium (Staessen et al., 1991).

The Cadmibel participants of two rural areas were invited for further examination in the context of the follow-up study named PheeCad (Public Health and Environmental Exposure to Cadmium, 1991-1995). In these two areas, exposure to cadmium decreased with time after measures were implemented to sanitize the environment. From the three zinc smelters present in these areas, one was dismantled already in 1974; a second ceased primary production in 1992 and in the third one, ore has been transported and stored in dust-tight facilities. Inhabitants of the most polluted area were informed as to how reduce exposure to cadmium by using tap instead. How and whether this changing environmental exposure influenced blood pressure and the incidence of hypertension was examined by Staessen et al. (2000) in a random sample of 692 subjects aged 20 to 83 years. Biomarkers of exposure (Cd-U, Cd-B) illustrated the decrease of environmental exposure. Blood pressure (conventional or 24-hr) was not correlated with Cd-B or Cd-U and no relationship could be demonstrated between the trends in Cd-B or Cd-U, or Cd-B or Cd-U at baseline and the incidence of hypertension. The authors concluded that there was no evidence supporting the hypothesis that environmental exposure to cadmium would lead to an increase in blood pressure and/or to a higher prevalence of hypertension. (Staessen et al., 2000).

Some information is also provided by the mortality studies.

A mortality study of the residents of Shipham, a cadmium-polluted area in England and of a nearby control village was reported by Inskip et al. (1982) (the study will be detailed later in Section 4.1.2.9.2). There was a small but statistically significant excess mortality rate in Shipham from cerebrovascular disease (SMR: 140 versus 102 in Hutton, $p < 0.05$).

In the mortality study conducted by Shigematsu et al. (1982) in Japan, the mortalities from cardiovascular diseases such as cerebrovascular and hypertensive diseases among the general population in the cadmium-polluted areas were not different from, or even lower than, those in the non-polluted areas (Shigematsu et al., 1982).

Inhalation route: occupationally exposed populations

Inhalation exposure to cadmium does not appear to have significant effects upon the cardiovascular system.

In the USA, a correlation between average air cadmium levels in cities and mortality associated with hypertension and heart disease has been reported by Carroll (1966) and Hickley et al. (1967) (cited in WHO 1992). However, inhalation of ambient air is generally a minor pathway of cadmium exposure in non-occupational groups, so it seems unlikely that inhalation exposure was the causal factor. Moreover, several confounding factors such as smoking habits, air pollutants other than cadmium, and other environmental factors made it difficult to draw conclusions concerning the effects of cadmium (ATSDR, 1999; WHO 1992).

Most studies of workers occupationally exposed to cadmium have not found cadmium-related cardiovascular toxicity (Friberg, 1950; Bonnell, 1955; Bonnell et al., 1959; Kazantzis et al., 1963, Holden, 1969; Smith et al., 1980; de Kort et al., 1987 cited in WHO 1992 and in ATSDR 1999).

Vorobjeva and Eremeeva (1980) examined 92 workers at a battery factory exposed to cadmium oxide dust at concentrations ranging from 0.04 to 0.5 mg/m³. There was no control group. Blood pressure and electrocardiograms were taken. The authors reported increased prevalence of hypertension and absence from work due to hypertensive and ischaemic heart disease among the exposed workers. Several types of abnormalities were observed in the electrocardiograms of the exposed workers. But because the results of this study were presented in a very condensed form, excluding details, WHO and CRC authors concluded that it was difficult to draw clear-cut conclusions (Vorobjeva and Eremeeva, 1980 cited in WHO 1992 and in CRC 1986).

Health records of 311 male workers in an alkaline battery factory were examined by Engvall et al. (1985) to investigate the relationship between exposure to CdO and hypertension. All the workers were employed in cadmium-exposed jobs for more than one year during 1950 to 1980. Levels in air were estimated to have exceeded 1 mg in air before 1947. Levels dropped to 200 µg/m³ in 1947 and to 50 µg/m³ in 1962. After 1974, levels were below 20 µg/m³.

The prevalence of hypertension in the group of workers over the age of 40 years was 23% (57/248). Only one employee below 40 years of age was hypertensive and had worked in the plant for 7 years. Within different age groups, the time of employment was compared between hypertensive and normotensive individuals. Hypertensive workers had worked in the company for a significantly longer time than the age-matched normotensives what was interpreted by the authors as an indication of a possible relationship between exposure to cadmium and the development of hypertension (Engvall and Perk, 1985).

There is no indication of excess mortality due to cardiovascular or heart disease in cadmium-exposed workers. On the contrary, lower than expected mortality from cardiovascular disease was reported in some of the cohort studies (Armstrong and Kazantzis, 1983; Kazantzis et al., 1988).

Conclusions: studies in humans

Results reported by the human studies do not speak for the hypothesis that cadmium may cause hypertension as a result of occupational or environmental exposure. If cadmium does affect blood pressure, the magnitude of the effect is small compared to other determinants of hypertension.

Conclusions: cardiovascular effects

The weight of evidence suggests that cardiovascular effects are not a sensitive end point indicator for cadmium oxide and metal toxicity.

4.1.2.7.5 Liver

Studies in animals

Oral route

No experiment specifically using cadmium oxide/metal was located.

Experiments using cadmium compounds were reported and are briefly summarised:

Oral administration in rats of doses ranging from 1.6 to 15 mg/kg/day caused histopathologic changes in the liver (e.g. necrosis of central lobules, focal hepatic fibrosis, biliary hyperplasia) (Cha, 1987; Gill et al., 1989; Miller et al., 1974a; Schroder et al., 1965; Stowe et al., 1972; Wilson et al., 1941 cited in ATSDR 1999). Exposure to doses of 0.05-10 mg/kg/day caused metabolic alterations (e.g., decreased cytochrome c oxidase activity in mitochondria, increased enzymatic activities) in rats (Groten et al., 1990; Muller and Stacey, 1988; Muller et al., 1988; Sporn et al., 1970, Steibert et al., 1984; Tewari et al., 1986, cited in ATSDR 1999).

Other studies have not found liver effects in animals following oral exposure; These studies include a daily gavage exposure of 14 mg/kg/day for 6 weeks in rats (Hopf et al., 1990 cited in ATSDR 1999), a 3-month exposure to cadmium in food at 3 mg/kg/day in rats (Loeser and Lorke, 1977), a 24-week exposure to cadmium in water at 8 mg/kg/day in rats (Kotsonis and Klaassen, 1978) and a 3-month exposure in food at 0.75 mg/kg/day in dogs (Loeser and Lorke, 1977b) (ATSDR, 1999).

Inhalation route

Liver effects have occasionally been found in studies in animals. When reported, signs of liver damage are mainly an increase in serum enzymatic activities or an increased liver relative weight (Kutzman et al., 1986, 1.06 mg $CdCl_2$ 6 hours a day, days a week for 62 days).

No increased liver weight was observed from a continuous exposure at 90 µg Cd/m³as CdO for 218 days (Oldiges and Glaser, 1986) nor from a 63-day exposure to 0.105 mg/m³, a dose that was toxic for the lungs (Prigge et al., 1978) (ATSDR, 1999).

Conclusions: Studies in animals

No data were located about the liver effects of cadmium oxide/metal, administered orally. Experimental studies using cadmium soluble compounds reported some morphologic and metabolic changes but this was not observed in other studies.

Inhalation studies reported conflicting results for cadmium oxide and compounds but even when signs of cadmium adverse effects occurred, they were usually mild.

No data were located on liver toxicity of cadmium metal.

Studies in humans

Oral route

Reports on the effect of cadmium on the human liver function are rare.

From Japan, slight signs of liver involvement (plasmatic enzymes) have been reported as occurring in Itai-Itai patients as well in persons under observation for suspected Itai-Itai disease (CRC, 1986). This was not confirmed by Kasuya (1996, cited by Ikeda et al., 1997) who stated in his review of Itai-Itai disease cases that the liver function remained essentially undisturbed among the Itai-Itai patients, even in the severest cases.

Nishino et al. (1988) reported increased serum concentrations of the urea-cycle amino-acids among individuals exposed to cadmium in the diet and that theses levels were reflecting liver as well as kidney damage (Nishino et al., 1988 cited in ATSDR, 1999).

Environmental exposure to cadmium (dietary exposure of up 79 µg/day) had not affected the integrity of the liver among a group of 371 non-smoking and non-habitually drinking Japanese women studied by Ikeda et al. (1997).

Inhalation route

Non-specific signs of liver disease (e.g. increased serum gamma-globulin) were found in an early study of cadmium-exposed workers (Friberg, 1950) but liver effects were rarely observed in subsequent studies involving exposed humans (ATSDR, 1999).

Onodera et al. (1996) found liver dysfunction (sub clinical elevation in ALT, and to a lesser extent in AST and γ-GTP) among 162 male workers exposed to cadmium in a battery plant (compound involved no more detailed). Exposure was reported to be below the occupational limit of 0.05 mg/m³ but some renal markers levels were considerably elevated, what might suggest that the exposure was higher than reported (Onodera et al., 1996 cited by Ikeda et al., 1997).

Conclusions: Studies in humans

No major effects of environmental cadmium on the liver function have been reported.

Liver effects have occasionally been associated with cadmium occupational exposure. In most of the occupational studies, liver function has not been extensively studied but it appears from all the collected data that compared to the sometimes-pronounced changes in renal function, major changes in liver function were seldom found in cadmium-exposed workers.

Conclusions: Liver

Exposure to cadmium compounds can cause liver damage in animals but generally only after high levels of exposure. There is little evidence for liver damage in humans exposed to cadmium.

4.1.2.7.6 Haematological effects

<u>Anaemia</u>

<u>Studies in animals</u>

Oral route

No experiments using cadmium oxide or cadmium metal were located.

In monkeys maintained on 4 mg/kg/day cadmium (as $CdCl_2$) in food, pale faeces and clinical signs of anaemia occurred after 90 weeks, but the anaemia was associated with a decreased food intake rather than an increase in reticulocytes (Masaoka et al., 1994). Anaemia was not present in rats exposed via drinking water for 12 months to the relatively low dose of 0.79 Cd mg/kg/day (as $CdCl_2$, Decker et al., 1958). The number of erythroid progenitor cells in bone marrow was decreased in mice exposed to 57 mg/kg/day of cadmium in drinking water for 12 months (Hays and Margaretten, 1985), but was increased in rats exposed to 12 mg/kg/day of cadmium (as in drinking water for up to 100 days (Sakata et al., 1988). The question remains open whether factors in addition to reduced gastro-intestinal absorption of iron such as direct cytotoxicity to marrow or inhibition of heme synthesis may contribute to anaemia (ATSDR, 1999).

Data have suggested that cadmium may cause anaemia by disturbing the renal erythropoietin production. There appears to be a correspondence between the target cells of cadmium and the erythropoietin (EPO)-producing cells in the kidneys. Horiguchi et al. (1994) reported that a close relationship was observed between the decrease in the haemoglobin level and the progression of renal dysfunction in Itai-Itai patients. Moreover, low serum erythropoietin levels were detected in spite of the severe anaemia. The hypothesis that the hypoproduction of erythropoietin contributes to anaemia in chronic cadmium intoxication was further explored in an experimental study conducted by Horiguchi et al. (1996):

Cadmium chloride (2.0 mg/kg bw) was administered in Wistar rats, subcutaneously, once a week, for 6 or 9 months. Control rats were injected with saline. Heart, spleen, liver, kidneys and bone marrow were taken for biochemical and pathological examination. Analysis of the EPO mRNA inducibility in kidney, in order to examine the EPO production capacity, was performed by the Northern blotting technique.

Haemoglobin, hematocrit and plasmatic iron levels were significantly decreased in the Cd-exposed rats. Plasma erythropoietin levels remained as low as those of the control rats despite obvious anaemia. At 6 months, EPO mRNA was expressed to the same or a slightly lesser extent compared with the control rats, and the expression was further decreased at 9 months. At 6 months, the EPO-producing cells were still viable according to the pathological and Northern blotting data, but the cells could not respond adequately to the haemoglobin decrease, implicating a functional inhibition of EPO induction by cadmium. At 9 months, not only the EPO mRNA expression was depressed but also numerous necrotic or fibrotic areas were observed in the interstitial tissues, indicative of the death of the cells. Postulated mechanism for the hypoinduction of EPO in the kidneys induced by long-term exposure to cadmium appears to include 2 stages: a functional inhibition of EPO-induction in the early stage followed by necrotic injury of the renal EPO-producing cells in the later stage (Horiguchi et al., 1996).

Inhalation route

Conflicting results on the haematological effect of cadmium after inhalation exposure have been obtained with studies in animals. Rabbits exposed to cadmium oxide dust at 4 mg/m^3 for 3 hours a day, 21 days a month for 9 months developed eosinophilia and a slightly lower haemoglobin in the experiment of Friberg (1950). In contrast, rats exposed to CdO dust at 0.052 mg/m^3 for 24 hours a day for 90 days had increased haemoglobin and hematocrit that were attributed to decreased lung function (Prigge, 1978). Other studies report no Cd-related haematological effects. A nearly continuous 218-day exposure in rats to CdO dust or fumes at 0.09 mg/m^3 had no effect on a routine haematological evaluation (Oldiges and Glaser, 1986). A partial explanation for these conflicting results may be that Cd-induced anaemia primarily results from impaired absorption of iron from the diet following gastro-intestinal exposure to cadmium and the amount of gastro-intestinal exposure following cadmium inhalation is variable depending upon the form and dose (ATSDR, 1999).

Conclusion: studies in animals

Conflicting results have been reported about the haematological effects of cadmium after long-term exposure. In the studies where haematological alterations (e.g. anaemia etc.) were observed, several mechanisms have been postulated: impaired absorption of iron, direct cytotoxicity to bone marrow, inhibition of the heme synthesis, hypoproduction of erythropoietin, etc.

Studies in humans

Oral route

Anaemia has been found in some instances among humans with chronic dietary exposure to cadmium (Kagamimori et al., 1986) but this has not been demonstrated in other studies.

In some patients with Itai-Itai disease, anaemia has been demonstrated beneath the signs of renal dysfunction and osteomalacia. The cause of this anaemia has not yet been completely clarified, although several mechanisms have been proposed.

Itai-Itai patients (from the Toyama prefecture) were investigated in regard to their renal and haematological function by Horiguchi et al. (1994). Clinical data used were the latest data obtained (1990) from ten women with Itai-Itai disease. Nine of these patients had anaemia of varying degrees and four had occasionally required blood transfusion. Red blood cell count (RBC), haemoglobin concentration (Hb), hematocrit (Ht), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), white blood cell count (WBC), platelet count, reticulocyte count, serum iron level, total iron-binding capacity (TIBC), serum ferritin level, blood urea nitrogen and serum creatinine level were reported. Serum erythropoietine level was also measured in order to clarify whether a renal mechanism was involved in producing the observed anaemia. Bone marrow aspiration was performed in some patients to evaluate hematopoiesis.

Findings suggested that the main cause of anaemia was a hypoproduction of erythropoietin rather than iron deficiency or bone marrow dysfunction: serum EPO levels remained low in the patients with Itai-Itai disease despite their severe anaemia. Serum iron and ferritin levels were not significantly altered and TIBC was low. Bone marrow aspiration examination in four of the patients revealed a slight hypocellularity but this was not thought to be specific to the anaemia of Itai-Itai disease since one of the patients had a haemoglobin concentration at 13.6 g/dl but showed the same findings. Authors suggested that the hypoproduction of EPO is a consequence of the damage caused to the renal tubular cells (EPO-producing) by the accumulated cadmium in these patients.

The relationship between the severity of the anaemia and the renal function (urinary creatinine β2M levels on 24-hour urine collection) was subsequently examined. A low creatinine clearance and a high fractional excretion of beta2-microglobulin level (Fractional Excretion β2M= (β2M-U · urinary volume per minute)/ (β2M-B · creatinine clearance) · 100%)) were observed, indicating that both renal glomerular and tubular function were altered. There was a positive correlation -with borderline statistical significance- between the level of haemoglobin and the fractional excretion β2M level. Anaemia was not associated with creatinine clearance. According to the authors, these results support the hypothesis that cadmium may damage the

EPO-producing cells of the kidney rather than the glomerular cells and that renal damage plays an important role in the anaemia developed in Itai-Itai disease (Horiguchi et al., 1994).

Inhalation route

Lowered haemoglobin concentrations and decreased packed cell volumes have been observed in some studies of workers occupationally exposed to cadmium (Bernard et al., 1979; Friberg et al., 1950) but changes were often not statistically significant.

Conclusion: anaemia

In accordance with ATSDR (1999), it can be concluded that cadmium-induced anemia is unlikely to be of concern for occupational or general population exposure.

Immunological effects

In 1992, a review published by IARC (Descotes 1992) concluded that “A number of investigations have suggested that cadmium may exert immunosuppressive effects in animals even though conflicting findings, due mainly to varying conditions of exposure, have been reported. Overall, cadmium has been shown to enhance humoral immune responses at low levels of exposure, whereas higher ones may result in either no effect or decreased antibody production. By contrast, cell-mediated immunity was more consistently shown to be depressed. Similarly, phagocytosis, natural killer cell activity and host resistance toward experimental infections were markedly impaired in most instances. Very few data are available regarding cadmium immunotoxicity in humans. Hypersensitivity reactions have so far not been described. No immune alterations were found to be associated with “chronic cadmium disease”, whereas a depressed phagocytosis, the clinical relevance of which remains to be established, was recently documented in cadmium-exposed workers. Further investigations are therefore needed to determine how immunotoxic cadmium actually is and what health consequences are to be expected in occupationally or environmentally exposed humans”. Since then, a number of additional data have been published.

Studies in animals

Oral route

Cd has been shown to act on the immune system of experimental animals and on biological mechanisms involved in local inflammatory reactions. Following exposure of mice to $CdCl_2$ (30, 100, 300 ppm in drinking water for 35 days), significant suppression of humoral and cell mediated immune response was noted which could be due to the cytotoxic action of the element on liver, kidney and immune cells (Dan et al., 2000), Chronic injections of $CdCl_2$ in micealso produced dose- and time-dependent splenomegaly (5x), with loss of lymphoid structure, inflammation, hyperplasia, appearance of giant cells, and fibrosis. Thymus weights were decreased by Cd in a dose-dependent manner (60%). Mice genetically deficient in metallothionein were approximately 10 times more susceptible than wild-type to these lesions (Liu et al., 1999). Apoptosis of B cells (involving the MAP kinase pathway),'and T cell reactivity to metallothionein and heat shock proteins induced by Cd exposure, are among the suspected mechanisms of action exposed to cadmium via drinking water.

Exposure of NZBW mice (strain susceptible to auto-immune diseases) to 0, 3, 30, 3,000 or 10,000 parts per billion (ppb) of cadmium in tap water for 2, 4, 28, or 31 weeks stimulated the production of immune complexes and induced the development of auto-immune glomerulonephritis (Leffel et al., 2003). Immunosuppression is supposed to be the cause of the increased susceptibility to virus infection observed in mice pre-treated with Cd (Seth et al., 2003). A reduction of the maturation and mobilisation of T and B lymphocytes, but increased humoral response, has been reported in Balb/c mice infected with coxsakie viruses given Cd (2 mM) in their drinking water during 10 weeks (Illback et al., 1994).

Studies in humans

In humans, few studies examined the possible impact of Cd exposure on the immune system.

Oral route

The effects of cadmium on measures of immune-system function were determined from a health survey of school children in heavily polluted regions of eastern Germany (Ritz et al., 1998). A representative sample of 842 students, aged 5-14 years, was included in logistic regression analyses in which the relationship between Cd-U and blood immunoglobulin levels was examined. Investigators further evaluated a subsample of 807 students to determine the effect of Cd on the immediate hypersensitivity reaction elicited by skin-prick challenges with 12 common aeroallergens. Several potentially confounding factors were controlled for, after which investigators found that increasing body burdens of cadmium were associated consistently with dose-dependent suppression of immediate hypersensitivity and of immunoglobin G, but not immunoglobulins M, A, or E levels. The immunoglobulin pattern observed in exposed children led investigators to suggest that secondary humoral responses were impaired by Cd.

In a population of adults living in communities with possible pollution by Cd but also Pb, urine cadmium levels over 1.5 microg/g were associated with higher levels of IgA and circulating B lymphocytes. No evidence of immunosuppression was noted. Similar changes were not observed in the juvenile population examined concurrently (Sarasua et al., 2000).

Inhalation route

Serum immunoglobulin (IGG, IgM and IgA) levels were not significantly affected in a group of 37 male workers from a zinc smelter and a small Cd plating factory (mean Cd-U 5.5 µg/g creat, 1.59-17.90, Cd-B 2.36 µg/dl, 0.37-6.52) compared to 30 unexposed controls (Cd-U 2.01, 0.57-4.00; Cd-B 0.69, 0.03-1.77) (Karakaya et al., 1994).

In vitro data

In vitro, Cd (0.1-10 µM) has been shown to inhibit the production of IgE by human B-lymphocytes (Jelovcan et al., 2003).

Cadmium sulfate (0.01-10 µM) did not affect the NK activity of human lymphocytes (Yucesoy et al., 1999).

Conclusions: immunological effects

Overall, there is little consistency in experimental data and, so far, the relevance of these observations for humans remains uncertain.

Human studies are limited in number and seem to indicate a potential immunotoxic effect of Cd exposure (not specifically Cd metal or CdO). These studies require, however, confirmation before they can be considered as robust epidemiological observations.

4.1.2.7.7 Neurological disorders

Studies in animals

There is some experimental indication that cadmium (not specifically CdO/Cd metal) has neurotoxic properties, especially on the immature brain (see Section 4.1.2.10.3).

In adult animals, neurological effects have been noted after exposure to very high levels of cadmium compounds; ATSDR (1993) reports that these effects occurred at doses ranging from 5 to 40 mg Cd/kg/day.

Table 4.146 Neurological symptoms in rats after exposure to cadmium compounds

Species	Manifestation	Route	Reference
Rats	peripheral neuropathy	Po	Sato (1978)
Rats	aggressive behaviour (muricidal)	Repeated sc	Arito et al. (1981)
Rats	increased self-administration of ethanol	Repeated po	Nation (1990)
Rats	alteration of odor-mediated performances	Po	Davis et al. (1995)

There are also some recent studies in rats suggesting that dietary cadmium (100 ppm) might influence the pharmacological response to drugs of abuse (e.g. Nation et al., 2000).

Early experimental work has shown that after cadmium chloride (0.5 mg Cd/kg, s.c.) was given to rats 6 days a week for 25 weeks, there was no difference from controls in wet weight of the olfactory bulb or the remaining brain. The Cd concentration in the olfactory bulb and the remaining brain was 770 and 90 times, respectively, that of the control rats (Suzuki and Arito, 1975).The distribution of cadmium within the brain and neighbouring nervous structures has been further examined by autoradiography following were intravenous injection of $^{109}CdCl_2$ in adult rats (Arvidson 1986). Cadmium accumulated in regions outside the blood-brain barrier such as the choroid plexus, pineal gland and area postrema, but did not appear in the brain parenchyma. Uptake of cadmium was observed in the trigeminal ganglia close to the nerve cells and in the olfactory bulbs. In addition, cadmium accumulated in the iris, ciliary body and choroid of the eye, but not in the optic nerves. In rats treated with 20 or 100 ppm Cd in their diet during more than 2 months, a selective accumulation of the metal was also observed in the olfactory bulbs (Clark et al., 1985). Other experimental results comparing different routes of administration indicate that for airborne Cd, although excluded from the CNS by the blood-brain barrier, the olfactory system may provide a direct route of entry into the CNS (Gottofrey and Tjälve 1991; Hastings and Evans 1991; Evans and Hastings 1992).

Recently, Sun et al. (1996) found, however, no significant functional olfactory change in rats exposed via inhalation up to 660 µg/m^3, 5 hours per day, and 5 days a week during 20 weeks. Although olfaction was not impaired, cadmium levels in the olfactory bulbs of exposed rats were significantly elevated compared to controls. Cardiac and respiratory histopathologies were observed at all exposure levels, but there was no evidence of nasal pathology related to exposure to cadmium. Failure of cadmium to produce olfactory dysfunction was interpreted by these authors as the protective effects of metallothionein and/or to the highly resilient nature of the rodent olfactory system.

Studies in humans

The evidence for neurotoxicity of chronic cadmium exposure in humans (not specifically CdO/Cd metal) is rather limited but it should be recognised that there is a paucity of robust data.

Oral route: general population

Important changes in organ development and function occur during the neonatal period; in particular, the central nervous system is in a rapid growth rate and highly vulnerable to toxic effects of metals such as lead or methylmercury. Furthermore, the kinetics of many metals, including Cd, is age-specific, with a higher gastrointestinal absorption as well as a less effective blood-brain barrier in newborns compared to adults. For these reasons, it seems plausible that, in very young children, the developing brain might represent a sensitive organ upon Cd exposure. Solid epidemiological data are, however, lacking to document this possibility.

According to ATSDR (1999), there exist a few studies reporting an association between environmental cadmium exposure and neuropsychological dysfunctioning, especially in children (Thatcher et al., 1982; Struempler et al., 1985 cited in ATSDR 1999). The relevance of these studies for assessing the neurotoxic potential of cadmium is however limited because of the influence of confounding parameters (e.g. lead), inadequate quantification of Cd exposure (hair measurements), and lack of control for sociogenic confounders (e.g. parental IQ, home environment, care giving etc.).

Marlowe et al. (1983) conducted a case-control study to assess the possible relationship between heavy metals and mental retardation/ impaired intelligence. They measured 5 metallic elements (Pb, Cd, As, Hg and Al) in the hair of 64 children with mild retardation or borderline intelligence with no evident etiology (IQ 55-84, 4-16 years) from 5 economically depressed counties in Tennessee and 71 controls drawn from the same schools (IQ not measured, 4-15 years). Significant differences were found for Pb and Cd hair content: 14.10 ± 7.60 versus 7.09 ± 5.22 and 0.62 ± 0.58 versus 0.37 ± 0.42 ppm, for cases versus controls, respectively. Although suggestive of a possible effect of metal exposure in these mentally retarded children, the evidence for an involvement of Cd is very weak because of the major contribution of lead, and in view of the limitations of metallic hair content measurements, especially for Cd.

The report of Bonithon-Kopp et al. (1986) who examined the relationship between psychometric tests of 26 children aged 6 years and Pb and Cd hair content measured at birth is discussed more extensively under "Toxicity for reproduction" (see Section 4.1.2.10.3). Briefly, scores of psychometric tests administered to children at 6 years of age were negatively correlated with their Cd-levels in hair estimated at birth. However, these parameters were also linked to the Pb hair content and significant correlations were observed with the quantitative scores. The specific contribution of Cd exposure is difficult to assess.

Inhalation route: occupational exposure

Olfactory dysfunction has been reported in workers formerly exposed to extremely high levels of cadmium. Friberg (1950) reported that 37% of 43 cadmium-exposed workers studied had olfactory impairment; but these workers were also exposed to nickel dust. Workers from an alkaline battery factory exposed to CdO and nickel also suffered from hyposmia and anosmia (Adams and Crabtree, 1961). Significantly more battery workers reported themselves to be anosmic than controls (15 versus 0%, respectively), and they performed less well than controls in a smelling test. Anosmia correlated well with proteinuria in these workers. Signs of local nasal irritation, ulceration, and dry crusting suggested likely direct damage to the olfactory mucosae.

Olfactory impairment was also found by Potts (1965) in battery factory workers exposed to CdO dust and nickel. Tsuji et al. (1972), on the other hand, reported impaired olfaction in workers exposed to cadmium in the absence of nickel in a zinc refinery. Cases of anosmia have also been mentioned among Chinese cadmium smelters (Liu et al., 1985). Rose et al. (1992) reported olfactory impairment (butanol detection threshold and odour identification) in 55 workers chronically exposed to Cd fumes during brazing operations (0.3 mg/m³ in 1980). The olfactory performances were particularly impaired in workers with high Cd-U (> 10 µg/g creat) and LMW proteinuria (ß2M > 370 µg/L). The authors of the study concluded that chronic occupational exposure to Cd sufficient to cause renal damage is also associated with impairment in olfactory function. This conclusion might, however, be questioned because it compares what is most conceivably a local irritative effect with systemic manifestations of chronic Cd poisoning which might be completely independent. Moreover, the contribution of other irritants such as fluoride used in brazing needs also to be taken into account to interpret the olfactory effects.

The effects of occupational exposure to cadmium (not further detailed) on the olfactory function has also been assessed in a group of 73 workers heavily exposed probably to CdO in a Polish plant producing nickel-cadmium batteries (Rydzewski et al., 1998). The mean ± SD age of the workers was 42 ± 18 years and they were employed for 12. ± 8.5. Mean Cd-B and Cd-U reflected high exposure levels (Cd-B, 34.84±22.47 µg/l and Cd-U, 86.15±78.24 µg/g creat). Olfactory function was evaluated qualitatively and quantitatively on the basis of the established odour detection and identification thresholds. 26% of the workers were diagnosed as suffering from hyposmia, 17.8% from paraosmia and 1.4% from anosmia. Olfactory disorders were generally associated with hypertrophic changes of the nasal mucosa. A significant association was found between olfactory impairment and higher Cd-B, Cd-U values, but not with duration of employment.

A recent clinical survey conducted among 13 retired long-term Cd-exposed workers (average 66.5 years old, Cd-U mean ± SD, 8.78 ± 3.80 µg/g creat) and 19 age-matched controls suggested on the basis of a battery of tests (neurological examination, nerve conduction studies, needle EMG and standardised questionnaire) that an increased Cd body burden may promote the development of a polyneuropathy in older subjects. Seven exposed workers (54%) versus 2 controls (11%) met the criteria for polyneuropathy (Viaene et al., 1999).

An epidemiological survey was carried out by the same authors among a group of 89 individuals (42 Cd-exposed (Cd-U 0.1-16.6 µg/g creat) and 47 controls (Cd-U 0.1-2.0 µg/g creat)) in order to examine the impact of Cd exposure on neurobehavioral performances. Each subject was submitted to a standardised battery of neurobehavioral tests (NES), a validated questionnaire to assess neurotoxic complaints (NSC-60), and a standardised self-administered questionnaire to detect signs of peripheral neuropathy and/or autonomous nervous system dysfunction. Slowing of psychomotor function and increase in complaints of polyneuropathy, equilibrium, concentration ability were dose-dependently associated with Cd-U in the absence of renal effects (Viaene et al., 2000).

Conclusion neurotoxicity

Evidence from experimental systems indicate a potential neurotoxic hazard for cadmium (not CdO/Cd metal specifically) in adult rats. In humans, heavy occupational exposure to cadmium dust has been associated with olfactory impairments and studies performed on a limited number of occupationally-exposed subjects are suggestive of an effect of Cd on the peripheral and central nervous system but these findings should be confirmed by independent investigators before firm conclusions can be reached.

In the young age, there is some experimental indication that Cd exposure (not specifically Cd metal or CdO) can affect the developing brain (see Section 4.1.2.10.3). This aspect has not received sufficient attention in humans and, in view of (1) the very well-characterised neurotoxic potential of other heavy metals (e.g. lead), and (2) the increased gastro-intestinal absorption of Cd in the very young age (see Section 4.1.2.2), it would be prudent to recommend a thorough investigation of this potential effect in well designed epidemiological studies.

4.1.2.7.8 Others

Other systemic effects have been occasionally reported, associated with long-term ingestion or/and inhalation of cadmium and are cited here without further comments: asthenia, yellow teeth etc., but these studies in humans are subject to a number of uncertainties, including the measurements of cadmium exposure, the magnitude of confounding by other toxicants and the evaluation of the effect.

Summary information related to the classification[32] as well as the judgement on the fulfilment of the base-set requirements

In summary, the weight of evidence of cadmium compounds adverse effects on multiple organ sites supports the classification as T; R 48/23/25 (= the presently applicable classification for cadmium oxide in conformity with Dir. 67/548/EC).

4.1.2.8 Genotoxicity

4.1.2.8.1 Introduction

The Technical Guidance Document (1996) refers to two terms in this section and proposes the following definitions:

Mutagenicity refers to the induction of permanent transmissible changes in the amount or structure of the genetic material of cells or organisms. These changes may involve a gene, a gene segment, a block of genes or a whole chromosome. Genotoxicity is a broader term and refers to potentially harmful effects on genetic material, which may be mediated directly or indirectly, and which are not necessarily associated with mutagenicity.

The aims of testing for genotoxicity are to assess the potential of chemical substances to be genetic carcinogens or to cause heritable damage in humans.

As specified in Annex VII A to Directive 67/548/EEC, the minimum data requirements for the effect assessment are that genotoxicity data should be available from at least two tests: a bacterial gene mutation test and a chromosomal aberration test which in the absence of contra-indications should be conducted *in vitro*. Additional data may be available from a number of

[32] The **classification was done for cadmium oxide** and based on specific substance data, if available, and/or data from other cadmium compounds (more soluble forms).

For metallic cadmium the same classification is extrapolated on the basis of the so-called 'ion theory' and as a 'worst case' approach related to the bio-availability of the metal.

different types of *in vitro* studies and studies in animals (bone marrow micronucleus, SCE tests, dominant lethal tests), and human studies (TGD, 1996).

The genotoxic potential of cadmium compounds (as a whole) has been reviewed in 1987 by Kazantzis who concluded that, in bacterial systems, cadmium compounds generally fail to induce point mutations. In mammalian systems, while toxic concentrations of cadmium compounds (not specifically CdO or Cd metal) have been shown to cause chromosome damage *in vitro*, exposure of rodents to such compounds failed to induce either chromosomal aberrations or micronuclei in bone marrow cells. Cytogenetic studies on workers exposed to cadmium gave conflicting results and were often confounded by exposure to other metals (Kazantzis, cited in IARC 1992).

Information on a possible genotoxic effect of cadmium are provided by *in vitro, in vivo* and human studies and will be reviewed in sections 4.1.2.8.2, 4.1.2.8.3, and 4.1.2.8.4, respectively.

Because it can be assumed that cadmium metal and/or cadmium oxide will to some extent be solubilised *in vivo*, especially in the lung, data obtained with soluble Cd compounds (Cd ions) may also be considered relevant to assess the possible genotoxic potential (hazard) of both Cd/CdO. The terms "cadmium compounds" used here below refer to other compounds of cadmium than the oxide and the elemental forms. Data relating to these compounds is given hereafter with another letter size and type.

4.1.2.8.2 *In vitro* studies

Several *in vitro* systems have been used to study the genotoxic effects of cadmium compounds:

No *in vitro* study specifically using cadmium metal was located.

Only two studies investigated the genotoxic effects of cadmium oxide: both used the Salmonella Typhimurium test system (Mortelmans, 1986; NTP report 1995) with similar protocols. Cadmium oxide (particle size not given) at doses of 1,466 µg/ml or 147 µg/ml did not induce reverse mutations (Mortelmans, 1986 cited in IARC 1993). No genotoxic effects were noted when CdO was tested at doses of 3.3 to 3,333 µg CdO/plate in four strains of Salmonella, using a preincubation protocol with and without liver S9 metabolic activation enzymes (from Aroclor-induced male SD rats and Syrian hamsters) (Zeiger et al., 1992 cited in NTP Technical Report, 1995).

Most experiments used water-soluble cadmium compounds and evaluations by several organisations are mainly based on findings with these compounds. According to the available reviews (IARC 1992, 1993; ATSDR 1993, 1999; WHO 1992), the results of genotoxic tests in cells treated *in vitro* with cadmium compounds remain conflicting, possibly because of differences between treatments, as well as between cells used. IARC (1993) listed all experiments conducted with cadmium compounds.

Cadmium ions accumulated in the cells may cause genetic damage by the following mechanisms: 1) direct damage by interacting with the chromatin to generate strand breaks, cross-links or structural alterations in DNA, 2) indirectly, by depleting antioxidant levels and thereby increasing intracellular hydrogen peroxide and other oxidants, 3) by interacting at metal-binding sites of proteins involved in transcription, DNA replication or DNA repair (Misra et al., 1998). There exists, however, no consensus on a single mechanism of action, and these mechanisms are not mutually exclusive. Each hypothesis is briefly discussed below.

Direct damage

There is some evidence that treatment of bacteria with Cd ions results in strand breaks (or at least DNA of smaller weight). This was first seen in E.Coli by Mitra et al. (1975). Authors reported moreover a cadmium tolerance mechanism in this strain: growing E.Coli in 3 µM Cd2+ led to an initial decrease in colony-forming ability followed by a gradual accommodation of the cells. During the initial phase, cellular DNA was found to contain single strand breaks which were later repaired (Mitra et al., 1975 cited in IARC 1992).

Ochi et al. (1983) demonstrated that cadmium could induce DNA damage in eukaryotic cells. Treatment of cultured Chinese hamster V79 cells with 2-5 10^{-5}M $CdCl_2$ for 2 hours resulted in repairable DNA-single strand scissions and possibly DNA-protein cross-links, detected by the alkaline elution technique combined with proteinase K digestion. One year later, the same group of authors reported that 2-hour treatment with the concentrations able to induce strand breaks also induced chromosomal aberrations (mainly chromatid gaps and breaks) with a dose-dependency, indicating, according to the authors, a good correlation between DNA lesions and the genetic effect of the metal ion. In contrast, only a slight increase in incidence of chromosomal aberrations was observed after continuous treatment (24 hours) with 5 µM, may be due cell cycle arrest (Ochi et al., 1984). Rossman (cited in IARC, 1993) suggested that the different results between such short- (2 hours) and long-term studies (24 hours) might be explained by the differences in treatment duration: a long-term exposure to a lower concentration may induce the synthesis of proteins which protect the cells from the genotoxic effects of Cd ions.

DNA strand breaks in mammalian cells were also reported by e.g. Robison et al. (1982, cited in IARC 1993) at concentrations of 10-100 µM for 3 hours on Chinese hamster ovary cells and by Coogan et al. (1992) on rat TRL 1,215 liver cells (1 hour, 500 µM).

In human cells, DNA strand breaks were reported by e.g. Zasukhina and Sinelschikova (1976) on human lymphocytes, Hamilton-Koch et al. (1986) on HSBP fibroblasts (IARC, 1993). Cadmium chloride was also shown to induce DNA strand breaks in human diploid fibroblasts as measured by two independent assays by Snyder (1988). DNA strand breaks were repaired within 2-4 hours after removal of the metal ion what could indicate that the damage was probably non-specific. Moreover, strand breaks occurred only at doses that reduced cloning efficiency by greater than 50% (Snyder, 1988).

Finally, four different rodent cell lines (Chinese hamster ovary cells, rat myoblast L6 cells, rat Clone 9 liver cells, and rat TRL1215 liver cells) were exposed to 0, 1, 5, 10, 50, or 100 µM $CdCl_2$ by Misra et al. (1998) and monitored for evidence of direct DNA damage. Two different assays were used to measure strand breaks and DNA-protein cross-links. Although variability in sensitivity to DNA damage was evident between the different cell lines, in all of the cell lines tested, increases in DNA damage were observed only at cadmium doses that completely arrested cell growth (50-100 µM). Authors concluded that direct modification of DNA was probably not the basis for Cd ion genotoxicity (Misra et al., 1998).

Oxidative damage

There is some evidence that the genotoxic effects of Cd ions may be mediated by oxidative damage to DNA. Various scavengers of active oxygen species were assayed for their abilities to block chromosome aberrations induced by cadmium chloride. Marked reductions in the induction of strand breakage were observed when $CdCl_2$ was administered under anaerobic conditions or when superoxide dismutase was added to the culture medium (Ochi et al., 1983).The incidence of chromosomal aberrations was dramatically reduced in V79 cells that received catalase, D-mannitol (a scavenger of hydroxyl radicals), or butylated hydroxytoluene (a diffusible radical scavenger) prior to 20 µM $CdCl_2$ treatment (Ochi and Ohsawa, 1985 cited in Misra et al., 1998). Similar results were obtained by Snyder (1988), when fibroblasts were treated simultaneously by the metal and mannitol, potassium iodide or catalase. These results support the theory that cadmium acts by stimulating the production of hydrogen peroxide which in turns forms highly reactive hydroxyl radicals in the presence of intracellular iron or copper (Misra et al., 1998, IARC 1992, IARC 1993).

Cadmium chloride treatment also reduced the cellular glutathione level (Ochi et al., 1987 cited in IARC 1992). In the absence of the protection afforded by glutathione, antioxidants such as vitamins A, C and E, and antioxidant enzymes, one might indeed expect increased DNA damage by endogenous oxygen free radicals as well as lipid peroxidation, whose products can also cause DNA damage and mutations (IARC, 1992). Two observations illustrate this assumption: a) doses of > 20 µM $CdCl_2$ that decreased the levels of cellular antioxidants (Ochi et al., 1987) were shown to induce lipid peroxidation by Stacey et al. (1980) and b) vitamin C (6 µg/l) added to a culture of mouse spleen cells treated with 20 µg/ml $CdCl_2$ was shown to significantly reduce the frequency of chromosomal aberrations induced by cadmium chloride (Fahmy and Aly, 2000).

Inhibition of DNA repair

Another line of evidence suggests the enhancement of genotoxicity of other DNA damaging agents by Cd ions, possibly by interfering with DNA repair processes involved in the removal of DNA damage induced by alkylating agents or UVC irradiation (Hartwig, 1994*)*. These effects are summarised in **Table 4.147**.

Table 4.147 Modulation of genotoxicity and interaction with DNA repair by Cd2+ (Hartwig, 1994)

Cd^{2+} in combination with	Cell line	Dose (µM)	Effect	Reference
Bacterial tests systems:				
Methylnitrosourea (MNU)	*E. Coli*	10-500	Enhanced mutation frequency	Takahashi et al. (19880
N-methyl-N'-nitro-N-nitroguanidine (MNNG)	*S. typhymurium*	250-500	Enhanced mutation frequency	Mandel and Ryser (1984)
Methyl methanesulfonate (MMS)	*E. Coli*	250-500	Enhanced mutation frequency	Takahashi et al. (1991)
Mammalian cells:				
UV light*	V79	0.5-2	Enhanced mutation frequency	Hartwig and Beyersmann (1989)
	Human fibroblasts	5	Reduction of colony forming ability	Nocentini (1987)
	Human fibroblasts	4	Inhibition of unscheduled DNA synthesis	Nocentini (1987)
	Human fibroblasts	4	Accumulation of DNA strand breaks during repair	Nocentini (1987)
	HeLa	5	Inhibition of thymine-thymine dimmer removal	Snyder et al. (1989)
Benzo(a)pyrene	SHE	1.9	Enhancement of morphological transformations	Rivedal and Sanner (1987)

* Repair of UVC-induced damage and its inhibition have been measured in three ways: (1) direct analyses of removal of pyrimidine dimers from DNA; (2) unscheduled DNA synthesis, reflection of repair replication; and (3) accumulation of DNA strand breaks resulting from the incision step(s) of removal (reflecting a failure of repair replication or ligation).

In E. Coli, the comutagenic effect of Cd ions and MNU was attributed to the inactivation of the O^6-methylguanine-DNA methyl transferase (Hartwig, 1994).

The accumulation of DNA strand breaks after UV irradiation obtained from alkaline elution in human fibroblasts suggests an inhibition of the polymerisation or ligation step in excision repair. This could be due to enzyme inactivation or changes in DNA structures, preventing repair enzymes from binding (Hartwig, 1994). An inhibition of DNA polymerase β (a polymerase involved in DNA replication) at low concentrations of cadmium has been observed (Popenoe and Schmaeler, 1979).

Hartwig (1994) suggested also that besides a direct interaction with repair enzymes, cadmium ions might also interfere with calcium-regulated processes involved in the DNA replication and repair. However, these mechanisms remain to be elucidated. It has also been recently reported that non-cytotoxic concentrations of cadmium ions ((5-40 µM), by substituting for zinc in the cysteinyl cluster of the p53 protein, induces conformational modifications and impairs the function of p53, which may contribute to affect DNA repair capacity (Meplan et al., 1999).

Several researchers have also reported that cadmium ions affect the spindle apparatus (Kogan et al., 1978; Ramel and Magnusson, 1979). Spindle disturbances and aneuploidy were observed in human lymphocyte cultures treated with 6µg/ml $CdCl_2$. However, correspondence between the spindle effects (assessed by % of c-mitoses) and genomic effects (aneuploid, polyploid cells) appeared limited: it seemed that a slight disturbance of the spindle movement without functional inactivation is induced by the $CdCl_2$ treatment, which may be the secondary effect of a mechanism of aneuploidy production other than mitotic arrest (Sbrana et al., 1993).

Several authors analysed the frequency of sister-chromatid exchanges after treatment of cultured cells with cadmium compounds. Results of Saplakoglu and Iscan (1998) demonstrated that the genotoxicity of $CdCl_2$ in human lymphocytes may depend on the cell cycle status. A highly statistically significant increase was observed in the SCE frequency with increasing cadmium chloride 0.1-100 µM) when cadmium was administered during the early S phase (24 hours after culture initiation). The increase in SCE frequency was higher when cultures were terminated at 54 hours, compared to termination at 72 hours. These results correlated well with the results of Han et al. (1992) who demonstrated an SCE-inducing effect in human lymphocytes with cadmium concentrations between 5 and 50 µM for the last 48 hours. Saplakoglu and Iscan (1998) suggested that this dependence on the stage cell cycle might be one of the reasons of contradictory findings in the literature.

Misra et al. (1998) concluded their paper by the following speculation: low doses of cadmium might be genotoxic by compromising the cell's ability to accurately replicate DNA and/or cope with DNA damage. At high doses, Cd ions might act by damaging DNA directly, or by stimulating the production of reactive intermediates which subsequently attack the genetic material.

Finally, when discussing the mechanism of action of genotoxic substances, it has to be reminded that *in vitro* studies may be prone to produce responses by mechanisms that are not necessarily applicable to physiologically relevant concentrations of the substance: e.g. high levels of cadmium may affect base pairing or suggest alteration in polymerase error rates, but the relevance of these phenomena to the *in vivo* situation may be questioned.

If cadmium acts as a co-mutagen rather than as a mutagen, by e.g. decreasing fidelity in DNA synthesis or by interfering with DNA repair mechanisms, this might also partially explain some of the conflicting results of cytogenetic studies in human populations exposed to cadmium. If cadmium acts by inhibiting the repair of DNA damage induced by other agents, chromosome aberrations might be increased in different populations/subjects with different additional occupational/environmental exposures as a result of unrepaired damage (Forni, 1992).

From a risk assessment perspective, it is also important to note that most of the mechanisms proposed to explain the genotoxicity of Cd ions are dose-dependent and support the possibility of a threshold for genotoxic effects (Madle et al., 2000, Kirsch-Volders et al., 2000).

Summary and conclusions

No *in vitro* study using cadmium metal was identified. Bacterial tests with cadmium oxide yielded negative results. No other test system using cadmium oxide was located. Most of the located *in vitro* studies used water-soluble cadmium chloride. While, as emphasised by the IARC Working Group (1993), water solubility does not necessarily reflect *in vivo* solubility, it can be assumed that Cd/CdO will to some extent be solubilised *in vivo*, especially in the lung, and data obtained with soluble Cd compounds may be considered relevant to assess the possible genotoxic potential (hazard) of cadmium oxide.

Although a clear and consistent pattern of action remains to be determined, it is concluded that cadmium metal and oxide can exert a genotoxic potential *in vitro* in consideration of several genotoxic effects reported with water soluble cadmium compounds.

Three possible and *a priori* non-mutually exclusive mechanisms have been identified: 1) direct DNA damage, 2) oxidative damage and 3) inhibition of DNA repair. While for classification purpose it is not critical to distinguish between these mechanisms, it may, however, be very relevant in the interpretation of carcinogenicity data (threshold versus non-threshold approach).

4.1.2.8.3 *In vivo* studies

No *in vivo* study using cadmium metal was located.

Inhalation exposure to cadmium oxide (0.025, 0.05, 0.1, 0.25, 1 mg/m³) for 13 weeks did not result in an increased frequency of micronucleated erythrocytes in peripheral blood of male or female $B6C3F_1$ mice (McGregor et al., 1990 cited in NTP Technical Report, 1995, **Table 4.148**). At the end of the 13-week study, smears were prepared and slides were scanned to determine the frequency of micronuclei in 2,000 normochromatic erythrocytes in each of five male and five female mice per exposure concentration. Criteria of Schmid (1976) were used to define micronuclei. According to this NTP report, no attention was apparently paid to verify that the bone marrow had actually been exposed to cadmium (e.g. signs of bone marrow toxicity), and it can therefore not be excluded that the absence of effect in blood erythrocytes reflects insufficient bioavailability to the bone marrow of the tested compound. Moreover, the most relevant cells in terms of carcinogenic risk, i.e. lung epithelial cells, were not examined in this assay.

Table 4.148 Frequency of micronuclei in peripheral blood erythrocytes of mice following treatment with cadmium oxide by inhalation for 13 weeks (NTP Report, 1995)

	Concentration (mgCdO/m³)	Micronucleated NCEs/1000 NCEs (mean ± standard error)
Male	Air	3.5 ±0.4
	0.025	2.8 ± 0.3
	0.050	3.7 ± 0.6
	0.100	3.1 ± 0.9
	0.250	3.1 ± 0.4
	1.000	4.3 ± 0.6
Female	Air	2.1 ± 0.2
	0.025	2.1 ± 0.4
	0.050	2.2 ± 0.3
	0.100	2.1 ± 0.3
	0.250	2.7 ± 0.4
	1.000	2.7 ± 0.3

NCEs Normochromatic erythrocytes
Further details are available in the IUCLID

Several experiments using cadmium water-soluble compounds were identified and were summarised by the Working Group of the IARC (1993). Results were judged conflicting by this working group.

Two additional recent studies were identified, all using cadmium chloride:

- The induction of micronuclei, sister chromatid exchange in mouse bone marrow and chromosomal aberration after single i.p. treatment (1.9, 5.7, 7.6 mg $CdCl_2$/kg bw) was investigated by Fahmy and Aly (2000). The three doses induced a statistically significant (dose-dependent) increase in the percentage of peripheral erythrocytes with micronuclei. The doses 5.7 and 7.6 mg/kg bw also induced bone marrow toxicity as indicated by a significant increase in the percentage of polychromatic erythrocytes over that of the control value. Cadmium chloride was also reported to induce chromosomal aberrations (after excluding the metaphases with chromosome or chromatid gaps). Intensity of effect was a function of the $CdCl_2$ dose and effect was maximum 24 hours post-treatment. Finally, a dose-dependent increase in the frequency of SCEs was also observed at the two highest doses (Fahmy and Aly, 2000),
- Single strand breaks were observed after acute treatment of male albino rats with $CdCl_2$ (4 mg/kg bw) injected intraperitoneally. Cadmium also increased the amount of single strand breaks in the kidney (Saplakoglu et al., 1997).

Regarding the mechanism of action of cadmium, Forni suggested that Cd ions might act rather as a co-mutagen than as a mutagen (Forni, 1992). Indeed, cadmium ions appear to inhibit the repair of DNA damaged by other agents. For example, cadmium chloride given to mice at 300 ppm in water for 7 days enhanced the frequency of micronuclei resulting from dimethylnitrosoamine, thereby enhancing its genotoxicity (Watanabe, 1982 cited in IARC 1993).

Summary and conclusions

No study using cadmium metal was identified. Only one study using cadmium oxide by inhalation was located. The negative results of this study of micronuclei in peripheral erythrocytes should, however, be interpreted with caution because 1) of the absence of evidence of sufficient bioavailability to the bone marrow; and 2) the most relevant target cells, i.e. lung cells, were not examined. Results of animal studies using water-soluble cadmium compounds, although conflicting, tend to indicate a potential of Cd ions to cause genotoxic effects *in vivo* and it is reasonable to extend this potential to CdO and Cd metal. Considering the debate on the potential carcinogenicity of CdO and its mechanism (see Section 4.1.2.9), it would be very useful to examine the potential co-mutagenic activity of CdO in the lung tissue.

Conclusions

Although the available data on the cadmium compounds of concern (Cd metal and oxide) are scarce and the results with water-soluble compounds conflicting, it is concluded that it cannot be excluded that cadmium metal and oxide can exert genotoxic effects *in vivo*.

4.1.2.8.4 Studies in humans

According to several reviews (CRC 1986, IARC 1992, IARC 1993,WHO 1992, ATSDR 1999), the results of genotoxicity studies in humans are conflicting. The reasons for these discrepancies are far from clear and it was tried to identify some of the elements that could explain the diverging results. All studies cited in the main reviews (See Section 4.1.2.1) and dealing with cadmium genotoxicity were included and evaluated. An additional search for data was conducted on MEDLINE using (a) MESH cadmium-poisoning, cadmium-adverse effects, cadmium-poisoning-genetics, cadmium-poisoning-blood, cadmium-poisoning-complications, mutagenicity-tests (b) text words: cadmium, chromosomal aberrations, sister chromatid exchange, cytogenetics, cadmium or Itai-Itai (chromoso$ or chromati$ or micronucl$ or cytogenet$) and (cadmium or Itai-It$), limited to human) (c) (explode cytogenetics/or explode micronuclei/) and (explode cadmium/ or explode cadmium poisoning/, limited to human). Finally, the search was completed by a careful reading of the bibliography of the papers and searching in the database of the Unit for Occupational and Environmental Health in Zürich, which is based on articles in the main journals for occupational health since 1986. Only original papers fully published in German, English or French were considered eligible. Papers in other languages or from which only the abstract was available were excluded. The influence that excluded studies could have had is assessed in the discussion. In case of duplicate publications, only the most recent and/or useful paper was included.

All studies were evaluated by two reviewers with a checklist relating to population (inclusion criteria, selection procedure, and lost cases), exposure, endpoints, biases and confounders. Divergences were resolved by consensus.

<u>Oral route: general population</u>

Table 4.149 lists the located studies:

Table 4.149 Located studies conducted on environmentally exposed populations

Reference	Design of the study	Population (N)	Endpoint §	Selected study (yes/no)*
Shiraishi and Yosida (1972) Shiraishi (1975)	Mainly cross-sectional (some longitudinal observations)	Itai-Itai patients (7-12)	Chromosome aberrations	Yes
Bui et al. (1975)	Cross-sectional	Itai-Itai patients (4)	Chromosome aberrations	Yes
Nogawa et al. (1986)	Cross-sectional	People with kidney disease living in Cd-polluted area in Japan (24)	Sister chromatid exchanges	Yes
Wulf et al. (1986)	Cross-sectional	Greenlandic Eskimos (92)	Sister chromatid exchanges	Yes
Tang et al. (1990)	Cross-sectional	People living in Cd-polluted region in China (40)	Chromosome aberrations	Yes
Tang (1991)	Cross-sectional	People living in Cd-polluted region in China	Sister chromatid exchanges	No
Cerna et al. (1997)		General Czech population from four districts (2 urban, 2 rural)	Chromosome aberrations	Yes
Fu et al. (1999)	Cross-sectional	People environmentally exposed to Cd in China	Chromosome aberrations, Micronuclei	Yes

§ All studies examined circulating lymphocytes (PBL)
* Selected: considered in discussion, reasons for exclusion are briefly discussed in the "summary and discussion"

Studies were classified according to the outcome considered: chromosomal aberrations, sister chromatid exchanges or micronucleus.

For each selected study, a first table gives an overview on overall results (+/-), study population, exposure assessment and confounders, a second summarises methods, major results and dose-effect relationship.

Some additional information for interpreting the results is given in the text.

Table 4.150 Study population/ environmental exposure/ confounders, chromosomal aberrations (Shiraishi 1975, Shiraishi and Yosida 1972)

Reference	Results/ Material	Main characteristics of the sample	Exposure assessment	Considered confounders
Shiraishi and Yosida (1972) Shiraishi (1975)	+ (PBL)	Final population: E: 7-12 (F only) Age: 52-73 years C: 6 (F) - 9 (6F/3M) Age: 58-78 years Selected from: E: "Itai-Itai patients" C: "subjects of similar age " Selection procedure: N.I. Lost subjects: N.I. Previous poisoning/Osteomalacia/Kidney Disease: yes, Itai-Itai disease	Type of exposure: environmental Type of compound: N.I. Duration of exposure: N.I. Environmental and biological monitoring: N.I. Other simultaneous exposures: N.I.	Age: yes Sex: no Drugs: ± (see text) X-rays: N.I. but possible (see text) Viral diseases: N.I. Alimentation/ Vitamins: N.I. Anaemia: N.I. but possible Smoking: N.I. Other diseases: yes, see text

N.I. No information available in this publication
PBL Peripheral blood lymphocytes
Cd-B Blood cadmium,
Cd-U Urinary cadmium
\- Negative result,
\+ Positive result
± Positive results for some particular endpoints
E Cd-exposed subjects,
C Non exposed subjects,
M Male,
F Female,
Y Years
Considered confounders: Age, Sex, Drugs, X-rays, Viral diseases, Alimentation/Vitamins, Anaemia, Smoking, Other diseases:
yes Were considered in selection of the population and/or in discussion,
no Not considered either in selection of the population or in the discussion.
± Some attempt to consider this factor was made

Table 4.151 Methods/ endpoints and results, chromosomal aberrations (Shiraishi 1975, Shiraishi and Yosida 1972)

Reference	Methods and Endpoints				Results			
Shiraishi and Yosida (1972) Shirashi (1975)	-heparinised and "freshly drawn" blood							
		1972	1975			1972	1975	
	-incubation time	72	72	50	-total cells with structural aberrations (mean (range)):	E: 50.6 (14-64) % C: 0.6 (0-2) %	E: 19.9 (8.9-30.8) %* C: 2.7 (1.6-3.8)% (endpoint: total abnormal cells)	E: 23.5 (19-34) %** C: 2.5 (1.5-4.0)%
	-number of cells observed	50	155-700	200-300	-total aneuploid cells:	N.I.	E: 4 (0-7.7)%* C: 0.6 (0.1-2%)	E: 11.7 (6.5-15) % C: 2.1 (1-3)%
	-number of endpoints	±5§	±12§	±14§				
	-slides coded, mixed, analysed blind: N.I				-dose-effect or dose-response relation not explored			

N.I. No information available
* Examination of 1972.4.27
** Examination of 1973.2
§ Endpoints considered in this study (±: exact number of endpoints can not always be determined with precision with the available information in the publication):
1972 Single chromatid breaks, isochromatid breaks or gaps, chromatid translocations, dicentric or dicentric like chromosomes, acentric fragments (N=5)/
1975 72 hours Chromatid break, isochromatid break, chromatid exchange, dicentric chromosome, acentric fragment, ring chromosome, stable cells with translocation, G(21) long arm deletion, G(21) short arm large/ aneuploid cells (hypo-hyperdiploid), polyploid cells, total abnormal cells (N= 12)
1975 50 hours Chromatid break, isochromatid break, chromatid exchange, dicentric chromosome, acentric fragment, ring chromosome, stable cells with translocation, G(21) long arm deletion, G(21) short arm large, total structural aberrations/ aneuploid cells, polyploid cells, endomitoses, total numerical aberrations (N=14)

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Table 4.152 Study population/ environmental exposure/ confounders, chromosomal aberrations (Bui et al., 1975)

Reference	**Results/ Material**	**Main characteristics of the sample**	**Exposure assessment**	**Considered confounders**
Bui et al. (1975)	(PBL)	Final population: E: 4 (F only) Age: 55-71 years C: 4 (3F, 1M) Age: 65-94 years Selected from: E:" Itai-Itai patients from Fuchu (endemic cadmium-polluted area)" C: "Living in an area known not to be contaminated by cadmium" Selection procedure: N.I. Lost subjects: 2 Previous poisoning/ Osteomalacia/ Kidney disease: yes, Itai-Itai disease	Type of exposure: environmental Type of compound: N.I. Exposure duration: N.I. Environmental and biological monitoring: *Cd-U (N=4, µg/gcreat, mean (range))* E: 12.4-31.2 (20.0) C: 5.3-10.9 (7.9) Cd-B (N=4, ng/g "wet weight , mean (range)) E: 19.5 (15.5-28.8) C: 5.05 (4.4-6.1) Other simultaneous exposures: N.I.	Age: ± Sex: no Drugs: no subject with chromosome-damaging drugs (not detailed) X-rays: no subject with X-ray therapy Viral diseases: no subject with viral disease Alimentation/Vitamins: N.I. Anaemia: N.I. Smoking: N.I. Other diseases: N.I.

N.I. No information available in this publication,
PBL Peripheral blood lymphocytes,
Cd-B Blood cadmium,
Cd-U Urinary cadmium,
\- Negative result,
\+ Positive result,
± Positive results for some particular endpoints
E Cd-exposed subjects,
C Non exposed subjects,
M Male,
F Female,
y Years
Considered confounders: Age, Sex, Drugs, X-rays, Viral diseases, Alimentation/Vitamins, Anaemia, Smoking, Other diseases:
yes Were considered in selection of the population and/or in discussion,
± Some attempt to consider this factor was made
no Not considered either in selection of the population or in the discussion,

Table 4.153 Methods/ endpoints and results, chromosomal aberrations (Bui et al., 1975)

Reference	Methods and Endpoints	Results
Bui et al. (1975)	-time between sampling and initiation of cell cultures was about 96 hours (air mail, temperature isolated box) -incubation time: 72 hours -number of cells observed: 82-100 metaphase cells in each case -technical problems: haemolysis and failed cell culture was noticed in 2 samples of the Itai-Itai patients (2/6) -number of endpoints: 8§ -slides coded, mixed, analysed blind: yes	-total cells with structural aberrations: E: 6.6 ± 3.11% C: 6.0 ± 1.41% -prevalence of aneuploidy: E: 2.3 ± 2.63% C: 4.5 ± 2.38% -dose-effect or dose-response relation not explored

§ Endpoints considered in this study (±: exact number of endpoints can not always be determined with precision with the available information in the publication): an/euploidy, endoreplication, structural aberrations, chromatid-type damage (breaks and exchange figures), chromosome-type damage (breaks, exchange figures) (N=8)

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Table 4.154 Study population/ environmental exposure/ confounders, chromosomal aberrations (Tang et al., 1990)

Reference	Results/ Material	Main characteristics of the sample	Exposure assessment	Considered confounders
Tang et al. (1990)	**±** (PBL)	Final population: E: 40 (21M/ 19 F) Age: 36.8 ± 17.6 y. C: 11 (9M/ 2 F) Age: 41.9 ± 14.5 y. Selected from: E: "lived in Cd-polluted area of Suichang (Cd-soil : 1.103 ppm)" C: "lived in unpolluted region of the same general area (Cd-soil: 0.20 ppm)" Selection procedure: N.I. Lost subjects: 7 Previous poisoning/Osteomalacia/ Kidney Disease: N.I.	Type of exposure: environmental Type of compound: N.I. Exposure duration: 11-62 years Environmental and biological monitoring : *Cd-U (µg/l, mean ± SD):* E: 3.32 ± 1.46 (M) 3.83 ± 1.82 (F) C: 2.34 ± 1.59 (M) 1.85 ± 0.65 (F) Other simultaneous exposures: N.I.	Age: yes Sex: no Drugs: no subject with chromosome-damaging drugs (not detailed X-rays: no subject with X-ray therapy Viral diseases: no subject with viral disease Alimentation/Vitamins: N.I. Anaemia: N.I. Smoking: partial data (see text) Other diseases: N.I.

N.I. No information available in this publication, ± Some attempt to consider this factor was made
PB Peripheral blood lymphocytes,
Cd- Blood cadmium,
Cd- Urinary cadmium,
\- Negative result,
\+ Positive result,
± Positive results for some particular endpoints,
E Cd-exposed subjects,
C Non exposed subjects,
M Male,
F Female,
y Years,
Considered confounders: Age, Sex, Drugs, X-rays, Viral diseases, Alimentation/Vitamins, Anaemia, Smoking,
Other diseases:
yes Were considered in selection of the population and/or in discussion,
no Not considered either in selection of the population or in the discussion,

Table 4.155 Methods/ endpoints and results, chromosomal aberrations (Tang et al., 1990)

Reference	Methods and Endpoints	Results
Tang et al. (1990)	-blood drawn 3-5 hours before	-total cells with structural aberrations:
		E: 5.53 ± 3.11%
	-incubation time: 72 hours	C: 2.73 ± 2.05 %
	-number of cells observed: 100 cells per subject	-prevalence of aneuploidy:
		E: 0.1 ± 0.38%
	-technical problems: coagulation of blood in several samples, only in controls (7/18)	C: 0
	-number of endpoints: 12§	-dose-effects relationship between chromosomal aberration frequency (%, y) and Cd-U (µg/l, ・) with linear regression equation: y= 1.960 + 0.949x; r=0.463, p < 0.001
		in whole study population
	-slides coded, mixed, analysed blindly: yes	

N.I. No information available

§: (±: exact number of endpoints can not always be determined with precision with the available information in the publication):endpoints considered in this study: aneuploidy, endoduplication, with structural aberration, gap, chromatid gap, isochromatid gap, chromatid breaks, chromosomal fragment, dicentric chromosome, translocations, multiradial, total abnormal cells (N=12)

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Table 4.156 Study population/ environmental exposure/ confounders, chromosomal aberrations (Cerna et al., 1997)

Reference	Results/ Material	Main characteristics of the sample	Exposure assessment	Considered confounders
Cerna et al. (1997)	- (PBL)	Final population: E: - at the most 670 adult blood donors Age: about 77% men with an approximate age of 32y. (range: 20-45) - at the most 632 children Age: about 51% of the boys with an approximate mean age of 9.3 y. - at the most 411 samples of umbilical blood Selected from: E: population examined in the frame of a monitoring system Selection procedure: Adults: blood donors Children: contacted through schools Lost subjects: not exactly known (moreover fairly large variations according to the determination taken into consideration) Previous poisoning/Osteomalacia/ Kidney Disease: N.I. but unlikely in adult blood donors and in children from the general population	Type of exposure: environmental Type of compound: N.I. Exposure duration: approximate mean length of residence in the district of about 24 and 8 years for adults and children, respectively Environmental and biological monitoring : <u>Cd-U (µg/ g creat, P50-P 97.5):</u> E: Adults: 0.58-4.61 Children: 0.37-2.51 <u>Cd-B (µg/100 ml, P50-P97.5)</u> E: Adults: 0.090-0.492 Children:0.070-0.719 Umbilical blood: 0.06-0.215 Other simultaneous exposures: N.I.	Age: yes Sex: yes Drugs: yes, at least for adults X-rays: yes, at least for adults Viral diseases: yes, at least for adults Alimentation/Vitamins: N.I. Anaemia: N.I., but unlikely in adult blood donors Smoking: yes (children: passive smoking) Other diseases: N.I. but unlikely in adult blood donors

N.I. No information available in this publication; PBL Peripheral blood lymphocytes; <u>Cd-B</u> Blood cadmium,
<u>Cd-U</u> Urinary cadmium; - Negative result,; + Positive result
E Cd-exposed subjects,; ± Positive results for some particular endpoints; C Non exposed subjects,
M Male,; F Female,; y Years
Considered confounders: Age, Sex, Drugs, X-rays, Viral diseases, Alimentation/Vitamins, Anaemia, Smoking, Other diseases: ± Some attempt to consider this factor was made
Yes Were considered in selection of the population and/or in discussion, no Not considered either in selection of the population or in the discussion,

Table 4.157 Methods/ endpoints and results, chromosomal aberrations (Cerna et al., 1997)

Reference	**Methods and Endpoints**	**Results**
Cerna et al. (1997)	-time between sampling and initiation of cell cultures N.I. -incubation time: 52 hours -number of cells observed: 100 well-spread metaphase cells per subject containing 46 centromeres -technical problems: N.I. -number of endpoints: 4§ -slides coded, mixed, analysed blind: slides coded and blind-scored	-total cells with chromosomal aberrations (mean (range)): adults: 1.71% (0-8) children: 1.27% (0-11) umbilical blood: 1.11% (0-7) -prevalence of aneuploidy: N.I. -dose-effect or dose-response relation : not explored

N.I. No information available

§ Endpoints considered in this study: chromatid breaks, chromosome breaks, chromatid exchanges chromosome exchanges

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Table 4.158 Study population/ environmental exposure/ confounders, chromosomal aberrations (Fu et al., 1999)

Reference	Results/ Material	Main characteristics of the sample	Exposure assessment	Considered confounders
Fu et al. (1999)	± (PBL)	Final population: E: 56 (26M/ 30 F) Age: 36.8 ± 17.6 y. C: 10 (4M/ 6 F) Age: 41.0 ± 10.6 y. Selected from: E: *"people environmentally exposed to Cd and in Suichang county of Zhejiang province"* C: *"living in areas known to be uncontaminated by Cd"* Selection procedure: N.I. Lost subjects: N.I. (7 subjects lost for examination of chromosome aberrations) Previous poisoning/Osteomalacia/ Kidney Disease: possible (scarce information)	Type of exposure: environmental Type of compound: N.I. Exposure duration: 33.6 ± 13.0 y. Environmental and biological monitoring : *Cd-U (µg/l, categories):* E: GM: 3.96, corrected for specific gravity ~2.5 (N=15) 2.5~ (N=17) 5.0~ (N=16) 10.0~ (N= 8) C: GM (GSM): 1.83 (1.49) Other simultaneous exposures: N.I.	Age: no Sex: no Drugs: no subject with chromosome-damaging drugs X-rays: no subject with X-ray examinations Viral diseases: N.I. Alimentation/Vitamins: N.I. Anaemia: N.I. Smoking: said to be comparable in the control and exposed group (no details given) Other diseases: N.I.

N.I.1	No information available in this publication.	PBL	Peripheral blood lymphocytes
Cd-B	Blood cadmium,	Cd-U	Urinary cadmium
GM	Geometric mean	GSM	Geometric standard deviation
-	Negative result,	+	Positive result
±	Positive results for some particular endpoints	E	Cd-exposed subjects,
C	Non exposed subjects,	M	Male,
F	Female,	y	Years

Considered confounders: Age, Sex, Drugs, X-rays, Viral diseases, Alimentation/Vitamins, Anaemia, Smoking, Other diseases:

Yes	Were considered in selection of the population and/or in discussion,
no	Not considered either in selection of the population or in the discussion,
±	Some attempt to consider this factor was made

Table 4.159 Methods/ endpoints and results, chromosomal aberrations (Fu et al., 1999)

Reference	Methods and Endpoints	Results
Fu et al. (1999)	-time between sampling and initiation of cell cultures N.I.	-total cells with structural aberrations:
		E:
	-incubation time: 72 hours	Cd-U ~2.5: 3.07 %*
		2.5~: 5.21%
	-number of cells observed: 100 metaphase cells per subject	5.0~: 7.21%
		10.0~: 8.50%
	-technical problems: N.I.	C: 2.33%
	-number of endpoints: 10§	-prevalence of aneuploidy:
		differences in numerical aberrations were not significant
	-slides coded, mixed, analysed blind: "blind-method"	
		-dose-effect or dose-response relation : between chromosome aberration rate (%, y) and Cd-U (µg/l,x) with linear regression equation: $y= 2.884 + 0.490x$; $r=0.63$, $p < 0.01$

N.I. No information available

* Categories

§ Chromatid gaps, chromatid breaks, chromosome gaps, chromosome breaks, fragments, dicentrics, translocations, multiradial, chromosome aberration rate, chromosome aberration cell rate (N=10)

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Two studies dealt with Itai-Itai patients exposed to cadmium (unspecified species) via the diet (water, rice, fish), and reported contradictory results:

Chromosome abnormalities in PBL obtained from Itai-Itai patients were investigated by a group of Japanese authors in a cross-sectional study that also included some longitudinal observations:

Shiraishi (1975) examined 12 female patients diagnosed with Itai-Itai disease and 9 control subjects. Seven patients were apparently already included in the paper of Shiraishi and Yosida (1972), which, therefore is not considered separately. As part of the study population was examined more than once in 1972 and again in 1973, the number of exposed subjects and analyses are not always the same (see **Table 4.120/4.151**). Exposure was defined only by the diagnosis of Itai-Itai disease. Cells with chromosomal aberrations were classified according to the type of aberration found. Methods and number of examined cells varied (see **Table 4.150/4.151**).

Overall, the authors reported a remarkably high frequency of chromosomal abnormalities in the blood cells of the patients as compared with the results in control subjects. Frequency of aneuploidy was also significantly higher than in the controls (see **Table 4.149**). In their conclusion, authors stressed the possibility that chronic cadmium poisoning is not the direct cause of the observed abnormalities and suggested that chromosomes of Itai-Itai patients may present an unusual high susceptibility to cadmium.

Some selection bias is likely as 5 patients were selected for the 1973 follow-up because of their “high frequency of aberrations in the examination of 1972”. Information on possible confounding factors such as anaemia, intake of chromosome damaging drugs or exposure to X-rays is very scarce or absent and could have distorted the results (Forni, 1992; O'Riordan et al., 1978; Nogawa, 1986; Barlow and Sullivan, 1982).

These positive results were not confirmed in the study carried out by Bui et al. (1975), who examined PBL from Itai-Itai female patients and from a similar number of controls (3F/1M) living in an area of Japan reported as “known not to be contaminated by cadmium”. Mean age was higher in the control group. Technical problems (haemolysis) justified the exclusion of two samples from the initial exposed group (6 Itai-Itai patients). Authors reported no significant difference between the patients and the control subjects with regard to the frequency of cells with structural aberrations (Bui et al., 1975). The significance of these negative results may also be questioned as both Itai-Itai patients and their controls had much higher rates of structural aberrations than those encountered in most series for controls (generally, < 1%). This was stressed by Forni (1992) who suggested that this might be due to (a) the technical problems associated with e.g. transportation or cell culture, and/or (b) the fact that the controls may have had some cadmium exposure from the environment too. Indeed, the four Japanese controls had higher values of Cd-U (reflecting body burden) than what could be expected in a non-exposed general population (mean: 7.9 µg/g creatinine, range: 5.3-10.9 µg/g creatinine). Moreover, two of the four controls had a suspected tubular pattern, according to the authors' classification of the electrophoretic pattern of urinary proteins. Finally, as for the study of Shiraishi and Yosida, one cannot exclude that Itai-Itai patients had undergone diagnostic X-ray irradiation as well as a potential confounding effect of drugs or anaemia.

More recently, three other groups studied the genetic effects of an environmental and dietary exposure to cadmium, outside Japan:

Tang et al. (1990) investigated 40 subjects (19 women) from a cadmium-polluted region of Suichang (Zhejuang Province, China). Exposure was estimated by the cadmium content of the soil and by the measurement of Cd-U as an indicator of the body burden. Main outcome was chromosomal aberration frequency.

The frequency of abnormal cells, including structural aberrations, aneuploidy and endoduplication was not significantly different in exposed and control subjects. However, transformed data (arcsinvP, not further detailed) differed in a statistically significant way between the groups and urinary cadmium correlated with chromosomal aberration frequency (r=0.46). More individuals in the exposed group (62.5%) had a high aberration prevalence (defined as > 5% aberration frequency detected at examination of the cells) than in the control group (18.2%). When the whole population was divided into high- and low-cadmium subgroups according to Cd-U (cut-off, set arbitrarily by the authors at 3 µg/l), there were more individuals in the high cadmium group with high aberration frequencies and with severe types than in the low cadmium group. Some methodological aspects limit, however, the interpretation of these results: selection procedure and representativity of the study population are only partly known, the small size of the control group (n=11, only 2 women), sex ratio is quite different in the exposed and unexposed groups, the effect of smoking is only crudely assessed, the potential confounding effect of previous occupational exposure is unknown, and subgroup analyses are based on cut-offs which might have been suggested by the results.

Cerna et al. (1997) examined subjects from the general Czech population. The exact size and characteristics of the study population having both a cadmium determination and a cytogenetic analysis cannot be determined exactly because the number of examined subjects may differ considerably according to the determination taken into consideration. The study design did not include a control group. Exposure was assessed by urine or blood concentration (measurements carried out with quality control). Endpoint was the frequency of chromosomal aberrations. The frequency of chromosomal aberrations was according to the authors "in line with reference values for the Czech population" (Cerna et al., 1997).

Fu et al. (1999) conducted a study on 56 environmentally exposed subjects and a smaller group of non-exposed subjects living in areas known not to be contaminated by cadmium.

Exposure was estimated by residential period (about thirty years for all groups) and urinary cadmium concentrations as a measure of body burden. Exposed subjects were divided in four subgroups according to their urinary cadmium values (~2.5, 2.5~, 5.0~, 10.0~µg/l). All people were examined for PBL chromosomal aberrations and micronuclei. Data were analysed statistically after application of an arcsin and square root transformation. Chromosomal aberration rates were significantly elevated when Cd-U exceeded 2.5 µg/l. Authors also reported a significant correlation between chromosomal aberration rate and Cd-U. Authors claimed that this study demonstrates that chromosomal aberrations might be more sensitive to environmental Cd exposure than renal function tests as only 3 of the 17 exposed subjects belonging to subgroups with chromosome aberrations had some abnormalities in their urine samples ("abnormal in total protein, low-molecular protein or β2-microglobulin", not detailed).

Table 4.160 Study population/ environmental exposure/ confounders, sister chromatid exchanges (Nogawa et al., 1986)

Reference	Results/ Material	Main characteristics of the sample	Exposure assessment	Considered Confounders
Nogawa et al. (1986)	- (PBL)	Final population: E: 24 (8 M/ 16F) Age:76.7 ± 5.9 y.(mean ± SD) C: 6 (2 M, 4 F) Age:68.3 ± 3.8 y. (mean ± SD) Selected from: E: *lived in Cd-polluted area (Kakehashi River Basin) + diagnosed as having Cd-induced renal damage* C: *lived in an unpolluted area (Uchinada-Machi)* Selection procedure: partially known Lost subjects: N.I. Previous poisoning/ Osteomalacia/ Kidney Disease: yes, kidney disease; possible Itai-Itai?)	Type of exposure: environmental Type of compound: N.I. Exposure duration: N.I. Environmental and biological monitoring : <u>*Cd-U (µg/g creat, GM .GSM)*</u> E: 9.1 ± 2.8 C: 2.7 ± 2.0 (N=4) <u>*Cd-B (µg/100 ml)*</u> E: 0.96 ± 0.58 C: not available for these 6 controls (see text) For other controls(5 men from the unpolluted area): 0.12 ± 0.06 Other simultaneous exposures: N.I.	Age: yes Sex: yes Drugs: no subject with chromosome-damaging drugs (not detailed) X-rays: no subject with X-ray therapy Viral diseases: no viral infection at the time of the examination Alimentation/Vitamins: N.I. Anaemia: N.I. Smoking: in both groups men had smoked whereas women were non-smokers (no further information) Other diseases: N.I.

N.I. No information available in this publication
<u>Cd-U</u> Urinary cadmium
\+ Positive result
C Non exposed subjects,
Y Years
PBL Peripheral blood lymphocytes
GM (GSM) Geometric mean (geometric standard deviation)
± Positive results for some particular endpoints
M Male,
<u>Cd-B</u> Blood cadmium,
- Negative result,
E Cd-exposed subjects,
F Female,

Considered confounders: Age, Sex, Drugs, X-rays, Viral diseases, Alimentation/Vitamins, Anaemia, Smoking, Other diseases:
yes Were considered in selection of the population and/or in discussion,
no Not considered either in selection of the population or in the discussion,
± Some attempt to consider this factor was made

Table 4.161 Methods/ endpoints and results, sister chromatid exchanges (Nogawa et al., 1986)

Reference	Methods and Endpoints	Results
Nogawa et al. (1986)	-whole blood	-sister chromatid exchanges rates: E: 7.97 ± 0.94%
	-incubation time: 72 hours	C: 9.00 ± 3.13%
	-number of cells observed: 21-115 metaphases per subject	-dose-effect, dose-response relations: no significant correlations between SCE rates and individual renal function, or Cd-B or Cd-U
	-technical problems: 2 subjects had preparations with very few metaphases	
	-number of endpoints: 1 (sister chromatid exchanges)	
	-slides coded, mixed, analysed blind: coded	

Table 4.162 Study population/ environmental exposure/ confounders, sister chromatid exchanges (Wulf et al., 1986)

Reference	Results/ Material	Main characteristics of the sample	Exposure assessment	Considered Confounders
Wulf et al. (1986)	+ (PBL)	Final population: E: 92 (M/ F: N.I.) Age: 24-37y. according to subgroup C: 0 Selected from: E: genetically pure Greenlandic Eskimos, level of heavy metals in one subgroup already known as rather high C: / Selection procedure: partially known Lost subjects: N.I. Previous poisoning/ Osteomalacia/ Kidney Disease: only healthy subjects	Type of exposure: environmental Type of compound: N.I. Exposure duration: N.I. Environmental and biological monitoring : Cd-U (µg/g creat, GM. GSM) Not performed Cd-B (µg/100 ml) E: 0.16-0.24 (range of mean values in the different subgroups) Other simultaneous exposures: Pb, Hg,Se measured in blood (preliminary results available for DDT)	Age: yes Sex: yes Drugs: no medication except contraceptives X-rays: N.I. Viral diseases: only healthy subjects Alimentation/Vitamins: considered Anaemia: N.I. Smoking: yes (g/day) Other diseases: only healthy subjects

N.I. No information available in this publication
PBL Peripheral blood lymphocytes
Cd-B Blood cadmium,
Cd-U Urinary cadmium
- Negative result,
+ Positive result
± Positive results for some particular endpoints
E Cd-exposed subjects,
C Non exposed subjects,
M Male,
F Female,
y Years

Considered confounders: Age, Sex, Drugs, X-rays, Viral diseases, Alimentation/Vitamins, Anaemia, Smoking, Other diseases:
Yes Were considered in selection of the population and/or in discussion,
No Not considered either in selection of the population or in the discussion,
± Some attempt to consider this factor was made

Table 4.163 Methods/ endpoints and results, sister chromatid exchanges (Nogawa et al., 1986)

Reference	Methods and Endpoints	Results
Wulf et al. (1986)	-time between sampling and cell culture: 3 to 7 days -incubation time: 72 hours -number of cells observed: 30 -technical problems: N.I. -number of endpoints: 1(sister chromatid exchanges) -slides coded, mixed, analysed blindly: yes, blind	-sister chromatid exchange rates: only regression analyses shown -dose-effect, dose-response relations: a linear correlation was found between SCE and Cd-B

N.I. No information available

Sister chromatid exchanges were analysed in PBL from two groups of Japanese men and women by Nogawa et al. (1986). The exposed group included people living in a cadmium-polluted area and all of them were diagnosed as having cadmium induced renal damage by the Research Committee of Ishikawa Health Authority. Renal damage was ascertained by large excretion of β-2 microglobulin in urine, and other parameters of renal function as creatinine clearance, % tubular reabsorption of phosphate (TRP), serum creatinine and serum inorganic phosphorus. Authors noted that the Cd-U and Cd-B values in the Cd-exposed group were lower than those reported for Itai-Itai patients.

There were no significant differences in SCE rates between the Cd-polluted group and their controls. No significant correlation could be found between SCE rates, the individual renal function expressed as creatinine clearance or amount of β-2 microglobulin, or the individual blood and urinary Cd level (Nogawa et al., 1986). Men had smoked in both groups, but the women had not. No differences were found in SCE rates between exposed and non-exposed subjects. Alike, there were no differences between exposed and non-exposed women (Nogawa et al., 1986). These results contrast with those of Shiraishi (1975) who found an increased prevalence of chromosomal aberrations in PBL from Itai-Itai patients in Japan. Several explanations are possible: low power, less intense exposure to Cd and/or lower prevalence of confounding factors than in the population studied by Shiraishi (1975), as well as a possible lower sensitivity of the SCE test to detect Cd-induced genotoxic effects in an environmentally exposed population.

Wulf et al. (1986) investigated the association between sister chromatid exchange and several factors (diet, residence, smoking, some metals including cadmium, etc.) in 92 Greenlandic Eskimos. Blood cadmium was associated with a statistically significant increased number of sister chromatid exchanges pro cell. It is unclear whether cadmium was the cause of sister chromatid exchanges or only a marker of exposure to some other agents present in the food and in environment.

Endpoint: micronucleus

Micronuclei were measured in PBL in the study conducted by Fu et al. (1999) on 56 environmentally exposed people and previously detailed (see Endpoint: chromosome aberrations). The exposed group was divided in four subgroups according to the urinary cadmium values. Micronucleus rates (MNR) appeared to be significantly elevated in all exposed subgroups when compared with the controls, except when Cd-U was < 2.5 μg/l. A linear correlation between MNR and urinary cadmium was reported by the authors.

Table 4.164 MN(C)R in PBL : 56 environmentally exposed people, 10 controls (Fu et al., 1999)

Groups (Cd-U μg/l)	Subjects (N)	Number of cells	Micronucleus rate (MNR ‰)§	Micronucleus cell rate (MNCR ‰)§
Control	**10**	**10,000**	**3.10**	**2.90**
Cd-U~2.5	15	15,000	3.47	3.33
2.5~	17	17,000	5.06*	4.77*
5.0~	16	16,000	8.06**	7.63**
10.0~	8	8,000	12.75**	11.88**

§ Arithmetic, geometric mean or median not specified;
MNCR Probably rate of micronucleated cells (not specified)
* $p < 0.05$,
** $p < 0.01$ compared with the control group

Summary and discussion: environmental (oral) exposure

The main features common to all the selected studies are as follows:

- all these studies have a cross-sectional design except that by Shiraishi (1972), in which part of the study population was re-examined 3, 6 or 12 months later (Shiraishi, 1975),
- population sizes are often so small that false-positive and false-negative findings may be due to chance findings and lack of power, respectively,
- many endpoints and inter-groups comparisons were used and independence of the different endpoints is not clearly stated. Therefore some chance findings are likely to have occurred,
- there is also a lack of consistency between the studies with regard to endpoints affected by cadmium exposure (see **Table 4.165**),
- information regarding a quality control for the cadmium measurements in blood or in urine is given in two studies only (Nogawa et al., 1986, Cerna et al., 1997). Individual data for Cd-B or Cd-U are not always available (mean ± SD or GM (GSD) are given for the group) and this did not allow to detect some outliers that could lead to inappropriate comparisons of the exposures. In several studies controls appear to have high urinary values when compared to European current Cd-U values,
- also, while it is difficult to known whether the higher cadmium body burden is the cause of cytogenetic changes or was only a marker of exposure to other variables (Itai-Itai disease, smoking, nutrition pattern, etc.), it is impossible to assess the specific contribution of Cd and/or CdO versus the other cadmium compounds in the observed genotoxic effects.

Some papers located in the literature search were excluded from the present discussion:

The paper by Tang et al. (1991) is written in Chinese. According to the English abstract, sister chromatid exchanges were the only outcome and no difference was found between the environmentally exposed and the control group (N=38 and 9 respectively). Whether this group is independent from the study population examined by Tang et al. (1990) is not known.

The impact of the exclusion from discussion of this paper on the conclusion appears to be limited as it seems to present the same methodological approach and weaknesses as the original study.

Several elements that may partly explain the conflicting results have been identified and have to be considered before reaching a conclusion:

- Design of the study: Most studies were not undertaken to test the relationship between a specific endpoint that was defined *a priori* and cadmium exposure but to compare the prevalence of several genetic endpoints in the exposed and control groups.
- Definition of the study population: selection procedure, representativity, comparability of the exposed and control groups:
  - as already mentioned, exposed and/or control groups were small (e.g. Bui et al., 1975) and the power to evidence effects is limited,
  - selection procedures and participation rate are seldom reported, and selection bias cannot be excluded in all studies,
  - representativity is generally unknown,

  * matching of the groups has often been insufficient: sex can be linked with differences in smoking habits, or alimentary patterns, etc.

- Exposure assessment: definition of the exposure characteristics may vary from study to study:

  * some studies gave no detailed information on exposure (e.g. Shiraishi, 1975),

  * other authors reported Cd-U or Cd-B, which does not have the same significance.

- Definition of outcome (**Table 4.165**):

  * generally, several endpoints were chosen by the authors. For some of these endpoints a clear definition is lacking which limits comparisons between the different studies,

  * significance for carcinogenicity of considered endpoints differed between the authors. For the present effect assessment in particular, it should be reminded that while chromosomal aberrations have been shown to predict to some extent cancer development, sister chromatid exchanges and micronuclei did apparently not (Hagmar et al., 1998; Bonassi et al., 2000).

- Results:

  * Some authors applied unusual mathematical transformations before statistical comparison of the results between exposed and control groups (e.g. arcsin√P),

  * Some results can hardly be extrapolated to other environmentally exposed populations: e.g. Itai-Itai patients belong to a particular subgroup of the general population exposed to cadmium as the disease was limited to a subgroup of women, from a defined area, at a defined period and could involve also other causal factors than cadmium (e.g. anaemia, poor nutrition, etc.).

- Analysis of the confounding factors in the different studies has not been systematic and probably incomplete, as revealed by the **Table 4.149** and **4.152**.

The lack of attention in the selection procedures and the small groups, the different technical procedures together with the "gaps" in the information about exposure and confounding factors, might contribute to explain most of the contradictory results.

Table 4.165 Endpoints and findings (type of aberration), environmental exposure

Reference	Chromosomal aberrations														Sister chromatid exchanges	Micro-nucleus
	Chromatid-type					Chromosome-type						Total	Aneuploidy	Others		
	cg	icg	cb	icb	exch	CG	CB	F	Dic	TR	MR					
Shiraishi (1972) Shiraishi and Yosida (1975)	-	-	x S	x S	x S	-	-	x S	x S	x S	-	x S	x S	*RC ,GLD,GSL, polyploid cells*	-	-
Bui et al. (1975-	-		x NS	-	x N.I	-	x NS	-	-	-	-	x NS	x NS	*Endoduplication, chromosome type exchange figures*	-	-
Tang et al. (1990)	x N.I.	x N.I.	x N.I.	-	-	-	-	x N.I	x NS	x NS	x NS	x S	x NS	*Endoduplication*	-	-
Cerna et al. (1997)	-*	-	x NS	-	x NS	-	x NS	-	-	-	-	x NS	-	*Chromosome exchanges*	-	-
Fu et al. (1999)	x N.I.	-	x N.I.	-	-	x N.I.	x N.I.	x N.I.	x N.I.	x N.I.	x N.I.	x S	-	-	-	x S
Nogawa et al. (1986)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x NS	-
Wulf et al. (1986)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x S	-

cg Chromatid gaps, icg Isochromatid gaps, cb Chromatid breaks, icb Isochromatid breaks, Exch Chromatid exchanges,
CG Chromosome gaps, CB Chromosome breaks, F Fragments, Dic Dicentrics, TRT Translocations,
MR Multiradial RC Ring chromosome, GLD G(21)long arm deletion, GSL G(21)short arm deletion * Not considered as an aberration
x Explored endpoint
S Statistically significant ($p < 0.05$),
NS Not statistically significant when compared to the control group,
N.I. No information available on the statistical analysis of the data

In addition, the fact that Cd may act as a co-mutagen (see sections 4.1.2.8.2 and 4.1.2.8.3) has not been considered in the above studies, which might also contribute to explain variability of the response. It is indeed possible that effects reported in some studies represent an amplification of the genotoxic effect induced by an associated agent (cigarette smoking, other heavy metals or medical irradiation). Interaction between Cd exposure and other potential sources of genotoxic effect has not (and, given the limited size of the study population, could not) been examined in these studies.

Taking all these elements into account, the study by Fu et al. (1999) is identified as a critical study for the effect assessment in the general population because of the size of the population examined, the dose response-relationship and the confirmation of the finding with two independent biomarkers (chromosomal aberrations and micronuclei). Significant increase in genotoxicity biomarkers were observed in environmentally exposed people with a Cd-U > 2.5 µg/l. It can therefore not be excluded that cadmium may be genotoxic but a causal relation between cadmium exposure and genotoxic effects is not definitely proved. These threshold values should be considered as very tentative.

Conclusion: oral route

It cannot be excluded, based on the available data, that cadmium (including Cd metal and oxide by assimilation) might exert genotoxic effects in populations exposed via the oral route.

Inhalation route: occupationally exposed population

Table 4.166 lists the located studies.

Table 4.166 Located studies, occupationally exposed populations

Reference	Design of the study	Population	Plant	Endpoint	Selected study (yes/no)*
Deknudt et al. (1973)	Cross-sectional	14 workers	Zinc industry	Chromosome aberrations	Yes
Deknudt and Léonard (1975)	Cross-sectional	35 workers	Cadmium plant	Chromosome aberrations	Yes
Bui et al. (1975)	Cross-sectional	5 workers	Alkaline battery factory	Chromosome aberrations	Yes
Bauchinger et al. (1976)	Cross-sectional	24 workers	Zinc smelting plant	Chromosome aberrations	Yes
O'Riordan et al. (1978)	Cross-sectional	40 workers	Manufacture of cadmium pigments	Chromosome aberrations	Yes
Dziekanowska (1981) cited in IARC (1993)	Cross-sectional	11 workers	Smelter	Chromosome aberrations, Sister chromatid exchange	No
Fleig et al. (1983)	Cross-sectional	14 workers	Manufacture of cadmium pigments and stabilisers	Chromosome aberrations	Yes
Forni et al. (1990) Forni et al. (1994)	Cross-sectional	40 workers	Production of cadmium, zinc, silver and copper alloys	Chromosome aberrations Micronuclei	Yes
Bonassi et al. (2000)	Nested Case-control	4 workers	N.I.	Chromosome aberrations	No

* Selected: Relevant studies were identified, selected and included according the same criteria as previously described for environmental exposure. The possible influence of excluding one study is considered in the discussion.

Studies were classified according to the following outcomes: chromosomal aberrations, sister chromatid exchanges or micronucleus. For each selected study, a first table gives an overview on overall results (+/-), study populations, exposure assessment and confounders, a second table summarises methods, major results and dose-effect relationship. Some additional information for interpreting the results is given in the text.

Table 4.167 Study population/ occupational exposure/ confounders, chromosomal aberrations (Deknudt et al., 1973)

Reference	Results/ Material	Main characteristics of the population	Exposure assessment	Considered confounders
Deknudt et al. (1973)	± (see text) (PBL)	Final population: E: 14 (M) classified into 3 groups Group I: high level of Zn, low levels of Cd and Pb (N=5) Group II: high levels of Zn, Cd, Pb (N=5) Group III: high levels of Cd and Pb, no Zn (N=4) Age: 27-56 y. C: 5 Age: 31-55 y. Selected from : E:"workers in a Zn industry classified into 3 groups according to the type and duration of exposure" C: N.I. Selection procedure: N.I. Lost subjects: N.I. Previous poisoning/ Osteomalacia/Kidney Disease: all workers have presented clinical symptoms of saturnism, otherwise N.I.	Type of exposure: occupational Type of compound: fumes and dust at a zinc melting and refining and cadmium manufacturing plant Duration (mean (range)): Group I: 15.6 (7-26) y. Group II: 11.9 (2-26) y. Group III: 3.3 (0.5-11)y. # Environmental and biological monitoring: Cd-air: N.I. Cd-U: N.I. Cd-B: N.I. Other simultaneous exposures: Lead (Pb-U, (µg/L mean) Group I: 223.6 (range:155-305) Group II: 260.2 (range: 183-351) Group III: 432.8 (range: 165-720) Zinc: N.I.	Age: yes Sex: N.I. about the controls Drugs: N.I. X-rays: N.I. Viral diseases: N.I. Smoking: N.I. Previous work: ± Other diseases: N.I.

N.I. No information available in this publication PBL Peripheral blood lymphocytes Cd-B Blood cadmium, Cd-U Urinary cadmium
- Negative result, + Positive result ± Positive results for some particular endpoints
E Cd-exposed subjects, C Non exposed subjects, M Male, F Female, y Years
Considered confounders: Age, Sex, Drugs, X-rays, Viral diseases, Smoking, Previous work, Other diseases:
yes: were considered in selection of the population and/or in discussion, no: not considered either in selection of the population or in the discussion,
±: some attempt to consider this factor was made #: (total duration of exposure, see text)

Table 4.168 Methods/ endpoints and results, chromosomal aberrations (Deknudt et al., 1973)

Reference	Methods and endpoints	Results
Deknudt et al. (1973)	-time between sampling and cell culture: N.I.	-total cells with structural aberrations: **E:** 3.87% in Group I, 1.60% in Group II, 2.76% in Group III
	-incubation time: 48 hours	**C:** 1.55%
	-number of cells observed: 300-400 cells examined from each worker, 100-400 from each control	-prevalence of aneuploidy: “only euploid cells were analysed”
	-technical problems: N.I.	-dose-response, dose-effects relation: not explored
	-number of endpoints: ±10§	-prevalence of "more complex aberrations increased in the exposed group when compared to the controls"
	-slides coded, mixed, analysed blindly: analysed independently by 2 persons	

N.I. No information

§ Endpoints considered in this study (±: exact number of endpoints can not always be determined with precision with the available information in the publication): chromatid gaps, chromatid breaks, chromatid exchange, chromosome gaps, chromosome fragments, disturbance of spiralisation, ring chromosome, dicentrics, cells with structural abnormalities, presence of “more complex chromosome aberrations”

Table 4.169 Study population/ occupational exposure/ confounders, chromosomal aberrations (Deknudt and Léonard, 1975)

Reference	Results/ Material	Main characteristics of the population	Exposure assessment	Considered confounders
Deknudt and Léonard (1975)	± (see text) (PBL)	Final population: E: 35 (M only?) classified into 2 groups: "Cd-service": high levels of Pb and Cd, no Zn (N=23) "Rolling-mill": exposed mostly to Zn, lower levels of Pb and Cd (N=12) Age (mean): "Cd-service": 40.2 y. "Rolling-mill": 34.8 y. C: 12 (M only?) Age (mean): 32.2 y. Selected from : E: "workers in a Cd plant classified into 2 groups according to the type and duration of exposure" C: "people from the administration department of the same plant" Selection procedure: N.I. Lost subjects: N.I. Previous poisoning/ Osteomalacia/Kidney Disease: 3/23 workers of the Cd-service presented signs of lead poisoning (no more information)	Type of exposure: occupational Type of compound: Cd fumes and dust at a cadmium plant Duration (mean (range)): Cd-service: 12 (3-26) y. Rolling-mill: 11 (2-42) y. Environmental and biological monitoring: Cd-air: N.I. Cd-B: (µg/100 ml, range (mean)) E: Cd-service: 0.6-17.9 (3.17) Rolling-mill: < 0.05-1.45 (0.62) C: N.I. Other simultaneous exposures: Cd-Service: Pb-B (µg/100 ml mean): 44.62 (range:23.5-75.9) Zn: N.I. Rolling-Mill: Pb-B (µg/100 ml, mean): 20.78 (range: 12.8-27.6) *Zn:* N.I. Controls: Pb: N.I.	Age: ± Sex: ± Drugs: N.I. X-rays: N.I. Viral diseases: N.I. Smoking: N.I. Previous work: known for part of the population (see text) Other diseases: N.I.

N.I. No information available in this publication; ± Positive results for some particular endpoints; M Male,
PBL Peripheral blood lymphocytes; + Positive result; y Years
Cd-B Blood cadmium, E Cd-exposed subjects, F Female,
Cd-U Urinary cadmium C Non exposed subjects, negative result,
Considered confounders: Age, Sex, Drugs, X-rays, Viral diseases, Smoking, Previous work, Other diseases:
yes Were considered in selection of the population and/or in discussion, ± Some attempt to consider this factor was made
no Not considered either in selection of the population or in the discussion,

Table 4.170 Methods/ endpoints and results, chromosomal aberrations (Deknudt et al., 1975)

Reference	Methods and endpoints	Results
Deknudt and Léonard (1975)	-time between sampling and cell culture was about 2 or 3 hours	-total cells with structural aberrations: E: 2.0% in Group I, 3.96% in Group II
	-incubation time: 48 hours	C: 3.04%
	-number of cells observed: 200 cells examined from each worker	-prevalence of aneuploidy: N.I.
	-technical problems: N.I.	-dose-response, dose-effects relation: not explored
	-number of endpoints: ±12	-prevalence of more complex chromosome aberrations: increased when compared to the control workers (see text)
	-slides coded, mixed, analysed blindly: N.I.	

N.I. No information available

§ Endpoints considered in this study (±: exact number of endpoints can not always be determined with precision with the available information in the publication): chromatid gaps, chromatid breaks, chromatid deletion, chromatid exchange, chromosome gaps, chromosome fragments, disturbance of spiralisation, translocations, ring chromosomes, dicentrics, cells with structural abnormalities, “prevalence of more complex aberrations”

Table 4.171 Study population/ occupational exposure/ confounders, chromosomal aberrations (Bui et al., 1975)

Reference	Results/ Material	Main characteristics of the sample	Exposure assessment	Considered confounders
Bui et al. (1975)	- (PBL)	Final population: E: 5 (M only) Age: 44-57 y. C: 3 (M only) Age: 52-54 y. Selected from: E: “electrode department of an alkaline battery factory” C: ″office workers of about the same age, from the same factory” Selection procedure: N.I. Lost subjects: N.I. Previous poisoning/ Osteomalacia/ Kidney Disease: 2 workers with "suspected tubular pattern at electrophoresis"	Type of exposure: occupational Type of compound: N.I. (alkaline battery factory) Duration: 5-24 years (mean:12 years) Environmental and biological monitoring: <u>Cd-air (µg/m³)</u> Area sampler: < 1961:“higher” than 35 1969-1972: 35 Exposure probably similar between 1961 and 1968 Personal sampler: average of about 70 <u>Cd-U (µg/gcreat, range (mean))</u> E: 5.4-31.4 (11.4) C: 1.0-3.1 (2.5) <u>Cd-B (ng/g “wet weight”, range (mean))</u> E: 24.7-61.0 (37.7) C: 1.4-3.2 (2.3) Other simultaneous exposures: N.I.	Age: ± Sex: yes Drugs: no subject with chromosome-damaging drugs (not detailed) X-rays: no subject with X-ray therapy Viral diseases: no subject with viral diseases Smoking: N.I. Previous work: N.I. Other diseases: N.I.

N.I. No information available in this publication
PBL Peripheral blood lymphocytes
Cd-B Blood cadmium,
Cd-U Urinary cadmium
\- Negative result,
\+ Positive result
± Positive results for some particular endpoints
E Cd-exposed subjects,
C Non exposed subjects,
M Male,
F Female,
y Years

Considered confounders: Age, Sex, Drugs, X-rays, Viral diseases, Smoking, Previous work, Other diseases:
Yes Were considered in selection of the population and/or in discussion,
No Not considered either in selection of the population or in the discussion,
± Some attempt to consider this factor was made

Table 4.172 Methods/ endpoints and results, chromosomal aberrations (Bui et al., 1975)

Reference	Methods and endpoints	Results
Bui et al. (1975)	-time between sampling and cell culture was about 24 hours	-total cells with structural aberrations:
		E: 2.4 ± 1.52% (48hours) 2.0 ± 0.71% (72hours)
	-incubation time: 48 and 72 hours	C: 3.3 ± 3.51% (48hours) 2.4 ± 1.52% (72hours)
	-number of cells observed: 100 metaphases from each worker	-prevalence of aneuploidy:
		E: 2.2 ± 2.39% (48hours) 1.0 ± 0.71% (72hours)
	-technical problems: N.I.	C: 1.0 ± 0.73% (48hours) 0.7 ± 1.15% (72hours)
	-number of endpoints: ±8§	-dose-response, dose-effects relation: not explored
	-slides coded, mixed, analysed blindly: yes	

N.I. No information available

§ Endpoints considered in this study (±: exact number of endpoints can not always be determined with precision with the available information in the publication): an/euploidy, endoduplication, structural aberrations, chromatid-type damage (breaks and exchange figures), chromosome-type damage (breaks, exchange figures) (N=8)

Table 4.173 Study population/ occupational exposure/ confounders, chromosomal aberrations (Bauchinger et al., 1976)

Reference	**Results/ Material**	**Main characteristics of the sample**	**Exposure assessment**	**Considered confounders**
Bauchinger et al. (1976)	+ (PBL)	Final population: E: 24 (M only) Age: 25-53 y. C: 15 (11M/4F) Age: 26-60 y. Selected from: E: "Workers at a smelting plant" C: "Unexposed, healthy controls from the general population" Selection procedure: N.I. Lost subjects: N.I. Previous poisoning/ Osteomalacia/ Kidney disease: no	Type of exposure: occupational Type of compound: Cd dust and fumes at a zinc smelting plant in zinc electrolysis Duration of exposure: 3 – 6.5 y. Environmental and biological monitoring: <u>Cd-air:</u> N.I. <u>Cd-U:</u> N.I. <u>Cd-B (mean ± SD, µg/100 mL):</u> E: 0.395 ± 0.27 C: N.I for the selected controls Other simultaneous exposures: zinc, lead (<u>*Pb-B (mean ± SD, µg/100 mL):*</u> E:19.29 ± 6.62, C:N.I for the selected controls	Age: ± Sex: no Drugs: no subject previously treated with cytostatic drugs X-rays: no subject previously irradiated Viral diseases: N.I. Smoking: N.I. Previous work: N.I. Other diseases: N.I. Others: no subject with clinical symptoms due to excessive exposure to Pb, Cd, Zn

N.I.	No information available in this publication	PBL	Peripheral blood lymphocytes	<u>Cd-B</u>	Blood cadmium,	<u>Cd-U</u>	Urinary cadmium
-	Negative result,	+	Positive result	±	Positive results for some particular endpoints		
E	Cd-exposed subjects,	C	Non exposed subjects,	M	Male,	F	Female,
Y	Years						

Considered confounders: Age, Sex, Drugs, X-rays, Viral diseases, Smoking, Previous work, Other diseases:

Yes Were considered in selection of the population and/or in discussion,

No Not considered either in selection of the population or in the discussion,

± Some attempt to consider this factor was made

Table 4.174 Methods/ endpoints and results, chromosomal aberrations (Bauchinger et al., 1976)

Reference	Methods and endpoints	Results
Bauchinger et al. (1976)	-time between sampling and cell culture: N.I.	-total cells with structural aberrations: E: 1.35 ± 0.99%
	-incubation time: 48 hours	C: 0.47 ± 0.92%
	-number of cells observed: 200 metaphases from each Cd worker, 100 metaphases from each control (in one case, 250 cells)	-prevalence of aneuploidy: "only cells with a complete number of chromosomes were scored" -No relationship detected between the prevalence of aberrations per person and Cd-B or Pb-B or length of exposure
	-technical problems: N.I.	
	-number of endpoints:± 8§	
	-slides coded, mixed, analysed blindly: N.I.	

N.I. No information available

§ Endpoints considered in this study (±: exact number of endpoints can not always be determined with precision with the available information in the publication): gaps per cell, chromatid breaks, acentric fragments, dicentrics, atypical chromosomes, chromatid exchanges, breaks per cell, structural aberrations

Table 4.175 Study population/ occupational exposure/ confounders, chromosomal aberration (O'Riordan et al., 1978)

Reference	Results/ Material	Main characteristics of the population	Exposure assessment	Considered confounders
O'Riordan et al. (1978)	- (PBL)	Final population: E: 40 (M only) Age: 17-61 y. C: 13 (M only) Age: 20-58 y. Selected from: E: "Workers employed in the manufacture of cadmium pigments, actively engaged in the processing of pigments" C: "same plant "on site controls", employed as laboratory and administrative staff" Selection procedure: N.I. Lost subjects: N.I. Previous poisoning/ Osteomalacia/ Kidney disease: 2 exposed subjects had clinical proteinuria (proved tubular origin), no further information	Type of exposure: occupational Type of compound: cadmium salts, pigments (not detailed) in a manufacture of cadmium pigments Duration of exposure: 6 weeks- 34 years Environmental and biological monitoring: Cd-air (µg/m³): 1964-1968: 600-1000 since 1968: 200 Cd-U: N.I. Cd-B (mean, range, µg/100 ml): E: 1.95 (< 0.2 –14.0) C: < 0.2 for 8 men, 0.6-2.9 for the remaining five Other simultaneous exposures: N.I.	Age: ± Sex: yes Drugs: no subject with chromosome-damaging drugs X-rays: no subject with X-ray therapy (exposure to diagnostic irradiation in some workers) Viral diseases: N.I. Smoking: N.I. Previous work: ± Other diseases: N.I.

N.I. No information available in this publication; PBL Peripheral blood lymphocytes; Cd-B Blood cadmium; Cd-U Urinary cadmium
- Negative result; + Positive result; ± Positive results for some particular endpoints
E Cd-exposed subjects; C Non exposed subjects; M Male
F Female; y Years

Considered confounders: Age, Sex, Drugs, X-rays, Viral diseases, Smoking, Previous work, Other diseases:
yes Were considered in selection of the population and/or in discussion
no Not considered either in selection of the population or in the discussion
± Some attempt to consider this factor was made

Table 4.176 Methods/ results and endpoints, chromosomal aberrations (O'Riordan et al., 1978)

Reference	Methods and endpoints	Results
O'Riordan et al. (1978)	-time between sampling and cell culture: N.I. -incubation time: 45-48 hours -number of cells observed: 100-102 cells from each subject (102 cells in the majority of the cases) -technical problems: N.I. -number of endpoints: ±7[§] -slides coded, mixed, analysed blindly: coded and analysed blind	<u>-total cells with structural aberrations:</u> E: 0.24% C: 0.482% -prevalence of aneuploidy: N.I. -dose-response, dose-effect relation: no relation with duration of pigment processing (≥ 15 y.) or Cd-B (> 2.0 µg/100 ml)

N.I. No information available

§ Endpoints considered in this study (±: exact number of endpoints can not always be determined with precision with the available information in the publication: chromatid gaps, chromatid breaks, chromatid interchanges, total N° cells with chromatid aberrations, dicentrics, free fragments, N° structurally abnormal chromosomes

Table 4.177 Study population/ occupational exposure/ confounders, chromosomal aberrations (Fleig et al., 1983)

Reference	**Results/ Material**	**Main characteristics of the population**	**Exposure assessment**	**Considered confounders**
Fleig et al. (1983)	– (PBL)	Final population: E: 14 (M only) Age: 25 – 56 y. C: 14 (M only) Age: 24 – 58 y. Selected from: E: "engaged in the manufacturing of cadmium stabilisers and cadmium pigments" C: "employed as administrative or office staff " Selection procedure: N.I. Lost subjects: N.I. Previous poisoning/ Osteomalacia/ Kidney Disease: N.I.; kidney disease: some workers with high laboratory parameters, workers with increased Cd-U and/or Cd-B transferred to non-exposed workplaces, urinary β2-µglobulin above "normal" in some workers	Type of exposure: occupational Type of compound: cadmium containing dusts Duration of exposure: 6 – 25 (mean:10.1) y. Environmental and biological monitoring: Cd-air (µg/m³): currently about 50 (TWA), higher in former years Cd-U (range, µg/l): E: 18.3 – 66.9 (1980) C: N.I. Cd-B (range, µg/100 mL): E: 0.3 – 2.9 (1980 for 13 workers) C: N.I. Other simultaneous exposures: N.I.	Age: yes Sex: yes Drugs: no subject with chromosome-damaging drugs X-rays: no subject with X-ray therapy (exposure to diagnostic irradiation in some workers) Viral diseases: N.I Smoking: N.I. Previous work: N.I. Other diseases: transaminases above "normal" in some workers

N.I. No information available in this publication
PBL Peripheral blood lymphocytes
Cd-B Blood cadmium
Cd-U Urinary cadmium
\- Negative result
\+ Positive result
± Positive results for some particular endpoints
E Cd-exposed subjects
C Non exposed subjects
M Male
F Female
y Years

Considered confounders: Age, Sex, Drugs, X-rays, Viral diseases, Smoking, Previous work, Other diseases:
yes Were considered in selection of the population and/or in discussion
no Not considered either in selection of the population or in the discussion
± Some attempt to consider this factor was made

Table 4.178 Methods/ endpoints and results, chromosomal aberrations (Fleig et al., 1983)

Reference	Methods and endpoints	Results
Fleig et al. (1983)	-time between sampling and cell culture: N.I.	-total cells with structural aberrations: E: 4.0% (including gaps) 1.5% (excluding gaps)
	-incubation time: 70 - 72 hours	C: 3.6% (including gaps) 1.3% (excluding gaps)
	-number of cells observed: 150 metaphases from each Cd worker, 100 metaphases from each control	-prevalence of aneuploidy: N.I.
	-technical problems: N.I.	-dose-response, dose-effect relation not explored
	-number of endpoints: ±10§	
	-slides coded, mixed, analysed blindly: N.I.	

N.I. No information available

§ Endpoints considered in this study (±: exact number of endpoints can not always be determined with precision with the available information in the publication): chromatid gaps, isochromatid gaps, breaks, fragments, deletions, chromatid interchanges, rings, dicentric chromosomes, percentage aberrant cells including cells, percentage aberrant cells excluding gaps (N = 10)

Table 4.179 Study population/ occupational exposure/ confounders, chromosomal aberrations (Forni et al., 1990)

Reference	Results/ Material	Main characteristics of the population	Exposure assessment	Considered confounders
Forni et al. (1990) Forni (1992) Forni (1994)	± (see text) (PBL)	Final population: E: 40 (M only) Age: 23 – 58 y. C: 40 (M only) Age: 23 –63 y. Selected from: E: "workers in a single factory producing cadmium, zinc, copper and silver alloys" C: " matched for age, sex and smoking" Selection procedure: ± Lost subjects: N.I. Previous poisoning/ Osteomalacia/ Kidney disease: No	Type of exposure: occupational Type of compound: cadmium fumes and dust in the alloys production Duration of exposure: NI Environmental and biological monitoring: Cd-air (µg/m³): Very high up to 1975 < 50 in 1982 Cd-U (range, µg/L): E:22 workers with Cd-U > 10 18 workers with Cd-U < 10 range: 1.5- 31.6 C: N.I. Cd-B (range, µg/100 mL): E: 0.03 -2.83 C: N.I. Cumulative exposure index (CEI) : mean yearly airborne Cd concentration x number of years of exposure Other simultaneous exposures: Cu, Zn,Ag (concentrations of Zn and Pb considered as negligible)	Age: yes Sex: yes Drugs: subjects who had taken cytotoxic drugs (not detailed) were excluded X-rays: subjects with X-ray therapy were excluded Viral diseases: subjects with recent viral disease were excluded Smoking: yes Previous work: subjects with previous occupational exposure to clastogens excluded Other diseases: N.I.

N.I. No information available in this publication PBL Peripheral blood lymphocytes Cd-B Blood cadmium, Cd-U Urinary cadmium
\- Negative result, + Positive result ± Positive results for some particular endpoints
E Cd-exposed subjects, C Non exposed subjects, M Male, F Female, y Years
Considered confounders: Age, Sex, Drugs, X-rays, Viral diseases, Smoking, Previous work, Other diseases: yes: were considered in selection of the population and/or in discussion,
no Not considered either in selection of the population or in the discussion, ± Some attempt to consider this factor was made

Table 4.180 Methods/endpoints and results, chromosomal aberrations (Forni et al., 1990)

Reference	Methods and endpoints	Results
Forni et al. (1990)	-time between sampling and cell culture: N.I.	-abnormal metaphases:
Forni (1992)		E: 2.6% (excluding gaps)
Forni (1994)	-incubation time: 48 hours	C: 1.7% (excluding gaps)
		Total rates of abnormal metaphases including gaps not different in the 2 groups
	-number of cells observed: 100 metaphases from each subject	
		-prevalence of aneuploidy: N.I.
	-technical problems: N.I.	
	-number of endpoints: ±8§	-dose-response, dose-effect relation: long-term exposure associated with significant increase in frequency of chromosome-type aberrations (2.37% in workers with CEI > 1,000 vs. 0.8 in workers with CEI < 100, vs.0.5% in controls
	-slides coded, mixed, analysed blindly: N.I.	

N.I. No information available
CEI Cumulative exposure index
§ Endpoints considered in this study (±: exact number of endpoints can not always be determined with precision with the available information in the publication: total abnormal metaphases (including and excluding gaps), cells with chromatid-type aberrations, cells with chromosome-type aberrations

Deknudt et al. (1973) reported chromosome observations performed on PBL from 14 workers employed in a zinc factory who presented signs of lead poisoning of different degrees. Workers were classified according to the type and duration of exposure into a group exposed to high levels of zinc and low levels of cadmium and lead (mean duration: 15.6 years), a group exposed to high levels of the three substances (mean duration: 12 years), and a group exposed to high levels of lead and cadmium in the absence of zinc. All the workers have presented clinical symptoms of saturnism with elevated Pb-B and Pb-U. The observed aberrations were dicentrics, rings, chromatid exchanges as well as gaps and fragments. The prevalence of "more complex aberrations" such as chromatid exchange, disturbance of spiralisation, ring and dicentrics was significantly different between the exposed workers and the controls and appeared to be also increased in the workers from group I exposed to low levels of cadmium and lead compared to the workers exposed to high levels of Cd, Pb, and Zn. Authors concluded that exposure to cadmium did not seem to increase the number of cells with severe chromosome anomalies and that lead intoxication should be considered responsible for the observed chromosome aberrations (Deknudt et al., 1973).

Deknudt and Léonard (1975) carried out a further study in workers exposed to cadmium, lead and zinc. 35 workers (classified in two subgroups, "Cd-service" and "Rolling-mill") were compared with a small group of 12 controls from the same plant. Exposure subgroups were defined according to type and duration of exposure. A biological monitoring for cadmium and lead was done in the exposed workers only. In contrast to the previous study, the cytogenetic analyses were apparently not done by two independent observers. No clear definition of the endpoint "severe chromosome anomalies" was given in the publication. While "more complex chromosome aberrations" were more frequent in the "cadmium group", three unexplained severe aberrations also occurred in the control group. The lowest mean percentage of cells with structural abnormalities was found in workers from the "cadmium service" subgroup. No obvious relationships between type of exposure and chromatid gaps and chromosome fragments were found. These results are difficult to interpret because they were influenced by an obvious outlier with 5% severe abnormalities and possibly by previous occupations such as miner, foundry worker or industrial plumber. Since an occupational history was available for part of the study population only, a detailed analysis is rendered difficult if not impossible. The fact that the study was mainly hypothesis-generating may explain the discrepancies with the previous investigation by the same authors (Deknudt et al., 1973).

Since there is for these two studies a combined exposure to high levels of cadmium and lead, it is difficult to conclude on which metal might be responsible for the increase in aberrations (Deknudt and Léonard, 1975). Bauchinger et al. (1976), citing Deknudt et al. (1973) in their own study, suggested a possible synergistic effect of several metallic and other compounds that may influence the induction of chromosome aberrations

Bui et al. (1975) examined chromosomal aberrations in five men employed in the electrode department of an alkaline battery factory. They were compared with three male office workers of about the same age as the exposed workers and from the same factory. Reported average cadmium concentration in the general air during 1969-1972 was 35 µg/m³ but cadmium concentrations in air of the electrode department amounted to about twice this general air value when exposure was estimated by personal air samplers. Before 1961, there were exposures to somewhat higher cadmium concentrations (data not available).

Mean cadmium concentrations were reported for urine and whole blood for both groups: the exposed group had significantly higher values than the control group and Cd-B values in the exposed workers were elevated indicating recent exposure. Electrophoretic examination of urinary proteins and determination of total urinary protein were also performed to allow, according to the authors, an estimation of the extent of cadmium exposure and cadmium accumulation as well as of renal tubular damage: 2 workers had a suspected tubular pattern.

No increased frequency of chromosome aberrations was found. However, interpretation of these negative results should take into account the fact that three of the five workers had low Cd-U (indicator of body burden): 2.4, 5.4, 7.4 µg Cd/g creatinine when compared to the other group of exposed subjects (Itai-Itai patients) in the same study (Bui et al., 1975).

Bauchinger et al. (1976) compared chromosomes in PBL from workers exposed to fumes and dust containing zinc, cadmium and lead from a cadmium-zinc smelter with chromosomes obtained from controls of the general population. Workers had no clinical sign of metal toxicity. Cd-B and Pb-B levels were not determined in the 15 persons selected as controls as they were assumed to be identical to the "normal values for an adult population of industrial workers not exposed to such heavy metals". The percentage of cells with structural aberrations was significantly increased in the exposed group (1.35 ± 0.99% for exposed workers versus 0.47 ± 0.92% for the controls, $p < 0.001$). No relationship was detected between the individual prevalence of aberrations and Pb-B, Cd-B or the duration of exposure.

Exposure to cadmium, however, does not appear to have been very significant since Cd-B levels were of 0.4 ± 0.3 µg/100ml. Bauchinger et al. (1976) suggested from their other existing cytogenetic data on heavy metals (subjects environmentally exposed to lead) that cadmium alone or in synergism with other metals (e.g. lead) may well be responsible for the increase in aberrations observed in this last study, which is reminiscent of the co-mutagenic activity of Cd ions discussed in the previous sections (4.1.2.8.2 and 4.1.2.8.3).

No significant increase in chromosome aberrations was reported by O'Riordan et al. (1978) in workers exposed to cadmium salts in a manufacture of cadmium pigments when they were compared with 13 on-site controls. Five of the 13 on-site controls had relatively high Cd-B values, what might reduce the possible differences between exposed and controls. Cd-B values and exposure ranged both widely, what could "dilute" possible positive results for the most highly exposed individuals (IARC, 1992). Cd-B values in the exposed subjects presented a non-normal distribution which suggests definitely that about half of the exposed group could have been exposed to low levels of cadmium (Cd-B < 0.5 µg/100 ml; no further details). Two subjects had clinical tubular proteinuria, what might suggest that cadmium toxicity had occurred. Four individual cells (out of 3,740 examined in total) with chromatid interchanges were observed in the exposed group but the authors stated that "if such an increase was a real phenomenon then it can only be a negligible one". Exposed and control groups working in the plant showed a higher overall frequency of aberrations than general population controls (6.6% and7.6% for workers of the exposed and the control group versus 3.4% in the general population), which might raise some doubt on the quality of selection of the control subjects.

Negative findings were reported by Fleig et al. (1983) in workers exposed to cadmium (compound not specified), used as the initial basic substance for the production of cadmium pigments and stabilisers. Exposed workers were compared with age-matched office workers.

No significant difference in the percentage of aberrant cells, including or excluding gaps, was found. No explanation is given for the fact that biological monitoring showed clearly increased Cd-U values despite the wearing of masks and the filtering of room air. In her comments, Forni noted the rather low values for aberrant cells excluding gaps, both for the exposed group and for the controls (Forni, IARC 1992).

Forni et al. (1990) compared male workers exposed to fumes and dusts emitted through the production of cadmium, zinc, copper and silver alloys in a single factory with the same number of controls matched for age, sex and smoking habits. Exposed workers were selected from a larger group monitored by Ghezzi et al. (1985). Subjects with signs of cadmium poisoning were excluded. A healthy worker effect may have biased the results because workers with increased blood or urine cadmium concentrations were transferred to workplaces without cadmium exposure. Atmospheric cadmium concentrations in the factory seem to have been very high up to 1975, after what they had progressively decreased to < 50 µg/m³. Mean urinary cadmium values were reported for the exposed workers but not for controls. Concentrations of zinc and lead had always been negligible and exposure data regarding Cu and Ag were not reported. Rates of abnormal metaphases excluding gaps were significantly higher in PBL of the 40 exposed men than in the controls, whereas the total rates of abnormal metaphases including gaps did not differ between the two groups. Chromosome-type aberrations accounted for most of the observed increase. When a cumulative exposure index was calculated for each subject (mean yearly atmospheric cadmium concentration · years of exposure, ranging from < 100 to > 1,000), only high-intensity, long-term exposure was associated with a significant increase in the frequency of chromosome-type aberrations.

Table 4.181 Rates of abnormal metaphases (excluding gaps) and of cells with chromosome-type aberrations in cadmium workers, subdivided by Cd cumulative exposure index, and in the matched controls (Forni et al., 1990)

Cumulative exposure index	% Abnormal metaphases		% Chromosome-type aberrations	
(µg/m³.y)	Workers	Controls	Workers	Controls
< 100	1.80	1.60	0.8	0.7
101 – 500	2.61	1.54	0.76	0.15
501 – 1,000	2.44	2.33	1.00	0.55
> 1,000	3.75	1.37	2.37*	0.50
	P < 0.05		P < 0.05	

* Different from the other subgroups (p < 0.01) Wilcox on matched pair test

The 22 workers with Cd-U > 10 µg/l had significantly higher rates of abnormal metaphases (excluding gaps) and chromosome type aberrations than the controls and the 18 other workers (see **Table 4.182**). No increase in chromosome-type aberrations was detectable in the group of subjects with mean Cd-U levels lower than 10 µg/l, the biological exposure limit value at the time of the study (Forni et al., 1990, Forni, 1992).

Table 4.182 Chromosome-type aberrations in relation to Cd-U (mean values of the last 4 years) (Forni et al., 1990)

Cadmium workers		Controls		
Cd-U (µg/l)	% Chrom. Aberr.	Cd-U (µg/l)	% Chrom.Aberr.	
< 10 (N=18)	0.67	N.I.	0.50	N.S.
> 10 (N=20)	1.55	N.I.	0.41	P < 0.005

N.S. Statistically non significant

<u>Endpoint: micronucleus</u>

Micronuclei were evaluated in PBL of the 40 cadmium workers previously tested for chromosome aberrations by Forni (1994). Rates of micronuclei in the exposed group did not differ from those of the 40 healthy, unexposed controls matched for age and smoking, not even in the subgroup with the highest cumulative exposure index or with the higher Cd-U values for which chromosomal aberrations were previously observed (Forni et al., 1990).

Results are summarised in **Table 4.183**.

Table 4.183 Micronucleus rates in lymphocytes of 40 cadmium workers and 40 controls matched for age and smoking habits (Forni, 1994)

Subjects	**N**		**MN rate (%, mean)**	
Controls	40		2.20	
Cd workers	40		2.03	
Cadmium cumulative exposure index (μg/m³.y)	**N**	**N**	**MN rate (‰, mean)**	
			Workers	**Matched Controls**
< 100	10	35.8	1.76	1.55
101-500	13	40.4	1.97	2.29
501-1,000	9	45.8	2.14	2.28
> 1,000	8	50.1	2.33	2.87

Author related the negative finding with MN in cadmium workers who had positive findings for chromosomal aberrations to the stronger age effect (also present in the controls) on micronuclei than on chromosomal aberrations (Forni et al. 1994). These results are in sharp contrast with those reported by Fu et al. (1999) (see **Table 4.158** and **4.159**) who found markedly increased MN rates in environmentally exposed people. It should however be considered that the methodology of the micronucleus test was at that time not standardised and that variations in the protocol might account for differences in the sensitivity of the test. This possibility is suggested by the fact that both authors reported different MN rates in the control population (see **Table 4.184**); however methodological information in both reports is insufficient to further discuss this issue. It should also be considered that the subjects examined by Fu et al. (1999) were on the average younger than the workers studied by Forni et al. (1994). Finally, it is also possible that the increased MN rate reported by Fu et al. (1999) is the results of a co-exposure to another environmental agent acting as a complete mutagen or in association with Cd (co-mutagenic effect of Cd ions).

Table 4.184 Comparison of the MN studies by Fu et al. (1999) and Forni et al. (1994)

	Fu et al. (1999)	**Forni et al. (1994)**
Type of exposure	**Environmental**	**Occupational**
Number of exposed/controls	56/10	40/40
Age of the exposed/controls	36.8/41.0 (mean)	23-58/23-63 (range)
Cd-U in exposed/controls	3.96/1.83 (μg/l, GM)	1.5-31.6 (μg/l, range) 18 workers with Cd-U > 10
Number of cells examined	100 metaphase cells/subject	1,000
MN rate in controls	3.10% (not specified)	2.20% (mean)
MN rate in exposed	Cd-U ~2.5 : 3.47% 2.5~: 5.06 5.0~: 8.06 10.0~: 12.75	2.03% (mean)

<u>Summary and discussion: occupationally exposed population</u>

The main features common to all the selected studies are as follows:

- all these studies have a cross-sectional design;

- many endpoints and inter-groups comparisons are used and independence of the different endpoints is not clearly stated. Therefore, some chance findings are likely to occur;
- no study mentions a quality control regarding the measurement of cadmium in urine, blood or air;
- in some studies, the involved cadmium compound is not precisely defined. It is difficult to assess the specific contribution of Cd and CdO versus other cadmium compounds;
- individual data for Cd-B or Cd-U are not always available (mean ± SD or GM (GSD) are given for the group) and this did not allow to detect some outliers that could lead to inappropriate comparisons.

Table 4.185 and **4.186** summarise the results of the selected studies.

Table 4.185 Summary of the selected studies: occupationally exposed populations, chromosomal aberrations

In the literature reported as	Reference	Population	Incidences of observed aberrations in exposed group compared to control group	Considered Confounders
+	Bauchinger et al. (1976)	24 workers	S	Age, drugs, X-rays
±	Deknudt et al. (1973)	14 workers	NS (but significantly increased prevalence of "more complex aberrations")	Age, sex
	Deknudt and Léonard (1975)	35 workers	NS (but significantly increased incidence of “more complex aberrations”)	Age, previous work
	Forni et al. (1990) Forni (1992) Forni (1994)	40 workers	Total abnormal metaphases rate : NS S when excluding gaps	Age, sex, drugs, X-rays, viral diseases, smoking, previous work
-	Bui et al. (1975)	5 workers	NS	Age, sex, drugs, X-rays, viral diseases
	O’Riordan et al.(1978)	40 workers	NS	Age, sex, drugs, X-rays,
	Fleig et al. (1983)	14 workers	NS	Age, sex, drugs, X-rays

Table 4.186 Summary of the selected studies: occupationally exposed populations, micronuclei

In the literature reported as	Reference	Population	Incidences of observed aberrations in exposed group compared to control group	Considered Confounders
			MN	
-	Forni (1994)	40 workers*	NS	Age, sex, drugs, X-rays, viral diseases, smoking, previous work

* Same workers as in Forni et al. (1990)

Two located papers were excluded from the discussion**:**

Dziekanowska (1981) was non eligible because it was only available as a short abstract (only available as a summary in the IARC 1993). Small increases in the prevalence of chromosomal aberrations in exposed workers (8.91 ± 4.99%) were reported when compared with 32 healthy non-smelter controls (6.66 ± 2.38%). No difference was, however, found in the frequency of sister chromatid exchange, conceivably because of the high SCE in the control group (IARC 1993). It is not known whether smoking habits and other confounding factors (radiotherapy, chromosome damaging drugs, etc.) were considered, moreover exposure was poorly documented (Dziekanowska,1981).

Insufficient data could be extracted from the paper of Bonassi et al. (2000) to allow a correct assessment of exposure and outcome.

Again, several elements that may partly explain the conflicting results have been identified and have to be considered before reaching a conclusion:

- Definition of the study population: e.g. selection procedure, representativity, comparability of the exposed and control groups:
  - in one study, exposed and control groups were small (e.g. Bui et al., 1975) and the power to evidence effects is limited,
  - selection procedures and participation rate are seldom reported, and selection bias cannot be excluded in all studies. Representativity is generally unknown, thus differences in the composition of the study population may have influenced the results.
- Exposure assessment: definition of the exposure characteristics may vary from study to study:
  - as stated previously, no quality control for these analyses is mentioned,
  - the type of cadmium compound is not always clearly defined,
  - it is difficult to assess the specific contribution of Cd and CdO in the observed genotoxic effects versus other simultaneous or previous exposures. **Table 4.187** summarises the available exposure characteristics in the selected studies, including the reported details about the presence of other toxicants at the workplace (e.g. lead) or past exposures (PAH).

No clear conclusion can be drawn from this table as to the possible contribution of other simultaneous exposures to the observed effects.

Persons working in this type of industry are usually exposed to a mixture of different metals. It is therefore extremely difficult to establish a causal relationship between a low increase in chromosome aberrations and one of the many components encountered in the environment because these agents may interfere with each other to produce synergistic or antagonistic effects. Therefore, the only conclusion that can be drawn from such studies is that the working conditions encountered in a given plant or workplace have or have not led to an increase in aberrations in the peripheral blood lymphocytes of exposed subjects (Léonard and Bernard, 1993).

In this regard, it should be stressed that almost no information is available on arsenic exposure. This issue may be critical as inspection of **Table 4.187** suggests that workers from studies showing increased prevalence of abnormal cytogenetic findings might have been exposed to arsenic as well whereas such an exposure seems less likely in the negative studies

- Definition of outcome

Table 4.188 summarises the explored endpoints and the findings in each study; a consistent pattern of genotoxic effects associated with occupational exposure to Cd compounds cannot be deduced.

Table 4.187 Summary of the reported studies considered in discussion: characteristics of exposure

Reference	Result	N	Type of setting	Exposure		Simultaneous exposures		Previous exposures (when known)
				Type of Cd compound	Available monitoring data	Reported in the selected studies	Might be presumed possible	
Deknudt et al. (1973)	S-NS	14	Zn melting and refining, manufacture of cadmium, lead	"cadmium"	Cd-air: N.I. Cd-U: N.I. Cd-B: N.I.	Lead Pb-U (µg/l, range): 165-759 Zinc: no quantitative information	Arsenic	N.I.
Deknudt and Léonard (1975)	S-NS	35	Cadmium plant	Cadmium fumes and dust	Cd-air: N.I. Cd-U: N.I. Cd-B(µg/100 ml, range (mean)): < 0.05-17.9 (3.17)	Lead fumes and dust, Pb-B (µg/100 ml, range (:mean)): 12.8-75.9 (*32.7*) Zinc: no quantitative information	Arsenic	Previous work: possibly PAH, silica, radon
Bui et al. (1975)	NS	5	Alkaline battery factory	Cadmium (compound not specified)	Cd-air: 35-70 µg/m^3 Cd-U (µg/gcreat, range (mean)) E: 5.4-31.4 (11.4) C: 1.0-3.1 (2.5) Cd-B (ng/g "wet weight", range (mean)) E : 24.7-61.0 (37.7) C : 1.4-3.2 (2.3)	N.I.	Ni compounds	N.I.
Bauchinger et al. (1976)	S	24	Zinc smelting plant: zinc electrolysis	Cadmium fumes and dust	Cd-air: N.I. Cd-U: N.I. Cd-B (, µg/100 ml, mean ± SD): E: 0.395 ± 0.27 C: N.I for the selected controls	Lead Pb-B (mean ± SD, µg/100 mL): 19.29 ± 6.62 Zinc: no quantitative information	H_2SO_4 Arsenic KCN	N.I.

Table 4.187 continued overleaf

Table 4.187 continued Summary of the reported studies considered in discussion: characteristics of exposure

Reference	Result	N	Type of setting	Exposure to cadmium		Simultaneous exposures		Previous exposures (when known)
				Type of compound	Available monitoring data	Reported in the selected studies	Might be presumed possible	
O'Riordan et al. (1978)	NS	40	Manufacture of Cd pigments	Cadmium salts, pigments	Cd-air: 200-1,000 µg/m^3 Cd-U: N.I. Cd-B (mean, range, µg/100 ml): E: 1.95 (< 0.2 –14.0) C: < 0.2 for 8 men, 0.6-2.9 for the remaining five	N.I.	H_2SO_4, zinc salts, sodium sulphide, mercuric sulphide, selenium, barium sulphide	Previous occupations not associated with chromosome damage (not detailed)
Fleig et al. (1983)	NS	14	Cadmium stabilisers and pigments	Cadmium containing dusts	Cd-air: 50 µg/m^3 Cd-U (range, µg/l): E: 18.3 – 66.9 (1980) C: N.I. Cd-B (range, µg/100 ml): E: 0.3 – 2.9 (1980 for 13 workers) C: N.I.	N.I.	H_2SO_4, zinc salts, sodium sulphide, mercuric sulphide, selenium, barium sulphide	N.I.

Table 4.187 continued overleaf

Table 4.187 continued Summary of the reported studies considered in discussion: characteristics of exposure

Reference	Result	N	Type of setting	Exposure to cadmium		Simultaneous exposures		Previous exposures (when known)
				Type of compound	Available monitoring data	Reported in the selected studies	Might be presumed possible	
Forni et al. (1990)	S- NS	40	Zn, Ag, Cu Alloys production	Cadmium fumes and dust	Cd-air: < 50 µg/m^3- "very high" Cd-U (range, µg/l): E: 22 workers with Cd-U > 10 18 workers with Cd-U < 10 range: 1.5- 31.6 C: N.I. Cd-B (range, µg/100 ml): E: 0.03 –2.83 C: N.I.	Zinc Copper Silver	Arsenic	Previous work: subjects with previous occupational exposure to clastogens were excluded

C.A. Chromosomal aberrations
N.I. No information available
S Difference statistically significant ($p < 0.05$)
NS Difference not statistically significant ($p > 0.05$)
S-NS Statistically significant for some specific endpoint (see study)

Table 4.188 Endpoints and findings (type of aberration), occupational exposure

Reference	**Chromosomal aberrations**														**Sister chromatid exchanges**	**Micro-nucleus**
	Chromatid-type					**Chromosome-type**						**Total**	**Aneuploidy**	**Others**		
	cg	**icg**	**cb**	**icb**	**Exch**	**CG**	**CB**	**F**	**Dic**	**TR**	**MR**					
Deknudt et al. (1973)	x N.I..	-	x N.I.	-	x N.I.	x N.I.	-	x N.I.	x N.I.	-	-	x S for complex aberrations	-	*Ring chromosomes, disturbance of spiralisation*	-	-
Deknudt and Léonard (1975)	x N.I.	-	x N.I.	-	x N.I.	x N.I.	-	x N.I.	x N.I.	-	-	x S for complex aberrations	-	*Chromatid deletion*	-	-
Bui et al. (1975)	-	-	x NS	-	x N.I	-	x NS	-	-	-	-	x NS	x NS	*Endoduplication, chromosome-type exchange figures*	-	-
Bauchinger et al. (1975)	x S	-	x S	-	x S	x S	-	x S	x NS	-	-	x S	-	*Breaks per cell, achromatic fragments Atypical chromosomes*	-	-
O'Riordan et al. (1978)	x NS	-	x NS	-	x NS	-	-	x NS	x NS	-	-	x NS	-	-	-	-
Fleig et al. (1983)	x N.I.	x N.I.	x N.I.	-	x N.I.	-	x N.I.	x N.I.	x N.I.	-	-	x NS (including or excluding gaps)	-	*Deletion, ring chromosomes,*	-	-
Forni et al. (1990) Forni et al. (1994)	x N.I.	*N.I.*	N.I.	N.I.	N.I.	x N.I.	N.I.	N.I.	N.I.	N.I.	N.I.	X NS including gaps, S excluding gaps	-	*Chromosome-type aberration*	-	x NS

cg Chromatid gaps, icg Isochromatid gaps, cb Chromatid breaks, icb Isochromatid breaks, Exch Chromatid exchanges,
CG Chromosome gaps, CG Chromosome breaks, CB Chromosome breaks, F Fragments, Dic Dicentrics,
TR Translocations, MR Multiradial RC Ring chromosome, GLD G (21) long arm deletion, GSL G (21) short arm deletion
X Explored endpoint S Statistically significant ($p < 0.05$),
NS Not statistically significant when compared to the control group, N.I. No information available on the statistical analysis of the data

- Analysis of the confounding factors in the different studies has not been systematic and probably incomplete, as revealed by the **Tables 4.167 - 4.180**.

Taking into account all these elements, the studies by Forni et al. (1990, 1992 and 1994) are identified as critical for the effect assessment in the occupational population because of the large number of subjects examined, the matching of controls and the dose-response relationship (long-term exposure). In this study, a significant elevation of chromosomal aberrations was observed in workers with Cd-U > 10 µg/l and/or a cumulative exposure index > 1,000 µg/m³ · years. A causal relation between cadmium exposure and chromosome aberrations is, however, not definitively proved and these thresholds should be considered as very tentative.

Conclusion: inhalation route

It cannot be excluded, based on the available data that cadmium (including Cd metal and oxide) might exert genotoxic effects in populations exposed by inhalation.

Conclusions: are cadmium oxide, cadmium metal genotoxic?

No definitive conclusions can be drawn about the genotoxicity of cadmium oxide and/or cadmium metal. Data from experimental systems indicate that cadmium, in certain forms, has genotoxic properties and it is reasonable to assume that these properties may also apply to cadmium oxide and probably metal species. With regard to human exposure to CdO, Cd metal and other compounds, data are conflicting but seem to indicate a genotoxic potential of cadmium metal and cadmium oxide, at least in occupational settings, but it is unclear whether these effects are solely attributable to CdO. Studies performed in environmentally exposed populations do not allow identifying the type of cadmium compound(s) to which subjects were exposed.

According to Annex VII A to Directive 67/548/EEC, minimum data requirements for the evaluation of the genotoxic potential of cadmium oxide (metal), had to be available from at least two tests: a bacterial gene mutation test (available and negative for cadmium oxide, not available for cadmium metal) and an *in vitro* chromosomal aberration test (not available for cadmium oxide nor for cadmium metal). An *in vivo* micronucleus test is available in $B6C3F_1$ mice exposed to CdO by inhalation but the negative results of this study are not sufficiently convincing. According to TGD, when there is not enough useful information already available on the genotoxic potential, further testing is necessary according to the strategy in Section 3.10.7 of the TGD (1996).

Keeping in mind that another important objective of genotoxicity testing is to predict a carcinogenic potential and to help interpret human data, it would be of higher value to conduct a well-designed *in vivo* study to assess the (co-)mutagenic activity of CdO particles in respiratory cells than to generate any additional *in vitro* data. Elucidation of the mechanism of genotoxicity and the issue of the possible co-mutagenic activity of cadmium is critical to better interpret the diverging results of human studies and to develop prevention strategies.

As long as the mechanism of genotoxicity is not completely elucidated it must be assumed that, when inhaled as a dust, Cd (and by extension Cd metal and oxide) is a direct acting genotoxic substance and that, according to TGD, it is prudent to consider that there is no threshold airborne exposure level below which effects will not be expressed.

If it could be demonstrated that the genotoxic effect of cadmium compounds is fully mediated through a mechanism such as inhibition of DNA repair enzymes, it would be reasonable to assume, from a theoretical perspective, that a threshold relationship applies to this kind of effects. Some epidemiological information is available on the relationship between effects (incidence, severity, etc.) and the dose or concentration of the substance (measured or estimated in environment, reflected by the biological monitoring). However, this quantitative information is of insufficient robustness to be formally used in a Risk Assessment.

Summary information related to the classification[33] as well as the judgement on the fulfilment of the base-set requirements

The available data are conflicting. The studies have many shortcomings and confoundings but the overall assessment suggests a genotoxic potential of the cadmium compounds involved.

Therefore, a classification as Muta Cat 3 (R68) is warranted.

4.1.2.9 Carcinogenicity

4.1.2.9.1 Introduction

Substances or preparations are defined as carcinogenic if they induce cancer or increase its incidence when they are inhaled, ingested or penetrate the skin (TGD, 1996).

Studies on carcinogenicity are not part of the minimum data requirements according to Article 9(2) of Regulation 793/93 for existing substances. However, all available information relevant to this endpoint has to be evaluated. Data useful in assessing the carcinogenic potential of substances may be obtained from available sources, including studies in humans, studies in animals, *in vitro* studies etc. and the final assessment will require the integrated evaluation of these different categories of data (TGD, 1996).

The idea that cadmium might cause cancer in humans was raised in 1967, before any positive laboratory evidence of carcinogenicity in animals, when four men who had worked in a UK cadmium-nickel battery factory were reported to have died of prostate cancer, although at national rates, less than one such death would have been expected. Interest focused afterwards on lung cancer, as cadmium compounds had been shown to produce bronchial carcinomas in rats following long-term inhalation (Takenaka et al., 1983; Oldiges et al., 1989). In humans, excess mortality from lung cancer has been reported in *some* studies among cadmium recovery, nickel-cadmium battery and cadmium processing workers. The role of cadmium with regard to the induction of lung cancer seems complex but most of the regulatory agencies have classified cadmium at least as a suspected or probable carcinogen. The Environmental Protection Agency EPA has classified cadmium as a probable human carcinogen by inhalation (group B1), based on its assessment of limited evidence of an increase in lung cancers in humans and sufficient evidence of lung cancer in rats. EPA has calculated an inhalation unit risk (the risk corresponding to lifetime exposure to 1 µg/m³) of $1.8 \cdot 10^{-3}$ (IRIS 1996, in ATSDR, 1999). The National Toxicology Program (NTP) has classified cadmium and cadmium compounds as "known to be human carcinogens" based on sufficient evidence of carcinogenicity from studies in humans, including epidemiological and mechanistic information which indicate a causal

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33 The **classification was done for cadmium oxide** and based on specific substance data, if available, and/or data from other cadmium compounds (more soluble forms).

For metallic cadmium the same classification is extrapolated on the basis of the so-called 'ion theory' and as a 'worst case' approach related to the bio-availability of the metal.

relationship between exposure to cadmium and cadmium compounds and human cancer (NTP, 2001). ACGIH (2001) noted cadmium, elemental form and its compounds, as (A2) suspected carcinogen: "human data are accepted as adequate in quality but are conflicting or insufficient to classify the agent as a confirmed human carcinogen (…) there is limited evidence of carcinogenicity in experimental animals with relevance to humans". In contrast, the International Agency for Research on Cancer (IARC) has classified cadmium as carcinogenic to humans (Group 1) based on an assessment of sufficient evidence for carcinogenicity in both human and animal studies (IARC 1993). Cadmium has been classified in category 2 in the European Union (Substances which should be regarded as if they are carcinogenic to man. There is sufficient evidence to provide a strong presumption that human exposure to this substance may result in the development of cancer, generally on the basis of: appropriate long-term studies in animals/ other relevant information).

For cadmium oxide, studies in animals and humans are available and reviewed in sections 4.1.2.9.2 and 4.1.2.9.3.

The term "cadmium compounds" refers to other compounds of cadmium than the oxide and the elemental forms. Data about these compounds are reported with another letter size and type.

4.1.2.9.2 Studies in animals

<u>Oral route</u>

No studies were identified in which rats or mice were exposed to cadmium oxide or cadmium metal by the oral route.

Most of the studies have been carried out with water-soluble cadmium compounds. They are summarised in **Table 4.189**.

Table 4.189 Cadmium by the oral route: summary of the main studies using cadmium compounds (adapted from Collins et al., 1992)

Species	Type of compound	Route	Dose (maximal)	Frequency duration	Number of exposed animals	Results	Reference
L.E rats	Cd acetate	Drinking water	0.5 mg/kg/day	Life span Life time	96	-	Schroeder et al. (1965)
Hooded rats	Cd acetate	Drinking water	0.36 mg/kg/day	Life span Life time	47	-	Kanisawa and Schroeder (1969)
Hooded rats	Cd sulfate	Gastric inst.	0.05 mg/kg/day	1x/week 24 months	90	-	Levy , Clack (1975)
Wistar rats	Cd chloride	Food	3.5 mg/kg/day	7d/week 104 weeks	50	-	Löser (1980)
Rats (strain not detailed)	Cd chloride	Food	6.75 mg/kg/day	n.d.	26-32	-	FDA (1977) cited in Collins et al. (1992)
Wistar rats	Cd chloride	Food	3.5 mg/kg/day (LOAEL)	77 weeks	56	+	Waalkes and Rehm (1992)
Swiss mice	Cd acetate	Water	1 mg/kg/day	36 months Life time	100	-	Schroeder , Balassa (1965)
Swiss mice	Cd sulfate	Gastric inst.	0.2 mg/kg/day	1x/week 18 months	50	-	Levy et al. (1975)
Albino Swiss mice	Cd chloride	Water	1.9 mg/kg/day (LOAEL)	280 days	41	+ *	Blakley (1986)
Mice (strain not detailed)	Cd chloride	Food	8 mg/kg/day	2 years	n.d.	-	Watanabe et al. (1986)

Number of exposed animals: number of animals in highest exposed group.
n.d. Not detailed
bw Body weight
* When trend test run, not statistically significant
\+ positive
\- negative

Most of the studies on chronic oral exposure to cadmium compounds administered to rats or mice have not reported an increased overall cancer incidence or an increased incidence of specific tumour types (Schroeder et al. (1965), Kanisawa and Schroeder (1969), Levy et al. (1975), Löser et al. (1980), Watanabe et al. (1986)). However, the failure of some oral studies to detect tumours may be due to inadequate study design, as indicated by low doses and variable study duration (Collins et al., 1992).

Blakley (1986) found that one-third more albino Swiss mice -exposed to a water-soluble cadmium compound at doses of 10 or 50 ppm, via the drinking water - died of leukaemia compared to controls (24/41 deaths at both doses versus 18/41 in controls) (Blakley, 1986 cited in Collins et al., 1992). However, the leukaemia incidence was very high in controls and a trend test was not statistically significant (Collins et al., 1992).

More recently, Waalkes and Rehm (1992) assessed the effect of chronic dietary zinc deficiency on the carcinogenic potential of dietary cadmium in male Wistar rats. Rats were exposed to several levels of dietary cadmium (0, 25, 50, 100, 200 ppm), given as cadmium chloride and mixed with diets either adequate in zinc or marginally deficient. A complete necropsy was performed on all animals.

A significant elevation in incidence of prostate proliferative lesions (hyperplasia and adenoma) occurred in both zinc adequate (22.7%) and zinc deficient (15.4%) rats fed 50 ppm cadmium, when compared to controls (1.9%). There was not a clear dose-response increase in prostate proliferative lesions.

Cadmium treatment resulted in an elevated incidence of leukaemia (large granular lymphocytes; maximum 28% leukaemia in exposed rats versus 5.4% in control rats) in both adequate and zinc-deficient groups. A significant increase in the incidence of leukaemia in the zinc-adequate diet was seen at 50 and 100 ppm cadmium, but not at 200 ppm. There was a consistent increase in the incidence of leukaemia with an increasing cadmium dose in the zinc-deficient group but the increase was statistically significant only at 200 ppm. Dietary zinc deficiency appeared to have a complex, apparently inhibitory effect on cadmium carcinogenesis as higher doses of Cd were needed in the zinc deficient group to observe comparable incidences of leukaemia.

The incidence of testicular tumours (benign interstitial cell tumours) increased significantly only in rats receiving 200 ppm of cadmium and diets adequate in zinc.

In conclusion, there appeared to be a carcinogenic potential for cadmium chloride after oral exposure in rats. This included cadmium-induced tumours in target sites of utmost human relevance such as the prostate. Cadmium exposure was also associated in this study with tumours of the testes and the hematopoietic system in rats (Waalkes and Rehm, 1992, ATSDR 1999).

Cadmium as $CdCl_2$ was given in drinking water at doses of 0, 25,100 and 200 ppm to groups of male rats (Noble rat, a strain known for its susceptibility to chemical induction of tumours of the prostate) observed for up to 102 weeks by Waalkes et al. (1999). At the lower doses of cadmium ($\leq$ 50 ppm), a dose-related increase in total proliferative lesions of the prostate (ventral and dorsolateral lesions combined) occurred. Authors observed also tumours of the adrenal gland (at 50 ppm) and proliferative lesions of the testes (significant increase in rats given 200 ppm) (Waalkes et al., 1999)

Summary

None but one of the studies in animals (Waalkes and Rehm, 1992) showed a cadmium-related significant increase in cancer when cadmium compounds were administered by the oral route. The early animal carcinogenicity experiments had however limited sensitivity because the maximum doses used were clearly below the maximum tolerated dose or because exposure duration was too brief. In some of these studies moreover, histopathological examination was limited in terms of number of animals and tissues.

Waalkes and Rehm (1992) reported an oral study, suggestive of carcinogenic activity of cadmium. Cadmium chloride, given to rats in diet, was associated with large granular lymphocyte leukaemia and proliferative lesions of the prostate. Another neoplastic, but benign, effect was associated with dietary cadmium: interstitial cell adenomas in the testes.

No data has been found about a carcinogenic effect of cadmium oxide given orally. Because of its low water solubility and the consequently uneasy administration to the animals, this compound has rarely been tested by the oral route.

Inhalation route

The first carcinogenicity result for inhaled cadmium was reported from the long-term inhalation study of Takenaka et al. (1983), in which highly significant and concentration-dependent primary lung tumours were induced in rats upon exposure to $CdCl_2$. Even if this study did not use cadmium oxide or cadmium metal, it will be detailed here because it has been used to derive the cancer potencies by several reviewers (theoretical slope of the dose-response curve for cancer at low doses) of cadmium.

Four groups of 40 male Wistar rats were exposed to 12.5, 25 or 50 µg Cd/m^3 as cadmium chloride aerosol (mass median aerodynamic diameter: 0.55 µm) for 23 hours a day, seven days a week for 18 months. A control group of 41 rats was exposed to filtered air. Animals were observed for an additional 13 months, at which time the experiment was ended.

At the end of the experiment, the retained Cd contents in the lung ranged from 5.6 ± 1.0 to 10.4 ± 4.2 µg/g wet weight for the different Cd doses (determined on 24 animals, controls: < 0.03 µg/g wet weight)

Dead or dying animals have been autopsied as soon as possible after they were detected. The surviving rats were killed after 31 months. Histological examination was performed on all animals.

A dose-related increase in the incidence of malignant pulmonary tumours (mostly adenocarcinomas) was observed in cadmium chloride-treated rats: at a dose of 12.5 µg/m^3: 6/39 carcinomas were observed (15% of examined animals); at 25 µg/m^3: 20/38 (53%); at 50 µg/m^3: 25/35 (71%). For controls, incidence of carcinomas was 0/38 animals. Multiple pulmonary tumours were observed frequently, several tumours showed metastases or were regionally invasive. The incidence of adenomatous hyperplasia was also increased by cadmium treatment (Takenaka et al., 1983; IARC 1993).

Preliminary results of an experiment by Maximilien et al. (1992) indicate that cadmium does not behave as a strong initiator of lung tumours in adult rats. Three months old S.D rats were exposed to $CdCl_2$ at a concentration of 700 µg/m³ (5 hours per day, 5 days a week, for 1 month) and received in addition, intramuscular injections of 5,6-β-naphthoflavone (BNF), known to promote the induction of lung tumours rapidly and specifically after treatment with different carcinogens. No evidence of tumour initiation by cadmium was found (Maximilien et al., 1992).

Inhalation studies were also performed with CdO dust and fumes, in rats and other species. The studies are summarised in **Table 4.190**.

Table 4.190 Main characteristics of the inhalation studies with CdO

Species	Type of compound	Particle size	Dose	Frequency duration	Number of exposed animals	Reference
Wistar rat	CdO dust	1.4 ± 1.9 µm (MMAD)	60 µg/l of air	1 · 30 minutes	61	Hadley et al. (1979)
Wistar rat	CdO fumes	0.01 µm	10, 30 µg Cd/m^3	22 h/d · 7d · 18 months	40	Oldiges et al. (1989)
Wistar rat	CdO dust	0.2-0.5 µm (MMAD)	30,30[a],30[b] 90,90[c] µg Cd/m^3	22 h/d · 7d · 18 months or 11 months40h/w · 6 months	40	Oldiges et al. (1989) actualised in Glaser et al. (1990)
NMRI mouse	CdO dust CdO fumes	0.2-0.6 ± 1.6 µm (MMAD) n.d.	10,30,90,270 µg Cd/m^3 10,30,90 µg Cd/m^3	19 or 8h/d · 5d for up to14 months	48	Heinrich et al. (1989) Heinrich (1992)
Golden Syrian hamster	CdO dust CdO fume	0.2-0.6 ± 1.6 µm (MMAD) n.d.	10,30,90,270 µg Cd/m^3 10,30,90 µg Cd/m^3	19 or 8h/d · 5d for up to14 months	48	Heinrich et al. (1989) Heinrich (1992)

Number of exposed animals: number of animals in each exposure group,
n.d. Not detailed,
MMAD Mass median aerodynamic diameter,
a + Zn depleted diet,
b + 300 µg Zn/m^3,
c + 900µg Zn/m^3,
For further details: see IUCLID Cd- CdO

Rat

Hadley et al. (1979) found only one lung tumour (adenocarcinoma) among the 34 surviving rats (12 months) acutely exposed to a massive dose of CdO.

Several publications from the group Fraunhofer-Institut in Grafschaft (Germany) report the results of a series of experiments conducted with CdO dust or fumes.

Long term exposure of rats to cadmium oxide dust or fumes was reported to produce primary lung tumours and indications of lung toxicity in rats (seen by bronchio-alveolar lavage analyses performed after 3, 6, and 18 months of exposure and by flow cytometric measurements of the rat lung cell DNA). No clinical signs were observed, except dyspnoea in the last 1-2 weeks before death (Glaser et al., 1990).

Groups of Wistar rats were exposed to aerosols of cadmium oxide dust. Two groups received both zinc oxide dust and cadmium oxide dust. One group was exposed to CdO dust and received a Zn-depleted diet. Exposure was generally for 22 hours a day for seven days a week, although some groups received discontinuous exposure for 40 hours per week for 6 months. Histological examination was performed on all rats.

When CdO dust was continuously administered at 30 µg/m^3 Cd for 18 months, this aerosol was well tolerated as it was by rats discontinuously exposed to 90 µg/m^3 for 40 hours per week and 6 months. The continuous exposure to 90 µg Cd/m^3 of CdO dust was however so noxious that exposure had to be ceased.

Highly significant tumour rates were found after continuous exposure to > 30 µg Cd/m^3 and after discontinuous CdO dust exposure but not after continuous exposure to CdO fumes (10 µg/m^3) and to CdO dust (30 µg/m^3) combined with ZnO dust.

The portion of cell debris, considered by authors as a measurement of the respiratory cytotoxicity, was found to be increased after CdO dust.

No clear dose-effect relationship could be ascertained since exposure durations were shortened at high levels (90 µg Cd/m^3 as CdO dust) (Glaser et al., 1990).

Table 4.191 Results of lung tumours and of flow cytometric measurements after long-term CdO inhalation in Wistar rats (Glaser et al., 1990)

Type of compound	Dose of cadmium (µg/m^3)	Sex	Duration (months[a])		Animals bearing primary lung tumours/ animals examined	%	Portion of debris (%)*
			of exposure	of study			
Air	0	m/f	0	31	0/40	0	2.5 ± 0.5
CdO dust	30	m	18	31	28/39	72	6.3 ± 1.9[e]
		f	18	31	15/20	75	
	90	m	7	31	12/39	31	n.d.
		f	11	31	14/19	74	
	90[b]	m	6	31	4/20	20	
		f	6	31	3/20	15	
	30[c]	m	18	29	25/38	65	
CdO fumes	10	m	18	31	0/40	0	1.2 ± 0.2
	30	m	18	31	8/38	21	1.4 ± 0.3
CdO dust/ZnO dust	30/300	m	18	31	0/20	0	4.0 ± 0.4[e]
		f	18	31	0/20	0	
	90/900	m	18	31	8/20	40	6.8 ± 2.0[e]
		f	18	31	7/20	35	

m Male
f Female
* 8 male rats per group during the study
a Exposure was stopped when 25% mortality had occurred, and the study was terminated when 75% of the animals had died
b Discontinuous exposure for 40 hours per week
c Rats maintained on a zinc-deficient diet
e $p < 0.01$, student's t test for test groups versus controls

Except in males exposed to 90 µg Cd/m^3 CdO and 900 µg/m^3 zinc oxide, zinc oxide reduced the carcinogenicity of cadmium oxide.

Groups of rats exposed to cadmium oxide fumes (10 µg CdO/m^3, 30 µg CdO/m^3) had significantly lower lung tumour incidences than those seen in groups exposed to cadmium oxide dust using the same the exposures modalities. However, these animals had only about half the cadmium content in their lungs compared to animals exposed to the same concentration of CdO dust over the same period, attributed to a lower pulmonary deposition of the chain-like electric arc-generated fume particles (IARC 1993 reporting Oberdörster and Cox, 1989).

<u>Mouse</u>

Groups of female NMRI mice were exposed to cadmium oxide fumes and cadmium oxide dust. Exposure was planned for 19 or 8 hours a day, for five days a week and duration of exposure ranged from 6 to 69 weeks. Exposure was terminated in some groups when the mortality rates started to increase. A control group for each treated group was available. Duration of the study reached 71 to 107 weeks. A histopathological examination was performed on all animals.

The incidence of lung tumours was significantly increased in the groups receiving 30 and 90 µg Cd/m^3 as CdO fumes (29.6% versus 20% of tumour-bearing animals at 30 µg, 34.0% versus 14.6%, at 90 µg for exposed and controls respectively and in the group receiving 10 µg Cd/m^3 as CdO dust (26.1% versus 14.6%). However, this was not observed in the group given the highest dose of CdO dust (Heinrich, 1989, 1992). In six other groups receiving cadmium oxide dust at various concentrations, survival was significantly decreased and probability of dying with a lung tumour was greater than in the controls (by life-table analysis). The IARC Working Group noted the variable spontaneous lung tumour rate. No details were reported about the histopathological types of the tumours (IARC 1993).

Hamster

Groups of 24 female and 24 male Syrian hamsters were exposed to CdO at 10, 30, 90 or 270 µg/m³ as cadmium oxide dust or 10, 30 or 90 µg/m³ as cadmium oxide fumes for 19 or 8 hours per day on five days a week. Exposure was terminated when mortality started to increase; exposure times ranged from 13 to 65 weeks, and total experimental time from 60 to 113 weeks. A control group received filtered air.

Survival was reduced in 12 of the 19 groups of exposed male hamsters but none showed an increased incidence of lung tumours.

Histological examination was performed on all animals. Dose-dependent significant incidences of bronchioalveolar hyperplasia, thickening of septa, and proliferation of connective tissue were found with the Cd-compounds tested.

No carcinogenic effect could be demonstrated: only six of the 19 cadmium-exposed groups of hamsters had one, or in one case two, animal(s) with a papilloma or a polypoid adenoma of the trachea; one papilloma was also found in the control group (Heinrich et al., 1989; IARC 1993). The IARC Working Group noted the insensitivity of the hamster to induction of tumours of the lung in studies by long-term inhalation (IARC 1993, Heinrich et al., 1989).

The significant species differences observed in the pulmonary carcinogenicity of inhaled CdO raised the question about underlying mechanisms of cadmium carcinogenicity in the lung and about the relationship of the carcinogenic potency to the pulmonary dose of cadmium.

Oberdörster et al. (1994) hypothesised that rats and mice respond differently to inhaled CdO with regard to pulmonary inflammation and cell proliferative effects and with respect to inducibility of metallothionein which could exert a protective effect by sequestering cadmium (Oberdörster et al., 1994). To corroborate their hypothesis, they compared the basic pulmonary responses, including the induction of MT (metallothionein), after exposure of rats and mice to the same concentration of cadmium chloride (100 µg Cd/m³, mass median aerodynamic diameter: 0.4 ± 1.4 µm) in a subchronic inhalation study (6 hours/day, 5 days/week for a total of 4 weeks).

Major findings were that: (1) Normalised lung burdens (expressed as Cd per g lung tissue) showed that mice retained about twice as much Cd as rats did, which is consistent with their greater ventilation rate per unit body weight; (2) Mice responded with a significantly greater inflammatory reaction in their lungs than rats did when percent PMN in pulmonary lavages were compared (35.7% and 19.8% in exposed mice versus 2.0% and 0.6% in exposed rats 1 day and 28 days after exposure); (3) Cytoplasmic and lysosomal enzymes (LDH and β-glucuronidase) were significantly increased in the pulmonary lavage fluid of mice (data not shown), but not in rats; (4) A greater pulmonary metallothionein baseline level was present in mouse lungs; (5) Induction of metallothionein in lungs was different in rat and mouse, as revealed by histochemical staining of lung sections: a significant induction of MT was found in the epithelial cells of the conducting airways as well in the alveolar region in mouse lungs, but not in rats. The sequestration of cadmium by metallothionein could prevent the interaction of Cd with DNA, and be protective. Rats responded with an increased induction of MT in lavagable free lung cells, i.e., alveolar macrophages; however these seem not to be target cells in tumorigenesis and may not offer the necessary protection against the carcinogenic effects of inhaled cadmium. Authors concluded that the observed greater resistance of mice to the pulmonary carcinogenic effects of cadmium chloride (100 $\mu g/m^3$) may be at least in part due to the greater base-line metallothionein level in mouse lungs, as well the greater inducibility at relevant sites in mice when both species are exposed to the same inhaled Cd concentration.

Further investigations confirmed these observations and demonstrated several important differences in inhaled Cd dosimetry, base-line metallothionein, and exposure-response relationships between rats and mice exposed to $CdCl_2$ by inhalation (0, 30, 50, 150 $\mu g/m^3$ or 0, 10, 30, and 100 $\mu g/m^3$ for rats and mice respectively). Species differences appeared also when comparing pulmonary inflammatory response and pulmonary metallothionein: mice had a longer-lasting polymorphonuclear and metallothionein response compared to the rats. This could be related to the much longer pulmonary retention half-time of cadmium in the mice. Comparison of the dose-response curves indicated however that both species were similar with respect to metallothionein induction in total lung.

In conclusion, these studies demonstrated that rats and mice exhibited dose-dependent lung inflammatory responses and dose-dependent lung metallothionein induction after inhaled $CdCl_2$ exposure. However, the differences in induced and baseline pulmonary metallothionein levels in concert with localised metallothionein protein expression in airway epithelial cells may represent increased protection from pulmonary carcinogenicity of inhaled cadmium compounds in mice (Kenaga et al., 1996).

McKenna et al. (1996, 1997) also explored the basis of interspecies and strain differences in the lung carcinogenicity of cadmium by evaluating early events of lung injury and metallothionein induction in rodents. WF rats, DBA mice and C57 mice were exposed to 1 mg/m^3 CdO for 3 hours and lung injury was assessed by examining histopathology and cell proliferation (considered as an important risk factor for carcinogenesis). Metallothionein and Cd were determined in lavaged lungs and lavaged free lung cells at sacrifice immediately or at 1, 3, and 5 days after exposure.

Cellular proliferative response was greater in C57 mice than in DBA mice or in WF rats for three cell types (alveolar macrophage, type II cells, bronchiolar epithelial cells) what might represent higher susceptibility of this mouse strain to lung carcinogenesis. Baseline concentrations of metallothionein were similar across species and strains but marked differences were observed after CdO exposure. Significant elevations were found in all groups 1 day after exposure; thereafter the increase was much larger in DBA mice than in rats or C57 mice. The greater induction of lung metallothionein, which has been associated with Cd detoxification by lowering its bioavaibility, together with the lower cell proliferative response in DBA mice than C57 mice, might indicate higher resistance to pulmonary carcinogenesis by inhaled CdO in DBA mice (McKenna et al., 1996, 1997).

Finally, considering the appropriateness of the rat model for cadmium induced lung tumours in humans, Maximilien et al. (1992) stressed that following parameters may influence the potential for carcinogenicity and have to be considered before extrapolation to humans: rate of deposition in the compartments of the respiratory tract, direct penetration of particles into the target cells, retention in target tissues, fixation of metals by transport proteins, notably the inducible metallothioneins. Respiratory deposition in animals differs from deposition in man. The clearance of particles resulting from mechanical cleaning of the ciliated passages is undoubtedly slower in man than in rodents. Speciation at the level of the target cell, transporters (as they relate to solubility and susceptibility) are not well characterised. Localisation of the tumours is different in animals and humans, regardless the route of administration: practically all the tumours are found in peripheral locations in animals, in the regions of prolonged retention of particles of low solubility. In humans, the vast majority are bronchial and in the ciliated passages, which are quickly cleaned of particles deposited on the mucociliary escalator. All these concerns seem to warrant further investigations.

Summary: inhalation route

An unequivocal relationship between Cd exposure and lung cancer incidence was demonstrated in chronic inhalation studies in Wistar rats exposed to $CdCl_2$, CdO fumes and CdO dust. In two inhalation studies in rats, malignant lung tumours were produced by cadmium oxide dust and fumes at low levels of exposure for short duration. The lowest dose to produce carcinogenic effects was 30 µg Cd/m³ as cadmium oxide dust as well as cadmium oxide fumes. For $CdCl_2$, lowest dose to produce lung tumours in rats was 12.5 µg Cd/m^3. In mice, some groups exposed to cadmium oxide fumes or dust had increased incidences of lung tumours, but the spontaneous lung tumour rate was high and variable. No increase in the incidence of lung tumours was found in hamsters exposed to cadmium oxide fumes and dust. Some authors hypothesised that expression of metallothionein protein in the lung after inhalation of Cd differs between species thereby providing different degrees of sequestration of Cd and protection from its carcinogenic effects.

Other routes

Although not relevant for a human risk assessment, these additional routes will be reported here with their main characteristics because some experiments were conducted with cadmium oxide.

Intratracheal route

In 1984, Sanders and Mahaffey reported no evidence of lung cancers in rats given several intratracheal instillations of cadmium oxide (median diameter: 0.5 µm) suspended in saline solution at dose levels close to (75%) the LD_{50}. Rats were divided in 4 groups: a control group and three groups with one, two or three instillations of 25 µg cadmium oxide respectively. Animals were observed for up to 880 days and all were examined histologically. Cumulative cancer incidence was very similar in the control and exposed groups. There was however a slight increase in fibroadenomas of the mammary gland: 7% in the control group, and 16, 12 and 23% in the three exposed groups (CRC, 1986).

Groups of about 40 female Wistar rats received 20 weekly intratracheal instillations of cadmium oxide (total doses: 20, 60 or 135 µg/rat). Controls received saline solution only. Only the lungs and trachea were examined histologically. Cadmium oxide induced lung tumours: 20 µg/rat, 2/37 (5, 4%); 60 µg/rat, 2/40 (5, 0%); 135 µg/rat, 0/39 (0%). These results were not significant compared to the controls. Lung tumours induced were primarily adenocarcinomas (2/4), although one adenoma and one squamous-cell carcinoma were also observed (Pott et al., 1987)

Intramuscular or subcutaneous routes

Intramuscular or subcutaneous administration of metallic cadmium or other cadmium compounds can induce sarcomas at the site of injection.

Kazantzis and Hanbury obtained tumours in eight out of ten rats injected subcutaneously with 25 mg cadmium oxide suspended in physiological solution.

The injection was followed by an intense inflammatory reaction with ulceration of the overlying skin. Fibrosarcomas developed within one year at the site of injection. No visceral metastases were seen (Kazantzis and Hanbury, 1966).

An intraperitoneal injection of cadmium oxide in three of 47 Wistar rats induced peritoneal cavity tumours, described as sarcomas, mesotheliomas and carcinomas (no further details reported). In the control group (204 rats, injected with saline), five intraperitoneal tumours were observed (Pott et al., 1987 cited in IARC 1993).

Intramuscular or subcutaneous administration of metallic cadmium or other cadmium compounds can induce sarcomas at the site of injection.

Heath and Daniel (1964) injected 20 hooded rats intramuscularly with 14 or 28 mg cadmium metal powder (spheres of 1.7 µm ϕ, ellipsoids and rods of 85 · 50 µm and pyramids and irregular forms of 220 · 50 · 50 µm) suspended in fowl serum. Injection was followed by severe inflammation 3 days after injection (Heath and Daniel, 1962). Total duration of the study was 84 weeks. Of the 20 rats, 15 developed rhabdomyosarcomas with large area of fairly well differentiated fibrosarcomas. Some fibrosarcomas were seen which metastasised to lymph nodes (inguinal, axillary and prevertebral lymph nodes).

Furst et al. (1973) injected cadmium metal powder (3 mg) or cadmium powder (3 mg) associated with zinc metal powder (6 mg) in the right inferior portion of the rib cage of Fischer rats (N= 2 groups of ten rats). Animals were compared to a group of controls injected with saline. Treated animals became emaciated and lethargic. When animals became moribund they were killed and autopsied. In the group treated with cadmium alone, too few animals survived and no tumours were reported. In the ten rats treated with cadmium + zinc, three tumours were found in the pleural cavity and were diagnosed as mesotheliomas. In another group, zinc alone was injected (6 mg) and no tumours were observed (Furst et al., 1973).

Summary: other routes

Single or multiple subcutaneous injections of cadmium oxide caused local sarcomas in rats. An intraperitoneal injection of cadmium oxide induced peritoneal cavity tumours. Cadmium metal powder produced local sarcomas in rats following intramuscular administration, including some fibrosarcomas which metastasised. An intrathoracic injection of cadmium metal associated with zinc metal induced pleural cavity tumours. These studies are reported as supporting data because administration routes are not relevant for this human RA

Conclusions: carcinogenicity of cadmium metal and oxide in animals

While the discussion on the carcinogenicity of cadmium in humans is still ongoing, there seems to be an agreement about cadmium as an animal carcinogen.

Only one study reported an increase in cancer upon oral exposure to soluble cadmium compounds; no data were located for cadmium metal or cadmium oxide.

In contrast, strong evidence exists that inhalation of CdO (dust and fumes) or $CdCl_2$ can cause lung cancer in rats. Mice exposed to equivalent levels of cadmium oxide, had only marginally significant elevations in lung cancer, but the rate of lung cancers in control mice was variable and elevated. No evidence for lung carcinogenicity was found in hamsters, possibly due to lung damage and subsequent decreased survival at high doses.

Interspecies but also interstrain differences seem to play a role in the sensitivity to Cd-induced carcinogenesis. Intratracheal instillation of cadmium oxide caused no increase in lung tumours in rats, but did increase the incidence of mammary fibroadenomas. Cadmium oxide is a carcinogen in rats when injected locally at the site of injection. Cadmium metal powder is a carcinogen in rats when injected intramuscularly forming malignant tumours.

4.1.2.9.3 Studies in humans

Food-borne cadmium is the major source of exposure for most of the non-smoking general population. Occupational exposure to cadmium is mainly by inhalation but includes additional intakes through food and tobacco. Studies included in this RA are presented and commented below according to the type of population considered: the general population exposed essentially via the oral route to various cadmium compounds and the occupationally exposed workers, mainly exposed to cadmium oxide and cadmium metal by inhalation.

<u>Oral route</u>

The general opinion is that the carcinogenic risk due to cadmium (in general) is considerably lower following dietary intake compared to inhalation. However, some authors have suggested that cadmium exposure in the general population may be associated with cancer (e.g. prostate cancer) (Waalkes and Oberdörster, 1990).

Information on this issue may be derived from two sources:

a) mortality studies in populations considered to be exposed to high levels of Cd (e.g. Shipham, Japan) and

b) the comparison of cadmium values measured in tissue of healthy, control subjects with the values obtained in tumour tissue of cancer patients.

None of the considered studies did specifically refer to Cd or CdO and it is not possible to identify which Cd species are involved in the effects examined in the general population (oral route).

<u>a) Mortality studies in exposed populations</u>

A number of studies of cancer rates among humans orally exposed to cadmium have been published.

Cadmium reaching abnormally high amounts was discovered in stream sediment from the village of Shipham (United Kingdom) in the course of a national geochemical reconnaissance in 1969. Cadmium was part of the remains of an old zinc mine and cadmium concentrations in soil ranged from 11 to 998 ppm. Average garden-soil cadmium levels ranged from 2 to 360 µg/g. Estimates of dietary cadmium intake by villagers revealed an average of 0.2 mg per week (0.04-1.08). The major source of excess cadmium in the diet was home-grown vegetables. The populations living in 1939 in Shipham (N=501) and in a nearby control village (N=410) were followed for 40 years by Inskip and Beral (1982), who compared standardised mortality ratios (SMRs) for all-causes and specific-causes of death in both villages. There was no difference between the two populations in mortality from all causes. For no type of investigated cancer (bladder, prostate, ovarian, breast, lung, gastrointestinal), SMRs were significantly different in Shipham from that in the control village. Besides the limited number of subjects, a weakness of this study, as acknowledged by the authors, was the limited information available about each individual's exposure to cadmium (Inskip and Beral, 1982).

An extension of the follow-up of the Shipham cohort was published recently (Elliott et al., 2000). Mortality analyses included a total of 351 residents of Shipham and 260 Hutton residents. No clear evidence of health effects from exposure to cadmium was found. The limitations of this study are similar to those of the original study (no individual exposure assessment, broad diagnostic categories and small sample size).

Analysis of the Hospital Activity Analysis database for a four year period (1974-1978) showed that exposure to cadmium in the soil of Shipham was unlikely to be influencing hospital admission patterns (Philipp and Hughes, 1982).

The geographic distribution of elevated rates of prostate cancer incidence was shown to parallel the distribution of elevated cadmium concentrations in river water in different areas of Alberta (Canada). Industrial effluents and run-off water from agricultural land released into the rivers and the use of fertilisers derived from phosphate rock (rich in cadmium) were responsible for these elevated cadmium concentrations. Agricultural practices, water supply and the percentage of population drinking water from the river differed between the low- and high- risk (for prostate cancer) areas of the province. The city with the highest incidence of prostate cancer (53.2 cases per 100,000 population) had consistently higher mean cadmium concentrations in the samples taken (0.006 ppm in waste water, 0.27 in soil, 0.004 in flowing water) compared to the city with the lowest incidence (10.6 cases/100,000 population) where cadmium concentrations in the samples reached < 0.001 ppm, 0.19 and 0.001 ppm for waste water, soil and flowing water, respectively. This study does however not demonstrate the involvement of Cd since many associated factors could be at play (Bako et al., 1982, IARC 1993).

Mortality was assessed in four pairs of populations in cadmium-polluted and unpolluted areas from four prefectures in Japan during 1948-1977, where exposure to cadmium occurred in polluted areas through the ingestion of cadmium-contaminated rice. Average concentrations of cadmium in rice ranged from 0.2 to 0.7 ppm, while those in the non-polluted areas ranged from 0.02 to 0.1 ppm. These levels were estimated to have prevailed for more than 30 years. No difference was seen between the two areas in the mortality rates from cancers "all sites" or from cancers of the stomach or liver. The mortality rate from prostate cancer was significantly higher (standardised mortality ratio, SMR: 1.66, 95% CI not reported) in the polluted than in the non-polluted area of one prefecture, as was the incidence of hyperplasia of the prostate. No data were reported for respiratory cancers (Shigematsu et al., 1982, IARC 1993).

Kjellström and Matsabura (unpublished data, cited in CRC 1986) carried out a study similar to that by Shigematsu et al. (1982) including cohorts from a total of nine different polluted areas in Japan. Each polluted area was matched with one or several adjacent control areas for which there was no known cadmium pollution but where geographic and meteorological conditions were similar. Age-adjusted death from different causes among inhabitants of the two types of areas was compared. The overall cancer mortality was not significantly different between cadmium-polluted and non-polluted areas. Leukaemia, cancer of the bladder, cancer of the kidney and cancer of the prostate were, however, reported to be more common among male inhabitants of the polluted areas compared to male inhabitants of the non-polluted areas. Among female inhabitants of the polluted area (less likely to have been occupationally exposed to cadmium), there was an excess mortality by cancer of the kidney, cancer of the lung and cancer of the breast (Kjellström and Matsabura, unpublished data, cited in CRC 1986).

Table 4.192 Age-standardised mortality rate ratios (AMRR): inhabitants of Cd-polluted areas versus non-polluted areas (Kjellström and Matsabura, cited in CRC, 1986)

Type of cancer	AMRR	
	Males	Females
Leukaemia	160	98
Bladder	144	78
Kidney	136	233
Prostate	134	-
Lung	N.I.	117
Breast	-	114

N.I. No information available

It has to be mentioned that for these two studies (Shigematsu et al., 1982; Kjellström and Matsabura), the classification of exposure incited the CRC author's group to make some comments: the exposed cohorts comprised people living in "polluted areas" chosen for practical purposes from administrative areas of the prefecture, village, town where increased levels of cadmium in rice were known to have occurred. However, this did not preclude that all the people of the exposed areas had eaten contaminated rice and were actually exposed to more than normal amounts of cadmium. When only a relatively small proportion of the group could have been in fact exposed to any significant extent, there is a risk that any possible effect on the causes of death will be extenuated and impossible to prove statistically (CRC, 1986).

The selection of an appropriate control area involves some difficulties too: large differences in causes of death are known to exist in different districts in Japan and differences in e.g. the frequency in which autopsies are carried out between polluted and non-polluted areas, may invalidate comparisons (CRC, 1986).

Inhabitants of cadmium-polluted areas in Japan with elevated urinary retinol binding protein excretion had an observed mortality rate from malignant neoplasms not different from the expected rate (Nakagawa et al., 1987 cited in ATSDR 1999).

Campbell et al. (1990) reported analyses of a comprehensive cross-sectional survey of possible risk factors for primary liver cancer in 48 counties in China. County mortality rates were correlated positively with mean daily cadmium intake (0-90 µg/day) from foods of plant origin, as estimated by dietary surveys (Campbell et al., 1990 cited in IARC, 1993).

Overall, these epidemiological studies had no reliable estimates of individual doses and so had limited sensitivity to detect a carcinogenic effect (ATSDR, 1993).

Wulff et al. (1996) conducted a study in the northern coastal region of Sweden to assess the risk of cancer in children born to women living during pregnancy near a smelter producing lead, arsenic, copper, cadmium and sulphur dioxide. The study group including 30,644 children born between 1961 and 1990 was linked to the Swedish Cancer Registry. The observed numbers of cancers were compared with those expected, calculated on the basis of the national sex- and age-specific incidence rates in Sweden for the same years.

The results showed a non-significantly increased incidence of childhood cancer among the children born near the smelter (13 cases observed, versus 6.7 expected, standardised incidence ratio: 195, 95% CI: 88-300). To explain the slight increase of incidence, authors suggested that some confusion may have occurred, by e.g. parental smoking. Unfortunately, parental smoking data were available only for a small part of the children who developed cancer and only from 1982 and onwards. Authors concluded that no association could be found between the environmental pollution from the smelter in the area and childhood cancer (Wulff et al., 1996).

b) Comparison of cadmium values measured in healthy subjects and in carcinogenic tissue of cancer patients

Elevated cadmium levels have been found in blood, in liver and kidneys of patients with bronchogenic carcinoma (Morgan, 1970, 1971). Aim of the study was to define the nature and the possible significance of altered concentrations of cadmium and zinc in cases of neoplasias after the coincidental observation of such an association. Zinc and cadmium levels were determined on blood taken during life and on tissues obtained post-mortem and compared to levels encountered in control subjects. There was no history of occupational exposure for the majority of the patients. Data about smoking habits were not reported but it is likely that smokers were overrepresented in patients with lung cancer, which may contribute to explain the higher Cd Burden.

Cadmium concentrations in both renal and hepatic tissue taken from patients dying of bronchogenic carcinoma were significantly increased (3,513 μg/g and 254 μg/g in renal and hepatic ashed tissues versus 2,406 and 182 μg/g for cancer patients and controls respectively, $p < 0.01$). The authors stressed the possibility that the observed differences could reflect altered protein binding or metabolic processes and would have in themselves no significance (Morgan, 1970).

In a first investigation, Feustel et al. (1982) found a continuous increase of the cadmium concentration in the prostate tissue (from normal, adenomatous prostate to carcinomas). The authors conducted another study (Feustel and Wennrich, 1984) to obtain more information about the localisation of cadmium in cell fractions of normal and of pathologically changed prostate glands. Distinct differences in the Cd content in the nuclear fractions of malignant tissues compared to adenomyomatous and normal prostatic tissues were reported. Cadmium levels were the highest in the nuclear fractions of poorly-differentiated carcinomas. Authors concluded that the accumulation of cadmium could be one of the factors causing the disturbance in RNA synthesis occurring in carcinogenesis of the prostate (Feustel and Wennrich, 1984).

Other studies have showed clear evidence that cadmium levels were elevated in cases of prostate carcinoma. In Nigerian black men, prostate cancer cadmium levels were 25 times greater than in normal prostate tissue (Ogunlewe and Osegbe, 1989 cited in Waalkes and Rehm, 1994). In Caucasians residing in Great Britain, cadmium levels in resected prostates from patients with prostatic carcinoma were 25 times greater than in normal tissues obtained at autopsy (Habib et al., 1986 cited in Waalkes and Rehm, 1994). This was not reported by Lahtonen (1985), who found no differences in cadmium concentrations between malignant and normal prostate tissue in Finnish men (Lahtonen, 1985 cited in Waalkes and Rehm, 1994).

In their review, Waalkes and Rehm emphasised that several points have to be considered in the interpretation of these last studies: first of all, the concentrations of cadmium in the normal prostate gland can vary widely with specific anatomical localisation and thus, sampling may be a major source of variability from study to study. Furthermore, the neoplastic cell proliferation could have diluted cellular cadmium concentrations. Finally, the level of cadmium present in the tissues may reflect recent exposure as well as chronic accumulation. However, given the very long biological half-life of cadmium, the current tissue levels may well reflect long past exposure at least in part (Waalkes and Rehm, 1994).

Levels of cadmium were also determined in operated kidneys from 31 patients suffering from renal cell carcinoma (20 men and 11 women) and compared to the levels of cadmium found at autopsy in kidneys from 17 autopsied patients (9 men and 8 women) who died of non-malignant diseases. Cases and controls were of the same age and smoking habits were assessed for all subjects. No one of the subjects had been occupationally exposed to cadmium. The cadmium levels were higher in smokers and authors divided the whole material into never-smokers or ever-smokers in subgroup analysis, but difference between smoking cases and smoking controls did not reach statistical significance. It was concluded that cadmium in kidney was not associated with an increased risk for renal cell carcinoma (Hardell et al., 1994).

Exploring the role of environmental pollutants in the aetiology of breast cancer, Antila et al. (1996) analysed cadmium in breast-fat tissue of 43 breast cancer patients and in 32 healthy control subjects. In cancer patients, the adipose sample was taken from excised tissue as near to the malignant tissue as possible. As controls, breast-tissue samples were taken during post-mortem examinations from women who died of a sudden non-malignant illness or accidental fatality. Age did not differ significantly between the two groups. Smoking was more prevalent among the breast cancer patients (43%) as compared with the general figures for smoking among women in the country (Finland, 20%). Cadmium levels in breast samples were high in cases and controls and ranged widely (cases: 3.2 – 86.9 µg/g, controls: 0.1 – 160.4 µg/g), what authors attributed to a tight binding of cadmium in breast tissue possibly submitted to individual variability. Mean cadmium concentrations found in breast cancer patients (mean ± standard deviation: 20.4 ± 17.5 µg/g) did not differ significantly from that of the healthy controls (31.7 ± 39.4 µg/g). The association between Cd levels and smoking was only suggestive ($r = 0.228$) (Antila et al., 1996).

Summary and conclusions: oral route

Available epidemiological studies on a possible increase of cancer mortality subsequent to oral exposure to cadmium (generic, not specifically cadmium metal or oxide) did not report reliable estimates of individual doses and so had limited sensitivity to detect a possible carcinogenic effect. Classification of exposure and selection of appropriate control groups are two methodological problems met after analysis of these studies.

Cadmium concentrations were measured in carcinogenic tissues from cancer patients. Elevated levels were found in malignant prostate tissue compared with normal prostate tissue. Other groups of authors have reported elevated levels of cadmium in other neoplastic tissues but differences with healthy subjects failed to reach statistical significance or were attributed to other factors, e.g. the effect of smoking.

Overall, there is currently no evidence that cadmium (and by extension Cd metal or oxide) acts as a carcinogen following oral exposure.

Inhalation route

The relationship between occupational exposure to cadmium (in general) and increased risk of cancer (in particular, lung and prostate cancer) has been explored in a number of epidemiological studies.

Some early studies reported an increase in prostate cancer but the increases were small, and subsequent investigations found either no increases in prostate cancer or increases that were not statistically significant (ATSDR, 1999).

The only cancers in humans that are currently thought to be associated with inhaled cadmium are lung cancers. A statistically significant increase in mortality from lung cancer has been reported in some studies but not in others. It is unclear whether study results differ because of genuine exposure differences, because of factors unrelated to exposure (confounding factors, biases, etc.) or whether these differences are chance findings.

To shed some light on this question, the studies included in the present section were assessed with a check-list (see Section 4.1.2.1) and the final results evaluated with criteria of causality.

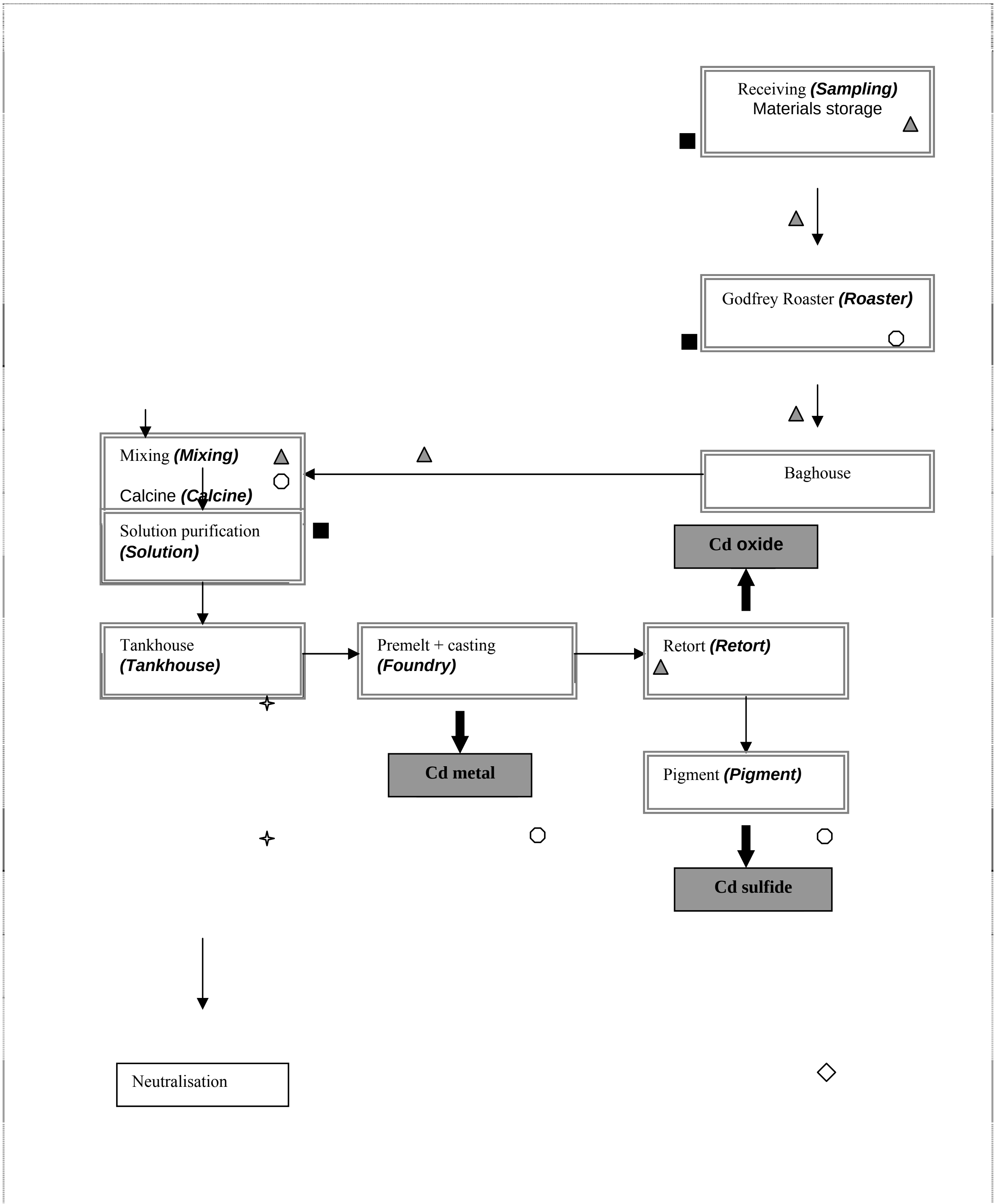
To take into account the differences in industrial conditions, considered exposures were classified into 4 broad types: 1) the recovery of cadmium from zinc refining; 2) the copper-cadmium alloy production as such; 3) the production of nickel-cadmium batteries; and 4) others.

1) Cadmium recovery plants

Seven studies which all concern the same study population have been conducted at a US recovery plant (Globe plant) and are summarised in **Table 4.195**. This plant has a history of activities: it originally began production as a lead smelter in 1880, switching to arsenic smelting about 1918. The plant ceased production of arsenic and began production of cadmium products about 1925. Then, the primary function of the plant has been to recover cadmium and a number of other trace metals from the precipitated dusts obtained as a by-product of pollution control at non-ferrous smelters, especially zinc smelters. The facility is reported as unusual in having a prolonged period of process with workers exposed predominantly to cadmium (Thun et al., 1985).

Cadmium production was performed in a complex of ten buildings and a flow-sheet is reported here to illustrate the process and the involved cadmium compounds. Cadmium entered the process as CdO dust and each shipment of raw material was assayed for its cadmium content when received. The cadmium-bearing materials were roasted, mixed with sulphuric acid, calcined, and dissolved in a sulphuric acid solution that was purified by precipitation and filtration. Highly purified metal was plated out of the solution in an electrolytic refinery (tank-house), melted and cast into shapes at the foundry. Some of the metal was reoxidised in gas-heated retorts to make high purity oxide, and some re-dissolved in sulphuric acid and treated with hydrogen sulphide to make yellow cadmium sulphide pigment. Each phase of the process was performed in a physically isolated building or section of a building (Smith et al., 1980).

Figure 4.6 Flow diagram of operations at the Globe plant (adapted from Varner et al., 1983 and Smith et al., 1980)



Jobs/work areas designation used for exposure assessment are indicated between brackets

Exposures to cadmium oxide dust (▲) occurred during sampling, loading, transporting of dust between roasting, mixing, and calcine operations, and during the loading of the purified oxide. Exposure to cadmium oxide fumes (○) occurred during the roaster, calcine, retort, and foundry operations. Exposures to cadmium sulphate (–✧–) occurred during the solution and tank-house operations (Smith et al., 1980). Exposure to cadmium sulphide (◇) occurred only in the pigment department.

Workers who unloaded, roasted and calcined feedstock were also exposed to arsenic (■).

Cadmium exposures in the different departments have been estimated by Smith et al. (1980). Consideration has been given to 1367 area measurements (static samples) carried out in the period 1943-1976.

Table 4.193 Cadmium measurements (mg/m3) by work area (Smith et al., 1980)

Years	Sampling	Roaster	Mixing	Calcine	Solution	Tank-house	Foundry	Retort	Pigments
1943-'44	-	-	7.62 (1)	1.39 (7)	-	-	4.0 (3)	1.79 (8)	-
1945-'49	0.69 (2)	35.8 (20)	16.6 (3)	35.8 (20)	0.95 (4)	0.18 (3)	2.71 (9)	45.2 (14)	0.08 (2)
1950-'54	0.05 (2)	0.12 (3)	-	20.4 (14)	4.42 (12)	-	0.30 (4)	0.39 (54)	1.27 (2)
1955-'59	-	-	-	1.36 (119)	0.44 (35)	-	-	0.53 (75)	-
1960-'64	-	-	-	0.36 (23)	0.47 (19)	0.05 (50)	-	-	-
1965-'69	-	-	-	0.12 (92)	0.06 (105)	0.02 (72)	-	0.23 (30)	-
1970-'76	-	0.34 (72)	0.61 (44)	0.15 (102)	0.05 (47)	-	-	0.56 (253)	0.04 (42)
Total N samples	4	95	48	377	222	125	16	434	46

These area sampling data were adjusted to estimate personal exposures (personal monitor measurements from 1973-1976 were used to determine the ratio between area - and personal sampling). Personal exposure estimates were then adjusted for the effect of respirator usage to obtain estimates of inhalation exposure (Smith et al., 1980a; Smith et al., 1980b; Sorahan and Lancashire, 1997).

These estimates were used in most of the studies (Thun et al., 1985; Stayner et al., 1992; Lamm et al., 1992; Sorahan and Lancashire, 1997) to construct a job-exposure matrix.

Table 4.194 Estimates* of cadmium inhalation exposures (mg/m3) by plant department and time period (Smith et al., 1980)

Years	Sampling	Roaster	Mixing	Calcine	Solution	Tank-house	Foundry	Retort	Pigments
Pre-1950	1.0	1.0	1.5	1.5	0.8	0.04	0.8	1.5	0.2
1950-54	0.6	0.6	0.4	1.5	0.8	0.04	0.1	0.2	0.2
1955-59	0.6	0.6	0.4	1.5	0.4	0.04	0.1	0.2	0.04
1955-'59	0.6	0.6	0.4	0.5	0.4	0.02	0.1	0.2	0.04
1960-'64	0.6	0.6	0.4	0.15	0.4	0.02	0.04	0.2	0.04

* Adjusted for personal exposure and respirator usage

Measurements of cadmium in urine were reported by Thun et al. (1985) and were available for 261 members of their cohort (43%). These measurements were obtained periodically by the company on production workers since 1948 but were reported as "representative" only of workers employed beyond 1960. The urine levels suggested a highly exposed population (reported as cumulative distribution of the median levels) and provided an index of group exposure: 81% of workers for whom urine cadmium levels had been measured had a median urine cadmium of at least 20 µg/l. Because of the small number of samples for most workers (median 2 samples/person), these urine levels could not been used to measure individual exposure in the study (Thun et al., 1985).

The question of other simultaneous exposures and in particular exposure to arsenic has been examined in most of the studies conducted in this setting. On one hand, the plant had facilities to produce small amounts of lead, arsenic, thallium and indium. These operations were reported to be performed "sporadically" or "at intervals" by a few individuals in three isolated buildings (Smith et al., 1980). On the other hand, substantial and widespread arsenic exposure occurred between 1918 and 1926 when the plant operated as an arsenic smelter. A second and continuing source of arsenic was the arsenic contamination from the incoming feed material, even after 1926 (Thun et al., 1985). The proportion of arsenic in the feedstock ore used in the smelter was reported to be ≥ 50% before 1926, about 7% in 1926-1927, 1.5-5.6% in 1928-1933, 1.9-3.7% in 1934-1940 and 1.0-2.0% after 1940. Summaries provided by Lamm et al. (1992) showed however that the annual mean percentage of arsenic in feed-stocks for the plant still ranged from 1-4% in the period 1940-58 (Lamm et al., 1992). Exposure to arsenic compounds was much higher in the early process departments. In 1950, airborne arsenic concentrations ranged from 300 to 700 µg/m³ (area sampling) near the roasting and calcine furnaces, the areas of highest exposure (see flow diagram). In 1979, arsenic exposures in those same areas had decreased to about 100 µg/m³ and personal exposures were lower due to respirator use. A survey in 1973 found 0.3 and 1.1 µg As/m^3 in the pre-melt department and 1.4 µg As/m^3 in the retort department (Thun et al., 1985). Urinary arsenic levels measured on workers in the high arsenic areas from 1960 to 1980 averaged only 46 µg/l, a level associated with an average inhaled arsenic concentration of 14 µg/m^3 by Pinto et al. (1977) (cited by Thun et al., 1985). These data are discussed in most of the studies considering the potential confounding effect of arsenic compounds for lung cancer.

In the examination of the dose-response relationship between lung cancer mortality and cadmium exposure, workers hired before 1926 were mostly excluded to minimise the contribution of arsenic exposure (indeed, the total study group included workers hired as early as 1902 with job assignments at many different operations at the site).

1940 has been used as surrogate for arsenic exposure by e.g. Stayner et al. (1992, 1993) as arsenic exposure was believed, from their data, to have drastically decreased after 1940.

Table 4.195 Cohort studies of lung and prostate cancer in workers exposed to cadmium at the cadmium recovery plant Globe plant (USA)

Reference	Follow-up period	Population, selection, lost cases	Exposure levels and categories	Prostate cancer (o/e)	SMR (95% CI) prostate	Lung cancer (o/e)	SMR (95% CI) lung	Considered confounders
Lemen et al. (1976)	1940- 1973	E: 292 (white M only) S: "who had achieved 2 years of employment between 01.01.1940 and 31.12.1969" Lost cases: 20	Overall (without categories) "in general, ranged below 1 mg/m³ ranged up to 24 mg/m³ during infrequent operations"	4/1.15	348 (94-891)	12/5.11	235 (121-410)	Smoking: N.I. Other simultaneous exposures: no
Varner (1983)	1940-1982	E: 625 (including F and black workers) S: "who were employed for a minimum of six months janitors and guards included" Lost cases: 11	Overall 0 – 4 5 – 15 16+ (mg Cd-years/m³)	5/N.I.	169 §	23£ 7 6 10	163 § 95 § 159 § 332 §	Smoking: yes Other simultaneous exposures: no
White (1985) cited by Lamm et al. (1992)	1940-1982	E: 646 (including F and black workers) S: "employed more than 6 months between 1940 and 1969" Lost cases: N.I.	-hired before 1940 -hired on or after 1940	N.I.	N.I.	11£ 10	244 § 78§	Smoking: N.I. Other simultaneous exposures: N.I.
Thun et al. (1985)	1940-1978	E: 602 (white M only) S: "who had worked more than 6 months between 01.01.1940 and 31.12.1969" Lost cases: 12	Overall -Hired before 1926 -Hired on or after 01.1926: ≤584 585-2,920 ≥ 2,921 (mg Cd.days/m³)	3/2.2	136	20/12.15 4/0.56 2£ 7 7	165 (101-254) 53 152 280 (113-577)	Smoking: yes Other simultaneous exposures: arsenic

Table 4.195 continued overleaf

Table 4.195 continued Cohort studies of lung and prostate cancer in workers exposed to cadmium at the cadmium recovery plant Globe plant (USA)

Reference	Follow-up period	Population, selection, lost cases	Exposure levels and categories	Prostate cancer (o/e)	SMR (95% CI) prostate	Lung cancer (o/e)	SMR (95% CI) lung	Considered confounders
Stayner et al. (1992)	1940-1984	E: 606 (white M only) S: "all hourly employees and foremen who had worked for at least 6 months in a production area of the facility between 01.01.1940 and 31.12.1969…and first employed at the facility on or after 1.1.1926" Lost cases: 12	Overall ≤584 585-1,460 1,461-2,920 ≥2,921 (mg Cd.days/ m^3)	N.I.	N.I.	24/16.07 2/5.73 7/4.28 6/2.75 9/3.30	149 (95-222) 34 163 217 272 (123-513)	Smoking: yes Other simultaneous exposures: arsenic
Sorahan and Lancashire (1997)	1940-1982	E: 571 (M only) S: "employed for at least 6 months as plant production workers between 1940 and 1969 and first employed after 1.1.1926" Lost cases: N.I.	< 400 400 – 999 1,000- 1,999 ≥ 2,000 (mg Cd.days/m^3)	N.I.	N.I.	6£ 6£ 4£ 5£	100 225 (72-702) 341 (66-872) 413 (121-1403)	Smoking: no Other simultaneous exposures: arsenic

E Exposed subjects,
S Selected from,
R Reference rates,
M Males,
F Females,
N.I. No information available,
N Number of subjects,
o Observed deaths,
e Expected deaths,
SMR Standardised mortality ratio,
95%CI Confidence interval,
Significant SMRs are reported in italics,
£ N.I. for expected number of deaths, only observed number was given in the publication,
§ Standardised cause ratio (SCR) (see text),
Considered confounders: yes, no,
± An attempt was made

Lemen et al. (1976) studied 292 male hourly paid workers exposed to cadmium fumes and cadmium dust for two or more years between 1940 and 1969 and followed from 1940 through to 1973. Employment histories were ascertained from company personal files. Lemen et al. (1976) reported cadmium concentrations in air, quantified in 1973 .Exposure to trace metals other than cadmium was considered insignificant because several refining processes and steps reduced drastically impurities in the ore, as determined by bulk sample analyses. However, arsenic concentrations of about 1 µg/m^3 were measured in 1973 in the premelt department, at the end of the process. 27 deaths from malignant neoplasms where observed whereas only 17.57 were expected: four were attributed to prostate carcinoma and 12 to lung cancer. The increased risk for respiratory tract cancer was demonstrated for each interval since onset of initial exposure, when workers were grouped in categories (2-14, 15-29, ≥ 30 years), with the greatest risk being apparent 30 years after initial employment. The relation between lung cancer and cumulative exposure to cadmium or other work-related exposures (like arsenic) was not examined (Lemen et al., 1976).

Varner (1983) and White (1985), of ASARCO Inc. (Owner of the cadmium-smelter plant) independently conducted a mortality study through 1982 including also non-white and non-male employees.

In the study of Varner, the study population (N=585) included janitors and guards because these individuals were considered to have been exposed to measurable, albeit low cadmium levels. Cumulative exposure values were calculated on the base of the measurements of intensity reported by Smith et al. (1980) (personal monitor measurements made from 1973 to 1976) and the categories/employment histories established by Thun et al. (1985). The resulting calculated cumulative exposures are based on the assumption that exposures over several decades have been consistent with the measurements made between 1973 and 1976. Authors stated that these cumulative exposures are overstated for recently-employed persons -because of the efforts of the company to reduce exposure- and underestimated for workers employed several decades ago. Mean length of exposure of the deceased employees was 11.2 years and latent period 27.6 years.

Results were reported by use of standardised cause ratios (SCR), calculated by dividing the observed numbers of death for each category or specific “cause of death” (according to the 7th ICD revision) by a calculated expected number of deaths. The latter was obtained by dividing the age-specific number of deaths attributable to each cause of death (extracted from the US vital statistics) by the normal number of deaths reported for that year in the age category related to the age at death of the deceased worker and summing up of the resultant for each cause of death. SCR were higher than expectation for lung cancer (N: 23) but not for prostate cancer (Varner, 1983).

White (1985) reported the mortality experience through 1982 for the cohort of production workers with more than 6 months employment between 1940 and 1969, including female and black workers (N=646). Analysis was stratified by date of hire prior to and after 1940. A significantly increased risk of lung cancer (N=21) was demonstrated in those hired prior to 1940 (11 cases) and no increased risk among those hired 1940 or later (10 cases) was found. All the cadmium exposure measurements on which Lemen et al. (1976) from the NIOSH had relied on were obtained during the period for which the corresponding “period-of-hire” cohort showed no increased lung cancer risk. White concluded that the attribution of pulmonary carcinogenicity to inhaled cadmium was incorrect (White, 1985, cited by Lamm, 1992).

Thun et al. (1985, 1986) extended the follow-up of the cohort described by Lemen et al. (1976) for an additional 5 years: the vital status of the workers was determined in 1978. The study population was expanded to include 257 more workers with brief (6-23 months) employment.

The total study population comprised thus 602 white males who had been employed at this cadmium production plant between 1940 and 1969 for at least 6 months. Only the workers hired on or after January 1926 were included in the mortality analyses (N=576) and the cohort was limited to the cadmium production workers The requirement of production-area employment excluded several guards, office workers and office area janitors who had been included in the Lemen et al. (1976) and the ASARCO's studies.

For each worker, cumulative exposure (mg.days/m^3) to cadmium was calculated according to the length of employment and jobs within the plant and computed as the sum of the number of days worked in a given job category multiplied by the average inhalation exposure (data from Smith et al., 1980) of that category for the relevant time period. "Job categories" were used as exposure categories rather than the "departments" because many of the personnel records specified general work categories rather than single departments. Seven broad job categories were established: e.g. category 1 included production work in any of the 6 high exposure departments (sampling, roasting and bag house, mixing, calcine, foundry, retort); category 2 included production work in the solution, tank-house and pigments departments.

No additional death from prostate cancer had occurred during the extended follow-up. As the cohort was limited to cadmium production workers, one of the four prostate cancers observed by Lemen et al. (1976) was excluded from the analysis (guard). The remaining three deaths from prostate cancer occurred among workers with two or more years of employment and with 20 or more years of latency.

The excess of malignant respiratory disease, noted previously by Lemen et al. (1976) persisted during the expanded observation period. Eight new deaths from respiratory cancer were identified, all among workers with over 2 years employment.

To analyse lung cancer mortality by cumulative exposure, authors classified the cumulative exposures of the 576 workers hired after 1926 into three categories (≤ 584, 585-2,920, ≥2,921 mg.days/m^3). These categories were defined a priori on basis of regulatory standards and on the assumption that such standards are intended to protect a worker over a 40-year working lifetime (e.g. a worker with 40 years exposure to the proposed NIOSH-TWA (40 µg/m^3) would have a cumulative exposure of: 40 years · 365 days · 40 µg = 584 mg.days/m^3, 40 years exposure at levels above the NIOSH TWA but within the OSHA 200µg/m^3 PEL would result in a cumulative exposure of up to 2,920 µg.days/m^3 worker).

The central finding of the study was a dose-response relationship between lung cancer mortality and cumulative exposure to cadmium (see **Table 4.196**).

Table 4.196 Lung cancer mortality by cumulative exposure to cadmium, workers hired after 01.1926 (Thun et al., 1985)

Cumulative exposure (mg-days/m^3)	40-year TWA equivalent	Deaths	SMR	95% CI
293- 584*		N.I.	100*	N.I.
≤ 584	≤ 40 µg/m^3	2	53	N.I.
584 – 2,920	41-200 µg/m^3	7	152	N.I.
≥ 2921	≥ 200 µg/m^3	7	280	113 – 577
U.S. white males		-	100	

* Cited by authors, detailed results not available

N.I. No information available Significant SMRs are reported in italics

However, the excess of deaths was statistically significant only for the stratum of workers whose cumulative exposure exceeded 2,920 mg-days/m³ (or 8 mg-year/m³), the level corresponding to a 40-year exposure above the OSHA limit (200 µg/m³).

The excess of lung cancer mortality did not increase with length of employment beyond 2 years: workers employed for 2-9 years, 10-19 years, and 20 or more year all showed approximately twice the number of deaths from lung cancer as expected from the U.S rates (**Table 4.197**) (Thun et al., 1985).

Table 4.197 Lung cancer mortality by duration of employment, workers hired on or after 01.1926 (Thun et al., 1986)

Duration of employment	Deaths	SMR
6-23 months	0	-
2-9 years	9	225
10-19 years	3	196
20+ years	4	273
U.S. white males	-	100

As stated by the authors, the observed excess of deaths from respiratory cancer could be due either to a true causal relationship between cadmium and lung cancer, to bias (effect of uncontrolled confounding), or to chance. Cigarette smoking and exposure to arsenic were considered as possible confounders and explored:

Individual smoking histories were collected from medical records and from a questionnaire survey mailed to surviving workers. Data were available for 49% (297 subjects) of the cohort. Cigarette smoking habits were computed and compared to the habits of the U.S. white male population for the same moment (1965, the earliest year that data are available for the U.S. white male population). As shown in **Table 4.198**, smoking habits were different in the two considered populations: cadmium workers were smoking less.

Table 4.198 Cigarette smoking habits 1965 (Thun et al., 1986)

	Non-smokers	Moderate smokers(1-24/day)	Heavy smokers(25+/day)	Rate ratio of smokers relative to U.S.
Cadmium workers	48.4%	40.8%	10.8%	0.70
U.S. male population	27.1%	53.0%	20.0%	1.00

The authors used a technique to estimate the change in the SMR likely to result from disparities in cigarette smoking (Axelson adjustment)*. The information required to compute this included the cigarette smoking habits (in terms of intensity of smoking, duration of smoking was not asked) of the exposed workers, comparable information for the comparison group and the relative risk for lung cancer associated with each level of smoking.

*Axelson's adjustment: In an attempt to evaluate quantitatively the confounding effect of smoking with regard to lung cancer, Axelson (1978) suggested the use of following model in occupationally exposed cohorts: $I = R\ I_o\ P_{CF} + I_o\ (1-P_{CF})$ where R: risk ratio, I: overall incidence of the illness in the overall population, P_{CF}: the proportion of the population with the factor in question, I_o: the incidence among those without the risk indicator. Using this model and assuming 2 different risk levels for smokers, i.e. 10 times and 20 times that of non-smokers for "moderate" and "heavy" smokers respectively. **Table 4.199** may be constructed.

Table 4.199 Cigarette smoking habits and Axelson's adjustment

	(NS) (1x)	(MS) (10x)	(HS) (20x)	Rate ratio of overall population (exposed or referents) vs. Non-smokers (I/I_o) $I: P_{NS}(1).I_o + P_{MS}(10).I_o + P_{HS}(20).I_o$
Exposed (N=250)	48.4	40.8	10.8	6.724
US reference population	27.1	53.0	20.0	9.571

NS Non-smokers,
MS Moderate smokers (1-24 cigarettes a day),
HS Heavy smokers (25+ cigarettes a day)

Because the cadmium workers smoke less, they would be expected, to have 30% fewer deaths from lung cancer than US males after adjustment. Instead, cadmium workers appeared to have more deaths from lung cancer. If SMR in the cadmium cohort was adjusted to reflect the lower levels of tobacco smoking, an overall SMR of about 250 would be found, compared to 176 (SMR for lung cancer in the cadmium cohort). Thun et al. (1986) stated that the important finding is that relatively lower smoking in this population of workers caused the study to underestimate the effect of cadmium and not to overestimate it.

The authors concluded that cigarette smoking alone was unlikely to account for the increase in deaths from lung cancer among the cadmium workers.

The authors addressed also the question of the extent to which exposure to arsenic could be held responsible for the excess of lung cancer observed in the cohort. When they stratified the cohort into workers employed before and those first employed on or after January 1, 1926, they observed a significantly elevated lung cancer mortality among the workers hired before 1926: the rate of lung cancer mortality among the 26 workers employed before 1926 was nearly 6 times the U.S rates (4 deaths observed, versus 0.56 expected, SMR: 714, 95% CI: 195-1829).

Authors estimated the number of lung cancer deaths attributable to arsenic by assuming a) an average airborne arsenic exposure of 500 $\mu g/m^3$ in the “high-arsenic work areas” during the years of this study, b) a respirator protection factor of 75% and c)an estimated 20% person-years of exposure spent in high-arsenic jobs, based on personnel and biological monitoring data. Average inhalation exposure would be 25 $\mu g/m^3$. As the workers hired after 1926 were employed for an average of 3 years, they acquired 1,728 person-years of exposure to 25 $\mu g/m^3$. Such an exposure should result in no more than 0.77 lung cancers, on the basis of a risk assessment model developed by the OSHA (1983) (Thun et al., 1985, 1986).

Authors concluded that arsenic alone did not appear to explain the observed excess of deaths from lung cancer (Thun et al., 1985).

Stayner et al. (1992) performed a quantitative and updated assessment of lung cancer risk based on the data from the historical prospective study conducted by Thun et al. (1985). Study population consisted of 606 workers employed for at least 6 months between January 1940 and December 1969 and vital status was successfully ascertained for approximately 98% of this cohort in December 1984. In order to minimise potential confounding by arsenic exposure, the analysis was restricted to workers who were first hired on or after January 1, 1926.

Exposure of the workers was assessed using the same cumulative exposure categories as Thun et al. (1985, 1986) relying on the same assumptions. Workers were classified into 4 groups by cumulative exposure (i.e., ≤ 584, 585-1,460, 1,461-2,920, and ≥2,921 mg.days/m^3) and in three time-since-first-exposure-categories (i.e., < 10, 10-19, ≥ 20 years) The study findings were analysed using a modified life-table analysis to estimate standardised mortality ratios (SMRs) and various functional forms (i.e., exponential, power, additive relative rate, and linear) of Poisson and Cox proportional hazards models to examine the dose-response relationship. Separate life-table analyses were performed for Hispanics and non-Hispanics, as Hispanics have been reported to experience lower lung cancer rates than non-Hispanics. The mortality rate for white U.S. males was used in this analysis as the referent rate for both the Hispanic and the non-Hispanic workers.

The excess in mortality from lung cancer was consistent with that in the previous reports on this cohort. The extended period of follow-up resulted in the identification of eight additional lung cancer cases (N=24) and a slightly stronger overall estimate of lung cancer risk (SMR=149) for workers employed after January, 1, 1926 than previously reported by Thun et al. (1985, 1986).

Lung cancer mortality was not so significantly elevated for the entire cohort (SMR= 149, 95% CI: 95-222, p=0.076), but significant elevations in mortality were observed in the highest-exposure (≥ 2921 mg-day/m³) for the combined (Hispanics and non-Hispanics) cohort and for the three highest exposure groups for the non-Hispanic groups. A significant excess of lung cancer mortality was also observed among workers in the longest time-since-first-exposure category (≥ 20 years) for the combined cohort and for non- Hispanics (see **Table 4.200**).

Table 4.200 Lung cancer standardised mortality ratios (SMR), observed (Obs.), expected (Exp.) deaths stratified by cumulative exposure to cadmium and time since first exposure (Latency) and Hispanic ethnicity (Stayner et al., 1992)

Category	Non-Hispanic			Hispanic			Combined		
	Obs.	Exp.	SMR (95% CI)	Obs.	Exp.	SMR	Obs.	Exp.	SMR (95%CI)
Overall	21	9.95	211	3	6.12	49	24	16.07	149
Exposure (mg.days/m³) ≤ 584	1	3.35	29	1	2.38	42	2	5.73	34
585-1,460	7	2.64	265[a]	0	1.64	0	7	4.28	163
1,461-2,920	6	1.55	386[a]	0	1.2	0	6	2.75	217
≥ 2921	7	2.41	290[a]	2	0.90	223	9	3.30	272[a] (123-513)
Latency (years) < 10	0	0.41	0	1	0.28	363	1	0.69	145
10-19	2	1.41	142	0	1.00	0	2	2.41	83
≥20	19	8.13	233[b] (141-365)	2	4.84	41	21	12.97	161[a] (100-248)

a $p < 0.05$
b $p < 0.01$

The significant dose-response relationship previously observed by Thun et al. (1985) was also evident in this study. Hispanics were observed to have a deficit in mortality from lung cancer relative to the U.S. population and because the inclusion of Hispanic ethnicity had little effect on the estimated cadmium exposure coefficients in their regression models, authors concluded that Hispanic ethnicity was not a strong confounder in the analysis.

Two sources of bias were considered in the interpretation of the results:

The influence of cigarette smoking was considered by the modelling procedures used, relying on internal comparisons within the cohort as opposed to the external comparisons made with the U.S. population in the SMR analysis. The potential influence of smoking was further reduced by the inclusion of a parameter for Hispanic ethnicity in the regression models. Hispanics smoke fewer cigarettes per day than do non-Hispanics and Hispanic ethnicity was thus thought of as a surrogate for lower cigarette smoking in this analysis. As previously said, Hispanic ethnicity (and hence smoking) was not considered as a strong confounder in the analysis. Authors concluded that given the internal nature of their analysis and the control of ethnicity in the models, it seemed unlikely that residual confounding by cigarette smoking would have a large influence on the findings.

The other major potential source of bias was confounding by exposure to arsenic. This was already reduced, but not eliminated, by the exclusion of workers first employed prior to January 1926, when the plant functioned as an arsenic smelter. An indirect assessment of the potential for confounding by arsenic was presented by the authors, based on an analysis of time period first employed. Based on the declining percentage of arsenic in the feedstocks (see Thun et al., 1985, 1986), arsenic exposures experienced before 1940 were thought to be substantially higher than those in later years. However, an increasing dose-response relationship between cadmium and lung cancer persisted when the variable representing year of hire prior to 1940 (as surrogate for arsenic exposure) was added to the model: the estimated coefficient for cadmium exposure increased rather than decreased, contrary to what could have been expected if year of hire (or arsenic) was a confounder. In fact, the dose-response pattern was stronger in workers hired after 1940, indicating that the result was not likely to be due to exposure to arsenic (Stayner et al., 1992, ATSDR 1999, IARC 1993).

In a subsequent analysis, Stayner et al. (1993) performed an SMR analysis on the same cohort using US general population rates stratified by year of first employment, Hispanic ethnicity and cumulative exposure (**Table 4.201**). Although the numbers were small the lung cancer SMR appeared to increase with cumulative exposure for workers hired after 1940 as well as before 1940.

Table 4.201 Cumulative exposure and lung cancer in a nested case-control analysis (Stayner et al., 1993)

	Cumulative cadmium exposure (mg.days/m³)							
	< 584		585-1,460		1,461-2,920		≥ 2,921	
Group	**Obs**	**SMR**	**Obs**	**SMR**	**Obs**	**SMR**	**Obs**	**SMR**
Non-Hispanic								
Year for hire < 1940	0	0	1	184	1	204	7	381§§
Year for hire ≥ 1940	1	32	6	281§	5	470§§	0	0£
Hispanic								
Year for hire < 1940	-*	-	-	-	-	-	-	-
Year for hire ≥ 1940	1	42	0	0	1	82	2	246

* Only one Hispanic worker in this study was first employed before 1940
£ The expected number of deaths was 0.6
§ $p < 0.05$;
§§ $p < 0.01$

They also performed a nested case-control (50 controls per case) and yielded consistent results with their full cohort analysis. A significant linear trend with cumulative exposure was observed in both overall analysis and analysis restricted to workers first employed during or after 1940. A significant odds ratio was observed for all of the exposure categories except for the highest exposure category among workers hired during or after 1940 (only 2 exposed cases in this last group) (**Table 4.202**).

Table 4.202 Stratified case-control analysis including ± 50 controls per case matched on survival to the same age as the case

	Cumulative exposure to cadmium			
	< 584 OR (95% CI)	585-1,460 OR (95% CI)	1,461-2,920 OR (95% CI)	> 2,920 OR (95% CI)
Overall	1.0	4.7§ (1.3,17.0)	8.8§ (1.5,52.5)	8.4§§ (1.8,39.5)
Year of hire≥1940	1.0	4.0§ (1.1, 15.0)	13.6§§ (2.3,80.3)	4.6 (0.4,48.8)

§ $p < 0.05$
§§ $p < 0.01$
OR Odds ratios
95%CI 95% confidence interval based on comparisons with the lowest exposure group

The IARC Working Group noted that the dose-response pattern was stronger in workers hired after 1940, indicating that the result was not likely to be due to exposure to arsenic (Stayner et al., 1993 cited in IARC 1993).

The studies by Thun et al. (1985, 1986) and Varner (1983) and White (1985) differed in a certain number of ways including cohort definition, analytical method, death certificate coding, and date-of-hire stratification. Lamm et al. (1988, 1992) merged the NIOSH demographic and work-history data tapes (of the Thun's study) and the ASARCO mortality data tapes (of Varner and White's study) and identified 599 of the 602 men in the NIOSH cohort and all of the lung cancer deaths. Using all the death certificates, authors observed that the workers hired prior to 1926 had an SMR for lung cancer mortality of 656, those hired from 1926 to 1939 an SMR of 283 and those hired from 1940 to 1969 an SMR of 88. This analysis revealed that lung cancer risk was dependent on the period of hire (Lamm et al., 1988, 1992).

In 1992, Lamm et al. presented a nested case-control analysis of the 25 cases of lung cancer known from death certificates through 1982, using three controls per case matched by age at hire and date of hire to the case. The objective was to examine the relative role of cadmium exposure when controlling for the period-of-hire risk factor, considered as a probable surrogate for arsenic exposure.

Cumulative cadmium exposure estimates were derived for each case and the three matched controls from job histories, using work category-time period exposure estimates developed by NIOSH et previously used in the Thun's study. Individual cumulative exposure estimates (expressed in mg.years/m^3) were used in this case-control study instead of the 4 cumulative exposure categories previously used by the NIOSH group (in mg.days/m^3). Cumulative exposures for employees in this study ranged from about 1 to 30 mg-years/m^3 for those hired prior to 1940 and from about 0.3 to 17 mg. years/m^3 for those hired subsequently.

The major finding of this study was that no difference could be observed between the mean cumulative cadmium exposure of lung cancer cases and the mean cumulative cadmium exposure of their date-of-hire, age-of-hire matched controls, either overall or within period-of-hire strata (**Table 4.203**).

Table 4.203 Relative cadmium cumulative exposure in cases and controls (Lamm et al., 1992)

Cadmium cumulative exposure (mg-years/m³)	Cases (N=25)	Controls (N=75)
Mean ± Standard Deviation of Mean	9.24 ± 7.46	9.29 ± 8.20

Calculations of the ratio of mean cadmium exposures of the cases and the controls were made for each of the three period-of-hire strata. The relative cadmium exposure ratio of the cases to the controls remained near unity for each of the period-of-hire strata (**Table 4.204**).

Table 4.204 Relative cumulative cadmium exposures for cases and controls, by period of hire (Lamm et al., 1992)

Period of hire	Mean cumulative cadmium exposure (mg.year/m³)		Relative ratio Cadmium exposure
	Cases	Controls	Cases/ Controls
< 1926	17.23	17.33	0.99
1926-1939		12.40	1.05
1940-1969	4.43	4.89	0.91
Total	9.24	9.29	0.99

This founding would suggest that the cumulative exposure, as assessed by the NIOSH's calculation technique was not a major determinant of lung cancer within the study group (Lamm et al., 1992).

Methodological issues (possibility of "overmatching", validity of the exposure assumptions and estimates, etc.) but also alternative aetiologies (cigarette smoking, arsenic exposure) were considered in an attempt to explain the differences of findings between this case-control study and the previous reported studies on the same cohort.

Overmatching: Authors matched cases and controls by age at hire and date at hire to increase the likelihood that subjects would not differ markedly in terms of unknown previous environmental, occupational, and personal risk factors that might be related to cancer risk.

Smoking histories were available for 72% (18/25) of the cases and for 75% (43/75) of the controls. According to Lamm et al., the cigarette smoking histories that had been obtained presented some difficulties with respect to consistency but were the same records as those that were previously used by both ASARCO's investigators and NIOSH (Thun et al., 1985, 1986) to assess the smoking habits of the cohort members. Subjects were classified as "ever smoker" or "never smokers". Only one of the lung cancer cases was known to be a non-smoker. For those for whom smoking information was available, odds ratio for smoking as a lung cancer risk factor was found to be 8.2 (95% CI: 1.04-367.05, $p < 0.05$), consistent with the accepted range of risk of lung cancer associated with smoking.

Cigarette was demonstrated to be a possible lung cancer risk factor in this study but there were insufficient data to assess whether it could explain the period-of-hire differences in cancer risk.

As individual arsenic exposure levels could not be determined, the arsenic concentrations in smelter feedstock ore were considered as a surrogate measure of arsenic exposure during the various time periods. Information concerning feedstock composition was asked to ASARCO and additionally from NIOSH, the same information that has been previously released to NIOSH by the company was obtained. The arsenic levels in the feedstock seem to have shifted similarly to the lung cancer risk (pre-1926 levels > 1926 to 1939 levels > 1940 to 1969 levels). Whether arsenic exposure is responsible for the excess lung cancer risk above smoking or whether it interacts synergistically with cadmium or with smoking could not be ascertained.

Authors concluded that the similarity in cadmium exposures for cases and controls strongly suggested that cadmium exposure, as defined by the NIOSH investigators, was not a major determinant of the lung cancer risk in this study population. Analysis of cigarette-smoking histories demonstrated the expectation that cigarette smoking was a significant lung cancer risk factor in the particular group of the lung cancer cases (in contrast to what was observed for the whole study population, see Thun et al., 1985). The previously described association with period of hire may also reflect continued arsenic exposure to airborne concentrations of 500 µg/m^3 from feedstock ores in excess of 1 to 2% arsenic concentration (Lamm et al., 1992).

Doll (1992, cited in IARC 1993) reviewed these two last studies (Stayner et al., 1992; Lamm et al., 1992) and noted that an explanation for the differences between the results could be that the two studies had only 21 cases in common. Lamm's population included four cases hired before 1926, excluded by Stayner et al. (1992) because they occurred in men hired before 1926. Three cases included by Stayner et al. (1992) were not reported by Lamm et al. (1992) because they died between 1982 and 1984 (analysis of the death certificates through 1982). The IARC Working Group noted that the methodological differences between the two studies might also account for the contradictory results reported (IARC 1993).

Sorahan and Lancashire (1994), in a short report, highlighted two problems about the quality of the data on job histories collected by Thun et al. (1985, 1986) and the estimated cumulative exposures to cadmium derived from the data used by Stayner et al.(1992), and Lamm et al. (1992). First of all, Thun et al.(1985, 1986) classified the worker's employment into general work categories (high cadmium exposure including production work in sampling, roasting/bag house, mixing, calcine, foundry and retort departments, medium cadmium exposure including production work in the solution, tank-house and pigments departments, and low cadmium exposure) rather than in departments. Sorahan and Lancashire (1994) pointed out that some misclassification may have occurred as it appeared that workers were assumed to be in the category high exposure employment unless the personnel records indicated something to the contrary. Moreover, this classification in departments becomes crucial in the adjustment for the effects of arsenic; exposure to arsenic compounds being much higher only in the departments involved in the early stages of the cadmium process (sampling, mixing, roasting, bag house, calcine, welders and burners).

Secondly, the investigators used the rather sparse information contained in service and personnel records, rather than consulting the very detailed time sheets which show for each month, how many hours each worker spent in different jobs (Sorahan and Lancashire, 1994).

In an attempt to rectify these issues, Sorahan and Lancashire (1997) reported an analysis making use of the detailed job histories, abstracted from the time sheet records. Analysis was restricted to 571 male workers first employed after 1 January 1926 and employed for at least six months between 1940 and 1969.

Individual estimates of cumulative exposures to cadmium were re-assessed and the potentially confounding role of an exposure to arsenic was again evaluated. Time sheet records were available for the period 1926 onwards and showed how many hours each day a worker spent in different jobs. A job dictionary was compiled from 600 job titles classified under one of 29 jobs and departments. For each cohort member, the principal job and department was selected as that in which the most hours were worked. Employment histories were abstracted for the period 1926-1976 and a useful comparison could be made between the original NIOSH data on job histories (defined as seven general work categories, see Thun et al., 1985) and these newly abstracted data on job histories (defined as 29 jobs and departments). Several misclassifications became visible: e.g. as no suitable category existed in the NIOSH scheme, 78.1% man-half-months of employment in the lead department (unconnected with the cadmium process) had been placed in the high exposure category in the NIOSH database.

The new data on job histories were also cross referenced with the existing job exposure matrix (from Smith et al., 1980) to provide an estimate of exposure to cadmium in mg. days/m³ for each half-month of employment. For each study subject, these estimates were summed over the entire job history to provide estimates of cumulative exposure to cadmium as a time dependent variable. These cumulative exposures were then grouped in categories (< 400, 400-999, 1,000-1,999, ≥ 2,000 mg.days/m^3), defined a priori on the basis of regulatory standards and on the assumption that such standards are intended to protect a worker over a 40-year working lifetime, as were the categories adopted by Thun et al. (1985) and by Stayner et al. (1992). It was assumed that a working year comprised of 250 days and time-weighted averages of 40, 100, 200 µg/m^3 were considered.

There was a significant positive trend between cumulative exposure to cadmium and risks of mortality from lung cancer.

Several variables were considered to have the potential for influencing mortality within this cohort: age attained at death or at follow up, year of starting employment, Hispanic ethnicity (as Hispanics have been reported to experience lower lung cancer rates than non-Hispanics), estimated cumulative exposure to cadmium, estimated cumulative exposure to cadmium in the presence of arsenic, ever being employed in the arsenic department. Data on smoking habits were not available for the entire cohort and available data on smoking were not incorporated into the analysis.

Table 4.205 shows the role of two potential confounding variables (year of hire, Hispanic ethnicity) on risk estimates for lung cancer. The left hand side of the table provides estimates of relative risk for different cumulative exposures to cadmium, year of hire and Hispanic ethnicity when these three variables are considered separately (Poisson regression) and the right hand side of the table provides similar estimates when the three variables are analysed simultaneously.

Table 4.205 Mortality from lung cancer by cumulative exposure with and without adjustment for two potential confounding variables(year of hire, Hispanic ethnicity) (Sorahan and Lancashire,1997)

		Separate analysis		Simultaneous analysis	
	N	RR§	95% CI	RR§	95% CI
Cumulative exposure					
< 400	6	1.0		1.0	
400-999	6	2.25	0.72 - 7.02	2.30	0.72-7.36
1,000-1,999	4	3.41	8.72	2.83	0.75-10.72
≥ 2,000	5	4.13*	1.21- 14.03	3.88*	1.04-14.46
Evaluation of trend$^{\pi}$		1.56*	1.06-2.28	1.58*	1.03-2.30
Year of hire					
1926-1933	3	1.0		1.0	
1934-1939	5	1.02	0.24-4.27	1.26	0.30-5.42
1940-1949	10	0.42	0.11-1.51	0.93	0.23-3.75
1950-1969	3	0.45	0.09-2.29	1.07	0.18-6.18
Hispanic ethnicity					
Yes	4	1.0		1.0	
No	17	2.73	0.92-8.12	2.68	0.81-8.85

* p < 0.05,
§ RR adjusted for six levels of age attained,
a Three variables: Cumulative exposure, Year of hire, Hispanic ethnicity,
π Relative risk for change in exposure of one level, obtained by treating cumulative exposure as a continuous variable.

Hispanic ethnicity and year of hire were not confounding variables in the analysis of risks of lung cancer and cumulative exposure to cadmium because the estimates of risk were little changed when simultaneous adjustment was made for Hispanic ethnicity or year of hire.

- A separate analysis was made for exposure to arsenic. As previously reported, exposure to arsenic was higher in the early cadmium process departments than in the other departments. **Table 4.206** shows the relative risks of lung cancer by levels of cumulative exposure to cadmium in three different occupational settings: departments with high exposure to cadmium (mainly CdO) and arsenic compounds (excluding the arsenic department), departments with high exposures to cadmium but minimal or no exposures to arsenic, and other departments.

A significant positive trend was found for risk of lung cancer and cumulative exposure to cadmium in the presence of high exposure to arsenic but not for cumulative exposure to cadmium received in the absence of high exposure to arsenic.

Table 4.206 Mortality from lung cancer by simultaneous analysis of four several aspects of occupational history (Sorahan and Lancashire,1997).

Cumulative	N	Cancer of lung	
Exposure to cadmium (mg-days/m³)#		RR£	95% CI
Department with high cadmium and high arsenic exposures (excluding arsenic departments)π			
< 200	11	1.0	
200-499	2	0.81	0.17- 3.82
500-999	2	1.83	0.36- 9.39
≥ 1,000	6	4.02*	1.34- 12.03
Evaluation of trend		1.54*	1.06-2.23
Departments with high cadmium and minimal or no arsenic exposureππ			
< 200	13	1.0	0.48-5.90
200-499	4	1.68	0.26-6.59
500-999	2	1.30	0.54-13.36
≥ 1,000	2	2.68	0.80-2.00
Evaluation of trend		1.26	0.80-2.00
Ever employed in the arsenic department			
No	20	1.0	0.63-167.0
Yes	1	10.25	
All other departments			
< 200	18	1.0	
200-499	2	0.97	0.19-4.91
≥ 500	1	0.45	0.04-5.35
Evaluation of trend		0.79	0.30-2.09

* $p < 0.05$

£ RR with simultaneous adjustment for six levels of attained age, four levels of year of hire and two levels of Hispanic ethnicity

π Calcine, mixer and screener, sampling, roasting, concentrated and dry dust, welder and burner

ππ Solution (operator and pressman), solution (charger), pigment (gasman), pigment (other operator), tank house and electrolytic, retort, caster, crushing

\# Cut-off values for exposure categories were set (by Sorahan and Lancashire) to be 50% of those used in other tables of their paper

The role of the variable “ever employed in the arsenic department” was also considered but there was only one death in one of the two categories of the variable.

A significant positive trend was also found for risk of lung cancer and cumulative exposure in the presence of high exposure to arsenic, including the arsenic departments (**Table 4.207**).

Table 4.207 Mortality from lung cancer by simultaneous analysis of four several aspects of occupational history) (Sorahan and Lancashire,1997)

Cumulative	N	Cancer of lung	
Exposure to cadmium ($mg\text{-}days/m^3$)#		RR£	95% CI
Department with high arsenic exposures$^{\pi}$ (including arsenic departments)			
< 200	10	1.0	
200-499	3	1.29	0.34-4.83
500-999	2	1.92	0.38-9.75
≥ 1,000	6	3.85*	1.28-11.56

* $p < 0.05$
£ RR with simultaneous adjustment for six levels of attained age, four levels of year of hire and two levels of Hispanic ethnicity
π Calcine, mixer and screener, sampling, roasting, concentrated and dry dust, welder and burner
Cut-off values for exposure categories were set (by Sorahan and Lancashire) to be 50% of those used in other tables of their paper

A limitation of the study, according to the authors, is the lack of independent evidence of the reliability of the individual estimates of cumulative exposure to cadmium (no evidence was provided by a comparison of these estimates with *in vivo* measurements of cadmium in liver, for example).

Analysis was also limited (as in the other studies) by the non-availability of follow-up for the workers employed before 1940. One may conceive that only a small proportion of these employees first employed in the 1920s appear in the cohort as defined in 1997.

Finally, estimates of exposure to cadmium did not all refer to cadmium oxide (fumes or dust). Exposures in the solution and tank-house departments refer mainly to cadmium sulphate mist and exposures in the pigment department refer mainly to cadmium sulphide dust. These latter exposures tended to occur in the absence of high exposure to arsenic compounds whereas exposures to cadmium oxide tended to occur in the presence of high exposure to arsenic trioxide.

In conclusion, there was a significant positive trend between cumulative exposure to cadmium and risks for mortality from lung cancer. Adjustment was made for age attained, year of hire and Hispanic ethnicity but not for smoking. Several hypotheses were, however, identified as possibly consistent with the study findings: a) cadmium oxide in the presence of arsenic trioxide is a human lung carcinogen; b) cadmium oxide and arsenic trioxide are human lung carcinogens and cadmium sulphate, cadmium sulphide are not (or are less potent) (as no significant positive trend was found for risk of lung cancer and cumulative exposure to cadmium in the departments where exposure to Cd sulphate and sulphide occurred); or c) arsenic trioxide is a human lung carcinogen and cadmium oxide, cadmium sulphate, cadmium sulphide are not (from findings reported in **Table 4.207**). Because there were only 21 deaths from lung cancer available for this analysis, it was, according to the authors “impossible to gauge which, if any, of the above hypotheses is correct” (Sorahan and Lancashire, 1997).

Discussion and conclusion: cadmium recovery plants

The ideal "critical" study would have used a detailed and reliable exposure assessment, identified all subjects diagnosed with lung cancer and taken Hispanic ethnicity, year of hire, smoking and arsenic exposure into account. Although no study meets all these conditions, the investigation conducted by Sorahan and Lancashire (1997) appears to be the most convincing.

Alternative aetiologies proposed for the reported excess of lung cancer are the exposure to arsenic at the plant and cigarette smoking:

A dose-effect relationship between arsenic exposure and lung cancer could not be investigated as no detailed job exposure matrix for arsenic compounds is available at present. However, it should be stressed that exposure to arsenic has continued well after the plant ceased operation as an arsenic smelter and that the time changes of exposure to arsenic - estimated as arsenic levels in the feedstock - seem to have shifted parallel to the lung cancer risk (pre-1926 levels > 1926 to 1939 levels > 1940 to 1969 levels) (Lamm et al., 1992). These findings are compatible with a co-carcinogenic activity of cadmium.

A bias due to smoking remains imaginable and could not be definitively ascertained as no sufficient, complete and consistent information on smoking habits was available.

Moreover, discrepancies between the results may also be explained by methodological differences (in the characterisation of exposure (to cadmium and to arsenic), and/or in the coding of lung cancer, the selection of the studied population etc.). Finally, the relatively small number of cases of lung cancer does not allow excluding the uncertainties related with small groups (broad confidence intervals, low level of significance, etc.)

Taken together, all these weaknesses are, however, not strong enough to refute the cadmium-as-causal factor hypothesis, but suggest other compatible explanations. As stated by Sorahan and Lancashire (1997), confident interpretation of the data from this plant may become possible when further follow-up data become available and a quantitative job exposure matrix for arsenic compounds could be integrated in the analysis.

2) Copper-cadmium alloys plant

Three studies were conducted at the same two UK plants and concern all the same population (Holden 1980a, Holden 1980b, Sorahan et al., 1995). Kjellström et al. (1979) investigated a copper-cadmium alloy plant located in Sweden. These studies are summarised in **Table 4.208**.

Typically, the manufacture of cadmium alloys consists of the addition of metallic cadmium to the molten metal(s) with which it is to be alloyed and after thorough mixing, the resultant alloy is cast into the desired form (ingot, wire, rod) (IARC, 1993). At the UK plants studied by Holden and Sorahan, the manufacture of the alloys included the production in a first step, of a master alloy (50:100 or 50/50 mix of Cd and Cu) by the addition of metallic cadmium to melted copper at a temperature of 1,100°C. As cadmium metal boils at 767°C, there is a considerable evolution of cadmium oxide fumes during this process. Both mixing and casting stage involve high production of cadmium fumes. In factory A, the master alloy was made at one end of the workshop in one coke fired pit furnace and the final copper cadmium alloys were produced at the other end of the shop. In the middle, induction furnaces were used to manufacture brass and bronze. In factory B, the cadmium alloy department was located 22 years long (1940-1962) at one end of a large building containing three large copper furnaces and casting wheels. Arsenical copper, bronze, phosphor bronze and silver bronze were cast in the central area of this workshop. The manufacture of arsenical copper was obtained by adding bags of arsenic trioxide to the molten copper and stirring manually what resulted in the evolution of dense white clouds of arsenic oxide fumes. Workers from the copper cadmium alloy operated some 60-80 m away. Exposure to silver, nickel was also reported to occur. One may conceive that the “cadmium workers” were also exposed to these substances however no quantitative information about these simultaneous exposures is available. In 1957, the production of the master alloy (50:50 Cu and Cd) was installed in an enclosed casting box and in 1962, production of master and final alloys were moved to a separate room (Holden, 1980a, 1980b, Kazantzis and Blanks, 1989, Sorahan et al., 1995). Factory B also included iron and brass foundries where workers were exposed to considerable amounts of other chemicals, including polycyclic aromatic hydrocarbons (Sorahan et al., 1995).

Table 4.208 Cohort studies of lung and prostate cancer in workers exposed to cadmium at copper-cadmium alloy plants

Reference	Follow-up period	Population, selection, lost cases	Exposure levels and categories	Prostate cancer (o/e)	SMR (95% CI) prostate	Lung cancer (o/e)	SMR (95% IC) lung	Considered confounders
Holden (1980a)	1940-1978	E: 347 (M only) D: ”who had been employed for at least 12 months between 1922 and 1978” Lost cases: E: 13 (+ 4 emigrated)	before 1953: > 1 mg/m³ 1953-1957: < 0.15mg/m³ since 1957: < 0.05 mg/m³	1/1.58	63 (1-352)	10/12.35	81	Smoking: N.I. Other simultaneous exposures: no
Holden (1980b)	1940-1979	E: 347 (M only) D: ”who had been employed for at least 12 months between 1922 and 1978” + 624 vicinity workers (M only) Lost cases: 25 (+ 27 emigrated)	before 1953: > 1 mg/m³ 1953-1957: < 0.15mg/m³ since 1957: < 0.05 mg/m³	1/1.58 8/3.0	63 (1-352) 267 (115-526)	10/13.14 36/26.08	76 138 (97-191)	Smoking: N.I. Other simultaneous exposures: no
Sorahan et al. (1995)	1946-1992	E: 347 (M only) D: “who had been employed for at least 12 months between 1922 and 1978” + 624 vicinity workers (M only) Lost cases: 26 (+ 27 emigrated)	1947-1954: 0.24 mg/m³ 1955-1962: 0.21 mg/m³ 1963-1972: 0.16 mg/m³ 1973: 0.085 mg/m³ since 1974: < 0.06 mg/m³	2/2.83 N.I.	71 (9-255) N.I.	18/17.8 55/ 34.3	101 (60-159) 160	Smoking: N.I. Other simultaneous exposures: N.I.
Kjellström et al. (1979)	1940-1975	Sweden E: 94 D: ”all workers with a 5 years or longer exposure to cadmium since the factory started (1930’s)” Lost cases:	1960’s: 0.1-0.4 mg/m³ since 1971: ± 0.05 mg/m³	4/2.69	149 (40-381)	N.I.	N.I.	Smoking: N.I. Other simultaneous exposures: N.I.

U.K. United Kingdom
E Exposed subjects
D Duration of exposure
M Males
N.I. No information available

N Number of subjects
o Observed deaths
e Expected deaths
SMR Standardised mortality ratio
95%CI Confidence interval

Considered confounders: yes, no, ±: an attempt was made

Holden (1980) described cadmium exposures at the plants A and B, located respectively in rural and urban areas in the United Kingdom, where copper-cadmium alloys were produced from 1922 to 1966 (A) and from 1926 to 1989 (B).

347 men, who had been employed for at least 12 months in these factories were included in the study. The numbers of workers in each plant were not given.

Exposures to cadmium fumes exceeded very probably 1 mg/m³, with a reported peak at 3.6 mg/m³ before 1953, < 0.15 mg/m³ from 1955 to 1957 and 0.05 mg/m³ thereafter.

Observed number of deaths was compared with expected number calculated from death rates in England and Wales in five-year groupings. Vital status of the workers was assessed in 1978.

Table 4.209 Mortality: deaths from cancer, 1921-1978 (Holden, 1980)

	Factory A* (Rural)			Factory B*(Urban)			Total		
	Obs.	Exp.	SMR	Obs.	Exp.	SMR	Obs.	Exp.	SMR
Respiratory system	2	7.85	25	8	4.5	177	10	12.35	81
Uro-genital system	3	2.22	135	1	1.06	94	4	3.28	122
All cancers	20	19.58	102	14	10.69	130	34	30.27	112

* Number of workers in the factories not given
95% CI not reported

Factory B had 8 observed deaths from respiratory cancer against 4.5 expected and this appeared high. However, according to the authors, when the rate for the urban district in which factory B was located was taken into account, the new expected number was 6.0 and the SMR became 133.

The four neoplasms of the genito-urinary tract consisted of three neoplasms of the bladder and one case of carcinoma of the prostate (versus 1.58 expected).

In a further study of the same workers, 624 "vicinity workers" producing arsenical copper and other alloys (and also exposed to silver and nickel during refining) in the same workshop (Factory B) were included too, as was a control group of 537 men employed for at least 12 months in the brass or iron foundries of the same factory.

The mean cadmium exposure of these vicinity workers was low (≤ 0.07 mg/m³, King 1955, cited in IARC 1993), but arsenic exposures were reported as "high". Vital status was assessed in 1979.

Table 4.210 Numbers of observed and expected cancer deaths (Holden, 1980)

Cause of death	Cadmium workers			Vicinity workers			Control group		
	Obs.	Exp.	SMR	Obs.	Exp.	SMR	Obs.	Exp.	SMR
Respiratory system	10	13.14	76	36*	26.08	138	11	10.56	104
Genito-urinary system	4	3.49	115	11*	6.69	164	2	2.59	77

* Significant at 5% level

The vicinity workers had significantly higher mortality rates from both respiratory and genito-urinary cancer than the general population of England and Wales. This may be due, according to the authors to exposure to other metals such as arsenic (exposure values not reported).

Smoking histories were not available (Holden, 1980 a, b).

A more detailed analysis of the mortality in this cohort was carried out by Sorahan et al. (1995) and included the analysis of deaths occurring in a further 13 years of follow up.

The study cohort comprised 168 copper cadmium alloy workers from factory A, 179 copper cadmium alloy workers from factory B, 624 vicinity workers from factory B and 521 iron and brass foundry workers from factory B. All of them had worked a minimum period of 12 months between 1922 and 1978. However, most of the workers from factory A started alloy work in the period 1922-1940 (N=134, against 39 in factory B) ands most of the alloy workers from factory B started alloy work in the period 1940-1962 (N=140 against to 34 in factory A). Sixteen members of Holden's original control group (1980) were excluded in this analysis because they started work before 1922. Vital status of the workers was assessed end December 1992. An assessment of the cadmium exposure was only available for the factory B: measurements of airborne cadmium made between 1951 and 1983 were reviewed by Davison et al. (1988) and are reported in **Table 4.211**.

Their results were used in this study to estimate individual cumulative exposures. The cumulative exposure for each man who worked with copper cadmium alloy was calculated as the sum of the estimated exposures to cadmium during each year worked with copper cadmium alloy in the period 1922-1980, expressed in µg · year/m³. It was intended to use the cut off values selected by Thun et al. (1985) for the categories of cumulative exposure to cadmium (1,600 µg years/m^3 or 584 mg. days/ m^3, 8,000 µg. years/m^3 or 2,920 mg. days/ m^3). However, the use of these values would have placed only a small percentage (8%) of observed deaths in the highest dose category so the highest cut-off value was reduced to 4,800 µg. years/m^3 (1,753 mg days/m^3). Distribution of the workers among these cumulative exposure categories is not reported. This available historical assessment of exposure in factory B was used thereafter for the estimation of exposure in factory A. Although this could have led to some errors in classification of the workers in the cumulative exposure levels, these misclassifications, according to Sorahan et al., would probably be modest given that processes in both factories were broadly similar and that improvements were made over time at both factories.

Table 4.211 Estimated exposure to cadmium (Davison et al., 1988)

Year	Cadmium (µg/ m³)
1926-1930	600
1931-1935	480
1936-1942	360
1943-1946	270
1947-1954	240
1955-1962	210
1963-1972	156
1973	85
1974	58
1975	43
1976	44
1977	48
1978	49

Table 4.211 continued overleaf

Table 4.211 continued Estimated exposure to cadmium (Davison et al., 1988)

Year	Cadmium (µg/ m³)
1979	58
1980	56

For lung cancer, there was a significantly depressed SMR for copper cadmium alloy workers from factory A (Obs/Exp. 3/10.3, SMR:29 95%CI: 6-86) and a significantly increased SMR for copper cadmium alloy workers from factory B (Obs/Exp. 15/7.6, SMR: 198, 95% CI: 111-325).

When the alloy workers from both factories combined were compared with the general population of England and Wales, the SMR for lung cancer was not significantly increased (O/E: 18/17.84, SMR: 101; 95%CI: 60-159). The unusually low SMR for lung cancer among copper cadmium alloy workers from factory A was unexpected and authors examined possible reasons for this deficit and could exclude an artefact in data collection. Some of the deficit might be due to regional differences (factory A is located in a rural setting whereas factory B is in an urban setting). Because the smoking histories were not available, it was not possible to assess the role of cigarette smoking in this deficit. Considering the mortality of the workers by their entry in the cohort, it appears that two of the three lung cancer cases observed in factory A (1946-1992) occurred in men who joined the cohort between 1922 and 1940 (8.3 cases expected) and one might question the quality of the registration of the lung cancer deaths among this subgroup exposed to high values of cadmium in air, according to Davison's estimates.

A significant overall excess for lung cancer was shown only for vicinity workers. These workers were exposed to a mixture of chemicals, including arsenic and this last exposure may be responsible, at least in part, for the increased SMR obtained. The sub-cohort of iron and brass foundry workers referred as control group worked also in an extremely dirty environment and was exposed to considerable amounts of chemicals others than cadmium, including polycyclic aromatic hydrocarbons (SMR for non-malignant diseases of the respiratory system was found to be increased in this group, O/E: 34/17.1, SMR= 199).

Table 4.212 Mortality from lung cancer in participants, 1954-1992 (Sorahan et al., 1995)

Group	Factory	Obs.	Exp.	SMR (95% CI)
Total alloy workers	A + B	18	17.8	101
alloy workers	A	3	10.3	29 (6-86)
alloy workers	B	15	7.6	198 (111-325)
Vicinity workers	B	55	34.3	160
Control group	B	19	17.8	107

Even when the used regression analysis (Poisson) was restricted to the alloy workers from factory B, the analysis did not find cumulative exposure to cadmium to be an important risk factor for lung cancer, there was even a non-significant negative trend between exposure to cadmium and risks of mortality (**Table 4.213**).

Table 4.213 SMRs for lung cancer by level of cumulative exposure (Sorahan et al., 1995)

Cumulative exposure to cadmium (µg · years/m³)	Deaths* (N)	SMR (95%CI)	SMR (95% CI) (when analysis restricted to factory B)
< 1,600	10	100	
1,600-4,799	5	50 (17-146)	134 (44-405)
≥ 4,800	4	46 (14-149)	54 (12-256)

* Cases selected as those death for which any part of the death certificate (1a, 1b, 1c or II) would be coded to ICD categories 162-163: cancer of the lung) (N=19)

As reported by the authors, this study has limitations: no quantitative data on occupational exposures other than cadmium and no smoking histories were available. The study was also limited in that an historical assessment of cadmium exposures was only available for factory B and was used to estimate exposures in factory A. As the results of the two alloy factories appeared to present large differences, it may be questioned whether studies of these factories should be combined or not. Authors concluded that their findings did not support the hypothesis that exposure to cadmium oxide fumes increases risk of lung cancer. The copper cadmium alloy workers studied in this cohort had rather excess risks of non-malignant diseases of the respiratory system (SMR: 230) than excess risks of lung cancer (see also Section 4.1.2.7 Lung) (Sorahan et al., 1995).

Kazantzis and Blanks (1989) reported briefly the results of a nested case-control study of lung cancer in the copper-cadmium alloy cohort previously studied by Holden (1980). Long-term employees were reported also to have been exposed to arsenic in the production of arsenical copper (obtained by adding bags of arsenic trioxide to the molten copper and stirring manually what resulted in the evolution of dense white clouds of arsenic fume). An analysis in which 50 lung cancer deaths were compared with 158 controls matched on age and year at hire showed a stronger association between lung cancer and exposure to arsenic (OR: 2.15, 90% CI: 1.22-7.39) than with exposure to cadmium (OR:1.27, 90% CI: 0.61-2.51). However, in his comments, the IARC Working Group found the results difficult to interpret in respect to cadmium because of the lack of information on exposure classification and because no simultaneous control of exposure to cadmium and arsenic was made in the analysis (Kazantzis et al., 1989 cited in IARC 1993, in WHO 1992).

Kjellström et al. (1979) also investigated a cadmium-copper alloy plant in Sweden where workers at the furnace had been exposed to cadmium oxide fumes. As company records went as far back as 1940, target exposed group was limited to the workers employed in 1940 or who started working after that year. The reference group comprised all other workers in the same factory who had been employed for at least 5 years and never exposed to cadmium. These workers were involved in the production of copper, brass tubes, and various aluminium products.

The production of copper-cadmium alloys started in the 1930's, but reliable measurements of the cadmium exposure via air was first carried out in the middle of the 1960's. Cadmium concentrations were then in the range 100-400 µg Cd/m³. In 1971, the average exposure level decreased to about 50 µg/m³, subsequent to the installation of local exhaust equipment.

Calculation of expected number of deaths was made using the "life-table" method. Expected and observed number of deaths were used to calculate risk ratios. Only a preliminary calculation of prostate cancer mortality was carried out.

Mortality from prostate cancer between 1940 and 1975 in the exposed group was above that expected from national rates (4 observed versus 2.7 expected). In the reference group, the mortality from prostate cancer was lower than expected what the authors attributed to the “healthy worker effect” (Kjellström et al., 1979, IARC 1993, WHO 1992).

Summary and conclusions

Sorahan et al. (1995) studied the lung cancer frequency for copper cadmium alloy workers from two factories. In one factory they found a significantly decreased SMR, while a significant increased SMR was found in the other factory. The authors concluded that their findings did not support the hypothesis that cadmium oxide fumes increase the risk of lung cancer. These authors identified several limitations of their study such as missing data on smoking habits, on exposures to other substances than cadmium (quantitative data) incomplete historical assessment of cadmium exposure in one of the two factories, etc.).

3) Nickel-cadmium batteries plants

Five studies have investigated the association between cadmium and cancer at two UK plants and four studies examined a Swedish cohort in two nickel-cadmium batteries factories. These studies are summarised in **Table 4.214** and **4.215**. The use of cadmium was noted to be increasing in the production of nickel-cadmium batteries but work-place air decreased by up to 100 times since the 1940s in the work sites studied.

United Kingdom

The first survey in the UK was conducted by Potts (1965) at two nickel-cadmium battery plants that amalgamated in 1947, factory A which opened in 1937 and factory B which opened in 1923 and closed after the amalgamation. Among 74 men, exposed to cadmium oxide dust for at least 10 years before 1965, Potts (1965) recorded 8 fatalities. Three of them were due to prostate cancer and one to lung cancer. No referent rates were used to compute the expected number of fatal cancers (Potts, 1965 cited in IARC 1993).

This study was extended by Kipling and Waterhouse (1967) to assemble a cohort of 248 men with at least one year of exposure at the same plant, including the 74 men reported by Potts (1965). Cancer incidence rates through 1966 were compared with regional rates from the local cancer register.

No published information on exposure levels was available.

One new case of prostate cancer was detected. This case, combined with the three cases reported by Potts (1965), exceeded the 0.58 expected. The incidence of lung cancer was not significantly elevated (5 observed, 4.4 expected) (Kipling and Waterhouse, 1967, cited in IARC 1993).

Sorahan and Waterhouse (1983) enlarged once more the cohort to include 3,025 people (2,559 men and 466 women) who started employment between 1923 and 1975 and had a minimum period of employment of one month. Vital status of the workers was assessed end 1981.

Detailed job histories were coded for each worker. Jobs were categorised by exposure to cadmium (high, moderate, or minimal).

Some cadmium measurements in air were made in early years: in 1949, concentrations ranged from 0.6 to 2.8 mg/m^3. The installation of extensive local exhaust ventilation reduced the concentrations to below 0.5 mg/m^3 in most parts of the factories. After 1967, working conditions below the 0.2 mg/m³ were achieved. Since 1975, levels ranged around 0.05 mg/m³. However, it was not possible to estimate exposure levels by department and calendar year.

The mortality experience of this cohort was compared with that which might have been expected to occur if rates of mortality for the general population of England and Wales had been operating on the study cohort. The excess for cancers of the respiratory system (SMR: 127) was significant at the 5% level (Sorahan and Waterhouse, 1983).

Table 4.214 Cohort studies of lung and prostate cancer in workers exposed to cadmium at nickel-cadmium battery plants (UK)

Reference	Follow-up period	Population , selection, lost cases	Exposure levels and categories	Prostate cancer (o/e)	SMR (95% CI) prostate	Lung cancer (o/e)	SMR (95% CI) lung	Considered confounders
Potts (1965) (cited in IARC 1993)	Through 1965	E: 74 D: "at least ten years of exposure" Lost cases: N.I.	N.I.	3/N.I.	-	1/ N.I.	-	Smoking: N.I. Other simultaneous exposures: N.I.
Kipling and Waterhouse (1967)	Through 1966	E: 248 (M only) D: "at least one year of exposure" Lost cases: N.I.	N.I.	4/0.58	690 (186-1766) (SIR)	5/4.4	114 (.37 – 265) (SIR)	Smoking: N.I. Other simultaneous exposures: N.I.
Sorahan and Waterhouse (1983)	1946-1981	E: 3025 (2559 men) D: "had a minimum period of employment of one month between 1923 and 1975" Lost cases:	1949: 0.6 – 2.8 mg/m³ post 1950: < 0.5 mg/m³ 1967: < 0.2 mg/m³ since 1975: 0.05 mg/m³ (description of job histories in terms of high, moderate, minimal exposure)	8/6.6	121 (52-239)	89/70.2	127	Smoking: no Other simultaneous exposures: NiOH ±, oxyacetylene fumes
Sorahan and Waterhouse (1985)	1950-1980	E: 2,995 (M only) D: "employed at least one month between 1923 and 1975" Lost cases: 80 (+68 emigrated)	(see above) -subgroup employed at least 1 year, high exposure (N=458)	15/11.02 8/1.99 (when 4 cases of Kipling and Waterhouse excluded: 4/1.78)	136 (76-225) 402 (173-792) 225 (60-575)	N.I.	N.I.	Smoking: no Other simultaneous exposures: NiOH, oxyacetylene fumes ±

Table 4.214 continued overleaf

Table 4.214 continued Cohort studies of lung and prostate cancer in workers exposed to cadmium at nickel-cadmium battery plants (UK)

Reference	Follow-up period	Population , selection, lost cases	Exposure levels and categories	Prostate cancer (o/e)	SMR (95% CI) prostate	Lung cancer (o/e)	SMR (95% CI) lung	Considered confounders
Sorahan (1987)	1946-1984	E: 3025 (2559 men) D: ”minimum period of employment of 1 month who started employment between 1923 and 1975” Lost cases: 78	(see above) none < 2 years 2- 4 years 5- 14 years ≥15 years	N.I.	N.I.	110/84.5 64/70.2 19/15.6 6/5.3 6/4.9 6/5.2	130 (107-157) 100 140 130 130 150	Smoking: N.I. Other simultaneous exposures: N.I.
Sorahan and Esmen (2004)	1947-2000	E: 926 (M) D: “workers first employed in the period 1947-1975 and having a minimum of 12 months of employment at the factory” Lost cases: 26 emigrated, 4 untraced	Cumulative exposure categories < 400 µg:m³/year 400-1,599 µg/m³/year 1,600-4,799 µg/m³/year ≥ 4,800 µg/m³/year	9/7.5	116 (53-221)	45/40.7	111(81-148)	Smoking: N.I. Other simultaneous exposures: N.I.

UK United Kingdom
E Exposed subjects
D Duration of exposure
M Males
F Females
N.I. No information available
N Number of subjects
o Observed deaths
e Expected deaths
SMR Standardised mortality ratio
SIR Standardised incidence ratio
95%CI Confidence interval

In a later paper, the same authors (Sorahan and Waterhouse, 1985) reported 15 incident cases of prostate cancer entered into the regional cancer registry between 1950 and 1980 (versus 11.0 expected). Eight of these cases occurred in a subgroup of 458 workers employed for at least one year in a job involving high exposure to cadmium oxide dust (expected 1.99). Exclusion of the cases identified by Kipling and Waterhouse left 4 cases: this number was greater than expected (1.78 expected) but not significant.

Results of the analyses carried out on the collected data suggested that a) there was an increased risk of mortality from cancer of the prostate, entirely dependent on the original four cases reported by Kipling and Waterhouse (exclusion of these four cases of prostate left 11 observed cases in the whole cohort, versus 10.67 expected); b) no association with mortality from cancer of the prostate was shown for cases subsequent to the initial report; c) some indication of an increased risk of mortality from cancers of the respiratory system among those first employed before 1940, although exposure to oxyacetylene welding fumes and to nickel hydroxide dust were important confounding exposures.

Analysis in this study did not allow distinguishing between exposure to cadmium oxide dust and exposure to nickel hydroxide, because almost all jobs entailing high cadmium exposures were also associated with high nickel exposures.

Data on smoking habits were not available (Sorahan and Waterhouse, 1983, 1985).

Sorahan (1987) further examined the lung cancer mortality between 1946 and 1984 in the same cohort. Job histories were updated to the closing date of the survey: as in the previous study (Sorahan and Waterhouse, 1983), eight jobs were considered to entail high exposure to cadmium (plate-making, assembly, negative active material departments); 14 to entail moderate exposure; 53 to entail minimal exposure.

102 deaths from lung cancer were reported, including 22 deaths not previously analysed. Among early workers (first employed in the period 1923-1946, SMR for lung and bronchus cancer: 126), there was some evidence of an association between the risk of death from lung cancer and duration of employment in jobs with high or moderate exposure, but this relied heavily on the findings for the single highest exposure category. Among late workers first employed in the period 1947-1975 (SMR for lung and bronchus: 136), there was no good evidence of an association between risk of dying from lung cancer and duration of employment in high exposure jobs, and no evidence for an association with duration of employment in high or moderate exposure jobs.

Exposure to nickel hydroxide could not be controlled for, only a few workers were exposed to cadmium in the absence of nickel. Data about smoking habits were not available.

The author concluded that these findings did not suggest that workers in this factory experienced raised risks of dying from lung cancer as a consequence of exposure to cadmium oxide dust (Sorahan, 1987, WHO 1992, IARC 1993).

An update of the mortality experienced in this cohort was recently published by Sorahan and Esmen (2004). Mortality from cancer and risk for chronic obstructive pulmonary disease for the period 1947–2000 was examined in the group of 926 male workers engaged in the manufacture of nickel-cadmium batteries at one factory located in the West Midlands of England . All subjects were first employed at the plant in the period 1947–75 and employed for a minimum period of 12 months. Work histories were available for the period 1947–86; the factory closed down in 1992.

There was a significantly increased mortality for cancers of the pharynx and non-malignant diseases of the respiratory system. Non-significantly increased SMRs were shown for lung cancer (O: 45, E: 40.7, SMR 111) and cancer of the prostate (O: 9, E: 7.5, SMR 116). Estimated cumulative cadmium exposures were not related to risks of lung cancer or risks of chronic obstructive pulmonary diseases, even when exposure histories were lagged first by 10, then by 20 years. This study has some limitations as reported by the authors themselves: data for the earlier years of exposure were not available, neither were direct measurements for workers in the “non-exposed” departments or smoking data. These factors could therefore not be considered in the analysis. Overall, authors concluded that the study findings did not support the hypothesis that cadmium compounds are human lung carcinogens (Sorahan and Esmen, 2004).

Table 4.215 Cohort studies of lung and prostate cancer in workers exposed to cadmium at a nickel-cadmium battery plant (Sweden)

Reference	Follow-up period	Population, selection, lost cases	Exposure levels and categories	Prostate cancer (o/e)	SMR (95% CI) prostate	Lung cancer (o/e)	SMR (95% CI) lung	Considered confounders
Kjellström et al. (1979)	1959-1975	E: 228 (M only) D: ”workers with a 5 years or longer exposure” Lost cases: N.I.	Overall < 1947: above 1 mg/m³ 1950’s: 200 µg/m³ 1962-1974: 50 µg/m³ 1979: < 5µg/m³	2/1.2	167 (19-602) (SIR)	2/1.35	148 (17-535)(SIR)	Smoking: no Other simultaneous exposures: NiOH ±
Andersson et al. (1983)	1951-1980	E: 528 (M only) D: ”at least one year of cadmium exposure” Lost cases: N.I.	< 1946: above 1mg/m³ 1977:< 20 µg/m³	4/3.09	130	6/5.03	119	Smoking: N.I. Other simultaneous exposure: Nickel, ±
Elinder et al. (1985)	1951-1983	E: 522 (M only) D: “exposed to cadmium for at least one year” Lost cases: 3 (+ 17 emigrated)	Overall < 1947: about 1 mg/m³ 1947-1962: 300 µg/m³ 1962-1974: 50 µg/m³ > 1975: about 20 µg/m³	4/3.7	108 (29-277)	8/6.01	133 (57-262)	Smoking: ± Other simultaneous exposures: NiOH Asbestos ±
Järup et al. (1998)	1951-1992	E: 869 (M and F) D: "employed at least one year between 1940 and 1980" Lost cases: 31	Total < 250 µg/m³ · years 250-< 1,000 µg/m³ · years > 1,000 µg/m³ · years	11/9	122 (61.1-219)	16/9.1	176 (101-287) 1.0 (-) 0.34 (0.09-1.31) 0.31 (0.09-1.05)	Smoking: yes Other simultaneous exposures: NiOH

E Exposed subjects
D Duration of exposure
M Males
F Females
N.I. No information available
N Number of subjects
o Observed deaths
e Expected deaths
SMR Standardised mortality ratio
95%CI Confidence interval
SIR Standardised incidence ratio
Considered confounders: yes, no,
± An attempt was made
* Males only

In Sweden, the mortality and the cancer morbidity in workers from a single cadmium-nickel battery factory was first investigated by Kjellström et al. (1979).

Target group included the workers employed in the factory in 1945 or who started working after that date, because company records (including name, birth date, address, sex, death date, exposure and employment experience in the company) were kept for all years after 1945. This study population included 269 male workers, born between 1874 and 1952.

Workers were exposed for 5 years or more to cadmium oxide dust and nickel hydroxide dust and exposures to nickel hydroxide were reported to have been at least the same as the cadmium exposure levels and often up to10 times higher, although no measurements were reported. The cadmium oxide concentrations were originally above 1 mg Cd/m³ in air, around 200 µg/m³ in the 1950's and about 50 µg/m³ between 1962 and 1974. Since 1974, most of the workers were exposed to levels below 5 µg/m³.

Incident cancers among the workers were identified from the Swedish National Cancer Registry, which started in 1959, and were compared with national rates of incidence. There was a tendency for an increased incidence of prostate, lung and colorectal cancer among these workers but the risk ratios were not statistically significantly except for naso-pharyngeal cancer.

Table 4.216 Expected and observed new cases of cancer(incidence) in 1959-1975 in the whole group of battery factory workers (Kjellström et al., 1979)

Site	Cancer cases		Risk ratio (95% CI)
	Observed	Expected	
Prostate	2	1.2	1.67 (0.19 – 6.02)
Lung	2	1.35	1.48 (0.17 – 5.35)
Colorectal	5	2.25	2.22 (N.I.)
Kidney	0	0.87	0 (N.I.)
Bladder	1	1.07	0.93 (N.I.)
Nasopharynx	2	0.20	10.0 (1.23 – 36.1)
Other	3	9.81	0.31 (N.I.)
Total	15	16.4	0.91 (N.I.)

The high and significant risk ratio for naso-pharyngeal cancer among the battery workers was connected by the authors with the exposure to nickel compounds. However, in its comments, the IARC Working Group (1993) noted that cancers of the nasal cavity and the sinuses and not naso-pharyngeal cancers could be associated with exposure to nickel.

Andersson et al. (1983) extended cohort and follow-up and included 528 male workers from the same factory. At the time of the study, the authors estimated that the cadmium levels in air were generally below 20 µg/m³ and that nickel levels in air were below 50 µg/m³. Because no individual levels could be estimated, exposure was defined as years of exposure. Periods of exposure varied from one to 52 years (median: 10 years).

Expected numbers of death due to different causes were calculated for the period 1951-1980.

There was a non-significant increase in deaths due to prostate cancer and lung cancer. One case of carcinoma of the nasopharynx, who died in 1972, was recorded (was also recorded by Kjellström et al., 1979). Another case had occurred among the workers but the man was still alive at the end of the follow-up (Andersson et al., 1983).

Elinder et al. (1985) extended the cohort to include 522 male workers from the same plant, who had been exposed for at least one year between 1940 and 1980 and who had not died before 1951 (because SMRs were calculated as the ratio between observed number of deaths and the expected number, calculated from the general (whole) Swedish population, available for the period 1951-1983).

In the cohort as a whole, the observed number of deaths for most causes of death was similar to the expected numbers. For all the 522 workers, the excess cancer (all sites) mortality was not statistically significant (SMR=115).

Authors incorporated latent periods of 10 or 20 years and a minimum of five years exposure in their calculations of the SMR for the types of cancer with two or more observed cases.

Because the exposure to cadmium before 1963 has been reported to be much higher, the subgroup of workers with a 20 year latent period (thus exposed before that year), was considered as of particular interest by the authors, in order to elucidate the possible carcinogenic effects from high exposure to cadmium. SMRs are reported in the **Table 4.217**.

Table 4.217 Observed numbers of deaths from certain types of cancer before age 80 (1951-1983) and SMR's, with different requirements on exposure times and time lapse since the first exposure (Elinder et al., 1985)

Cause of death	All workers			Workers with at least 5 years of exposure, 10 years latency (N=340)		Workers with at least 5 years of exposure, 20 years latency (N=295)	
	Observed	Expected	SMR (95% CI)	Observed	SMR	Observed	SMR
Cancer of lung	8	6.01	133 (57-262)	8	163	7	175
Cancer of prostate	4	3.70	108 (29-277)	4	125	4	148
Cancer of intestines	8	-	195 (-)	6	182	4	148
Cancer of pancreas	3	-	130 (-)	2	105	1	67
Cancer of bladder	2	-	181 (-)	2	222	2	250

For lung, prostate and bladder cancer, the SMR was increased but did not reach statistical significance, even in the "high exposure group" (20 years latency, at least 5 years of exposure). Seven deaths (on eight reported) from lung cancer occurred among 295 men who had experienced at least five years exposure to cadmium and were employed before 1963 and had thus been exposed to about 0.3 mg/m³ or more for at least a part of their exposure period (4.0 expected, SMR= 175, 95% CI: 70-361). Authors concluded that this supported an association between lung cancer and cancer of the prostate and the exposure to cadmium.

Again, exposure to nickel hydroxide was reported as a potential confounder. One death (versus near zero expected) in the cohort was due to nasopharyngeal cancer, what according to the authors, raised the suspicion of an effect of nickel as well as of cadmium. The possibility of an exposure to asbestos was also cited by the authors.

Data about smoking habits were available for the whole plant in 1981: 52% of the currently employed workers were smokers, 11% were former smokers, and 37% had never smoked and these percentages were similar to the smoking habits of the general Swedish population; Unfortunately, more detailed information about the smoking habits of the workers (and in particular the workers who died from lung cancer) were not available (Elinder et al., 1985).

Järup et al. (1998) extended this cohort once more to investigate mortality and cancer incidence with new detailed exposure estimates and regional reference data. The extended cohort comprised 900 (717 male, 183 female) workers employed for at least one year in the nickel-cadmium battery plant between 1931 and 1982.Vital status was obtained by search in the national Swedish cause of death registry. Cancer morbidity was assessed by search in the Swedish cancer registry. No age limit was applied for the inclusion of the cases. Smoking habits data were collected by means of a postal questionnaire and qualitative data were obtained for 88% of the cohort members.

The collection of exposure data included examination of employment records and workplace measurement reports as well as interviews with “key informants” in the factory. The compilation of the description of the production history provided the foundation for a consensus approach in which exposure concentrations were assigned to 23 generic job titles in three periods for cadmium and nickel exposure on two separate scales. Quantitative estimates were made from monitoring data covering the period 1946-1992. These estimates were linked to the combinations of generic job titles and periods to form a job-exposure matrix, applied to the individual work histories. The resulting individual exposure profiles were used for the calculation of estimated cumulative exposures (µg/m³ · years).

The previous follow-up studies (Kjellström 1979, Elinder 1985) used reference data from the general population from all of Sweden as regional rates were not available. In this study, regional rates (death rates as well as cancer incidences) could be used.

Table 4.218, **4.219** and **4.220** summarise the main results of the study:

Table 4.218 Observed numbers of death and SMRs in male battery workers (1951-1992), regional reference rates (Järup et al., 1998)

Cause of death	Obs.	Exp.	SMR	95%CI
All cancers	75	60.1	125	98.2-157
Lung cancer	16	9.1	176	101-287
Prostate cancer	11	9.0	122	61.1-219
Cancer of the bladder	3	1.7	176	36.4-515
Cancer of the pancreas	6	4.0	148	54.5-323

Table 4.219 SMRs for lung cancer in male battery workers in relation to cumulative cadmium exposure and latency (Järup et al., 1998)

	Cumulative cadmium exposure							
	< 250		250-< 1,000		> 1,000		Total	
Latency	N	SMR	N	SMR	N	SMR	N	SMR
< 20 years	2	415	1	115	1	380	4	248
≥ 20 years	3	378	3	151	6	128	12	161
Total	5	392*	4	140	7	142	16	176*

* $p < 0.05$

Table 4.220 SMRs for lung cancer in male battery workers in relation to duration and intensity of exposure (Järup et al., 1998)

	Duration							
	< 5 years		$5 \leq 10$ years		> 10 years		Total	
Mean intensity (µg/m³)	N	SMR	N	SMR	N	SMR	N	SMR
< 50	1	518	1	359	7	275*	9	298*
50-< 100	1	170	0	-	3	150	4	124
≥ 100	0	-	1	389	2	85	3	106
Total	2	202	2	169	12	174	16	176

* $p < 0.05$

There was an increased risk of lung cancer among the nickel-cadmium battery workers, but there was no increase in SMR with increasing cumulative exposure.

The influence of smoking on the relative risks for lung cancer was analysed with Poisson regression. Adding smoking to the regression equation changed the relative risks only marginally. Similar findings were obtained for exposure to nickel and the risk of lung cancer.

Authors noted that the comparatively high relative risks for lung cancer in workers with the lowest cumulative exposures and short duration of exposure were most likely explained by exposures to other carcinogens: for example some workers worked periodically at a shipyard which had the same owners as the battery plant. Another explanation they suggested for the negative exposure-response relation, was the healthy worker effect.

Authors concluded that there was an overall increased risk of lung cancer, but no exposure-response relation between cumulative exposure to cadmium and risk of lung cancer. There was a highly significant increased risk of cancer of the nose and nasal sinuses which may be caused by exposure to nickel or cadmium or a combination of both exposures (Järup et al., 1998).

Summary and discussion

The most convincing study from the UK plants is that of Sorahan (1987). Whereas the SMR for lung cancer was increased for all workers, there was no relationship with duration of employment and the association was weak (SMR < 150).

Regarding the Swedish study population, the most convincing study is that of Järup et al. (1998). The SMR for lung cancer was again increased but the dose-effect relationship followed a pattern which was the contrary of that expected. In the subgroups with the highest mean intensity and the highest cumulative exposure, the SMR amounted to 106 and 142, respectively. This rather low SMR may suggest a weak carcinogenic effect but is also compatible with the effect of bias or/and confounding.

4) Cadmium oxide, alloys and pigments plants: cadmium processing

In the "17-plant study of cadmium-exposed workers in England", the mortality of almost 7,000 workers from 17 processing plants in England was examined, initially until the end of 1979 (Armstrong and Kazantzis, 1983). Two updates (follow-up to 1984 and 1989, respectively) have been carried out (Kazantzis et al., 1988; Kazantzis and Blanks, 1992; Kazantzis et al., 1992).

Table 4.221 summarises the results of these studies.

Armstrong and Kazantzis (1983) have investigated the mortality rate for cadmium-exposed workers in 17 plants in the U.K. where cadmium is produced or used, including primary production, silver cadmium-alloy production, oxide and pigments production and stabiliser production. The cohort included workers born before 1940 and employed for more than a year on, or in the vicinity of, a cadmium process between 1942 and 1970. Workers of these plants had never been included in any previous mortality study. On the 6,995 subjects included in the study in 1983, most of the workers (N= 4,453) were involved in primary cadmium production. The remaining (N= 2,452) were engaged in the production of cadmium alloys (N= 1,559), pigment and oxides (N= 531) and stabilisers (N= 452).

Jobs were assessed for each relevant year as involving high, medium or low exposure to cadmium on the basis of discussions with hygienists and others with knowledge of past working procedures, taking into account available results of biological or environmental monitoring (e.g. Cd-U > 20 mg/l in the high-exposure group). The years at risk of the study population were divided on the basis of these categories and recorded job histories into three groups: (i) "ever high" (minimum one year, 3% of the workers), (ii)"ever medium (minimum one year, 17%) and (iii) "always low" (all others, 80% of the workers). The mean duration of exposure was 11 years and the mean interval from initial exposure to the end of the follow-up was 27 years. In the "ever high" exposure group, 45% were born before 1920, and 71% were first employed before 1960, when exposures to cadmium were particularly high, e.g. in some recorded circumstances over 2 mg/m^3 (Kazantzis et al.,1992). The small number of selected subjects who experienced heavy exposure to cadmium (N=199), compared to the number of subjects belonging to the "always-low" exposure group (N=5,596), constituted one limitation of the study, according to the authors.

Deaths from 1943 to the end of 1979 were investigated and only deaths occurring at ages below 85 (N=1,902) were considered. Expected numbers of deaths were calculated from mortality rates for the population of England and Wales corrected for regional variation, and the results were expressed as SMRs (standardised mortality ratios).

Among the 199 men considered to have ever been subjected to high exposure levels of cadmium, 13 had died from cancer (compared to an expected number of 10.4) and 5 of these patients had suffered from lung cancer (versus 4.4 expected). When including both "ever-high" and "ever-medium" in the cohort, there was a slight increase in lung cancer, a total of 32 cases compared to 28.6 expected but a deficit in prostate cancer (0 cases versus 2.9 expected). The only group showing a significant excess of lung-cancer deaths was that of the men employed for more than 10 years in the "always-low" exposure category (SMR= 126, 18 cases of lung cancer versus 13.7 expected, $p < 0.05$).

Smoking histories were not available so lung cancer mortality data have to be interpreted with caution. However, the authors stated that manual workers tend to smoke more than average, so that some excess in lung-cancer mortality in all exposure groups would not be unexpected. This, together with the absence of any relation between the frequency of lung cancer and the intensity of exposure allowed the authors to conclude that it was unlikely that the small excess of lung cancers in the "always-low" exposure group was related to cadmium (Armstrong and Kazantzis, 1983, IARC 1993, CRC 1986, WHO 1992).

A five-year update of this "17-plants" study was made by Kazantzis et al. in 1988. Re-scrutiny of the initial population identified a small number of erroneous entries, which reduced the number of workers included in the SMR analysis from 6,995 to 6,958 subjects for the five-year period. Mean duration of cadmium exposure was 12 years and the mean interval from first exposure to the end of follow-up was 29 years.

This update confirmed the findings of the first study for prostate cancer: no excess risk from prostate cancer over the total study period (from 1943 to 1984) could be observed and no cases of prostate cancer occurred in the medium- or high-exposure groups.

75 additional cases of lung cancer over the five-year period gave a significant excess mortality in the cohort as a whole and also in the high-exposure group (high-exposure group: 12 deaths versus 6.2 expected, SMR:194, 95% CI: 100-339). The increased lung cancer risk was most marked in men first employed before 1940, with long exposure and with a long period of follow-up.

When the lung cancer mortality of the whole cohort was examined in relation to the type of industry, it was observed that the majority (182/277) of the lung cancer deaths were from a large non-ferrous smelter starting before 1940 and which provided over 60% of the total study population. In a subsequent case-control analysis (Ades and Kazantzis, 1988 see below), the excess lung cancer mortality was found to be related to length of employment in this smelter, but not to cumulative exposure to cadmium. However, there were no workers from the smelter in the ever high category (Kazantzis et al., 1988; WHO 1992).

Kazantzis et al. (1992) and Kazantzis and Blanks (1992) extended follow-up through 1989 for 6,910 workers. In 1989, at the end of the second 5-year update, 43% of the cohort had died, with 52% of the total cohort born before 1920.

The absence of an increased risk from prostate cancer seemed to be confirmed, although there was now in the last follow-up period one death from prostate cancer in the “ever high” group (0.4 expected).

There was a significant excess mortality from lung cancer in both the last 5-year follow-up period and the total study period(SMR: 134, 95% CI: 103-164, SMR 112, 95% CI: 100-124 respectively). The SMR increased with intensity of exposure, but SMR did no longer attain a 5% significance level in the high exposure group. Again, increased risk appeared to be the most marked in men first employed before 1940 with long exposure and with a long period of follow-up.

Table 4.221 Cohort studies of prostate and lung cancer in cadmium workers, cadmium oxide, alloys and pigments (UK)

Reference	Follow-up period	Population, selection, lost cases	Exposure levels and categories	Prostate cancer (o/e)	SMR (95% CI) prostate	Lung cancer (o/e)	SMR (95% CI) lung	Considered confounders
Armstrong and Kazantzis (1983)	1943-1979	E: 6995 (M only) D: "exposed for more than 1 year between 1942 and 1970" Lost cases: 90	Overall ever high (N=3%) ever medium (N=17%) always low (N=80%)	23/23.3 0/0.4 0/2.5 23/20.4	99 (63-148) 0 (0-962) 0 (0-147) 113 (72-170)	199/185.6 5/4.4 27/24.2 167/157.0	107 (92-122) 113 (37-263) 112 (74-163) 106 (90-123)	Smoking: N.I. Other simultaneous exposures: N.I.
Kazantzis et al. (1988)	1943-1984	E: 6958 (M only) D: "exposed for more than 1 year between 1942 and 1970" Lost cases: 67 + 184 emigrated	Overall ever high (N=3%) ever medium (N=17%) always low (N=80%)	30/33.2 0/0.6 0/4.0 30/28.6	90 (61-129) 0 (0-615) 0 (0-92) 105 (71-150)	277/240.9 12/6.2 41/34.0 224/200.7	115 (101-129) 194 (100-339) 121 (84-158) 112 (97-126)	Smoking: N.I. Other simultaneous exposures: N.I.
Kazantzis and Blanks (1992) Kazantzis et al. (1992)	1943-1989	E: 6910 (M only) D: "exposed for more than 1 year between 1942 and 1970"	Overall ever high (N=3%) ever medium (N=17%) always low (N=80%)	37/49.5 1/1.0 0/6.2 36/42.3	75 (53-103) 97 (1-540) 0 (0-59) 85 (60-118)	339/304.1 14/8.6 55/45.6 270/249.9	112 (100-124) 162 (89-273) 121 (91-157) 108 (96-122)	Smoking: N.I. Other simultaneous exposures: arsenic, beryllium, nickel, tin, chromium, heated mineral oils, etc.

U.K. United Kingdom
E Exposed subjects
D Duration of exposure
M Males
F Females
N.I. No information available
N Number of subjects
o Observed deaths
e Expected deaths
SMR Standardised mortality ratio
95%CI Confidence interval

As the majority of lung cancer deaths (namely 237/339, 70%) still were from the large zinc-lead-cadmium smelter providing the greatest part of the total study population, authors also reported the mortality pattern for prostate and lung cancer after excluding the data from the large smelter. In the 16 remaining plants, there was some evidence of an increased risk of lung cancer in the high exposure group, however not reaching the 5% significance level.

There was a significantly increased lung cancer risk in the smelter population as a whole, with 212 lung cancer deaths (89% of the total) in the “always low” exposure group. There were no “ever high” cadmium exposed workers in the smelter.

Table 4.222 Cause specific mortality in relation to cadmium exposure 1943-1989: smelter and all plants excluding smelter (Kazantzis et al., 1992)

Disease	Always low			Ever medium			Ever high			Total		
	Obs.	SMR	95%CI	Obs.	SMR	95%CI	Obs.	SMR	95%CI	Obs.	SMR	95%CI
Lung cancer												
Smelter	212	119	104-137	25	149	96-219	-	-	-	237	122	102-139
Plants excl. smelter	58	80	61-104	30	104	70-149	14	162	89-273	102	93	76-113
Prostate cancer												
Smelter	24	74	47-110	0	-	0-125	-	-	-	24	68	43-101
Plants excl. smelter	12	124	64-217	0	-	0-111	1	97	1-540	13	93	49-159

Obs. Observed deaths,
SMR Standardised mortality ratios,
95% CI Confidence interval no ever high exposed workers in the smelter.

In this same smelter, a nested case-control analysis was performed by Ades and Kazantzis (1988) to examine the contribution of specific departments, processes and contaminants. For each case of lung cancer (N= 174) with at least 10 years of follow-up, a set of controls (N=2,717) was selected to satisfy following criteria: a) controls were born within the year of the case b) they started work within three years of the case c) they had been followed up for at least 10 years, and had necessarily worked for at least one year at the time of the death of the case, and d) exit from the study was later than the death of the case.

Estimates of exposure to cadmium, lead, arsenic, zinc, sulphur dioxide and total dust were used to calculate cumulative exposures from job histories.

This study provided no evidence that cadmium, in the concentrations encountered in the smelter, was a cause of lung cancer, although there was an excess risk of lung cancer overall. Only 21 (12%) cases of lung cancer ever worked in the departments (sinter and cadmium plant) with substantial exposures to cadmium (> 0.01 mg/m³). But lung cancer mortality was positively related to duration of employment and to cumulative exposure to arsenic and lead. The effect of duration of employment could have arisen due to a real association between lung cancer mortality and cumulative exposure to arsenic or lead, or both, together with a correlation between the latter and duration of employment. This was supported by data the authors reported, suggesting that increasing levels of exposure to arsenic and lead for a given period were associated with a higher risk (see **Table 4.223**).

Table 4.223 Estimated relative risks associated with 10 years employment at each exposure level (Ades and Kazantzis, 1988)

	Exposure level (µg/m³)	N	Relative risk
Cadmium	1	88	1.30
	2-5	114	1.34
	10-30	4	2.11
	40-60	21	1.34
Arsenic	0	66	1.25
	1	134	1.36
	2	2	2.05
Lead	0	57	1.25
	1	73	1.28
	2	72	1.36
	3	27	1.54

N Number of cases working at least one year
Results for each contaminant are not adjusted for exposure to others

Arsenic was processed in certain of the plants and Kazantzis et al. (1992) reported a particular mortality pattern with regard to lung and prostate cancer: the SMRs in those plants without known arsenic exposure were below 100, (Lung cancer: 85, 95% CI: 68-106, Prostate cancer: 88, 95% CI:44-157) while in those plants with known past exposure they were raised (lung cancer: 147, 95% CI: 90-227, prostate cancer: 137, 95% CI: 15-495), although not significantly.

Summary and discussion: processing

Again, although it cannot be excluded that cadmium compounds including Cd metal/Cd oxide are carcinogen to the lung, reasonable alternative explanations should be considered. It also appears that the relationship between cadmium exposure and lung cancer was not strong (highest SMR 194, 95% CI: 100-339), a finding compatible with both a weak carcinogenic effect and/or the role of a confounder.

All these cohort studies are summarised again, to facilitate comparisons in **Table 4.224** and **Table 4.225**. Critical studies are highlighted with a grey background.

Table 4.224 Cadmium and lung cancer. Summary of the available studies

Reference	Type of plant	Study population	Exposure to	Findings		Confounders & Comments
				O/E	**SMR (95% CI)**	
Lemen et al. (1976)	Cd recovery	292	Cd fumes and dust	12/5.11	235 (121-410)	Smoking: N.I.
Varner (1983)	Cd recovery	625	CdO dust and fumes, $CdSO_4$, CdS, arsenic	23/N.I.	163 (N.I., SCR)	Smoking: yes SCR for malignant neoplasms (respiratory system)
White (1985)	Cd recovery	646	CdO dust and fumes, $CdSO_4$, CdS, arsenic	11/N.I.	244 (N.I., SCR)	Smoking: N.I.
Thun et al. (1985)	Cd recovery	602	CdO dust and fumes, $CdSO_4$, CdS, arsenic	20/12.15	165 (101-254)	Smoking: yes Dose-response relationship for the workers hired after 1926
Stayner et al. (1992)	Cd-recovery	606	CdO dust and fumes, $CdSO_4$, CdS, arsenic	24/16.07	149.95 (95-222)	Smoking: yes SMR significant among workers in the highest exposure group and among workers with 20 or more since first exposure
Sorahan and Lancashire (1997)	Cd recovery	571	CdO dust and fumes, $CdSO_4$, CdS, arsenic	5/N.I.	413 (121-1403)	Smoking: no SMR reported is for the highest exposure group
Holden (1980a, b)	Cu-Cd alloy	347 (Vicinity workers: 624)	CdO fumes, copper Vicinity workers: arsenical copper, silver, nickel	10/12.35	81	Smoking: N.I. Elevated risk of lung cancer in vicinity workers (arsenic smoking)
Sorahan (1995)	Cu-Cd alloy	347 (Vicinity workers: 624) (Control group: 521)	CdO fumes, copper Vicinity workers: arsenical copper, phosphor bronze, other copper alloys Control group: iron, brass foundry	18/17.84	101 (60-159)	Smoking: N.I. Increased SMR for lung cancer in the vicinity workers (arsenic smoking)

Table 4.224 continued overleaf

Table 4.224 continued Cadmium and lung cancer. Summary of the available studies

Reference	Type of plant	Study population	Exposure to	Findings		Confounders & Comments
				O/E	SMR (95% CI)	
Potts (1965)	Batteries	74	CdO dust	1/N.I.	-	Smoking: N.I. Cancer of bronchus
Kipling and Waterhouse (1967)	Ni-Cd batteries	248	CdO dust	5/4.4	114 (37-265)	Smoking: N.I.
Sorahan and Waterhouse (1983)	Ni-Cd batteries	2,559	CdO, Cd(OH)2 dust, Nickel hydroxide, oxyacetylene fumes	89/70.2	127	Smoking: N.I. (SMR for cancers of the respiratory system)
Sorahan (1987)	Ni-Cd batteries	3,025	CdO dust, Cd(OH)2 dust, Nickel hydroxide	110/84.5	130 (107-157)	Smoking: N.I.
Sorahan and Esmen (2004)	Ni-Cd batteries	926	Nickel hydroxide, cobalt, graphite, iron oxide, potassium hydroxide	45/40.7	111 (81-148)	Smoking : N.I.
Kjellström et al. (1979)	Ni-Cd batteries	228	CdO, Nickel hydroxide	2/1.35	148 (17-535)	Smoking: no Excess nasopharyngeal cancer (Nickel)
Andersson (1983)	Ni-Cd batteries	528	Cd (not detailed), Nickel (not detailed)	6/5.03	119	Smoking: N.I. 1 case of nasopharyngeal cancer (Nickel)
Elinder (1985)	Ni-Cd batteries	522	CdO dust, Nickel hydroxide, asbestos	8/6.01	133 (57-262)	Smoking: data from 1981 1 case of nasopharyngeal cancer (Nickel)

Table 4.224 continued overleaf

Table 4.224 continued Cadmium and lung cancer. Summary of the available studies

Reference	Type of plant	Study population	Exposure to	Findings		Confounders & Comments
				O/E	SMR (95% CI)	
Järup et al. (1998)	Ni-Cd batteries	869	CdO dust, Nickelhydroxyde	16/9.1	176 (101-287)	Smoking: yes
Armstrong and Kazantzis (1983)	Cd-processing	6,995	CdO dust and fumes, CdS, dust from Cd stabilisers, silver, copper + beryllium, nickel, mineral oils, arsenic, lead *	199/185.6	107 (92-122)	Smoking: N.I. Excess of lung cancers in the always low group, more than 10 years exposure (probably not related to cadmium)
Kazantzis (1988)	Cd-processing	6,958	CdO dust and fumes, CdS, dust from Cd stabilisers, silver, copper + beryllium, nickel, mineral oils, arsenic, lead *	277/240.9	115 (101-129)	Smoking: N.I. Majority of lung cancer deaths came from a large smelter, providing 64% of the study population (see text)
Ades and Kazantzis (1988)	Cd-processing	4,173	CdO dust and fumes, polycyclic hydrocarbons (in mineral oils, until 1955), lead, arsenic, copper, beryllium, sulphur dioxide	182/146.2	124.5 (107-144)	Smoking: No data for the whole cohort The increasing risk for lung cancer could not be accounted for by cadmium exposure
Kazantzis and Blanks (1992) Kazantzis et al. (1992)	Cd-processing	6,910	CdO dust and fumes, CdS, dust from Cd stabilisers, silver, copper + beryllium, nickel, mineral oils, arsenic, lead	339/304.1	112 (100-124)	Smoking: N.I

N.I. No information available
O/E Observed/expected deaths
SMR Standardised mortality ratio

Table 4.225 Cadmium and prostate cancer. Summary of the available studies

Reference	Type of plant	Study population	Exposure to	Findings		Comments
				O/E	SMR (95% CI)	
Armstrong and Kazantzis (1983)	Cd-processing	6,995	CdO dust and fumes, CdS, dust from Cd stabilisers, silver, copper + beryllium, nickel, mineral oils, arsenic, lead *	23/23.3	99 (63-148)	Mortality study
Kazantzis (1988)	Cd-processing	6,958	CdO dust and fumes, CdS, dust from Cd stabilisers, silver, copper + beryllium, nickel, mineral oils, arsenic, lead *	30/33.2	90 (61-129)	Mortality study
Kazantzis and Blanks (1992) Kazantzis et al. (1992)	Cd-processing	6,910	CdO dust and fumes, CdS, dust from Cd stabilisers, silver, copper + beryllium, nickel, mineral oils, arsenic, lead	37/49.5	75 (53-103)	Mortality study
Lemen et al. (1976)	Cd recovery	292	Cd fumes and dust	4/1.15	348 (94-891)	Mortality study
Varner (1983)	Cd recovery	625	CdO dust and fumes, $CdSO_4$, CdS, arsenic	5/N.I.	169 (N.I., SCR)	Mortality study
Thun et al. (1985)	Cd recovery	602	CdO dust and fumes, $CdSO_4$, CdS, arsenic	3/2.2	136	Mortality study
Holden (1980a, b)	Cu-Cd alloy	347 (Vicinity workers: 624)	CdO fumes, copper Vicinity workers: arsenical copper, silver, nickel	1/1.58	63 (1-352)	Mortality study Elevated risk of prostate cancer in vicinity workers (SMR=267, 95% CI: 115-526)
Sorahan (1995)	Cu-Cd alloy	347 (Vicinity workers: 624) (Control group: 521)	CdO fumes, copper Vicinity workers: arsenical copper, phosphor bronze, other copper alloys Control group: iron, brass foundry	2/2.83	71 (9-255)	Mortality study
Kjellström et al. (1979)	Cu-Cd alloy	94	CdO fumes	4/2.69	149 (40-381)	Mortality study

Table 4.225 continued overleaf

Table 4.225 continued Cadmium and prostate cancer. Summary of the available studies

Reference	Type of plant	Study population	Exposure to	Findings		Confounders and Comments
				O/E	SMR (95% CI)	
Potts (1965)	Batteries	74	CdO dust	3/N.I.	-	Mortality study
Kipling and Waterhouse (1967)	Ni-Cd batteries	248	CdO dust	4/0.58	690 (186-1766)	Incidence study.
Sorahan and Waterhouse (1983)	Ni-Cd batteries	2,559	CdO, Cd(OH)2 dust, Nickel hydroxide, oxyacetylene fumes	8/6.6	121 (52-239)	Mortality study
Sorahan and Waterhouse (1985)	Ni-Cd batteries	2,995	CdO, Cd(OH)2 dust, Nickel hydroxide, oxyacetylene fumes	15/11.02	136 (76-225)	Mortality study Significant for a subgroup (N=458), high exposure (SMR=402 (173-792))
Sorahan and Esmen (2004)	Ni-Cd batteries	926	Nickel hydroxide, cobalt, graphite, iron oxide, potassium hydroxide	9/7.5	116 (53-221)	Mortality study
Kjellström et al. (1979)	Ni-Cd batteries	228	CdO, Nickel hydroxide	2/1.2	167 (19-602)	Mortality/cancer incidence study
Andersson (1983)	Ni-Cd batteries	528	Cd (not detailed), Nickel (not detailed)	4/3.09	130	Mortality study
Elinder (1985)	Ni-Cd batteries	522	CdO dust, Nickel hydroxide, asbestos	4/3.7	108 (29-277)	Mortality study
Järup et al. (1998)	Ni-Cd batteries	869	CdO dust, Nickelhydroxyde	11/9.0	122 (61.1-219)	Mortality and cancer incidence study

N.I. No information available
O/E Observed/expected deaths
SMR Standardised mortality ratio
* From Kazantzis et al. (1992)

5) Other epidemiological studies on cadmium carcinogenicity

In addition to these cohort studies, the search in the literature and in the aforementioned reviews (IARC 1992,1993; CRC 1986; ATSDR 1993, 1999; WHO 1992) identified some other publications concerning the potential carcinogenicity of cadmium:

A hospital-based case-control study in the USA suggested an increased risk of prostate cancer for occupational exposure to cadmium (assessed by interviews) alone (or in addition to smoking) but these values were not statistically significant (Kolonel and Winkelstein, 1977).

In a study of cancer mortality patterns in Massachusetts, prostate cancer was elevated in three occupational categories, including welders that were stated as having potential exposure to cadmium (Dubrow and Wegman, 1984 cited by Waalkes and Rehm, 1994). In a similar study comprising of data from over 3,000 counties throughout the USA, a significant association between prostate cancer in white males and occupation in primary metal products or fabricated metal products industries was observed. Though no direct cadmium exposure data were available, this finding suggested to the authors that metals such as cadmium may be involved in the pathogenesis of prostatic cancer (Blair and Fraumeni, 1978 cited in Waalkes and Rehm, 1994).

The cancer mortality among male workers (number of employees not given) employed for at least one year in a smelter in China was followed from 1972 to 1985 and compared with rates for the city in which the smelter was located (Ding et al., 1987 cited in IARC 1993). When the plant was divided into 5 areas, industrial hygiene sampling indicated that exposures to cadmium were the highest in the cadmium and the sintering shops, with mean air concentrations of 0.186 and 0.014 mg/m^3 , respectively. The levels in the cadmium shop were reported to have been much higher prior to 1980 (0.535 mg/m^3). Exposure to arsenic was also reported to have occurred in the sintering area (0.196 mg/m^3 As_2O_3).

Table 4.226 Reported cancers among smelters in China (Ding et al., 1987, cited in IARC 1993)

Type of cancer	Area of the plant	Obs.	Exp.	SMR
Lung cancer	Cadmium shop	1	0.15	665
	Sintering shop	4	0.24	1,680
Stomach cancer	Sintering shop	1	0.31	318
Liver cancer	Cadmium shop	2	0.11	1,790
	Sintering shop	3	0.18	1,700

The men who died from cancer were reported to have had 10-30 years of cadmium exposure. Mortality from lung cancer was also increased in three other areas of the plant. Authors stated that there was no obvious association of the mortality from lung cancer with smoking (Ding et al., 1987 cited in IARC 1993).

Abd Elghany et al.(1990) conducted a population-based case-control study of exposure to cadmium based on 358 cases of prostate cancer newly diagnosed in 1984-1985 and 679 controls in four urban USA counties. The aim of the study was to investigate potential associations between prostate cancer and cadmium exposure, longest industry and longest occupation held. Occupational exposures to cadmium were ascertained from self-reported data, through several a priori suspect industries (suspect because of potential exposure to cadmium) and occupations, through an occupation-exposure linkage system, and through dietary food frequency questionnaires. Analyses were also conducted for the subgroup of cases classified as aggressive tumours (the aggressiveness was characterised by a combination of histologic criteria -

differentiation and stage of diagnosis-localisation), in order to differentiate more clearly the cases from the controls. Indeed, controls were identified through a random-digit dialling telephone sampling procedure and selected on the basis of their age, and this procedure could not exclude the inclusion of some latent prostate tumours.

In general, there was little evidence of an increased risk for prostate cancer associated with occupations with potential exposure to cadmium (odds ratio: 0.9, 95% CI: 0.7-1.2), with cigarette smoking (odds ratio: 1.1, 95% CI: 0.8-1.4) or with diet (odds ratio: 1.4, 95% CI: 1.0-2.1). A composite measurement of potentially high exposure to cadmium from any source was not associated with prostate cancer in general but was associated with aggressive tumours (OR: 1.7, 95% CI: 1.0-3.10) (Abd Elghany et al., 1990; IARC 1993).

In a hypothesis-generating case-control study of 20 cancer sites conducted in the Montreal metropolitan area by Siemiatycki (1991), the only type of cancer associated with the exposure to cadmium compounds (not detailed) was the bladder cancer (6 exposed cases, odds ratio: 1.6, 90% CI: 0.7-3.8). When the analysis was restricted to substantial exposure, only four cases of bladder cancer had been exposed (odds ratio: 4.9, 90% CI: 1.2-19.6). No association was found with cancers of the lung or prostate (Siemiatycki, 1991 cited in IARC 1993).

The risk of brain-nervous system cancer has been investigated in a cohort of 413,877 Finnish women with blue-collar occupations in 1970 (Wesseling et al., 2002). Exposure to 25 occupational agents was linked to job titles and cadmium exposure was found associated with an increased risk of cancer (SIR 1.26; CI 0.72 to 2.22). The authors noted that the ecological design of the study and the possible misclassification for exposure may have contributed to limit the possibility to detect an existing risk.

Several case-control studies have examined the possible association between occupational exposure to Cd and the risk of renal carcinoma.

The relationship between renal-cell cancer (RCC) and occupation was investigated in an international multicentre population-based case-control study (Mandel et al., 1995). Study centres in Australia, Denmark, Germany, Sweden and the United States interviewed 1,732 incident RCC cases and 2,309 controls. A statistically significant association was found for occupational exposure to cadmium (crude RR, 2.0; 95% CI, 1.0-3.9), but with an inverse dose-response effect (RR declined from 4.3 for 1 to 10 years of exposure to 1.0 for 31 to 41 years of exposure)

In another multicentre case-control study conducted in Germany (935 incident RCC cases and 4298 controls matched for region, sex, and age), occupational exposure was evaluated by job exposure matrices (low, high and substantial) and excess risks were shown for high exposure to cadmium (OR = 1.4, 95% CI : 1.1-1.8, in men, OR = 2.5, 95% CI : 1.2-5.3 in women). No relationship with the intensity of Cd exposure was, however, detected (Pesch et al., 2000). In Canada, another case-control study examined the same association (exposure assessed by postal questionnaire) in 935 incident RCC cases and 4,298 controls matched for region, sex, and age. A significant association was found with occupational exposure to Cd salts (adjusted OR 1.7 (1.0-3.2)) and a significant relationship with the duration of exposure (never, 1-5, ≥ 6 years) was also reported (Hu et al., 2002).

In a pilot study, the concentration of cadmium was determined quantitatively in samples of renal cortex of 22 kidney cancer patients and 19 controls (Muller et al., 1994). Data on the three main sources of exposure to cadmium-diet, cigarette smoking and occupation-were obtained through interviews. No significant difference in Cd concentration between the tumour samples and the controls could be found (50.9 ± 25 versus 55.2 ± 50 mg/kg dry weight, respectively).

Summary and discussion: other epidemiological studies

Study designs, exposure assessments and/or consideration of confounding factors in these studies do not offer a definite refinement of the assessment in comparison to the other groups of previous studies. Altogether, no clear indication for an increased risk of prostate or lung cancer due to cadmium exposure appears from these studies.

Conclusions: studies in humans

The first site of cancer which was considered to be possibly associated with cadmium exposure in humans was the prostate. An early study was based on four observed (versus 0.58 expected) prostate cancer cases among 248 workers in a nickel-cadmium battery plant in the United Kingdom (Kipling and Waterhouse, 1967). Three of these cases had been previously reported by Potts (1965) in a survey conducted at the same plant. Three other cohorts from the United States (Lemen et al., 1976) and from Sweden (Kjellström et al., 1979 copper-cadmium alloy plant, Kjellström et al., 1979 nickel-cadmium batteries) reported cases of prostate cancer but SMRs were not significantly increased. In the 1980's several larger and carefully conducted cohort studies (Armstrong and Kazantzis, 1983; Thun et al., 1985; Elinder et al., 1985) failed to confirm the increased risk of prostate cancer among workers exposed to cadmium. Altogether, it is now generally accepted that there is no increased risk for prostate cancer associated with occupational exposure to cadmium.

However, open questions remain in the overall database of epidemiological studies concerning cadmium and prostate cancer. Most of the studies have exclusively used populations of European origins and it has been reported that there are major differences in population rates for cancer of the prostate based on ethnicity (Bosland, 1994). Indeed, race is reported to be an important risk factor both for developing clinically evident disease and for dying of prostate cancer. For example, incidence and mortality rates for prostate cancer are among the highest in the world in African American men in the United States (Flanders, 1984; Greenwald, 1982) while these rates are lower for native American men and Asians living in the United States (Flanders, 1984; Higgins, 1975; Ross et al., 1984).

Furthermore, most studies have been limited to fatal cancers. Many cases of prostate cancer are missed when death alone is used as the end point for incidence of prostate malignancy. Moreover, survival has progressively improved with early detection from therapeutic and/or surgical intervention and this may be of importance in a population that might be alerted or otherwise sensitised to their risk. Finally, possible cofactors such as zinc, androgens, estrogens, etc. in prostate carcinogenesis have never been analysed. As suggested by Waalkes and Rehm (1994), ideal studies would include pathological analysis of prostate tissue obtained at resection or autopsy from a population with defined levels of cadmium exposure compared to samples from non-exposed individuals. In addition to the cadmium exposure data, data from repeated diagnostic testing (including digital rectal examination or transrectal ultrasonography and prostate-specific antigen levels) would be precious to definitely explore causation (Waalkes and Rehm, 1994).

The relationship between occupational exposure to cadmium and the risk of lung cancer has been explored in an appreciable number of epidemiological studies, as reported above, but seems to remain conflicting.

Before reaching a conclusion, some methodological issues have to be considered:

1) assessment of the exposure to cadmium;

2) dose-response relationships;

3) possibility of concomitant exposure to other carcinogens;

4) confounding from non-occupational risk factors and

5) interaction between cadmium and other risk factors.

1) Assessment of the exposure to cadmium

In most of the cohort studies, some monitoring data on cadmium air levels were available to the investigators (see **Table 4.227**). In a number of studies, these data were used as the basis for ordinal categories of exposure (high, medium, low).

Table 4.227 Type of exposure data and exposure classification given in the different cohort studies

Reference	Type of plant	Exposure data	Exposure quantification
Armstrong and Kazantzis (1983)	Cd-processing	Discussions with hygienists and others, biological and environmental results	Categories: always low, ever medium, ever high
Kazantzis (1988)	Cd-processing	Discussions with hygienists and others, biological and environmental results	Categories: always low, ever medium, ever high
Ades and Kazantzis (1988)	Cd-processing	Environmental monitoring, consultation with plant hygienist and staff Urine cadmium levels	Quantitative cumulative exposure (job histories)
Kazantzis and Blanks, Kazantzis et al. (1992)	Cd-processing	Discussions with hygienists and others, biological and environmental results	Categories: always low, ever medium, ever high
Lemen et al. (1976)	Cd recovery	Air Cd (+As) levels from the 1970's	Duration of employment (years)
Varner (1983)	Cd recovery	Air Cd levels + personal sampling	Quantitative cumulative exposure
Thun et al. (1985)	Cd recovery	Urine cadmium levels	Quantitative cumulative exposure (general work categories)
Stayner et al. (1992)	Cd recovery	Air monitoring data 1943-1976 Personal sampling data 1973-1976	Quantitative cumulative exposure (general work categories)
Holden (1980)	Cu-Cd alloy	Air Cd levels: surveys 1953,1957, data mid 1960's	Duration (years)
Sorahan et al. (1995)	Cu-Cd alloy	"All available measurements, changes in techniques, ventilation, levels of production, and discussions with staff and work force…"	Quantitative cumulative exposure
Kjellström et al. (1979)	Cu-Cd alloy	Data from the 1960's	Overall
Potts (1965)	Batteries	N.I.	Overall
Kipling and Waterhouse (1967)	Ni-Cd batteries	N.I.	Overall
Sorahan and Waterhouse (1983)	Ni-Cd batteries	Air Cd levels: 1949, 1950's,1967, 1975	Categories: high, moderate, minimal (on job histories) – Duration
Sorahan and Waterhouse (1985)	Ni-Cd batteries	As above	Categories: high, remainders
Kjellström et al. (1979)	Ni-Cd batteries	Data from 1947,1950's, 1962-1974, 1979	Duration (years) – Time starting work
Andersson (1983)	Ni-Cd batteries	Air Cd levels: < 1946, 1980's	Duration (years)
Elinder (1985)	Ni-Cd batteries	Air Cd levels: 1947-1975	Duration (years)- Time lapse since first exposure

Table 4.227 continued overleaf

Table 4.227 continued Type of exposure data and exposure classification given in the different cohort studies

Reference	Type of plant	Exposure data	Exposure quantification
Järup et al. (1998)	Ni-Cd batteries	Workplace measurements reports (1946-1992)	Quantitative cumulative exposure (job histories)
Sorahan (1987)	Ni-Cd batteries	Air Cd levels: surveys 1953, 1957, data mid 1960's	Categories: high, moderate, minimal
Sorahan and Esmen (2004)	Ni-Cd batteries	Air Cd levels: 1957-1992, personal sampling 1964-1992	Cumulative cadmium exposure categories

Boffetta noted, in 1992, that in spite of the availability of a substantial amount of data on cadmium levels, most epidemiological studies did not attempt to classify workers according to a quantitative index of cumulative exposure. In the last years, several authors have tried to have a more precise assessment of the cadmium exposure in their cohorts.

This heterogeneity in the characterisation of exposure does not allow an appropriate comparison between the studies.

2) Dose-response relationships

A number of studies yielded results allowing the investigation of the dose-response relationships between lung cancer risk and cadmium exposure.

Several studies showed an increase in lung cancer risk with duration of exposure (Elinder et al., 1985; Ades and Kazantzis, 1988, Sorahan and Waterhouse, 1983, Sorahan, 1987) or cumulative exposure (Varner, 1983; Thun et al., 1985; Stayner et al., 1992; Sorahan and Lancashire, 1997) but not with latency time.

3) Concomitant exposure to carcinogens

The possibility of a confounding effect due to exposure to other potential carcinogens is a major limitation of most of the occupational cohort studies. In the available studies on cadmium workers, the most important co-exposures were nickel in the Ni-Cd batteries factories, arsenic in the Cd-recovery plants but also welding fumes, mineral oils, lead, zinc, beryllium and other metals. Not all the studies reported the exposure levels to these agents and several were unable to control for the possible confounding effect of these factors.

4) Confounding from non-occupational risk factors

The most important non-occupational risk factor that may confound the association between cancer and cadmium exposure is tobacco smoking. It is a well-known cause of lung cancer and has also been associated with an increase in prostate cancer risk. On the other hand, tobacco smoking is an important route of non-occupational exposure to cadmium.

Combined exposure to cadmium in the industry and from tobacco smoke may have greater deleterious effects on the workers' health by initiating or enhancing disease because of possible additive or multiplicative biological effects (Shaham et al., 1996).

Smoking may act in two ways in confounding the association between occupational exposure to cadmium and lung cancer. On the one hand, if workers exposed to cadmium smoke more than the reference population, an association may be found suggesting a false carcinogenic effect of cadmium. On the other hand, a large number of cigarettes smoked will result in an individual dose of cadmium higher than that estimated from workplace monitoring data and in an overestimation of the carcinogenic effect of cadmium (Boffetta, 1992).

5) Interaction between cadmium and other risk factors

Very few epidemiological data are available on the possible interaction between cadmium and other risk factors in the causation of cancer. In the case-control study conducted by Kolonel (1976), a multiplicative effect between cigarette smoking and occupational exposure to cadmium was observed for the smokers. In the case-control study of Abd Elghany et al. (1990), an additive effect between smoking, diet high in cadmium and occupational exposure to cadmium was reported. No synergistic effect was found, on the other hand, by Ades and Kazantzis, when they tested interactions between pairs of exposures (cadmium, zinc, sulphur dioxide, arsenic, lead, dust) (Boffetta, 1992).

Conclusions: are cadmium metal and cadmium oxide carcinogens?

There is no indication or evidence that cadmium oxide or metal may act as carcinogens in the general population exposed by the oral route.

Considering the working population, there is currently no solid evidence that cadmium (generic) acts as a prostatic carcinogen following occupational exposure.

Interest in the possible carcinogenicity of cadmium is focused primarily on the lung since cadmium compounds, including cadmium oxide (but not Cd metal), have been shown to produce bronchial carcinoma in rats. Several cohort studies have been conducted in cadmium plants over the world in the hope to allow an assessment of the carcinogenic potential of cadmium compounds. However, most of the studies have had to camp with methodological difficulties, or could not totally exclude the effect of confounding factors (smoking, simultaneous exposures to other carcinogens, etc.). The possibility that cadmium oxide might cause a risk of lung cancer by inhalation has neither been excluded nor affirmed by several reviewers.

Overall, however, the weight of evidence collected in genotoxicity tests (see Section 4.1.2.8), long-term animal experiments and epidemiological studies (see Section 4.1.2.9) leads to conclude that cadmium oxide has to be considered at least as a suspected human carcinogen (lung cancer).

Summary information related to the classification[34] as well as the judgement on the fulfilment of the base-set requirements

Overall, the weight of evidence collected in genotoxicity tests, long-term animal experiments and epidemiological studies leads to consider cadmium oxide as a suspected human inhalation carcinogen (lung cancer) and the TM would therefore maintain its classification as carc.cat 2 (T; R49 i.e. may cause cancer by inhalation).

However, the CMR WG reviewed the classification and agreed (May 2002) to classify CdO with Carc.Cat 2; R45 (may cause cancer): i.e. carcinogenic potential irrespective of the exposure route (ECBI/42/02 Rev2).

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[34] The **classification was done for cadmium oxide** and based on specific substance data, if available, and/or data from other cadmium compounds (more soluble forms). The extrapolation is done on the basis of the so-called 'ion theory' and as a 'worst case' approach related to the bio-availability of the metal.

Cadmium metal is a carcinogen when injected in experimental animals. No study was specifically conducted with cadmium metal in animals exposed by inhalation or in humans specifically exposed to this species, which does not allow to sufficiently document its carcinogenic potential.

Summary information related to the classification of Cadmium metal

In the absence of specific information for Cd metal, but given the Carc. Cat 2 (T; R45) classification of CdF_2, $CdSO_4$, $CdCl_2$ and CdO, a Cat 2 (T; R45 i.e. may cause cancer) classification was agreed for cadmium metal by analogy.

4.1.2.10 Toxicity for reproduction

4.1.2.10.1 Introduction

The placenta provides a relative barrier protecting the fœtus against cadmium exposure (see Section 4.1.2.2). However, cadmium has been reported to possibly affect structure and function of the placenta itself and so to be potentially associated with developmental effects such as a decreased birth weight. Moreover, an association between cadmium exposure and toxicity for the developing brain has been suggested, but the mechanism is not yet elucidated. Effects of cadmium on fertility and sex organs have been reported in animals and occasionally in humans but data are limited and the meaning of the observed variations is not always clear in terms of "adverse effects". Concern about this issue has recently been revived by the finding (in a single laboratory) that cadmium salts could possess oestrogenic activity (see below, other routes).

Experimental and epidemiological data reporting potential effects of Cd on fertility/sex organs and/or development will be reviewed in sections 4.1.2.10.2 and 4.1.2.10.3, respectively. Some *in vitro* experiments have been conducted to address on mechanisms of action of cadmium on placenta and spermatozoids. These studies are reported in **Annex E**.

The terms "cadmium compounds" used here below refer to other compounds of cadmium than the oxide and the metallic forms. Data relating to these compounds are given hereafter with another letter size and type.

4.1.2.10.2 Effects on fertility and sex organs

Studies in animals

Oral route

No studies in animals specifically using cadmium oxide or metal administered by the oral route has been located. Most studies used water-soluble cadmium compounds.

Effects on male organs and male fertility

The acute and chronic toxicity of cadmium on the testis has been investigated in several experiments conducted with cadmium compounds. Main characteristics of these experiments are summarised in **Table 4.228**.

Table 4.228 Located experiments conducted with cadmium compounds in rats and mice dealing with the effects of Cd on male fertility and sex organs

Doses of Cadmium	Duration	Reproductive NOAEL	Reproductive NOAEL(mg Cd/ kg/day)	ReproductiveLOAEL(mg Cd/ kg/day)	Reference	Comments
Rats						
0-6.25-12.5-25 mg $CdCl_2$/ kg (W)	single dose	25 mg	15	-	Dixon et al. (1976) cited in ATSDR (1999)	Only abstract available
0-25-50-100-150 mg $CdCl_2$/ kg (G)	single dose	50 mg $CdCl_2$/ kg	30.6	61.2	Kotsonis and Klaassen (1977)	
0-50-100-200 mg $CdCl_2$/ kg (G)	single dose	50 mg $CdCl_2$/ kg	30.6	61.2	Bomhard et al. (1987)	
0-25-51-107-225 mg $CdCl_2$/kg (G)	10 days	51 mg $CdCl_2$/ kg	31.3	65.6	Borzelleca et al. (1989)	
13-323 mg $CdCl_2$/l (W)	10 days	323 mg $CdCl_2$ /L	24.7*	-	Borzelleca et al. (1989)	
0-5 mg $CdCl_2$ /kg (G)	10 weekly doses	5 mg $CdCl_2$/ kg	3.6	-	Bomhard et al. (1987)	
- -	30-90 days		5 [&]	-	Dixon et al. (1976) cited in ATSDR (1999)	Details of dosing not available (Only abstract)
0-17.2-34.4-68.8 mg Cd/L (W) as $CdCl_2$)	70-80 days	34.4 mg Cd/L	4.64	-	Zenick et al. (1982)	
- (W) (as $CdCl_2$)	10 weeks	-	-	8.58[&]	Cha et al. (1987) cited in ATSDR (1999)	Only abstract available. Details of dosing not available
- (W)	14 weeks	5 mg $CdCl_2$/kg/day	2.9	5.8[&]	Pleasants et al., (1992, 1993) cited in ATSDR (1999)	Only abstract available. Details of dosing not available
- (W)	6 months	N.I.	N.I.	3	Krasovskii et al. (1976)	Only abstract available. Details of dosing not available
0-10-30-100 mg Cd/L (W) (as $CdCl_2$)	24 weeks	100 mg Cd/L	12.5*	-	Kotsonis and Klaassen (1978)	

Table 4.228 continued overleaf

Table 4.228 continued Located experiments conducted with cadmium compounds in rats and mice dealing with the effects of Cd on male fertility and sex organs

Doses of Cadmium	Duration	Reproductive NOAEL	Reproductive NOAEL(mg Cd/ kg/day)	ReproductiveLOAEL(mg Cd/ kg/day)	Reference	Comments
50 ppm (W) (as Cd acetate)	120 days	-	-	12.6	Saxena et al. (1989) cited in ATSDR (1999)	Only abstract available. Details of dosing not available
10 mg $CdCl_2$/L (W)	52 weeks	10 mg $CdCl_2$/ L	-	± 0.8*	Saygi et al. (1991)	Number of animals with pathological findings not given
Mice						
0-270-530-790 µmol Cd/kg (as $CdCl_2$) (G)	single	270 µmol/kg	30.4	59.6	Andersen et al. (1988)	

* Estimated consumption of water: 25 ml/day,
Estimated weight of the rat: 200 g (Derelanko, 2000),
(G) Gavage
(W) Water
For further information on these experiments see IUCLID and N(L)OAEL reported in ATSDR 1999 without further details on the experiments themselves

Dixon et al. (1976) examined the effects of a single dose of Cd in drinking water. No effects on body weight, weight of testis, prostate and seminal vesicles were observed. No change in testis histopathology was reported, neither was an effect on clinical parameters or serum hormone levels.

Kotsonis and Klaassen (1977) treated rats with a single dose of Cd. Histopathological examination indicated focal testicular necrosis and reduced spermatogenesis at 100 and 150 mg/kg but no changes at the lower doses. Concentrations of cadmium in the testicles were ~0.35 µg/g for the two highest dosed groups 2 days after dosing and decreased 20-35% after 14 days.

25 males were each treated once with 200 mg $CdCl_2$/kg and 35 males with 100 mg $CdCl_2$/kg in an experiment conducted by Bomhard et al. (1987). Animals were sacrificed 6 months later. Animals having received both 100 and 200 mg $CdCl_2$/kg showed severe lesions of the whole testicular parenchyma with massive calcification of the necrotic tubuli and pronounced fibrosis of the interstitium.

By gavage (10 days), a dose of 107 mg $CdCl_2$/kg produced testicular atrophy and loss of spermatogenic element in the study of Borzelleca et al. (1989). A dose-dependent increase in mortality, kidney and hepatic changes was also observed in the treated rats. In the drinking-water study conducted by the same authors, dose-dependent effects on body weight and organ weights were observed but did not concern the testes.

Bomhard et al. (1987) examined also the chronic effects of repeated oral Cd administration on the testis of mature Wistar rats. Animals were necropsied after 12 and 18 months, or were kept up to 30 months. Findings were comparable to controls.

No effects on testis histopathology, clinical parameters or hormone levels were reported to have occurred after repeated exposure to cadmium (30-90 days) in the experiment conducted by Dixon et al. (1976).

A dosing regimen of 4.64 mg Cd/kg/day via water did not result in any effect on reproductive parameters (Zenick et al., 1982).

Male rats exposed to 8.58 mg Cd/kg/day for more than two months developed necrosis and atrophy of seminiferous tubule epithelium (Cha et al., 1987).

Pleasants et al. (1992, 1993) reported a cadmium-related increase in testis weight, reduced by simultaneous administration of vitamins A and D_3.

Krasovskii et al. (1976) have reported significant reductions in sperm number and motility and a significant desquamation of spermatogenic epithelium in rats receiving cadmium orally for 6 months. Authors noted that this gonadotoxic effect of cadmium was manifested on the same level as the general toxic effect (3 mg/kg of body weight).

When Kotsonis and Klaassen (1978) investigated the effects of a prolonged administration of Cd to rats, no altered testicular function was observed. Testicular tissue was within normal limits at histopathological examination although the concentration of Cd in the testes after 12 weeks was greater (± 0.9 µg Cd/g) than that which caused testicular injury in the previous acute study (Kotsonis and Klaassen,1977).

Rats exposed to 12.6 mg/kg/day for 120 days developed significantly increased relative testis weight, decreased sperm count and motility, decreased seminiferous tubular diameter and seminiferous tubular damage (pyknotic nuclei, multinucleated giant cells, interstitial oedema and dilated blood vessels) (Saxena et al., cited in ATSDR 1999).

Saygi et al. (1991) examined the effect of cadmium (administered during 52 weeks) on the histological and morphological patterns of the testis. At the end of the treatment, animals were kept for mating for an additional period of 30 days. On gross pathological examination, no testicular alterations were observed in animals sacrificed within the exposure period. However, histologically, necrosis of spermatogonia, spermatocyte and spermatid was observed in some tubuli seminiferi at the end of the 10^{th} month of cadmium intake. Some tubuli showed atrophy, oedema and vascular hyperaemia in the interstitium. At the end of the 13^{th} month, a slight atrophy of the testis and hyperaemia was observed in the tunica vaginalis and serosal vessels of the interstitium as compared with the controls. Necrosis of spermatogonia, spermatocyte and spermatid were more apparent than at the end of the 10^{th} month intake. Some tubuli had no spermatozoa. Beneath these testicular effects, kidney alterations were also observed (cystic dilatation in cortical tubuli, some glomerular atrophy, etc.). Some rats were reported to have "lost their reproduction capacities" when fertility was assessed; however, it is not indicated whether these rats are those in which histopathological anomalies were observed. Because of the incomplete test report, and despite the interesting findings noted at 10 mg/l (± 0.8 mg Cd/kg/day), the study of Saygi et al. (1991) could not be identified as the most critical study to describe effects on fertility.

Andersen et al. (1988) reported a relative testicular deposition of cadmium in mice that was nearly constant at doses not inducing testicular damage but that decreased at doses inducing necrosis of tubules and interstitial tissue (60-90 mg Cd/kg). They attributed this decrease to the cadmium-induced vascular damage and reduced circulation. At this dose, tissular damage was also observed in the gastro-intestinal tract and in the liver.

In several of these studies male fertility was assessed by placing males after dosing with untreated females and recording the fractions of females producing offspring:

Table 4.229 Effects on male fertility assessed in above mentioned studies

Effect on male fertility	Reference
Higher dose rats (100-150 mg Cd/kg) were significantly less fertile than the control rats (1/6 vs. 5/6 females pregnant in the lower dose groups)	Kotsonis and Klaassen (1977)
Fractions of females producing offspring were not significantly different from controls	Kotsonis and Klaassen (1978)
"Reduced reproductive function" (no pregnancies or deliveries in 38.9% of the rats)	Saygi et al. (1991)

A dose of 10 mg/kg/day (as $CdCl_2$) for 9 weeks did not affect the fertility of male rats in dominant lethal tests (Sutou et al., 1980). The five analysed fertility indices (copulating ability and impregnating ability of males and copulated ratio, pregnant ratio, and pregnancy efficiency of females) did not reveal a difference with control rats when males were mated with untreated females. When treated males were mated with females having undergone the same Cd treatment, adverse effects were observed in the 10 mg/kg/day group on number of copulation and pregnancies, on the number of implants and live fetuses (NOAEL: 1 mg Cd/kg/day). This study with acceptable test design and study reporting appears to be the most critical study related to effects on fertility.

Effects on female organs and female fertility

Higher doses of cadmium compounds were generally needed to elicit a reproductive toxic response in females compared to the males (ATSDR, 1999). Effects included decreased percentage of fertilised females and percentage of pregnancies, and increased duration of the oestrus cycle.

Table 4.230 Located experiments conducted with cadmium compounds on effects on female sex organs and fertility

Doses of Cadmium	Duration	Reproductive NOAEL (mg Cd/kg/day)	ReproductiveL OAEL(mg Cd/k g/day)	Reference	Observed effect
Rats					
0-0.1-1.0-10 mg Cd/kg/day (G)	6 weeks + 3 weeks during	1.0	10	Sutou et al. (1980)	> 50% fewer copulating and pregnant females
0.04-0.4-4.0-40 mg Cd/kg/day (G) (as $CdCl_2$)	14 weeks	4.0	40	Baranski and Sitarek (1987)	Length of oestrous cycle twice as in control rats
Mice					
2.5 mg/kg/day (W) (unspecified form of Cd)	6 months	N.D.	2.5	Schroeder and Mitchener (1971)	"low mating index"
0.25-5.0 or 50 ppm Cd (as $CdCl_2$) (D)	6 consecutive rounds of 42 days	5.0	50 (with deficient diet)	Whelton et al. (1988)	Decreased fertility and litter size

(G) Gavage
(W) Water
(D) Diet

In females treated with 10 mg/kg/day by gavage, adverse effects were found on numbers of copulations and pregnancies. These females showed signs of toxicity like depressed body and organ weights (Sutou et al., 1980).

Repeated administration of cadmium chloride by gavage to female rats at doses of 0.04, 0.4 or 4 mg Cd/kg/day did not change the length of the oestrous cycle and the duration of its phases. At a dose of 40 mg Cd/kg/day the length of the oestrous cycle was twice as long as in control rats. However, in this high dose group other signs of toxicity appeared (animals became emaciated, aggressive with ruffled hair coat) and lethality was elevated as summarised in **Table 4.231**. Authors attributed these signs of toxicity to the Cd treatment.

Table 4.231 Mean length (± SD) of the oestrous cycle in days and lethality in female rats given $CdCl_2$ (Baranski and Sitarek 1987)

Dose (mg Cd/kg/day)	Before treatment	7-8 weeks of exposure		13-14 weeks of exposure	
		Length (days)	Lethality (%)	Length (days)	Lethality (%)
0	4.1 ± 0.2 (12)	4.1 ± 0.2 (12)	0	5.2 ± 3.3 (12)	0
0.04	4.1 ± 0.1 (12)	4.0 ± 0.1 (12)	0	5.4 ± 3.5 (12)	0
0.4	4.0 ± 0.1 (11)	4.0 ± 0.1 (11)	0	4.0 ± 0.1 (11)	0
4.0	4.0 ± 0.2 (13)	4.1 ± 0.2 (13)	0	4.2 ± 0.5 (13)	0
40.0	4.1 ± 0.1 (13)	10.8 ± 4.0* (9)	31	10.3 ± 3.9* (9)	54

Authors concluded that exposure to cadmium did not affect the sexual cycle unless other overt signs of Cd toxicity were induced (Baranski and Sitarek, 1987).

Female mice were bred for 6 consecutive, 42-days rounds of gestation-lactation (Whelton et al., 1988). Diet contained either 0.25-5.0 or 50 ppm Cd and were either sufficient or deficient in certain vitamins, minerals, and fat. The dose of 5 ppm cadmium combined with a deficient diet was designed to simulate conditions implicated in the aetiology of Itai-Itai disease. Exposure to Cd did not decrease fertility for mice on sufficient diet. Combined exposure to cadmium and nutritional deficiencies had a synergistic effect on fertility and litter size that was statistically significant at 50 ppm:

Table 4.232 Summary of the effects of 50 ppm cadmium and dietary deficiencies on reproductive success (Whelton et al., 1988)

Exposure	Percentage decrease	
	Fertility (% of litters per females bred)	Litter size
50 ppm cadmium [a]	0	15
Deficient diet [b]	12	30
50 ppm cadmium + deficient diet [c]	45	43

a Percentage decrease are from the 0.25 ppm Cd (sufficient diet) group to the 50 ppm Cd (sufficient diet) group

b Percentage decrease are from the 0.25 ppm Cd (sufficient diet) group to the 0.25 ppm Cod (deficient diet) group

c Percentage decreases are from the 0.25 ppm Cd (sufficient diet) group to the 50 ppm Cd (deficient diet) group

Authors suggest that the low calcium content of the deficient diet possibly allowed Cd to interfere with calcium pathways important to maintain fertility. Authors noted as of particular interest the invariance in the magnitude of responses to Cd and nutritional deficiencies with successive rounds of breeding. Increases with time in the extent of dietary deficiencies and in cadmium burdens of maternal organs had no measurable effect on reproduction.

Table 4.233 Reproductive results for the population of mice - rounds 2-5* (Whelton et al., 1988)

Cd (ppm)	Diet	Round			
		2	3	4	5
Fertility (percentage of litters per females bred)					
0.25	+	73	61	64	60
0.25	-	55	71	45	55
5	+	72	69	67	65
5	-	49	60	42	62
50	+	75	80	64	55
50	-	27	48	32	38
Litter size: live pups per litter on the day of birth (mean ± SE)					
0.25	+	11.2 ± 0.4	12.2 ± 0.4	10.7 ± 0.6	10.8 ± 0.7
0.25	-	8.0 ± 0.5	8.4 ± 0.6	7.3 ± 0.7	7.7 ± 0.7
5	+	10.0 ± 0.5	11.6 ± 0.5	9.0 ± 0.6	9.4 ± 0.6
Litter size: live pups per litter on the day of birth (mean ± SE)					
5	-	8.0 ± 0.5	8.3 ± 0.6	9.3 ± 0.8	8.2 ± 0.6
50	+	9.6 ± 0.4	9.7 ± 0.4	9.4 ± 0.5	9.2 ± 0.6
50	-	6.2 ± 0.6	6.7 ± 0.5	6.4 ± 0.5	6.1 ± 0.5

* Data from rounds 1 and 6 have been omitted because round 1 mice were in a period of adjustment to the purified diets, while at the terminus of round 5 large numbers of the most reproductively successful females were diverted to an ovariectomy experiment

The soil of the Dutch part of Kempenland (Netherlands) has been contaminated with cadmium by various industries in the Netherlands and Belgium since the last century. Kreis et al. (1993) conducted a historic follow-up study that addressed the possibility of diminished fertility, decreased twinning rate and other developmental effects (increased foetal death) in cattle. Red-white Meuse-Rhine-Yssel cows from dairy farms located in Kempenland and in a reference area (remote from major cadmium emissions but in the same Veterinary Health Service region) constituted two cohorts. Data on accumulated exposure to cadmium had been recorded at slaughter over a 3-year period for cows in the 2 cohorts. Each cow was registered for fertility characteristics (fertility, foetal death, complications at birth, and twinning rate) and milk production; birth defects and body weights were not recorded.

Data on cadmium ground water and soil levels were available for the two cohorts (cadmium soil levels of 1-2.5 and 0.4 mg/kg dry weight for exposed and reference areas, respectively). Herd sizes, feeding practices and productivity were comparable between the farms.

Overall conclusion was that reproduction of dairy cows in Kempenland appeared to be slightly impaired when compared to the reference area. When only artificial inseminations were compared (exclusion of the old-fashioned methods), the number of inseminations needed for conception seemed somewhat increased in the exposed area. Fewer twins were born to cows from the exposed area compared to control area. Authors suggested that long-term exposure to low levels of cadmium in soil, grass and food is associated with impaired reproduction in cows. However, confounding exposures to other chemicals might have been possible and this is not precisely documented in the study (Kreis et al., 1993).

Multigenerational studies

Both female and male mice were treated by Schroeder and Mitchener (1971) over two generations with 2.5 mg $CdCl_2$/kg/day via the drinking water. Five pairs of mice were given Cd from weaning and allowed to breed freely up to 6 months of age. In the F1 litters, average litter size at birth was normal. Three of five pairs failed to breed in the second generation (Schroeder and Mitchener 1971 cited in Barlow and Sullivan 1982).

The effects of a low-level exposure to cadmium (0-0.1-1.0-5.0 ppm) on reproduction and growth were evaluated in SD rats by Laskey et al. (1980). Exposure started with conception of the first generation and continued throughout the experiment (130 days). According to the water consumption data, the F1 rats received approximately 1.3 mg Cd/kg/day as young animals which decreased to 0.5 mg Cd/kg/day as they reached adulthood. No gross testicular pathology or depression in fertility was observed. Epididymal sperm count at 130 days was reduced approximately 20% in the 5 ppm Cd group but not at 50 days. No increase in serum FSH accompanied this reduced sperm count. Liver weight was decreased in the 5.0 ppm group.

Three consecutive generations of Wistar rats were treated by gavage with 3.5, 7.0 or 14.0 mg/kg cadmium (as cadmium chloride) over the period of pregnancy, lactation and 8 weeks after weaning in a study carried out by Nagymajtenyi et al. (1997). Aim of the study was to investigate possible behavioural and functional neurotoxicological changes caused by cadmium. However, the effects on the reproductive function were not assessed (for more details on this study, see Section 4.1.2.10.3).

Summary: oral route, effects on sex organs and fertility

No studies in animals specifically using cadmium oxide or metal has been identified.

Effects of Cd treatment on male and female reproductive organs were observed after oral administration (as Cd compounds) in rats and mice. In several studies, effects were detected at dose levels which caused also general toxicity (effects on kidney, liver or body weight).

In male rats and mice, acute exposure cadmium compounds at doses higher than 50 mg/kg can cause testicular atrophy and necrosis, and concomitant decreased fertility. In females, effects on length of oestrous cycle after administration of Cd compounds by gavage were observed at a dose of 40 mg/kg/day. Fertility was however reported to be affected at doses of 10 mg/kg/day.

Overall, the lowest concentration of cadmium reported to affect fertility in rats was 10 mg Cd/kg/day (number of copulations and pregnancies, number of implants and fetuses were decreased) when males and females rats were both treated (no effect was seen at 1 mg Cd/kg/day : NOAEL).

Inhalation route

Some experiments were conducted with cadmium oxide in male rats and mice. No study specifically using cadmium metal was located.

Effects on male organs and male fertility

Male rats were exposed for 13 weeks to 0-0.025-0.05-0.1-0.25-1 mg CdO/m³ (as CdO aerosol) to assess effects on reproductive function at the end of the study (NTP Report, 1995). Number of spermatids per testis was reduced (72.1 ± 2.31/ 10^{-4} ml testis suspension versus 90.8 ± 0.44/ 10^{-4}

ml in controls) at 1 mg CdO/m^3. At this exposure level, other signs of toxicity were observed and are summarised in **Table 4.234**.

Table 4.234 Reproductive and systemic toxicity in MALE F344/N rats exposed to CdO (13 weeks) (NTP Report, 1995)

		Concentration (mg/m^3)			
		0	0.025	0.1	1
Reproductive toxicity	Testis/epididymis weight	NS	NS	NS	NS
	Spermatid count	NS	NS	NS	↓
	Sperm motility	NS	NS	NS	NS
Toxicity in other systems	Lung				
	Weight (absolute and relative)	NS	NS	↑	↑
	Alveolar histiocytic infiltrate	-	-	+	+
	Alveolar epithelial hyperplasia	-	-	+	+
	Inflammation	-	-	-	+
	Fibrosis	-	-	+	+
	Mediastinal lymph node				
	inflammation	-	-	+	+
	Larynx				
	Epithelial degeneration	-	+	+	+
	Nose				
	Olfactory epithelium				
	Degeneration	-	-	-	+
	Resp.metaplasia	-	-	-	+
	Squamous metaplasia	-	-	-	+
	Respiratory epithelium				
	Inflammation	-	-	-	+
	Degeneration	-	-	-	+
	Kidney				
	Weight (relative)	NS	NS	↑	↑
	Urinalysis parameters*	NS	NS	NS	NS
				Reproductive NOAEL	

- \- No lesions present (histopathology)
- NS Not significantly different from the control group
- \+ Significantly different from the control group
- * Aspartate aminotransferase levels(mU/mg creat)
- ↑ Increased

In male mice exposed to same concentrations of CdO, no reproductive toxicity was observed at any exposure level (NTP Report, 1995) (NOAEL: 1 mg CdO/m^3)

Effects on female organs and fertility:

Female rats were exposed by inhalation to CdO for 20 weeks (5 hours a day, 5 days a week) at concentrations of 0.02-0.16 and 1 mg Cd/m^3. In the high dose group (1 mg Cd/m^3) marked changes in the oestrous cycle occurred: a pronounced increase in the main duration of the oestrous cycle was observed 7-8 weeks after exposure (7.1 ± 3.8 days versus 4.9 ± 2.0 in controls). Body weight gain of the females exposed to 1 mg Cd/m^3 was significantly decreased and lethality was significantly higher in this group compared to the other experimental groups and increased with duration of exposure.

Table 4.235 Mean length (± SD) of the oestrous cycle in days and lethality in female rats exposed by inhalation to CdO (Baranski and Sitarek 1987)

Dose (mg Cd/kg/day)	Before treatment	7-8 weeks of exposure		13-14 weeks of exposure		19-20 weeks of exposure	
		Length (days)	Lethality (%)	Length (days)	Lethality (%)	Length (days)	Lethality (%)
0	4.3 ± 0.4 (14)	4.9 ± 2.0 (14)	0	5.1 ± 2.6 (13)	8	7.0 ± 3.7 (12)	14
0.02	4.5 ± 0.5 (14)	5.6 ± 1.7 (14)	0	5.6 ± 2.5 (14)	0	10.0 ± 4.3§ (13)	7
0.16	4.2 ± 0.3 (14)	4.7 ± 0.7 §(14)	0	5.5 ± 2.6 §(14)	0	10.3 ± 3.4§ (14)	0
1.0	4.3 ± 0.5 (13)	7.1 ± 3.8 §(11)	15	8.6 ± 3.7*§(8)	38	-	100*

Number of exposed animals are reported between brackets
* Significantly different ($p < 0.05$) from the control group in the same period of the experiment
§ Significantly different ($p < 0.05$) from the same group before treatment

At lower exposure levels (0.02 and 0.16 mg Cd/m^3), no changes in the main duration of the oestrous cycle were found when compared with that of controls, although at the end of exposure it was significantly longer than before the onset of treatment. During the last 2 weeks of exposure, the percentage of females (93%) with prolonged cycle (> 6 days) in the group exposed to 0.16 mg Cd/m^3 group, was significantly higher than in the control group but mean duration of the cycle was not reported to be significantly different from that in the non-exposed group (LOAEL: 1 mg Cd/m^3). Body weight gain of females exposed to 0.02 and 0.16 mg Cd/m^3 remained unchanged. Authors concluded that alterations of the oestrous cycle evoked by repeated exposure to Cd appeared only in female rats exhibiting other signs of Cd intoxication (depressed body weight gain, increased lethality) (Baranski and Sitarek, 1987).

In the NTP study, a significant increase in the length of the oestrous cycle (5.45 ± 0.33 vs. 4.75 ± 0.08 days in exposed and controls respectively) was observed in female rats exposed to 1.0 mg CdO/m^3 (NTP Report, 1995). However, there were no histopathologic lesions indicative of toxicity of the reproductive system, suggesting that reproductive effects at the highest exposure level in rats may be related to other effects of cadmium such as hormonal changes (NTP Report, 1995).

Table 4.236 Reproductive and systemic toxicity in FEMALE F344/N rats exposed to CdO (13 weeks) (NTP Report, 1995)

		Concentration (mg/m^3)			
		0	0.025	0.1	1
Reproductive toxicity	**Oestrous cycle length**	**NS**	**NS**	**NS**	↑
Toxicity in other systems	Lung				
	Weight (absolute and relative)	NS	NS	↑	↑
	Alveolar histiocytic infiltrate	-	-	+	+
	Alveolar epithelial hyperplasia	-	-	+	+
	Inflammation	-	-	-	+
	Fibrosis	-	-	+	+
	Mediastinal lymph node				
	Inflammation	-	-	+	+
	Larynx				
	Epithelial degeneration	-	+	+	+
	Nose				
	Olfactory epithelium				
	Degeneration	-	-	-	+
	Resp.metaplasia	-	-	-	+
	Squamous metaplasia	-	-	-	+
	Respiratory epithelium				
	Inflammation	-	-	+	+
	Kidney				
	Weight (relative)	NS	NS	NS	↑
	Urinalysis parameters*	NS	NS	NS	↑
				Reproductive NOAEL	

- No lesions present (histopathology)
NS Not significantly different from the control group
+ Significantly different from the control group
* Aspartate aminotransferase levels (mU/mg creat)
↑ Increased

In female $B6C3F_1$ mice exposed for 13 weeks to CdO (0-0.025-0.05-0.1-0.25-1 mg CdO/m^3) (NTP Report 1995), no indication fore reproductive toxicity was reported at any exposure level (NOAEL: 1 mg CdO/m^3).

Summary: inhalation route, effects on sex organs and fertility

No study specifically using cadmium metal was located.

In male rats exposed by inhalation to 1 mg cadmium oxide/m^3 for 13 weeks, the number of spermatids per testis, as evaluated at necropsy, was reduced compared to controls. No histopathological changes of the reproductive system were observed (Reproductive LOAEL: 1 mg CdO/m^3 ($\cong$ 0.9 mg Cd/m^3)). This effect on the number of spermatids was not observed in mice.

Exposure to cadmium oxide at a concentration of 1 mg/m^3 (for more than 10 weeks) has been associated with an increase in oestrous cycle length in rats in two studies. It has been suggested that the effects on the oestrous cycle occur only when other signs of Cd intoxication are present and might be related to other Cd-induced effects such as hormonal changes. However, current data do not allow concluding that the effect on the oestrous cycle is a consequence of the other toxic effects. Reproductive LOAEL used is: 1 mg CdO/m^3 ($\cong$ 0.9 mg Cd/m^3), derived from the NTP study. This change in oestrous cycle length was not observed in mice exposed to the same concentrations of CdO.

The overall NOAEL is 0.1 mg CdO/m^3 (about 0.09 mg Cd/m^3).

Other routes

Effects of Cd (compounds) treatment on male and female reproductive organs have been observed after subcutaneous, intratesticular or intraperitoneal administration.

Martin and colleagues found that cadmium administered by single intraperitoneal injection mimics oestrogen activity in breast cancer cells and that cadmium binds to and activates oestrogen receptor-α (Martin et al., 2003; Stoica et al., 2000). Recently, they reported vaginal epithelial cornification and increased uterine weight after a single dose of cadmium (5µg/kg body weight) in ovariectomised rats and these effects did not occur in the presence of anti oestrogenic drugs (Johnson et al., 2003). While these studies may help to understand how Cd may cause adverse effects on reproduction, their relevance for humans has not been explored yet.

However, these routes are not considered to be relevant for a human risk assessment.

Epidemiological studies

Whether chronic exposure to cadmium may have a deleterious effect on fertility and reproductive organs in humans is still an open question.

To take into account the different exposure conditions to cadmium, studies were grouped in subchapters according to the concerned population: the general population exposed to cadmium by the oral route (not necessarily Cd or CdO), the workers exposed by inhalation, and the smoking population.

Oral route: general population

Table 4.237 lists the located studies and presents the main characteristics of the selected population, the exposure assessment and the considered endpoint reported in all the identified studies. Only a limited number of studies have assessed the effects of Cd in populations indirectly exposed to cadmium. An overview of the selected studies is given in **Tables 4.238** to **4.243**. **Table 4.238**, **4.239** and **4.240** gives an overview of study population, exposure assessment and considered confounders. **Table 4.238**, **4.241** and **4.243** reports objectives of the study and results. Some comments on the study are given in **Table 4.239**, **4.241** and **4.243**.

Table 4.237 Available epidemiological studies: effects on sex organs and fertility, environmental exposure

Reference	Country	Population	Exposed to	Endpoint
Noack-Fuller et al. (1992)	Germany	22 volunteers	N.I.	Cd and Pb in semen, conventional semen characteristics and sperm motion parameters
Xu et al. (1993)	Singapore	221 men undergoing initial screening for infertility	N.I.	Semen volume, sperm density, motility, morphology and viability
Keck et al. (1995)	Germany	176 patients attending an infertility clinic	N.I.	Cd in semen, seminal parameters

N.I. No information available

Table 4.238 Study conducted by Noack-Füller et al. (1992): Study population, exposure, confounders

Main characteristics of the sample	Exposure assessment	Considered Confounders
Final population:	Type of exposure: occupationally unexposed to Cd, Pb, Se, Zn	Age: ±
E: 22 (M)	Exposure duration: N.I.	Drugs: N.I.
Age: 21 – 50 y.	Environmental and biological monitoring:	Alimentation/Vitamins: N.I.
C: 0	Cd air: N.I.	Smoking: yes
	Cd-U: N.I.	Other diseases: N.I.
Selected from:	Cd-B: N.I.	Others: N.I.
E: "occupationally unexposed volunteers"	Cd-seminal plasma(µg/l):	
C: 0	0.34 ± 0.19 (0.1 – 0.66)	
Selection procedure: N.I.	Cd-semen (µg/l):	
Lost subjects: N.I.	0.4 ± 0.23 (0.10 – 0.92)	
Previous poisoning/ Osteomalacia/ Renal disease: N.I.	Other simultaneous exposure : N.I.	

N.I. No information available in this publication,
* No further details available,
E Cd-exposed persons,
C Non exposed persons,
M Male,
F Female,
y Years,
Cd-B Blood cadmium,
Cd-U Urinary cadmium
Considered confounders by the authors: Alimentation, Drugs, Smoking, Other diseases, Others:
yes Means that these factors were considered in the selection of the population and/or in discussion,
no Not considered in selection of the population nor in the discussion,
± Some attempt to consider this factor was made,
Exposure assessment: if not other wise indicated, values are means ± SD (range).

Table 4.239 Study conducted by Noack-Füller et al. (1992): Methods/endpoints and results

Methods and endpoints	Results	Comments
Objectives of the study: 1/parallel determinations of the concentrations of four elements (Cd,Pb, Se, Zn in whole semen and seminal fluid of occupationally unexposed volunteers, 2/evaluation of the intra-individual variability of element concentrations in comparison to semen parameters and 3/examination of the results for statistical associations between element concentrations and conventional semen characteristics/sperm motion parameters -Semen characteristics and sperm motion parameters: ejaculate volume, sperm concentration, total sperm count, motility, linear velocity, curvilinear velocity	-Extremely high within-subject variations were observed for the concentrations of Cd and Pb in semen -No correlation was found between cadmium concentration in semen and sperm density -Authors found a positive correlation between Cd concentration in semen and sperm motility ($r = 0.53$, $p < 0.05$), linear ($r = 0.757$, $p < 0.001$) and curvilinear velocity ($r = 0.643$ $p < 0.002$) assessed by computer video micrography.	-According to Noack-Füller et al., concentrations of Cd within the group of donors were very low -Authors reported that values of Cd in smokers were slightly elevated (but results are not available)

Table 4.240 Study conducted by Xu et al. (1993): Study population, exposure, confounders

Main characteristics of the sample	Exposure assessment	Considered Confounders
Final population:	Type of exposure: general population	Age: ±
cases: 221 (M)	Exposure duration: N.I.	Drugs: N.I.
Age: 24 – 54 y.	Environmental and biological monitoring:	X-rays: N.I.
controls: 38 (M)	Cd air: N.I.	Alimentation/Vitamins: N.I.
Age: N.I	Cd-U: N.I.	Smoking: ±
Selected from:	Cd-B (µg/l ,mean):	Other diseases: yes
cases: "subjects who were undergoing initial screening for infertility in the Andrology Clinic at the Singapore General Hospital from January 1990 to June 1992"	E: 1.25 ± 0.9 (0.1 – 3.7) (N= 191)	Others: occupational exposure, living habits, alcohol drinking, medical history (e.g urinary tract infection, sexually transmitted disease, testicular injuries)
controls: " cohort of fertility proven males (wives had recently conceived) analysed during same study period"	Cd-seminal plasma (µg/l): E: 0.61 ± 0.21 (N.I.) (N=74)	
Selection procedure: known for "E", exclusion of individuals with significant past medical history, and/or signs of defective androgenisation or abnormal testicular examinations, and occupational exposure to metals	Other simultaneous exposure : N.I.	
Lost cases: N.I.		
Previous poisoning/ Osteomalacia/ Renal disease: No		

N.I. No information available in this publication
* No further details available
M Male,
F Female,
Y Years
Cd-B Blood cadmium,
Cd-U Urinary cadmium
Considered confounders by the authors: Alimentation, Drugs, Smoking, Other diseases, Others:
yes Means that these factors were considered in the selection of the population and/or in discussion,
no Not considered in selection of the population or in the discussion,
± Some attempt to consider this factor was made
Exposure assessment: if not other wise indicated, values are means ± SD (range)

Table 4.241 Study conducted by Xu et al. (1993): Methods/endpoints and results

Methods and endpoints	**Results**	**Comments**
Objective of the study: to examine the relationships between the concentrations of Cd, Pb, Se and Zn in blood and seminal plasma, and sperm quality -subjects were interviewed using a questionnaire to obtain information on occupational exposure, general health, living habits, including cigarette smoking and alcohol drinking and medical history -a medical examination was conducted by an andrologist - Measured parameters included semen volume and sperm density, motility, morphology and viability	-The volume of semen was inversely proportional to the cadmium concentration in seminal plasma ($r = -0.29$; $p < 0.05$). -Cadmium levels in blood had a significant inverse relationship with sperm density ($r = -0.23$, $p < 0.05$) in oligospermic (sperm density below 20 million/ml) but not in normospermic men. There was a significant reduction in sperm density in men with blood cadmium of > 1.5µg/l (7.8 ± 7.1 million/ml versus 17.8 ± 4.5 million for men with Cd-B < 1 µg /L). -No differences were observed in sperm quality (density, motility, morphology, volume and viability) in the cohort when compared to 38 fertility proven men	According to Xu et al., Cd-B mean (1.25 µg/l) measured in this population was slightly higher when compared with other studies. Authors attributed this elevated Cd-B among Singaporeans to the diet.

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Table 4.242 Study conducted by Keck et al. (1995): Study population, exposure, confounders

Main characteristics of the sample	**Exposure assessment**	**Considered Confounders**
Final population:	Type of exposure: general population	Age: ±
Cases: 44 (group II) + 118 (group III)	Exposure duration: N.I.	Drugs: N.I.
Age: 35 – 36 y.	Environmental and biological monitoring:	Alimentation/Vitamins: N.I.
Controls: 12 (group I)	Cd air: N.I.	Smoking: ±
Age: N.I.	Cd-U: N.I.	Other diseases: N.I.
	Cd-B: N.I.	Others: socio-economic status
Selected from:	Cd-seminal plasma(µg/l, mean ± SD):	
Cases: Group II: " patients(of the infertility clinic) with unexplained infertility whose semen analysis revealed normozoospermia"	E: Group II: 0.43 ± 0.69 Group III: 0.44 ± 0.73	
Group III: "consecutive patients attended the infertility clinic due to barrenness"	C: 0.38 ± 0.64	
Selection procedure: known		
Lost subjects: N.I.	Other simultaneous exposure : N.I.	
Previous poisoning/ Osteomalacia/ Renal disease: N.I		

N.I. No information available in this publication
* No further details available
M Male,
F Female,
Y Years
Cd-B Blood cadmium,
Cd-U Urinary cadmium
Considered confounders by the authors: Alimentation, Drugs, Smoking, Other diseases, Others:
Yes Means that these factors were considered in the selection of the population and/or in discussion,
No Not considered in selection of the population nor in the discussion,
± Some attempt to consider this factor was made
Exposure assessment: if not other wise indicated, values are means ± SD (range)

Table 4.243 Study conducted by Keck et al. (1995): Methods/endpoints and results

Reference	Methods and endpoints	Results	Comments
Keck et al., 1995	Objective of the study:1/define a normal range of values for Cd concentrations in seminal plasma of nonexposed fertile men and patients of a fertility clinic and 2/ to investigate if these Cd concentrations correlate with parameters of conventional semen analysis and fertility assessment 3/the effect of cigarette smoking on Cd concentrations in seminal plasma was examined -semen parameters assessed: volume, pH, motility, concentration, normal forms, amorphous forms, midpiece defect, tail defect, glucosidase, fructose, zinc	-Mean Cd concentrations in seminal plasma did not differ significantly for groups I (fertility proven men), II (normozoospermic patients), III (unselected patients) -There was no significant correlation between seminal Cd concentrations and conventional semen parameters or between cadmium concentrations and the fertility status of the patients. -In normozoospermic patients, seminal plasma cadmium concentrations were significantly higher in the group of smokers, compared with the group of non-smokers (0.55 ± 0.81 versus 0.42 ± 0.67 µg/l)	-Data about tobacco smoking were not available for all the groups

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Summary and discussion: oral route (general population)

One group of authors reported a significant inverse correlation between semen volume and the concentration of cadmium in the seminal plasma (Xu et al., 1993). In their conclusions, they suggested that cadmium may have a possible adverse effect on the prostate gland, as a significant amount of seminal plasma is derived from this gland.

However, no clear prostate-specific Cd accumulation could be demonstrated by Oldereid et al. (1993). They determined the tissular concentrations of cadmium in various reproductive organs removed at necropsy from men who had died suddenly. The epididymides and to a lesser extent, the seminal vesicles, appeared to be more efficient than both the prostate gland and testis in their capacity to accumulate cadmium. The age-related rise in tissue cadmium in the testes and other organs was most apparent after the fourth decade, a time when a potentially negative influence on spermatogenesis might have limited relevance. Amount of cadmium in the tissues was not influenced by the rural or urban backgrounds of the subjects or their occupation in this study (Oldereid et al., 1993).

Xu et al. (1993) reported also a significant reduction in sperm density in men with blood cadmium of > 1.5µg/l; however, no differences were observed in sperm quality (including density) in the whole group when compared to fertility proven men. One group of authors reported a positive correlation between Cd concentration in semen and some parameters of sperm motility (motility, linear and curvilinear velocity) (Noack-Füller et al., 1992). However, to draw some conclusions and to assess the clinical relevance of the modification of some seminal parameters, studies on higher number of subjects are required where correlations between seminal plasma or serum Cd concentrations and ejaculate parameters or fertility status will be looked for.

Overall, the epidemiological evidence of a clinically relevant reproductive effect of Cd (including by assimilation Cd metal and CdO) in humans exposed by the oral route is weak.

Inhalation route: occupational exposure

Some cases of acute poisoning in human males may have displayed histological damage to reproductive organs, including the testes.

This was first reported by Smith et al. (1960) (cited in Barlow and Sullivan, 1982 and by Elinder in CRC, 1986). Authors reported the results of examination of the testes in 4 men autopsied after having suffered from cadmium fumes poisoning. The 4 men had experienced intermittent exposure to high levels of cadmium fumes in a copper-cadmium alloy factory, due to inadequate ventilation of the working area. Exposure duration ranged from 7 to 9 years, and occurred at various ages (above 30 years). The four workers had to be transferred to other work (light or office work) because of respiratory problems. Smoking habits were not reported. Results of the testis examination are summarised in **Table 4.244**.

Table 4.244 Results of the testis examination at autopsy in 4 men previously exposed to Cd fumes in a manufacture of copper-cadmium alloy (Smith et al., 1960)

Patient n°	Age	Exposure duration (years)	Clinical reportings	Results of the testis examination				
				Macro.	**Sperm.**	**Mitoses**	**Fibrosis**	**Others**
1	46	9	Respiratory problems	Normal	Absent	+++	-	No atrophy, normal interstitial cells
2	55	7	Emphysema	Normal	Absent	++	-	No atrophy, normal interstitial cells
3	57	8	Dyspnoea (Emphysema was later diagnosed)	Normal	Infrequent	++	+	Tubular atrophy
4	67	8	Dyspnoea	Normal	Infrequent	N.I.	-	Inconspicuous interstitial cells

N.I. No information available in this publication
Macro. Macroscopical aspect
Sperm. Spermatids and Spermatozoa
+++ Abundant
++ Many
\+ Present

Cadmium tissue levels measured in three men ranged from 9 to 38 µg/g in the testis (body) for 2 of them, and last case had a value that amounted to 3.5 mg/g tissue. These levels were compared with levels in 3 unexposed men of comparable age at autopsy (0.16-0.2 µg/g).

The authors suggested, in view of a) the long time lag (5-19 years) between last exposure and autopsy, b) the lack of any gross histological lesions in the testes and c) the plentiful mitotic activity of the spermatocytes; that the effects on later stages of spermatogenesis could rather be the result of the terminal illness of these people than of their previous exposure to Cd fumes. Barlow and Sullivan, in their comments on this study, did, however, not rule out the cadmium as possible causal agent of a specific action on spermatogenesis (Smith et al. (1960) cited in Barlow and Sullivan (1982) and by Elinder in CRC (1986)).

Considering workers exposed chronically to cadmium, only a few studies have investigated the question of the potential reproductive hazards (including effects on libido and potency, fertility, menstruation and sperm etc.). Studies have assessed either the effect on the endocrine/gonadal function, the fertility status of the workers or both.

Table 4.245 lists the located studies. An overview of the selected studies is given in **Tables 4.246 - 4.251**. **Table 4.246**, **4.248** and **4.250** gives an overview on study population, exposure assessment and considered confounders. **Table 4.247**, **4.249** and **4.251** reports objectives of the study and results. Some comments on the study are given in **Table 4.247**, **4.249** and **4.251**.

Table 4.245 Available epidemiological studies, effects on sex organs and fertility: occupational exposure

Reference	Country	Population	Exposed to	Endpoint	Selected study (yes/no)
Favino et al. (1968)	Italy	10 male workers at an alkaline storage battery plant	Cd, Ni, Pb	Androgen function	yes
Mason et al. (1990)	UK	101 current and ex-workers who had produced copper-cadmium alloys	Cu, Cd	Testicular endocrine function	yes
Gennart et al. (1992)	Belgium	112 smelter workers	Cd, some of them were also exposed to Pb	Fertility	yes
Keck et al. (1995)	Germany	2 workers with occupational exposure to cadmium	Cd	Semen analysis	no*
Tsvetkova (1970)	Russia	106 women employed in 3 Cd factories: 1 alkaline batteries factory, 1 chemical reagent kit factory, 1 zinc moulding factory	N.I.	Menstrual cycle	no*

* These studies will be briefly evoked in discussion

Table 4.246 Study conducted by Favino et al. (1968): Study population, exposure, confounders

Main characteristics of the sample	Exposure assessment	Considered Confounders
Final population:	Type of exposure: occupational	Age: yes, matching
E: 10 (M only)	Type of compound: alkaline storage batteries plant: $Cd(OH)_2$, Cd powder and "Cd vapours"	Drugs: N.I.
Age: 32-75 y.		X-rays: N.I.
C: 10 (M only)	Duration:	Smoking: N.I.
Age: 28-76 y.	first area (preparation): 2-5 y.	Previous work: N.I.
Selected from:	second area (assembly): "continuously until some	Others: body weight
E: "workers selected from two areas of the plant, (preparation: of the material for the negative electrode of the battery :Cd powder mixed with kerosene and water/ assembly: supply the elements of the battery and connecting the electrodes) -some actively employed at time of investigation, some had left the plant some years before"	years ago and then employed alternatively also in other jobs in the factory"	
C: "men working in other jobs in the factory: the majority worked in lead (N=8)storage battery manufacture"	Environmental and biological monitoring:	
	Cd-air : N.I.	
Selection procedure: partially known	Cd-B : N.I.	
Lost subjects: N.I.	Cd-U:	
	E : first area (preparation): 30-550 µg/l	
Previous poisoning/ Osteomalacia/ Kidney Disease: no proteinuria in all examined samples, further no details	Second area (assembly): not detected	
	C : not detected	
	Other simultaneous exposures : nickel, lead	

N.I. No information available in this publication
E Cd-exposed persons,
C Non exposed persons,
M Male,
F Female,
y Years
Cd-B Blood cadmium,
Cd-U Urinary cadmium
Considered confounders by the authors: Alimentation, Drugs, Smoking, Other diseases, Others:
Yes Means that these factors were considered in the selection of the population and/or in discussion,
No Not considered in selection of the population nor in the discussion,
± Some attempt to consider this factor was made

* No further details available
Exposure assessment: if not other wise indicated, values are means ± SD (range)

Table 4.247 Study conducted by Favino et al. (1968): Methods/endpoints and results

Methods and endpoints	Results	Comments
Objective of the study:"… to look for an evaluation of the androgenic function of people exposed to cadmium to see whether or not the level of industrial hazard for cadmium can compromise the genital function" -17 ketosteroids, androsterone, etiocholanolone, testosterone, epitestosterone were measured on collected urine of two consecutive days	-No considerable difference in 17 ketosteroids, androsterone, and etiocholanolone, testosterone excretion were detected between controls and Cd exposed groups -Epitestosterone excretion tended to be higher in the exposed group, however this was not considered to be significant	Conclusions cannot be drawn from this study because of a number of flaws: -Firstly, exposure history of the exposed subjects was variable (some had worked for 2-5 years or more and were still active, others had been exposed for some years and were transferred to other areas, some had left the plant and numbers of subjects in the different categories are not given), -Secondly, Cd-U levels were not given for each worker and could not be related to the different exposure patterns, -Thirdly, hormone levels showed considerable variability in both control and exposed groups, -The subjects chosen as controls were exposed to another heavy metal (lead). Two men of the cadmium-exposed group complained of impotence and one of them had elevated Cd-U (but values are not given) and low testosterone urinary levels compared with the group mean. Remark: the 10 men exposed to cadmium had a small family size (average 1.5 children). But insufficient details are given on numbers conceived before exposure, desired family size, etc., to evaluate fertility (Favino et al., 1968 commented by Barlow and Sullivan, 1982).

Table 4.248 Study conducted by Mason et al. (1990): Study population, exposure, confounders

Main characteristics of the sample	**Exposure assessment**	**Considered Confounders**
Final population:	Type of exposure: occupational	Age: yes
E: 77 (M)	Type of compound: cadmium oxide fumes	Drugs: N.I.
Age: 54 ± 13 y. (mean ± SD)	Environmental and biological monitoring:	X-rays: N.I.
C: 101 (M)	Cd-air: Exposure index (µg/m³, years):	Smoking: N.I.
Age: 56 ± 12 y. (mean ± SD)	E: 808 ± 40 (mean ± SD)	Other diseases: N.I.
Selected from:		Previous work: N.I.
E: "all male current and ex-workers who had produced copper-cadmium alloy for one or more years since the factory opened in 1926"	Cd-B: N.I	Others: N.I.
C: "from the current or past workforce of the same company, hourly paid workers without occupational exposure to cadmium"	Cd-liver: N.I. (correlated with the derived cumulative exposure index)	
Selection procedure: known		
Lost subjects: 26	Other simultaneous exposures: N.I.	
Previous poisoning/ Osteomalacia/ Kidney Disease: yes, 37% of the exposed subjects showed evidence of renal tubular damage		

N.I. no information available in this publication
* No further details available
E Cd-exposed persons,
C non exposed persons,
M male,
F female,
y years
Cd-B blood cadmium,
Cd-U urinary cadmium
Considered confounders by the authors: Alimentation, Drugs, Smoking, Other diseases, Others:
yes means that these factors were considered in the selection of the population and/or in discussion,
no not considered in selection of the population nor in the discussion,
± some attempt to consider this factor was made
Exposure assessment: if not other wise indicated, values are means ± SD (range)

Table 4.249 Study conducted by Mason et al. (1990): Methods/endpoints and results

Methods and endpoints	**Results**	**Comments**
Objective of the study: to report on testicular endocrine function in a well-characterised male population -*in vivo* measurements of kidney and liver cadmium by neutron activation analysis -measure of plasma testosterone, FSH and LH levels	- no change in testicular endocrine function (as measured by serum levels of testosterone, luteinising hormone, and follicle-stimulating hormone) was observed in men exposed to cadmium at levels causing dose-related changes in glomerular and tubular function in the same population.	-For the same population, cadmium exposures have been estimated in another study (Davison et al., 1988) and decreased from 600 µg/m³ (in 1926) to 36 µg/m³ (in 1983) -For each worker, cumulative exposure indices have been calculated and correlated with the *in vivo* measurement of liver cadmium.

Table 4.250 Study conducted by Gennart et al. (1992): Study population, exposure, confounders

Main characteristics of the sample	Exposure assessment	Considered Confounders
Final population:	Type of exposure: occupational	Age: yes
E: 83 (M only)	Type of compound: Cd dust and Cd fumes	Drugs: N.I.
Age: 23.4 - 72.2 y.	Duration (range, years): 1.1 - 52.3	X-rays: N.I.
C: 138 (M only)	Biological monitoring:	Smoking: yes
Age: 19.9 - 71.9 y.	Cd-air: N.I.	Other diseases: yes, detailed
Selected from:	Cd-B: N.I.	Previous work: N.I.
E: "workers from two primary cadmium smelters, exposed uninterruptedly to cadmium for at least 1 year before the study and at the time of the study: Cd-U > 2µg/g creatinine, Pb-B < 30 µg/100ml"	Cd-U (µg/g creat): E: 6.94 ± 4.56 (mean ± SD)	Others: wife's age, birth cohort, parity, time interval since previous birth, wife's occupational status, age at marriage, alcohol consumption, educational level
C: "workers from factories located in the same area, never occupationally exposed to heavy metals, at the time of the survey: Cd-U < 2µg/g creatinine, Pb-B < 20µg/100ml"	2.07 – 24.15 (range)	
For E and C, no pathologic conditions which might interfere with reproductive function, Belgian nationality and married at least once"	Other simultaneous exposures: E: Lead: (Pb-B (µg/100 ml)	
Lost subjects: 29 in E, 127 in C	18.6 ± 5.8 (mean ± SD)	
Previous poisoning/ Osteomalacia/ Kidney Disease: 21/83 workers had signs of kidney dysfunction	8.0 - 30. 0 (range) C: possibility of an intermittent exposure to cutting oil and a few solvents	

N.I. No information available in this publication * No further details available
E Cd-exposed persons, C Non exposed persons,
M Male,
F Female,
y Years
Cd-B Blood cadmium,
Cd-U Urinary cadmium
Considered confounders by the authors: Alimentation, Drugs, Smoking, Other diseases, Others:
yes Means that these factors were considered in the selection of the population and/or in discussion,
no Not considered in selection of the population nor in the discussion,
± Some attempt to consider this factor was made
Exposure assessment: if not other wise indicated, values are means ± SD (range)

Table 4.251 Study conducted by Gennart et al. (1992): Methods/endpoints and results

Methods and endpoints	Results	Comments
<u>Objective of the study:</u> to examine the effect of exposure to cadmium on the reproductive function. -By questionnaire, information was gathered on age, residence, educational level, occupational and health history, actual and previous occupations, smoking, coffee and alcohol consumption. The fertility section of the questionnaire contained the questions proposed by Levine et al. for the monitoring of the fertility of workers (Levine et al., 1980 cited by Gennart et al., 1992).	-No significant reduction in fertility was detected in the exposed group compared with the unexposed population.	The main limitation of this study was the fact that the workers' wives could not be interviewed and therefore some factors that might have affected their reproductive ability could not be assessed (Gennart et al., 1992).

Further information on fertility was also derived from studies considered elsewhere because reproductive effects were not the primary target effect explored by the authors:

Kazantzis et al. (1963), in a study of renal and pulmonary effects, interviewed workers from a manufacture of cadmium pigments and took fertility histories but found no evidence of decreased fertility (no further details given) (Kazantzis et al., 1963 cited in Barlow and Sullivan, 1982).

A case-control study based on data collected from medical records and mailed questionnaires showed an association between female occupational exposure to lead, mercury and cadmium and idiopathic infertility in the case-control comparison. Exposure was defined as contact with cadmium a minimum of once per week for a period of at least one year. However, this study was rather designed to generate hypotheses and to be a preliminary step in pointing the way to further research (Rachootin and Olsen, 1983).

No data were located about the mechanism underlying the reproductive effects of cadmium.

Summary and discussion: inhalation route

Two located studies were not discussed. In a previously detailed study (see oral route), cadmium concentrations and seminal parameters in samples of 2 men occupationally exposed to cadmium and attending an infertility clinic were determined by Keck et al. (1995).

Results were compared with those obtained in 12 men with proven fertility and non-occupationally exposed to cadmium. Values of cadmium in seminal plasma were much higher than in the control group and the two exposed patients had abnormal seminal parameters. However, as exposure to cadmium was not documented regarding duration, intensity, type of compound or other concomitant exposure and as the number of patients is very small, no conclusions on a particular level of cadmium in seminal plasma which can be associated with infertility can be drawn from these data. Moreover, the 2 patients may not be considered as representative as they were recruited from patients attending an infertility clinic (Keck et al., 1995).

The study of Tsvetkova (1970) was excluded as only an English abstract was available and consequently too less details were known on the effects and on the toxicity that must have occurred in the exposed women at the levels of cadmium encountered in the factories.

Evidence is insufficient to determine an association between occupational inhalation exposure to cadmium (including by assimilation Cd metal and CdO) and effects on fertility or sex organs. A post-mortem study of men occupationally exposed to cadmium fumes (with intermittent high levels) found high levels of cadmium in the testes but no histologic lesions and authors attributed the findings to the terminal illness (emphysema) rather than to exposure. Two studies (in men) dealing with endocrine and gonadal function found no effects that may be attributed to cadmium. Fertility was not significantly different in exposed workers compared to unexposed age-matched subjects.

<u>Population exposed to cadmium by smoking</u>

Saaranen et al. (1989) carried out a study to determine cadmium concentrations in seminal fluid and serum of 62 men and to compare these results with semen parameters, fertility and smoking habits. Semen samples were obtained from 24 donors admitted to a fertility clinic, and from 38 fertile men whose wives had conceived within 6 month. None of the men had any known occupational exposure to cadmium. About the half of them were smokers (28/62) and a subgroup of heavy smokers (smoking more than 20 cigarettes/day) was constituted.

Smokers had significantly higher serum cadmium concentrations than non-smokers (0.33 ± 0.10 µg/l versus 0.24 ± 0.09 µg/l). Seminal fluid cadmium was also elevated in smokers and was the highest in the subgroup of heavy smokers (0.4 ± 0.4 µg/l versus. 0.28 ± 0.24 µg/l in smokers, and 0.19 ± 0.21 µg/l for non-smokers). Thus, there appeared to be no barrier to prevent the cadmium to enter the male reproductive system from the circulation.

Semen quality was measured for volume, sperm density, morphology, motility and number of immature germ cells. No differences were found in semen quality or fertility between smokers and non-smokers. There was no significant correlation between seminal fluid cadmium levels and semen quality and fertility. Authors concluded that the concentrations of cadmium observed in their material did not reach concentrations able to cause any adverse effects on the male fertility but that the observed increased concentrations in smokers might, however, potentiate any other detrimental toxic effect on the reproduction (Saaranen et al., 1989).

Oldereid et al. (1993), already mentioned, observed that cadmium concentration in the seminal fluid of smokers was similar when compared to non-smokers except when consumption of cigarettes exceeded 20 cigarettes per day (Oldereid et al., 1993).

Chia et al. (1994) also examined the relationship between cigarette smoking, blood and seminal plasma concentrations of cadmium (and lead) and sperm quality. All male partners of couples who were undergoing initial screening for infertility during 1.5 year were included in the study (222 cases). Great care was taken to ensure that only individuals with no known cause for infertility were included in the study. Subjects were interviewed about the use of alcohol, hallucinogenic drugs and tobacco smoking. Smokers were classified on the basis of cigarette-years (number of cigarettes smoked per day · number of years smoked). Ex-smokers (N=21) were excluded because their number was small and might have confounded the results. Results of cadmium in blood were available for the 184 subjects who fulfilled the selection criteria. A significant correlation was observed for the different categories of cigarette-years. Cadmium in semen (reported for 59 subjects) was significantly correlated with cigarette-years and sperm volume ($r= -0.35$, $p < 0.01$). Significant positive trends were observed for different categories of cigarette-years with Cd-B, Cd in semen and sperm density and significant differences were also noted between smokers (> 100 cigarettes-year) and non-smokers for sperm density (9.2 versus 18.2 million/ml for smokers and non-smokers, respectively). Authors concluded that cigarette smoking appeared to affect sperm density, especially in heavy smokers and that the cadmium present in cigarettes could be a possible responsible agent for the low sperm density among the smokers of their study (Chia et al., 1994).

Telisman et al. (1997) reported significant differences in Cd exposure between a group of smokers and a group of non-smokers when exposure was assessed by the measurement of the Cd-B and Cd in seminal fluid levels. The absolute increase in Cd-B was more pronounced than that of seminal fluid-Cd in smokers compared to non-smokers. Although a highly significant correlation ($p < 0.0001$) was found between the Cd-B and the Cd in seminal fluid levels in the studied population, the results showed considerable differences in individual Cd-seminal fluid levels for the same Cd-B level (Telisman et al., 1997).

Summary

In man, cigarette smoking is an important source of cadmium and studies showed that there appears to be no barrier to prevent the cadmium to enter the male reproductive system from the circulation. Smokers have higher cadmium concentrations in both serum and seminal plasma than non-smokers.

Cadmium in semen was significantly influenced by smoking habits and associated with reduced sperm volume in one study. Significant differences were noted between smokers (> 100 cigarettes-year) and non-smokers for sperm density and authors suggested that cadmium content in cigarette could be involved. In another study, although a highly significant correlation was found between the Cd-B and the Cd in seminal fluid in the studied population, some individual results showed considerable differences in Cd-seminal fluid levels for the same Cd-B level.

Overall, the epidemiological evidence of an association between Cd exposure through tobacco smoking and reduction of reproductive function is weak.

Overall conclusion: Effects on fertility and sex organs

Experimental studies indicate that administration of cadmium by the oral route (as Cd water-soluble compounds) or by inhalation (as CdO) has been associated with damage to the testes, decreased fertility, and an increase of the length of the oestrous cycle. These effects were reported to occur at dose levels which mostly caused other manifestations of toxicity (body or organ weights, lethality. Overall, epidemiological evidence does not speak for an association between exposure to cadmium and relevant effects on fertility or sex organs. The number of studies investigating these endpoints is limited and the toxicological significance of some of the reported effects might be questioned in terms of adverse effects for fertility. Therefore, the LOAEL that will be used for the Risk Characterisation are derived from studies in animals:

Table 4.252 LOAEL/NOAEL derived from different routes of exposure in animals

Route	LOAEL/NOAEL	Species
Oral (general population)	NOAEL: 1 mg Cd/kg/day	rat, male and female
Inhalation (occupationally exposed population)	NOAEL: 0.1 mg CdO/m³	rat, male and female

Cadmium is classified in Repr. Cat 3, R62, as a substance which causes concern for human fertility on the basis of the results reported in the studies in animals.

4.1.2.10.3 Developmental effects

In humans, Cd has been incriminated by some authors as a possible causal factor in preterm labour and decreased birth weights (Tsvetkova 1970; Huel et al.,1984; Fréry , 1993). Maternal hypertension has also been associated with elevated levels of cadmium in the neonate (WHO, 1992).

The potential developmental toxicity of cadmium has been investigated in animals by the oral, inhalation and parenteral routes. A number of these studies indicate that exposure to cadmium prior to or during gestation can be foetotoxic (in rats and mice). This foetotoxicity is most often manifested as reduced foetal or pup weight but malformations (primarily skeletal) have been found in some studies (ATSDR, 1999). Another indicator of developmental toxicity of cadmium in animals appears to be altered neurobehavioral development of the pups.

Studies in animals

Oral route

No study specifically using cadmium oxide or cadmium metal was located.

Experimental studies in animals have generally used soluble Cd salts in food, drinking water, and gavage exposures.

Main characteristics of the located studies reporting developmental effects are summarised in **Table 4.253**. Studies are briefly described subsequently according to a developmental endpoint (reduced weight, malformations, and neurobehavioral alterations) in an attempt to identify the relevant L(N)OAELs. All these studies have used cadmium chloride or acetate.

Table 4.253 Main characteristics of the studies on developmental effects in rats and mice

Effect	Doses of Cd	Duration	Developmental NOAEL (mg Cd/kg/day)	Developmental LOAEL (mg Cd/kg/day)	Maternal NOAEL/LOAEL (mg Cd/kg/day)	Reference	Comments
Rats							
Reduced fœtal or pup weight	0-19.7 mg/kg/day (F) (as $CdCl_2$)	Gd1-Ld1	N.D.	12	12 (LOAEL)	Pond and Walker (1975)	
	0.1-1.0-10 mg/kg/day (W) (as $CdCl_2$)	Throughout pregnancy	1	10	1 (NOAEL)	Sutou et al. (1980)	
	4.2-8.4 µg/ml (W) (as Cd acetate)	Gd1-Ld21	0.7	1.4	N.I.	Ali et al. (1986) cited in ATSDR (1999)	Only abstract available
	2-12-40 mg/kg/day (G) (as $CdCl_2$)	Gd 7-16	2	12	2 (LOAEL)	Baranski (1985)	
	0-5-50-100 ppm (W) (as $CdCl_2$)	Gd 6-20	≅ 0.6	≅ 5	≅ 0.6	Sorell and Graziano (1990)	Significantly different from control group with α-level at 0.1
	4.8 mg/kg/day (W) (as $CdCl_2$)	10 w (4 before mating, until weaning)	N.D.	2.9	N.I.	Kostial et al. (1993)	Only abstract available
	5-8 mg/kg/day (W) (as Cd acetate)	Gd1-Ld21	< 3.1	3.1	N.I.	Gupta et al. (1993)	Only abstract available
Malformations	3-10-30-100 mg/kg (G) (as $CdCl_2$)	Gd 6-15	6.1	18.4	3.5 (NOAEL)	Machemer and Lorke (1981)	
	10-30-100 ppm (F) (as $CdCl_2$)	Gd 6-15	12.5	-	12.5 (NOAEL)		
	2-12-40 mg Cd /kg/day (G) (as $CdCl_2$)	Gd 7-16	< 2	2	2 (LOAEL)	Baranski (1985)	

Table 4.253 continued overleaf

Table 4.253 continued Main characteristics of the studies on developmental effects in rats and mice

Effect	Doses of Cd	Duration	Developmental NOAEL (mg Cd/kg/day)	Developmental LOAEL (mg Cd/kg/day)	Maternal NOAEL (mg Cd/kg/day)	Reference	Comments
Pup behavioural alterations	17.2 µg Cd^{2+}/ml (W)	90 days before breeding then during gestation	-	≅2.2	≅2.2 (NOAEL)	Hastings et al. (1978)	Small number of animals
	0.04-0.4-4 mg Cd/kg/day(G) (as $CdCl_2$)	5d/w, 11w (5 before mating, then throughout gestation)	N.D.	0.04	4 (NOAEL)	Baranski et al. (1983)	
	4.2 -8.4 µg/ml (W) (as Cd acetate)	Gd 1- Ld 21	N.D.	0.7	N.I.	Ali et al. (1986)	Only abstract available
	3.5-7.0-14.0 mg/kg/day (G) as $CdCl_2$)	7 d/w, from 4 weeks of age through mating 5d/w from gestation through parturition	N.D.	3.5	N.I.	Nagymajtenyi et al. (1997)	
	3.5-7.0-14.0 mg/kg/day (G) as $CdCl_2$)	Gd 5-15 Gd 5-15 + 4 weeks of lactation Gd 5-15 + 4 weeks of lactation + treatment of F1 male rats for 8 weeks	N.D.	3.5	3.5 (NOAEL)	Desi et al. (1998)	
	0.25-1.0-1.75-2.5-3.25-4.0-7.0 mg/kg (G) as $CdCl_2$)	10 days from sixth day of life	4.3	-	N.I.	Smith et al. (1982)	

Table 4.253 continued overleaf

Table 4.253 continued Main characteristics of the studies on developmental effects in rats and mice

Effect	Doses of Cd	Duration	Developmental NOAEL (mg Cd/kg/day)	Developmental LOAEL (mg Cd/kg/day)	Maternal NOAEL (mg Cd/kg/day)	Reference	Comments
Mice							
Reduced foetal or pup weight	10-20-40 ppm (W) as $CdCl_2$	Throughout pregnancy	1.2	2.4	N.I.	Webster (1978,1979)	
	0.25-5.0-50 mg/kg food (F) as $CdCl_2$	Gd1-Ld21 for 6 successive rounds	5.0	50	50	Whelton et al. (1988)	
Malformations	2.5 mg/kg/day (W) (unspecified form of Cd)	6 months	N.D.	2.5	N.I.	Schroeder and Mitchener (1971)	Only abstract available

G Gavage
W Water
F Food
Gd Gestation days
Ld Lactation days
d Days
W Week
N.I. No information available
N.D. Not determined
Further information available in IUCLID

1. Significantly reduced foetal weight (when compared to the control group)

Female rats receiving 200 ppm Cd in diet from day following mating through parturition significantly depressed their feed consumption and body weight gain (Pond and Walker, 1975). Number of pups per litter was not significantly affected by diet. However, pup birth weight was significantly less in dams fed high Cd compared to those receiving a diet without Cd ($p < 0.01$).

Sutou et al. (1980) have given Cd at doses of 0-0.1-1.0 or 10 mg Cd/kg/day throughout pregnancy. Foetal body weight was reduced in a dose-related way but was only significantly reduced in the highest dose group, which had a 33% reduction in comparison to controls (2.32 ± 0.23 g versus 3.48 ± 0.16 g in exposed and control groups, respectively). Foetuses were small and yellowish in colour, indicative of anaemia and malnutrition. At this dose, toxic symptoms such as reduced weight gain and water and food consumption, depilation, bleaching of the incisors, salivation, reduced copulation ratio were observed in the mothers.

The developmental and behavioural toxicity of gestational exposure to cadmium has been assessed in rats by Ali et al. (1986). Significant decreases in birth weight and growth rate were observed in the 1.4 mg Cd/kg/day (8.4 µg/ml) group (Ali et al., 1986 cited in ATSDR 1999). No details are reported on maternal toxicity.

Cadmium chloride administered intragastrically to pregnant rats lead to a retardation of the prenatal development of foetuses manifested by a significantly lower body weight (and a retarded osteogenesis) compared to a control group at doses of 12 and 40 mg Cd/kg/day (Baranski, 1985). Body weight increase during pregnancy of exposed females was reduced at all Cd doses.

Table 4.254 Effect of cadmium chloride gavage on prenatal development of progeny (Baranski, 1985)

	Cadmium chloride dose (mg Cd/kg/day)			
	Control	**2**	**12**	**40**
Foetus weight (g) (mean ± SD)	3.76 ± 0.26	3.62 ± 0.26	3.42 ± 0.38*	2.90 ± 0.93*

* Significantly different from mean in control group ($p < 0.05$)

To examine the effect of cadmium exposure on maternal and foetal zinc metabolism, rats were exposed to cadmium chloride in drinking water on days 6 through 20 of pregnancy (Sorell and Graziano, 1990). Maternal weight and weight gain during exposure period were significantly decreased in the 50- and 100-ppm exposure groups (but not in the 5-ppm group). At the highest concentration tested, decrease of foetal weight appeared to be largely secondary to the decreased maternal weight gain and presumably water and food intake. However, in the 50-ppm group the adjusted foetal weight (for maternal weight) was significantly different from control weight, indicating an effect that was not solely a consequence of decreased maternal weight. At this concentration, cadmium caused a substantial Zn retention in maternal liver and kidney, considered to be partially responsible for the decreased concentration of Zn in the foetal liver. The changes in the maternal and foetal disposition of Zn, accompanied by a modification in the activities of Zn metalloenzymes in both maternal and foetal tissues (delta-aminolevulinic acid dehydratase) support the author's hypothesis that the Cd-induced maternal zinc retention is responsible for an impaired foetal growth (Sorell and Graziano, 1990).

Table 4.255 Effect of cadmium chloride administered in drinking water on maternal and fœtal weight and zinc content (Sorell and Graziano, 1990)

	Cadmium exposure (ppm)			
	0	5	50	100
Maternal weight gain (g/day) (days 6-20)	9.85 ± 0.3	8.84 ± 0.22	8.53 ± 0.28*	6.89 ± 0.22*
Maternal water intake (ml/day) (days 6-20)	42.6 ± 3.0	44.0 ± 2.79	33.0 ± 2.0	28.6 ± 2.4*
Fœtal weight (day 20)	4.26 ± 0.027	4.26 ± 0.025	3.90 ± 0.036*	4.06 ± 0.038*
Adjusted fœtal weight	4.22 ± 0.025	4.14 ± 0.027	3.95 ± 0.032**	4.24 ± 0.025
Zinc content of maternal liver	25.3 ± 1.7	27.8 ± 0.9	29.7 ± 1.0*	29.4 ± 0.7
Zinc content of placenta	11.0 ± 0.4	10.8 ± 0.2	10.9 ± 0.4	9.9 ± 0.2*

Values are expressed as x ± SE (N)
* Significantly different from control ($p < 0.1$)
** Significantly different from control ($p < 0.05$)

Cadmium given to female rats for a total of 10 weeks induced a 12% decrease in pup body weight at weaning in a study designed to assess cadmium deposition in rats and their pups and the depleting efficiency of a chelator (sodium N-(4-methoxybenzyl)-D-glucamine-N-carbodithioate monohydrate) after the discontinuation of exposure (Kostial et al., 1993 cited in ATSDR 1999). No details on maternal toxicity are reported.

A study by Gupta et al. (1993) examined the developmental effects of an exposure to cadmium acetate during gestation and lactation. Pup body weights were significantly decreased in the cadmium exposed pups during lactation (Gupta et al. 1993 cited in ATSDR 1999). No details on maternal toxicity are reported.

Exposure of mice to 40 ppm cadmium in their drinking water throughout pregnancy resulted in foetal growth retardation (1.14 ± 0.04 g versus 1.42 ± 0.04 g, in exposed mice and controls respectively) (Webster 1979). In a previous study by the same author (Webster 1978), the small foetuses observed after exposure to the same concentration of cadmium were also very anaemic. Both anaemia and effect on growth were prevented by parenterally administered iron during pregnancy (Webster 1978).

Pup weights on the day of weaning were measured for the litters of dams that experienced 6 consecutive rounds of pregnancy and lactation, exposed to 0.25, 5.0 or 50.0 ppm in their diet. At each cadmium level, diets were either sufficient or deficient in vitamins, minerals and fat (Whelton et al., 1988). For sufficient diet groups, cadmium at 5 ppm had no effect on pup mass at weaning but had a moderate effect at 50 ppm (~25%). The reduction in pup growth was not caused by decreases in dietary consumption in the dam. For deficient diet groups, a larger reduction of pup weaning weight was observed at 50 ppm Cd (41%). This reduction may, however, have been caused partly by a significant (31%) decrease in diet consumption by the dams in this combined Cd-dietary deficient group.

2. Malformations

Administration of 30 mg $CdCl_2$/kg (18.4 mg Cd/kg) by gavage in an experiment conducted by Machemer and Lorke (1981) resulted in a significant increase in malformations compared to the control group ($p < 0.05$). The malformations occurring at that dose were varied and affected different organ systems but were reported to be unusual in type and frequency.

Table 4.256 Details on the reported malformations (study of Machemer and Lorke, 1981)

Effects					
Dose (mg Cd/kg/day)	**Effects on foetuses**		**Developmental NOAEL/LOAEL**	**Maternal toxicity**	**NOAEL**
	n (%)*				
0	0 (0)	Telencephalic hypoplasia		/	
1.2 (F)	1 (0.41)			/	
3.5 (F)	1 (0.46)	Microphtalmia		/	NOAEL
12.5 (F)	5 (2.39)	Telencephalic hypoplasia, wavy ribs, microphtalmia		Effect on weight gain	
1.84 (G)	1 (0.49)	Dysplasia of the facial bones		/	
6.13 (G)	2 (0.98)	Costal fusion, anophtalmia	NOAEL	3/23: coarse fur, effect on weight gain, no death	
18.39 (G)	10 (5.62)	Dysplasia of the facial bones and the rear limbs, general oedema, palatoschisis, cryptorchism, exenteration	LOAEL	1/28 died, 8/28: bristly fur, weight gain was significantly depressed	
61.32 (G)		Resorption of all the embryos in the surviving pregnant rats		15/25 animals died	

* Number of malformed foetuses: n (percentage)
F Food
G Gavage

This dose of 18.4 mg Cd/kg/day was not well tolerated by the exposed female rats.

When the same authors administered cadmium in food in concentrations up to 100 ppm (corresponding roughly to 12.5 mg Cd/kg/day), no adverse effects with respect to the development of the embryos were observed compared to controls. However, 100 ppm had a negative effect on the weight gain of the females (weight gain was significantly lower than in the control group, $p < 0.05$).

Developmental anomalies such as sirenomelia or amelia were observed after exposure to a cadmium dose of 40 mg Cd/kg/day, administered intragastrically (Baranski, 1985). Examination of the bone system did not disclose congenital defects. A retarded process of ossification of the sternum and ribs was observed at any of the doses tested. However, at least for the two highest doses, body weight of the foetuses was also significantly lower compared to controls (see **Table 4.254**) and the delayed ossification was considered by the author as a manifestation of the retardation of the intrauterine development induced by cadmium and not as a congenital anomaly of the skeleton.

Table 4.257 Details on the reported malformations (study of Baranski, 1985)

Effects					
Dose (mg Cd/kg /day)	Effects on foetuses		Developmental NOAEL/ LOAEL	Maternal toxicity	Maternal NOAEL
	n (%)*				
2	N.I.	delayed ossification of the sternum and ribs		Body weight gain significantly depressed	LOAEL
12	N.I.	delayed ossification of the sternum and ribs	NOAEL	Body weight gain significantly depressed	
40	N.I.	Slowed down osteogenesis sirenomelia (fused lower limbs), amelia (absence of one or more limbs), and delayed ossification of the sternum and ribs	LOAEL	Body weight gain significantly depressed	

* Number of malformed foetuses: n (percentage)
N.I. No information

In the multigenerational study carried out by Schroeder and Mitchener (1971), there was a 14% incidence of runts (defined as animals with large heads but small bodies) and a 21% incidence of postnatal deaths of the young compared with none in controls. By the F2 generation, 2/5 litters were born dead and postnatal deaths had increased to 47% of the young. Kinked tail was seen in both F1 and F2 offspring (Schroeder and Mitchener, 1971; Barlow and Sullivan, 1982; Whelton et al., 1988).

Table 4.258 Details on the reported malformations (study of Schroeder and Mitchener, 1971)

Effects					
Dose (mg/kg /day)	Effects on foetuses		Developmental NOAEL/LOAEL	Maternal toxicity	Maternal NOAEL
	n (%)*				
2.5	N.I.	Runts, sharp angulation of the distal third of the tail, increased mortality	LOAEL	N.I.	N.I.

* Number of malformed foetuses: n (percentage)
N.I. No information

In contrast to these three studies reporting malformations, Saxena et al. (1986) reported no developmental effect from an exposure to 21 mg Cd/kg/day (as Cd acetate) via drinking water in pregnant rats during gestation (Gd0-20). No maternal effect was seen either. This study evaluated the effect of simultaneous exposure to lindane (20 mg/kg via gavage on Gd 6-14) and cadmium acetate. Whereas cadmium or lindane alone did not produce any significant malformations in the 20 day old foetuses, their combination caused significant reduction in the body weight of dams and pups and increased total embryonic deaths. Skeletal deformities like wavy ribs, reduced skull ossification and reduced caudal vertebrae were observed in the coexposure group (Saxena et al., 1986 cited in ATSDR 1999).

3. Reported neurobehavioral changes

The most sensitive indicator of developmental toxicity of cadmium in animals is reported to be the neurobehavioral development (ATSDR 1999). Several studies have attempted to assess the possible effects on neurobehavioral or neurophysiological parameters of an indirect (by exposing the dams) or a direct (during lactation and post-weaning periods) exposure to cadmium compounds.

Cadmium exposure via drinking water (about 2.2 mg Cd^{2+}/kg/day) has been reported to decrease significantly spontaneous locomotor activity levels of male offspring evaluated from 5 weeks of age during 5 weeks as daily wheel running activity. This reduction in spontaneous locomotor activity was not accompanied by a reduced consumption of food or water, neither by other signs of toxicity. No difference between exposed and control rats was observed in regard of the acquisition of the spatial discrimination task (Hastings et al., 1978).

The locomotor activity of female offspring of rats treated with 0.04 mg Cd/kg/day by gavage and evaluated at 2 months of age, was significantly reduced and the length of stay on a rotating rod by males born to rats exposed to the same dose was significantly shorter than that of respective controls. Exploratory locomotor activity of both males and females was reduced at a Cd dose of 0.4 mg Cd/kg/day. At these levels, no maternal effects were reported. No overt foetotoxicity effects such as viability, body weight gain, delayed ossification were observed (Baranski et al., 1983).

A significant hyperactivity and delay in the development of cliff aversion and swimming behaviour were observed in neonatal pups from dams exposed to 0.7 mg/kg/day during gestation. In post-weaning measurements, locomotor activity shuttle box performance was significantly decreased at 60 days but not at 90 days of age. The apomorphine-induced hyperactivity was not affected in these rats at either age (Ali et al., 1986 cited in ATSDR 1999). No details on maternal toxicity are available.

Three consecutive generations of Wistar rats were treated by gavage with 3.5, 7.0 or 14.0 mg/kg cadmium chloride over the period of pregnancy, lactation and 8 weeks after weaning. Behavioural (open field behaviour) and electrophysiological parameters (spontaneous and evoked cortical activity, etc.) were investigated at the age of 12 weeks. The main behavioural outcomes were change in vertical exploration activity and increased exploration of an open field centre. The spontaneous and evoked electrophysiological variables showed dose- and generation-dependent changes (increased frequencies in electrocorticogram, lengthened latency and duration of evoked potentials, etc.) signalling a change in neural functions. No visible signs of cadmium intoxication were observed during the whole period over the three generations. However, treatment with the two highest cadmium doses resulted in a significantly lower body weight in F3 compared to controls of the same generation at 12 weeks of age (Nagymajtenyi et al., 1997).

Behavioural and electrophysiological changes in the offspring of exposed female rats were investigated by the same group of authors, using same doses of cadmium. Dams were given cadmium chloride in three different treatment regimes: pregnancy only, pregnancy + lactation, pregnancy + lactation + post weaning. The changes of electrophysiological phenomena were significant only in the high dose pregnancy + lactation + post weaning group. Only combining treatment during the prenatal development and the suckling period resulted in a significant dose-dependent decrease of horizontal and vertical exploratory activity and a significantly lower exploration frequency of the open-field centre. However, behavioural effects were not significant in the longest treated group (pregnancy + lactation + post-weaning). No explanation was offered for this contradictory reaction. No visible signs of chronic cadmium intoxication were found in any of the treated groups (Desi et al., 1998).

Neither the mechanism nor the critical period of cadmium-induced central nervous system dysfunction in offspring due to maternal exposure to Cd is yet completely elucidated. Direct action of cadmium on the foetal brain seems improbable because this element has not been reported to accumulate to a significant extent in foetuses of female rats repeatedly exposed to cadmium in drinking water or via inhalation (Baranski et al., 1983). For example, in the study of Andersson et al. (1997) where young rats were exposed to 5 ppm cadmium chloride (either directly in the drinking water, or indirectly via lactation, or during lactation and post weaning), brain cadmium levels (at day 45-51 after birth) were below the limit of detection in all treatment groups.

A first explanation that has been suggested is that cadmium should affect the metabolism of copper and zinc (as for the foetal growth impairment) as both Cu and Zn deficiency in new-born or suckling rats were reported to induce brain lesions or behavioural disturbances.

Baranski (1986) has reported an association between reduced brain Cu and Zn concentrations and the impairment of behaviour in the adult offspring of female rats exposed to 60 ppm cadmium (as $CdCl_2$, in drinking water) during gestation. However, these reductions in Cu and Zn brain content were observed only in suckling and/or adult offspring and not in the foetuses at term, what indicated that the alterations in Cu and Zn distribution in pups of Cd-treated dams appeared after birth, leading to deficit of behaviour being pronounced only in adult offspring. Hypothesised mechanism for the decreased content in Cu and Zn of the brain was a Cd-induced decreased gastro-intestinal absorption of these elements. The behavioural defects as seen in adult offspring (Baranski, 1984) would be indirect rather than direct results of their Cd exposure during the prenatal and/or suckling period (Baranski, 1986).

Another suggested explanation for the changes in the behavioural and electrophysiological activity is an effect of cadmium on the neurotransmitter systems: “low” (not detailed) doses of cadmium were reported to change the release of acetylcholine from presynaptic nerve resulting in higher EEG frequency (Casali et al., 1995 cited by Nagymajtenyi et al., 1997). Cadmium also inhibits to some extent the activity of brain cholinesterases (Desole et al., 1991, cited by Nagymajtenyi et al., 1997). It has also been shown that repeated administration of cadmium in adult rats resulted in increased levels of 5-HT in the brain whereas decreased levels of 5-HT were seen after cadmium exposure in growing rats (0.4 mg/kg a day, IP) (Gupta et al., 1993 cited by Andersson et al., 1997).

Another possible explanation suggested by Nagymajtenyi et al. (1997) for the cadmium- induced functional disorders in the sensory pathway could be a blocking effect of cadmium on certain ionic channels, primarily the Ca^{2+} channels. Consequently, the conduction of the action becomes slower and the latencies and also the interpeak durations of evoked potentials will be lengthened. Cadmium may also interfere with cellular energy metabolism by inhibiting ATP synthesis and ATP hydrolysis reactions (Andersson et al., 1997). All these findings appear to be of potential relevance as the catecholaminergic and serotoninergic systems are known to be involved in a number of important functions such as motor activity. The monoaminergic and the cholinergic systems appear to be involved in cadmium-induced behavioural alterations (Andersson et al., 1997).

In an attempt to elucidate the mechanism of the neurotoxicity of cadmium when given to pregnant animals, Andersson et al. (1997) exposed S.D. rats to 5 ppm cadmium in drinking water. Exposed animals were developing rats (day 19-42 of life) or dams (from partus to day 19 of lactation) to evaluate indirect exposure. No significant alterations were seen in body weight gains of the growing pups or in the dams. The serotoninergic system appeared to be particularly sensitive to cadmium exposure. Small alterations were also seen after cadmium exposure in noradrenalin levels but not in dopamine or acetylcholine levels. The most prominent effects were found in the offspring indirectly exposed to cadmium via the lactating dam.

However, the kidney cadmium concentrations in the rats belonging to this group were 60 times lower than those observed in the group directly exposed to cadmium after weaning.

Table 4.259 Cadmium concentrations in offspring (Andersson et al., 1997)

	Control	Lactation	Post wean	Lactation-post weaning
Brain	< 0.004	< 0.004	< 0.004	< 0.004
Kidney	0.01 ± 0.01	0.02 ± 0.00	1.21 ± 0.28*	1.26 ± 0.32

Authors suggested two explanations for this finding: either the suckling period is very sensitive even to extremely low levels of cadmium or the cadmium interacts in the mammary tissue with the transfer of essential elements into milk thereby disturbing normal mechanisms in the new-born and inducing serotoninergic effects (Andersson et al., 1997).

The effects of a gestational and early lactational exposure to cadmium acetate (10 mg Cd acetate/L; ~ 1.1 ± 0.2 mg Cd/kg/day) on the monoaminergic metabolism in rat brain were examined by Antonio et al. (1998). At birth or on postnatal day 5, pups were weighed and sacrificed. Cd brain content and levels of dopamine (DA), 5-hydroxytryptamine (5-HT) and their metabolites (3,4 -dihydroxyphenylacetic acid DOPAC, and 5-hydroxyindolacetic acid (5-HIAA), respectively) were measured. No effects of cadmium exposure were observed on body weight gain or water consumption of exposed dams and no decrease in birth weight of the pups was observed. Cd increased the 5-HT and 5-HIAA contents in all areas of the brain and the DA and DOPAC levels in mesencephalon but decreased the DA and DOPAC levels in the metencephalon. From these results, authors concluded that the alterations of the monoamines depended on the specific area of the brain and may be related to their different pattern of development (Antonio et al., 1998).

Finally, beside these investigations on the effects of a gestational or lactational exposure to cadmium, one experiment was located in which cadmium chloride was administered to very young rats for 10 consecutive days. The objective was to assess possible long-term effects on activity and learning (Smith et al., 1982). Animals were tested for spontaneous locomotor activity at either 45 or 46 days of age. Learning trials started from 75 days of age. The highest dose group was the only one to have a mean level of activity below the control level (although not reaching statistical significance). Surprisingly, in the learning task cadmium treated animals were reported to perform significantly better. Authors suggested that the exposed rats might present Cd-induced impaired olfactory capabilities, and that this effect, instead of handicapping the rats, would reduce the exploratory behaviour, improving thereby their performances and shortening the latencies in a trial that includes immediate reinforcement (Smith et al., 1982).

Summary: oral route, developmental effects

No studies in animals specifically using cadmium oxide or metal has been identified.

Cadmium compounds have been reported to induce reduced body weight and malformations (primarily of the skeleton) in offspring of animals exposed via gavage or diet at doses that produced maternal toxicity. In some studies, information on maternal toxicity is lacking, but cross reading with studies that provide this information indicates that the reported developmental effects occur at doses levels expected to cause maternal toxicity (overall > 5 ppm or about ~0.6 mg $CdCl_2$/kg/day).

Neurobehavioral effects or changes in electrophysiological parameters were reported to occur at doses that did not induce maternal toxicity. Lowest dose reported to generate behavioural changes in pups is 0.04 mg Cd/kg/day (LOAEL) (Baranski et al., 1983). Significance of these changes and underlying mechanisms for the observed effects on behavioural endpoints are not completely elucidated yet; some authors suggested that the toxic effects might be mediated by placental toxicity or by interference with the normal fœtal metabolism of Zn and/or Cu. Several other mechanisms of action (neurotransporters, ions channels) were suggested to explain the neurobehavioral changes in the pups of exposed dams. There is a need for further studies to better describe the effects of cadmium on the developing brain.

Because the oral bioavailability of CdO and Cd metal is not fundamentally different from the compounds tested (see Section 4.1.2.2), it can reasonably be considered that these observations can be extended to Cd metal and CdO by the oral route. Taken together, these results indicate concern for developmental toxicity.

Inhalation route

No study using cadmium metal was located. Some studies using cadmium oxide and investigating foetal body weight, malformations or neurobehavioral effects of inhaled cadmium have been identified (Baranski, 1984; Baranski, 1985; NTP Report 1995).

Table 4.260 Main characteristics of the studies on developmental effects in rats and mice exposed by inhalation Rats

Effect	Doses of Cd	Duration	Developmental NOAEL ($mg\ Cd/m^3$)	Developmental LOAEL ($mg\ Cd/m^3$)	Maternal NOAEL ($mg\ Cd/m^3$)	Reference	Comments
Rats							
Reduced fœtal or pup weight	0-0.02-0.16 mg Cd/m^3	5 days/week, 5 hour daily for 5 months + 3 weeks of mating + days 1-20 of gestation	0.02	0.16	N.I.	Baranski (1984)	Body weight at birth similar in all doses. At 0.16 mg Cd/m^3: delayed growth, reduced viability at 0.16 mg Cd/m^3
	0-0.02-0.16-1 mg Cd/m^3	0.02-0.16 mg Cd/m^3:5 days/week, 5 hour daily for 5 months + 3 weeks of mating + days 1-20 of gestation 1 mg Cd/m^3: 5 days/week, 5 hour daily for 4 months + 3 weeks of mating + days 1-20 of gestation	0.02	0.16	0.16	Baranski (1985)	At 0.16 and 1 mg Cd/m^3, "increased number of foetuses with retarded development" (no statistical data). At 0.16 mg CdO/m^3: body weight significantly lower during the first two months of life compared to controls (no statistical analysis reported)
	0-0.05- 0.5-2 mg CdO/m^3	gestation days 4–19	0.4	1.75	< 0.04	NTP Report (1995)	Maternal NOAEL of < 0.05 mg CdO/m^3 is based on clinical signs (dyspnea); another NOAEL could be set at 0.5 mg CdO/m^3 based on pregnancy index and maternal weight change
Malformations	0-0.02-0.16-1 mg Cd/m^3	0.02-0.16 mg Cd/m^3:5 days/week, 5 hour daily for 5 months + 3 weeks of mating + days 1-20 of gestation 1 mg Cd/m^3: 5 days/week, 5 hour daily for 4 months + 3 weeks of mating + days 1-20 of gestation	N.D.	0.02	0.16	Baranski (1985)	Significantly higher number of foetuses with pronounced signs of retarded ossification (data and statistical analysis not reported)
	0-0.05- 0.5-2 mg CdO/m^3	gestation days 4–19	0.4	1.75	< 0.04	NTP Report (1995)	Effect: reduced ossification Maternal NOAEL of < 0.05 mg CdO/m^3 is based on clinical signs (dyspnea); another NOAEL could be set at 0.5 mg CdO/m^3 based on pregnancy index and maternal weight change

Table 4.260 continued overleaf

Table 4.260 continued Main characteristics of the studies on developmental effects in rats and mice exposed by inhalation

Effect	Doses of Cd	Duration	Developmental NOAEL (mg Cd/m³)	Developmental LOAEL (mg Cd/m³)	Maternal NOAEL (mg Cd/m³)	Reference	Comments
Pup behavioural alterations	0-0.02-0.16 mg Cd/m³	5 days/week, 5 hour daily for 5 months + 3 weeks of mating + days 1-20 of gestation	N.D.	0.02	N.I.	Baranski (1984)	
	0-0.02-0.16-1 mg Cd/m³	0.02-0.16 mg Cd/m³:5 days/week, 5 hour daily for 5 months + 3 weeks of mating + days 1-20 of gestation 1 mg Cd/m³: 5 days/week, 5 hour daily for 4 months + 3 weeks of mating + days 1-20 of gestation	N.D.	0.02	0.16	Baranski (1985)	
Mice							
Reduced fœtal weight	0-0.05- 0.5-2 mg CdO/m³	0-0.05- 0.5-2 mg CdO/m³	0.04	0.4	< 0.04	NTP Report (1995)	Maternal NOAEL of < 0.05 mg CdO/m³ is based on clinical signs (dyspnea), other NOAELs could be set at 0.05 mg CdO/m³ based on pregnancy index and at 0.5 mg CdO/m³ for maternal weight change
Malformations	0-0.05- 0.5-2 mg CdO/m³	gestation days 4–17	0.4	1.75	< 0.04	NTP Report (1995)	Effect: reduced ossification Maternal NOAEL of < 0.05 mg CdO/m³ is based on clinical signs (dyspnea); other NOAELs could be set at 0.05 mg CdO/m³ based on pregnancy index and at 0.5 mg CdO/m³ for maternal weight change

N.D. Not determined
N.I. No information

Inhalation exposure of female rats to cadmium oxide aerosol (mass median aerodynamic diameter < 0.65 µm) at concentrations of 0.02 and 0.16 mg Cd/m^3 before and during gestation did not produce any increased embryonic or foetal lethality, congenital malformations or changes in mean foetal body weight at term. However, viability of offspring born to females exposed at 0.16 mg CdO/m^3 was significantly reduced (indices of viability: % of pups born alive that survived to 4 days = 75% and 98% in exposed and controls, respectively, $p < 0.05$) (Baranski, 1984).

Pups from Cd-exposed rats did not differ from age-matched controls in either appearance or food and water consumption. However, growth of offspring whose dams were exposed to 0.16 mg Cd/m^3 was delayed in comparison with controls.

Exploratory motor activity of 3-month-old females delivered by female rats exposed at a concentration of 0.16 mg Cd/m^3 and that of male offspring from the 0.02 and 0.16 mg Cd/m^3 groups were significantly reduced when compared with respective control values. The reduction of exploratory motor activity was apparently dose-dependent. Avoidance acquisition of 3-month-old female rats prenatally exposed to Cd was significantly depressed when compared with the controls. Data on the open-field behaviour recorded at 5 months of age are summarised in **Table 4.261**.

Table 4.261 Total mean (± SD) calculated across 5 days of testing of 2 categories of open field-behaviour for 5-month-old male and female offspring of Cd-exposed and control female rats (activity counts/5 min)

Behaviour	Females			Males		
	Control	0.02 mg Cd/m^3	0.16 mg Cd/m^3	Control	0.02 mg Cd/m^3	0.16 mg Cd/m^3
Locomotor activity	31.0 ± 14.1	50.8 ± 26.4*	34.3 ± 17.2§	28.4 ± 13.1	29.1 ± 15.1	22.4 ± 11.8§*
Rearing	7.8 ± 4.8	9.7 ± 7.7	6.5 ± 5.4§	6.5 ± 5.7	8.0 ± 7.1	5.8 ± 5.7§

* Significantly different ($p < 0.05$) from the control group

§ Significantly different from the 0.02 mg Cd/m^3 group

The locomotor activity of female offspring group appeared to be higher in the 0.02 mg Cd/m^3 group compared to controls and the 0.16 mg Cd/m^3 exposed group. Activity of males born to females exposed to 0.16 mg Cd/m^3 was significantly lower than in both other groups. The vertical activity (rearing) of male and female offspring from the high exposure group was significantly reduced in comparison with animals from the other groups. Cadmium-induced CNS dysfunction was still observable in 7-month-old female offspring (Baranski, 1984).

In another report (it is not exactly known whether this report deals with an experimental group independent of the one described above, Baranski, 1984), female rats were exposed to cadmium oxide at a concentration of 0.02-0.16 or 1 mg Cd/m^3. No embryotoxicity was observed and no effect on the foetus (length, weight) was noted on day 21 of pregnancy when dissection was performed:

Table 4.262 Prenatal development of progeny of female rats chronically exposed to CdO. Dissection performed on the 21st day of pregnancy

	Controls	0.02 mg CdO/m³	0.16 mg CdO/m³	1 mg CdO/m³
Length of fœtus (cm)*	4.12 ± 0.19	4.23 ± 0.31	3.75 ± 0.76	4.09 ± 0.3
Weight of fœtus (g)*	3.52 ± 0.37	3.44 ± 0.21	2.96 ± 0.93	3.57 ± 0.53

* Mean of mean values for litters ± standard deviation

However, authors report that macroscopic examination of foetuses and internal organs revealed an increased number of foetuses with retarded development in the females exposed to 0.16 and 1 mg CdO/m³ (not further detailed). A significantly higher number of foetuses with pronounced signs of retarded ossification was found in the exposed groups than in the controls (no statistical analysis available in the publication). Due to the high death rate (55.1%) of females exposed to 1.0 mg/m^3, no analysis of the postnatal development of their offspring was undertaken. Body weight in the progeny of females exposed to 0.16 mg Cd/m^3 is reported to have been significantly lower during the first two months of life than in the progeny of control animals and female rats exposed to 0.02 mg Cd/m^3. The offspring of females exposed to 0.02 mg/m^3 displayed lowered motor activity and worsened consolidation of the conditioned-reflex response compared to the controls. Inhalation exposure to 0.16 mg/m^3 of females induced in their young a prolongation of latency in the negative geotaxis test, lower locomotor activity (especially in the female offspring) and worsened consolidation of the conditioned-reflex response, compared to the control group (Baranski, 1985). Large variations were however observed between the groups (e.g. female controls vs. 0.02 mg/m^3).

The robustness of the observations by Baranski (1984 and 1985) may, however, be questioned in view of the :

- high and unexplained mortality rate in certain groups,
- apparent inconsistencies in the dose-effect relationship in a single test (e.g. locomotor activity at 0.02 and 0.16 mg/m³),
- apparent inconsistencies in the response between tests (e.g. locomotor activity and rearing).

Developmental effects were also reported in a more recent study which assessed the toxicity of CdO in rats and mice exposed to 0.05, 0.5, or 2 mg/m³ (mean mass median aerodynamic diameter: 1.5 µm) cadmium oxide aerosol during gestation (NTP Report, 1995).

In rats, maternal toxicity expressed as change in body weight gain was reported to be significant only in the highest dose group. However, clinical signs of toxicity occurred in all exposed groups and included dyspnea (its duration, incidence and severity increased in an exposure-related manner) and hypoactivity. There was no evidence of embryolethality at any exposure level. However, in the highest exposure group (2 mg/m³), developmental toxicity was evidenced by lower foetal weights and a significant increase in the incidence of reduced skeleton ossification (assessed by examination of the carcasses at necropsy and expressed as % per litter) (results are summarised in **Table 4.263**).

Table 4.263 Maternal and developmental toxicity in SD rats exposed to CdO (NTP report 1995)

		0 mg/m³	0.05 mg/m³	0.5 mg/m³	2 mg/m³
Maternal toxicity	Maternal weight change (g) (Gd 0-20)	133 ± 3§	135 ± 3	131 ± 3	78 ± 5**
	Clinical signs	/	Dyspnea +	Dyspnea ++	-Dyspnea +++ -1/32 died -Hypoactivity in most of the rats
	Pregnancy index (number of pregnant females/number of sperm positive females)	26/32	28/32	29/32	31/32§
Developmental toxicity	Embryolethality	0	0	0	0
	Average fœtal body weight				
	Male foetuses	3.83± 0.05	3.76 ± 0.05	3.70 ± 0.05	3.20 ± 0.06##
	Female foetuses	3.64 ± 0.06	3.52 ± 0.05	3.52 ± 0.06	3.01 ± 0.06##
Morphologic abnormalities observed in foetuses	Malformations:				
	Foetuses with malformations	1 (0.3%)	2 (0.5%)	0 (0.0%)	1 (0.2%)
	Malformed foetuses per litter (%)	0.3 ± 1.5	0.5 ± 1.8	0	0.2 ± 1.1
	Reduced ossifications per litter (%)				
	Pelvis	2.4 ± 5.5	2.3 ± 5.2	3.4 ± 7.3	12.0 ± 19.6*
	Sternebrae	4.4 ± 7.0	7.5 ± 10.5	8.4 ± 8.4	24.7 ± 32.1*

Further details are available in the IUCLID
§ Mean ± SD
* Significantly correlated with exposure concentration by an orthogonal test after arc sin transformation
** Significantly different ($p < 0.0 1$) from the control group by William's test
Significantly different from the control group by Shirley's test
§ Significantly different ($p \leq 0.05$)from the control group by a chi-square test
+ Moderate
++ Severe
+++ Very severe

Maternal NOAEL: < 0.05 mg/m^3 (dyspnea).

Developmental NOAEL: 0.5 mg/m^3 (decreased fœtal weight and reduced ossification).

In mice exposed to same inhalation levels, maternal toxicity was the most pronounced in the high exposure group: clinical signs of toxicity included dyspnea and hypoactivity in all mice in the 2 mg CdO/m³ and in most mice in the 0.5 mg CdO/m³. Dyspnea increased in incidence, duration and severity with increasing exposure concentration. The mean body weight and maternal weight change of pregnant females exposed to the highest concentration of CdO were significantly lower than those of the controls. A decreased pregnancy rate was also observed at the highest doses (30% versus 97% in the control group at 2 mg CdO/m³). Developmental toxicity was evidenced by a decrease in foetal weights in the 0.5 and 2 mg/m³ groups and an increase in the incidence of reduced sternebral ossification in the highest exposure group (results are summarised in **Table 4.264**).

Table 4.264 Maternal and developmental toxicity in Swiss mice exposed to CdO (NTP Report, 1995)

		0 mg/m³	**0.05 mg/m³**	**0.5 mg/m³**	**2 mg/m³**
Maternal toxicity	Maternal weight change (g) (Gd 0-18)	27.5 ± 0.6	28.3 ± 0.7	27.7± 0.7	14.8 ± 3.4
	Clinical signs	/	Dyspnea +	-Dyspnea ++ -Hypoactivity in most of the mice	-Dyspnea +++ -5/32 died -Hypoactivity in all of the mice
	Pregnancy index (number of pregnant females/number of sperm positive females)	32/33	32/33	23/33§§	10/33§§
Developmental toxicity	Embryolethality	0.033 ± 0.033§	0	0	0
	Average fœtal body weight per litter§				
	Male foetuses	1.389± 0.015	1.386 ± 0.013	1.265 ± 0.018##	0.985 ± 0.104##
	Female foetuses	1.328 ± 0.014	1.328 ± 0.015	1.224 ± 0.018##	0.931 ± 0.082##
Morphologic abnormalities observed in foetuses	Malformations:				
	Foetuses with malformations	6 (2.0%)	7 (2.1%)	8 (2.7%)	1 (1.8%)
	Malformed foetuses per litter (%)	1.7 ± 3.5	1.7 ± 3.3	2.7 ± 4.4	1.7 ± 3.7
	Reduced ossifications per litter[a] (%) Sternebrae	6.0 ± 8.7	7.1 ± 14.0	11.1 ± 5.4	65.8± 34.0*

Further details are available in the IUCLID §; mean ± SD
* Significantly different (p < 0.0 5) from the control group by Turkey's t-test after arc sin transformation
Significantly different (p < 0.01) from the control group by Shirley's test
a Reduced ossification occurred in other skeletal components but only the significantly reduced ossification are given here
§§ Significantly different ($p \leq 0.01$) from the control group by a chi-square test
\+ Moderate
++ Severe
+++ Very severe

Maternal NOAEL: < 0.05 mg/m3

Developmental NOAEL: 0.05 mg/m3 (decreased fœtal weight)

Summary: inhalation route, developmental effects

No study specifically using cadmium metal was located.

Decreased foetal weight and a significant increase in retarded ossification frequency were reported in offspring of rats and mice exposed to CdO by inhalation at levels that produced maternal toxicity (2 mg CdO/m^3 and 0.5 mg CdO/m^3 in rats and mice, respectively). Neurobehavioral changes were reported in young rats from dams exposed to CdO (0.02 mg Cd/m^3 or about) in an apparently single experiment but these observations should be confirmed in an independent study.

Other routes

Most other experiments on the foetal effects of cadmium have been performed on animals given relatively large doses (> 1 mg/kg body weight) of cadmium compounds parenterally in a single or small number of doses. These routes are not considered to be relevant for a human risk assessment.

Epidemiological studies

Some authors have incriminated cadmium as a possible causal factor in preterm labour and decreased birth weights (Tsvetkova 1970; Huel et al.,1984; Fréry , 1993). Maternal hypertension has also been associated with elevated levels of cadmium in the neonate (WHO, 1992). Effects of an exposure to cadmium on the developing brain have been reported by some authors but the role of a simultaneous exposure to other potentially neurotoxic substances such as i.e. Pb could not be excluded.

To take into account the different exposure conditions to cadmium, studies were grouped in subchapters according to the concerned population: the general population exposed to cadmium by the oral route (not necessarily Cd or CdO), the workers exposed by inhalation, and the smoking population.

Oral route: general population

Table 4.265 lists the located studies conducted in different countries from 1981 to 1995. Several studies assessed primarily the environmental exposure to cadmium by measuring Cd in hair or in the placenta rather than specifically investigating the association between an exposure to cadmium and an effect of this substance on development. An overview of the selected studies is given in **Tables 4.266** to **4.277**. **Table 4.266**, **4.268**, **4.270**, **4.272**, **4.274** and **4.276** gives an overview on study population, exposure assessment and considered confounders. **Table 4.267**, **4.269**, **4.271**, **4.274**, **4.275** and **4.277** reports objectives of the study and results. Some comments on the study are given in **Table 4.267**, **4.269**, **4.271**, **4.273**, **4.275** and **4.277**.

Table 4.265 Available epidemiological studies: developmental effects, environmental exposure

Reference	Country	Population	Exposed to	Endpoint	Selected study (yes/no)*
Huel et al. (1981)	France	110 births in a maternity	At least Pb and Cd	Cd -hair related to parity, birth weight and maternal hypertension	yes
Bonithon-Knopp et al. (1986)	France	26 children (6 y.-old) probably previously studied by Huel et al., 1984	At least Pb and Cd	Psychomotor development	yes
Lazebnik et al. (1989)	US	86 women studied at the time of delivery	N.I.	Cd-B and placental Cd related to hypertension and zinc status	yes
Laudanski et al. (1991)	Poland	136 women from village highly contaminated with lead and cadmium	Pb, Cd	Reproductive outcome	yes
Loiacono et al. (1992)	Yugoslavia	106 women living in the vicinity of a Pb smelter	Pb, Cd	Birth weight	yes
Fréry et al. (1993)	France	102 mothers and new-borns in a obstetrical care unit	N.I.	Birth weight	yes
Tabacova et al. (1994)	Bulgaria	71 prenatal patients residing in the vicinity of a copper smelter	As, Cu, Mn, Zn, Se, and to a lesser extent Pb and Cd	Some complications of pregnancy	yes
Wulff et al. (1995)	Sweden	Children born to women living around a Swedish smelter (N=N.I.)	Sulfur dioxide, Pb,Cu, Zn, Cd, Hg, As	Birth weight, perinatal death	no*

* Reasons for exclusion and possible impact of this exclusion on the conclusions are considered in the discussion
N.I. No information available

Table 4.266 Study conducted by Huel et al.(1981): Study population, exposure assessment, confounders

Main characteristics of the sample	**Exposure assessment**	**Considered Confounders**
Final population:	Type of exposure: environmental	Age: yes
E: 108 F	Type of compound: N.I	Drugs: N.I.
Age: 25.4 y. (mean)	Exposure duration: N.I.	Alimentation/Vitamins: N.I.
105 newborns	Environmental and biological monitoring:	Smoking: yes
C: 0	Cd air: N.I.	Other diseases: N.I.
	Cd-U: N.I.	Others: N.I.
Selected from:	Cd-B: N.I.	
E: "110 births that occurred during the spring of 1978 in Hagenau Maternity"	Cd-hair(ppm):	
	E: Mothers: 0.43 ± N.I. (N.I.)	
Selection procedure: N.I.	Newborns: 0.54 ± N.I. (N.I.)	
Lost subjects: N.I.	Other simultaneous exposure: "several chemical and metallurgical factories are present in the area…"	
Previous poisoning/ Osteomalacia/ Kidney disease: of the mothers: N.I.	*Pb-hair (ppm):*	
	E: Mothers: 8.4± N.I. (N.I.)	
	Newborns: 7.3 ± N.I. (N.I.)	

N.I. No information available in this publication
E Cd-exposed persons,
C Non exposed persons,
M Male,
F Female,
Y Years
Cd-B Blood cadmium,
Cd-U Urinary cadmium
Cd-P Placental Cd
Cd-H Cd in hair
Considered confounders by the authors: Alimentation, Drugs, Smoking, Other diseases, Others:
yes Means that these factors were considered in the selection of the population and/or in discussion,
no Not considered in selection of the population or in the discussion,
± Some attempt to consider this factor was made
Exposure assessment: if not other wise indicated, values are means ± SD (range)

Table 4.267 Study conducted by Huel et al. (1981): Methods/endpoints and results

<table>
<tr><th>Methods and endpoints</th><th>Results</th><th>Comments</th></tr>
<tr>
<td rowspan="3">Objective of the study: 1/ to test the reliability of hair values of Cd and Pb as indicators for the direct foetal environment and 2/ to assess the possible implications of these trace metals in the mother upon certain pathologic changes in the infant during the in utero life

-Hair taken at delivery

-Outcomes of pregnancy: information available at delivery</td>
<td>-a correlation was observed between Cd-H mother and Cd-H infant
(0.48, p < 0.0001)

-cadmium in mothers' and new-borns' hair according to outcomes of pregnancy:</td>
<td>-according to the authors of the paper, results remain only suggestive because of several drawbacks of the study</td>
</tr>
<tr>
<td><table>
<tr><th></th><th>Mothers</th><th>New-borns</th></tr>
<tr><td>Preterm births*:
Cd-Hair (GM)</td><td>0.47</td><td>0.54</td></tr>
<tr><td>Small-for-dates*:
Cd-H (GM)</td><td>0.69</td><td>1.04§</td></tr>
<tr><td>Malformed infants*:
Cd-H (GM)</td><td>0.65</td><td>0.64</td></tr>
<tr><td>Normal infants:
Cd-H (GM)</td><td>0.38</td><td>0.46</td></tr>
</table></td>
<td>(small number of subjects, lack of information on the selection of the study population, poor exposure assessment, endpoints not precisely defined, incomplete results, etc.)</td>
</tr>
<tr>
<td>-Higher levels of Cd were found in infant's hair of hypertensive mothers (0.79 ppm (N=13)) compared to the infants of normotensive mothers (0.52 ppm (N=72)) (p < 0.05). Authors attributed this to a preferential accumulation in the infants of hypertensive mothers</td>
<td></td>
</tr>
</table>

§ Difference significant ($p < 0.05$) when compared with the normal group
Cd-H Cd in hair
GM Geometric mean
* No definition available

Table 4.268 Study conducted by Bonithon-Kopp et al. (1986): Study population, exposure assessment, confounders

Main characteristics of the sample	**Exposure assessment**	**Considered Confounders**
Final population:	Type of exposure: environmental	Age: yes
E: 26 children	Type of compound: N.I	Drugs: N.I.
Age: 6 y.	Exposure duration: N.I.	Alimentation/Vitamins: N.I.
	Environmental and biological monitoring:	Smoking: yes
C: 0	Cd air: N.I.	Other diseases: N.I.
	Cd-U: N.I.	Others: social class, mother's and father's educational level, birth weight
Selected from:	Cd-B: N.I.	
E: " new-born babies from whom samples of hair were taken in 1977 in the Hagenau Maternity"	Cd-hair(ppm, mean ± SD (range)):	
	E: Mothers: 0.40 ± N.I. (0.16-1.15)	
	Newborns: 0.63± N.I. (0.23-1.90)	
Selection procedure: N.I.	Other simultaneous exposure: "several chemical and metallurgical factories are present in the area, etc."	
Lost subjects: N.I.		
Previous poisoning/ Osteomalacia/ Kidney disease: of the mothers: N.I.	Pb-hair (ppm, mean ± SD (range)):	
	E: Mothers: 25.4± N.I. (8.1-72.4)	
	Newborns: 19.3 ± N.I. (4.6-104.7)	

N.I. No information available in this publication
E Cd-exposed persons,
C Non exposed persons,
M Male,
F Female,
y Years
Cd-B Blood cadmium,
Cd-U Urinary cadmium
Cd-P Placental Cd
Cd-H Cd in hair
Considered confounders by the authors: Alimentation, Drugs, Smoking, Other diseases, Others:
yes Means that these factors were considered in the selection of the population and/or in discussion,
no Not considered in selection of the population or in the discussion,
± Some attempt to consider this factor was made
Exposure assessment: if not other wise indicated, values are means ± SD (range)

Table 4.269 Study conducted by Bonithon-Kopp et al. (1986): Methods/endpoints and results

Methods and endpoints	Results	Comments
Objective of the study: evaluate the late consequences of an exposure to both Pb and Cd upon the psychomotor development of children aged 6 years (Cd and Pb measured on hair samples taken at delivery)	-with the exception of verbal or memory scores, other scores of the used McCarthy scales correlated significantly with Cd-H levels in mothers -in regard to Cd-H levels in children (at birth), there was a negative significant correlation with the perceptual and motor scores -a decrease in the mean of the general cognitive index is observed when children whose degree of exposure levels (Cd-H) falls above the third quartile are compared to those falling below the first quartile	-a significant decrease of birth weight in babies belonging to the highest Cd-H quartile was reported -children and mothers are very probably already included in the study carried out by Huel et al.(1981)

Table 4.270 Study conducted by Lazebnik et al. (1989): Study population, exposure, confounders

Main characteristics of the sample	Exposure assessment	Considered Confounders
Final population:	Type of exposure: environmental	Age: yes, matched controls
Cases: 43	Type of compound: N.I.	Drugs: N.I.
Age: N.I.	Exposure duration: N.I.	Alimentation/Vitamins: N.I.
Controls: 43	Environmental and biological monitoring:	Smoking: yes, matched controls
Age: N.I.	Cd air: N.I.	Other diseases: N.I.
Selected from:	Cd-U: N.I.	Others: N.I.
E: " women attending the Cleveland Metropolitan General Hospital"	Cd-B: N.I.	
Selection procedure: N.I.	Other simultaneous exposure: N.I.	
Lost subjects: N.I.		
Previous poisoning/ Osteomalacia/ Kidney disease: N.I.		

N.I. No information available in this publication
E Cd-exposed persons,
C Non exposed persons,
M Male,
F Female,
y Years
Cd-B Blood cadmium,
Cd-U Urinary cadmium
Cd-P Placental Cd
Cd-H Cd in hair
Considered confounders by the authors: Alimentation, Drugs, Smoking, Other diseases, Others:
yes Means that these factors were considered in the selection of the population and/or in discussion,
no Not considered in selection of the population or in the discussion,
± Some attempt to consider this factor was made
Exposure assessment: if not other wise indicated, values are means ± SD (range)

Table 4.271 Study conducted by Lazebnik et al. (1989): Methods/endpoints and results

<table>
<tr><th>Methods and endpoints</th><th>Results</th><th>Comments</th></tr>
<tr>
<td>Objectives of the study: 1/ assess the different zinc indices in normotensive and hypertensive parturient women to determine whether they are altered 2/ assess whole-blood cadmium and placental cadmium levels with regard to hypertension and zinc status

-Blood sample taken at delivery

-Criteria were used to classify the patients in preeclamptic toxaemia or chronic hypertension on basis of blood pressure measurements</td>
<td>-No differences were found in the various zinc indices between chronic hypertensive parturient patients and normal control subjects. Plasma zinc levels were lower in patients with preeclamptic toxaemia (12% lower when compared with normal control subjects)

-Cd-B and Cd-P were not statistically significant between hypertensive patients (chronic hypertension/preeclamptic toxaemia) and control patients
<table>
<tr><th></th><th>Cd-B (ng/gm) (mean ± SD)</th><th>Cd-P (ng/gm) (mean ± SD)</th></tr>
<tr><td>Non-smokers</td><td></td><td></td></tr>
<tr><td>Preeclamptic toxaemia</td><td>0.63 ± 0.3</td><td>5.95 ± 2.3</td></tr>
<tr><td>Controls</td><td>0.60 ± 0.3</td><td>5.89 ± 2.3</td></tr>
<tr><td>Chronic Hypertension</td><td>0.64 ± 0.3</td><td>5.66 ± 3.3</td></tr>
<tr><td>Controls</td><td>0.63 ± 0.3</td><td>6.41 ± 2.6</td></tr>
<tr><td>Smokers</td><td></td><td></td></tr>
<tr><td>Preeclamptic toxaemia</td><td>1.98 ± 1.2</td><td>10.53 ±1.5</td></tr>
<tr><td>Controls</td><td>0.99 ± 0.2</td><td>6.86 ± 1.2</td></tr>
<tr><td>Chronic Hypertension</td><td>1.29 ± 0.4</td><td>14.1 ± 8.4</td></tr>
<tr><td>Controls</td><td>1.22 ± 0.8</td><td>11.7 ± 4.0</td></tr>
</table>
None of the values were significantly different from controls at $p < 0.05$

-By regression analysis, a significant correlation was found between the level of Cd-B and plasma zinc in non-smoking parturients with preeclamptic toxaemia</td>
<td>According to the authors the role of Cd in the cause of preeclamptic toxaemia remains unclear</td>
</tr>
</table>

Cd-B Blood cadmium,
Cd-U Urinary cadmium
Cd-P Placental Cd

Table 4.272 Study conducted by Laudanski et al. (1991): Study population, exposure, confounders

Reference	Main characteristics of the sample	Exposure assessment	Considered Confounders
Laudanski et al. (1991)	Final population: E: 136 (F) Age: 20 - > 80 y. C: 264 (F) Age: 20 – 79 y Selected from: "405 of the total of 814 women aged 17-75 y. and living in the rural area of Suwalki" E: "136 came from villages where the soil…has approximately twice the normal content of lead and cadmium…" C: "nearby villages with no increased soil content" Selection procedure: partially known (positive response to a written invitation) Lost subjects: N.I. Previous poisoning/ Osteomalacia/ Kidney disease: N.I.	Type of exposure: environmental Type of compound: N.I Exposure duration: N.I Environmental and biological monitoring: Cd-soil: N.I. Cd-U: N.I Cd-B (µg/l) E: 2.9 ± 1.2 (N=89, 65%*) C: 2.5 ± 1.4 (N=175, 65%*) Other simultaneous exposure: lead Pb-B (µg/100ml): E: 6.75 ± 6.53 C: 6.21 ± 3.36	Age: yes Drugs: no Alimentation/Vitamins: yes Smoking: yes Other diseases: yes Others: alcohol, education, occupation, contact with contaminated substances(cosmetics), living conditions, source of water, gynaecological and obstetrical histories

N.I. No information available in this publication
* No further details available
E Cd-exposed persons,
C Non exposed persons,
M Male,
F Female,
Y Years
Cd-B Blood cadmium,
Cd-U Urinary cadmium
Cd-P Placental Cd
Cd-H Cd in hair
Considered confounders by the authors: Alimentation, Drugs, Smoking, Other diseases, Others:
Yes Means that these factors were considered in the selection of the population and/or in discussion,
no Not considered in selection of the population or in the discussion,
± Some attempt to consider this factor was made
Exposure assessment: if not other wise indicated, values are means ± SD (range)

Table 4.273 Study conducted by Laudanski et al. (1991): Methods/ endpoints and results

Methods and endpoints	**Results**	**Comments**
Objective of the study: to study the influence of lead and cadmium on human reproductive outcome - data on complications of pregnancy (stillbirths, miscarriages, pre-term labour), occurrence of gynaecologic and neoplastic processes, gynaecological history (e.g. menstrual cycle disturbances, age at menarche, etc.) were obtained by personal interviews. The interviewer was aware of the exposure status of the women. -gynaecological and general physical examination, plasma samples were obtained for 65% of the population	-There was a lower number of women with three or more pregnancies and deliveries at full term in the exposed group compared to the control group	- no quantitative data available on the high levels of Cd in soil -Weak correlation, not confirmed when results for this endpoint in the exposed and control groupare compared

N pregnancies	N deliveries at full term and percentage of total	
	Exposed group (E)	Control group (C)
0	8 (6)§	10 (4)
1	18 (13)	20 (8)
2	36 (26)	49 (18)
3	27 (19)	70 (26)
> 3	47 (35)*	115 (44)
total	136	264

N complicated pregnancies	Miscarriages		Still births		Preterm labours£	
	E	C	E	C	E	C
1	12 (8.8)	46 (17)	3(2.2)	13 (4.8)	7 (5.4)	14 (5)
2	3 (2.2)	3 (1.1)	0	1 (0.3)	1 (0.7)	0
> 2	0	4 (1.4)	0	0	0	

-The only correlation found was that between Cd levels and number of preterm labours ($r=0.17$, $p < 0.05$)

§ Percentages indicated between brackets
E Exposed
C Control
* Significant differences between exposed and normal groups ($p < 0.05$)
£ Deliveries before the end of the 36th week of pregnancy

Table 4.274 Study conducted by Loiacono et al. (1992): Study population, exposure, confounders

Main characteristics of the sample	Exposure assessment	Considered Confounders
Final population: E: 106 (F only) Age (mean ± SD, years): 26.8 ± 5.0 C: 55 (F only) Age (mean ± SD): 27.0 ± 4.8 Selected from: E and C:"1502 women from areas in and around the Yugoslavian cities of T.Mitrovica and Pristina, attending a single-out patient clinic, who were in approximately 12 to 20 weeks of gestation, during the period from May 1985 through December 1986" Selection procedure: known Lost subjects: 1,341 Previous poisoning/ Osteomalacia/ Kidney disease: No	Type of exposure: environmental Type of compound: N.I Exposure duration: N.I. Environmental and biological monitoring: Cd-air: N.I. "Emissions contained approximately 0.02% Cd" Cd-B: N.I. Cd-U : N.I. Cd-P(nmol/g dry weight): E: 0.73 ± 0.52 (N=106) C: 0.5 ± 0.19 (N=55) Other simultaneous exposure: lead Pb-air: 0.9 - 12.8 µg/m³ ("immediately prior the current study") Pb-B (mother, at delivery ,µmol/l) E: 1.05 ± 0.33 C: 0.33 ± 0.23 Pb-B (umbilical cord blood, µmol/l) E: 0.98 ± 0.37 C: 0.27 ± 0.19	Age: yes Drugs: no X-rays: no Alimentation/Vitamins: no Smoking: yes Other diseases: no Others: ethnicity, alcohol, parity, live-births, maternal education

N.I. No information available in this publication, * No further details available, E Cd-exposed persons,
C Non exposed persons, M Male, F Female,
y Years Cd-B Blood cadmium, Cd-U Urinary cadmium,
Cd-P Placental Cd, Cd-H Cd in hair,
Considered confounders by the authors: Alimentation, Drugs, Smoking, Other diseases, Others:
yes Means that these factors were considered in the selection of the population and/or in discussion,
no Not considered in selection of the population or in the discussion,
± Some attempt to consider this factor was made, Exposure assessment: if not other wise indicated, values are means ± SD (range)

Table 4.275 Study conducted by Loiacono et al. (1992): Methods/ endpoints and results

<table>
<tr><th>Methods and endpoints</th><th>Results</th><th>Comments</th></tr>
<tr>
<td><u>Objective of the study:</u> to test the hypothesis that placental Cd is associated with reduction in birth weight

-Placental sample and birth weight/gestational age data obtained at delivery</td>
<td>-No association was detected between placental Cd and birth weight or gestational age at delivery

<table>
<tr><th></th><th>E</th><th>C</th><th>p</th></tr>
<tr><td>Birth-weight (g)</td><td>3,405 ± 555</td><td>3,435 ± 468</td><td>0.733</td></tr>
<tr><td>Gestational age at delivery</td><td>274.4 ± 18.4</td><td>276.4 ± 14.5</td><td>0.500</td></tr>
</table>
</td>
<td>-Incomplete exposure assessment

-Notable is the considerable lost of cases and controls from the initial study population (E: 602/C:900)</td>
</tr>
</table>

Table 4.276 Study conducted by Fréry et al. (1993): Study population, exposure, confounders

Main characteristics of the sample	Exposure assessment	Considered confounders
Final population:	Type of exposure: environmental	Age: yes
E: 102	Type of compound: N.I.	Drugs: N.I.
Age:	Exposure duration: N.I.	X-rays: N.I.
C: 0		Alimentation/Vitamins: N.I.
Selected from:	Environmental and biological monitoring:	Smoking: yes
E: "attending an obstetrical care unit"	Cd-U: N.I.	Other diseases: N.I.
	Cd-B: N.I.	Others: mother's height and weight, gestational age
Selection procedure: N.I.	Cd-H (ppm, range):	
Lost subjects: N.I.	E: mothers: 0.04-0.65	
	new- borns: 0.04-0.47	
Previous poisoning/Osteomalacia/ Kidney Disease: N.I.	Cd-P (ng/g ww):	
	E: 3.6-22.7	
	Other simultaneous exposures: N.I.	

N.I. No information available in this publication
* No further details available
E Cd-exposed persons,
C Non exposed persons,
M Male,
F Female,
y Years
Cd-B Blood cadmium,
Cd-U Urinary cadmium,
Cd-P Placental Cd
Cd-H Cd in hair
Considered confounders by the authors: Alimentation, Drugs, Smoking, Other diseases, Others:
yes Means that these factors were considered in the selection of the population and/or in discussion,
no Not considered in selection of the population or in the discussion,
± Some attempt to consider this factor was made
Exposure assessment: if not other wise indicated, values are means ± SD (range)

Table 4.277 Study conducted by Fréry et al. (1993): Methods/endpoints and results

<table>
<tr><th>Methods and endpoints</th><th>Results</th><th>Comments</th></tr>
<tr><td><u>Objective of the study</u>: investigate the effect of low levels of Cd on birth-weight

-Placenta and hair samples obtained at delivery</td><td>-a relationship was reported between a decrease in birth-weight (mean ± SD) and an increase of Cd (for the first and last quartiles) in new-born hair, depending on the presence or absence of placental calcifications

Birth weight (mean ± SD)
<table>
<tr><td>Quartile</td><td>Calcifications</td><td>N</td><td>No calcifications</td><td>N</td></tr>
<tr><td>First quartile of Cd</td><td>3,248 ± 173</td><td>7</td><td>3,051 ± 310</td><td>21</td></tr>
<tr><td>Last quartile of Cd</td><td>2,775 ± 347*</td><td>7</td><td>2,929 ± 414</td><td>20</td></tr>
</table>
-Other placental parameters were not significantly related to placental Cd concentrations</td><td>Authors could give no clear-cut interpretation for the "higher toxicity of Cd in presence of calcifications"</td></tr>
</table>

Birth weight in g,

* Significant ($p < 0.01$)

Table 4.278 Study conducted by Tabacova et al. (1994): Study population, exposure, confounders

Main characteristics of the sample	Exposure assessment	Considered Confounders
Final population:	Type of exposure: environmental	Age: yes
E: 66 (F)	Exposure duration: N.I.	Drugs: yes
Age: 17 – 36 y.	Environmental and biological monitoring:	X-rays: no
C: 0		Alimentation/Vitamins: ±
	Cd-U: N.I.	Smoking: yes
Selected from:	Cd-B (µg/l)	Other diseases: yes
E: "patients residing in the vicinity of a copper smelter…volunteered for study…all pregnant women of more than 24 weeks gestation"	E: < 0.1- 1.67	Others: hospitalisation during pregnancy, reproductive history, familial medical history, occupation (mother & father), residence, location of workplace, education, chemical exposure, drinking habits
Selection procedure: partially known	Other simultaneous exposure:	
Lost subjects: 5 patients excluded for evidence of pre-existing medical conditions	Lead Pb-B (µg/l): < 5 – 103.6	
	Arsenic As-U (µg/l): 2.2 – 62.9 µg/L	
Previous poisoning/ Osteomalacia/ Renal disease: No	Copper, manganese, zinc, selenium	

N.I. No information available in this publication,
* No further details available,
E Cd-exposed persons,
C Non exposed persons,
M Male
F Female,
Y Years,
Cd-B Blood cadmium,
Cd-U Urinary cadmium,
Cd-P Placental Cd,
Cd-H Cd in hair,
Considered confounders by the authors: Alimentation, Drugs, Smoking, Other diseases, Others:
Yes Means that these factors were considered in the selection of the population and/or in discussion,
no Not considered in selection of the population or in the discussion,
± Some attempt to consider this factor was made,
Exposure assessment: if not other wise indicated, values are means ± SD (range)

Table 4.279 Study conducted by Tabacova et al. (1994): Methods/endpoints and results

<table>
<tr><th>Methods/endpoints</th><th colspan="5">Results</th><th>Comments</th></tr>
<tr><td rowspan="6">-Objective of the study: "to assess the relation of maternal lipid peroxides, glutathione, and metal exposure to some complications of pregnancy in an area polluted by the local copper industry"
-diagnosis of pregnancy complications made on basis of interviews and clinical records
-Cd-blood: prenatal sample</td><td colspan="5">-There were no statistically significant differences between the mean values of metals in different diagnostic groups and the normal pregnancy group
Biochemical changes suggestive of increased lipid peroxidation were found in the diagnostic group toxaemia.</td><td>-11 of the patients had more than one diagnosis
-In a previous study (Tabacova, 1992) authors</td></tr>
<tr><td rowspan="2"></td><td colspan="3">Complication of pregnancy</td><td rowspan="2">No major complication (n=19)</td><td>noted significantly higher levels of lipid peroxides in the highly</td></tr>
<tr><td>Toxaemia[£] (n=17)</td><td>Anaemia[££] (n=16)</td><td>Threatened abortion[£££] (n=24)</td><td rowspan="3">polluted area even in the absence of pregnancy complications

-the environmental
situation in the studied area involved pollution by multiple metals: elevated levels of arsenic, copper, manganese, zinc, selenium and to a lesser extent lead and cadmium, were</td></tr>
<tr><td>Cd-B:
Mean ± SD
Range</td><td>0.30 ± 0.28
ND-0.83</td><td>0.32 ± 0.29
ND-0.83</td><td>0.21 ± 0.18
ND-0.83</td><td>0.32 ± 0.37
ND-1.67</td></tr>
<tr><td>Lipid peroxides in blood
Mean
Range</td><td>0.19 ± 0.20*
ND-0.55</td><td>0.13 ± 0.19
ND-0.55</td><td>0.08 ± 0.09
ND-0.26</td><td>0.05 ± 0.08
ND-0.25</td></tr>
<tr><td colspan="5">-Smoking tended to result in higher Cd-B and Pb-B
-In conclusion, authors suggested that exposure to metals during pregnancy could enhance the development of pregnancy complications(toxaemia) by increasing lipid peroxidation via depletion or reduced glutathione reserves (although changes in glutathione reserves did not reach statistical significance in the toxaemia group, perhaps because of the small number of samples)</td><td>found in soil, surface waters and food chain and observed effect may be hardly attributed to cadmium alone</td></tr>
</table>

ND Below detection limit (0.1 µg/l)
£ Toxaemia is defined as a group of disorders occurring after 20 weeks of pregnancy that variably includes hypertension, proteinuria and oedema
££ Anaemia: hemoglobin levels of 10 g/dl or less measured on 2 or more occasions without a history of anaemia before the present pregnancy
£££ Threatened abortion: onset of bleeding and/or lower abdominal pain in the first 20 weeks of pregnancy in a patient with intact membranes and a closed cervix
Cd-B Cd in blood

Discussion

Several studies addressing developmental effects in humans exposed to cadmium via the oral route were located. However, study population were mostly exposed to different pollutants and no study specifically addressed the effects of an environmental exposure to cadmium. Moreover, several of these studies are of limited value for hazard assessment because of significant drawbacks i.e. in the definition of the study endpoints, the selection of the population, the assessment of exposure. One located study has not been discussed. This study had as purpose to determine if emissions from a smelter would affect the birth-weight of offspring and increase the risk of perinatal death (Wulff et al., 1995). A historical cohort was formed from register of births. Reasons for exclusion of this study were that cadmium was not addressed specifically and that no data on exposure to cadmium were available. No differences in birth-weight were found between the children born to people living near the smelter exposed to multiple pollutants (including cadmium), and those of a reference population. Risk of perinatal death was apparently not affected by the emissions of the smelter.

Summary

No study specifically dealing with Cd metal or CdO could be located.

Decreased birth-weight (or small-for-date) was reported only in two studies, related to concentration of cadmium in infant's hair, which is not a robust estimate of exposure. In a single study this association was different according to the presence or not of placental calcifications. Cd-hair content was also reported to be increased in infants of hypertensive mothers compared to normotensive mothers.

No other major morphologic alterations of the placenta were evidenced that could explain an adverse effect on the foetus (possibly due to the relatively low levels of cadmium compared to other studies and experimental systems). Biochemical changes in maternal blood suggestive of decreased antioxidant protection have been reported by one author in some cases of complicated pregnancies. One study evaluated the late consequences of an exposure to cadmium and lead upon the psychomotor development of children. Samples of hair had been taken from these children when they were new-born and probably included in the study population of Huel et al. (1981). Results showed a significant negative relationship between the Cd-H content and the perceptual and motor scores obtained at 6 years of age. However a similar correlation was observed in these children between the same scores and the Pb-H levels in mothers and babies and the specific effect of Cd is difficult to assess.

Overall, the epidemiological evidence for a developmental effect (on birth weight, malformations, neurobehavioral performances) of Cd compounds in the general population mainly exposed by the oral route (conceivably including Cd metal and CdO) appears weak.

Inhalation route: occupational exposure

There is limited evidence that occupational maternal cadmium exposure may cause decreased birth weight in humans (Tsvetkova (1970), Huel (1984)).

Table 4.280 lists the located studies. Only four studies were identified. An overview of the selected studies is given in **Tables 4.281- 4.284**. **Table 4.281** and **4.283** gives an overview on study population, exposure assessment and considered confounders. **Table 4.282** and **4.284** reports objectives of the study and results. Some comments on the study are given in the **Table 4.282** and **4.284**.

Table 4.280 Available epidemiologic studies: developmental effects, occupational exposure

Reference	Country	Population	Exposed to…	Endpoint	Selected study (yes/no)*
Tsvetkova (1970)	Russia	106 women employed in 3 Cd factories: 1 alkaline batteries factory, 1 chemical reagent kit factory, 1 zinc moulding factory	N.I.	Birth-weight, malformations	no*
Huel et al. (1984)	France	26 women whose occupations involved heavy metals	At least Pb and Cd	Cd-H content related to exposure, Adverse effects related to Cd exposure: gestational age, birth-weight, Apgar and placental weight	yes
Berlin et al. (1992)	UK	Women employed at a nickel-cadmium battery manufacturing plant	Ni-Cd	Birth-weight	yes
Wulff et al. (1995)	Sweden	Employees in a smelter (N=N.I.)	Sulfur dioxide, Pb,Cu, Zn, Cd, Hg, As	Birth-weight and perinatal death	no*

* Reasons for exclusion and possible impact of this exclusion on the conclusions are considered in the discussion
N.I. No information available

Table 4.281 Study conducted by Huel et al.(1984): Study population, exposure, confounders

Main characteristics of the sample	**Exposure assessment**	**Considered Confounders**
Final population:	Type of exposure: occupational	Age: yes
E: 26 (F)	Type of compound: N.I.	Alimentation, Vitamins: N.I.
Age: N.I.	Exposure duration: N.I. (min. 3 months)	Drugs: N.I.
C: 26 (F)	Biological monitoring:	Smoking: yes
Age: N.I.	Cd-air: N.I.	Other diseases: N.I.
Selected from:	Cd-B: N.I.	Previous work: N.I.
E: "women whose occupations involved heavy metals, seeking obstetrical care at the Hagenau Maternal Hospital"	Cd-U: N.I. Cd-hair (ppm):	Others: parity, maternal weight and height, socio-economic status: yes
C: "unexposed women who delivered at the (same) hospital "	E: Mothers :1.45 ± N.I. (N.I.)	Hair coloration: no
Selection procedure: known	New-borns: 1.27 ± N.I. (N.I.)	
Lost cases: 53/105	C: Mothers: 0.59 ± N.I. (N.I.)	
	New-borns: 0.53 ± N.I. (N.I.)	
Previous poisoning/ Osteomalacia/ Kidney Disease: N.I.	Other simultaneous exposures: Lead	
	Pb-hair (ppm):	
	E: Mothers: 13.3 New-borns: 7.2	
	C: Mothers : 6.0 New-borns: 5.3	

N.I. No information available in this publication,
* No further details available,
E Cd-exposed persons,
C Non exposed persons,
M Male,
F Female,
y Years
Cd-B Blood cadmium,
Cd-U Urinary cadmium,
Cd-P Placental Cd,
Cd-H Cd in hair,
Considered confounders by the authors: Alimentation, Drugs, Smoking, Other diseases, Others:
Yes Means that these factors were considered in the selection of the population and/or in discussion,
no Not considered in selection of the population or in the discussion,
± Some attempt to consider this factor was made
Exposure assessment: if not other wise indicated, values are means ± SD (range)

Table 4.282 Study conducted by Huel et al. (1984):Methods/ endpoints and results

Methods and endpoints	**Results**	**Comments**
Objective of the study: to discuss advantages and problems related to hair sampling for measuring fœtal exposure to heavy metals	-Cd-H values for both mothers and new-borns were twice as high as the values for the matched controls and for the authors, this suggested that women whose occupations involved heavy metals passed substantially more cadmium to their offspring as did controls.	-according to the authors significant differences in obstetric parameters would not be expected in a study of this size
-Hair taken at delivery -Outcomes of pregnancy: information was obtained from each subject including e.g. babies' length of gestation, sex, height, weight, cranial and thoracic perimeters, placental weight, Apgar score, complications during pregnancy and at delivery and malformations	-A non-significant decrease in birth weight of exposed new-borns was observed (250 g less when compared to controls) -No other adverse effects (by the clinical parameters measured) from this exposure were documented in these new-borns	

Table 4.283 Study conducted by Berlin et al. (1992): Study population, exposure, confounder

Main characteristics of the sample	Exposure assessment	Considered Confounders
Final population:	Type of exposure: occupational	Age: yes
E: "case births": 157	Type of compound: N.I.	Alimentation, Vitamins: N.I.
C: "control births": 109	Duration of exposure: at least 6 months (no further details)	Drugs: N.I.
	Environmental and biological monitoring:	Smoking: yes
Selected from:	<u>Cd-air:</u> N.I.	Other diseases: N.I.
E: "case births: children who were born after the women had worked for at least 6 months in an area in which they were exposed to cadmium"	<u>Cd-B (µg/L):</u>	Previous work: N.I.
	E: 7.71 ± 5.59 (in mothers of 62/157 of the case births)	Others: parity, maternal weight and height
C: "children born before their mothers worked at the nickel-cadmium plant"	C: N.I.	
Selection procedure: N.I.	<u>Cd-U:</u> N.I.	
Lost subjects: N.I.	<u>Cd-P (µg/g wet weight):</u>	
Previous poisoning/Osteomalacia/Kidney disease: N.I.	(N=27):	
	dry weight: 0.119 ± 0.122 (range: < 0.012-0.535)	
	wet weight: 0.021 ± 0.022 (range: < 0.002-0.095)	
	Other simultaneous exposures: N.I.	

N.I. No information available in this publication,
* No further details available,
E Cd-exposed persons,
C Non exposed persons,
M Male,
F Female,
y Years,
<u>Cd-B</u> Blood cadmium,
<u>Cd-U</u> Urinary cadmium,
Cd-P Placental Cd,
Cd-H Cd in hair,
Considered confounders by the authors: Alimentation, Drugs, Smoking, Other diseases, Others:
yes Means that these factors were considered in the selection of the population and/or in discussion,
no Not considered in selection of the population or in the discussion,
± Some attempt to consider this factor was made,
Exposure assessment: if not other wise indicated, values are means ± SD (range)

Table 4.284 Study conducted by Berlin et al. (1992): Methods/endpoints and results

Methods and endpoints	Results	Comments
Objective of the study:1/investigate whether an exposure to cadmium had any effect on the birth weight (retrospective study), 2/assess the degree of cadmium accumulation in the placenta caused by an occupational exposure and investigate whether any morphological, histological or ultra structural changes have occurred (prospective study) -Details of occupational and reproductive history were obtained by postal questionnaires. Occupational history was checked with company records, while birth weight was checked against hospital records	-exposure to cadmium was not associated with birth-weight. Regression analysis showed that the main factors contributing to birth weight were maternal height, habitual maternal weight and smoking -Cd-P concentrations were positively correlated with maternal Cd-B levels (r=0.6) -Morphological and ultra structural studies of the placental tissue did not reveal any effect of cadmium	-Some mothers contributed children to both groups -Detailed exposure status and environmental exposure were not available in this publication -Authors noted that the mean placental concentrations they measured lied towards the lower end of a range of published data (0.012-0.055 µg/g wet weight)

Discussion

Two located papers were not discussed. The paper of Tsvetkova (1970) is written in Russian and was excluded from our analysis as only the abstract is available in English. However, this paper has been cited in several reviews. The author reports that 106 Russian women, occupationally exposed to cadmium oxide/metal (20-250,000 $\mu g/m^3$) but also to other cadmium compounds (160-35,000 $\mu g/m^3$), had offspring (67 births) with decreased birth weights compared to unexposed controls (20 births). Course and duration of pregnancy were normal in both groups but mean birth weight of children born to those working in the alkaline battery factory and in the zinc smelter were significantly lower than controls. For 4 of the 27 children born to women in the zinc smelter, author reports signs of rachitism, 1 child had retarded tooth eruption and 2 had dental disorders. The impact of this study on the conclusions is however limited because of several limitations characterising this paper (for instance, it cannot be deduced from the abstract if some women had contributed to more than one birth in the study group, whether other factors known to influence birth weights were considered, no details are given either on the observed malformations or as to how these manifestations were assessed, etc.). In view of the rather excessive exposure, other effects of cadmium would be expected to have occurred but no information was reported (Tsvetkova (1970), cited in CRC, 1986; Barlow and Sullivan, 1982, ATSDR 1993, 1999). ATSDR (1999) concluded for this study that no association was found between birth weights of offspring and length of maternal cadmium exposure.

The determination of the offspring birth weight and the number of perinatal deaths for parents working in a Swedish smelter were the aim of the study conducted by Wulff et al. (1995). Groups exposed and unexposed to the potentially reprotoxic agents from the smelter were compared, using information obtained from birth registers. Mother's age, parity, and smoking were considered as possible confounding factors. Reasons for exclusion of this study were that cadmium was not addressed specifically and that no data on exposure to cadmium were available. Authors report a tendency towards an increased risk for children born to smelter employees regarding low birth-weights, although not significant. Any interpretation of these results has to consider the multiple other toxicants used in the smelter: lead, mercury, arsenic, copper, zinc, gold, silver, sulfur dioxide before this effect can be attributed to cadmium (Wulff et al., 1995).

Summary

No clear evidence indicates that cadmium had adverse effects on the development of the offspring of women occupationally exposed to cadmium (generic). Decreased birth weight and skeletal malformations were reported in a paper written in Russian and often cited by reviewers. However, this last study can hardly be used to draw definite conclusions on developmental effects associated with cadmium exposure as information on exposure, offspring and maternal effects is fragmentary.

This generic assessment can reasonably be extended to Cd metal or CdO.

Population exposed to cadmium via tobacco smoking

It is well established that babies of mothers who smoke are smaller than those of non-smokers and that cigarette smoking causes cadmium uptake.

Urinary cadmium content was measured by Cresta et al. (1989) in women three days after giving birth and compared to smoking habits and birth weight of offspring. Women who smoked during the pregnancy ran a risk of giving birth to small-weight children one time and half higher (C.I.

not available) than women who did not smoke and urinary cadmium levels in women who smoked were higher too. The cadmium levels in urine were on average higher in women who gave birth to small-weight children, independently of smoking habits. Authors did not find a significant relationship between cadmium levels in urine and new born weight (Cresta et al., 1989).

Kuhnert et al. (1987) have suggested that a cadmium–zinc interaction takes place in the maternal-foetal-placental unit of pregnant women who smoke and results in less favourable zinc status in the infants.

In a first study, they investigated whether the increased levels of cadmium (Cd-B, Cd in placenta) found in smoking pregnant women may affect the distribution of zinc in the maternal-foetal-placental unit. In smokers, maternal whole blood cadmium levels were determinant (a stepwise multiple regression was used) of the placental cadmium levels and the placental zinc levels. A decrease in red blood cells zinc was observed in the cords of infants of mothers who smoked (230 ng/g of Hb ± 55 for smokers versus 250 ng/g ± 60 for non-smokers, $p < 0,05$) and this decrease was found to correlate with the levels of thiocyanate (an index of the number of cigarettes smoked) in maternal blood.

Authors suggested that the increased levels of cadmium as the result of smoking would induce the production of metallothionein, protein that binds both cadmium and zinc. An increased binding of cadmium and zinc and consequently a sequestering of these metals in the placenta would follow the production of the protein. The binding of zinc by metallothionein may reduce the amount of zinc available to the foetus, what could explain the decreased red blood cell zinc in the infants of smoking women. Another possibility is that less zinc is being transported by the placenta like in cadmium injected pregnant rats (Kuhnert et al., 1987).

In a second paper, Kuhnert et al. (1987) tried to relate these findings with the observable effect of smoking on human birth weight. Clinical confounding variables that were considered were gestational age, gravidity, maternal age, race, parity and maternal red blood cell count.

Biochemical variables considered were the levels of plasmatic thiocyanate, the maternal whole blood cadmium and the cord vein red blood cell zinc. Birth weights in infants of smokers were significantly lower than in infants of non-smokers (3,143 ± 554 versus 3,534 ± 555 g). Using simple correlations, the authors showed that there were different relationships between the biochemical variables and the birth weight depending on the smoking status. In smokers, negative correlations were found between birth weight and the cadmium and the zinc variables (Cd-B, Cd and Zn in placenta). Cord vein red blood cell zinc and the ratio of placental zinc to placental cadmium were positively related to infant birth weight in smokers.

Authors considered these observations as supporting data for their hypothesis: in smoking mothers, the more they smoked (as measured by thiocyanate), the higher the levels of Cd-B, Cd and Zn in placenta and the lower the birth weight. Inversely, the more zinc in the cord vein red blood cells, the greater the birth weight. A trapping of the zinc in the placenta, as previously suggested, would result in less zinc in the infant's red blood cells and theoretically less zinc to grow (Kuhnert et al., 1987).

Among smokers, the reduction in birth weight became more pronounced with increasing maternal age as reported by Cnattingius et al. (1985), cited by Kuhnert et al. (1988). Kuhnert et al. (1988) examined the relationships among placental cadmium, placental zinc, placental Zn/Cd ratio, age and parity in smokers and non-smokers. Increased parity was related to an increased placental cadmium level in smokers ($r = 0.42$, $p < 0,05$) and to a decreased placental zinc level in both smokers and non-smokers ($r=-0,14$, $p < 0,05$). An increase in placental cadmium with parity supports increases in the body burden of cadmium with age what is coherent with the long half life of cadmium. Age was inversely related to the placental Zn/Cd ratio in smokers and non-smokers. These results were consistent with a depletion of body zinc stores with increasing parity and the long half-life of cadmium (Kuhnert et al., 1988).

In the previously cited retrospective study of Berlin et al. (1992), on the birth weight of children born to female workers in a nickel-cadmium battery factory, the mean reduction in birth weight attributable to smoking after confounding factors (maternal height and habitual weight) were taken into account was 169 g. The hypothesis that cadmium accumulation in the placenta due to smoking would be the major factor in causing the birth weight reduction seen in the children of smokers (compared with those of non smokers) was rejected as the reported mean placental Cd concentrations lied towards the lower end of a range of published data cited by the authors (Finklea and Creason, 1972; Baglan et al., 1974; Creason et al., 1978; Roels et al., 1978 cited by Berlin et al., 1992).

Conclusion

It is well known that the babies of mothers who are cigarette smokers are smaller at birth than are those of non-smokers and that smoking increases the uptake of cadmium. Some authors suggested that in pregnant smokers, a cadmium – zinc interaction takes place in the maternal-foetal-placental unit and results in zinc deficiency in the foetus. A trapping of the zinc in the placenta, would result in less zinc in the fœtus's red blood cells and theoretically less zinc to grow.

The weight of evidence to specifically attribute these developmental effects to CdO or Cd metal from tobacco smoke is insufficient.

Overall assessment of developmental effects in experimental and epidemiological studies

Most studies performed with CdO or Cd salts given by the oral, inhalation or other routes reported developmental effects at dose levels that produced maternal toxicity.

Neurobehavioral changes occurring in young rats born to females treated orally ($CdCl_2$, Baranski et al. 1983) or by inhalation (CdO, Baranski 1984, 1985) have been reported by a single group of authors and the data are not completely convincing. There seems to be a consistency in the dose levels reported to produce these effects by the oral and inhalation routes :

Table 4.285 Comparison of oral and inhalation studies - Neurobehavioral effects

	LOAEL	Absorption factor	Systemic LOAEL
Oral route Baranski et al. (1983)	40 µg Cd/kg/day	5%	2 µg Cd/kg/day
Inhalation Baranski (1984)	6 µg Cd/kg/day	30%	2 µg Cd/kg/day

The underlying mechanisms of the neurobehavioral action of cadmium are not well characterised.

In humans, no clear evidence indicates that cadmium had adverse effects on the development of the offspring of women exposed indirectly via the environment or occupationally to cadmium (generic). Effects on birth weight, motor and perceptual abilities of offspring have been reported related to Cd in hair which is not a robust estimate of exposure. It is not clear whether these effects are specifically due to cadmium or were influenced by a simultaneous exposure to other substances such as lead.

Overall conclusion

Do cadmium metal and/or cadmium oxide exert reproductive and/or developmental effects?

Effects on fertility and sex organs

Only a few publications concerning the effects of cadmium on human fertility were found. Overall, epidemiological evidence does not speak for an association between exposure to cadmium and relevant effects on fertility or sex organs. In studies in animals, effects of Cd (compounds, oxide) on male and female reproductive organs were observed after oral or inhalation exposure. These effects were reported to occur at dose levels which generally caused other manifestations of toxicity (body or organ weights, lethality).

The LOAELs that will be used for the Risk Characterisation are derived from studies in animals:

Table 4.286 LOAEL/NOAEL derived from different routes of exposure in animals

Route	LOAEL/NOAEL	Species
Oral (general population)	NOAEL: 1 mg Cd/kg/day	rat, male and male
Inhalation (occupationally exposed population)	LOAEL: 1 mg CdO/m^3/0.1 mg CdO/m^3	rat, male and female

A classification for effects on fertility and sex organs of cadmium metal and cadmium oxide is warranted: Repr. Cat 3, R 62.

Developmental effects

No clear evidence indicates that cadmium had adverse effects on the development of the offspring of women exposed indirectly via the environment or occupationally to cadmium (generic). Effects on birth weight, motor and perceptual abilities of offspring have been reported by some authors. However, these studies suffer from drawbacks either in the definition of their study population, in the definition of the effects or in the assessment of exposure. Moreover, it is not clear whether the effects on psychomotor development were related to Cd or a simultaneous exposure or to other substances such as Pb. This aspect has not received sufficient attention in humans and, in view of (1) the very well-characterised neurotoxic potential of other heavy metals (e.g. lead), and (2) the increased gastro-intestinal absorption of Cd in the very young age (see Section 4.1.2.2), it would be prudent to recommend a thorough investigation of this potential effect in well designed epidemiological studies.

In studies in animals, effects of Cd on the development (reduced fœtal weight, malformations, behavioural performances) were observed after oral or inhalation exposure to Cd compounds or CdO in rats and mice. Neurobehavioral changes were reported to occur in the absence of signs of maternal toxicity but the robustness of these observations is not sufficient to derive a NOAEL for the Risk Characterisation. Further studies are needed to better document the possible effects of Cd/CdO on the developing brain (see also Section 4.1.2.7.7).

Overall, further information is needed to better document the possible effect of low doses of CdO on neurobehavioral performances suggested in experimental animals. In view of the concerns expressed for several other health effects, including repeated dose toxicity and carcinogenicity, it is urgent to address these issues adequately and to implement appropriate control measures without delay.

Conclusion (i) on hold is reached.

Cd metal and CdO have been classified in Repr. Cat. 3 (substances which cause concern for humans owing to possible developmental toxic effects) and labelled with R63 (possible risk of harm to the unborn child) considering the effects in animal testing with water soluble Cd compounds and acknowledging that possible differences in physical-chemical properties (bio-availability) may exist and that general toxicity cannot be ruled out.

4.1.3 Risk characterisation (human health)

4.1.3.1 General aspects

Uptake of cadmium can occur in humans via the inhalation of air, the ingestion of food and drinking water and, to a minor extent, through the skin.

The major route of exposure to cadmium for the non-smoking general population is via food; the contribution of other pathways (inhalation, dermal) to total uptake is small. Tobacco is an important additional source of cadmium uptake in smokers.

In exposed workers, lung absorption of cadmium following inhalation of workplace air is the major route of exposure. Additional uptake can also occur as a consequence of contamination of food and tobacco (mainly in workers who eat or smoke at the workplace).

Toxicokinetics

Toxicokinetic studies specifically dealing with CdO are limited in number. Since, following absorption, the biodisposition of cadmium (Cd^{+2}) is assumed to be independent of the chemical form to which exposure occurred, information obtained with other Cd compounds was considered relevant for this RA.

In non-smokers, the diet provides 99% of the cadmium intake, probably not as CdO. Although accurate data are lacking, it is reasonable to assume that the gastrointestinal absorption of CdO is not significantly different from that of other Cd compounds, mainly because of the high solubility of CdO in gastric juice (94%). Data from studies conducted with other Cd compounds are, therefore, used for assessing the gastro-intestinal absorption of CdO in this RA. Overall, it is considered that a large proportion of ingested Cd (including CdO) is eliminated in the faeces and that only a few percent (maximum 5%) is absorbed via the gastrointestinal tract. This rate is, however, subject to variations according to:

- age: studies in animals indicate that absorption rate is markedly higher during the first weeks of life,
- composition of the diet : low Ca, Fe, Zn and protein contents tend to increase Cd absorption,
- source of Cd : the bioavailability of soil-absorbed and seafood Cd is lower than that of ionic Cd; that of rice-associated Cd (Asia) is reported to be higher than from other sources,
- the concomitant presence of Zn in contaminated food reduces the absorption rate of Cd,
- depleted iron status (mainly women) increases Cd absorption rate by a factor of 2.

Therefore it is concluded that the gastro-intestinal absorption rate of CdO is generally below 5% when iron stores are adequate and may increase up to twice when iron stores are depleted (mainly women). A validation study showed that in mathematical modelling, a GI absorption rate of 3% is appropriate to relate Cd intake to life-time body burden in the general population, even for subgroups of the populations with depleted iron stores (see Section 4.1.2.2.5).

The alveolar absorption rate of the element from CdO varies depending on the type of exposure (fumes > dust). It is a slow process that continues for many weeks after a single inhalation exposure. Absorption rates after inhalation of CdO derived from studies in animals range from 50% (fumes) to maximum 30% (dust, depending on particle size). In humans, figures of 10-30% of absorption rate according to particle size are derived for CdO dust. For CdO fumes, based on cigarette smoke studies, it can be calculated that the respiratory absorption of CdO is between 25 and 50% in humans.

Although specific data are not available for CdO, it can be deduced from experimental studies performed with soluble Cd salts that percutaneous absorption is likely to be significantly less than 1%.

In blood, most cadmium is found in the erythrocytes (about 90%). In plasma, Cd is predominantly bound to proteins of high molecular weight (albumin or larger) a short time after exposure. To a large extent Cd bound in this form will be taken up by the liver where it accumulates. After induction of metallothionein (4-24 hours after a single exposure), Cd is present in liver mainly bound to this protein.

Cd is widely distributed and retained in the body where it accumulates throughout life. Hence, the body burden increases due to the continuous exposure and the element has a biological half-life of about 10-20 years. While the new-born baby has a total body burden of less than 1 µg of Cd, the average total body burden at age 50 has been estimated to range from 5 to 30 mg. After long-term low-level exposure, about half the body burden of cadmium is localised in the kidneys and liver, a third of the total being in the kidneys with the major portion located in the cortex. The distribution of Cd in the kidney is of particular importance as this organ is a critical target after long-term exposure to low concentrations of cadmium. The ratio between the cadmium concentration in the kidney and that in the liver decreases with the intensity of exposure; it is for instance much lower in occupationally exposed persons than in the general population. High body burden values have been found in cadmium-exposed workers without functional renal impairment (up to 450 or even 600 ppm). In non-occupationally exposed subjects the cadmium concentration in the kidneys is generally between 10 and 50 ppm (2-5 fold increase in smokers). A decrease of the Cd body burden in the European population over the last 20 years has been suggested by some authors. It must, however, be recognised that the evidence for such a decrease, based on Cd kidney content measurements, is not robust. Indirect elements supporting a decrease of the Cd body burden over the last decades include the reduction observed in the Cd content in deciduous teeth in German children and the reduction in Cd-U observed in the Pheecad study after implementation of risk reduction measures.

The considerable age-related accumulation of Cd in the body indicates that only a small part of cadmium absorbed from long-term low level exposure will be excreted. Most absorbed Cd is excreted very slowly, with urinary and faecal excretion being approximately equal. The daily excretion which takes place via faeces and urine represents only about 0.005-0.02% of the total body burden of Cd, which corresponds to a biological half life of about 10-20 or even 40 years.

After the development of severe Cd-induced renal dysfunction, Cd is lost from the renal tissue. When renal dysfunction occurs, the cadmium level in the renal cortex decreases and urinary excretion increases. The reduction of renal Cd is very likely due to a release of cadmium from the kidney combined with a depressed re-absorption of circulating Cd. This phenomenon explains why in most severely poisoned individuals the concentration of Cd in the renal cortex may be relatively low in contrast to the liver level.

The placenta provides a relative barrier protecting the foetus against cadmium exposure. There is some build up of cadmium in the placenta and levels are significantly higher in smokers than in non-smokers. The mechanism involved is still unknown but the most plausible hypothesis is that Cd is retained by binding to metallothionein in the placenta. An interaction between the essential metals zinc and copper and cadmium is suggested but its mechanism and potential consequences for toxicity to the foetus is not known. Decreases in placental Zn-Cd ratios are observed in smoking mothers. Cd can cross the placenta but at a low rate. The cadmium concentration in new-born blood is on average 40-50% lower than in maternal blood.

Cadmium is found in human breast milk at low concentrations (< 1µg/l).

Biomarkers

In humans with long-term high exposure, whole blood Cd (Cd-B) may be about 30 times higher than plasma Cd. The Cd-B value is generally below 3 µg/l in European subjects not occupationally exposed to cadmium. Concentrations in the order of 5-10 µg/l are extremely rare, unless in heavily contaminated areas. Much higher levels have been reported in Japanese women living in Cd polluted areas. Reported Cd concentrations in the blood of exposed workers are generally between 5 and 50 µg/l but, in the past, levels between 100 and 300 µg/l have resulted from extreme exposure. As tobacco smoking is an additional source of cadmium intake in the general population, values for Cd-B are generally 2-5 fold higher in smokers than in non-smokers.

In workers, after the start of exposure, Cd concentration in blood increases linearly then levels off when equilibrium is reached. Blood Cd level is considered to be related to recent exposure, it is a useful indicator of exposure during recent months. After long-term high Cd exposure, in non-smokers, an increasing proportion of blood Cd will be related to body burden. After cessation of long-term high exposure, blood Cd reflects mainly the body burden and the decrease of whole blood Cd displays an initial fast component with a half-time of 3-4 months and a slow component with a half-time of about 10 years.

Cd urinary excretion (Cd-U, expressed as µg Cd/L, as µg Cd/g creatinine, as nmol Cd/mmol creatinine or µg Cd/ 24 h) is correlated with the body burden and has been extensively used as a biomarker of long-term exposure in human studies. The mean urinary cadmium level in individuals neither occupationally exposed to cadmium nor living in a cadmium-polluted area is generally below 1-2 µg/g creatinine. Several studies have shown that in the general population, urinary Cd excretion increases with age and this increase coincides with an increased body burden. On the average, women have generally higher urinary Cd concentrations than men, probably as a reflection of higher body burden associated with increased gastro-intestinal absorption (relative iron depletion). At the group level, there is a close relationship between the cadmium concentrations in urine and kidneys. If one assumes a linear relationship between cadmium in urine and kidney, which, however, may not always be totally correct (e.g. after an acute exposure to high Cd levels or after renal damage has occurred), a Cd-U of 2.5 µg/g creatinine in urine corresponds to about 50 ppm in the kidneys cortex. In cadmium exposed workers, high urinary Cd cadmium concentrations (> 10 µg/g creatinine) have been observed and, when associated with tubular proteinuria, even higher urinary excretion may occur.

Acute toxicity

CdO is toxic by the oral and inhalation routes.

LD_{50} oral values (rat and mouse) range from 72 to 300 mg CdO/kg (63-259 mg Cd/kg) and from 50 to 400 mg Cd/kg for water-soluble compounds. Experiments using cadmium compounds provide additional information about the target organs of ingested cadmium at acute toxicity doses: targets were the proximal parts of the intestinal tract. The emetic threshold dose for cadmium (element) in drinking water has been estimated to be in the order of 15 mg/l. The no-effect level of a single oral dose for humans is estimated at 3 mg elemental Cd and the lethal doses range from 350 to 8,900 mg.

In animals, acute inhalation exposure to cadmium oxide aerosols was found to produce pulmonary inflammation and oedema. Several biochemical changes have been shown to parallel the morphological alterations. Minimal CT_{50}[35] was 450 mg CdO · min/m^3 for CdO fumes but the reliability of this figure may be questioned. Concentrations above 5 mg/m^3 have caused clear pulmonary damage (destruction of lung epithelial cells, resulting in pulmonary oedema, tracheobronchitis, and pneumonitis). The lowest dose (LOAEL) reported to cause mild pulmonary damage (hypercellularity indicative of hyperplasia) in experimental animals was an 3-hour exposure to 0.5 mg/m^3 CdO fumes, and is considered as reliable data. Acute poisonings and, in some cases, deaths have been reported among workers shortly after exposure to fumes when cadmium metal or cadmium-containing materials were heated to high temperatures. At an early stage, the symptoms may be confused with those of “metal fume fever”. However, these conditions are different, with Cd-lung leading to delayed pulmonary oedema and possibly death. Subjects who survive the acute cadmium poisoning may recover without damage, although some authors have reported delayed development of lung impairment. Cadmium concentrations in air were not reported in most case-reports. It has been estimated that an 8-hour exposure to 5 mg/m^3 may be lethal and an 8-hour exposure to 1 mg/m^3 is considered as immediately dangerous for life.

Available information does not allow a N(L)OAEL to be derived for acute dermal exposure to CdO. However, acute toxicity effects of cadmium via the dermal route are not expected to be significant as uptake of soluble and less-soluble cadmium compounds applied on the skin appears to be very low (see above).

Irritation, sensitisation, corrosivity

No specific data were located regarding the irritation potential of CdO on the skin, eye or respiratory tract neither in animals nor in humans. Based on the effects observed after acute and repeated inhalation exposure, it seems possible that CdO (as fumes) is irritant for the respiratory tract in animals as well as in humans.

Examination of the available experimental and human studies leaves the picture unclear as to whether CdO has properties of skin sensitisation. CdO is apparently not a respiratory sensitiser.

Repeated dose toxicity

A substantial body of information is available indicating that the lung, kidney and bone are the target organs upon repeated exposure to CdO in occupational settings (mainly by inhalation). Environmental exposure to Cd (generic, not specifically CdO), mainly by the oral route, is associated with bone and kidney toxicity.

35 CT50 : concentration x time , causing the death in 50% of a defined experimental animal population

Long-term inhalation exposure of experimental animals to CdO results in similar effects as seen upon acute exposures, i.e. pneumonia accompanied by histopathological alterations and changes in the cellular and enzymatic composition of the bronchoalveolar fluid. Some tolerance to cadmium appears to develop so that lung lesions developed after a few weeks of exposure do not progress, and may even recover after longer exposure. Multiple mechanisms could explain this tolerance, including the synthesis of lung metallothionein and proliferation of type II cells. Identified NOAELs are: 0.025 mg CdO/m^3 in F344/N rats exposed for 13 weeks and 0.01 mg Cd/m^3 in hamsters exposed for 16 months.

Several authors concluded that, in humans, long-term inhalation exposure to cadmium (generic) leads to decreased lung function and emphysema. Chronic obstructive airway disease has been reported to lead in severe cases to an increased mortality. A moderate increase in residual volume was observed in workers exposed to cadmium fumes (CdO) at a cumulative exposure of < 500 µg $Cd/m^3 \cdot$ years. This increase in residual volume is considered a critical effect. The LOAEL derived from this study is 3.1 µg Cd/l (Cd-U) taking into consideration that this value is for CdO fumes and may not necessarily apply to CdO dust.

The bone tissue is another target organ for the general and occupational populations exposed to cadmium compounds, including CdO. The hazard is relatively well identified both in experimental and epidemiological studies. *In vitro* studies have demonstrated that cadmium compounds (not specifically CdO) might exert a direct effect on bone affecting both bone resorption and formation, and inducing calcium release. In animals, cadmium has been shown to affect bone metabolism. These effects have manifested themselves as osteopetrosis, osteosclerosis, osteomalacia and/or osteoporosis and have been produced experimentally in several species. The most severe form of bone disease caused by cadmium intoxication is Itai-Itai disease which associated in the past kidney and bone lesions in aged Japanese women.

Thus there are solid experimental and clinical arguments to demonstrate that Cd poisoning entails bone toxicity, generally in association with overt kidney damage. Overall, however, because most of the experimental studies were designed to explore the pathogenesis of Itai-Itai disease and because animals were generally exposed during a relatively short period with relatively high doses of Cd they do not allow to derive a robust NOAEL relevant for humans exposed chronically to low doses via the diet or by inhalation. In most experimental studies, bone effects were accompanied or preceded by renal damage induced by the Cd-treatment. Young age (growing bones), gestation, lactation, and ovariectomy (used as an animal model of menopause) appeared to exacerbate Cd-induced bone toxicity.

In humans, the mechanism of bone toxicity is not fully elucidated and types of bone lesions associated with cadmium exposure are not clearly identified. One likely mechanism is disturbance of bone metabolism but another explanation is that Cd-induced kidney damage and/or hypercalciuria might promote osteoporosis and osteoporotic fractures. Results in the general Swedish population reported by Alfvén et al. (2000) suggest a LOAEL of 3 nmol Cd/mmol creatinine or 3 µg/g creatinine (not specifically CdO). This threshold would be in line with the idea that bone effects follow or are accompanied by kidney dysfunction which appears within the same range of body burden (2 µg Cd/g creatinine; Buchet et al. 1990). Some MS supported a LOAEL at 0.5 nmol Cd/mmol creatinine based on the finding of a significantly increased risk in men > 60 years; but this effect should be interpreted with caution mainly because of the presence in this subgroup of occupationally exposed subjects with previously high Cd-U values.

In workers exposed to cadmium compounds (not specifically CdO), clinical bone disease has been described but the number of cases is limited. One cross-sectional study reported results compatible with a role of cadmium in the genesis of osteoporosis in exposed workers but no critical Cd dose could be derived.

The kidney is another target organ for cadmium (not specifically CdO) toxicity following repeated exposure by the inhalation and oral routes.

Numerous studies in rats, mice, rhesus monkeys and rabbits have indicated that exposure to cadmium compounds administered orally or by inhalation causes kidney damage including increase or decrease of relative kidney weight, histological (necrosis of the proximal tubules, interstitial renal fibrosis) and functional changes (reduced glomerular filtration rate, proteinuria).The first manifestation of cadmium nephrotoxicity in occupationally exposed subjects (mainly by inhalation) is usually a tubular dysfunction associated with an increased urinary excretion of low molecular weight (LMW) proteins such as protein HC, ß2M and RBP. An effect on the glomerulus may also be observed in cadmium-exposed workers, as indicated by increased urinary excretion of high molecular weight (HMW) proteins including albumin, immunoglobulins G or transferrin. In workers occupationally exposed to cadmium, a Cd body burden corresponding to a Cd-U of 5 µg/g creatinine constitutes a LOAEL based on the occurrence of LMW proteinuria. There is consensus in the literature concerning the health significance of this threshold because of the frequent observation of irreversible tubular changes above this value and in view of its association with further renal alteration.

On the basis of the most recent studies conducted in Europe, it appears that renal effects can be detected in the general population (mainly exposed by the oral route) for Cd body burdens below 5 µg Cd/g creatinine and even from 2 µg Cd/g creatinine (LOAEL). These studies detected associations between Cd body burden and LMW proteinuria but also urinary calcium excretion and its possible relationship with bone effects. There is, however, a lingering scientific debate about the health significance of the changes observed at Cd-U levels < 5µg/ g creatinine and this was reflected in the contrasting views expressed by the experts during the TMs.

Although mortality studies were not able to detect an excess of end-stage renal diseases in populations exposed to cadmium compounds, a recent epidemiological study suggests that the incidence of renal replacement therapy is increased in a population with occupational/environmental exposure to Cd.

The most significant difference between occupational and environmental exposure is that the populations at risk are different (mainly healthy young individuals in occupational settings. It is plausible that the lower LOAEL in the general population exposed by the oral route is the consequence of an interaction of Cd exposure with pre-existing or concurrent renal disease. As workers exposed to Cd may also suffer from such disease during or after their occupational career, it appears prudent to recommend that they should be offered the same degree of health protection than individuals from the general population. For this reason, a single LOAEL of 2 µg/g creatinine will be used in the Risk Characterisation section, both for oral and inhalation exposure.

Evidence for cardiovascular toxicity resulting from oral and inhalation exposure to CdO and other Cd compounds (chloride, acetate) in animals is suggestive of a slight effect on blood pressure. Results from human studies do not speak for the hypothesis that cadmium may cause hypertension as a result of occupational or environmental exposure. If cadmium does affect blood pressure, the magnitude of the effect is small compared to other determinants of hypertension. Overall, the weight of evidence suggests that cardiovascular effects are not a sensitive end point indicator for CdO toxicity.

Exposure to cadmium compounds can cause liver damage in animals but generally only after high levels of exposure. There is little evidence for liver damage in humans exposed to cadmium (including CdO).

Cadmium-induced haematological effects reported in experimental animals (anaemia) exposed to very high doses of Cd compounds (not specifically CdO) are unlikely to be of concern for occupational or general population exposure.

Evidence from experimental systems indicates a potential neurotoxic hazard for cadmium (not CdO specifically) in adult rats. In humans, heavy occupational exposure to cadmium dust has been associated with olfactory impairments and studies performed on a limited number of occupationally-exposed subjects are suggestive of an effect of Cd on the peripheral and central nervous system but these findings should be confirmed by independent investigators before firm conclusions can be reached. In the young age, there is some experimental indication that Cd exposure (not specifically CdO) can affect the developing brain. This aspect has not received sufficient attention in humans in view of (1) the very well-characterised neurotoxic potential of other heavy metals (e.g. lead), and of (2) the increased gastro-intestinal absorption of Cd in the very young age.

Overall, based on the concurrence of epidemiological studies indicating both kidney and bone effects in the general population at body burden below 5µg Cd/g creatinine, a single LOAEL of 2 µg/g creatinine is considered for the risk characterisation. It should be recognised that uncertainties remain as to the accuracy of this value. The clinical significance of the biochemical changes observed at these levels is also subject to a scientific debate.

Genotoxicity

Data from experimental systems indicate that cadmium, in certain forms, has genotoxic properties and it is reasonable to assume that these properties may also apply to CdO. Three possible and *a priori* non-mutually exclusive mechanisms have been identified: 1) direct DNA damage, 2) oxidative damage and 3) inhibition of DNA repair. With regard to human exposure to CdO and other compounds, data are conflicting but seem to indicate a genotoxic potential, at least in occupational settings, but it is unclear whether these effects are solely attributable to CdO. Studies performed in environmentally exposed populations do not allow to identify the type of cadmium compound(s) to which subjects were exposed but it cannot be excluded, based on the available data, that cadmium (including CdO by assimilation) might exert genotoxic effects in populations exposed via the oral route.

A classification as Muta. Cat. 3, R68 is warranted.

Carcinogenicity

CdO is carcinogenic in animals (especially lung tumours in rat inhalation studies). The possibility that, in humans, cadmium might cause a risk of lung cancer by inhalation is suggested by several epidemiological studies but the possible contribution of confounding factors (mainly co-exposure to other carcinogens) could not be clearly defined. Overall, however, the weight of evidence collected in genotoxicity tests, long-term animal experiments and epidemiological studies leads to conclude that CdO has to be considered at least as a suspected human carcinogen (lung cancer) upon inhalation exposure. There is no indication or evidence that CdO acts as a carcinogen in the general population exposed by the oral route.

The TM would therefore have maintained the classification of CdO as Carc.Cat 2 (T; R49 i.e. may cause cancer by inhalation).

However, the CMR WG classified CdO with Carc.Cat 2; R45 (may cause cancer): i.e. carcinogenic potential irrespective of the exposure route.

Reproductive toxicity

With regard to reprotoxicity, epidemiological studies do not speak for an association between exposure to CdO and relevant effects on fertility or reproductive organs. Based on the human data available, there is no indication of a potential developmental effect of CdO. While effects on reproductive organs and fertility have been noted in experimental studies at high doses of CdO and Cd compounds (oral: NOAEL 1 mg/kg/day and inhalation NOAEL 0.1 mg/m³), further information is needed to better document the possible effect of low doses of CdO on the developing brain of young children suggested in experimental animals.

The CMR WG classified CdO in Repr. Cat 3 (substances which cause concern for humans owing to possible developmental toxic effects) and labelled it with R63 (possible risk of harm to the unborn child).

Table 4.287 Endpoints and L(N)OAELs identified in the effect assessment

Endpoint	NOAEL (as Cd)	LOAEL (as Cd)	Based on
Acute toxicity		437.5 µg/m³	studies in animals
Repeated toxicity			
lung		3 µg/g creat	studies in humans (fumes)
	0.01 mg/m³		studies in animals (dust)
bone		3 µg/g creat	studies in humans
kidney and bone		2 µg/g creat	studies in humans
Reprotoxicity			
effects on fertility and sex organs	1 mg/kg/d		studies in animals (oral)
	0.1 mg/m³		studies in animals (inhal)
developmental effects		-	-

The characterisation of the health risks associated with cadmium oxide exposure will consider three potentially exposed human populations, i.e. workers, consumers and man exposed indirectly via the environment. The risk is estimated by comparing estimated N(L)OAEL values to exposure levels measured or estimated in the target population. For each health effect, the ratio of the N(L)OAEL to the exposure level will be assessed for each scenario, e.g. workers in a particular type of production or general population. This ratio is termed the Margin of Safety (MOS).

Exposure data supplied by industry, Member States and other sources are used for the calculation of the MOS.

It is important to remind the reader that for cadmium oxide, unlike most other substances examined in the framework of this RA programme, relevant and validated biomarkers of exposure exist and allow to characterise the risk with a better accuracy and/or relevance. Cd in blood mainly reflects the last few months of exposure in workers moderately exposed to cadmium. Cadmium is a cumulative toxicant and the systemic manifestations of toxicity (mainly bone and kidney toxicity) are related to the body burden accumulated over several years of exposure, which is closely reflected by the concentration of Cd in urine (Cd-U) (see Section 4.1.2.2). The biomarker approach offers the advantage that, to characterise both effects and exposure, one can rely on measured (Cd-U measurements) rather than on estimated or calculated doses that would need to be derived with a number of assumptions and uncertainties. Another advantage of using the body burden (Cd-U) to characterise exposure is that this biomarker integrates all possible exposure pathways and allows a global assessment of the health risks, including combined exposure. Therefore, when dealing with systemic effects of Cd, the risk will preferably be characterised by comparing Cd-U values when biologically relevant**.** **Table 4.288** compares the increases in Cd-U and Cd-B in the different occupational scenarios and indicate a relative consistency except for the first occupational scenario. It can therefore be reasonably assumed that both parameters reflect current exposure conditions.

Since the use of biomarkers integrates all possible routes of exposure, no differentiation will be made between oral, dermal or inhalation exposure and only a single systemic MOS will be calculated.

Table 4.288 Fold increases above normal in different scenarios

	Urine (normal < 2 µg/g creatinine)		Blood (normal < 1 µg/L)	
	fold increase above normal			
	Typical value	Worst case	Typical value	Worst case
CdO production	5	35	1	3
Cd metal production	1.5	11	3	15
Ni Cd batteries	1.75	10	2.3	80
Pigments	2	5	4	10

4.1.3.2 Workers

4.1.3.2.1 Exposure

Occupational exposure data have been reported in Section 4.1.1.2.

CdO is produced and/or used in different industrial activities. In the identified scenarios, exposure may be to cadmium oxide and/or to cadmium metal and/or to other cadmium compounds. For clarification, **Table 4.289** summarises for each scenario which Cd compound is used or produced, to which Cd compound exposure occurs and in which risk characterisation and corresponding conclusion file (i.e. Cadmium metal or Cadmium oxide) this is respectively discussed and included.

Table 4.289 Involvment of different Cd compounds for various occupational scenarios

Scenario	Substance produced /used			Substance to which main exposure occurs			RC and conclusion file(s)	
	Cd metal	CdO	Remark	Cd metal	CdO	Remark	Cd metal	CdO
1. The production of cadmium oxide	+	+		-	+		-	+
2. The production of Cd metal	+	-		+	+		+	-

Table 4.289 continued overleaf

Table 4.289 continued Involvment of different Cd compounds for various occupational scenarios

Scenario	Substance produced /used			Substance to which main exposure occurs			RC and conclusion file(s)	
	Cd metal	CdO	Remark	Cd metal	CdO	Remark	Cd metal	CdO
3.The production and recycling of Ni-Cd batteries	+	+		+	+		+	+
4. The production of Cd alloys	+	-		-	+	+ exposure to alloy fumes	+	-
5. Cd pigments production	+	+	starting material	(+)	(+)	other Cd compounds	+	+
6.Cd plating	+	+		+	+		+	+
7.Cd stabilisers	+	+	starting material	(+)	(+)	other Cd compounds	+	+
8.Brazing	+	-		(+)	+		+	-
9. Others	+	+		+	+	other Cd compounds	+	+

Values used for risk characterisation are reported in **Table 4.290**.

Table 4.290 Summary of occupational exposure data used in the risk characterisation

Production type	Mean exposure in air* (µg/m³)		Biomonitoring data Urine (µg/g creat)		Blood (µg/L)	
	Typical value	Worst case	Typical value	Worst case	Typical value	Worst case
CdO production	15	150	10	70	1	3
Ni-Cd batteries	50	320	3.5	20	2.3	80
Pigments	22	80	4	10	4	10
Plating	5	10	-	-	-	-
Stabilisers		2				5
Others	-	2	-	-	-	-

* For this RC assumed to be 8-hour TWA concentrations

4.1.3.2.2 Health effects

The health effects of concern covered in the risk characterisation are acute toxicity, skin/eye/respiratory tract irritation, sensitisation, repeat dose toxicity to lung, kidney, bone, neurotoxicity, genotoxicity, carcinogenicity, reproductive toxicity. The main route of occupational exposure is inhalation as significant oral exposure is not expected to occur in the workplace. Although dermal exposure might occur during handling of powders or activities of cleaning /maintenance, there would be no prospect of systemic effects arising via dermal exposure because exposure is limited, CdO is a solid particulate compound and skin absorption is low. Furthermore, all routes of exposure are considered by using biological monitoring data, which evaluate the body burden of cadmium.

Acute toxicity

The acute inhalation of cadmium fumes has been reported to cause metal fume fever and chemical pneumonitis, the latter being potentially lethal. These fumes result from burning cadmium metal and are readily generated in many industrial processes. In a conservative approach, the margin of safety for the different scenario will be calculated for the worst case exposure data in order to take into account exceptional or extreme situations that could give rise to acute manifestations.

No human data were located allowing the determination of a LO(A)EL for chemical pneumonitis, specifically. The lowest dose reported to cause mild pulmonary damage in animals (slight increase of the number of cuboïdal epithelial cells lining the alveoli, indication of hyperplasia) was a 3-hour exposure to 500 µg/m³ cadmium oxide fumes (or 437.5 µg Cd/m³).

Table 4.291 Acute toxicity

Scenario	**Critical concentration 437.5 µg Cd/m³ (3 h TWA)**		
	Cd air (µg/m³) worst case 8-hour TWA*	**MOS**	**Ccl**
CdO production	150	3	iii
Batteries	no CdO fumes	-	ii
Pigments	no CdO fumes	-	ii
Plating	10	44	ii
Stabilisers	no CdO fumes	-	ii
Others	2	220	ii

* Assuming that pneumonitis is a concentration-related effect and that Haber's rule is not applicable

The following parameters should be taken into consideration when evaluating the magnitude of the MOS value: interspecies differences (rat to human), differences between experimental conditions and exposure pattern of the workers, nature and severity of the effect (from hyperplasia to chemical pneumonitis). A minimal MOS of 10 is therefore recommended.

Conclusion (iii) for all scenarios with production and/or use of CdO and with potential exposure to CdO fumes, except “plating” and “others” for which **conclusion (ii**) is proposed.

Scenarios where no CdO fumes are formed **conclusion (ii),** see **Table 4.291**.

However, it should be considered that appropriate reduction measures may already be in place to control the risk of chemical pneumonitis (e.g. by educational measures and the use of respiratory protection). Chemical pneumonitis caused by CdO exposure has been relatively rarely reported in recent years and the few recent cases of chemical pneumonitis caused by CdO fumes were associated with non industrial circumstances.

Irritation

Acute dermal irritation

No dermal irritation study with CdO is available but the extensive clinical literature does not report on any effects of CdO with respect to skin irritation. Given the toxic properties of the substance (including its carcinogenic potential in occupational settings), it is supposed that risk reduction measures are in place to prevent irritation, if any, to occur. It is concluded that CdO is probably of limited concern for workers with regard to dermal irritation.

Conclusion (ii).

Eye irritation

Exposure of the eyes is possible via fumes or dust. No study was, however, located regarding ocular effects in animals or in workers after exposure to CdO. Although exposure has been significant in a large array of industrial settings since the beginning of this century, the toxicological literature does not report on any ocular effects. Given the toxic properties of the substance (including its carcinogenic potential in occupational settings), it is supposed that risk reduction measures are in place to prevent irritation, if any, to occur. It is concluded that eye irritation is probably not a concern for CdO.

Conclusion (ii).

Respiratory tract irritation

No studies in animals specifically regarding local irritation of the respiratory tract after exposure to CdO was located. However, as several studies in animals and case reports are available on acute and chronic respiratory effects after inhalation of CdO (see Section 4.1.2.4.3), it is reasonable to consider that this substance is an irritant for the respiratory tract. **Conclusion (iii)**. Given the toxic properties of the substance (including its carcinogenic potential in occupational settings), it is, however, supposed that risk reduction measures are in place to prevent irritation to occur. Personal protective equipment, properly selected and worn, will also significantly reduce exposure.

Corrosivity

Corrosivity studies with CdO are not available and the extensive clinical literature does not report on any corrosive effects. In view of the toxic nature of the substance (including its carcinogenic potential in occupational settings), it is supposed that risk reduction measures are in place to prevent corrosion, if any, to occur. It is concluded that the substance is of no concern for workers with regard to corrosivity effects.

Conclusion (ii).

Sensitisation

A skin sensitisation test with CdO, conform with the current regulatory standards, is not available. The medical literature does not report cases of sensitisation in workers exposed to CdO. Given the toxic properties of the substance (including its carcinogenic potential in occupational settings), it is supposed that risk reduction measures are in place to prevent sensitisation, if any, to occur. It is concluded that the substance is of no concern for workers with regard to sensitisation.

Conclusion (ii).

Repeated dose toxicity

Section 4.1.2.7 (Effect assessment, repeated dose toxicity) considers several target organs of which the kidney appears to be the most sensitive. Kidney effects are relevant for workers exposed to cadmium by inhalation and typical exposure data reported under Section 4.1.1.2 are used to calculate the margins of safety for the different scenarios.

Kidney and bone

For workers exposed to cadmium (mainly by inhalation), a Cd body burden corresponding to a Cd-U of 5 µg/g creatinine constitutes a LOAEL based on the occurrence of LMW proteinuria. There is consensus in the literature concerning the health significance of this threshold because of the frequent observation of irreversible tubular changes above this threshold and in view of its association with further renal alteration. It appears, however, prudent to recommend that workers should be offered the same degree of health protection than people from the general population, in which renal and/or bone effects were already detected at lower exposure levels and to adopt a LOAEL of 2 µg Cd-U /g creatinine which is used in **Table 4.292** to calculate the MOS in the different scenarios.

Table 4.292 Repeated dose toxicity: kidney and bone (critical Cd-U: 2 µg/g creat)

Scenario	Critical Cd-U 2 µg/g creatinine		
	Cd-U typical (µg/g creatinine)	MOS	Ccl
CdO production	10	0.20	iii
Batteries	3.5	0.60	iii
Pigments	4	0.50	iii
Plating	-	-	iii*
Stabilisers	-	-	iii*
Others	-	-	iii*

* By extrapolation from other scenarios

The amplitude of the calculated MOS indicates a cause for concern, at least in three scenarios. For most scenarios for which Cd-U data are not available (Plating and Stabilisers and Others), airborne measurements indicate a lower exposure than in CdO production, Batteries and Pigments, suggesting a relatively lower level of concern.

On the basis of available data, it is concluded that CdO is of concern under typical (and thus by extension also under RWC) occupational exposure conditions (**conclusion (iii)**) for all scenarios.

For information, the same assessment given below (see **Table 4.293**) for a critical Cd-U of 5 µg/g creatinine indicates a MOS < 2 for all scenarios where data are available.

Table 4.293 Repeated dose toxicity: kidney and bone (critical Cd-U: 5 µg/g creat)

Scenario	Critical Cd-U 5 µg/g creatinine	
	Cd-U typical (µg/g creatinine)	MOS
CdO production	10	0.50
Batteries	3.5	1.50
Pigments	4	1.25
Plating	-	-
Stabilisers	-	-
Others	-	-

Neurological effects

Further information is needed to better document the possible effect of low doses of CdO on the developing brain of young animals suggested in experimental studies (see Section 4.1.2.10). However, in view of the concerns expressed for several other health effects, including repeated dose toxicity and carcinogenicity, it is urgent to address these issues adequately and to implement appropriate control measures without delay.

Conclusion (i) "on hold" for all scenarios**.**

Genotoxicity

Data from experimental systems indicate that cadmium, in certain forms, has genotoxic properties and it is reasonable to assume that these properties may also apply to CdO. Data concerning humans exposed to CdO seem to indicate a genotoxic potential, at least in occupational settings, but it is unclear whether these effects are solely attributable to CdO. As long as the mechanism of genotoxicity is not completely elucidated it must be assumed that Cd compounds (and by extension CdO) is a direct acting genotoxic substance and that it is prudent to consider that there is no threshold exposure level below which effects will not be expressed.

Conclusion (iii) for all scenarios.

There is a need for limiting the risks and risk reduction measures which are already being applied shall be taken into account.

Carcinogenicity

In view of the sum of data collected in long-term animal experiments and in epidemiological studies, it was concluded in Section 4.1.2.9 that cadmium oxide has to be considered at least as a suspected inhalation carcinogen (lung cancer). Risks cannot be excluded, as the substance is considered as a non-threshold carcinogen. Given the serious and irreversible nature of the effect and the fact that it is not possible to exclude the risk of this being expressed at occupational levels, there is cause of concern across all industrial uses, leading to **conclusion (iii)**. There is a need for limiting the risks and risk reduction measures which are already being applied shall be taken into account.

Reprotoxicity

a. effects on fertility and sex organs

Epidemiological studies do not indicate evidence of any effects of occupational exposure to CdO on fertility and/or sex organs. Effects on sex organs (testes, reduced fertility and increased length of oestrus cycle) were reported in experimental animals (rat) at high dose levels (LOAEL 1 mg/m³, NOAEL 0.1 mg/m³). These levels mostly caused other manifestations of toxicity (reduction of body or organ weights, lethality). Calculated MOS values are reported below and, on the basis of a minimal MOS of 10, indicate a cause for possible concern in 3 scenarios (typical and/or RWC). It can however be expected that measures already in place or that will be implemented to prevent repeated dose toxicity (respiratory, kidney, bone or carcinogenicity) will be protective for reproductive organs also. The MOS calculated for the scenarios Plating (typical and RWC), Stabilisers and Others (RWC) do not lead to concern.

Conclusion (iii) for scenarios CdO production, Batteries and Pigments.

Conclusion (ii) for scenarios Plating, Stabilisers and Others.

Table 4.294 Fertility and sex organs: Cd-air (typical value)

NOAEL Cd air : 100 µg/m³		
Scenario	**Cd air typical (µg/m³)**	**MOS**
CdO production	15	6.6
Batteries	50	2
Pigments	22	4.5
Plating	5	20
Stabilisers	-	-

Table 4.295 Fertility and sex organs: Cd-air (reasonable worst case value)

Scenario	**NOAEL Cd air : 100 µg/m³**	
	Cd air RWC (µg/m³)	**MOS**
CdO production	150	0.66
Batteries	320	0.31
Pigments	80	1.25
Plating	10	10
Stabilisers	2	50
Others	2	50

b. developmental effects

Based on the data available in occupational settings, there is no indication of a potential developmental effect of CdO. Further information is, however, needed to better document the possible effect of low doses of CdO on neurobehavioural performances suggested in experimental animals (see Section 4.1.2.10.3). However, in view of the concerns expressed for several other health effects, including repeated dose toxicity and carcinogenicity, it is urgent to address these issues adequately and to implement appropriate control measures without delay.

Conclusion (i) "on hold".

Table 4.296 Summary of the risk characterisation for occupational exposure

Endpoint	Conclusion	Remarks
Acute toxicity	iii	except "Plating" and "Others" (conclusion ii) and the scenarios where no CdO fumes are formed i.e. Batteries, Pigments and Stabilisers
Skin and eye irritation	ii	
Respiratory tract irritation	iii	
Corrosivity	ii	
Sensitisation	ii	
Repeated toxicity		
kidney and bone	iii	
neurological effects	i	(on hold)
Genotoxicity	iii	
Carcinogenicity	iii	
Reprotoxicity		
effects on fertility and sex organs	iii ii	for scenarios CdO production, Batteries, Pigments for scenarios Plating, Stabilisers and Others.
developmental effects	i	(on hold)

Occupational exposure limits

In European countries, national exposure limits for Cd and compounds (including CdO and Cd metal) aimed at protecting workers from adverse renal effects vary from 0.002 to 0.030 mg/m³ TWA for airborne concentrations and from 5.6 to 15 µg/l or µg/g creatinine for Cd-U used as a biological limit value (BLV) (see Exposure assessment, occupational exposure, Section 4.1.1.2). Since, according to the conclusions of the effect assessment (see Section 4.1.2), it seems prudent not to exceed Cd-U values of 2 µg/g creatinine to protect from renal and bone toxicity, a re-evaluation of these limit values is recommended.

4.1.3.3 Consumers

Among the 5 scenarios examined under Section 4.1.1.3, CdO is involved only for the manufacture of Ni-Cd batteries (Scenario 1). In this case, consumer exposure is considered non-existent or negligible.

Conclusion (ii) is proposed.

4.1.3.4 Humans exposed via the environment

4.1.3.4.1 Methodology: actual and future exposure of man via the environment

The risk characterisation of man indirectly exposed to Cd via the environment is performed at the current exposure and at the predicted future exposure. The latter assessment is made to characterise the risk of current diffuse Cd emissions to soil which may lead to a Cd exposure via the foodchain in the future. In this respect, this assessment is based on the information concerning environmental exposure (see environmental part of the Risk Assessment Report).

The risk characterisation at the current exposure is described under Section 4.1.3.4.2 and is mainly based on the current Cd body burden of the general population (urinary Cd, i.e. Cd-U). The Cd-U values are either measured or derived from Cd uptake under different scenario's for the general population. The conversion of Cd intake to Cd-U requires a toxicokinetic model which is addressed in parts of Section 4.1.2.2.5.

The risk characterisation at the predicted exposure in the future is described under Section 4.1.3.4.4. This risk characterisation is not a standard procedure and does not calculate MOS values between exposure and effect levels. Instead, this characterisation is based on the comparison of predicted soil concentrations (PEC, see environmental part of the Risk Assessment Report) with a so-called critical soil Cd concentration. The PEC values are predicted soil Cd concentrations that will occur in future at current Cd emissions and depositions. The critical soil Cd concentration is defined as that concentration in soil not causing excessive Cd exposure via the human diet. This concentration will be derived below in Section 4.1.3.4.3 using food chain modelling and with a critical dietary Cd intake.

4.1.3.4.2 Current exposure conditions

Environmental exposure data have been reported under Section 4.1.1.4 and are summarised below in **Table 4.297**. This table is based on average values for ambient environmental Cd levels and for two groups of the general population, adults with sufficient body iron stores and adults with depleted body iron stores. An additional scenario is included representing a local condition where Cd concentrations in soil, air and diet are all elevated.

The GI absorption rate for cadmium in the general population is generally < 5%. Individuals with low iron stores may absorb more Cd via the GI route, on average 2 times more, and absorption rates up to 10% have been reported above. The model validation study reported under Section 4.1.2.2.5 indicates that a 3% absorption rate (at $t_{1/2}$=13.6 years) most adequately describes Cd-U levels measured in the general population (predicted/observed ratio 0.9-1.3), even for upper percentile values. This 3% absorption rate as a 'best fit' parameter, while acknowledging that individuals with larger absorption rates exist, may indicate that it is incorrect to apply the largest absorption rates on also the largest dietary Cd intake values and for a constant period of 50 years. In a conservative approach, however, and for the subsequent calculations, a GI absorption rate twice this figure, i.e. 6%, is used in the scenario including individuals with depleted iron stores. The overall GI absorption rate used in **Table 4.297** is therefore 3% for adults with sufficient iron stores, and 6% for adults with low iron stores.

The data show that smoking and dietary Cd are the main pathways of Cd exposure in uncontaminated areas. It can also be derived from these data that Cd intake through smoking 20 cigarettes per day increases the Cd systemic dose 2 to 3-fold above that in non-smoking individuals with equivalent Cd intake through other sources.

Scenario 3 is based on reasonable worst case air concentration estimates for battery production, recycling and waste management (all **c**admium sources in the municipal solid waste included) in the range of 22 to 28 ng/m^3 (TRAR section 3.1.3.2.3, p. 191). This leads to a daily uptake of Cd via inhalation estimated at 0.11-0.15 µg/day (i.e. 440 to 600 ng/day · 0.25) which is 'low' compared to the dietary intake. When applied to certain point sources with very high air emissions and predicted local air concentrations in the range of 1µg/m^3 (see Section 3.1: a few number of cadmium metal producers) the contribution of inhalation is dominant.

The contribution of air Cd to dietary Cd neglects the Cd deposition on locally produced food. While there is indirect evidence that this might largely contribute to crop Cd concentrations (see Section 4.1.1.4.8), there are, however, no data to estimate this contribution correctly. On the other hand, restrictions on food production near point sources are often in place but there is no information to generalise the current situation in EU.

It should also be reminded that very young children fed on a cereal-based infant formula may have higher Cd intake (up to 12 times) than breast-fed children (see Section 4.1.1.4.5). The mean weekly intake of dietary cadmium was estimated to vary between 0.10 and 3.05 µg Cd/kg bw, if the recommended amount of formula were to be consumed at the recommended age, and if the child were of average weight. This condition might be relevant for possible neuro-developmental effects of cadmium (see **conclusion (i)** "on hold", developmental toxicity below).

Table 4.297 Estimated daily Cd uptake in adults through environmental exposure in areas at ambient Cd concentrations (scenario's 1-2) and near point sources with largest atmospheric Cd emissions in EU (scenario 3)

Scenario 1: adults with sufficient body iron stores		
Source	**Cd uptake (µg day^{-1})**	**Assumptions**
Air	0.025 -0.075	Air Cd 5-15 ng m^{-3}; daily inhalation 20 m^3; absorption rate = 0.25
Soil and dust	0.021	Dust or soil Cd 7 mg kg^{-1}; 100 mg dust or soil per day; absorption rate = 0.03
Smoking	0.5-2.0	Smoking of 20 cigarettes; 1-2 µg Cd $cigarette^{-1}$; absorbed fraction 0.025-0.05
Drinking water	< 0.06	Cd water<1 µg L^{-1}; absorption rate = 0.03 2L day^{-1} consumption
Dietary intake	0.21-0.96	Dietary Cd 7-32 µg day^{-1}, absorption rate = 0.03
Sum	non smokers: 0.32-1.12 smokers: 0.82-3.12	
Scenario 2: adults with depleted body iron stores		
Source	**Cd uptake (µg day^{-1})**	**Assumptions**
		As above, but absorption rate of 0.06 for dietary Cd, soil/dust/water Cd
Sum	non smokers: 0.53-2.08 smokers: 1.03-4.08	

Table 4.297 continued overleaf

Table 4.297 continued Estimated daily Cd uptake in adults through environmental exposure in areas at ambient Cd concentrations (scenario's 1-2) and near point sources with largest atmospheric Cd emissionsin EU (scenario 3)

Scenario 3 : near point sources (adults with sufficient body iron stores)		
Source	**Cd uptake (µg day^{-1})**	**Assumptions**
Air	0.11-5.0	Air Cd is 22[36]-1,000[37] ng m^3; daily inhalation 20 m^3; absorption rate = 0.25
Soil and dust	0.21	Dust or soil Cd 70 mg kg^{-1}; 100 mg dust or soil per day, absorption rate = 0.03
Drinking water	< 0.06	Cd water< 1 µg L^{-1}; absorption rate = 0.03 2L day^{-1} consumption
Dietary intake	0.51 –1.02	Dietary Cd 17-34 µg day^{-1}
Sum	non-smokers : 0.89 – 1.40 (22 $ng.m^{-3}$) smokers: 5.9-6.4 (1,000 $ng.m^{-3}$)	

Relationship between Cd uptake and Cd-U

Based on the data derived from the Nordberg-Kjellström model reported under Section 4.1.2.2 (t1/2: 13.6 y; 1/3 of the body burden in the kidney and a daily urinary excretion of 0.016% of Cd kidney content), it can be calculated that a continuous uptake of 1 µg Cd/day is equivalent to an urinary excretion of about 0.5 µg Cd/24 hours or 0.5 µg/g creat at the age of 50 years. The conversion in Cd-U values of the daily uptakes calculated in the different scenarios is reported below in **Table 4.298**.

Table 4.298 Conversion of Cd daily uptake in Cd-U for individuals indirectly exposed via the environment

Scenario		**Daily uptake (µg/day)**	**Cd-U (µg/g creat)**
1.	Adults with sufficient body iron stores, non-smokers	0.32-1.12	0.16-0.56
	Adults with sufficient body iron stores, smokers	0.82-3.12	0.41-1.56
2.	Adults with depleted body iron stores, non-smokers	0.53-2.08	0.26-1.04
	Adults with depleted body iron stores, smokers	1.03-4.08	0.51-2.04
3..	Near point sources (adults with sufficient body iron stores), non-smokers	5.9-6.4 0.89 – 1.40	2.95-3.2 0.44 – 0.7

The Cd-U values calculated by this approach can be compared for validation with the data reported in large epidemiological studies conducted in Europe reported in **Table 4.299** (Umwelt Bundes Amt 2000; Fiolet et al., 1999) and **Table 4.135** (Buchet al. 1990, Hotz et al. 1999 and Järup et al. 2000):

36 22 $ng.m^{-3}$: the NiCd producing plant for which this value was reported may have ceased its activity during the preparation of this report. Figure based on RWC calculated estimate for the year 1999 and in the absence of more recent Industry's exposure data.

37 1,000 $ng.m^{-3}$: some of the Cd producing plants for which these values were reported may have ceased their activities during the preparation of this report. Figure based on RWC calculated estimate for the year 1996 and in the absence of more recent Industry's exposure data.

Table 4.299 Measured Cd-U values in European samples of the general population

		Cd-U (µg/24 h or nmol/mmol creat)
Buchet et al. (1990) Hotz et al. (1999)* Scenarios1, 2 and 3	Belgium	Geometric mean 0.84 Geometric mean (GSD) M: 0.6 (1.9) 95th percentile : 2.1 F: 0.9 (2.0) 95th percentile : 3.6
Järup et al. (2000)** Scenarios1, 2 and 3	Sweden	Mean (10-90th percentile) M : 0.82 (0.18-1.80) F : 0.66 (0.21-1.30)
Umwelt Bundes Amt. (2000) *Scenarios 1 and 2*	Germany	Median (10-90th percentile) 0.18 (0.06-0.55)
Fiolet et al. (1999) (RIVM) *Scenarios 1 and 2*	The Netherlands	Geometric mean: 0.44 Median: 0.34 P95: 1.35

* Baseline before implementation of preventive measures
** Including occupationally exposed individuals

While the calculated values fit reasonably well with the measured data reported in Belgium and Sweden, they notably overestimate the values from Germany and the Netherlands. It should be noted that the studies by Buchet et al. (1990), Hotz et al. (1999) and Järup et al. (2000) were conducted, at least in part, in regions with known environmental contamination by Cd (Scenarios 1, 2 and 3) whereas the German and Dutch surveys examined individuals from the general population with no specific source of environmental exposure (mainly Scenario 1 and 2). It can therefore be concluded that the calculated Cd-U values in **Table 4.298** represent a conservative estimate of the general population exposure and can be used for a conservative characterisation of the health risk in the general population.

It must be remembered that no attempt is made in this risk assessment to evaluate the specific contribution of CdO in the contamination of the diet by cadmium.

Risk associated with repeated dose exposure in the general population

Except for Scenario 3, exposure is mainly via the diet and the lung is not expected to be a target organ in the general population. The critical target organs for cadmium in the general population are the kidney and the bone.

When inhalation exposure is significant (Scenario 3, near point sources), the possible relevance of respiratory toxicity (including carcinogenicity by inhalation) cannot be excluded.

Kidney and bone

- As stated in the conclusions of Section 4.1.2.7.3, an accurate risk estimate is presently not possible for several reasons. On the basis of the available studies, it appears probable, however, that the earliest renal effects (HC proteinuria), may occur in the general population at Cd-U < 5 µg/g creatinine (LOAEL 2 µg/g creatinine). This figure is based on the association between Cd and not only LMW proteins but also calcium excretion in urine and its possible relationship with bone effects (see Section 4.1.2.7.3 Effect Assessment, Repeated dose toxicity, Kidney). Some scientists (including the rapporteurs of the present document) are convinced that clear adverse renal effects with demonstrated clinical relevance occur only at Cd-U levels 2.5-fold above this LOAEL (> 5 µg Cd/ g creat).

- Bone effects (bone mineral density and increased risk of fractures) directly caused by Cd and/or secondary to kidney damage are seen at relatively low exposure (LOAEL 3 µg/g creatinine; see Section 4.1.2.7.2, Effect Assessment, Repeated dose toxicity, Bone).

Before defining the amplitude of a MOS that would be acceptable for health effects in the general population, a number of issues need consideration:

- These LOAEL values are derived from a large set of epidemiological data directly collected in the population at risk (including individuals exposed during their childhood, smokers, women with depleted iron stores, and individuals with possible predisposing conditions such as renal diseases or diabetes but also workers with previously high exposure),
- Ambient Cd-U levels in the European population are < 2 µg Cd/g creat (see Toxicokinetics **Table 4.95**) with, in the most recent surveys (e.g. Umweltbundesamt 2000), a median around 0.20 and a 90th percentile around 0.50 µg Cd/g creat. Other values measured in Europe are reported in **Table 4.90** (Toxicokinetics). Mean Cd-U levels in the reference population against which odds ratios of increased urinary protein HC were calculated in the most sensitive study (Järup et al. 2000) is also 0.20 µg Cd/g creat.

It is therefore proposed that a MOS of 3 would be sufficient to protect the population in order to mainly take into account the conversion of a LOAEL→NOAEL.

Other factors that are usually included in the definition of a MOS such as incompleteness of the database, inter-species extrapolation, variations in exposure route or particularities of the dose-response relationship do not need consideration here. Intra-species variation in sensitivity (e.g. renal disease, diabetes) is implicitly included in the LOAEL and variations in exposure are taken into account by the different scenarios examined.

Table 4.300 Margin of Safety factors for the different scenarios of Human exposure via the Environment (A)

		Critical dose : 2 µg/g creatinine	
Scenario		**Cd-U (µg/g creatinine)**	**MOS**
1a.	Adults non-smokers	0.16-0.56	12.2-3.58
1b.	Adult smokers	0.41-1.56	4.88-1.28
2a.	Adults depl. iron stores, non-smokers	0.26-1.04	7.72-2.00
2b.	Adults depl. iron stores, smokers	0.51-2.04	3.92-0.98
3.	Adults, near point source, non-smokers	2.95-3.20	0.68-0.62
		0.44-0.7	4.5-2.85
Measured data			
Buchet et al. (1990)		GM 0.84	2.4
Hotz et al. (1999)		GM M : 0.6	3.4
		P95 2.1	1.0
		GM F : 0.9	2.2
Scenarios 1,2 and 3		P95 3.6	0.6
Järup et al. (2000)		Mean M : 0.82	2.4
		P10 : 0.18	11.0
		P90 : 1.80	1.2
		Mean F : 0.66	3.0
		P10 : 0.21	10
Scenarios 1,2and3		P90 : 1.30	4.0
Fiolet et al. (1999) (RIVM)		GM : 0.44	6.4
		Median : 0.34	5.8
Scenarios 1 and 2		P95 : 1.35	1.4
Umwelt Bundes Amt. (2000)		Median 0.18	11.0
		P10 : 0.06	33.4
		P90 : 0.55	3.6
		P95 : 0.74	2.8
Scenarios1 and 2		P98 : 1.10	1.8
NHNES (1999) (CDC, US)		GM : 0.29	6.6
		P10 : 0.11	18
		P25 : 0.17	11.8
		P50 : 0.27	7.4
		P75 : 0.46	4.2
Scenarios 1 and 2		P90 : 0.74	2.8

Calculations indicate that, the MOS may be below 3 in smokers with adequate iron stores or not, and borderline for non-smokers with depleted iron stores (Scenario 2a). The MOS is clearly below 3 for Scenario 3, and this would even more be the case for individuals with depleted iron stores and/or smokers in such a scenario. **Conclusion (iii)** is proposed for all scenarios except Scenario 1a (non-smokers) for which c**onclusion (ii)** applies.

When confronted with the measured data, the MOS are substantially greater but still below 3 for a significant fraction of the population in the studies conducted in polluted areas (Buchet et al. 1990, Hotz et al. 1999 and Järup et al. 2000; scenarios 1, 2 and 3). Considering the data from the general German population (equivalent to Scenarios 1 and 2), the amplitude of the MOS is > 3 for more than 90% of the population. It should be noted that these environmental population surveys included smokers and ex-smokers which, most likely, contributed largely to the highest values. The MOS for the non-smoking population cannot be estimated precisely and there is a need for data to characterise Cd exposure specifically in the non-smoking population. Data obtained in selected non-smoking women in Sweden indicated upper Cd-U values of about 0.60 µg/g creatinine (Berglund et al. 1994, n = 57 and Olsson et al. (2002), n = 37 after exclusion of one outlying value, 0.99 µg/g creatinine). The average Cd-U in non-smoking pregnant Swedish women (with relative iron deficiency) was 0.31 (0.11-1.1, n = 193) µg/L (Åkesson et al. 2002).

The same calculation is given, for comparison purpose, with the data from the recent NHNES survey conducted in 1999 in the US (CDC 2001).

For information, the same assessment is done below with a critical value of 3 µg/g creatinine at which adverse bone effects were detected.

Table 4.301 Margin of Safety factors for the different scenarios of Human exposure via the Environment (B)

		Critical dose: 3 µg/g creatinine	
Scenario		**Cd-U (µg/g creatinine)**	**MOS**
1a.	Adults non-smokers	0.16-0.56	19-5
1b.	Adult smokers	0.41-1.56	7-2
2a.	Adults depl. iron stores, non-smokers	0.26-1.04	12-3
2b.	Adults depl. iron stores, smokers	0.51-2.04	6-1.5
3.	Adults, near point source, non-smokers	2.95-3.20 0.44-0.7	1 6.82-4.28
Measured data			
Buchet et al. (1990) Hotz et al. (1999)		GM 0.84 GM M : 0.6 P95 2.1 GM F : 0.9 P95 3.6	3.6 5 1.5 3.3 0.8
Järup et al. (2000)		Mean M : 0.82 P10 : 0.18 P90 : 1.80 Mean F : 0.66 P10 : 0.21 P90 : 1.30	3.6 17 1.7 4.5 15 2.3

Table 4.301 continued overleaf

Table 4.301 continued Margin of Safety factors for the different scenarios of Human exposure via the Environment (B)

	Critical dose: 3 µg/g creatinine	
	Cd-U (µg/g creatinine)	**MOS**
Fiolet et al. (1999) (RIVM)	GM : 0.44 Median : 0.34 P95 : 1.35	6.8 8.8 2.2
Measured data		
Umwelt Bundes Amt. (2000)	Median 0.18 P10 : 0.06 P90 : 0.55 P95 : 0.74 P98 : 1.10	17 50 5.5 4.1 2.7
NHNES (1999) (CDC, US)	GM : 0.29 P10 : 0.11 P25 : 0.17 P50 : 0.27 P75 : 0.46 P90 : 0.74	10 27 18 11 6.5 4

Respiratory toxicity

The LOAEL for respiratory effects (3 µg Cd/g creat equivalent to an integrated inhalation exposure of 500 µg Cd/m³ · years) is based on the finding of functional changes in workers exposed to CdO fumes. Because it is unlikely that the general population is exposed to CdO fumes when locally exposed to nearby emitting sources, the MOS is calculated against the NOAEL derived from studies in animals (0.01 mg CdO dust/m³, 5 days/week, 8 hours/day). Adjusting to a constant exposure from the experimental conditions, an adjusted NOAEL of 2.4 µg CdO/m³ for human exposure to ambient air can be derived.

By using an uncertainty factor of 10 for interindividual differences in humans and a factor of 10 for interspecies extrapolation, the MOS should be at least 100.

Under scenario 3, the most important route of exposure could be inhalation near cadmium metal producing plants (reasonable worst case estimate of 1 µg Cd/m³). Assuming that ambient exposure is mainly to CdO (which is not demonstrated), this would be equivalent with 1.14 µg CdO/m³. At those exposure levels, respiratory effects cannot be excluded and a **conclusion (iii)** is proposed for Scenario 3.

Carcinogenicity/genotoxicity in the general population

There is no evidence that CdO when given by the oral route increases the risk of cancer in the general population and the TM agreed formerly to propose a **conclusion (ii)** for scenarios 1 and 2.

In view of the possibility of significant inhalation exposure for populations living nearby certain emitting sources, **conclusion (iii)** was proposed by the rapporteur and supported by the TM for Scenario 3. Following the decision of the CMR WG for CdO (see Section 1.4), a carcinogenic potential cannot be excluded irrespective of the route of exposure, and a **conclusion (iii)** applies to all scenarios. Along the same line, a **conclusion (iii)** also applies for genotoxicity.

Reprotoxicity

a. effects on fertility and reproductive organs

The NOAEL (1 mg Cd/kg/day) derived from experimental studies is based on effects noted both in male and female reproductive systems upon repeated exposure by the oral route (9 weeks). This level is three orders of magnitude greater than environmental exposure (µg/kg/day), which is judged sufficient to protect the general population (composite MOS of 100 to account for interspecies extrapolation (10) and variability in humans (10)).

Conclusion (ii).

b. developmental effects

Based on the data available in the general population, there is no indication of a potential developmental effect of CdO. Further information is needed to better document the possible effect of low doses of CdO on neurobehavioural performances suggested in experimental animals (see Section 4.1.2.10).

Conclusion (i) "on hold".

Table 4.302 Summary of the risk characterisation for the general population

Endpoint	Conclusion	Scenario
Repeated toxicity		
Kidney and bone	iii	all except 1a
Respiratory effects	iii	3 only
Carcinogenicity/genotoxicity	iii	all
Reprotoxicity		
Effects on fertility and reproductive organs	ii	All
Developmental effects	i "on hold"	

4.1.3.4.3 Risk characterisation for future conditions: modelling.

The risk characterisation for current exposure (see Section 4.1.3.4.2) leads to **conclusion (iii)**, except for Scenario 1a (non-smoking adults with sufficient iron stores). It might therefore be useful to examine whether a risk may be expected in the future for this Scenario (1a).

The risk characterisation at the predicted exposure in the future is based on predicted future exposure via the food chain and applies specifically to adult non-smokers with sufficient body iron stores. No further calculations will be made for scenarios for which a concern was already identified at current exposure conditions.

The assessment for future conditions is only made for the regional and continental scale and not for local sites. This risk characterisation is not a standard procedure and does not calculate MOS values between exposure and effect levels. Instead, this characterisation is based on the comparison of predicted soil concentrations (see PEC, in the environmental part of this report) with a so-called critical soil Cd concentration. The critical soil Cd concentration is defined as that concentration in soil not causing excessive Cd exposure via the human diet. This concentration will be derived below using food chain modelling and with a critical dietary Cd intake.

This section describes the conversion of critical Cd body burden into critical soil Cd concentrations.

A critical soil Cd concentration ($Cd_{soil,crit}$) can be defined as the highest concentration in soil not causing excessive Cd exposure via the human diet. This concentration will be derived with foodchain modelling by changing the variable amount of dietary Cd until a critical dietary Cd intake is reached.

The critical dietary Cd intake is defined as that value above which a tolerable systemic Cd dose (body burden) would be exceeded in humans. The critical target organs in humans are the kidney and bone and critical Cd body burdens are derived here from urinary Cd concentrations (Cd-U). A LOAEL of 2 µg/g creatinine is proposed based on early renal changes. The significance of this value is subject to contrasting views: while some scientists (including the rapporteurs of the present document) expressed the view that early renal effects associated with low levels of environmental exposure (Cd-U < 5 µg/g creatinine) most likely reflect benign, non-adverse responses (Hotz et al. 1999; Section 4.1.2.7.3: health significance of early renal changes and ESRD), other scientists (mainly Swedish experts) indicated that an elevated concentration of low molecular weight proteins in urine is widely accepted, as such, as an indicator of kidney damage.

The NOAEL for urinary Cd can be estimated by dividing the LOAEL by an uncertainty factor

NOAEL Cd-U=LOAEL/3= 0.66 µg Cd/g creatinine

The uncertainty factor of 3 is the lowest value suggested by IPCS **(**Environmental Health Criteria 210: Principles for the assessment of risks to human health from exposure to chemicals, WHO, 1999).

The flow of information needed to derive critical soil Cd concentrations from the critical urinary Cd concentrations for the general population is depicted in **Figure 4.7**.

The critical dietary Cd intake can be calculated with a one compartment model assuming several toxicokinetic parameters, age and body weight. This one compartment model is a simplification of the 8 compartment model of Nordberg-Kjellström (Annex 1) and in which the contribution of air Cd to the body burden is neglected, in line with the figures discussed above (**Table 4.298**, excluding scenario near point sources).

The assumptions behind the model to convert critical urinary Cd values into critical dietary Cd intake values are:

1. Cd-U is proportional to kidney cortex Cd and Cd-U=2.5 µg/g creatinine is equivalent to 50 mg Cd/kg FW in kidney cortex (see Section 4.1.2.2.3)
2. Kidney weight is 300 g FW at body weight 70 kg and 235 g FW at body weight 55 kg.
3. Fraction of body burden Cd retained in kidney (f_k) is 1/3 (Annex 1).
4. Cd concentration in the renal cortex is 25% higher than renal average (see Section 4.1.2.2)
5. Constant daily Cd intake during the last 53 years
6. No contribution from smoking, i.e. the assessment is made for non-smokers

Table 4.303 shows the daily Cd intake that would be required to reach the critical urinary Cd concentrations of 0.66 µg/g creatinine for various parameter values. Critical Cd intake values largely depend on the assumed half-life and on the fraction of Cd that is absorbed by the GI tract (f_u).

Figure 4.7 Flow of information to derive critical soil Cd concentrations from critical urinary Cd in the general population not occupationally exposed to Cd. The risk characterisation of Cd in soil to protect the general population is based on the PECsoil and the critical soil Cd concentrations.

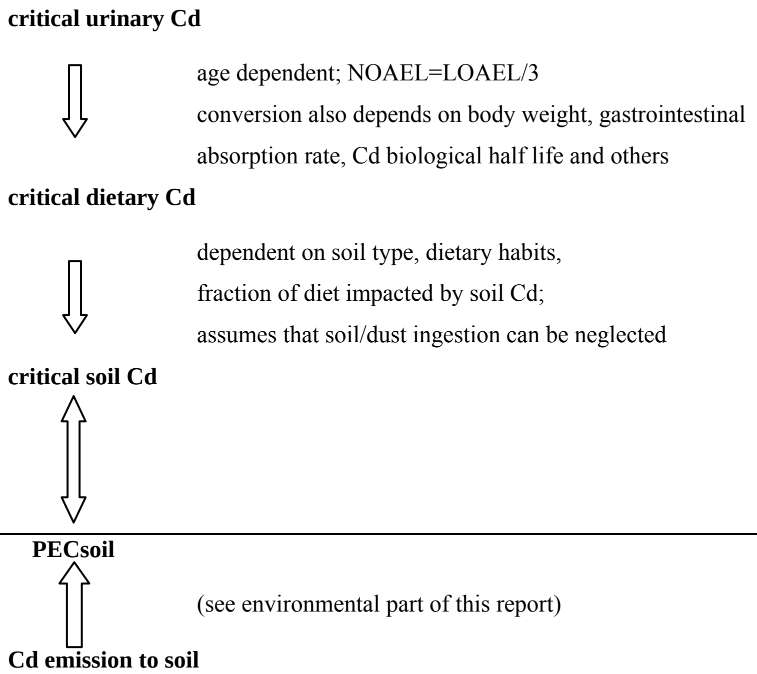

Table 4.303 The calculated Cd intake through ingestion (µg/day) to reach the NOAEL of urinary Cd concentrations (0.66 µg/g creatinine) at age 53 in non-smoking adults. Calculations are based on a one compartment model with various assumed parameter values

	$t^{**}_{1/2}$ (y)	10		13.6		40	
F^{*}_{u}	Body weight (kg)	70	55	70	55	70	55
0.03		62	48	47†	37†	25	20
0.05		37	29	28	22	15	12
0.10		19	15	14	11	8	6

* Fraction of dietary Cd that is absorbed by the GI tract;
** Estimated half life of Cd in kidney;
† Selected for risk characterisation, see 4.1.2.1.5 and text.

The following calculations will further be done for a body weight 70 and 55 kg and using the 3% GI absorption rates. The model validation study reported under Section 4.1.2.2.5 indicates that a 3% absorption rate (at $t_{1/2}$=13.6 years) most adequately describes Cd-U levels measured in the general population (predicted/observed ratio 0.9-1.3), even for upper percentile values. This 3% absorption rate as a ‘best fit’ parameter, while acknowledging that individuals with larger absorption rates exist, may indicate that it is incorrect to apply the largest absorption rates on also the largest dietary Cd intake values and for a constant period of 50 years. This indicates that the critical dietary Cd intake for non smokers with body weights of 70 kg and 55 kg respectively is:

Critical dietary Cd intake = 47-37 µg Cd/day (**Table 4.303**)

Conversion of dietary Cd intake to soil Cd

The relationship between soil Cd and dietary Cd intake can be calculated using food consumption data and food Cd concentrations that are predicted from soil Cd concentrations and the appropriate soil-plant transfer factors (TF's[38]). The biotransfer of Cd from soil to the foodchain has been dicussed in Section 4.1.1.4.8. This calculation must consider the amount of dietary Cd that is impacted by the level of Cd in the soil. For a local risk assessment, it can be assumed that dietary Cd intake is only influenced by local soil Cd through locally produced food. This section only deals with the regional and continental risk assessment. Rather than making a single prediction for a risk assessment, dietary Cd intake is predicted for several scenarios of dietary habits and soil types. Four scenarios are included for a continental risk assessment. These scenarios are chosen to represent a Scandinavian situation (Norway) with either neutral or acid soils, a central western European situation (Belgium) and a Mediterranean situation (Italy).

The calculations assume that vegetables, potatoes and cereals are 100% produced within the continent. The Cd in all other food groups (basal Cd intake) is assumed to be unaffected by the soil Cd content. There is only little error involved with this assumption since this basal Cd intake, diminished with Cd intake from fish and shellfish, is typically below 5 µg Cd day^{-1} (EUR 17527, 1997). The basal Cd intake at a continental scale is calculated from dietary Cd intake excluding the contribution of vegetables, potatoes and cereals. Market basket data of Norway, Belgium and Italy are selected from EUR 17527, 1997, similarly to the local calculations.

The soil-plant transfer factors were chosen from **Tables 4.71** and **4.72** (see Section 4.1.1.3.8). The contribution of cereals was calculated from whole grain data. The Cd concentrations in white flour are, on average, 31% less than that in wholemeal flour (Chaudri et al., 1995). The TF's of Scandinavian grain are based on the Swedish data in the **Table 4.72** and the other TF's of wheat grain were averaged to obtain representative TF's for grain for central Western Europe and for Mediterranean countries. The TF's for vegetables and potatoes were calculated as given above.

The dietary Cd intake is predicted for ambient soil Cd concentrations and for elevated soil Cd concentrations (see **Table 4.304**). At ambient Cd concentrations, dietary Cd is predicted to range between 10 and 21 µg day^{-1}, corresponding well with market basket studies in the respective countries (see **Table 4.66**). At an average soil Cd concentration of 1 mg Cd kg^{-1}, dietary Cd intake is predicted to range between 36 and 59 µg Cd day^{-1}.

38 TF, plant to soil Cd concentration ratio: (predicted Cd crop concentration)/soil Cd; see Section 4.1.1.3.8

Table 4.304 Calculated dietary Cd intake in 4 scenarios with either ambient soil Cd or elevated soil Cd (1 mg Cd kg^{-1}) at a continental scale. Potatoes, vegetables and cereals (wheat grain) are 100 % grown within the continent. Food consumption and basal Cd intake are based on data of European market basket studies (EUR 17527, 1997) and Cd soil-plant Transfer Factors (TF's) based on the compilation given in Section 4.1.1.4.8. See text for more details.

Scenario	**Food group**	**Consumption g fresh weight day^{-1}**	**TF (dimensionless)**	**dietary Cd intake (µg Cd day^{-1}) at ambient soil Cd**	**dietary Cd intake (µg Cd day^{-1}) at Cd_{soil}=1 mg kg^{-1}**
1. Scandinavian neutral soils (pH 6.8, ambient soil Cd=0.25 mg kg^{-1})	Potatoes	131	0.09	3.0	11.8
	leafy vegetables	7	0.09	0.1	0.7
	other vegetables	52	0.04	0.5	2.1
	cereals	142	0.14	5.0	19.6
				total continental 8.6	total continental 34.2
				basal intake 1.7	basal intake 1.7
				total intake **10.3**	total intake **35.9**
2. Scandinavian acid soils (pH 5.8 ambient soil Cd=0.25 mg kg^{-1})	Potatoes	131	0.18	5.9	23.5
	leafy vegetables	7	0.18	0.3	1.3
	other vegetables	52	0.08	1.0	4.1
	cereals	142	0.17	6.0	24.6
				total continental 13.3	total continental 53.5
				basal intake 1.7	basal intake 1.7
				total intake **15.0**	total intake **55.2**

Table 4.304 continued overleaf

Table 4.304 continued Calculated dietary Cd intake in 4 scenarios with either ambient soil Cd or elevated soil Cd (1 mg Cd kg^{-1}) at a continental scale. Potatoes, vegetables and cereals (wheat grain) are 100 % grown within the continent. Food consumption and basal Cd intake are based on data of European market basket studies (EUR 17527, 1997) and Cd soil-plant Transfer Factors (TF's) based on the compilation given in Section 4.1.1.4.8. See text for more details

Scenario	**Food group**	**Consumption** **g fresh weight day-1**	**TF** **(dimensionless)**	**dietary Cd intake (µg Cd day-1) at ambient soil Cd**	**dietary Cd intake (µg Cd day-1) at Cdsoil=1 mg kg-1**
3. Central western Europe (ambient soil Cd=0.30 mg kg^{-1})	Potatoes	240	0.08	5.8	19.2
	leafy vegetables	47	0.12	1.7	5.6
	other vegetables	155	0.03	1.4	4.7
	cereals	224	0.11	7.4	24.6
				total continental 16.2	total continental 54.1
				basal intake 4.9	basal intake 4.9
				total intake **21.1**	total intake **59.0**
4. Mediterranean (ambient soil Cd=0.30 mg kg^{-1})	Potatoes	54	0.08	1.3	4.3
	leafy vegetables	27	0.12	1.0	3.2
	other vegetables	175	0.03	1.6	5.3
	cereals	266	0.11	8.8	29.3
				total continental 12.6	total continental 42.1
				basal intake 7.4	basal intake 7.4
				total intake **20.0**	total intake **49.5**

The critical soil Cd concentrations are now derived for the proposed critical dietary Cd intake values (see **Table 4.305**). The $Cd_{soil,crit}$ range for continental exposure is 0.59-1.32 mg Cd $kg^{-1}{}_{dw}$.

The $Cd_{soil,crit}$ values derived to protect the human food chain (see **Table 4.305**) are generally lower than the $PNEC_{soil}$ that was calculated in the environmental effects assessment (1.1-2.3 mg Cd kg^{-1}, see the environmental part of this report in a separate document) or than the critical soil Cd concentrations (0.9 mg Cd/kg) to prevent small mammals toxicity (see the environmental part of this report in a separate document). It can therefore be concluded that protecting the human food chain is the most critical pathway of soil Cd. The derivation of the critical soil Cd values most critically depend on the choice of the actual ambient soil Cd concentration that is associated with the actual mean dietary Cd intake. This risk characterisation has however used identical choices for average ambient soil Cd concentrations at t=0 in both the exposure and the effects analysis and the conclusions of the risk characterization for future exposure are only marginally affected by the choice of the background.

Table 4.305 The critical concentrations of Cd in soil that is predicted to protect the general population from Cd transferred through the foodchain

Scenario	$Cd_{soil,crit}$ (mg Cd $kg^{-1}{}_{dw}$)
at critical dietary Cd intake = 47 µg/day (body weight 70 kg)	
1. Scandinavian neutral soils (pH 6.8)	1.32
2. Scandinavian acid soils (pH 5.8)	0.85
3. Central western Europe	0.78
4. Mediterranean	0.94
at critical dietary Cd intake = 37 µg/day (body weight, 55 kg)	
1. Scandinavian neutral soils (pH 6.8)	1.03
2. Scandinavian acid soils (pH 5.8)	0.66
3. Central western Europe	0.59
4. Mediterranean	0.70

Additional safety factors to account for the large group of individuals with low or depleted iron stores have been asked by some Member States at the TM on several occasions. The validation study discussed under Section 4.1.2.2.5, has shown that application of the 3% GI absorption rate adequately predicts the values observed in the population, including the upper percentiles. In this sense, an additional safety factor to protect Fe deficient individuals is not explicitly but implicitly included in the assessment. Therefore, the rapporteur proposes to minimise the accumulation of safety factors in the derivation of critical dietary Cd intake and it may become more transparent that only a safety factor of 3 is used in the conversion of LOAEL to NOAEL. The conversion of dietary Cd to soil Cd is obviously also uncertain but there are no data to predict if safety factors are embedded or not. The entire conversion of Cd-U to soil Cd leads to thresholds well below ambient or pre-industrial situations in some conditions.

4.1.3.4.4 Future exposure conditions: risk characterisation (soil contribution)

Model 2 was proposed in the environmental part of this report (see separate document) to assess risk of Cd in agricultural soils at a regional and continental scale. The predicted soil Cd concentrations after 60 years with current input range from 0.2-0.4 mg Cd/kg_{dw} (see **Table 4.306**). As mentioned above, there is little effect of the choice of the soil background at t=0 for risk characterisation because identical choices were made for exposure and effects analyses at the current conditions. Risk factors between 0.2-0.7 are predicted depending on the scenario and the critical dietary Cd intake (depending on body weight). This suggests that a **conclusions (ii)** can be proposed for the average soil compartment in the environmental risk assessment taking risks to the non-smoking population into account. It should be noted that those risks factors were derived using a best fit GI-uptake of 3%. A higher uptake (6%) will increase the risk factor by a factor of two.

This assessment is based on PEC_{soil} derived from mean measured Cd concentrations at t=0. A risk can, however, not be excluded for local/regional situations i.e. when PEC_{soil} calculations would be based on 90^{th} percentiles of measured Cd concentrations. Moreover, even risk factors that are below 1.0 may not be protective enough for all sections of the general population because of the large variability in food Cd concentrations, dietary habits and nutritional status. This warrants that existing food surveillance programs should be continued.

Table 4.306 Risk characterisation for agricultural soil to protect the human food chain. The factor risk = PEC/$Cdsoil_{crit.}$ The PEC values are derived from the environmental part of this report in a separate docement (see environmental exposure)

Exposure scenario	PEC_{soil}	$Cd_{soil,crit}$	Factor risk soil	Effect scenario*
	mg/kg_{dw}			
at critical dietary Cd intake = 47 µg/day				
1. low input-low output (pH 6.8)	0.257	1.32	0.2	Scandinavian neutral soils
2. low input-high output (pH 5.8)	0.203	0.85	0.2	Scandinavian acid soils
3. average input-low output	0.385	0.78-0.94	0.4-0.5	Central western Europe and mediterranean
4. average input-high output	0.310	0.78-0.94	0.3-0.4	Central western Europe and mediterranean
5. high input-low output	0.411	0.78-0.94	0.4-0.5	Central western Europe and mediterranean
6. high input-high output	0.339	0.78-0.94	0.4	Central western Europe and Mediterranean
7. EU average	0.318	0.78-1.32	0.2-0.5	All
at critical dietary Cd intake = 37 µg/day				
1. low input-low output (pH 6.8)	0.257	1.03	0.2	Scandinavian neutral soils
2. low input-high output (pH 5.8)	0.203	0.66	0.3	Scandinavian acid soils
3. average input-low output	0.385	0.59-0.70	0.5-0.7	Central western Europe and Mediterranean
4. average input-high output	0.310	0.59-0.70	0.4-0.5	Central western Europe and Mediterranean
5. high input-low output	0.411	0.59-0.70	0.6-0.7	Central western Europe and Mediterranean
6. high input-high output	0.339	0.59-0.70	0.5-0.6	Central western Europe and Mediterranean
7. EU average	0.318	0.59-1.03	0.3-0.5	All

* Continental scenarios for deriving the critical soil Cd concentrations, see Section 4.1.1.4.8

4.1.3.5 Combined exposure

For occupationally exposed people, all or not living nearby an emitting plant and possibly also exposed via consumer goods, the dominant exposure route is presumably the inhalation route especially when the occupational exposure is high.

In case the occupational exposure is low, the oral route may become predominant as this is the case in people indirectly exposed to the substance (generic) via the environment.

In all these cases, because of the use of biomarkers of exposure that integrate all possible routes, the risk characterisation conducted under Section 4.1.3.2 and 4.1.3.4 also includes “combined exposure”. Thus, the results of risk characterisation for those populations will not differ from those already derived under the mentioned sections.

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

The physicochemical properties of cadmium metal and cadmium oxide are well known and there is a general consensus as to the values of the particular physicochemical parameters relating to each of these substances. Note that the testing on pyrophoric properties of cadmium metal powder[39], as requested by the MSR and the TM, was recently performed by Industry on a voluntary basis.

Due to the relatively low melting and boiling point, these substances, when heated sufficiently can give rise to irritative fumes. For exposure and risk related to this property, reference is made to the relevant sections in Section 4.1 (human toxicity).

Given the level of control in manufacture and use – extensive legislative instruments being already in place e.g. at the workplace - the risks from physicochemical properties are small.

Overall risk assessment for physicochemical properties is **conclusion (ii)**.

39 The outcome of these studies is: commercial cadmium ‘powder’ is found to be non pyrophoric: the criteria for flammability, self-ignition and explosivity are not met (see Section 1).

5 RESULTS

The results in this document of the risk assessment for human health relate to cadmium oxide only.

5.1 ENVIRONMENT

(see separate document).

5.2 HUMAN HEALTH

5.2.1 Human health (toxicity)

5.2.1.1 Workers

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (i) There is a need for further information and/or testing.

Conclusion (iii) is reached because at the mentioned exposure levels, health risks (acute toxicity; respiratory irritation; kidney and bone repeated dose toxicity; genotoxicity; carcinogenicity, effects on fertility and reproductive organs) cannot be excluded upon inhalation exposure.

Conclusion (i) is reached because further information is needed to better document the possible neurotoxic effects of CdO suggested in experimental animals, especially on the developing brain. The collection of this additional information should, however, not delay the implementation of appropriate control measures needed to address the concerns expressed for several other health endpoints including repeated dose toxicity and carcinogenicity

Conclusion (i) "on hold".

The information requirements are further epidemiological and experimental information to identify more precisely the nature of the effects, the characterisation of the exposure and the mechanism of action related to neurotoxicity. These investigations should mainly focus on effects on the developing brain (prenatal and early childhood exposure). Effects on the adult nervous system should also be characterised.

Table 5.1 Overview of the formal occupational health conclusions on cadmium oxide as produced/used in the scenarios relevant for the life-cycle of cadmium oxide i.e. 'CdO production', 'Ni-Cd batteries', 'Pigments', 'Stabilisers', 'Plating' and 'Others

End point	Conclusions proposed for the occupational scenario's											
	CdO production		Ni-Cd batteries		Pigments		Metal plating		Stabilisers		Others	
	MOS	Ccl	MOS	Ccl	MOS	Ccl	MOS	Ccl	MOS	Ccl	MOS	Ccl
Acute toxicity	3	(iii)	-	(ii)	-	(ii)	44	(ii)	-	(ii)	220	(ii)
Irritation												
eye	-	(ii)	-	(ii)	-	(ii)	-	(ii)	-	(ii)	-	(ii)
skin	-	(ii)	-	(ii)	-	(ii)	-	(ii)	-	(ii)	-	(ii)
respiratory tract	-	(iii)	-	(iii)	-	(iii)	-	(iii)	-	(iii)	-	(iii)
Corrosivity	-	(ii)	-	(ii)	-	(ii)	-	(ii)	-	(ii)	-	(ii)
Sensitisation	-	(ii)	-	(ii)	-	(ii)	-	(ii)	-	(ii)	-	(ii)
Repeated dose toxicity												
Kidney and bone	0.20	(iii)	0.6	(iii)	0.50	(iii)	-	(iii)*	-	(iii)*	-	(iii)*
Neurotoxicity	-	(i)§	-	(i)§	-	(i)§	-	(i)§	-	(i)§	-	(i)§
Genotoxicity	-	(iii)	-	(iii)	-	(iii)	-	(iii)	-	(iii)	-	(iii)
Carcinogenicity	-	(iii)	-	(iii)	-	(iii)	-	(iii)	-	(iii)	-	(iii)
Reprotoxicity												
Effects on fertility ands sex organs	0.66	(iii)	0.31	(iii)	1.25	(iii)	10	(ii)	50	(ii)	50	(ii)
Developmental effects	-	(i)§	-	(i)§	-	(i)§	-	(i)§	-	(i)§	-	(i)§

§ "on hold"
* by extrapolation from other scenarios

5.2.1.2 Consumers

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) is reached because among the examined scenarios, CdO is only involved for the manufacture of Ni-Cd batteries and, in this case, consumer exposure is considered to be non-existent or negligible.

5.2.1.3 Humans exposed via the environment

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (i) There is a need for further information and/or testing.

Conclusion (iii) is reached because at the mentioned exposure levels, health risks (kidney and bone (all scenarios except adult non-smokers with sufficient iron stores) and lung (scenario 3) repeated dose toxicity, carcinogenicity/genotoxicity) cannot be excluded upon environmental exposure.

Related to the Scenario 3 (‘near point sources’): the **conclusion (iii)** for kidney and bone repeated dose toxicity is based on RWC calculated estimates derived from the highest exposure data per life-cycle step i.e. data from 1996 (three Cd metal producers) or 1999 (one NiCd battery producer) and in the absence of more recent emission and/or reliable measured data from Industry. To date, some of the plants for which these values were reported may have ceased activity or changed their production process.

For the same scenario, the **conclusion (iii)** for lung repeated dose toxicity is applicable to Cd metal producers only (RWC calculated estimate based on emission data of 1996 at three sites and in the absence of more recent emission and/or reliable measured data from Industry: to date, some of the plants for which these values were reported may have ceased activity or changed the production process).

Conclusion (i) is reached because further information is needed to better document the possible neurotoxic effects of Cd metal suggested in experimental animals, especially on the developing brain. The collection of this additional information should, however, not delay the implementation of appropriate control measures needed to address the concerns expressed for several other health endpoints including repeated dose toxicity and carcinogenicity.

Conclusion (i) “on hold”.

The information requirements are further epidemiological and experimental information to identify more precisely the nature of the effects, the characterisation of the exposure and the mechanism of action related to neurotoxicity. These investigations should mainly focus on effects on the developing brain (prenatal and early childhood exposure). Effects on the adult nervous system should also be characterised.

5.2.2 Human health (risks from physico-chemical properties)

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) is reached because given the level of control in manufacture and use, the risks from physicochemical properties are small.

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ABBREVIATIONS

ADI	Acceptable Daily Intake
AF	Assessment Factor
ASTM	American Society for Testing and Materials
ATP	Adaptation to Technical Progress
AUC	Area Under The Curve
B	Bioaccumulation
BBA	Biologische Bundesanstalt für Land- und Forstwirtschaft
BCF	Bioconcentration Factor
BMC	Benchmark Concentration
BMD	Benchmark Dose
BMF	Biomagnification Factor
BOD	Biochemical Oxygen Demand
bw	body weight / *Bw*, *bw*
C	Corrosive (Symbols and indications of danger for dangerous substances and preparations according to Annex II of Directive 67/548/EEC)
CA	Chromosome Aberration
CA	Competent Authority
CAS	Chemical Abstract Services
CEC	Commission of the European Communities
CEN	European Standards Organisation / European Committee for Normalisation
CEPE	European Committee for Paints and Inks
CMR	Carcinogenic, Mutagenic and toxic to Reproduction
CNS	Central Nervous System
COD	Chemical Oxygen Demand
CSTEE	Scientific Committee for Toxicity, Ecotoxicity and the Environment (DG SANCO)
CT_{50}	Clearance Time, elimination or depuration expressed as half-life
d.wt	dry weight / dw
dfi	daily food intake
DG	Directorate General

DIN	Deutsche Industrie Norm (German norm)
DNA	DeoxyriboNucleic Acid
DOC	Dissolved Organic Carbon
DT50	Degradation half-life or period required for 50 percent dissipation / degradation
DT90	Period required for 90 percent dissipation / degradation
E	Explosive (Symbols and indications of danger for dangerous substances and preparations according to Annex II of Directive 67/548/EEC)
EASE	Estimation and Assessment of Substance Exposure Physico-chemical properties [Model]
EbC50	Effect Concentration measured as 50% reduction in biomass growth in algae tests
EC	European Communities
EC10	Effect Concentration measured as 10% effect
EC50	median Effect Concentration
ECB	European Chemicals Bureau
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
ECVAM	European Centre for the Validation of Alternative Methods
EDC	Endocrine Disrupting Chemical
EEC	European Economic Communities
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EN	European Norm
EPA	Environmental Protection Agency (USA)
ErC50	Effect Concentration measured as 50% reduction in growth rate in algae tests
ESD	Emission Scenario Document
EU	European Union
EUSES	European Union System for the Evaluation of Substances [software tool in support of the Technical Guidance Document on risk assessment]
F(+)	(Highly) flammable (Symbols and indications of danger for dangerous substances and preparations according to Annex II of Directive 67/548/EEC)
FAO	Food and Agriculture Organisation of the United Nations
FELS	Fish Early Life Stage
foc	Organic carbon factor (compartment depending)

GLP	Good Laboratory Practice
HEDSET	EC/OECD Harmonised Electronic Data Set (for data collection of existing substances)
HELCOM	Helsinki Commission -Baltic Marine Environment Protection Commission
HPLC	High Pressure Liquid Chromatography
HPVC	High Production Volume Chemical (> 1000 tonnes/annum)
IARC	International Agency for Research on Cancer
IC	Industrial Category
IC50	median Immobilisation Concentration or median Inhibitory Concentration
ILO	International Labour Organisation
IPCS	International Programme on Chemical Safety
ISO	International Organisation for Standardisation
IUCLID	International Uniform Chemical Information Database (existing substances)
IUPAC	International Union for Pure and Applied Chemistry
JEFCA	Joint FAO/WHO Expert Committee on Food Additives
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
Koc	organic carbon normalised distribution coefficient
Kow	octanol/water partition coefficient
Kp	solids-water partition coefficient
L(E)C50	median Lethal (Effect) Concentration
LAEL	Lowest Adverse Effect Level
LC50	median Lethal Concentration
LD50	median Lethal Dose
LEV	Local Exhaust Ventilation
LLNA	Local Lymph Node Assay
LOAEL	Lowest Observed Adverse Effect Level
LOEC	Lowest Observed Effect Concentration
LOED	Lowest Observed Effect Dose
LOEL	Lowest Observed Effect Level
MAC	Maximum Allowable Concentration

MATC	Maximum Acceptable Toxic Concentration
MC	Main Category
MITI	Ministry of International Trade and Industry, Japan
MOE	Margin of Exposure
MOS	Margin of Safety
MW	Molecular Weight
N	Dangerous for the environment (Symbols and indications of danger for dangerous substances and preparations according to Annex II of Directive 67/548/EEC
NAEL	No Adverse Effect Level
NOAEL	No Observed Adverse Effect Level
NOEL	No Observed Effect Level
NOEC	No Observed Effect Concentration
NTP	National Toxicology Program (USA)
O	Oxidising (Symbols and indications of danger for dangerous substances and preparations according to Annex II of Directive 67/548/EEC)
OC	Organic Carbon content
OECD	Organisation for Economic Cooperation and Development
OEL	Occupational Exposure Limit
OJ	Official Journal
OSPAR	Oslo and Paris Convention for the protection of the marine environment of the Northeast Atlantic
P	Persistent
PBT	Persistent, Bioaccumulative and Toxic
PBPK	Physiologically Based PharmacoKinetic modelling
PBTK	Physiologically Based ToxicoKinetic modelling
PEC	Predicted Environmental Concentration
pH	logarithm (to the base 10) (of the hydrogen ion concentration $\{H^+\}$
pKa	logarithm (to the base 10) of the acid dissociation constant
pKb	logarithm (to the base 10) of the base dissociation constant
PNEC	Predicted No Effect Concentration
POP	Persistent Organic Pollutant

PPE	Personal Protective Equipment
QSAR	(Quantitative) Structure-Activity Relationship
R phrases	Risk phrases according to Annex III of Directive 67/548/EEC
RAR	Risk Assessment Report
RC	Risk Characterisation
RfC	Reference Concentration
RfD	Reference Dose
RNA	RiboNucleic Acid
RPE	Respiratory Protective Equipment
RWC	Reasonable Worst-Case
S phrases	Safety phrases according to Annex IV of Directive 67/548/EEC
SAR	Structure-Activity Relationships
SBR	Standardised birth ratio
SCE	Sister Chromatic Exchange
SCHER	Scientific Committee on Health and Envionment Risks
SDS	Safety Data Sheet
SETAC	Society of Environmental Toxicology And Chemistry
SNIF	Summary Notification Interchange Format (new substances)
SSD	Species Sensitivity Distribution
STP	Sewage Treatment Plant
T(+)	(Very) Toxic (Symbols and indications of danger for dangerous substances and preparations according to Annex II of Directive 67/548/EEC)
TDI	Tolerable Daily Intake
TG	Test Guideline
TGD	Technical Guidance Document
TNsG	Technical Notes for Guidance (for Biocides)
TNO	The Netherlands Organisation for Applied Scientific Research
ThOD	Theoritical Oxygen Demand
UC	Use Category
UDS	Unscheduled DNA Synthesis

UN	United Nations
UNEP	United Nations Environment Programme
US EPA	Environmental Protection Agency, USA
UV	Ultraviolet Region of Spectrum
UVCB	Unknown or Variable composition, Complex reaction products of Biological material
vB	very Bioaccumulative
VOC	Volatile Organic Compound
vP	very Persistent
vPvB	very Persistent and very Bioaccumulative
v/v	volume per volume ratio
w/w	weight per weight ratio
WHO	World Health Organisation
WWTP	Waste Water Treatment Plant
Xn	Harmful (Symbols and indications of danger for dangerous substances and preparations according to Annex II of Directive 67/548/EEC)
Xi	Irritant (Symbols and indications of danger for dangerous substances and preparations according to Annex II of Directive 67/548/EEC)

Annex A The Nordberg-Kjellström kinetic model

The Nordberg-Kjellström model (Kjellström and Nordberg, 1978; Kjellström and Nordberg, 1985) is a linear eight-compartment kinetic model of cadmium metabolism which has the advantage of being able to calculate not only accumulation in the kidney, but in other tissues as well. It is the most detailed and commonly used model for cadmium risk assessment and is discussed in the ATSDR (1999).

The model is based on a number of approximate assumptions, but it appears to be able to calculate the long term accumulation of tissue levels under a number of different exposure situations with reasonable accuracy.

The coefficients C1 - C19 determine the transfer between compartments. In most cases, the daily transfer is assumed to be a fixed proportion of the accumulated amount in the compartment.

It describes the disposition of cadmium via the oral and inhalation routes of exposure. Dermal exposure and skin absorption were assumed to be negligible.

Description of the model by Nordberg and Kjellström (1985):

Absorption and uptake

For inhalation exposure, the model takes into account the different deposition patterns for different size particles in nasopharyngeal, tracheobronchial, and alveolar regions of the respiratory tract. Cadmium compounds are inhaled as particulate matter, either as fumes with very small particle size or as dust. The general principles for deposition and absorption of particulate matter described by the Task Group on Lung Dynamics * and by the Task group on Metal Accumulation ** were taken to be valid for cadmium and were used in this model. Particles with MMAD (mass median aerodynamic diameter) of 5 µm were assumed to distribute mainly to the nasopharyngeal region (75%) with lesser amounts depositing in the alveolar (20%) and tracheobronchial (5%) regions. Particles of 0.05 µm MMAD (i.e., cigarette smoke) were assumed to deposit 55% in the alveolar compartment, 10% in the tracheobronchial compartment and none in the nasopharyngeal compartment. The remaining amounts are exhaled. The respiratory Cd intake (A) can be diverted to the gastro-intestinal tract (C · A) due to the clearance of Cd deposited on the mucosa of nasopharynx, trachea, or bronchi. It can also be deposited in the alveoli (C2 · A) and from there be absorbed into the blood (C3 · E1). The remainder of the respiratory intake is exhaled. Some of the Cd in the alveoli is transported via alveolar clearance back to the bronchi (C4 · E1) and eventually to the gastro-intestinal tract after swallowing. Based on data given by the Task Group on Lung Dynamics, C1 was estimated at 0.1 to 0.2 for Cd fumes and at 0.4 to 0.9 for Cd dust. Calculations with different values were carried out and a best fit between calculated and empirical values was found for C1 = 0.1 (fume) and 0.7 (dust). In accordance with the difference in the distribution of small (fume) and large (dust) particles, C2 was estimated to be 0.4 to .06 for fume and 0.1 to 0.3 for dust. The best fit values for all coefficients are listed in **Table A.1**. The alveolar clearance is likely to be small in comparison with the rest of the lung clearance and C4 was assumed to be 0.1 · C3.

Cadmium intake via the gastro-intestinal tract consists of food cadmium (G) and Cd cleared from alveoli (C4 · E1) and respiratory tract (C1 · A). Most of Cd in the intestinal lumen will pass unabsorbed and the retention C5 was assumed to be in the range 0.03 to 0.1. The Cd retained in the intestinal wall will accumulate to a certain extent before being absorbed into blood. C6 was assumed to be 0.05/day, but available data are insufficient to estimate this coefficient with accuracy. The total amount of Cd absorbed into blood each day (C3 · E1 + C6 · E2) is called daily uptake (I µg/day).

Transport and distribution

The blood was divided into three compartments: the albumin-bound Cd (B1), the cell-bound Cd (B2), and the metallothionein-bound Cd (B3). The turn-over of Cd in B1 and B3 is very rapid and all Cd input into these compartments is assumed to have continued to other compartments within less than a day. Thus the contribution of B1 and B3 to whole blood Cd concentration is less than the calculated amounts in these compartments. This fraction (C20) was assumed to be in range 0.05 to 0.5. The part of Cd uptake (C7 · I) which is bound to metallothionein (B3) will continue mainly to kidney and urine. As about a third of the body burden after long-term exposure is in the kidneys, C7 was assumed to be 0.2 to 0.4. The B3 compartment has a limited number of binding sites and therefore, the daily flow from I to B3 was maximised by C8 (0.5 to 5 µg/day).

Accumulation in B2 is determined by the turn-over rate of red blood cells. The mean life of erythrocytes is 120 days which implies a half-time of 83 days and C16 would be 0.008/day. For the modelling, it was assumed that C16 would be in the range of 0.004 to 0.015/day. From B1, Cd is transferred to red blood cells (B2), liver (L), and other tissues (T), and via intestinal wall cells to faeces (F). The proportions of B1 distributed to L and T were assumed to agree approximately with their proportion of whole body burden of Cd (16% for L, 50% for T). Thus, C12 was assumed to be 0.1 to 0.4 and C9 was set at 0.4 to 0.8. The liver is a main organ for metallothionein production and it was assumed that most of the cadmium in B3 came from the liver (C14 · L). From B2, metallothionein-bound Cd will add to the B3 compartment and the B3-Cd is cleared through the kidney glomeruli. Some Cd is reabsorbed in the proximal tubuli (C17 · B3) and adds to kidney accumulation (K) and the rest is excreted via urine (U). About 95% of the glomerular filtrate of Cd-metallothionein is reabsorbed in the renal tubuli of mice, hence C17 was assumed to be in the range 0.8 to 0.98. Tubular reabsorptive capacity decreases with age. Between 30 and 80 years, it decreased 33%. In the model a similar decrease was assumed. Cd is transported back from liver, kidney, and other tissues to the blood. This is assumed to occur mainly to the B compartment (C10 · T, C13 · L, and C18 · K), but the liver also contributes to B3 (C14 · L).

Excretion

Almost all Cd in the body is excreted via faeces and urine. Faecal Cd consists mainly of the non-absorbed part of ingested Cd. "True" faecal excretion originates from blood via the intestinal wall (C11 · B1) and from bile (C15 · L). The main part of biliary cadmium is correlated with the amount of cadmium in liver. C15 was assumed to be in the range 0 to 0.0001/day. With long-term low level exposure faecal and urinary excretion are about the same. Urinary excretion is mainly a function of the body burden, but a part of this excretion is directly dependent on blood Cd. This has been taken into consideration by splitting urinary excretion into two parts: (1-C17) · B3 coming from blood and C19 · K coming from kidney. At steady state, the total daily excretion would be the same as total daily uptake. In Sweden, the average adult daily Cd intake via food is about 16 µg and the average body burden of non-smokers is about 5 mg at 50 years. With a gastro-intestinal absorption rate of 5%, the daily uptake (0.8 µg) would be 0.016% of body burden.

Average adult (30-60 years) urinary excretion is approximately 0.35 µg/day. Thus, the daily excretion rate for urine would be 0.007% of body burden and, by subtraction from the estimated total excretion; the faecal excretion would be 0.009% of body burden.

Retention and accumulation

The main part of body burden will be found in the liver (L), the kidneys (K) and other tissues (T) (muscles, skin, and bones). C13 was set at 0 to 0.0001/ay and C14 at 0.001 to 0.003/day which in combination with C15 gave a half-time in liver between 4 and 19 years. C19 was estimated to be in the range 0.00002 to 0.0002/day, and C18 in the range 0 to 0.0001/day. The corresponding range of kidney half-times would be 6 to 38 years. It was also assumed that C19 increases linearly after age 30 with C21 each year. Initially, C21 was set at 0 to 0.000002/day. Very little data are available regarding half-times in other tissues. It was found that age-dependent accumulation curves for Cd in muscle indicate an even longer half-time than for kidney. With long-term low level exposure about half of the body burden is in other tissues, indicating that a major accumulation occurs there as well as in liver and kidneys. C10 was assumed to be in the range 0.00004 to 0.0002/day corresponding to half-times between 9 and 47 years.

Table A.1 Assumed and modelled values of coefficients (Kjellström and Nordberg, 1985)

Coefficients	Initially assumed ranges [a]	Unit	Values fitting to empirical data
C1	0.1- 0.2 (cigarette smoke) 0.4 - 0.9 (factory dust)		0.1 0.7
C2	0.4- 0.6 (cigarette smoke) 0.1 - 0.3 (factory dust)		0.4 0.13
C3	0.01 - 1	day^{-1}	0.05
C4	0.1 ・ C3 = 0.001 - 0.1	day^{-1}	0.005
C5	0.03 - 0.1		0.048
C6	0.05	day^{-1}	0.05
C7	0.2 - 0.4		0.25
C8	0.5 - 5	µg	1
C9	0.4 - 0.8		0.44
C10	0.00004 - 0.0002	day^{-1}	0.00014
C11	0.05 - 0.5		0.27
C12	0.1 - 0.4		0.25
C13	0 - 0.0001	day^{-1}	0.00003
C14	0.0001 - 0.0003	day^{-1}	0.00016
C15	0 - 0.0001	day^{-1}	0.00005
C16	0.004 - 0.015	day^{-1}	0.012
C17b	0.8 - 0.989		0.95
C18	0 - 0.0001	day^{-1}	0.00001
C19cadmium	0.00002 - 0.0002	day^{-1}	0.00014
CXd	0.01 - 0.05		0.04

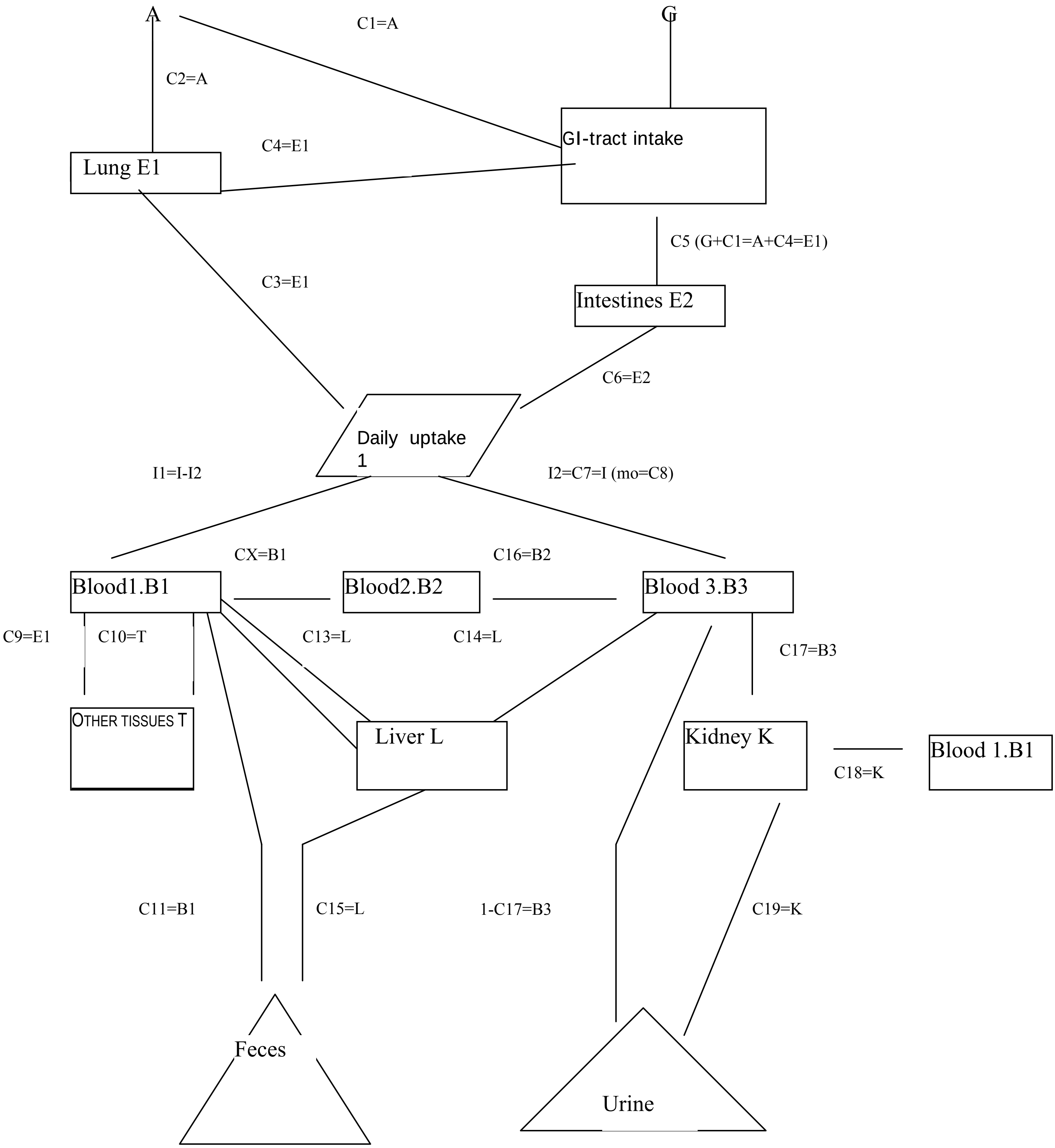
Table A.1 continued overleaf

Table A.1 continued Assumed and modelled values of coefficients (Kjellström and Nordberg, 1985)

Coefficients	Initially assumed ranges a	Unit	values fitting to empirical data
C20	0.05 - 0.5		0.1
C21	0 – 0.000002	day^{-1}	0.0000011

a If no unit is given, this means that the coefficient is a unitless proportion
b C17 decreases from age 30 to age 80 by 33%
c C19 increases from age 30 with C21 each year
d Cx = 1 - C9 - C11 - C12
* Task Group on Lung Dynamics, Deposition and retention models for internal dosimetry of the human respiratory tract. Health Phys, 12, 173-208, 1966
** Task Group on Metal Accumulation, Accumulation of toxic metals with special reference to their absorption, excretion and biological half-times. Environ Physiol Biochem, 3, 65-107, 1973

Figure A.1 Flow scheme of the Nordberg-Kjellström kinetic model of cadmium metabolism



Annex B Metallothionein

Metallothionein

In tissues, the majority of cadmium is bound to metallothionein, a low molecular weight protein (approximately 6,600 kDa) rich in cysteinyl thiol groups but deficient in aromatic amino acids. Metallothionein has been detected in human kidney, liver, heart, brain, testis, skin epithelial cells and in human embryonic fibroblasts from skin, muscles and lung. In animals, the protein has also been found in placenta, spleen and intestinal mucosa.

Separation techniques based on the charge properties of metallothionein, such as ion-exchange chromatography and iso-electric focusing, have shown that different forms of metallothionein often exist in the same organ. Usually two main forms of metallothionein are found: MT-I and MT-II. As a rule the total amount of metal ions bound to each metallothionein molecule is constant, but the types of metal ions might differ. Apart from having a different molar ratio of metals, the two different forms of metallothionein from the same species and tissues have also been shown to have slightly different amino acid composition (CRC, 1986). Transgenic mice deficient for MT-I and MT-II have been produced (Michalska and Choo; 1993)

Metallothionein is normally present in animal tissues in only trace amounts. Induction of its synthesis is under the control of a large group of genes and is stimulated by glucocorticoids and the essential metals Zn and Cu. Exposure to certain metals such as Cd, Hg, Zn, Ag, Cu, Mg can increase the concentration of MT in the liver and/or kidney, and possibly other tissues. It has also been observed that metallothionein can be induced by formaldehyde, carbon tetrachloride, hormones, drugs, alkylating agents, alcohol, infection, inflammation, food deprivation, irradiation (UV-X), cold, strenuous exercises. Certain metals appear to show organ specificity in regard to their ability to increase concentration of MT. For example, Hg and Zn induce the synthesis of MT in the kidney and the liver, respectively, whereas Cd induces synthesis in both the liver and the kidney (Waalkes and Goering, 1990; Kotsonis and Klaassen, 1978).

The exact physiologic functions of metallothionein are not known but it is thought to play an important role in the biological detoxification of metals, including Cd. It has been shown that following Cd exposure, Cd is predominantly associated with metallothionein and pretreatment with metals known to stimulate the synthesis of metallothionein prevents the toxicity of subsequent Cd exposure (Leber and Miya, 1976; Yoshikawa, 1973; Jin et al., 1986). A deficiency in metallothionein appears to occur in several mammalian tissues that are highly susceptible to the toxic effects of Cd. Rat, mouse, monkey testes, rat ventral prostate, hamster ovary are known to be susceptible to either the acute or/and chronic carcinogenic effects of Cd and appear to be deficient in metallothionein as assessed by biochemical analysis of Cd-binding protein (Waalkes and Goering, 1990).

The observed correlation between cellular Cd and MT is the result of the cell’s responding to increased intracellular Cd levels by increasing the synthesis of MT. Experiment carried out on MT I and MT II null mice also support the conclusion that the persistence of Cd in the body is at least partially due to Cd binding to metallothionein in tissues (Liu et al., 1996). More than 60-80% of the Cd in the kidneys and liver is bound to MT. MT is , however, also found in other tissues, usually in amounts proportional to the Cd or Zn content. The biological half-time of Cd-MT appears to be in the order of days; this is considerably shorter than the biological half-life of Cd. Thus a constant synthesis of MT must take place in order to sequester the Cd ions which have been released from the degraded MT (Elinder and Nordberg, 1985, CRC).

The low molecular weight of metallothionein enables the protein to be filtered through the kidney glomerular membrane; it is subsequently reabsorbed by the proximal tubule cells where it can compete with other proteins for the reabsorption site. The Cd-metallothionein complex is degraded in lysosomes with release of Cd, which may induce metallothionein synthesis in the proximal tubule. This process continues until the capacity of the cell to synthesise metallothionein is exceeded. The renal toxicity of Cd is associated with Cd not bound to metallothionein. However, brush-border membranes of the renal tubule may be damaged by cadmium that is bound to metallothionein (Suzuki and Cherian, 1987; Cherian and Goyer, 1976).

The synthesis of MT in the kidney cells is considerably slower than in the liver cells. The tissue MT level is mainly related to the tissue deposition of the inducing metal.

In rats, the concentrations of MT and Cd in both kidney and liver increase with dose and time. However, the rates of increase of MT and Cd are not the same in the liver and the kidney. In the kidney , the ratio of Cd to MT increases with time; in the liver, however, the ratio reaches a plateau. This phenomenon may explain why in rats the liver apparently has a tolerance to Cd during prolonged exposure that is the synthesis of MT in the liver appears to keep abreast with continually increasing concentration of Cd and thus limits the concentration of the non-MT-bound-Cd. However, in the kidney the ratio continues to increase with time that may explain why renal injury is observed during prolonged Cd exposure. In other words, the amount of Cd taken up by the kidney increases at a faster rate than does the amount of MT (Elinder and Nordberg, 1985).

LD_{50} of $CdCl_2$ by the intraperitoneal route are not different in wild type and MT-deficient animals and the distribution of Cd in tissues (24 hour post-treatment) was not different between the two strains, indicating that the basal level of MT does apparently not protect against acute Cd toxicity. Pretreatement with Zn (MT induction) protected however wildtype but not MT-deficient mice (Conrad et al., 1997). Using a similar dosing regimen (single administration of radiolabeled Cd, ip). Liu et al. (1996) confirmed that the initial distribution of Cd was not affected by the presence of MT. However, the elimination of Cd was found much faster in MT-null mice, with a 2-fold reduction of the Cd dose retained in the liver after 24 hours and later. Cd concentration in kidney continued to increase with time in control but not in MT-null mice, indicating that an important source of Cd in the kidney is the uptake of CdMT.

Alveolar macrophages were recovered by BAL from 10 healthy nonsmokers and 10 cigarette smokers to determine whether increased concentrations of Cd were present in the macrophages of cigarette smokers and whether metallothionein accumulated in response to the presence of cadmium. Cd was detected in the alveolar macrophages of all subjects, with a higher mean in cigarette smokers (3.4 ± 0.5 versus. 1.3 ± 0.2 ng/10^6 cells; $p < 0.005$). There was a correlation between current smoking history (cigarettes per day) and the alveolar macrophage content of cadmium. The mean metallothionein content was similar in both groups, despite the higher Cd content in the alveolar macrophages of smokers. This could be due, according to the authors, either to the fact that Cd concentrations in cigarette smoke are insufficient to induce metallothionein synthesis or to a greater saturation of this protein (Grasseschi et al., 2003).

MT and nephrotoxicity

Results from experimental studies carried out mainly with $CdCl_2$ suggest that the Cd-metallothionein complex is a nephrotoxin when injected but when it is synthesised within the cell it may protect from cadmium toxicity temporarily.

The distribution of Cd from a nephrotoxic dose of radiolabeled Cd-MT was compared in subcellular fractions of kidney cortex of rats with pre-induced MT synthesis (by $CdCl_2$) and of controls. In the pretreated rats, Cd in the plasma membrane and microsome fractions of renal cortex cells was mainly bound to MT and other low molecular weight proteins. In nonpretreated rats, the major part of Cd was bound to high molecular weight proteins. The animals with pre-induced MT synthesis were protected against the toxic effects of Cd-MT, whereas the control animals later developed nephrotoxic effects (Nordberg et al., 1994).

The prevalence of nephrotoxicity rather than hepatotoxicity in chronic Cd exposure may be due to several factors (WHO, 1992):

- the release of hepatic Cd-MT or its presence in the blood can result in preferential accumulation of Cd in kidneys;
- the kidney can accumulate MT mRNA in response to Cd exposure to only about half the level of the liver (Koropatnick and Cherian, 1988)

Thus the kidney may not be able to synthesise MT as efficiently as the liver in response to Cd exposure, resulting in an accumulation of non MT-Cd in the kidney but not in the liver.

Pretreatment with Cd entails increased tolerance to subsequent exposure to Cd.

Parenterally administered Cd-MT is highly nephrotoxic. The distribution of a single dose of Cd salts differs considerably from that of Cd-MT. A couple of hours after Cd salt was administered, about 50% of the dose was found in the liver and only about 10%, or less, in the kidney. However, when Cd-MT was administered, up to 90% was found in the kidneys 2 hours later (Elinder and Nordberg, 1985).

When Cd is given in the form of Cd-MT the LD_{50} is only about one tenth of that for inorganic Cd salts. It has been suggested that the mechanism underlying this phenomenon is, probably, glomerular filtration of Cd-MT and a subsequent efficient uptake from the tubular fluid into the tubular cells by pinocytosis followed by a rapid degradation in lysosomes and release of Cd from its protein ligand in the cytoplasm. Tubular cells have a certain capacity for producing their own metallothionein which can bind Cd and thereby prevent the toxic effects of Cd ions. Following large doses of Cd-MT, the cells cannot cope with all the Cd being released and cell damage occurs. The occurrence of non MT-bound-Cd ions in the tubular cells produces the toxic effects.

The free Cd pool is sufficiently large to gives rise to interact with membrane targets to block calcium transport routes, and there is deficient uptake and transport of calcium through the cell.

When injected parenterally, a high influx of Cd-MT occurring in the tubules can overload the sequestration mechanism of the de novo cellular synthesis of MT. Such acute toxicity does not occur in human exposure that takes place by oral or inhalation routes, which can only provide a limited flow of Cd-MT (Elinder and Nordberg, 1985; Vahter, 1996).

In a further experiment using a single dose of Cd intraperitoneally (25 µmole/kg as $CdCl_2$ or as Cd-MT complex), Liu et al. (1996) compared the heptoxic and nephrotoxic responses to $CdCl_2$ and Cd-MT, respectively. They concluded that MT plays less of a protective role in protecting against CdMT-induced nephrotoxicity than CdCl2-induced hepatotoxicity, and that Zn-induced protection against CdMT-induced nephrotoxicity does not appear to be mediated through MT.

Table B.1 Comparison of the heptoxic and nephrotoxic responses to $CdCl_2$ and Cd-MT

	Liver toxicity ($CdCl_2$)	Renal toxicity (Cd-MT)
MT +/+ mice	+++	+++
MT-/- mice	+	+++
effect of Zn pretreatment	protects +/+ only	protects +/+ and -/-

Chronic toxic effects of Cd in the kidney are likely to occur when tubular cell capacity for producing MT is insufficient to sequester all the Cd ions in the cell cytoplasm.

Chronic Cd administration of $CdCl_2$ produces renal injury in MT-null mice, indicating that Cd-induced nephrotoxicity is not necessarily mediated through the CdMT complex (Liu et al., 1998; Liu et al., 2000). However, MT protects against chronic $CdC1_2$ nephropathy, suggesting that intracellular MT is an important adaptive mechanism decreasing $CdC1_2$ nephrotoxicity (Liu et al., 1999), and that a single injection of CdMT may not be a good model to study chronic Cd nephropathy (Klaassen and Liu, 1998).

There are likely species differences with regard to the capacity of different animals to produce MT in the renal cortex. Therefore, signs of renal toxicity may occur at different total concentrations of Cd. In the case of human exposure, constitutional factors as well as age and simultaneous exposure to other nephrotoxic agents may influence renal MT in production capacity and thus the susceptibility of the kidneys to Cd (CRC, 1986). The exact impact of these possible variations in humans is however not clearly identified.

Zn pretreatment protects against the nephrotoxicity of Cd-MT. Several mechanisms have been suggested (Tang et al., 1998):

- the induction of the synthesis of MT by Zn and sequestration of Cd^{++} released from the lysosomial degradation of exogenous Cd-MT by the newly synthesised renal MT. However even MT-null mice are protected by Zn (Liu et al., 1996);
- plasma Zn seems to displace some of the Cd from Cd-MT and thus decreases renal Cd accumulation
- it appears to reduce the pinocytic uptake of Cd-MT complex by affectng the stability of the renal brush border membrane (Chvapil, 1973)
- more recently, GSH has been proposed as an important factor in regulating Cd-MT nephrotoxicity. Exogenous GSH can reduce Cd-MT nephrotoxicity in MT-null mice, while depletion of GSH severely enhanced the nephrotoxicity of Cd-MT. Although Zn does not require elevation of renal cortex GSH levels for protection against Cd-MT nephrotoxicity, the protection depends on the maintenance of normal intracellular GSH levels. While Zn reduces both Cd and MT accumulation, it does not alter the subcellular distribution of Cd. Zn protection in the MT-null mice appears to be through the reduction of Cd accumulation in the renal cortical epithelial cells to a level where the normal GSH levels are sufficient to prevent toxic interactions of Cd^{++} with sensitive intracellular sites (Tang et al., 1998).

Habeebu et al. (2000) have shown that MT also protects against the bone toxicity of Cd. Upon repeated sc injections of $CdCl_2$ over a wide range of doses for 10 weeks, they found no difference in bone Cd content between wild-type and MT-null mice. Repeated Cd injections produced, however, a dose-dependent loss of bone mass (up to 25%), as shown by analysis of the femur, tibia, and lumbar vertebrae. The loss of bone mass was more marked in MT-null mice than in wild-type mice, as shown by dry bone weight, defatted bone weight, bone ash weight, and total calcium content. X-ray photography showed decreasing bone density along the entire bone length with increasing dose and time of Cd exposure.

Annex C Cadmium exposure and End-Stage Renal Disease (ESRD)

Critical original studies

a) Retrospective mortality studies

Studies from Japan: Jinzu River basin, Toyama Prefecture

Nakagawa et al. (1990) examined the mortality (20-year follow-up) of Itai-Itai disease patients, patients suspected of having Itai-Itai disease, and control subjects matched for age, gender, and place of residence. Most cases were women (186 out of 190). Control subjects had neither proteinuria nor glucosuria (sulfosalicylic acid method and Benedict's reaction, respectively). Briefly summarised, Itai-Itai patients had the highest mortality and patients suspected of having Itai-Itai disease had a higher mortality than the control subjects. The increased mortality of patients with and suspected of Itai-Itai became statistically significant after three and 18 years of follow-up, respectively. However, some questions remain open. Firstly, the Cd body burden and the values of the renal parameters are not given and it is not known whether there was a relationship between these variables and mortality. Secondly, it is not clear whether the cause of death was due to end-stage renal disease or to another cause. This is an important issue because some observations suggest that the relationship between cadmium exposure and Itai-Itai disease is not univocal as several factors may have influenced cadmium toxicity in humans including nutritional deficiencies in calcium, protein, vitamin D, and iron, or zinc intake (ATSDR, 1999). As most of these factors may reflect unfavourable living conditions (low socio-economic level), it cannot be excluded that they were to some extent responsible for the increased mortality. Thirdly, regarding renal function it would be extremely important to know whether the patients diagnosed with Itai-Itai disease used non-steroidal anti-inflammatory drugs. Indeed, some authors have stressed the potential role of these agents in the progression to chronic renal disease (De Broe and Elseviers, 1998), the use of analgesic therapy for relief of pain due to osteomalacia has been reported in Itai-Itai patients (Kagamimori et al., 1986), and an interaction between acetaminophen and Cd effects has been described in experimental animals (Bernard et al., 1988). In human studies conducted in Belgium also, the use of analgesics was found to significantly influence tubular parameters alone or in interaction with the Cd body burden (Buchet al., 1990; Hotz et al., 1999).

A last issue is the possible publication bias. Indeed, two other surveys dealing with the mortality of the population from the Jinzu River basin found no increased mortality and were published in Japanese only (abstracts unavailable on Medline), one of them reported that the mortality was low especially in the highly polluted area (Shigematsu et al., 1982; Shigematsu et al., 1980). Similarly, the publication dealing with the possible confounding factors is available in Japanese only (Kawano et al., 1981). Thus, no overall assessment of all these studies can be made. Furthermore, the study by Nakagawa et al. (1990) extends the findings reported by Kawano et al. (1986); both reports can, therefore, not be considered as independent with which consistency can be examined.

To summarise, the aforementioned study (Nakagawa et al., 1990) concludes to an association between Itai-Itai disease and increased "all causes" mortality. However, both the causal role of Cd and its association with end-stage renal disease remain unclear. In particular, it would be interesting to know whether men with a similar Cd body burden had an increased mortality as well. Moreover, the fact that results showing an increased mortality were published in English and in international journals (Nakagawa et al., 1990; Kawano et al., 1986) unlike the results of the negative study (Shigematsu et al., 1982; Shigematsu et al., 1980) or those of the report on the comparability of the control group (Kawano et al., 1981), may suggest a publication bias.

Studies from Japan: Kosaka Town, Akita Prefecture

Iwata et al. (1992) found an increased "all causes" mortality in women (but not in men) with increased urinary β2M and/or total amino nitrogen concentration which was attributed to exposure to Cd in the environment. These results were published in English in an international journal whereas a negative study (Ono and Saito, 1985) from the same region is available in Japanese only (a very short abstract could be found in Nakagawa et al., 1990).

Again, only the "all causes" mortality is known, there is no specific data on ESRD, and the publication of the negative study in Japanese only makes an overall evaluation of the results extremely difficult and suggests a publication bias.

Studies from Japan: Kakehashi River basin, Ishikawa Prefecture

Nishijo et al. (1995) reported an increased mortality from "nephritis and nephrosis" in persons with tubular dysfunction diagnosed in 1974-1975 (15 year follow-up, 930 deaths or 38.6% of the subjects having participated in the 1974-1975 survey, tubular dysfunction assessed by semi-quantitative urinary RBP concentration) thought to be due to environmental cadmium exposure in the Kakehashi River basin. However, a diagnostic suspicion bias is possible. Indeed, all cases of "urinary tract diseases" were recorded in the group without increased RBP whereas no case with this diagnosis was found in the group with increased RBP. That some persons with "urinary tract diseases" and increased RBP were diagnosed erroneously with "nephritis and nephrosis" is likely because diagnoses were apparently not confirmed objectively. Furthermore, the authors noted that the quality of the death certificates was not very satisfactory (Nishijo et al., 1995).

More importantly, Nishijo et al. (1994) examined the mortality in the population from the same region using β2M instead of RBP as an indicator of tubular dysfunction. Although they found an increased mortality in subjects with increased β2M "most deaths were due to non-specific cardiac disease such as heart failure and cerebro-vascular diseases". A further important fact was that cases with increased total urinary protein were overrepresented and total urinary protein concentrations higher in the group with increased β2M concentrations (Nakagawa et al., 1993). Further analysis of the results presented by these authors (Nishijo et al., 1994) suggests that the group of subjects with increased β2M was not homogenous and included a subgroup of subjects with cardiovascular risk factor (as indicated by increased urinary protein) (Ruggenenti et al., 1998; Grimm et al., 1997) but without increased urinary β2M. Therefore, increased cardiovascular risk factors could be considered as associated with but not due to the cadmium exposure. Finally, an association between individual cadmium body burden and mortality from renal disease was not reported. Taken together, these results suggest that patients with cardiovascular risk factors as indicated by an increased urinary protein concentration could have been overrepresented in the subgroup with increased β2M and that this finding may not have been associated with cadmium exposure. Indeed, others have found that it is unlikely that Cd exposure could be associated with the risk of cardiovascular diseases in a causal way (Staessen et al., 1991 and 2000). It should also be borne in mind that the association between age and β2M excretion has been suggested as a possible source of error (Park, 1991).

In 1999, the same authors published a 15 year follow-up of 3,119 inhabitants living in the same Cd polluted areas of the Kakehashi River bassin (1,403 men, and 1,716 women) (Nishijo et al., 1999). The age-specific cumulative survival curves were lower with increasing Cd-U measured in 1981-82 (< 5, 5-9.9, 10-19.9 and > 20 µg/g creatinine), suggesting a dose-response relationship between Cd exposure and mortality. As this study is an extension of the previous follow-up published by Nakagawa et al. (1993), the same comments hold for the present report.

To summarise, these studies from the Kakehashi River basin are compatible with Cd causing ESRD but other explanations seem plausible as well.

Studies from Japan: Sasu, Nagasaki Prefecture

In their historical cohort study, Iwata et al. (1991) examined the mortality of 256 subjects (participation rate over 80%) living in a Cd-polluted area. After a 10-year follow-up, 65 subjects (25.4%) had died. In a subgroup of residents (with a urinary β2M concentration greater than 1,000 µg/g creat in 1979), observed deaths were greater than expected. Using a Cox's proportional hazard model, the influence of age, mean blood pressure, Cd-U, and β2M on all causes mortality was examined. β2M proved to be a predictor of mortality in men (but not in women) whereas Cd-U was not ($p > 0.4$). The association between β2M and mortality in men only is surprising because both β2M and Cd-U concentrations were higher in women than in men. Cause-specific mortality was not calculated because of "uncertainty of the diagnosis". It is reported that the serum creatinine concentration of the most severe case was 3.2 mg/100 ml (no further details on serum creatinine or GFR measurements).

To summarise, no straightforward relationship between Cd body burden and uraemia was demonstrated in this study.

Mortality studies conducted outside Japan

The village of Shipham (UK) was contaminated by considerable quantities of toxic metal cadmium from nearby extinct calamine workings. Harvey et al. (1979) have conducted a limited study on 21 adults living in the most heavily polluted areas of the village to measure their liver-cadmium concentration. Their mean age was 53 years (40-62) and they had lived there on the average for more than 20 years, 3 were light smokers and 50% of the vegetables they consumed were of local origin. The mean liver-cadmium concentration in these villagers was 11.0±2.0 ppm which was significantly higher than that of 10 non-Shipham controls (2.2±2.0 ppm) of similar age (Harvey et al., 1979). The results of the survey conducted later in Shipham (Inskip et al., 1982) do neither refute nor support an association between renal diseases and environmental cadmium exposure because of small sample size, crude exposure assessment, and lack of dose-response relationship. A follow-up of the mortality in this cohort has been reported by Elliot et al. (2000). There was an excess mortality from cerebro-vascular disease, hypertension, nephritis and nephrosis (for the latter SMR 128, 95% CI: 99-162). However, it was not possible to separate the diagnoses included in the latter category, so that it remains unclear whether the effect is associated with nephritis or nephrosis (Elliot et al., 2000).

Lauwerys and De Wals (1981) wrote a letter drawing attention to a possible relationship between Cd exposure (environmental) and nephritis and nephrosis. Owing to the limitations of this type of publication, definitive conclusions relative to a causal relationship between Cd exposure and ESRD are not possible.

b) Longitudinal morbidity studies

Besides retrospective mortality studies, there are also publications dealing with the renal function in Cd-exposed subjects followed-up for some years.

Kido et al. (1990) assessed the course of glomerular function in members of the same population as Nishijo et al. (1995). These authors concluded that Cd exposure is capable of causing progressive glomerular damage. Although it cannot be excluded on the basis of the available data that long-term and high-level exposure to Cd in the environment causes glomerular dysfunction, several potential sources of error should also be considered. Indeed, although the renal parameters were non-specific for the effects of Cd, other causes of renal dysfunction were not systematically ruled out. Moreover, there was no clear dose-effect relationship, latency time did not show a consistent trend, it seems possible that the definition of the groups was based on criteria defined a posteriori, and it is not clear whether the study population was a representative sample of the whole exposed population.

In the longitudinal study by Kido et al. (1988) only tubular markers were considered and it is not known whether the subjects examined are the same as those included in the publication of 1990.

The frequently cited study of Nogawa et al. (1984) included glomerular markers but was a cross-sectional study, a design that is not very suitable to establish a causal relationship.

c) Case reports and case series

A case series including four persons exposed to cadmium and diagnosed with uremia is discussed by Tsuchiya (1992) and Kido et al. (1990) reported one case of renal insufficiency attributed to environmental exposure. Nagakawa et al. (1990) described briefly an autopsy series but it is unclear whether Cd-induced renal failure was the main cause of death (original report is available in Japanese only). Although case reports and case series are useful for drawing attention to some problem, they are weak study designs to demonstrate the existence of a causal relationship.

Annex D Kidney effects

Buchet et al. (1990). Renal effects of cadmium body burden of the general population. Lancet 336:699-702 – Detailed calculations.

In the logistic model, the probability of "elevated" value is:

$P=1/1+\exp-(a+ß_1X+ß_2Y)$

Table D.1 Parameters of the logistic model

	ß coefficient	SE on ß	p value
Constant	-1.5793	0.3906	< 0.001
Age	-0.0303	0.0088	< 0.001
U-Cd*	1.6093	0.4087	< 0.001

SE Standard error
* Cd-U is expressed as log µmol Cd-U/24h centered on the mean of the group (0.837 µg/24h)

Therefore, at age 47 years and Cd-U=2 µg/24 hours (centered log = 0.378)

$P=1/1+\exp-(-1.5793+1.6093 \cdot 0.378-0.0303 \cdot 47)$

= 0.084 or about 10% probability of elevated Ca-U

Probability of elevated Ca-U

Table D.2 Probability of elevated Cd-U

	Age 40 years	Age 50 years
Cd-U (µg/24hours)		
0	0.058	0.045
1	0.065	0.049
2	0.101	0.076

Järup et al. (2000). Low level exposure to cadmium and early kidney damage: the OSCAR study Occup Environ Med 57:668-672 - Detailed recalculations based on the raw data provided by the authors.

1) Total population

In a logistic regression analysis the estimated probability (p) can also be expressed as:

$p = [\exp(a + ß_1X + ß_2Y)]/[1 + \exp(a + ß_1X + ß_2Y)]$

Table D.3 Parameters of the logistic model

	ß coefficient	SE on ß	95% CI	p value
Constant	-5.07	0.428	-5.908 to -4.227	< 0.001
Age	0.056	0.007	0.0425 to 0.070	< 0.001
U-Cd	0.295	0.086	0.125 to 0.464	0.001

CI Confidence intervals

Therefore, at age 53 years and Cd-U=1.2 µg/g creat,

p = exp(-5.07+ 0.056 · 53 + 0.295 · 1.2)/(1 + exp(-5.07 +0.056 · 53 + 0.295 · 1.2))

= 0.147 or about 15% probability of elevated HC values.

Probability of HC proteinuria

Table D.4 Probability of HC proteinuria

	Age 40 years	Age 53 years
Cd-U (µg/g creatinine)		
0	0.056	0.10
1.2	0.078	0.15
2.62	0.113	0.20

<u>2) Subgroup after exclusion of individuals with occupational exposure</u>

Table D.5 Parameters of the logistic model

	ß coefficient	SE on ß	p value
constant	-5.02	0.476	< 0.001
Age	0.045	0.007	< 0.001
U-Cd	1.535	0.297	0.0001

Probability of HC proteinuria

Table D.6 Probability of HC proteinuria

	Age 52-y
Cd-U (µg/g creatinine)	
0	0.06
0.5	0.13
1.0	0.24

Annex E *In vitro* studies

Some *in vitro* studies were conducted in an attempt to elucidate about the mechanism of the developmental and reproductive effects associated with an exposure to cadmium (generic). These studies were performed with water-soluble cadmium compounds.

No study specifically using cadmium oxide was located. One study using cadmium metal is reported here.

Studies have suggested that Cd accumulates in the placenta and exerts its toxicity either directly by creating placental damage or through perturbation of placental transport of nutrients such as calcium and zinc.

Wier et al. (1990) perfused lobes of placenta from normal-term deliveries of non-smoking women with cadmium (as cadmium chloride) at 0-11 mg/l for up to 12 hours. Cadmium content in the perfused tissue was dose-dependent. Alterations of circulatory parameters appeared at doses of 2.2 and 11 mg/l and were correlated with ultra structural alterations (between 5 and 8 hour perfusion): stromal oedema appeared with microvesicular changes in the endoplasmic reticulum, mitochondrial swelling in the syncitiotrophoblast; followed by subsyncitiotrophoblastic vesiculation and finally necrosis of the trophoblast (occurring between 5 and 8 hours of perfusion). There were no effects reported on glucose consumption or lactate production. However, cadmium (at 1.1 mg/l) reduced the placental transfer of zinc into the foetal circuit (Wier et al., 1990). Page et al. (1992) reported that cadmium at 5-50 µM inhibited zinc uptake by placental microvillous membranes (Page et al., 1992 cited in Lin et al., 1997).

Cadmium may also perturb the placental transport of calcium. To investigate the involved mechanism, Lin et al. (1997) used a human choriocarcinoma cell line, which exhibits trophoblastic properties. Culture medium contained low concentrations (0.04, 0.16, 0.64 µM) of cadmium as $CdCl_2$. Cadmium treatment at low, physiological doses (0.04 µM), for 24 hours did not compromise cellular integrity but decreased cellular calcium uptake and transport, calcium ion binding and modified intracellular Ca^{2+} profile. Higher doses (≥ 16µM) affected cell integrity (as assessed by lactate dehydrogenase release). The 24-hour treatment resulted also in a reduced expression of the trophoblast-specific cytosolic Ca^{2+}-binding protein (HcaBP). These results suggested that cadmium exposure compromised the calcium handling ability of trophoblastic cells as a consequence of alterations in subcellular, cytosolic Ca^{2+} binding activities (Lin et al.,1997).

Wier et al. (1990) also reported that the perfusion of cadmium (as cadmium chloride) in lobes of placenta decreased the synthesis and the release of human chorionic gonadotropin at all experimental concentrations (0-11 mg/l). This was confirmed by the study of Eisenmann and Miller (1994) that compared the toxicity of cadmium (2.2 mg/l) and selenium in a similar experimental system.

Cadmium induces the synthesis of metallothionein which may exert a protective effect against the toxicity of several heavy metal ions. To illustrate this and also the competition with other elements such as zinc, Lehman and Poisner (1984) used an *in vitro* system and studied the induction of metallothionein in human tissues exposed to Cd or Zn. Human chorionic trophoblast cells were exposed to different concentrations of cadmium (compound not specified): for dose-response experiments, Cd (1-32 µM) or Zn (5-20 µM) was added and incubation was continued for 24 hours. For time-course experiments, doses of 0.5-2 µM Cd were applied in medium and incubation was continued for 8, 24 or 48 hours. To determine the effect of simultaneous addition of Cd and Zn, an experiment was done in which Cd (0.5, 1µM) and Zn (2.5, 5µM) were added separately or together to the cells and incubation was continued for 24 hours.

Concentrations of cadmium as low as 0.5 µM significantly increased MT synthesis. Higher concentrations of zinc were required to obtain the same phenomenon (2.5 µM). When the cells were exposed to the metals for 24 hours, the increased MT levels remained elevated at least 48 hours after removing Cd or Zn. When Cd and Zn were applied simultaneously to the trophoblasts, the resulting increase in the concentration of MT was similar to the increase in MT found in cells exposed to Cd alone (data reported on histogram).

Cd has been reported to bind MT approximately 3,000 times more strongly than Zn (see Section 4.1.2.2). It has been reported that Cd may displace zinc, by competing for the same binding site. The results of this study demonstrated the ability of cultured human trophoblasts to synthesise MT in response to Cd or Zn and that lower concentrations of cadmium than zinc are required for this synthesis.

Considering this, authors concluded that MT synthesised in foetal membranes may play a role in protecting the foetus from cadmium-toxicity (Lehman and Poisner, 1984).

In relation to a possible role of cadmium in mechanisms of preterm labour, effects of cadmium on the activity of myometrial strips from term pregnant women were examined by Sipowicz et al. (1995). Cadmium (Cd^{2+}) in a concentration of 10^{-9} M inhibited spontaneous contractile activity. Responses to Ca^{2+} and oxytocin were significantly increased by exposure to cadmium in low concentrations (10^{-9} M), whereas higher concentrations (10^{-3} M) had inhibitory action. These results suggest that cadmium not only blocks Ca^{2+} channels in the human myometrium, but also interferes with intracellular mechanisms involved in excitation-contraction coupling. The increased responses to Ca^{2+} and oxytocin in the presence of low amounts of Cd^{2+} support a role of cadmium in mechanisms of preterm labour (Sipowicz et al., 1995).

Clough et al. (1990) reported that cultured rat Sertoli cells were more sensitive to cadmium chloride than interstitial (primary Leydig) cells. Different cell populations within a same tissue differed markedly in susceptibility to the toxicant: the 72-hour LC_{50} for Sertoli and interstitial cells were 4.1 and 19.6 µM, respectively. Because the Sertoli cell provides support for the seminiferous epithelium, the differential sensitivity of this cell may in part explain cadmium-induced testicular dysfunction, particularly at doses that leave intact the vascular epithelium (Clough et al., 1990).

Laskey and Phelps (1991) also showed a reduction of rat Leydig cell function following *in vitro* exposure to cadmium chloride at concentrations of 1 to 5,000 µM for 3 hours (Laskey and Phelps, 1991, cited in IARC 1993).

The toxicity to the human spermatozoa of cadmium metal (200 mm^2 in a flask) was already tested by Holland and White in 1979. Human ejaculates were obtained and motility of the spermatozoa was estimated before to be incubated with the metal for 3 hours under constant shaking. Oxygen uptake, glucose utilisation and oxidation, lactate accumulation were also measured. Cadmium reduced significantly the percentage of motile spermatozoa (73.0 ± 2.5% and 43.0 ± 2.0% at 0 and 3 hours respectively) and decreased the quantity of glucose used by the spermatozoa. As cadmium had a detrimental effect on the motility of the spermatozoa but only moderately depressed glycolysis and had even less effect on oxidative metabolism, authors suggested that cadmium may specifically inhibit the motility apparatus of the spermatozoa (Holland and White, 1979).

Fertility of ejaculates of rabbit sperm after *in vitro* exposure to $CdCl_2$ (0.02-0.05-0.1 mM) was tested by Foote (1999). Semen was washed to remove seminal plasma and minimise possible bindings of the metal by proteins. Exposure of the sperm was followed by insemination of superovulated does. The concentrations used to treat the sperm *in vitro* were, as reported by the authors, higher than the concentrations found in semen and/or blood of men exposed to heavy metals in occupational studies. The tested concentrations of Cd^{2+} did not reduce hyperactivity of the sperm. The fertility tests also resulted in little or no difference, consistent with the findings that Cd did not affect the proportion of hyperactive sperm , a variable often associated with capacitation (required for fertilisation) (Foote, 1999).

Conclusions: in vitro studies

Most of the located studies have used water-soluble cadmium compounds and not cadmium metal or cadmium oxide.

Different mechanisms, which may account for reprotoxic effects of cadmium, have been suggested, involving a direct placental damage, an indirect action via a perturbation of the placental transport of other nutrients or an effect on the synthesis or release of human chorionic gonadotropin.

Some cell populations (Sertoli cells) were reported to be more susceptible than others to a toxic effect of cadmium compounds, which could explain the rather specific action of cadmium compounds on the testes in experimental animals when injected.

Cadmium metal appeared to reduce motility of human spermatozoa *in vitro* after 3 hours of incubation. This was not observed with rabbit sperm exposed to cadmium chloride.

Although, some mechanistic explanations are suggested, no definite conclusion can be drawn from these *in vitro* studies about the toxicity of cadmium oxide/metal.

Annex F The occurrence of cadmium (metal) in products according to the Swedish product register

Trades that use products containing metallic cadmium and product functions.

Trade	Product functions
Paint industry	Activators* Dyestuffs, pigments Fillers (plastic, paint,…)
Industry for rubber products	Activators* Dyestuffs, pigments Fillers (plastic, paint,…)
Industry for ceramic tiles and flags	Activators* Dyestuffs, pigments Fillers (plastic, paint,…)
Treatment and coating of metals; workshops for gen. mech. engin.	Activators* Degreasing agents* Dyestuffs, pigments Fillers (plastic, paint,…)
Retail trade; repair shops	Adhesives, glues* Cast compounds*
Fabricated metal products, except machinery and equipment	Alloy metals* Fillers (plastics, paint, etc)
Soap and detergents, cleaning and polishing preparations	Corrosion inhibitors* pH-regulating agents*
Textile	Dyestuffs, pigments
Pulp, paper and paper products	Dyestuffs, pigments
Other organic basic chemicals	Dyestuffs, pigments
Agricultural establishment and related	Feedstuff/feedstuff additives*
Basic metals industry	Metal surface coating agents*
Glass and glass products industry	Other paints and varnishes, solvent-based*
Whole sale and retail	Paints, varnishes*
Pharmaceutical preparations	Skin protection agents*

* Less than three products in the product category

In total 35 products (total volume less than 1 ton per year) whereof two consumer products with a cadmium concentration lesser or equal at 10% of the product (Swedish Product Register for the year 1996, 15/09/97). No further details could be identified related to these latter products (KEMI, pers. com 2000/2001)

Annex G The occurrence of cadmium oxide in products according to the Swedish product register

Trades that use products containing cadmium oxide and product functions.

Trade	Product functions
Industry for radio, television and communication apparatus	Contact agents*
Treatment and coating of metals; workshops for gen. mech. engine.	Electrolytes*
Industry for glass and glass products	Enamels, glazes Paints, varnishes*
Industry for ceramic products, other than non-refractory for construction purposes	Enamels, glazes
Industry for plastic products	Intermediates (plastic manufacture)*
Manufacture of chemicals and chemical products	Metal surface treatment agents*

* Less than three products in the product category

In total 45 products whereof 37 with a cadmium concentration less than or equal at 10% of the product. Mainly in the Industry for glass and glass products and Industry for ceramic products with the following use/function: enamels, glazes. The Register further mentions seven products with a substance concentration in the range 10-20% and 1 product with a high (80-100%) content. No consumer products have been registered. The overall total volume accounts for less than 1 ton per year. (Swedish Product Register for the year 1996, 15/09/97).

Annex H Check-list for evaluating epidemiological studies

(check-list established by Professor Philippe Hotz from the Institut für Sozial- und Präventivmedizin der Universität Zürich)

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ABTEILUNG FÜR ARBEITS-
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CROSS-SECTIONAL STUDIES.

1. Other publications on the same population.

Consider possible overlapping with other studies by quite different authors which included part of the same study population.
If relevant : on the first page indications about possible redundancy (part of the same authors have already published results on part of this study population). Indicate references for easy retrieval of publications. Briefly comment on differences / similarities between former and latter pubications and justify the exclusion of the study not considered.

2. Location.

Country / region / institution (selection bias !).

3. Purpose

precisely defined ?

4. Study population

4.1. and 4.2. Exposed and nonexposed.

- size of study population, men /women, age. If possible : socioeconomic class, smoking, alcohol, and other relevant factors in that context.
- is the study population young ?
- definition of the study population :
a) beginning of work at...

b) end of work at ...; b) if sequential cross-sectional study or inclusion of retired workers
c) minimal duration;

d) all workers presently working and exposed ? Retired and currently nonexposed workers ? Time since last exposure ?

Are workers previously diagnosed with poisoning included ?

4.3. Final study population.

- initial vs final study population (as a summary showing the lost cases and controls at each step of constitution of study population with the most important data on age, sex, employablity, and other important variables in that context).
- comparability of cases and controls as for : age, sex, socioeconomic group, education, and other important variables in that context.
Are workers previously diagnosed with poisoning included ?
IMPORTANT : considerable differences may be found between initial and final study population. A presentation of the results (for example in tables) should take this issue into account.

5. Selection, participation rate, representativeness.

- selection of the study population
- selection of the study sample
- participation rate
- representative sample ?

If sequential cross-sectional study : are the samples comparable ?

6. Exposure.

6.1. Specific aspects : exposed workers

Is the word "exposed" clearly defined (with respect to type, minimal intensity, duration, frequency ?). Observational period (if not mentioned under 4.; important because of time-related changes of exposure intensity) ? Previous poisonings ?

- type :
== general population or industry ?
== type of industry (for example Cd exposure : cadmium production, alloys, soldering and/or cutting, Cd-Ni battery, etc.) ?
== is "exposure" defined by occupation and/or industry, group of agents, agent ? Are the groups specific or very broad (= how specific if this definition ?) ? Are concomitant exposures possible (for example : heavy metals vs Cd + As inorg or Pb or Ni vs Cd only ? Benzene in garages, oil refineries, printing plants represent three quite different exposure conditions).

- information on exposure frequency, duration, and intensity :
== yes/no
== only present exposure (strictly cross-sectional) or information on previous exposure (in this plant, in the same occupation but in other plants, in all occupations for the lifetime)
== minimal intensity, duration, frequency : based on exposure reconstruction or objective measures ?
== if exposure reconstruction : type of variable (dichotomous if exposed vs nonexposed, ordinal, exposure score, etc.) ?
== if dichotomous classifications : is the cut-off clearly described, credible, arbitrary ? Are minimal intensity, duration, frequency taken into account to define the word "exposed" ?
== if ordinal categories or of exposure score : is the classification / score credible, consistent ? Is there any indication of the validity of the classification / score ?
== objective measures available ? air sampling (area vs. personal, total vs respirable dust); biol.monitoring (blood/urine/neutron activation analysis/x-ray fluorescence, etc.)

samples from controls and exposed workers examined in the same series ?
quality control (exposure assessment) ?

6.2. Specific aspects : control workers

6.3. Summary

7. Diagnosis.

Is the endpoint clinically relevant (predictive value) ? Methods ? Quality control ?

If relevant :
Classification scheme
Are there objective criteria required for ascertaining diagnosis (example : FAB, SLE) ?
Blind review of medical records, slides, if any ?
Panel review ?
Other important methodologic aspects (example : biopsy for kidney diseases, immunofluorescence for glomerulonephritis, histolological confirmation for cancer).

8. Bias.

- preplacement examination
- healthy worker effect
- is it clear that the endpoint is really an effect of the exposure (cross-sectional design !)

9. Interview and coding, laboratory.

Blind interview / interview procedure / structure and content of the interview.
Blind coding of the answers / coding according to .... (are criteria mentioned, credible, arbitrary).

samples from controls and exposed workers examined in the same series and quality control (exposure assessment : see exposure). Are these units adequate and do they consider age- or sex-relaed differences (mg/l, mg/g, mg/24h for metabolite; ml/mn or ml/mn/1.76m2 for clearance)

10. Design and statistics.

- design
- control population : regional, other industrial workers, office workers, low vs high exposure (definition of control group : see 4.2.; exposure assessment in the control group : see 6.2.)
- statistical methods

11. Confounding factors

Age, sex, hospital, smoking, alcohol ?
If relevant : socioeconomic group, residence, genetic / familial factors, ethnicity, race. Are these factors clearly defined (nationality may change after wedding) ? If subgroups are used are these subgroups relevant ?

Considerable sources of misclassification ? (for exposure and disease see 6. and 7., respectively)

IMPORTANT : were the confounding factors taken into account in the analysis or were they only mentioned as items in the interview and not considered in the statistical analysis ?

12. Results.
12.1. Results
12.2. What about power ?

13. Identification, latency, DRC.

Identification : of a specific causal agent, specific causal occupation ?
Latency time (lagging of some years) : yes / no ? biologically credible ?
Dose - response curve : was it examined ?

14. Physiopathology.

Physiopathologial mechanisms

15. Miscellaneous.

26.9.1997

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ABTEILUNG FÜR ARBEITS-
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RETROSPECTIVE COHORT STUDIES, MORTALITY.

1. Other publications on the same population.

. Consider possible overlapping with other studies by quite different authors which included part of the same study population. If relevant : on the first page indications about possible redundancy (part of the same authors have already published results on part of this study population). Indicate references for easy retrieval of publications. Briefly comment on differences / similarities between former and latter pubications and justify the exclusion of the study not considered.

2. Location.

Country / region / institution.

3. Purpose

precisely defined / hypotheses - generating

4. Study population

4.1. and 4.2. Exposed and nonexposed.

- cohort size, men /women, age, number / percentage of deaths (obs. /exp. numbers of deaths). If possible : socioeconomic class, smoking, alcohol, and other relevant factors in that context.
- is the percentage of deaths higher than 10 % ?
- is the cohort young ?
- definition of the cohort :
a) begin of work at...
b) end of work at ...
c) minimal duration
d) other characteristics

Definition of follow - up : begin / end of follow - up
Are workers previously diagnosed with poisoning included ?

4.3. Final study population.

- initial vs final study population (as a summary showing the lost cases and controls at each step of constitution of study population with the most important data on age, sex, employablity, and other important variables in that context).
- comparability of cases and controls as for : age, sex, socioeconomic group, education, and other important variables in that context.
Are workers previously diagnosed with poisoning included ?
IMPORTANT : considerable differences may be found between initial and final study population. A presentation of the results (for example in tables) should take this issue into account.

5. Selection, participation rate, representativeness.

- selection
- participation rate
- representative sample
If register : is the coverage good ?
If morbidity / mortality statistics : data quality ?

6. Exposure.

6.1. Specific aspects.

Is the word "exposed" clearly defined (with respect to type, minimal intensity, duration, frequency ?). Observational period (if not mentioned under 2.; important because of time-related changes of exposure intensity) ? Previous poisonings ?

- type :
== general population or industry ?
== type of industry (for example : exposure to heavy metals/to Cd + As inorg or Pb or Ni/or to Cd only ? Benzene in garages, oil refineries, printing plants represents three quite different exposure situations).

== is "exposure" defined by occupation and/or industry, group of agents, agent ? Are the groups specific or very broad (= how specific if this definition ?) ? Are concomitant exposures possible (for example : heavy metals vs Cd + As inorg or Pb or Ni vs Cd only ? Benzene in garages, oil refineries, printing plants represent three quite different exposure conditions).
== if coding of occupations : clearly standardized ? Based on which coding system (for example : Dictionary of Occupational Titles of the Census) ? Blind ?

- information on exposure frequency, duration, and intensity :
== yes/no
== minimal intensity, duration, frequency : based on exposure reconstruction or objective measures ?
== if exposure reconstruction : type of variable (dichotomous if exposed vs nonexposed, ordinal, exposure score, etc.) ?
== if dichotomous and based on death certificates, registers, or similar sources of information : longest, usual, current, last occupation or occupation at diagnosis ?
== if other dichotomous classifications : is the cut-off clearly described, credible, arbitrary ? Are minimal intensity, duration, frequency taken into account to define the word "exposed" ?
== if ordinal categories or of exposure score : is the classification / score credible, consistent ? Is there any indication of the validity of the classification / score ?
== objective measures available ? air sampling (area vs. personal, total vs respirable dust); biol.monitoring (blood/urine/neutron activation analysis/x-ray fluorescence, etc.)

7. Diagnosis.

Classification scheme (ICD, ICD - O, etc.)
Are there objective criteria required for ascertaining diagnosis (example : FAB, SLE) ?
Blind review of medical records, slides, if any ?
Panel review ?
Other important methodologic aspects (example : biopsy for kidney diseases, immunofluorescence for glomerulonephritis, histolological confirmation for cancer).
If death certificates : underlying vs. contributing cause of death.
- high / low mortality rate ?

8. Bias.

- surveillance bias
- changes in the course of the study (for example : job changes in comparison to the job used as exposure surrogate)
- diagnostic access bias
- diagnostic suspicion bias

9. Interview and coding.

Blind interview / interview procedure / structure and content of the interview.
Blind coding of the answers / coding according to .... (are criteria mentioned, credible, arbitrary).

10. Design and statistics.

- design
- SIR, SMR, PMR
- reference population : national, regional, other industrial workers, low vs high exposure
- statistical methods

11. Confounding factors

Age, sex, hospital, smoking, alcohol ?
If relevant : socioeconomic group, residence, genetic / familial factors, race, ethnicity

Considerable sources of misclassification ? (for exposure and disease see 6. and 7., respectively)

Sensitivity analysis ?

IMPORTANT : were the confounding factors taken into account in the analysis or were they only mentioned as items in the interview and not considered in the statistical analysis ? Are these factors clearly defined (nationality may change after wedding) ? If subgroups are used are these subgroups relevant ?

12. Results.
12.1. Results
12.2. What about power ?

13. Identification, latency, DRC.

Identification : of a specific causal agent, specific causal occupation ?
Latency time (lagging of some years) : yes / no ? biologically credible ?
Dose - response curve : was it examined ?

14. Physiopathology.

Physiopathologial mechanisms (plausibility)

15. Miscellaneous.

26.9.1997

European Commission
DG Joint Research Centre, Institute of Health and Consumer Protection
European Chemicals Bureau

EUR 22766 EN **European Union Risk Assessment Report**
cadmium oxide – Part II – Human health, Volume 75

Editors: S.J. Munn, K. Aschberger, O. Cosgrove, W. de Coen, S. Pakalin, A. Paya-Perez, S. Vegro

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The report provides the comprehensive risk assessment of the substance cadmium oxide. It has been prepared by Belgium in the frame of Council Regulation (EEC) No. 793/93 on the evaluation and control of the risks of existing substances, following the principles for assessment of the risks to humans and the environment, laid down in Commission Regulation (EC) No. 1488/94.

Part I – Environment

This part of the evaluation is published in a separate document.

Part II – Human Health

This part of the evaluation considers the emissions and the resulting exposure to human populations in all life cycle steps. The scenarios for occupational exposure, consumer exposure and humans exposed via the environment have been examined and the possible risks have been identified.

The human health risk assessment concludes that there is concern for the endpoints acute toxicity, respiratory irritation, kidney and bone repeated dose toxicity, genotoxicity, carcinogenicity, and effects on fertility and reproductive organs upon inhalation exposure of workers. No concern for any endpoints applies to consumers. With regard to humans exposed via the environment, health risks (kidney, bone and lung repeated dose toxicity plus genotoxicity/carcinogenicity) cannot be excluded.

The conclusions of this report will lead to risk reduction measures to be proposed by the Commission's committee on risk reduction strategies set up in support of Council Regulation (EEC) N. 793/93.

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Toxicology and Chemical Substances (TCS)
European Chemicals Bureau (ECB)

European Union Risk Assessment Report

cadmium oxide

Part II – human health

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