European Chemicals Bureau

Institute for Health and Consumer Protection

European Chemicals Bureau

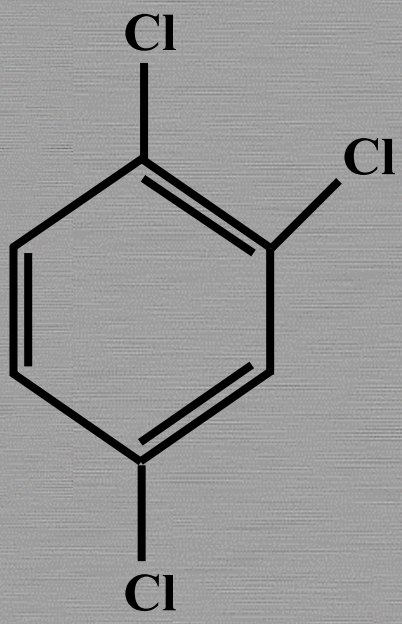
Existing Substances

European Union Risk Assessment Report

CAS No: 120-82-1

EINECS No: 204-428-0

1,2,4-trichlorobenzene



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1,2,4-TRICHLOROBENZENE

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RISK ASSESSMENT

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1,2,4-TRICHLOROBENZENE

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RISK ASSESSMENT

Final Report, 2003

Denmark

This document has been prepared by the Danish Environmental Protection Agency on behalf of the European Union.

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The scientific assessments included in this report have been prepared by the following organisations in co-operation with and by request of the rapporteur:

Institute of Food Safety and Toxicology, The Danish Veterinary and Food Administration.
The Danish Technological Institute.
The Danish National Institute of Occupational Health.
The Danish National Working Environment Authority.

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Final report:	**2003**

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 Toxicity, Ecotoxicity and the Environment (CSTEE) 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.

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.

Barry Mc Sweeney
Director-General
DG Joint Research Centre

Catherine Day
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

CAS-No.: 120-82-1
EINECS-No.: 204-428-0
IUPAC name: 1,2,4-trichlorobenzene

Environment

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.

This conclusion applies to production by the main manufacturers and for atmosphere.

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 is reached because of:

- concerns for effects on the aquatic ecosystem and terrestrial ecosystem as a consequence of exposure arising from the use of the substance as a dye carrier and other uses;
- concerns for sewage treatment plants as a consequence of exposure arising from use as an intermediate, as well as from the use sectors of basic chemicals as a solvent, textile industry as dye carrier and other downstream uses.

Risk reduction measures should be considered that will ensure a reduction in the levels of 1,2,4-trichlorobenzene (1,2,4-TCB) found in the environment. Risk reduction measures in relation to downstream open use resulting in environmental exposure is indicated because of risks identified for STP and soil receiving sludge from STPs. This conclusion is supported by the identified risks to the aquatic environment (including the sediment compartment) in relation to use of the substance as a dye carrier and for "other" downstream uses.

The risk indicated above were identified by employing generic release and exposure scenarios because of lack of specific information of the possible open use and subsequent environmental release of the substance. Recent environmental monitoring data however indicate that such uses and environmental releases may still occur in the EU.

The risk assessment indicates that it should be further investigated if the substance should be considered in relation to national or international programmes addressing persistent organic pollutants.

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.

This conclusion is reached because of:

- concerns for general systemic toxicity as a consequence of repeated inhalation exposure arising from drumming activities in the production of the substance, from the production of products containing the substance in the sector of pigment production and from the use of products containing the substance in the sector of spray painting;
- concerns for eye and respiratory tract irritation as a consequence of repeated exposure to the vapour of the substance arising from the production of products containing the substance in the sector of pigment production and from the use of products containing the substance in the sector of production of plastic pellets;
- concerns for general systemic toxicity and local dermal effects as a consequence of repeated dermal exposure arising from the use of the products containing the substance in the sectors of spray painting, dismantling transformers and polishing.

Adverse effects due to eye/respiratory tract irritation and due to repeated dose toxicity after inhalation and dermal exposure cannot be excluded for workers. Risk reduction measures should therefore be considered that will ensure a reduction in the levels of 1,2,4-TCB found in the workplace during the production of 1,2,4-TCB, the production of 1,2,4-TCB containing products, and the use of products containing 1,2,4-TCB.

Irritating effects on skin after repeated dermal exposure cannot be excluded for workers using 1,2,4-TCB containing products. Proper use of personal protective equipment (PPE) should be recommended.

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

This conclusion is reached because of:

- concerns for effects as a consequence of exposure.

The information and/or test requirements are

- information on occupational exposure during the use of the substance as a dye carrier and as a process solvent, during production of products containing the substance in the sector of production of dielectric fluids and during the use of products containing the substance in the sector of production of wire and cabling.

The need to actually obtain the information allowing the performance of the risk characterisation will be considered when the recommended risk reduction strategy is published in the Official Journal.

In order to make a formal risk characterisation for the scenarios R4 (Use of 1,2,4-TCB as a dye carrier), R5 (Use of 1,2,4-TCB as a process solvent), S4 (Production of dielectric fluids) and T4 (Production of wire and cabling) further information on occupational exposure is necessary.

The actual need to obtain this information allowing the performance of the risk characterisation for these scenarios (R4, R5, S4, and T4) will be considered when the risk reduction strategy is addressed. Hence, any formal request for further information on these processes should be seen in the light of other possible risk reduction measures for these scenarios based on concerns identified elsewhere in this report.

Consumers

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 is reached because of:

- concerns for eye and respiratory tract irritation as a consequence of repeated exposure to vapours and general systemic toxicity as a consequence of repeated inhalation and dermal exposure arising from spray painting and car polishing.

For consumers, adverse effects due to inhalation and dermal exposure cannot be excluded. Risk reduction measures should therefore be considered that will ensure a reduction in the levels of 1,2,4-TCB found during use of products containing 1,2,4-TCB (anti-corrosive paint and maintenance products). However, this conclusion should be seen in the light of a) the products concerned are almost certainly identical to those used by workers, b) for some consumers the use of these products may be highly infrequent, while for others, the use pattern may more closely resemble that of a professional user, and c) it is uncertain whether these products are in fact used at all by consumers.

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.

This conclusion is reached because of:

- concerns for indirect exposure as calculated exposures can exceed WHO TDIs, and WHO guideline values in drinking water for local use scenarios.

Human health (risks from physico-chemical properties)

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

This conclusion is reached because:

- the risk assessment shows that risks are not expected. Risk reduction measures already being applied are considered sufficient.

CONTENTS

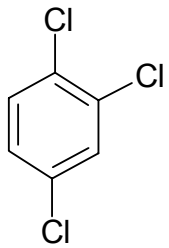
Euses Calculations can be viewed as part of the report at the website of the European Chemicals Bureau: http://ecb.jrc.it

TABLES

1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTITY OF THE SUBSTANCE

CAS-No.:	120-82-1
EINECS-No.:	204-428-0
IUPAC name:	1,2,4-trichlorobenzene
Synonyms:	1,2,4-TCB[4], 1,2,4-trichlorbenzol, 1,2,5-trichlorobenzene, 1,3,4-trichlorobenzene
Molecular weight:	181.46
Molecular formula:	$C_6 H_3 Cl_3$
Structural formula:	



1.2 PURITY/IMPURITIES, ADDITIVES

Purity:	≥ 99%
Impurity:	information from manufacturers (one or more of mentioned below): total tetrachlorobenzenes, ≤0.2% w/w 1,2,3-trichlorobenzene <1% w/w (usually 0.1-0.4%) 1,3,5-trichlorobenzene < 2 % w/w 1,2-dichlorobenzene <0.25 1,4-dichlorobenzene < 0.25% dichlorotoluenes <0.2% 2/4-bromo-chlorobenzenes <0.15%
Additives:	No information

[4] The abbreviation 1,2,4-TCB is used for this substance throughout the report. The abbreviation TCB is used in cases where the substitution position is unspecified. Specific isomers, e.g. 1,2,3-trichlorobenzene are similarly abbreviated to 1,2,3-TCB.

1.3 PHYSICO-CHEMICAL PROPERTIES

Table 1.1 Physico-chemical properties

Physical state	liquid	
Melting point	17°C 16.05°C 16.95°C	Merck Index (1996) BUA (1987) Weast (1975)
Boiling point	213.5°C at 1,013 hPa	Weast (1975)
Relative density	1.456 g/cm^3 at 20°C	BUA (1987)
Vapour pressure	21.5 Pa at 20°C 36 Pa at 20°C 0.29 mm Hg at at 25°C (38.6 Pa) 46.8 Pa at 25°C 80 Pa at 30°C 270 Pa at at 50°C	BUA (1987), Bayer Bayer (1994) US EPA (1980) DIPPR (1998 Bayer (1994) Bayer (1994)
Surface tension	38.5 dyn/cm	US EPA (1977a)
Water solubility	36 mg/l at 20°C 48.8 mg/l at 20°C	BUA (1987), Bayer (1986) Chiou et al. (1983)
Octanol/water	log Kow: 4.2 log Kow: 4.05 log Kow: 4.02 log Kow: 3.93	BUA (1987) Bruijn et al. (1989) Hansch and Leo (1985) Meylan and Howard (1995), calc
Flash point	110°C	DIN 51758, Bayer (1994)
Auto Flammability	≥500°C	DIN 51794, Bayer (1994)
Henry's Law constant	101 Pa m^3/mol (20ºC) 290 Pa m^3/mol (25ºC) 181 Pa m^3/mol (20ºC)	ten Hulscher et al. (1992) EPIWIN (1995), est. calc. according to TGD (1996)
Air calculation factor	1 ppm = 7.42 mg/m^3 (25ºC, 1,013 hPa) 1 mg/m^3 = 0.133 ppm	WHO (1991) WHO (1991)

Comments to physico-chemical data

Purity

The value on purity relates to the pure substance as produced by the main manufacturers. The purity of the technical 1,2,4-TCB is between 70% and 85% (cf. Section 2.1.1) but may be chlorinated and purified up to ≥99%.

Melting point

The melting point data range from 16.1°C to 17.3°C. Most values are literature or handbook citations of which most values concentrate around 17°C (IUCLID, 1996; Ullmann, 1986). The value 17°C is used in the risk assessment.

Boiling point

The boiling point data range from 206°C to 213.8°C. The measured value of 213.5°C at 1,013 hPa (IUCLID, 1996) is used in the risk assessment.

Vapour pressure

Data on the vapour pressure range from 21.5 Pa to 40 Pa at 20°C and from 38 Pa to 56 Pa at 25°C (IUCLID, 1996). Using the melting point 17ºC the QSAR estimation of vapour pressure is 33.2 Pa at 25ºC (EPIWIN, 1995). The measured vapour pressure of 36 Pa at 20°C (Bayer, 1994) is used in the risk assessment for environmental distribution estimations. For EUSES calculations, the vapour pressure of 46.8 Pa at 25 °C calculated by regression (DIPPR) has been used.

Water solubility

The data on water solubility range from 19 mg/l to 49 mg/l. The solubility of pure substance was observed to be 31.3 mg/l (25°C, HPLC, Banerjee, 1984) in distilled water. Korte and Freitag (1986) observed a water solubility of 49 mg/l by the "flask method" (UBA, OECD), a literature value of 30 mg/l, VCI found 36 mg/l and GSF (1982) 19 mg/l at 20°C.

The solubility in water at 25°C was found to be $2.54 \cdot 10^{-4}$ mol/l (46.1 mg/l) by the modified generator column coupled with a HPLC method (Miller et al., 1984) which cites $1.91 \cdot 10^{-4}$ mol/l (34.7 mg/l) as a literature value from Yalkowsky et al. (1979). The value of 30 mg/l (Callahan et al., 1979) is used by the US EPA. Using model calculations based on log Kow 4.02 resulted in a water solubility of 20 mg/l at 25°C and using QSAR based on log Kow and the melting point a water solubility of 33 mg/l at 25ºC was obtained (EPIWIN, 1995).

The water solubility of 36 mg/l calculated from measured values (BUA, 1987; IUCLID, 1996) is used in the risk assessment.

Log octanol/water partition coefficient (log Kow)

The data on log Kow range from 2.33 to 4.8 (IUCLID, 1996). The log Kow, studied using the OECD guideline and the ^{14}C-labelled substance, was observed to be 3.63. The value being a little less than other values could be explained by methodological conditions. Using the "slow stirring" method (Bruijn et al., 1989) resulted in log Kow 4.05. Eadsforth (1986) found by application of reverse phase HPLC a log Kow of 4.21 and Kock and Lord (1987) measured a log Kow of 4.22 also by reverse HPLC. The reverse HPLC is an indirect but rapid method, unaffected by impurities which might affect the shake-flask method (Kock and Lord, 1987) which is cited in Eadsforth (1986) to result in a log Kow of 4.8. The shake-flask method resulted in a log Kow of 4.02 by Chiou (1985).

The log Kow was found to be 3.98 by the modified generator column coupled with a HPLC method (Miller et al., 1984) which cites Yalkowsky et al. (1979) for 4.27 as an experimental value. Köneman et al. (1979) using HPLC found an experimental log Kow of 3.94. The mean log Kow value from literature (n=10) was 4.06 (Rippen, 1991). The Medchem database containing evaluated and recommended log Kow values (LOGPSTAR) recommends a log Kow of 4.05 (Sabljic et al., 1995).

Based on fragment structure analyses, the log Kow is estimated to be 3.93 (EPIWIN, 1995; Meylan and Howard, 1995).

Giving heavier weight to direct measurement than to indirect HPLC methods and evaluating the "slow stirring" method to be preferred in this case (Chessells et al., 1991), the log Kow value of 4.05 is used in the risk assessment.

Hydrolysis

The hydrolysis was studied in buffer solutions at pH 3, 7 and 9 using radioactive 1,2,4-TCB at the initial concentration of 17.7 mg/l. During a study period of 5 days, the half-lives of 1,2,4 TCB at 50°C were estimated to be 1,806 hours (75 days) at pH 3, 4,577 hours (190 days) at pH 7 and 6,889 hours (287 days) at pH 9 (Korte and Freitag, 1986). The large half-lives for hydrolysis which indicate hydrolytic stability mean that it has not been taken into account in the risk assessment.

1.4 CLASSIFICATION

Classification and labelling according to the 28th ATP of Directive 67/548/EEC[5]:

Classification

Xn; R22	Harmful if swallowed
Xi; R38	Irritating to skin
N; R50-53	Very toxic to aquatic organisms. May cause long-term adverse effects in the aquatic environment.

Specific concentration limits: None

Labelling

Xn; N
R: 22-38-50/53
S: (2-)23-37/39-60-61

[5] The classification of the substance is established by Commission Directive 2001/59/EC of 6 August 2001 adapting to technical progress for the 28th time Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances (OJ L 225, 21.8.2001, p.1).

2 GENERAL INFORMATION ON EXPOSURE

1,2,4-Trichlorobenzene (1,2,4-TCB) is a synthetic organic chemical which is not known to occur as a natural chemical. 1,2,4-TCB is manufactured and used in the chemical industry as an intermediate in closed systems in the manufacture of herbicides and higher chlorinated benzenes. Furthermore, 1,2,4-TCB is used as a process solvent (IUCLID, 1996), as a dye carrier, in metal working fluids, and sprays as a corrosion inhibitor (Nordic Product Registers, 1997). Significant quantities may still be used in existing electrical equipment as a dielectric fluid, solvent, and heat transfer medium (Hooftman and Kreuk, 1982; US EPA, 1984; Soldner and Gollmer, 1982; BUA, 1987; Srour, 1987; UBA, 1998). Unintentional release and leakage e.g. during use, recycling or disposal of existing electrical equipment may therefore occur.

Former uses include use of the substance in degreasing agents, septic tanks and drain cleaners, wood preservatives, and abrasive formulations (US EPA, 1980). It has also been reported as being used as a termite exterminator (Carlson, 1977). It has not been possible totally to exclude that such uses still occur.

Besides direct exposure from production and use of 1,2,4-TCB, indirect exposure may take place from the forming of trichlorobenzenes during the combustion of organic material when chlorine is also present (for example during incineration of waste, PVC, and other plastic materials). 1,2,4-TCB is also formed during industrial cracking or environmental degradation of hexachlorocyclohexanes (HCH) and other higher chlorinated benzenes (cf. Sections 2.1 and 3.1, respectively).

2.1 PRODUCTION

2.1.1 Production methods

The following production methods exist:

1. 1,2,4-TCB is manufactured by chlorination of benzene and further chlorination of mono- and dichlorobenzenes in the presence of various catalysts (e.g. sublimed ferric chloride, anhydrous aluminium chloride, stannic chloride, iron or aluminium). The reaction is exothermic. Hydrogen chloride is formed as a by-product (Ullmann, 1986):

$$C_6H_6 + Cl_2 \rightarrow C_6H_5Cl + HCl \quad (-131.5\ kJ/mol)$$
$$C_6H_5Cl + Cl_2 \rightarrow C_6H_4Cl_2 + HCl \quad (-124.4\ kJ/mol)$$
$$C_6H_4Cl_2 + Cl_2 \rightarrow C_6H_3Cl_3 + HCl \quad (-122.7\ kJ/mol)$$

After one chlorine has substituted onto the benzene ring, further substitution takes place principally in the ortho and para positions. All three dichlorobenzenes yield a preponderant amount of 1,2,4-TCB on further chlorination (US EPA, 1977a).

The process results in a mixture of various chlorination stages and isomers which are separated by fractionated distillation. The main product is 1,2,4-TCB and the proportion of 1,2,3-TCB is about 15% (BUA, 1987). The impurities in crude trichlorobenzenes mainly consist of isomers and homologues. To obtain higher purity, further purification or distillation methods are used.

2. 1,2,4-TCB can be obtained more directly by starting with pure 1,4-dichlorobenzene. Because of the directing influence of the chlorine substituents present, only 1,2,4-TCB and higher chlorobenzenes are formed (Ullmann, 1986).

3. Another production method is based on the *dehydrohalogenation* of 1,2,3,4,5,6-hexachlorocyclohexane (stereoisomeric mixture) which is a by-product of gamma-hexachlorocyclohexane ("Lindane") production. In the presence of catalysts, hexachlorocyclohexane is converted mainly to trichlorobenzenes at temperature of 90-250°C. The yield lies between 80 and 99% with the product mixture consisting of 70-85% 1,2,4-TCB and 13-30% 1,2,3-TCB (Ullmann, 1986).

According to Srour (1989, 1994), most trichlorobenzenes available on the market are obtained through hexachlorocyclohexane cracking. Hexachlorocyclohexanes are manufactured as part of the synthesis of the gamma isomer (gamma-HCH, "Lindane") which is obtained by subjecting cyclohexane to a photochlorination reaction. The resulting mixture contains about 15% of gamma isomer and the rest is a mixture of hexachlorocyclohexane isomers which can only be upgraded to trichlorobenzenes by cracking (Rhône-Poulenc, pers. comm. 1996).

2.1.2 Former production in the EU

A total of 14,000 tonnes of 1,2,4-TCB were manufactured in Europe in 1988 (Bayer, 1995). Fifty percent of the production was exported and the other 50% used in manufacturing.

Literature values on 1,2,4-TCB production and end-use:

- EU: 16,000 tonnes in 1983 (Wagner et al., 1989)
- EU: 17,000 tonnes in 1983, 14,000 tonnes in 1988 (Srour, 1989), 9,000 tonnes in 1993 and 6,000 tonnes in 1995 (Srour, 1996), cf. **Table 2.1**.

Table 2.1 Production and use of trichlorobenzenes in Western Europe 1983, 1988, 1993, and 1995 (Srour, 1989; 1996)

Years	1983	1988	1993	1995
Production	17,000	14,000	9,000	6,000
Imports	500	-	-	-
Exports	7,000	7,000	5,000	3,500
Consumption	9,500	7,000	3,700	1,800
of which:				
Dielectric fluids	1,500	1,200	500	-
Solvent uses	3,300	3,500	1,400	-
Manufacture of Tetrachlorobenzenes	3,000	-	-	-
- Dichlorophenols	400	-	-	-
- Aclonifen	-	1,000	1,500	1,500
- Trichloroaniline	200	250	300	300

The production of 1,2,4-TCB was 1,000-5,000 tonnes in 1993 in Germany (IUCLID, 1995).

Table 2.2 Main manufacturers of trichlorobenzenes in Western Europe

Country	Company	Reference
Germany	Bayer AG, Leverkusen Hoechst AG, Frankfurt am Main	IUCLID (1995), BUA (1987), Hooftman and Kreuk (1981), Ullmann (1986) BUA (1987), Hooftman and Kreuk (1981), Ullmann (1986)
France	Rhône-Poulenc, Paris ESAR S.A. ELF Atochem S.A. Produits Chimiques Ugine Kuhlmann S.A.	IUCLID (1995), BUA (1987), Hooftman and Kreuk (1981), Ullmann (1986) IUCLID (1995) IUCLID (1995) Ullmann (1986)
Italy	ACNA Aziende Colori Nazionale Affini, Milano Anic SpA	Hooftman and Kreuk (1981) Ullmann (1986)
Spain	Ugimica	BUA (1987)
United Kingdom	unknown	Atri (1985)

During 1994, Rhône-Poulenc stopped the production of Lindane and 1,2,4-TCB by its cracking. The pure 1,2,4-TCB is now produced by distillation by Halterman and sent back to be used as an intermediate in the synthesis of a pesticide by Rhône-Poulenc in a continuous process in a closed system. Emissions are expected to occur at reactor loading and sampling (Rhône-Poulenc, personal communication, 1996).

2.1.3 Current production in the EU

According to the manufacturers, there are two major manufacturers in the EU which were high-production volume producers between 1990 and 1993: Bayer in Germany and Rhône-Poulenc in Belgium (Halterman, Antwerp). One of them is distilling trichlorobenzene mixtures and the other chlorinating dichlorobenzene. The two manufacturers produced together approximately 7,000 tonnes in 1994/1995, but they have provided information showing a slight decrease in the level of production and marketing since then. There are no UK manufacturers of 1,2,4-TCB (HSE (UK), 1999).

According to these major manufacturers, the EU production was approximately 7,000 tonnes in 1994/1995. Based on information from these major manufacturers, 75% to 90% of the production was exported, and the average export was 80%. Twenty percent (1,400 tonnes) of the production was used or sold in the EU.

The rapporteur has been informed about specific plans on a temporary production in a Member State of approximately 3,000 tonnes of 1,2,4-TCB from a HCH ("Lindane") dumpsite during 1998 to 1999. The manufacturers have not submitted a HEDSET as they are not legally obliged to do so according to the Council Regulation 793/93. Therefore an assessment of the release, exposure and risk of TCB produced by this current additional major manufacturer has not been included in this report.

The recent production, import/export and use are summarised in **Table 2.3**.

Table 2.3 Production, import, export and consumption in the EU in tonnes/year (manufacturer data, 1996, covering 1994/95)

	Production (t)	Import (t)	Export (t)	Consumption (t)
Total	7,000	2,000	7,600	1,400

The values presented in **Table 2.3** are used in the risk assessment.

2.2 USE PATTERN

From 1994 to 1995, 1,2,4-TCB was predominantly used as an intermediate in the manufacture of herbicides and as a process solvent in closed systems (Bayer, 1996). Besides, 1,2,4-TCB has other minor uses as a solvent, a dye carrier, a corrosion inhibitor, etc.:

Main category: Produced in continuous production process (Ib)

Industrial category: Chemical industry: used in synthesis
Chemical industry: basic chemical
Textile industry

Use category: Intermediate
Dye carrier
Additive (including dielectric fluid additives)
Process solvent
Corrosion inhibitor and minor diverse uses

The use is divided in several minor categories.

The use can be broken down into use for (BUA, 1987):

40-60% used as an intermediate
<5% dye carrier in the textile industry
<5% as a solvent or extraction
30-50% exported outside the EU

Information on the use of 1,2,4-TCB outside the EU is limited. The Australian authorities report that it is unlikely that 1,2,4-TCB is in use in significant quantities in Australia, but that it has been used as a dye carrier in the past, perhaps as recently as five years ago. Further, it may have been used in dry cleaning (NICNAS, 1998).

Intermediate

Other uses are associated with textile auxiliaries and pesticide production where 2,5-dichlorophenol serves as an intermediate in the manufacturing (e.g. hydrolysed to 2,5-dichlorophenol and processed to 2,5-dichloro-6-methoxybenzoic acid (*dicamba*)) (Srour, 1994; Ullmann, 1986). According to Slooff et al. (1991), 1,2,4-TCB may also be used in the production of the pesticide 1,2,4-trichloro-5((4-chlorophenyl)-sulfonyl)-benzene (*tetradifon*). The UK usage has dropped dramatically in the last few years and is now around 5 tonnes annually and 1,2,4-TCB is no longer used in the production of insecticides in the UK. The main impetus behind this decline is environmental factors and it is likely that this trend will continue (HSE (UK), 1999).

Dye carrier

Where used as a dye carrier, 1,2,4-TCB is mixed with a disperse dye and a levelling agent and then applied to mainly polyester materials for several hours at 100°C (US EPA, 1977a). According to Ullmann (1986), 1,2,4-TCB is used as a dye carrier and via 2,4,5-trichloronitrobenzene and 2,4,5-trichloroanilin in the production of dyes and pigments.

According to information from the major manufacturers, the use as a dye carrier is recommended to be substituted by other substances. According to a survey by the German textile association (TEGEWA) concerning the use of trichlorobenzene as a dye carrier, the use is substituted in most countries. However, it is stated that a few companies may still use trichlorobenzene e.g. in Belgium (Bayer, letter 22.11.1996). Supporting evidence for the use of TCB in the industry (chemical, paint, and textile industry) is found in monitoring data from 1993 in France where residues of 1,2,4-TCB in effluents from especially textile industries indicate that the substance may still be used as a dye carrier (cf. Section 3.1.4.1).

Additive in dielectric fluids

In the field of electrical engineering, TCB (varying isomer composition) has been used together with tetrachlorobenzenes as additives to PCBs for insulating and cooling dielectric fluids for optimising the physical properties (Ullmann, 1986). The content of TCB in the dielectric fluids was between 20 and 40 % (Soldner and Gollmer, 1982). The use for transformer fluid production is stated to have been discontinued in Germany in 1984 (BUA, 1987). Another reference mentions the quantities for this type of use in Western Europe to be 1,500 tonnes in 1983, 1,200 tonnes in 1988, 500 tonnes in 1993 and 0 tonnes in 1995 (Srour, 1996). A Canadian report from 1993 states that “substantial quantities are also present in some electrical transformers and capacitors as a result of trichlorobenzenes past use in dielectric fluid” (CDN, 1993). Germany has discontinued the use for transformer fluid production in 1984 (BUA, 1987), but use of older equipment containing TCB still occurs. The present total volume in use of 1,2,4-TCB in electric equipment still in function is difficult to estimate by using available data. Because the insulating and cooling fluids used in transformers and capacitors mainly consisted of PCB they were subjected to a special waste regulation concerning PCB and containing receptacles including transformers and capacitors (Council Directive 96/59/EC). Assuming a lifetime of 20 to 30 years for transformers and that the use of TCB for new electrical equipment ceased during 1981-1984 in the EU approximately half of the transformers which contained TCB may still be in use. On the basis of a rough estimation, a volume of about 1,000 tonnes of TCB can be assumed for Germany (UBA, 1998). Only by making a crude estimation employing data specific for Germany, it is possible to get an impression of the current total tonnage of TCB still in use in electrical equipment in the EU. Taking the population size of Germany relative to the whole EU into account, a total level of around 5,000 t TCB used in existing electrical equipment in the EU can be estimated. However, no information is available about which specific isomers have been used for this purpose, or for exact amounts used at different time periods in the EU. However according to worst-case approximation in regard to 1,2,4-TCB a total volume of 5,000 t in dielectric fluids still in use in the EU is employed in this risk assessment (cf. Section 3.1.2).

Process solvent

The chlorobenzenes are used as solvents in a wide variety of processes in the chemical industry but according to the main manufacturers they presently only supply a minor volume for this use, if at all.

Corrosion inhibitor and other uses

1,2,4-TCB containing products have been used in the textile, iron, and metal industry as well as in trade and repair. In the Nordic countries 1,2,4-TCB is only registered in few products for the following uses:

- cooling agent and lubricant in the metal industry,
- additive in polish and maintenance products,
- anti-corrosives paint or rust removing agent (corrosion inhibitor - use category 14). It can be sprayed or applied by brush onto e.g. vehicles or steel constructions.

In the Nordic Product Registers, 1,2,4-TCB has been found in five products. The total volume of these 1,2,4-TCB containing products registered is generally very small (< 1t). In all five products, the content of 1,2,4-TCB was below ten percent. In one product the concentration of 1,2,4-TCB has been found to be below 1 w/w%. The products have been sold to both professional users and consumers (Pers. comm.: Danish Product Register, 1996; National Product Control Agency, Finland, 1997; National Chemical Inspectorate, Sweden, 1997). Information was provided indicating that none of these products are in the market today, since the last was withdrawn in 1997.

As the total number of products found in the Nordic Product Registers is low, it cannot be considered to be representative for the EU market. However, it cannot be excluded that these or similar products are available in the European market, as 1,2,4-TCB is a cheap substance and a realistic substitute for other solvents.

1,2,4-TCB emissions to the environment from the above mentioned products are considered negligible and therefore not included in the environmental risk assessment. For the sake of completeness, however, these uses have been included in the risk assessment for workers and consumers.

In addition, in the UK there is a small use of 1,2,4-TCB as an additive in the manufacturing of high performance insulation for use in wire and cable products (3 to 4 tonnes annually) and a much smaller use (300 kg annually) as a blend in the production of a brightener solution for use in lead/tin plating baths (HSE (UK), 1999).

Use scenarios

Based on main manufacturer information (1996), the breaking down of the yearly consumption of 1,2,4-TCB in the EU is estimated to be:

- 1,100 tonnes (79%) used in industry as an intermediate and
- 200 tonnes (14%) used in industry as a process solvent and
- 100 tonnes (7%) are used as a dyestuff carrier, lubricant, additive and other minor uses.

The amount exported out of the EU has been mentioned previously.

In the risk assessment, the use has been separated into industrial categories (IC) and use categories (UC) according to the TGD (cf. **Table 2.4**).

Table 2.4 Industrial categories and use categories

Industrial category	IC no.	Use category	UC no.	Percentage
Chemical industry: used in synthesis	3	Intermediates	33	79%
Chemical industry: basic chemicals	2	Solvents *	48	14%
Others	0	Process regulator, etc. *	43	7%
Textile industry	13	Dye carrier *	43	0.1%

* The main manufacturers or other sources of information do not indicate whether the pure (≥99%) or technical 1,2,4-TCB with a lower grade of purity are used for these purposes, therefore, the use of the pure 1,2,4-TCB has been assumed.

Based on the information from the major manufacturers during 1998, their supply for use as a process solvent has significantly been reduced or totally ended. Because the use has ceased only recently and for the sake of completeness the scenario has been included in the risk assessment. However, the change in use has been included in the sections with conclusions and recommendations.

Besides the yearly consumption of the continued manufacturing of 1,2,4-TCB, a rough worst-case estimate of the present use of formerly produced 1,2,4-TCB as an additive in dielectric fluids in electrical equipment still in use in the EU yields around 5,000 t.

Conclusion

1,2,4-TCB is produced by further chlorination of dichlorobenzene resulting in approximately 85% 1,2,4-TCB and 15% 1,2,3-TCB or in distillation campaigns by dechlorination of hexachlorocyclohexanes (HCH) resulting in approximately 75% 1,2,4-TCB and 25% 1,2,3-TCB. For higher purities, further purification is needed. The marketed substance consists of >99% 1,2,4-TCB.

The total production in the EU was in 1994/1995 approximately 7,000 tonnes per year, the import was approximately 2,000 tonnes, the export approximately 7,600 tonnes and the use approximately 1,400 tonnes per year.

The more recent production volumes by the main manufacturers are slightly less than the figures presented here, however, it is known that approximately 3,000 t are being produced during 1997 and 1998 by a new manufacturer not covered by the Regulation.

1,2,4-TCB is predominantly used as an intermediate in the manufacture of pesticides and is further used as a process solvent in closed systems. In addition, 1,2,4-TCB has several minor uses as a process regulator, an additive, a dye carrier, a corrosion inhibitor, etc. Considerable amounts of 1,2,4-TCB are likely to occur in existing electrical equipment. Previous wide dispersive use types of 1,2,4-TCB (e.g. as solvents) have significantly decreased during the last decade according to the information from the main manufacturers who, however, cannot exclude that such uses may still occur in the EU.

The total amount of 1,2,4-TCB still in use as a dielectric fluid additive is in the EU at a level of around 5,000 t according to a rough worst-case estimation based on information from Germany.

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

3.1.1 General discussion

1,2,4-TCB may be released into the environment during its production, use and disposal. 1,2,4-TCB is released into and detected in most environmental compartments. The atmospheric compartment is estimated to be the primary recipient (based on the relatively high vapour pressure) in some of the use areas (e.g. solvent); in other use areas, the aquatic compartment is the primary recipient (e.g. intermediate in industrial processes, dye carrier).

The present exposure scenarios only include a very rough estimation of the release of 1,2,4-TCB from the accumulated volume of the substances in electrical equipment still in function or such equipment at the recycling/disposal place.

According to Hooftman and Kreuk (1981), it is reported that trichlorobenzenes are formed, together with other chlorinated benzenes, during the combustion of PVC.

However, exposure of the soil compartment via sludge application may occur from municipal sewage treatment plants (STPs) receiving wastewater containing 1,2,4-TCB e.g. from processing of TCB. The sludge from the main manufacturers' production of 1,2,4-TCB, however, is incinerated at the production sites according to the information provided by the main manufacturers (pers. comm., 1996).

It should be noted that when comparing estimated and measured concentrations it has not been possible to quantitatively estimate the indirect release of 1,2,4-TCB either from combustion processes generating 1,2,4-TCB or from transformations to 1,2,4-TCB in the environment from higher chlorinated substances such as polychlorinated benzenes (PCB) and lindane (γ-HCH). Also the release of formerly produced 1,2,4-TCB from dielectric fluids in electrical equipment still in use has not been employed in the quantitative estimations of environmental concentrations. However, the measured data of environmental concentrations will also reflect contributions from such sources.

Until now, the rapporteur has tried to find more information on the use of 1,2,4-TCB based on the appearance of 1,2,4-TCB in the STP sludge (cf. Section 3.1.6.1). The presence of 1,2,4-TCB in municipal STP sludge in STPs without industrial influents indicates that currently unquantifiable sources of 1,2,4-TCB may exist, e.g. caused by release from present installations containing 1,2,4-TCB, from formation of 1,2,4-TCB from combustion of certain products and/or formation of 1,2,4-TCB as a degradation products from lindane and other highly chlorinated compounds. Another possibility of the continued occurrence of 1,2,4-TCB in municipal STP sludge may be not-reported uses such as use in drain cleaning agents (HSDB, 1995).

3.1.2 Environmental releases

3.1.2.1 Release from production

The European production volume is set at 7,000 tonnes. The emission from production is estimated in the scenarios primarily based on manufacturer information if available. The further estimated values performed by using estimation methods according to the Technical Guidance Document (TGD, 1996);

- the scenario A uses main manufacturer data on production release,
- the scenario B uses main manufacturer data on production release.

Table 3.1 Estimated release from production

Production	Tonnes/year	Environment	Release fractions	Tonnes/year (region)	kg/d (local)
Scenario A [1)]	*	Air		0.230 ***	0.63
		Wastewater	**	0.0045 ***	0.015
		Soil	0 **	0	0
Scenario B [1)]	*	Air		<0.025 ***	<0.083
		Wastewater	**	0.120 *** [a)]	0.4
		Soil	0 **	0	0
Total				0.38	

1) Site-specific production release scenario based on main manufacturer data.

* Confidential data not publically available. It can be made available by the Danish EPA to Member States Competent Authorities on request.

** Wastewater and other wastes were incinerated according to the two major manufacturers. However minor releases may be expected from scrubber, rinsing, etc. as indicated by actual measurements.

*** Manufacturer information based on site-specific measurements, cf. Table 3.21.[a)]: the figure has been reduced to 0.063 t in 1997 (pers. comm., main manufacturer). However, since the previous figure relates to 1994/95 no change has been made.

3.1.2.2 Release estimates from processing

In the release estimates for processing, the estimations are based on 1,400 t/year used in the EU. Of the 1,400 tonnes, 1,100 tonnes (79%) are used as an intermediate in production of other substances, 200 tonnes (14%) are used as a process solvent, 100 tonnes (7%) as a solvent and other purposes (lubrication and additive), and 1.4 tonnes (0.1%) as a dye carrier in the textile industry (cf. Use pattern, Section 2.2). The estimated emissions from processing and other uses are calculated in scenarios based on the TGD (1996);

- The scenario D1 is based on the use of 1,2,4-TCB as an industrial intermediate in the production of pesticides [6].
- The scenario D2 is based on the use as a process solvent. As the release is actually included in the release from scenario B, the estimations are based on the TGD as generic scenario.

[6] The worst-case exposure estimates for indirect human exposure via soil, ground water and drinking water for scenarios D1 and D2 are not relevant according to the main manufacturers, because sludge from the STPs concerned is incinerated or disposed of on controlled landfills.

According to the main manufacturer the use of 1,2,4-TCB as a process solvent in the chemical industry has stopped by 1997 at this specific production site[6].

- The scenario D3 is based on the release from several minor uses.
- The scenario D4 is based on the use in the textile processing industry as a dye carrier.

Table 3.2 Estimated release from processing (TGD, Appendix 1)

Processing	IC/UC	Tonnes/year	Environment	Release fractions	Tonnes/year *	kg/d **
Scenario D1	3/33 intermediate	1,100	Air	0.00001	0.01	0.04
			Wastewater	0.007	7.7	25.7
			Soil	0	0	0
Scenario D2	2/48 process solvent	200	Air	0.001***	0.2	0.67
			Wastewater	0.02***	4.0	13.33
			Soil	0.0001***	0.1	0.25
Scenario D3	0/55 others	100	Air	0.01	1.0	4.95
			Wastewater	0.01	1.0	4.95
			Soil	0.005	0.5	5.0
Scenario D4	13/43 dye carrier	1	Air	0.05	0.05	0.525
			Wastewater	0.85	0.85	8.93
			Soil	0.005	0.005	0.002
Total:					15.415	

* Regional estimates
** Local estimates of release during emission episodes
*** The release fraction from the use of 1,2,4-TCB as a process solvent is assumed to be more correctly a "formulation" process than an actual "processing"

Regional and continental releases estimated by employing EUSES[7]:

	kg/d	Tonnes/year
Total regional emission to air	0.868	0.317
Total regional emission to wastewater	22.9	8.359
Total regional emission to surface water	9.8	3.577
Total regional emission to industrial soil	0.138	0.050
Total continental emission to air	2.61	0.953
Total continental emission to wastewater	3.77	1.376
Total continental emission to surface water	1.61	0.588
Total continental emission to industrial soil	1.24	0.453
Total emission to the EU environment	1.284	15.673

Ten persistent organic pollutants (POPs) including TCB are part of the air emission inventory for Europe performed by the European Environment Agency. Based on EU Member States information, the total emission to air of TCB in the EU in 1994 was 629 tonnes (a value reached

[7] Euses calculations can be viewed as part of the report at the website of the European Chemicals Bureau: http://ecb.jrc.it

for UK alone) equivalent to 10.08 g TCB/capita[8]. The emission source is stated to be production processes: "solvent and other production use" (EEA, 1997).

The air emission presented by EEA (1997) is higher than the amount estimated for the whole EU in this Risk Assessment Report, especially since the former was based on information from only one country (UK) and furthermore specified to be released from production processes only. It is, however, stated in the report that the included emission estimates on POPs may be uncertain due to less developed release estimation methodologies. In addition the figure includes other TBCs than 1,2,4-TCB. However, the value of 629 tonnes for 1994 supports the assumption of the significance of other sources releasing 1,2,4-TCB (cf. below).

The total current content of 1,2,4-TCB in electrical equipment in the EU was roughly estimated to around 5,000 tonnes. However, based on available information it is only possible to make a very rough estimation of the possible release of 1,2,4-TCB from electrical equipment during current use and when the equipment is collected and handled for PCB destruction. In 1993 the consumption of TCB in Western Europe for additive in dielectric fluids was 500 t (cf. **Table 2.1**). Based on this, a worst-case assumption is that 10% of 1,2,4-TCB in dielectric fluids in current use is released to the environment each year. It is possible to make a very crude estimation of the yearly worst-case release of 1,2,4-TCB from this source: 10% of 5,000 t = 500 t for the EU per year.

Because the worst-case estimation of the environmental release of 1,2,4-TCB is so rough and uncertain, this environmental release will not be carried further in this risk assessment for quantitative estimations of environmental concentrations. Instead a rough comparison with the total estimated environmental release from the current industrial production and use will be made:

Total regional release from current production and processing:

Production:	0.380 t/year (cf. **Table 3.1**)
Processing:	15.415 t/year (cf. **Table 3.2**)
Total:	15.8 t/year

Total regional release from electrical equipment employing "the 10 % rule":
500 t / 10 = 50 t per year (worst case)

Conclusion

A very rough estimation of the environmental release of 1,2,4-TCB from dielectric fluids in existing electrical equipment indicates that it may be of the same order of magnitude as the total release from the current production and processing of this substance. Because of present EU and national legislation regarding the destruction of PCB and other chlorinated compounds in dielectrical fluids in electrical equipment it can be foreseen that the future level of environmental release of 1,2,4-TCB from this source will decrease significantly in the EU.

[8] In the EEA report (1997) a wrong value of 10.08 kg TCB/capita is reported.

3.1.2.3 Release from other sources

Other sources of 1,2,4-TCB in the environment exist apart from the direct releases from production and processing of 1,2,4-TCB and from the accumulated volume of the substance in existing electrical equipment. Based on available literature such diffuse sources include:

- combustion processes in waste incinerators,
- degradation processes of higher chlorinated benzenes
- bleaching processes in craft paper mills or in the textile industry,
- leakage from landfills,
- contaminated sites e.g. industrial sites of former pesticide production.

Occurrence in combustion processes

Lahaniatis et al. (1981) simulated the waste combustion at 800ºC with an organic matrix (synthetic waste of cellulose) containing polyethylene and sodium chloride as the only chlorine source. The molar ratio of chlorine to ethylene was 1:1. The exhaust fumes were analysed for chlorinated benzenes. All chlorinated benzenes were present between 0.005 µg/g (hexachlorobenzene) to 10 µg/g (chlorobenzene), 0.1 µg/g (1,2,4-TCB) related to the amount of polyethylene. The authors conclude that, under combustion conditions, both the organic and inorganic components can contribute to the formation of chlorinated benzenes via chlorine radicals, chlorine molecules or hydrochloride acid.

Simple prototype plastic waste, ranging from polyethylene to PVC was burned in a laboratory-scale rotary kiln simulator. Uneven combustion conditions and oxygen depletion can result in pollutant puffs resulting in heavy transient loadings of unburned gaseous and particulate hydrocarbons leaving the kiln. Results demonstrate in test burning at 1,066°C and excess air that dichlorobenzenes, 1,2,4-TCB, penta- and hexachlorobenzene are formed in the exhaust, when polyethylene and PVC were burned together. No chlorinated aromatics were formed, when polyethylene was burned alone. No higher chlorinated (>2) benzenes were formed, when PVC was burned alone (Linak et al., 1987).

Panagiotou et al. (1996) conducted a study on semi-volatile aromatic hydrocarbon emissions from the pyrolysis/combustion of polystyrene, polyethylene and PVC particles. In the drop-tube furnace, pyrolysis/combustion took place at gas temperature ranging from 900 to 1,200°C; particle heating rates were in the order of 1,000 to 10,000°C/s. The total residence time of gases in the furnace were 1 or 2 seconds. A large number of substances, about 80, were identified as pyrolysis/combustion products of PVC: substituted mono-aromatic hydrocarbons, oxygenated compounds, polyaromatic hydrocarbons, and to a lesser extent chlorinated aromatics - among them 1,2,4-TCB. 1,2,4-TCB was not detected in the pyrolysis/combustion of polystyrene and polyethylene.

Two kinds of wrapping film made of PVC were pyrolysed at 200 to 600ºC under an air stream. The pyrolysis products were identified by GC/MS. Beginning from 200ºC important products were chlorinated compounds of benzenes, among them 1,2,4-TCB, styrenes, phenols, phenylacetylenes, naphthalins, biphenyls, and benzofuranes. Chlorodibenzofuran and dichlorodibenzofurans were formed at 600ºC (Yasahara and Morita, 1988).

A laboratory-scale fluidised-bed reactor filled by a synthetic waste and reflecting the main components of the Swedish household waste, was used to study the influence of the flue gas temperature profile after the combustion on the formation of chlorinated aromatic compounds.

Flue gas samples with residence time in the cooling section of the reactor between 0.9 and 2.9 s were collected at temperatures between 260 and 510ºC. Polychlorinated dibenzo-p-dioxins, dibenzofurans, and benzenes were analysed as a function of temperature and residence time. All tri- and higher chlorinated benzenes were present; 1,2,4-TCB: 0.48 to 4.9 µg/std m^3 (Fängmark et al., 1994). The same experiments were performed with a cyclone at the entrance of the cooling section that removed the large fly ash particles. The formation of the chlorinated aromatics occurred at the same extent as in the earlier experiment without the cyclone. The authors conclude that the small fly ash particles are responsible for the formation of the chlorinated combustion products in which the fly ash may act as a catalyst (Fängmark et al., 1995).

Ethylene and ethane were burned together with hydrochloric acid in air at temperatures between 300 and 600ºC. Model catalyst mixtures of silica/aluminium oxide/copper oxide were compared with municipal waste incinerator fly ash. All polychlorinated benzenes were formed (Froese and Hutzinger, 1996). In a similar experiment benzene was reacted with hydrochloric acid over the same catalysts. The authors concluded that during post-combustion reactions aliphatic C_2-hydrocarbons undergo synthesis to polychlorinated benzenes and phenols - maybe via an intermediate benzene - and that copper in fly ash of municipal incinerators plays a critical role as catalyst and that aluminium oxide supports the formation of benzene rings (Froese and Hutzinger, 1997).

Stieglitz et al. (1989) demonstrated that in thermal laboratory experiments with a model mixture of magnesium-alumina-silicate, potassium chloride and charcoal, doped with copper chloride as a catalyst, polychlorinated benzenes, PCDDs and PCDFs are formed at 300ºC. These experiments support the hypothesis of the *de-novo* synthesis of polychlorinated benzenes, among them 1,2,4-TCB, PCDDs and PCDFs by the reaction of carbonaceous particulate matter of the fly ash with inorganic halides occurring in the cooler post-combustion zones of the incinerator.

Jay and Stieglitz (1995) identified about 250 compounds from the emission of a municipal waste incinerator plant at a concentration over 50 ng/m^3, among them 1,2,4-TCB in a concentration of 0.55 µg/m^3. These identified emissions represent about 42% of the total organic carbon on the emission. The rest could be shown to consist of non-identified aliphatic hydrocarbons.

Conclusion

Different quantitative data are available:

On the basis of laboratory experiments (Lahaniatis et al., 1981) it can be calculated that 100 kg 1,2,4-TCB are formed during the combustion of 1 Mio. tonnes of polyethylene mixed with sodium chloride.

An experiment from Fängmark et al. (1994) with a laboratory-scale reactor results to a maximum amount of 4.9 µg 1,2,4-TCB/m^3.

For calculating the emissions to the atmosphere it must be taken into account that in modern combustion plants the exhaust gases are cleaned by filtering techniques with high efficiency, due to the regulations on the emissions of chlorinated dioxins and furans.

Therefore the calculation should be based on measured data from combustion plants and not on laboratory results.

In the emissions from a municipial waste incinerator 1,2,4-TCB was detected in a concentration of 0.55 µg/m^3 (Jay and Stieglitz, 1995).

Following the calculation of the BUA (1993) published in the BUA report No. 185 on "1,4-dichlorobenzene" in Chapter 4.4.3 using:

- 5.5 m^3 exhaust gas per kg waste,
- capacity of 200,000 t/a for a combustion plant,
- 50 plants in West Germany,
- and a factor of six for Western Europe,

the following amounts can be calculated:

1,2,4-TCB: 0.55 µg/m^3	→	0.605 kg/plant
	→	30.25 kg in West Germany
	→	181.5 kg in the EU.

On the basis of this very rough estimation it can be assumed that in Western Europe the yearly emission of 1,2,4-TCB to the atmosphere via combustion plants is below 1 t/y.

Occurrence in effluents from bleaching processes

Chlorine compounds have decreased in craft paper mill effluents, when in 1993 the use of chlorine as bleaching agent was ceased in Finland. Instead of elemental chlorine free bleaching with ClO_2 and the total chlorine free bleaching process was introduced. For 1,2,4-TCB the authors reported negative results in two mills and a positive result in one mill that used the elemental chlorine free bleaching process. Wastewater influent (2 µg/l) and effluent concentration (0.7 µg/l) were found in this mill (Juuti et al., 1996).

In 1989 the worldwide production amount of paper was 233 million tonnes (Römpp Chemie Lexikon, 1989, page 3212); the amount for Western Europe is calculated to be 30% = 70 million tonnes.

The amount of water used for production has been lowered in the last years and now the mean value in Germany is about 20 l/kg paper (Römpp Chemie Lexikon 1989, page 3208).

Assuming that 20% of the paper mills are using elementary chlorine as a bleaching agent, an effluent concentration of 0.7 µg/l and a water amount of 40 l/kg paper the following calculation can be made:

70 Million tonnes/a · 40 m^3 of water/t · 0.7 mg/m^3 1,2,4-TCB · 20%

→ 392 kg/year

On the basis of this very rough estimation it can be assumed that in Western Europe the yearly emission of 1,2,4-TCB to the hydrosphere via paper mill effluents is below 1 t/y.

Environmental release of 1,2,4-TCB from other chlorinated organic compounds.

TCB including 1,2,4-TCB can be released to the environment from industrial cracking or during the biodegradation of lindane (Hooftman and Kreuk, 1982).

Production involving other chlorobenzenes may also result in therelease of TCB. For example, in an investigation of chlorine compounds in the wastewater at a location in the Netherlands where

dichlobenil and chlorfenvinphos were manufactured, 1,2,4-TCB was measured and the release estimated to be about 100 kg/year (Slooff et al., 1991).

Hexachlorobenzene is dechlorinated under anaerobic sewage conditions to tri- and dichlorobenzenes. The major dechlorination route stopped at 1,3,5-trichlorobenzene; the minor route proceeded via 1,2,4-TCB to dichlorobenzenes. Fresh anaerobic sludge was obtained from a primary digester. The STP receives about 40 % of its wastewater from industrial sources and the rest from residential sources (Fathepure et al., 1988).

Nowak et al. (1996) showed that a methanogenic mixed culture enriched from Saale River sediment was able to transform chlorobenzenes by reductive dechlorination via monochlorobenzene to unsubstituted benzene after a short lag phase of one week.

With respect to the estimated high amounts of lindane which have been produced and used in Western Europe until 1985 of at least 5,000 t/a (Rippen, Handbuch Umweltchemikalien, 1994) photochemical degradation of lindane in the atmosphere and biodegradation in soil and sediment may cause significant environmental releases of 1,2,4-TCB.

Occurrence from disposal sites and leachate from landfills

Sievers and Friesel (1989) examined the origin of polychlorinated benzenes, PCDDs and PCDFs in several waste disposal sites in Hamburg. They concluded from the analysis that the waste from the lindane and 2,4,5-trichlorophenoxyacetic acid pesticide production was deposited in these landfills. The technical by-products of α-, β-, δ-, and ε-HCH in the lindane production were thermally decomposed to 1,2,4-TCB, then chlorinated to 1,2,4,5-tetrachlorobenzene and transformed via trichloroanisol and trichlorophenol into 2,4,5-T. It is now known that these processes produce residues with high concentrations of polychlorinated benzenes, phenols, PCDDs, and PCDFs. Trichlorobenzenes concentration reached 35.9 and 13,900 mg/kg waste respectively at two different sites.

Trichlorobenzes were detected in leaching water and oil from a Hamburg landfill site (Georgswerder) that had been filled with industrial waste during 1967 to 1974. Götz (1985) measured 1,2,4-TCB in the aqueous leachates in concentrations between 0.016 to 351 µg/l and in the oily leachates up to 6,200 mg 1,2,4-TCB/kg.

On the basis of the single case study “Georgswerder” and the general knowledge of the occurence of such dumpsites throughout Europe, environmental releases of 1,2,4-TCB from contaminated sites and old waste disposal sites all over Western Europe might be likely to occur even though it is not possible to quantify further, if no supplementary information regarding such sites are gathered and evaluated. This is outside the scope of the current report.

Lubrication oils

Used oils collected for recycling contain chlorinated aliphatic and aromatic compounds, among them 1,2,4-TCB (average 1, range 0-60 µg/ml). An analysis of the origin of the used oil revealed that trichlorobenzenes (including all TCB derivatives) resulted primarily from industrial used oils (19% of samples contain 10 µg/ml, max. 321 µg/ml) and to a lower extent from automotive used crankcase oils (average 1 µg/ml) (Brinkmann and Dickson, 1995).

It is not possible to make even rough quantitative estimations on the environmental release of 1,2,4-TCB from this source based on the available information.

Other sources

Another source of TCB may be from environmental transformation of benzene which can be photochemically chlorinated to HCH which can be dechlorinated to TCB (Jensen, 1969). It is theoretically possible that this kind of environmental formation of TCB may occur at places where such chlorination processes are likely, for example in the atmosphere when fume gasses are emitted from incineration plants.

It is not possible to make even rough quantitative estimations on the environmental release of 1,2,4-TCB from these theoretical sources based on the available information.

Conclusion regarding environmental release of 1,2,4-TCB from other sources

On the basis of the available data it seems to be possible to estimate that:

- dielectrical fluids,
- bio- and photodegradation of HCB, lindane and lindane isomers and,
- emissions from landfills and contaminated sites

should be the main sources for the environmental release of 1,2,4-TCB in Europe besides the release originating from the current production and processing of 1,2,4-TCB.

In comparison to that, combustion processes and effluent from paper mills and some other sources seem to be of only minor importance.

3.1.3 Environmental fate

3.1.3.1 Degradation

3.1.3.1.1 Abiotic degradation

Hydrolysis

Based on the experimental data (Korte and Freitag, 1986) on hydrolysis at 50°C, 1,2,4-TCB is not expected to hydrolyse under normal environmental conditions (Howard, 1989; Schmidt-Bleek et al., 1982).

Photolysis

Degradation by direct photolysis is not expected to be essential because the maximum absorption value is 286 nm (Bayer spectral data). The half-life for sunlight photolysis in pure surface water at 40^{o} latitude in summer was 450 years (Dulin et al., 1986). The recovery of 1,2,4-TCB from isopropanol solution in Pyrex glass tubing (with a cut-off at 285 nm) irradiated with 300 and 310 nm fluorescent lamps for 30 minutes was 89.4% under anaerobic conditions where O_2 was replaced with N_2 and 8.1% under aerobic conditions. The products of photodegradation were 1,3- and 1,4-dichlorobenzene (Akermark et al., 1976).

In a laboratory study using artificial light (high pressure mercury vapour lamp at wavelengths > 290 nm), the photodegradation was studied at a concentration of 2-5 ppm. 1,2,4-TCB was dissolved in distilled water and filtered river water. The photolytic half-life was estimated to be

16.7 hours in distilled water and 12.2 hours in river water. The photolysis products in river water were 1,4-dichlorophenol and 4-chlorophenol (Mansour et al., 1989).

The photolysis was studied by exposing 5 ml 1,2,4-TCB at 4 µg/ml at a distance of 30 cm from artificial light (Fluorochemical lamps 20W·2) at 25°C. After 144 hours, 0% was degraded (Kondo et al., 1988).

In a test where 1,2,4-TCB was adsorbed on silica gel and irradiated with light at wavelengths > 290 nm for 17 hours, 9.8% of the applied amount was degraded to CO_2 (Freitag et al., 1985).

In addition to the direct photolysis, the photodegradation may also follow an indirect photolysis by sensitisation by secondary reactions with OH- and O_2-radicals. The photolysis was studied in water solutions 600 ml at 4-20 mg/l irradiated for 3 hours. The photoreactivity in solutions in the presence of nitrite was observed to increase the photodegradation rate. The rate constant in pure water was $1.5 \cdot 10^{-4} s^{-1}$ resulting in T½ to be 1.2 hours. In water added nitrite, the rate constant k was $3.1 \cdot 10^{-4}$ s^{-1} and the resulting T½ 0.4 hours (Kotzias et al., 1982). The study was conducted under artificial conditions but indicates that photolysis may be affected by the contents in water. In the study, salts were used but other organic substances and organic matter may also affect the photodegradation rate.

Atmospheric photooxidation

The photodegradation of 1,2,4-TCB by hydroxyl radicals in the atmosphere is estimated to be in the order of a month. However, the values should been considered as the upper limit of stability since other degradation modes are not considered. **Table 3.3** summarises the photodegradation data.

Table 3.3 Photooxidation rate constants

Rate constant cm^3 / molecule / s	Half-life (days)	Method	Reference
$5.32 \cdot 10^{-13}$	18.5	Experimental	Atkinson et al. (1985)
$5.32 \cdot 10^{-13}$	30.2	Measured, 296ºK	Rinke and Zetzsch (1984)
$2.82 \cdot 10^{-13}$	38.0	Calculated by AOP programme	AOPWIN (1995)

The reaction of 1,2,4-TCB with OH radicals was investigated in the presence of helium at pressures from 5 to 800 mbar using a pulsed vacuum UV photolysis-resonance fluorescence apparatus. At 23°C and 133 mbar helium, the rate constant k was observed to be $0.5 \cdot 10^{-12}$ cm^3/s (Rinke and Zetzsch, 1984). Assuming an average tropospheric OH radical concentration of $5 \cdot 10^5$ molecules/cm^3, the half-life is about 30 days (BUA, 1987).

In the atmosphere, the estimated vapour phase half-life of 1,2,4-TCB was 18.5 days estimated as a result of reaction with photochemically produced hydroxyl radicals at $8 \cdot 10^5$ molecules/cm^3 giving a reaction rate of $0.532 \cdot 10^{-12}$ cm^3/molecules/sec (Atkinson et al., 1985).

The photochemical oxidation was estimated using the structure analysis by the model AOPWIN (1995) for comparison. The estimated half-life of 38 days is based on the OH-radical concentration of $1.5 \cdot 10^6$ molecules/cm^3 and a 12-hour daylight period. The previous model used $5 \cdot 10^5$ molecules/cm^3 which was a 24-hour average value that included nighttime. Using $5 \cdot 10^5$ molecules/cm^3 (24 hours) would result in a T½ of 57 days estimated by AOPWIN (1995).

It is mentioned in IUCLID that using an experimental value for the OH rate constant of $0.55 \cdot 10^{-12}$ cm^3/molecules/s and by setting the OH radical concentration to $5 \cdot 10^5$ molecules/cm^3, a T½ of 29 days would be estimated (IUCLID, 1995; Rippen 1991). The value is based on the geometric mean of the measured absolute K_{OH} value (296ºK) $0.5 \cdot 10^{-12}$ cm^3/s and a relative measured K_{OH} value (300ºK) $0.6 \cdot 10^{-12}$ cm^3/s (Rippen, 1991). However, the mentioned value is the weighted average from the study and not the 296ºK, cf. the table.

The removal of 1,2,4-TCB in air may be by degradation by chemical- or sunlight-catalysed reactions or absorption onto particles that settle or are removed from the atmosphere by rain. A measure of the effectiveness of these factors is the atmospheric residence time. In a field study in California and Arizona, air samples during a two-week period included an unspecified trichlorobenzene. The estimated residence time was 116 days assuming an average daily (24 hours) abundance of OH radicals of 10^6 molecules/cm^3. The daily loss rates estimated for 12 hours was 0.9% (Singh et al., 1981).

Conclusion on photodegradation

Photodegradation in water may result in formation of the degradation products 1,3- and 1,4-dichlorobenzenes, 1,4-dichlorophenol and 4-chlorophenol. Photodegradation in water is very slow and is therefore not included in the risk assessment. This risk assessment does not include an assessment of the reaction products formed by indirect photolysis. Atmospheric photodegradation occurs with a half-life of approximately 30 days which is used in the risk assessment.

It is noted that an experiment with artificial UV light yielded 1,3- and 1,4-dichlorobenzene as photodegradation products from 1,2,4-TCB (Akermark et al., 1976) For an assessment of the risk caused by these chemicals cf. available literature on these substances (including the EU Risk Assessment Report on 1,4-dichlorobenzene).

3.1.3.1.2 Biotic degradation

Biodegradation in laboratory studies

The ready biodegradability was studied with a method corresponding to the OECD TG 301C, Modified MITI (I) test. The test concentration was 100 mg/l and activated sludge concentration 30 mg/l. In the aerobic study, the degradation measured as Biochemical Oxygen Demand (BOD) was 0% after 14 days (MITI, 1992). However, the high concentration of 1,2,4-TCB employed in the test may have resulted in toxicity to the microorganisms.

The BOD_{20} value for 1,2,4-TCB was studied using microorganisms from an industrial wastewater treatment plant normally exposed to phenolics and other industrial chemicals (i.e. adapted inoculum). The concentration of 1,2,4-TCB was 1.69 and 2.61 mg/l. Although no apparent degradation was indicated by the BOD oxygen uptake until day 10, GC-ECD analysis of the remaining 1,2,4-TCB indicated that the substance began to disappear within 1 to 5 days. 99% and 100% of the 1,2,4-TCB had disappeared in 10 days as determined by the GC-ECD analysis when the BOD test indicated 55% of the theoretical oxygen demand (ThOD). The remaining 45% ThOD was stated to be incompletely oxidised metabolites of 1,2,4-TCB. BOD_{10} and BOD_{20} were 55% and 55% using 1.7 mg/l and 19% and 55% using 2.6 mg/l, respectively (Simmons et al., 1977).

A static culture flask biodegradation screening study was used to determine the biodegradability at two concentrations of 1,2,4-TCB (5 and 10 mg/l), a 7-day static incubation at 25°C followed by three weekly subcultures of yeast and settled domestic wastewater (non-adapted) as microbial inoculum. A gradual adaptation process followed by a de-adaptive process in subsequent subcultures (reduced degradation and accumulation of 1,2,4-TCB in the media) was observed. For the original culture 54% and 43% degradation were observed after 7 days at 5 and 10 mg 1,2,4-TCB/l, respectively (Tabak et al., 1981). The employed test is less stringent than a standard ready biodegradability test, because of the use of an extra carbon source (yeast) allowing for co-metabolism. Further it is not clear whether the reported biodegradation percentages are referring to the removal of parent compound or the mineralisation.

Therefore, the studies indicate that 1,2,4-TCB may be regarded as not ready biodegradable.

Removal in the sewage treatment plant (STP)

In a study by Simmons et al. (1977) using ^{14}C-labelled substance at 0.345 mg/l, the degradation was studied in activated sludge from a textile plant wastewater (i.e. adapted) by measuring $^{14}CO_2$ development. After 5 days, 56% was recovered as $^{14}CO_2$, 23% as polar metabolites, 7% was evaporated, 12% was unchanged in the sludge and 2% was dissolved in water. The reduced volatilisation is stated to be caused by the high organic sludge environment since 80% was adsorbed to solids and 20% was actually in the water. The amount of ^{14}C-1,2,4-TCB converted to $^{14}CO_2$ was 33% in 1 day and 56% in 5 days. These results suggest that mineralisation may have continued if the duration of the test had been prolonged and that 70% mineralisation to CO_2 could have been reached in e.g. 15 days resulting in the 1,2,4-TCB being characterised as "inherent ultimate biodegradable" according to OECD guidelines.

The study by Simmons et al. (1977) also contains data on the distribution in STP: 79% degraded (56% to CO_2, and 23% degradation products), 7% released to air, 12% in sludge, and 2% in water. However, because of inaccurate description in the study on how the distribution is reached the more conservative approach from the TGD and the updated Simpletreat (ver. 3) is used in the risk assessment. The model EUSES estimates a removal of 84.7% (61.3% to air, 11,3% to sludge and 12.1% degraded) and 15.3% to water.

Removal from another industrial wastewater treatment plant was about 75% using activated sludge with a 6-hour retention time (Simmons et al., 1977). No further details are given.

The concentration of 1,2,4-TCB in influents to an advanced wastewater treatment plant was measured at the average value of 0.46 µg/l. The effluent concentration in the same period was 0.01 µg/l in percolating filter effluent treated by lime clarification, ammonia stripping, activated charcoal, chlorination and reverse osmosis. (McCarty and Reinhard, 1980). This removal of 97.8% of 1,2,4-TCB is a special case which is not to be considered a worst case. The "water factory" was designed to improve the quality of biologically treated municipal wastewater before injection into the aquifer system.

The influent to a water factory was the effluent from a municipal STP (Orange county, California). In 1976, the STP trickling effluent contained 1,2,4-TCB in the range <0.02-4.1 µg/l (geometric mean 0.46 µg/l) and in 1978 after switching from trickling-filter to activated sludge treatment, the measured range in STP effluent was <0.02-0.5 µg/l and the geometric mean 0.18 µg/l (McCarty and Reinhard, 1980).

The removal from 30 STPs measured in a study by the US EPA (1982) resulted in a removal of 62% and another report from the US EPA (1986) measured a removal of 86% in acclimatised and unacclimatised STPs (In: Danish EPA, 1990).

Table 3.4 Wastewater concentrations, measured values and removal %

Wastewater treatment plant (STP)			No. / % pos.	Max, µg/l	Average, µg/l	Removal	Ref.
Industrial	foundries	raw water treated water	2 / 100% 2 / 100%	1,000 570	500 290	42%	US EPA (1980)
	textile mills	raw water treated water	50 / 16% 50 / 32%	2,700 1,400	410 14	96%	
	electronics	raw water	2 / 100%	27,000	16600		
Municipal		influent effluent	1 / 9% 1 / 9%		0.07 0.02	71%	Kröber and Häckl (1989)

In Danish municipal STPs, 40% to 60% reduction (recovered in sludge) has been measured (Grüttner et al., 1996).

Removal in surface water

The removal in seawater was studied in mesocosmos studies including the volatilisation (Wakeham et al., 1983). The tanks were 5.5 m high and 1.8 m in diameter and contained 13 m^3 seawater. In the study, a mixture of volatile organic compounds was added. The dissipation was studied at conditions equal to spring (8-16°C), summer (20-22°C) and winter (3-7°C). The initial concentration 0.5 µg/l was equivalent to the concentration measured in a moderately polluted bay. The concentrations were measured during 1-2 months.

Table 3.5 Removal in mesocosmos (Wakeham et al., 1983)

	Temperature (°C)	Initial concentration (mg/l)	Rate constant	T½ (days)
Spring (Apr. 15-Jun. 18)	8-16	0.5	-0.032	22
Summer (Aug. 19-Sep. 8)	20-22	0.2	-0.066	11
Winter (Mar. 4-May 4)	3-7	2.2	-0.058	12
Water with $HgCl_2$ (Sept. 9th to 15th) Water without $HgCl_2$		0.2 0.3	-0.073 -0.066	9.5 10.6

The dissipation was relatively temperature independent with half-life of 2-3 weeks regardless of the season. Retardation of the biological activity by adding $HgCl_2$ (2 mg/l) did not increase the summer dissipation time. Therefore, the dissipation was assumed to be primarily dissipation by volatilisation and not biodegradation. Thus, volatilisation dominates the dissipation of 1,2,4-TCB whereas biodegradation is of less importance according to the authors (Wakeham et al., 1983).

The half-lives in rivers in the Netherlands were estimated to be 2.1, 1.5 and 28 days based on monitoring data taken along the River Rhine (Zoeteman et al., 1980). These half-lives differ considerably and are likely to be very inaccurate since only a limited number of samples were taken.

Removal in sediment

Trichlorobenzenes are chemically stable in both aerobic and anaerobic environments. In studies on the degradation in anaerobic sediments, trichlorobenzenes were reductively dechlorinated to monochlorobenzenes via dichlorobenzenes. 1,2,4-TCB was transformed via 1,4-dichlorobenzene (Bosma et al., 1988) and via 1,2- and 1,3- dichlorobenzenes (Peijnenburg et al., 1992). The study by Bosma et al. (1988) was performed as a column study using 25 cm high and 5.5 cm internal diameter wet packed with sediment from the River Rhine near Wageningen. The columns were percolated continuously at a flow rate of 1 cm/h in an upflow mode. It was concluded that the observed removal was a biological process because of the long lag-phase preceding the disappearance and that there was no elimination in anaerobic batch with autoclaved sediment. The study by Peijnenburg et al. (1992) was performed in a methanogenic sediment-water system maintained at 22ºC in a nitrogen atmosphere. The sediments were taken from a slow flowing river and a eutrophic pond. The anaerobic degradation rates were $\log k = -5.64\ min^{-1}$ and $\log k = -5.62\ min^{-1}$ (corresponding to the half-lives 212 days and 202 days), respectively. 1,2-, 1,3- and 1,4-dichlorobenzenes were formed in ratios of approximately 1.5:1:1.5 as confirmed by GC. Almost immediately after incubation began, monochlorobenzene could be detected.

Degradation in soil

1,2,4-TCB can be degraded in soil, although very slowly (Marinucci and Bartha, 1979; Wilson et al., 1981). The aerobic mineralisation was studied using ^{14}C-labelled 1,2,4-TCB and a mineralisation rate measured as CO_2 development/day (Marinucci and Bartha, 1979).

In a study using a sandy loam (pH 6.5) added 1,2,4-TCB at a concentration of 50 µg/g soil, the degradation in soil was observed to be slow. The incubation was performed at 20°C for 3 to 12 weeks. 1,2,4-TCB was subject to mineralisation as soil poisoned with 1% $HgCl_2$ or NaN_3 reduced the CO_2 evolution consistently. Anaerobic conditions either continuously or alternated weekly with aerobic incubation periods markedly depressed the mineralisation. The mineralisation rate was 0.181 µg/day/20 g soil equivalent to 9 µg/d/kg. The turnover rate (% 1,2,4-TCB converted to CO_2/day = 0.075%) was maximal at 10 µg/g soil and sharply declined at higher concentrations (Marinucci and Bartha, 1979). Haider et al. (1974) used 10 µg/g (in 100 g soil) and observed a mineralisation rate about twice as high.

3.1.3.1.3 Conclusion on degradability

1,2,4-TCB is not ready biodegradable. However, it can be concluded from the above that 1,2,4-TCB is to some extent biodegradable. Although degradation in activated sludge can be considerable, the level of degradation depends on the STP conditions (especially on the adaptation of microorganisms to the substance but also the residence time of solids and liquids). In sediments and in anaerobic digesters of STPs, degradation is by reductive dechlorination of trichlorobenzene to di- and mono-chlorobenzenes.

The study by Simmons et al. (1977) using ^{14}C-labelled trichlorobenzene resulted in 56% ultimately biodegraded after 5 days using activated sludge from industrial STP (i.e. not specifically adapted to 1,2,4-TCB but the presence of TCB was likely from its use as textile dye carrier). The conclusion from this study and supported by the other studies is that 1,2,4-TCB can be regarded as inherently biodegradable.

Degradation rates in STP, surface water, sediment and soil

The degradation rate in STP, based on the conclusion inherently biodegradable, results according to the TGD in an estimated $kbio_{STP}$ of 0.1 h^{-1} corresponding to a half-life of 6.9 hours.

Degradation rates for surface water cannot be obtained directly from available simulation studies. However, an approximate and generic half-life for surface water can be estimated based on the result of standardised tests for inherent biodegradability. Using the estimated half-life of the TGD for inherently biodegradable substances 1,2,4-TCB is concluded to have a $k_{surface\ water}$ of 0.0047 d^{-1}, corresponding to a half-life of 150 days.

Supporting this conclusion, Rodan (1997) estimated the half-life of 1,2,4-TCB to be in the order of 180 days for persistence in both water and soil whereas the EPIWIN QSARs, the Biodegradability Probability Program 1 and 3 (BPP1 and BPP3, respectively) for rapid and ultimate degradation respectively, estimated the degradation to be "slow" (BPP1=0.15) and with a half-life in the order of "more than a month" (BPP3 = 2.18 where 2 is equivalent with a range of a month, and 3 with a year).

The degradation rate in soil cannot be estimated based on soil degradation simulation studies. Therefore, the half-life value from the TGD is used for estimating the half-life in soil of inherently biodegradable substances, i.e. a biodegradation rate $kbio_{soil}$ is estimated to be 0.0023 d^{-1}, corresponding to a half-life of 300 days.

A degradation rate in sediment may be estimated based on the reported anaerobic half-life of 210 days for an anaerobic water-sediment system. It is concluded that a k_{sed} of 0.0023 d^{-1}, corresponding to a half-life of 300 days, is justified.

3.1.3.2 Distribution

The result of a Mackay model estimation of the distribution in the environmental compartments may vary according to the age of the model as they develop in time and the input data used.

The distribution in the environment, based on the EQC model (developed by Di Guardo according to Mackay et al., 1996) using the relevant physico-chemical data from this report at 20ºC results in the distribution: 76.9% in air, 2.1% in water, 20.5% in soil, 0.5% in sediment, 0.014% in suspended sediment, and 0.002% in fish. Another Mackay Level I model calculation employing also slightly different relevant physico-chemical data (Mackay, 1991; Bayer, 1996) is included for comparison in **Table 3.6**.

Table 3.6 Distribution in the environment, Mackay Level I

Mackay Level I ref.:	Input data				Mackay level I distribution			
	water-solubility	log Kow	vapour pressure	H Pa·m³/mol	Air	Water	Sediment	Soil
Bayer (1996)	36 mg/l	4.21	21.5 Pa	108	91.6%	2.4%	2.9%	3.1%
EQC (1996)	*36 mg/l*	*4.05*	*36 Pa*	*181*	*76.9%*	*2.1%*	*0.5%*	*20.5%*

Mobility (Leaching studies)

Mobility was studied in a soil column study on a sandy soil in a 5 cm diameter and 140 cm high soil column. The soil contained 92% sand, 2.1% clay, 0.067% organic carbon and pH was 6.4. The soil column received 14 cm water per day over 45 days with the measured concentrations 3.4 and 0.57 mg/l 1,2,4-TCB. When 3.4 mg/l was applied, 46% was leached and 54% was degraded or not accounted for. When 0.57 mg/l was applied, 39% was found in eluate and 61% was degraded or not accounted for. The amount of volatiles was not determined (Wilson et al., 1981) although other studies indicated volatility to be essential. The study indicates that 1,2,4-TCB may leach into groundwater in sandy soils with low content of organic carbon. The potential for mobility is confirmed by recoveries in groundwater surveys (see **Table 3.15**).

Adsorption

The adsorption was studied according to OECD TG 106 in three soils; alfisol clay soil (0.76% organic carbon (OC)) using the concentration range 6-25 µg/l, spodosol (sandy soil, 3.56% OC) in the concentration range 7-127 µg/l and entisol (clay soil 1.11% OC). The adsorption coefficient K values were 9.7, 82 and 10.7 and the estimated Koc values were 1,300, 2,300 and 970 for alfisol, spodosol and entisol, respectively (Broecker et al., 1984).

Three silty clay soils are used in an adsorption study of soils with low organic carbon content (1.2, 0.11 and 0.06% OC, respectively). The initial concentrations were 0.5-1.0 mg/l. Koc values were estimated to be 885, 2,100 and 1,300, respectively for the three soils. (Southworth and Keller, 1986). The soils were all clay soils with a clay content of 60, 86 and 68%, respectively.

The Freundlich adsorption constant in a peaty soil (29% organic matter) was 241.4 resulting in a Koc of 1,441 (Friesel et al., 1984). The difference between adsorption and desorption (K_{des} 200.8) indicates a high degree of reversibility of sorption.

In the study by Chiou et al. (1983), the adsorption was studied in a silt loam with 1.9% OM and a log Kom of 2.70 is presented. Recalculating Kom to Koc would result in a Koc of 864.

In an American study on an alluvial soil with low carbon content, the adsorption distribution constant K varied between 1.2 and 11.6 (l/kg) and the Koc values were calculated to be in the range 800 to 2,490 with the mean ± SD to be 1,460 ± 440 (Banerjee et al., 1985)

Other reported Koc values were 2,042 (US EPA, 1980; Howard, 1989; Calamari et al., 1983) and 1,000 (Wilson et al., 1981). Higher values of Koc have been found in the literature and using the TGD estimation (log Koc = 0.81 log Kow + 0.1) would result in Koc = 2,401.

A QSAR estimation performed by first order molecular connectivity index resulted in an estimated Koc of 718 (PCKOC in EPIWIN, 1995; Meylan and Howard, 1994).

The average Koc value from the data mentioned in this report is 1,424 and a Koc of 1,400 is used in the risk assessment estimations.

Conclusion on mobility and adsorption

1,2,4-TCB has a high adsorption capacity and the mobility in soil is expected to be low. However, because the degradation is slow in soil, 1,2,4-TCB may leach through sandy soils low in organic carbon content and reach groundwater.

Volatility

Volatilisation from surface water is estimated by means of 1,2,4-TCB's Henry's Law constant (H). Using a vapour pressure of 36 Pa at 20°C and a water solubility of 36 mg/l, the estimated Henry's Law constant would be 181 $Pa \cdot m^3/mol$ which indicates that volatilisation from shallow waters and after accidental spillage to water may take place.

A more reliable value may be obtained by measuring H directly by direct measurement of concentrations in the gas phase and the water phase in a system at equilibrium. Using a gas-purge technique, a water concentration of 10 µg/l and GC determination, ten Hulscher et al. (1992) measured the dimensionless Henry's Law constant ($K_{air\text{-}water}$) to 0.041 equivalent to a H of 101 $Pa \cdot m^3/mol$ for 1,2,4-TCB. The measurements were carried out in a buffer solution at pH 6.4 which may have changed the solubility of 1,2,4-TCB. Other measured values of H at 20ºC were 122 $Pa \cdot m^3/mol$ ($K_{air\text{-}water}$ 0.050) and 185 $Pa \cdot m^3/mol$ ($K_{air\text{-}water}$ 0.076) (Oliver, 1985; Ashworth et al., 1988, respectively).

QSAR estimation of Henry's Law constant by the bond contribution method resulted in a H estimated to be $2.19 \cdot 10^{-3}$ $atm \cdot m^3/mol$ (290 $Pa \cdot m^3/mol$) (EPIWIN, 1995).

The volatilisation rate in an aqueous solution has been observed to be 6.5 hour/m depth at 20°C (Geyer et al., 1985). The volatility from an aqueous solution was studied using the water sampling method. The initial concentration was 10.7 mg/l and the half-life was estimated to be 22 minutes at 20°C using ^{14}C-labelled substance (Korte and Freitag, 1986). These studies confirm that volatilisation takes place but the results are not in a form that can be used quantitatively in this risk assessment.

The volatilisation from soil is reduced at increasing content of organic matter due to adsorption. In soil incubated with 1,2,4-TCB at the concentration 50 ppm, the amount of volatile substances recovered from the test systems was 4 to 18% of the initial concentration from soil with high organic matter and 20 to 40% at low organic matter (Marinucci and Bartha, 1979).

Conclusion on volatility

The volatilisation of 1,2,4-TCB in clean water may be high but will be reduced in natural surface water according to the depth of the water body, possible stratification or turbulence of the water body and to the content of dissolved organic carbon (DOC) and particulate organic carbon (POC). The volatilisation is slow from soil and sludge because adsorption to organic carbon takes place.

3.1.3.3 Bioaccumulation

The log K_{ow} is >3 indicating that bioconcentration in aquatic organisms may occur. In a number of bioaccumulation studies, the bioconcentration factor values (BCF) values observed in fish ranged from 120 to 3,200. Comparatively, the QSAR estimated BCF (fish) are 250 according to EPIWIN, and 600 according to Bintein. Finally, according to the equation recommended in the TGD the estimated BCF (fish) is 550.

Table 3.7 Reliable bioconcentration factors (BCF)

Organism	Exposure mg/l	Exposure days	BCF (whole body)	Reference
Fish:				
Salmo gairdneri	0.0000032	119 days	1300	Oliver and Niimi (1983)
Salmo gairdneri	0.000052	105 days	3200	Oliver and Niimi (1983)
Cyprinus carpio	0.005	42 days	120-1320	MITI (1992)
Cyprinus carpio	0.05	42 days	420-1140	MITI (1992)
Jordanella floridae	0.0038	28 days	2026	Smith et al. (1990)
Leiostomus xanthurus	0.010	28 days	135	Heitmüller and Clark (1989)
Brachydanio rerio	0.0085	28 days	1412	Ballhorn et al. (1984)
"	0.1129	28 days	865	"
"	0.1709	28 days	683	"
"	0.2141	28 days	574	"
Cyprinus carpio	0.004		830	Broecker et al. (1984)
"	0.04		805	"
Poecilia reticulata	0.136	17 days	1139	Eck et al. (1997)
Crustaceans: *Daphnia*	0.003		142	Callahan et al. (1979) (static)
Penaeus duorarum (shrimp)	0.0085	12 days	69	Heitmüller and Clark (1989)
Algae: *Chlorella fusca*	0.05	24 hours	250	Freitag et al. (1985) Geyer et al. (1984)

* Comments to the table values are presented below

Carlson and Kosian (1987) and Freitag et al. (1985) derived BCF values in fish of 410 and 490 in short-term tests of 4 and 3 days, respectively. These BCF values are not considered valid because steady state had not been reached (cf. OECD TG 301E).

The rainbow trout exposed for 119 days in a flow through system at 3.2 ng/l showed a bioconcentration factor of 1,300 while exposed to water containing 52 ng/l for 105 days showed a BCF of 3,200 (Oliver and Niimi, 1983). The ng/l concentration level was chosen as this concentration was observed in water and effluents of the Great Lakes in Canada.

In the study on juvenile American flagfish (*Jordanella floridae*) exposed to 3.8 µg/l for 28 days followed by a depuration period of 5-7 days, the elimination time half-life was estimated to be 1.21 days and the whole fish bioconcentration factor 2,026 (Smith et al., 1990).

The bioaccumulation from water and food sources was studied in the marine fish Spot (*Leiostomus xanthurus*) in a 28-day flow through study (Heitmüller and Clark, 1989). The measured concentration in water was about 8.5 µg/l. Fish exposed to TCB in water and given no food resulted in a BCF of 69. Fish fed with unexposed food showed a BCF of 135. If the food (pink shrimp, *Panaeus duorarum*), previously exposed to TCB for 12 days, was available the fish BCF was 122. Thus, 1,2,4-TCB was accumulated from contaminated water and the

accumulation from contaminated food was negligible (Heitmüller and Clark, 1989). The depuration half-life was estimated to be 0.2 days.

The study on Zebrafish (*Brachydanio rerio*) was performed as a semi-static test (renewal every other day) almost following OECD TG 305 B. The concentrations were measured initially and at water changes. After 48 hours, 50-90 % remained in the glass plate covered aquaria. The values presented in the table above are average values. The BCF increased at reduced concentration levels (Ballhorn et al., 1984).

The daphnia continuously exposed to 3.1 µg/l had a mean equilibrium ^{14}C- residue body burden of 0.44 mg/l, resulting in a BCF of 142 (Callahan et al., 1979).

The bio-uptake of 1,2,4-TCB from spiked sediment by oligochaete worms was studied using mainly *Tubifex tubifex* and *Limnodrilus hoffmeisteri*. The sediment with a 4.6% organic matter content was placed in water tanks at 3 kg (5-6 cm depth), spiked with 1,2,4-TCB and aged for 6 weeks before 13 g of worms (~7,000 worms/m^2) were added. The exposure period was 79 days at 8°C and 20°C. After 4 and 79 days, the sediment concentration was 650 and 550 ng/kg dry weight. The exposed worms accumulation factor (worms / sediment) was 0.3 after 4 days and 0.2 after 79 days of exposure at 8°C. The water concentration was 1.8 ng/l after 14 days at 8°C and 2.5 ng/l at 20°C (Oliver, 1987).

Lipid normalised BCF

Studies on *Jordanella floridae* using the procedure proposed by ASTM in 1978 where the juvenile fish, 4 to 6 month-old and with a lipid content of 11.4% of total body weight were kept in a flow-through system at 25°C. At the test concentration 3.8 µg/l during 28 days, the BCF based on the lipid content (BCF_l) was 17,750 (Smith et al., 1990).

The study on carp (*Cyprinus carpio*) was performed as a flow through test according to OECD TG 305 C. The test concentrations were measured. The fish had a lipid content of 4.8% and based on this the maximum BCF_l of about 17,000 was found, compared with about 800 for the whole fish (Broecker et al., 1984). No time dependent increase was observed and the steady state is expected within 7 days.

Normalising the BCF based on wet weight with the fish lipid content, the data from several studies resulted in an average lipid content of 5.2% and a BCF 847 and an average BCF_l (lipid) of 15,403 (BUA, 1987).

Field-measured bioaccumulation factors (BAFs)

Field-measured bioaccumulation factors (BAFs) include site-specific considerations, e.g. food chain structure of the ecosystem, trophic level of the organisms of interest, and concentration of dissolved organic content (DOC) and particulate organic carbon (POC) in the water. BAFs for 1,2,4-TCB have been measured in 4 species living in an American effluent/cooling water canal receiving discharge from a chemical manufacturing plant that produced a variety of synthetic organic chemicals (Burkhard et al., 1997). The results are presented as lipid-normalised BAFs and corrected by determining BAFs using only the freely dissolved concentrations of the chemicals in the water (BAF_l^{fd}). The water concentration ranged from 81.9 to 382 ng/l and averaged 269 ng/l. The sediment ranged from 2 to 299 mg/kg organic carbon and averaged 100 mg/kg organic carbon (Burkhard et al., 1997).

Table 3.8 Field measured bioaccumulation factors, lipid normalised and corrected for freely dissolved organic carbon (BAF_l^{fd}) used to correct for bioavailability
(Burkhard et al., 1997)

Animal	Species	Concentration, average (range) mg/kg of lipid	BAF_l^{fd}	BCF * estimated , whole body
Crab	*Callinectes sapidus* (Blue crab)	10.0 (4.0-19.1)	41,700	
Fish	*Fundulus heteroclitus* (Mummichog)	15.8 (3.7-35.1)	47,900	2,395
	Micropoganias undulatus (Atlantic croaker)	10.0 (3.1-17.0)	56,200	1,810
	Brevoortia patronus (Gulf menhaden)	13.2 (8.8-15.8)	72,400	3,620

* Lipid concentration in fish assumed to be 5% w/w.

Accumulation in earthworms

The accumulation in earthworms was studied by Beyer (1996) in a standard soil (69.7% sand, 20% clay, 10% peat and 0.3% $CaCO_3$) where clitellate, i.e. sexually mature, *Lumbricus terrestris* were exposed to 10 ppm 1,2,4-TCB during 8 and 26 weeks. The BCF was 0.09 in the 8-week experiment and 0.06 in the 26-week experiment (Beyer, 1996). Because of 1,2,4-TCB's high-adsorption capacity and the high-soil organic matter content in the study, BCF would be expected to be lower than under most field conditions. Taking these results into consideration results from other organochlorines including hexachlorobenzene indicate according to Beyer (1996) that BCF of 1,2,4-TCB for earthworms may be around 1 in soil with normal ranges of organic matter. Beyer (1996) shows that $BCF_{earthworm}$ for chlorobenzenes increases with the degree of chlorination and that the BCF of hexachlorobenzene for *Lumbricus terrestris* was 0.27. He compares this result in a study with an OECD standard soil with 10 % organic matter with a study where a BCF for *Lumbricus terrestris* was 2 to 3 in a soil with 2.6% organic matter (Lord et al., 1980).

In comparison by employing the equilibrium method, the bioconcentration factor for earthworm, according to the TGD (equations 62 and 63) and taking the soil-water partition coefficient into account, is estimated to be:

$$BCF_{earthworm} = K_{earthworm\text{-}porewater} \cdot ((RHO_{soil} \cdot 10^{-3})/K_{soil\text{-}water}) = 0.25 \cdot 0.16 \cdot K_{ow} \cdot (1.700/42.2)$$

= 18; i.e an order of magnitude higher than the BCF based on experimental data, which however is regarded more reliable, because of the existence of comparable results in several studies with other chlorinated benzenes.

Accumulation in activated sludge

The bioconcentration in activated sludge from municipal sewage treatment plant was studied after aerobic degradation at low concentration (0.05 mg/l) with 5 days incubation. The bioconcentration factor (concentration in sludge/concentration in water) was 1,400 (Freitag et al., 1985).

Conclusion on bioaccumulation

1,2,4-TCB has a log K_{ow} of 4.05 indicating a bioaccumulation potential. This was confirmed by several tests on different fish species and other aquatic species.

The bioconcentration factor BCF for fish/water (whole body) is according to the realistic worst-case concept approximately 2,000, which is used in the risk assessment.

Based on experimental data, the BCF on earthworms (worm/sediment) is estimated to be 1, which is used in the risk assessment.

3.1.4 Aquatic compartment

3.1.4.1 Measured exposure data

Concentrations measured in industrial effluents

The measured concentrations in industrial effluents are usually not available in open literature. However, a French monitoring study from 1993 was available. The effluents of 114 industrial sites in the Rhône-Alpes region in France were monitored in 1993 for several chemical substances. A single 24-hour mixing sample was taken at each site. 1,2,4-TCB was detected in 10 of the monitored effluents:

Table 3.9 Releases of 1,2,4-TCB in the Rhône-Alpes region in France (INERIS, 1994)

Industrial activity	Daily release (kg/d)	Concentration in effluent (µg/l)
Chemical industry	0.582	20
Chemical industry	13.591	77
Chemical industry	0.0001 *	19
Chemical industry	0.601	43
Chemical industry	0.420	23
Paint manufacturing	0.006 *	11
Paint manufacturing	0.0005	9
Textile dying	0.048	80
Textile dying	2.645	6,150
Solvent recycling	0.0034 *	102

* Release into sewer system; not clear whether further treatment or not

The reference (INERIS, 1994) confirms that textile dying may release substantial amounts of 1,2,4-TCB.

In industrial effluents measured by US EPA, concentrations of 10-100 µg/l were measured in industrial effluent (Perry et al., 1979).

Concentrations measured in STP

The concentrations in wastewater treatment plants (STPs) were measured at several occasions and some of the results considered representative are presented in **Table 3.10**.

Table 3.10 Concentrations measured in wastewater

Wastewater		No. of samples / % positive or total no.	Max (µg/l)	Average (µg/l)	Reference
Denmark:					Grütner and Jacobsen (1994), Mikkelsen (1995)
Municipal STPs	influent 1992	12 / 50%	0.03	<0.02	
	effluent 1992		<0.01		
Germany:		11 / 9%			Kröber and Häckl (1989)
Municipal STPs	influent 1987		2.0	<0.5	
	influent 1988		0.07		
	effluent 1988		0.02		
Municipal STP at production site					Manufacturer information (1996)
	effluent 1993-1995		14, 28		
USA: Industrial wastewater:					US EPA (1980)
foundries	raw w.	2 / 100%	1,000	500	
	treated w.	2 / 100%	570	290	
textile mills	raw w.	50 / 16%	2,700	410	
	treated	50 / 32%	1,400	14	
electronics	untreated	2 / 100%	27,000	16,600	
Municipal STPs, Cincinnati, 1982	influent	16 / 81%	1,800	640	Dunovant et al. (1986)
		6 / 33%	0.43, 12	2	
		4 / 25%	18		
Industrial and municipal STPs US surveyeffluent			0.25-500		US EPA, 1985 (Ware and West, 1977)
California, LA Municipal	effluent		130		US EPA (1985)
Industrial wastewaters	1978-1979	3,268/30 (~1%)	1,012-607	161	US EPA (1985)
California Municipal STP, effluent:			**1975** Jun-Jul.:	Dec.:	1975: Young and Heesen (1980)
Los Angeles County			6.0	1.8	
Los Angeles City	"5-Mile"		5.7	3.1	
Los Angeles City	"7-Mile"		275	130	
Orange County			0.32		
San Diego City			0.23	<0.01	
Oxnard City			0.93	0.25	
California Municipal STP, effluent:			**1976** May-Jun.:	Dec.:	1976: Young et al. (1980)
Los Angeles County			3.6	1.8	
Los Angeles City	"5-Mile"		2.9	0.76	
Los Angeles City	"7-Mile"		100	43	
Orange County			0.18	0.76	
San Diego City			0.16	0.25	
Oxnard City			0.89	0.27	
Canada:					Oliver and Nicols (1982)
effluents, four STPs	1980		0.005-0.018	0.011	

Measurements from three Danish municipal STPs in October 1992 resulted in 0.01 to 0.03 µg/l (mean <0.02 µg/l, 6 positive out of 12 samples) in the influent and below detection limit to 0.01 µg/l in the effluent (1 positive out of 12 samples) (Grüttner and Jacobsen, 1994; Mikkelsen, 1995).

The effluent from a STP at a major production site was measured during 1994-1995. The concentrations of 1,2,4-TCB were measured to be <50 µg/l (28 and 14 µg/l, manufacturer information, 1996).

Composite influents from 3 municipal wastewater plants in Cincinnati, USA, were measured. Industrial wastewater contributions to the plants were approximately 30%, 10% and 2%. The detection limit was 0.4 µg/l in 8-hour averaged samples (Dunovant et al., 1986). For results, cf. **Table 3.10**.

In the studies by Young and Heesen (1980) and Young et al. (1980), the concentrations in the municipal effluents from the largest STPs in Southern California were measured at the submarine discharge zone. The samples were averages of two replicates of 1-week composites collected twice a year (cf. **Table 3.10**).

Some monitoring data include concentrations measured after sewage treatment but before further treatment. These data are not included in the table but are mentioned hereafter. The influent to a "water factory" was the effluent from a municipal STP (Orange county, California). The "water factory" was designed to improve the quality of biologically treated municipal wastewater before injection into the aquifer system. In 1976, the STP trickling effluent contained 1,2,4-TCB in the range <0.02-4.1 µg/l (geometric mean 0.46 µg/l) and in 1978 after switching from trickling-filter to activated sludge treatment, the measured STP effluent range was <0.02-0.5 µg/l and the geometric mean 0.18 µg/l (McCarty and Reinhard, 1980).

The effluent of the Los Angeles County wastewater treatment plant was sampled weekly from November 1980 to August 1981 and quarterly composites were analysed. The effluent contained a mean of 0.77 µg/l 1,2,4-TCB (Gossett et al., 1983).

In conclusion, most data are historic data reflecting previous uses. However, municipal STPs receiving industrial wastewater still contribute to the environmental load of 1,2,4-TCB. Sources to continued release may come from release from e.g. old transformers or as degradation product from substances or preparations containing chlorinated benzenes or combustion products from chlorinated polymers.

Concentrations measured in surface waters

Some literature references on the 1,2,4-TCB concentrations measured in surface water are summarised in **Table 3.11** below. After the table, some of the values are commented upon.

Table 3.11 1,2,4-TCB concentrations measured in surface waters

Location	Date	Range (µg/l)	Mean (µg/l)	Reference
The Netherlands River Rhine, NL	Jul 1979		1	Zoeteman et al. (1980)
Germany Rhine	1975-86	<0.01-5.1		IUCLID Borneff et al. (1978)
River Rhine (Düsseldorf-Flehe)	1985	<0.01-0.13	0.03	ARW (1985)
River Rhine Wiesbaden Köln/Cologne Düsseldorf-Flehe Wesel	1986	 0.02-0.13 0.02-0.06 0.03-0.37 <0.01-0.07	 0.05 0.04 0.05 0.03	ARW (1986)

Table 3.11 continued overleaf

Table 3.11 continued 1,2,4-TCB concentrations measured in surface waters

Location	Date	Range (µg/l)	Mean (µg/l)	Reference
Rhine (Duisburg)	1982 1983 1984	90% percentile: 90% percentile: 90% percentile:	0.1 µg/l 0.1 µg/l 0.1 µg/l	NRW (1985)
Rhine (right bank at side river mouths)	1984-1986	<0.1-0.2	<0.1 l	NRW (1987)
Rhine	1990 1991	0.3 0.14		BUA (1987) IUCLID (1996)
Rhine (Middle river)	1990	<0.1-0.3		NRW (1991)
Rhine (Middle Rhein) River Wupper	1991 1991	<0.1-0.14 <0.1-0.15		NRW (1992)
River Main	1977	max. 0.135	0.06 µg/l	Arendt et al. (1977)
Emscher	1989	<0.1-0.1		NRW (1990)
River Elbe Elbe river mouth Outside river mouth Marine/North See	1982-1983		0.0059 0.00034 0.00005 <0.00003	UBA (1987)
River Elbe Elbe river mouth Outside river mouth /North See	1989		0.0074 0.00052 0.0002	UBA (1989), sampled at 5 m depth
Hamburg (channels)	1982	0.007-0.305		Hamburger Umweltbericht (1985)
Switzerland Lake Zürich	 1973 1976	 0.006+ 0.042 0.004-0.012		 Atri (1986) (surface + 30m depth) Giger et al. (1978) incr. from top to 120 m depth
Scotland Forth estuary	1987 1990	0.04-5.49 <0.0012-0.084		Rogers et al. (1989) Harper et al. (1992)
Spain Besós river mouth llobregat river mouth Marine Barcelona La Pineda	 1985-1986	 8.100 ±0.12 1.200 ±0.14 0.0054 ±0.21 0.0081 ±0.25 0.0036 ±0.08		Gomez-Belinchon et al. (1991)
Japan (Kyushu) River Sea	1988 2/13 2/12	 ND-0.03 ND-0.12		Uchimura and Shinohara (1988)
Canada Lake Huron (5 stations) Lake Ontario (5 stations) Grand River Niagara River	1980	 0.0001-0.0004 0.0003-0.001 <0.0001-0.008 0.0001-0.107	 0.0002 0.0006 0.002	Oliver and Nicol (1982) 0.107 just below chemical plant
Canada, Niagara river at Niagara-on-the-Lake at Fort Erie	1981-1983	 0.0058-0.120	 0.016 0.00053	Oliver and Nicol (1984)

Scotland

In water samples from the Forth estuary in Scotland, it was observed that the concentration of 1,2,4-TCB had been reduced by between one and two orders of magnitude between 1987 and 1990. The reduction was mainly due to alterations in the manufacturing processes by a factory (ICI), which discharged chlorobenzenes to the estuary. The concentration in the ICI effluent was reduced from 3,400 µg/l in 1987 to 1.32-480 µg/l (mean 172 µg/l) measured monthly during 1990. The concentrations found in the estuary water lie within the ranges <0.0012-0.084 µg/l (Harper et al., 1992).

Spain

The monitored rivers, Besós and Llobregat, are located north and south of Barcelona. Their waters share multiple uses (domestic, industrial, agricultural etc.) and receive a wide spectrum of waste. The River Llobregat is used as a major source of municipal water for the city of Barcelona. The samples were taken monthly at the river mouth and from open seawater in front of the rivers at a maximum distance of 2 miles (3 km) (Gomez-Belinchon et al., 1988).

Canada

The River Niagara receives large input from industries during its course. The flow was 6,400 m^3/s. The measurements were taken weekly during two years. The mean measured value was 16 ±16 ng/l and the median value 12 ng/l (Oliver and Nicol, 1984).

Germany

Measurements (14 days mixed samples) from the River Rhine at Düsseldorf found the geometric means 0.05 µg/l in 1982, 0.02 µg/l in 1983 and 0.06 µg/l in 1984. Based on 1984, the transportation of 1,2,4-TCB at the measured place using the annual flow mean of 2,400 m^3/s was calculated to be 12.4 kg/day (ARW, 1984). A water plant using bank filtrated water measured an increasing amount of 1,2,4-TCB after bank passage. The time for filtration in the river banks was estimated to be 4 to 6 weeks. The measured geometric mean in the River Rhine was 0.05 µg/l, after bank filtration 0.09 µg/l, after ozonation of the raw water 0.04 µg/l, and after filtration by active carbon below detection level. The increased levels in the bank filtrated water are stated to be caused by earlier higher concentrations in the River Rhine (ARW, 1984).

The River Rhine has been monitored for several years and most concentrations of 1,2,4-TCB were below 0.1 µg/l. The changes in concentrations in water were time-dependent (BUA, 1987). A review of the data obtained from German monitoring programmes from 1988 to 1991 (UBA, 1994) supports that most measured values are reduced during the years except for the River Main where an increase in 1991 was observed with an average of 0.138 µg/l and a maximum of 0.35 µg/l. The 90% percentile was <0.1 µg/l in 1991 in most German rivers except for the Main where the 90% percentile was 0.25 µg/l (UBA, 1994), cf. **Table 3.12**.

In a study on a River Main bank-filtration water works, it was also observed that the bank-infiltrated water contained a higher concentration of 1,2,4-TCB than the river from which the water was taken. The River Main mean concentration was 0.013 µg/l, from the collected bank infiltration well, the concentration was 0.027 µg/l, and in a single well the concentration was 0.020 µg/l. It is stated to be because 1,2,4-TCB has a low degradability, is adsorbed during the infiltration and is in time accumulated, and at events with higher flow desorbed again (Haberer and Drews, 1985).

Table 3.12 Recent data on rivers

Location	Year	Range (µg/l)	Mean (µg/l)	90% percentile (µg/l)	Reference
Germany River Elbe at: Zollenspieker Seemannshöft	1992/93	 0.003-0.024 0.003-0.022		Median: 0.0053 90-percentile: 0.015	Götz et al. (1998)
River Elbe (Schnackenburg)	1993	<0.001-0.010	0.003		Arbeitsgemeinschaft für die Reinhaltung der Elbe (1994)
Rhine at: Village Neuf Lauterburg Koblenz Bimmen	1993	 <0.02-0.30 <0.01-0.04 <0.01-0.01 <0.2-<0.2	 0.04 0.01 <0.01 <0.2		IKSR (1993)
Rhine: Most values Lauterburg Main: Mosel:	1994	 <0.01-<0.2 <0.01-0.24 <0.01-0.07 <0.01-<0.01	 <0.2 0.03 0.02 <0.01	 <0.2 0.16 0.03 <0.01	 DKR (1996) IKSR (1996) DKR (1996) DKR (1996)
France Rhône and its affluents River Rhine in eastern France	 1993/97 1997	 <1-1.4 <0.02	 0.01 <0.02		 Banque nationale de l'eau, France, pers. comm. (1998) Agence de l'eau Rhin-Meuse, pers. comm. (1998)

More recent monitoring (after 1992)

Twenty samples taken during 1992/93 in the River Elbe near Hamburg at a 1-2 m depth from two locations were all above the detection limit of 1 ng/l (Götz et al., 1998).

The River Elbe has been monitored weekly during 1993 (Arbeitsgemeinschaft für die Reinhaltung der Elbe, 1994). The measured concentrations at Schnackenburg were <0.001-0.010 µg/l.

In a monitoring programme in France of the surface waters of the River Rhône and its affluents from September 1993 to December 1997, one positive result out of 153 samples was observed. The determination level was either 1 or 10 µg/l (Banque nationale de l'eau, France, personal communication, 1998).

In a monitoring study from in the Rhine and Meuse area (eastern France) during 1997, the concentrations of 1,2,4-TCB were all (n=88) below the determination level of 0.02 µg/l (Agence de l'eau Rhin-Meuse, France, personal communication, 1998).

According to a Fraunhofer study compiling data from Germany, Spain, France and Luxemburg (Herrchen and Müller, 1997) 1,2,4-TCB has been measured above the determination limit in 156 out of 593 measurements (26%) from 1985 to 1996 in surface waters. The mean concentration was 0.692 µg/l and the median concentration was 0.001 µg/l.

A further analysis of the data from 1993 and 1994 in surface water is performed in a second study from the Fraunhofer Institute (Klein et al., 1997). The results are presented below to show the difference in including values below the determination limit set equal to 0 or to ½ the determination limit.

Table 3.13 Concentrations in German surface water (Klein et al., 1997)

Location	Year	Number	No. >d.l.	Mean (µg/l)		Median (µg/l)	
				c<d.l=0	c<d.l.=½d.l.	c<d.l=0	c<d.l.=½d.l.
Rivers*	1993	344	110	0.00639	0.0641	0.0001	0.1
	1994	149	20	0.00502	0.0342	0.0001	0.1
NRW	1993/1994	20	0				
total	1993/1994	513	130				

* German rivers to the North Sea including their affluents. NRW: Nordrhein-Westfalen

Conclusion for surface waters

Monitoring data from rivers and lakes in Europe and North America show 1,2,4-TCB levels up to around 1 µg/l, and the vast majority of levels being one or two orders of magnitude less than this concentration level. Generally, monitoring data later than 1992 show levels of two to three orders of magnitude less than earlier monitoring data.

Concentrations measured in marine water

Table 3.14 Concentrations measured in marine surface water

Location	Year	Range (µg/l)	Mean (µg/l)	Reference
North Sea, SE German Bay	1983 1989	<0.00003-0.0059 0.0002-0.0074		UBA (1987) UBA (1989)
North Sea 2-70 km from NL coast	1983-1984	<0.0003-0.024	0.0016	van de Meent et al. (1986)
W. Mediterranean STP dispersion zone Rhône river mouth Rhône dispersal zone open sea	1984	 <0.020-0.082 <0.002-0.023	 0.300 <0.002	Marchand et al. (1988)

In the studies in the North Sea, the concentrations decreased with increasing distance to the coast indicating the dilution of the organic substances discharged from the rivers and the air-sea exchange by volatilisation and dry and wet deposition processes (van de Meent et al., 1986).

Concentrations measured in ground and drinking water

Table 3.15 Concentrations measured in ground and drinking water

Location	Year	Range (µg/l)	Mean (µg/l)	Reference
Canada: 3 cities, 1 sample each		0.001-0.004	0.002	Oliver and Nicol (1982)
USA: 113 cities		0.002-0.58	0.008	Kraybill (1983)
Switzerland: Groundwater	1976	<0.001-0.012		Giger et al. (1978)
Netherlands: 259 wells	1976	max. 1.2		Zoeteman et al. (1980)

The results from ground water in the Zürich area, Switzerland, were obtained from monitoring 44 drinking water wells. Only one single event of 0.012 µg/l was observed, the other wells contained 1,2,4-TCB below the detection limit of 1 ng/l (Giger et al., 1978).

More recent data have not been provided.

In conclusion, in ground water, monitored levels of 1,2,4-TCB two decades ago are generally at or below the detection limit of 1 ng/l.

Concentrations measured in sediment

Measurements of 1,2,4-TCB in river sediments reveal considerable fluctuations between <0.1 µg/kg and a single value of 1,000 µg/kg (Rhine sediment 1979, IUCLID). Of recent measurements, the harbour sediments in Hamburg averaged 83.5 (range 9 to 1,064) µg/kg dry weight in 1990 (IUCLID, 1996; BUA, 1987).

In a German river, sediments were measured at 0.6 µg/kg and 2.1 µg/kg (BUA, 1987). The sediment near the discharge zone of Los Angeles County STP contained 9 µg/kg dry weight (Gossett et al., 1983).

Table 3.16 Concentrations measured in sediments

Location	Year	Range	Mean	Reference
Germany				LUA NRW (1996)
River Rhine (n=34)	1994-1995	3-64 µg/kg dw	13 ±12 µg/kg dw	
River Sieg (n=6)	1993-1994	<2-<16 µg/kg dw		
River Wupper:	1994			
river mouth		3.6 µg/kg		
Wipperaue		1.7 µg/kg		
near by STP		5.6 µg/kg		
River Rhine	1985-1988	<0.3-97 µg/kg dw		Kröber and Häckl (1989)
River Main		<0.3-69 µg/kg dw		
Schwarzbach		<0.3-15 µg/kg dw		
Fulda		<0.3-392 µg/kg dw		
Hamburg harbour		nd-1,064 µg/kg dw	83.5 µg/kg dw	Götz et al. (1990)
Hamburg channels	1981	nd-89 µg/kg dw		Hamburger Umweltberichte (1985)
	1982	nd-17.9 µg/kg dw		
The Netherlands				Beurskens et al. (1994)
Lake Ketelmeere	1965		240 µg/kg	
(Rhine estuary)	1985		70 µg/kg	
France				
Rhône river	1989			Santiago et al. (1994)
suspended sediment		nd-676 µg/kg	90 µg/kg	
bed sediment		nd-90 µg/kg	42 µg/kg	
Rhône and affluents:	1993-1997			Banque nationale de l'eau, pers.
suspended matter		nd-3,260 µg/kg	34.3 µg/kg	comm. (1998)
sediment		nd-370 µg/kg	5.1 µg/kg	
River Rhine in eastern	1992-1996			Agence de l'eau Rhin-Meuse,
France	42/88	<0.2-42 µg/kg dw	3.5 µg/kg dw	pers. comm. (1998)
Denmark				
5 lakes, Aarhus county	1997 4/5	<0.5-3.3 µg/kg dw	1.6 µg/kg dw	Aarhus Amt (1998)
5 rivers, Aarhus county	1997 2/5	<0.5-2.8 µg/kg dw	1.7 µg/kg dw	
Marine: Fjords	1997 4/68	<1-20 µg/kg dw	9 µg/kg dw	
USA				Kuntz and Warry (1983)
Niagara-on-the-Lake	1980		61 ±42 µg/kg dw	
suspended sediments				
Niagara-on-the-Lake	1981			Fox et al. (1983)
suspended sediments		33-210 µg/kg dw	100 µg/kg dw	
bed sediments		59-220 µg/kg dw	95 µg/kg dw	
Canada	1980			Oliver and Nicol (1982)
Lake Superior	13/	0.1-4 µg/kg	1 µg/kg	
Lake Huron	42/	1-26 µg/kg	6 µg/kg	
Lake Erie	5/	1-9 µg/kg	3 µg/kg	
Lake Ontario	11/	20-220 µg/kg	94 µg/kg	
Niagara Basin	1976-1980		260 µg/kg	
Japan	1988			Uchimura and Shinohara (1988)
River sediment	6/12	nd-190 µg/kg dw		
Sea sediment	4/8	nd-38 µg/kg dw		

nd: not detected

Sediment cores from Lake Ketelmeere (NL), which is a sedimentation area of the River Rhine, were analysed to detect historical changes (Beurskens et al., 1994). As presented in **Table 3.16**, the concentrations were highest in the oldest layers.

Historical records from analysing sediment cores were performed in Lake Ontario near the Niagara River at a 70 m water depth. The sediment core was sectioned at 1 cm intervals and dated by ^{210}Pb content in depth. The maximum value was measured to be 410 ppb (about 1960). The content in sediment decreased to the latest deposited sediments from 1980-1981 where 66 ppb 1,2,4-TCB was measured (Durham and Oliver, 1983).

In 1982, the upper sediments in Western, Central and Eastern Lake Erie were sampled. The range in 46 samples was 1.3-14 µg/kg dw and the mean values were 5.3, 2.3 and 2.5 µg/kg dw, respectively (Oliver and Bourbonniere, 1985).

The concentration of 1,2,4-TCB in settling particulates and the sedimentation rate in the Niagara vicinity of Lake Ontario were measured by sediment traps placed at different depths in the lake. The traps were collected monthly during May-Nov. 1982. The average concentration at a 20 m depth ranged from 23-55 µg/kg and the downflux was calculated to vary between 18-400 ng/m^2/day. The Niagara River averaged 11 ng/l in the same period. The lake Ontario bottom sediments averaged 110 µg/kg dw (Oliver and Charlton, 1984).

Table 3.17 Measured concentrations of 1,2,4-TCB in suspended matter/particulate matter in fresh water

Location	Year	Range (µg/kg dw)	Mean (µg/kg dw)	Reference
Germany River Elbe	 (n=12)		 143	 Götz et al. (1990)
River Rhine, Lauterburg	1991	<10-90	58	IKSR (1991)
River Rhine at: Koblenz Bad Honnef Kleve-Binnen Mosel	1992 (n=12)	 8-55 27-120 70-190 <1-16	 22 61 121 7	Deutsche Kommission zur Reinhaltung des Rheins (1995)
River Rhine at: Lauterburg Koblenz Mosel Bimmen	1993 (n=12)	 <2-30 6-42 <1-9 8-170	 18 20 5 87	IKSR (1993)
USA Niagara on the Lake Lake Ontario		 33-210 59-220		Fox et al. (1983)

Table 3.18 Concentrations of 1,2,4-TCB in suspended matter of Hessian Rivers (µg/kg dw) (Fooken et al., 1997)

Year	Detection limit (DL)	Minimum	Maximum	No. of rivers	No. of values above DL:
1991	2	<DL	20	2	1
1992	5	77	100	2	2
1994	1	3	71	10	10
1995	1	<DL	17	12	10
1996	1	2	86	13	13

The Hamburg harbour sediment was measured to contain the median value of 35 µg/kg dw (95% confidence interval 23.6 to 56.3 µg/kg dw (n=36)) 1,2,4-TCB. The concentration is suggested to be a result of the sedimentation of particulate matter (Schwebstoff) from the Elbe River which at Schnackenburg had the median value of 143 µg/kg dw (95% confidence limit 130.5 to 155.5 µg/kg dw) (n=12) (Götz et al., 1990).

The concentration of 1,2,4-TCB in suspended solids in the Niagara river mouth at Niagara-on-the-Lake varied between 33 and 210 µg/kg dw. The concentration in the water was 6.4 ng/l water in July where the suspended solids ranged 33-90 µg/kg dw. The concentration in superficial sediments in Lake Ontario (just outside the river) ranged from 59 to 220 µg/kg dw (59 to 120 in July 1981) (Fox et al., 1983).

An analysis of the data from 1993 and 1994 in German river suspended sediments is performed in a second study from Fraunhofer (Klein et al., 1997). The results are presented below to show the difference in concentrations including values below the determination limit set equal to 0 or to ½ the determination limit.

Table 3.19 Concentrations in German suspended sediments (Klein et al., 1997)

Location	Year	Number	No. >d.l.	Mean (µg/kg)		Median (µg/kg)	
				c<d.l=0	c<d.l.=½d.l.	c<d.l=0	c<d.l.=½d.l.
Rivers	1993	175	164	44.1	44.1	24	24
Rivers	1994	155	101	6.15	7.81	0.02	0.5
total	1993/1994	330	265				

France

A monitoring programme in France of the suspended matter and sediments of the River Rhône and its affluents during 1993 to 1997 indicated that, in suspended matter 6 positive results out of 153 samples were observed and for sediments 6 positive results out of 153 samples were observed. The determination level varied between 10, 50 and 100 µg/kg. The mean concentration in sediments was 5.1 µg/kg and in suspended matter 34.3 µg/kg (Banque nationale de l'eau, France, personal communication 1998).

In a monitoring study in the Rhine and Meuse area (Eastern France) during 1992-1996, the mean concentration of 1,2,4-TCB was 3.4 µg/kg in sediments and 8.2 µg/kg dw in suspended matter. The determination level was 0.2 µg/kg dw (Agence de l'eau Rhin-Meuse, France, pers. comm. 1998).

Denmark

As part of a national monitoring programme for hazardous substances in the aquatic environment in Denmark, the results from screening programmes were currently available (Danish EPA, Marine Division, personal communication, 1998). The results of the analysis of 1,2,4-TCB in sediments from lakes, rivers (streams) and coastal waters (fjords) in the county of Aarhus sampled in 1997, and the results from marine sediments from the South-western part of the inner Danish waters sampled from December 1996 to March 1997, are presented in **Table 3.16**.

In sediments from 5 lakes in the county of Aarhus, 1,2,4-TCB was measured in 4 mixed samples from above the detection limit 0.5 to 3.3 µg/kg dw with the mean value 1.6 µg/kg dw (1.1 µg/kg in a lake without point source, 0.69 µg/kg in a lake with previous emissions from scattered settlements, 1.2 µg/kg in a river-lake system 500 m downstream from a paper mill outlet and 3.3 µg/kg in the lake sediments 100 m downstream from a STP outlet).

From the measurements of the sediments from 5 rivers (streams in the county of Aarhus), two mixed samples were above the detection limit: 0.5 and 2.8 µg/kg dw, both receiving wastewater emissions. In the sediments of the Bay of Aarhus 0.5 µg/kg dw was measured.

From the Maine sediments sampled in the south-western part of the inner Danish waters Little Belt and adjacent fjords 4 out of 68 samples were above the detection limit of 1 µg/kg dw. Three from Vejle Fjord (5, 6, 20 µg/kg dw) and 1 from Kolding Fjord (5 µg/kg dw), the average of measured values was 9 µg/kg dw.

Conclusion for sediments

Thus, the measured levels of 1,2,4-TCB in sediments from rivers and lakes in Europe and North America range from less than 1 µg/kg sediment (dw) to more than 200 µg/kg sediment (dw). The monitoring data generally indicate a reduction in concentrations of 1,2,4-TCB in the more recent observations and generally concentrations less than 100 µg/kg dw except for measurements from highly polluted areas (e.g. harbours). The monitoring data, however, also indicate that 1,2,4-TCB at least until recently, and possibly still, is being released to the environment not only from industrial manufacturing but also from downsteam uses and/or from processes forming 1,2,4-TCB.

3.1.4.2 Model estimations (PEC_{water})

PEC_{local} for the aquatic compartment

The PEC local of the aquatic compartment is calculated according to the TGD (1996). Using the values from the table in TGD, Appendix II at log K_{ow} of 4.05 and log H of 2.2, the removal was 83%, if the substance is considered inherently biodegradable (TGD corrigendum, 1997). However, the model EUSES ver. 1 estimates the removal in STPs to be 84.7% and 15.3% remains in water. The latter values are used in the risk assessment. The discrepancy can probably be attributed to the Koc used. In the EUSES calculations, the Koc value was set to 1,400 while in

the TGD corrigendum on SIMPLETREAT, the Karickhoff equation has been used by default. The Karickhoff equation results in a Koc of 4,571, which explains the larger fraction to sludge.

Table 3.20 Estimated fate of 1,2,4-TCB in STP

Estimation according to	% to air	% sludge	% degraded	% removal	% to water
TGD Corrigendum 1997	27	44	12	83	17
EUSES ver.1	61.3	11.3	12.1	84.7	15.3

The estimated concentrations in surface waters for the generic scenarios presented in Section 3.1.2.1 are presented in the tables below.

Table 3.21 Estimations of concentration in local surface water during emission episodes

Scenario	E_{water} kg/d	$C_{influent}$ mg/l	$C_{effluent}$ mg/l	Dilution	PEC_{water}** mg/l
Production					
A [1)] *			0.028	240,000	$9.6 \cdot 10^{-6}$
B [2)] *	0.4	0.2	0.031	698	$53.2 \cdot 10^{-6}$
Processing					
D1: intermediate	25.7	12.8	1.96	240,000	$17.7 \cdot 10^{-6}$
D2: process solvent	13.3	6.6	1.02	698	$1.46 \cdot 10^{-3}$
D3: others	4.95	2.47	0.378	10 (d)	0.038
D4: dye carrier	8.93	4.46	0.682	10 (d)	0.068

[1), 2)] cf. Table 3.1, Section 3.1.2.1
* Estimations based on information from the main manufacturer regarding dilution, further estimations based on the TGD
** The local PEC_{water} is $Clocal_{water}$ + PECregional (PEC regional, cf.below)
(d) Default

Since the two site-specific scenarios (A and B) are located at specific emission points from the main manufacturers at large rivers, the site-specific information on dilute factors can be used in the risk assessment for these production sites. However, not all emissions are covered by this and therefore the estimations for the default scenarios D1 to D3 are included according to the TGD. A dilution factor of 10 is used in these PEC estimations, except in scenario D1 and D2 where a dilution factor of 240,000 and 698 is used based on manufacturer information.

Comparison between measured and estimated concentrations for water

$C_{influent}$

The measured concentration of 1,2,4-TCB in STP influents ranged from <0.00001 to 27 mg/l. The estimated values are within the same range.

$C_{effluent}$

The measured concentrations in STP effluent ranged from <0.00001 to 0.29 mg/l. The estimated values are ranging from 0.02 to 2 mg/l which is one to two orders of magnitude higher than the measured values. The difference is probably caused by larger dilution factors at the actual sites than those used in the model calculations of the fate in STP according to the TGD.

$PEC_{local, water}$

The measured concentration of 1,2,4-TCB in surface water ranged from <0.0001 µg/l to 8 µg/l. The estimated values C_{water} are within the range 0.001 to 68 µg/l, i.e. one to two orders of magnitude greater. In most cases, however, the measured values are not from samples taken 100 meters from the industrial discharge and therefore represent more diluted values probably more closely representative for regional concentrations.

PEC_{local} for sediment

The concentration in bulk sediment can be estimated from the concentration in the corresponding water body assuming a thermodynamic partitioning equilibrium according to the TGD.

Estimations based on the previously mentioned scenarios are presented in **Table 3.22**.

Table 3.22 Estimations of concentration in local sediments

Scenario	PEC_{water} mg/l	PEC_{sed} mg/kg ww
Production		
A*	0.0000096	0.0003
B*	0.0000532	0.0017
Processing		
D1: intermediate	0.000018	0.00055
D2: process solvent	0.00147	0.046
D3: others	0.038	1.18
D4: dye carrier	0.068	2.12

* Estimations based on the main manufacturer information on dilution factors
The remaining estimations are based on the TGD

Comparison of measured and estimated concentrations in sediment

The measured concentrations of 1,2,4-TCB in sediment ranged from <1 to >200 µg/kg dw. The estimated concentrations PEC_{sed} ranged from 0.8 to 5,500 µg/kg dw using the conversion factor wet-dry sediment: 2.6 kg ww/kg dw (EUSES). The estimated local concentrations are approximately of the same order of magnitude as the measured concentrations. However, the estimated concentrations are estimated at a distance of 100 m from the point source whereas the measured values are mostly at unknown distances to the sources.

$PEC_{regional}$ and $PEC_{continental}$ for water and sediment

The concentrations of 1,2,4-TCB in the various environmental compartments on the regional and continental scales were estimated with the EUSES v.1.0 programme. A printout from the programme estimations can be viewed as part of the report on the European Chemicals Bureau website (http://ecb.jrc.it).

EUSES estimates the continental PEC in sediment to 0.86 ng/kg ww.
EUSES estimates the $PECregional_{sed}$ to 0.38 µg/kg ww sediment which is in the same level as the lower end of the measured concentrations.

Summary of regional and continental PECs (EUSES)

Regional		
Regional PEC in surface water (total)	$9.52 \cdot 10^{-6}$	mg/l
Regional PEC in surface water (dissolved)	$9.49 \cdot 10^{-6}$	mg/l
Regional PEC in sediment (total)	$3.75 \cdot 10^{-4}$	mg/kg wwt
Continental		
Continental PEC in surface water (total)	$2 \cdot 10^{-8}$	mg/l
Continental PEC in surface water (dissolved)	$2 \cdot 10^{-8}$	mg/l
Continental PEC in sediment (total)	$8.6 \cdot 10^{-7}$	mg/kg wwt

3.1.5 Atmospheric compartment

1,2,4-TCB in relation to persistent organic pollutants (POPs) with a high potential for long-range atmospheric transport is discussed in the risk characterisation section (Section 3.2.2).

3.1.5.1 Measured concentrations in the atmospheric compartment

A few values measured more than ten years ago are summarised in **Table 3.23**.

Table 3.23 Concentration in air

Locality	Concentration range	Average	Reference
Hamburg, Germany (1986-1987)	1.6-6.1 ng/m³ 173 ng/m³ **	3 ng/m³	Bruckmann et al. (1989)
Portland, OR, USA	3.4-4.7 ng/m³	3.8 ng/m³	Ligocki et al. (1985)
Los Angeles, CA, USA Phoenix, AZ, USA Oakland, CA, USA	2.0-33.9 ppt 0.9-10.2 ppt 1.0-15.1 ppt	6.9 ppt ~51.2 ng/m³ 3.1 ppt ~23.0 ng/m³ 3.0 ppt ~22.3 ng/m³	Singh et al. (1981) WHO (1991) *

* The conversion factor at 25°C and 101.3 kPa for trichlorobenzenes in air is: 1 ppt = 7.42 ng/m³, 1 ng/m³ = 0.13 ppt (WHO, 1991)
** Peak value, cf. text

The measurements from Hamburg were taken in the city and surroundings at 12 sites for 25 working days (275 samples) during the daytime over a year (1986-1987) at 1.5 m above the ground. The yearly average air concentrations were mostly within the range 1-6 ng/m³ except a single location in an industrialised area where up to 173 ng/m³ was measured. This site was a

contaminated industrial area where in 1984 a pesticide production was closed down (Bruckmann et al., 1989).

The air concentrations in urban environments were measured at four sites in the USA during 2 weeks at hourly intervals. The min/max and average results are presented in **Table 3.23** (Singh et al., 1981; Ligocki et al., 1985).

The emission of trichlorobenzenes in the Netherlands in 1980 was estimated to 43 tonnes/year (Guicherit and Schulting, 1985). The average and 1-hour concentrations were measured in the most polluted parts of the Netherlands (Delft, Vlaardingen) and in the least polluted part of the country (Island of Terschellingen). The mean concentration range was 10 to 20 ppb v/v (74 to 148 μg/m^3) and maximum 40 to 1,350 ppb (300 to 10,000 μg/m^3) of trichlorobenzenes (total sum of 1,2,3-, 1,2,4- and 1,3,5-TCB) (Guicherit and Schulting, 1985).

Wet deposition

In a rain sampler with a 0.89 m^2 collection surface recovering rain from 4 rain storm events in a semi-rural area in Oregon, USA, the concentration of 1,2,4-TCB in the rain was 0.10 ng/l in one occasion and not detected in the others (resulting in a mean sample concentration of 0.025 ng/l). The collector opened automatically at rain events to exclude dry deposition (Pankow et al., 1984). Based on the equilibrium scavenging for raindrops falling through the atmosphere, the authors estimate the predicted concentration in the atmosphere to be 3.6 ng/m^3, i.e. in the same range as measured in urban air.

The same rain sampler placed at an urban site in Oregon during 5 storm events collected 0.086, 0.11 ng/l and no detectable levels in the rest. The mean concentration was estimated to be 0.049 ng/l rain. The equivalent atmospheric concentration estimated to be 6.9 ng/m^3 (Pankow et al., 1984).

The amount of trace organic compounds in rain was also studied in a residential area in Oregon during 7 rain events using a sampler which collected trace organics in rain in both the suspended particulate and dissolved phases while an air sampler simultaneously collected the atmospheric organics in both particulate and gas phases. Rain sample volumes of 5 to 27 l and air samples of 50-230 m^3 were collected over periods of 1 to 5 days in February through to April of 1984. The temperatures ranged from 3 to 14°C and averaged 8°C. During the 7 rain events, the analyses of dissolved rain concentration showed that 3 were positive (0.13, 0.18 and 0.45 ng/l). The mean concentration was estimated to be 0.25 ng/l in rain. In simultaneous analyses of the atmospheric gas phase concentration, 1,2,4-TCB was observed during all events in the range 3.5 to 4.7 ng/m^3 with the mean concentration 3.8 ng/m^3 (Ligocki et al., 1985).

3.1.5.2 Model estimations of PEC_{air}

Estimates of the release to air from production and processing were made in Section 3.1.2. The TGD provides a method for estimating the air concentration and deposition fluxes from the emission rates.

The estimated concentration in air based on emissions from production and processing and from the emissions from STP, and the atmospheric deposition are estimated for the different scenarios below.

Table 3.24 Estimations of concentrations in local air during a STP emission episode

Scenario	$E_{local, air}$ kg/d	$E_{STP, air}$ kg/d	$Clocal_{,air}$ mg/m³	$PEClocal_{air,ann}$ mg/m³	$PEClocal_{air,ann}$ ng/m³
Production					
A*	0.63	0¤	0.000175	0.000144	144
B*	<0.08	0¤	<0.000023	<0.00002	<19.5
Processing					
D1: intermediate	0.04	0¤	0.000011	0.000004	3.9
D2: process solvent	0.67	8.17	0.0023	0.00187	1870
D3: others	4.95	3.03	0.0138	0.00007	76
D4: dye carrier	0.525	5.47	0.0015	0.00004	42

$Elocal_{air}$: Local direct emission to air during emission episode
$E_{STP, air}$: Local indirect emission to air from STP during emission episode
$C_{STP, air}$: Local concentration in air during STP emission episode
$C_{STP, ann}$: Annual average concentration in air, 100 m from STP
* Estimation based on the main manufacturer information
¤ The exhaust air is incinerated according to the main manufacturers

Continental and regional PECs

The regional and continental PEC were estimated by EUSES to be:

Regional PEC in air (total) $5.46 \cdot 10^{-7}$ mg/m³
Continental PEC in air (total) $5.86 \cdot 10^{-8}$ mg/m³

Comparing measured and estimated concentrations

It is difficult or impossible to compare the different techniques used in the monitoring studies. A uniform standard for the collection of air concentration data has not been employed (collection equipment, time, frequency, etc.).

The estimated local air concentrations are two orders of magnitude greater than the measured air concentrations. The former, however, are concentrations estimated at a distance of 100 m from point source whereas the measured concentrations are from unknown distances to the source. The measured concentrations may more or less represent regional values, except for the single value of 173 ng/m³ from a polluted industrial site in Hamburg (Brockmann et al., 1989). The regional PEC_{air} is estimated to 0.5 ng/m³ by employing EUSES. Thus, the estimated concentrations are considered to be in the relevant concentration range in comparison with measured concentrations.

Deposition

The deposition of 1,2,4-TCB from air is estimated based on the direct releases from production and use and the indirect release from STP.

The estimations of the total deposition flux (DEP_{total}) and the annual average total deposition flux ($DEP_{total, ann}$) are shown below.

Table 3.25 Estimations of deposition from local air

Scenario	E_{air} kg/d	$E_{STP,air}$ kg/d	DEP_{total} µg/m²/d	$DEP_{total, ann}$ µg/m²/d
Production				
A *	0.63	0 ¤	0.189	0.16
B *	<0.08	0 ¤	0.025	0.02
Processing				
D1: intermediate	0.04	0 ¤	0.012	0.004
D2: process solvent	0.67	8.17	2.65	2.18
D3: others	4.95	3.03	2.39	0.13
D4: dye carrier	0.525	5.47	1.80	0.05

* Estimations based on manufacturer information. The remaining estimations are based on the TGD
DEP_{total}: deposition during emission episode. $DEP_{total, ann}$: deposition averaged over a year (365 days)
¤ The exhaust air is incinerated according to the main manufacturers

3.1.6 Soil compartment

3.1.6.1 Measured concentrations

Soil

No monitoring data on 1,2,4-TCB in soil are available.

However, in the control soils in a study on the fate of chlorobenzenes in field soils with several sludge applications from 1942 to 1991, a range of 0.06 to 0.17 µg/kg of 1,2,4-TCB (0.15 in 1984 and 0.19 µg/kg in 1991) were measured (Wang et al., 1995). These data may be used in the risk assessment as background values indicating regional concentration levels.

Two soil samples from the Buffalo riverbank were analysed for trichlorobenzenes. The measured concentrations of trichlorobenzenes were 10 and 40 mg/kg soil. This site was however suspected to have been used as chemical dump by a nearby dyestuff manufacturer (Nelson and Hites, 1980).

The fate and loss kinetic characteristics of 1,2,4-TCB introduced into soil either by spiking or by addition of sewage sludge were studied by Wang and Jones (1994b). Volatilisation was the main loss pathway from soil while biodegradation and abiotic loss were minor processes by comparison. The soil was a sandy loam with 1.4-4.7% organic matter. The anaerobically digested sewage sludge was collected at a STP serving 60% municipal and 40% industrial catchment. The sludge was 3% dry matter of which 68% was organic matter. The initial concentration was 0.11 µg/kg soil and 276 µg/kg sludge. The soil was either amended with sludge or a mixture of chlorobenzenes. The loss was fast initially and decreased later. For 1,2,4-TCB, the loss in standard spiked soil was from 12.2 mg/kg at day 0 to 1.93 µg/kg after 259 days and the half-life was estimated to be 12.5 days in the first step (22 days: loss 65%) and 194 days in the second step (22-259 days: loss 20%) which resulted in a general half-life of 19.4 days and a loss of 84%. In the sludge amended soil, the concentration was reduced from 19 µg/kg to 2.76 µg/kg after 259 days. The half-life for sludge-amended soil was estimated to be 22.5 days in the first step (75 days: loss 83%) and 49,500 days in the second step (75-259 days: loss 2%)

which results in a general half-life of 23.3 days and a loss of 86%. The retention in soil increased with the organic content of the soil and the volatilisation from soil decreased with the organic content and thus also with addition of sewage sludge (Wang and Jones, 1994b).

Sludge

The sludge from wastewater treatment may be either applied to soil, landfilled, incinerated or dumped into the sea. Because the TGD includes a soil exposure scenario from sludge application to soil, the results from measuring 1,2,4-TCB concentrations in sludge are presented here. Comments are applied after the table.

All studies were from municipal sewage treatment plants receiving mainly household effluents but in some cases also wastewater from industries.

Table 3.26 Concentrations in sludge

Location	Range	Mean	Median	Reference
USA 217 sludges (56% positive)	5.51 – 51,200 µg/kg dw	2,140 µg/kg dw	274 µg/kg	Jacobs and Zabik (1983)
DK. 9 sludges municipal STP industrial STP	 <5 and 5µg/kg dw <5 and 110 * µg/kg dw			Kjølholt et al. (1995)
DK, 2 sludges	12 and 570 * µg/kg dw			Krogh et al. (1996)
DK, 1 sludge		34 * µg/kg dw		Krogh et al. (1997)
DK. 20 sludges (6 positive)	<1 - 420 µg/kg dw	25.9 µg/kg dw	<3 µg/kg	Kristensen et al. (1996)
DK, 3 sludges	8-11 µg/kg dw	9 µg/kg dw		Grüttner et al. (1996)
DK,2 sludges	8.1 and 14 µg/kg dw			Aarhus Amt (1998)
S. 8 sludges	< DL – 1,330 µg/kg dw			Swedish EPA (1992)
UK, 12 sludges	20 – 4,810 µg/kg dw	920 µg/kg dw	360 µg/kg	Rogers et al. (1989)
UK, 12 sludges	140 – 1,070 µg/kg dw 0.5 - 53.8 µg/l ww	264 µg/kg dw 10 µg/l ww	51 µg/kg 3.6 µg/l	Wang and Jones (1994)
Germany, Bad Herzfeld 1985 1987 1988 Limburg 1985 1987 1988 Hilda 1985 1987 1988	 17,900 µg/kg dw 4,625 µg/kg dw 20 µg/kg dw 16,300 µg/kg dw 67 µg/kg dw 8 µg/kg dw 4,800 µg/kg dw <20 µg/kg dw 6 µg/kg dw			Kröber and Häckl (1989)

dw: dry weight
ww: wet weight
* Monitoring data from STP receiving wastewater from textile industries

USA

In Michigan, USA, the sludges from 204 municipal sewage treatment plants were analysed for 73 organic chemicals. 217 samples were analysed for 1,2,4-TCB which was detected in 121 samples (56%). The measured range was from 5.5 to 51,200 µg/kg dw (Jacobs and Zabik, 1983).

Denmark

The concentration of 1,2,4-TCB in sludge measured in a Danish STP receiving municipal wastewater was 5 µg/kg, and in a STP receiving industrial wastewater 110 µg/kg dry weight during winter. Both STPs had concentrations <5 µg/kg dw in summer (Kjølholt et al., 1995). The same report cites literature values in sludge between 10 and 1,400 µg/kg dry weight (dw).

The sludge from two Danish STPs (Ringkøbing and Herning municipal STP) was analysed in a project before the sludge was disposed of onto soil. The two sludges contained 12 and 570 µg/kg dw sludge of 1,2,4-TCB. The detection level was 5 µg/kg dw (Krogh et al., 1996).

In 19 typical Danish STPs representing average STP types and municipal and industrial loading, the sludges were analysed between Sept. 1995 and Feb. 1996. The STP flow varied from 1,000 to 39,000 m^3/year and the total sludge production was approximately 30,000 tonnes dw/year. The industrial load varied from 0% to 70%. From the 19 STPs, 20 sludge samples were analysed and 6 were measured to have a concentration of 1,2,4-TCB above the detection limit 1.0 µg/kg dw. The range was <1.0 to 420 µg/kg dw and the mean value was 25.9 µg/kg dw including values below detection limit. The positive samples contained 5.4, 5.6, 5.9, 11, 40 and 420 µg/kg dw. The highest value was found in a STP with 50% industrial load, the others varied from 0% to 20% industrial load (Kristensen et al., 1996).

In 3 sludges from municipal STPs in Denmark, an average of 9 µg/kg dw in 1992 was measured. Avedøre STP (A) loading was 350,000 person equivalents (PE) and treated 65,000 m^3/d, and the industrial loading was 50%. Marselisborg STP (M) had 205,000 PE and treated 35,000 m^3/d and the industrial loading was 50%. Skævinge STP (S) had a loading of 9,000 PE, 1,200 m^3/d and 0% industrial loading. The influent was estimated to be 0.02 g/d (S), 0.26 g/d (M) and 0.23 g/d (A). In the sludge, 8, 11 and 9 µg/kg dw were found resulting in a reduction of 62% (A) and 43% in M (Grüttner et al., 1996). It was noted that the concentration of monochlorobenzenes was accumulated and that this might be the result of reductive dechlorination following adsorption of 1,2,4-TCB in sludge and anaerobic degradation (Bosma et al., 1988; Grüttner et al., 1996).

United Kingdom

Twelve UK sewage sludges of varying catchments were analysed to provide an indication of the typical concentrations of chlorobenzenes in raw and digested sludge. The relative concentrations of chlorobenzenes found in sewage sludge reflect the extent of domestic and industrial usage of the different compounds. 1,2,4-TCB was found in the concentration range of 20 to 4,810 µg/kg. The mean concentration was estimated to be 920 µg/kg dry weight (Rogers et al., 1989). In the American study on sludges, a wider range was found: 10 to 51,000 µg/kg (Rogers et al., 1989; Jacobs and Zabik 1983). The highest concentrations were found in samples from catchments including significant chemical industry.

The same picture emerge was observed in a study on 12 contemporary UK sewage sludges from North-west of England. The results are reported in dry weight basis and in wet weight basis. The concentrations based on wet weight were affected by the sludge solid content (Wang and Jones, 1994). The quantitative detection limits were 0.6-1 µg/kg. Comparisons of chlorobenzenes from urban and urban/industrial sludges resulted in mean values of 111 µg/kg dw in urban and 476 µg/kg dw in urban /industrial sludges (Wang and Jones, 1994).

Germany

In a report on monitoring results from 12 municipal STPs in Germany, 1,2,4-TCB was observed in 3 STP sludges in 1985 at 4,800, 16,300 and 17,900 µg/kg dw. In 1987, the samples were stripped using N_2 and recovered in two fractions part in the stripped sample: in the same STPs as before nd/nd, 67/nd and 925/3,700 µg/kg dw were found (cf. **Table 3.26**). The concentrations in the other STPs were below the detection levels which were 120-360 µg/kg dw in 1985, 20-51 µg/kg dw in 1987 and 5-10 µg/kg dw in 1988 (Kröber and Häckl, 1989). In 1988 with the lowest detection limit, 1,2,4-TCB was detected in 10 out of 12 samples (average 9.5 µg/kg dw).

Conclusion

In STP sludge, the monitoring data on 1,2,4-TCB indicate that the concentrations in German STP sludges have reduced during the last decades. Most recent monitoring data from STP sludge in 4 EU countries (UK, D, DK, S) show 1,2,4-TCB levels <1 up to 400 µg/kg (dw), the vast majority of levels being 10 to 100 µg/kg (dw). The Danish data suggest that 1,2,4-TCB may still be used as a dye carrier and/or that 1,2,4-TCB is released to the wastewater from textile industries processing textiles treated with TCB containing dyes. (Support for the latter suggestion may be provided by the US EPA Toxic Release Inventory, which contains data on 1,2,4-TCB release from textile processing industries such as weaving and knitting textile mills (US EPA, Office of Water)). Furthermore, the monitoring data may also suggest that 1,2,4-TCB may be dispersively released to wastewater.

3.1.6.2 Estimation of PEC_{soil}

1,2,4-TCB is not applied directly to the soil or crops, but it occurs in sewage sludge and thus may be applied to soil. 1,2,4-TCB is also released to air and may undergo deposition to soil. The PEC_{soil} is a summation of the concentration due to these two separate processes.

The values used are referring to the generic model and for the initial risk assessment the estimation procedures of the TGD are closely followed.

Removal from soil

The substance is removed from the soil by volatilisation, leaching to deeper soil layers and/or by biodegradation. The estimated removal rate constants are shown in **Table 3.27**.

Table 3.27 Estimated removal rate constants for soil

	d^{-1}
Total rate constant for degradation in bulk soil	0.00231
Rate constant for volatilisation from agricultural soil	0.0056
Rate constant for volatilisation from grassland soil	0.0113
Rate constant for leaching from agricultural soil	0.0000568
Rate constant for leaching from grassland soil	0.000114
Total rate constant for removal from agricultural top soil	0.00801
Total rate constant for removal from grassland top soil	0.0137

Concentration in soil due to atmospheric deposition

The aerial deposition flux per kg of soil (D_{air}) is derived by converting the total annual deposition flux and estimate the concentrations in soil after 10 years of deposition for agricultural soil (0.2 m soil depth) and for grassland (0.1 m soil depth) according to the TGD (cf. EUSES estimations on the ECB website: http://ecb.jrc.it).

Table 3.28 Local concentration in soil from air deposition

Scenario	**$Cdep_{agr.\ soil}$ (mg/kg)**	**$Cdep_{grassland}$ (mg/kg)**
Production		
A	$5.88 \cdot 10^{-5}$	$6.87 \cdot 10^{-5}$
B	$7.34 \cdot 10^{-6}$	$8.59 \cdot 10^{-6}$
Processing		
D1: intermediate	$1.47 \cdot 10^{-6}$	$1.72 \cdot 10^{-6}$
D2: process solvent	$8.00 \cdot 10^{-4}$	$9.36 \cdot 10^{-4}$
D3: other	$4.77 \cdot 10^{-5}$	$5.58 \cdot 10^{-5}$
D4: dye carrier	$1.84 \cdot 10^{-5}$	$2.15 \cdot 10^{-5}$

Concentration due to sludge application

Table 3.29 Local concentration in sludge and soil after sludge application

Scenario	Elocal $_{water}$ (kg/d)	C_{sludge} (mg/kg dw)
Production		
A ** #	-	-
B ** ##	-	-
Processing		
D1: intermediate**	25.7	3,690
D2: solvent**	13.3	1,910
D3: other	4.95	710
D4: dye carrier	8.93	1,280

** Sludge from A, B, D1, D2 is incinerated according to the main manufacturers. However, scenarios D1 to D4 are included for illustration of potential concentrations (i.e. generic scenarios)
# At production site A, 1,2,4-TCB is also used for processing (as an intermediate)
At production site B, 1,2,4-TCB is also used for processing (as a solvent)

Local concentration in soil

The concentration in soil from atmospheric deposition and from sludge deposition can be estimated according to the TGD for those exposure scenarios where sludge is applied to soil. Sludge from scenario A and B is incinerated according to the main manufacturers. Therefore, sludge deposition is not included in these scenarios. The main manufacturers declare that all their customers are represented in scenarios D1 or D2, and that these customers, which are well known companies, do not apply sludge to soil. The sludges are incinerated or kept in controlled landfills. However, scenarios D1 to D4 are estimated including sludge application and may for risk assessment purposes be considered generic scenarios. Without sludge application, the concentration in soil is the result of atmospheric deposition (cf. **Table 3.29**) and the contribution from regional depositions. The deposition from air is negligible in relation to the exposure from sludge.

Table 3.30 Local concentration in soil

Scenario	PEClocal $_{soil}$ (mg/kg)	PEClocal$_{agr.\ soil}$ (mg/kg)	PEClocal$_{grassland}$ (mg/kg)	PEClocal$_{natural\ soil}$ (mg/kg) *
Production				
A**	0.079	0.047	0.013	$1.4 \cdot 10^{-4}$
B**	0.079	0.047	0.013	$1.7 \cdot 10^{-5}$
Processing				
D1: intermediate ***	5.09	3.03	0.810	$3.6 \cdot 10^{-6}$
D2: process solvent ***	2.64	1.57	0.421	$1.9 \cdot 10^{-3}$
D3: other	0.98	0.58 ****	0.156	$1.1 \cdot 10^{-4}$
D4: dye carrier	1.77	1.05	0.281	$4.3 \cdot 10^{-5}$

* For natural soil, only deposition from air is included (no sludge application assumed)

* For the site-specific scenarios A and B only atmospheric deposition is included because sludge application does not take place

*** According to main manufacturers sludge application does not take place. However, the scenarios are retained as generic scenarios

**** Based on the monitored levels of 1,2,4-TCB in sludge it is possible to estimate the soil concentration resulting from the application of these actual sludges. The concentration in agricultural soil would be 0.33 μg/kg for a concentration in sludge of 400 μg/kg (the highest recent value as indicated in Table 3.28) and 0.04 mg/kg for the highest measured value of 51.2 mg/kg. The activities which give rise to these levels are unknown. Therefore they could be taken as indicative of levels from the wider "other uses" as they are apparently not related to the major activities which use this substance. In conclusion: the local PEC for agricultural soil onto which sludge is applied is according to monitoring data and employment of the sludge application scenario of the TGD one to three orders of magnitude lower than the estimation in the table employing the TGD estimation method

PEClocal$_{soil}$ was estimated as C local$_{soil}$ + PECregional$_{natural\ soil.}$

The contribution from atmospheric deposition is small (cf. PEClocal$_{natural\ soil}$). The highest PEC soil is found where sludge application may take place.

Continental and regional PECs

The continental and regional PECs are presented below based on the EUSES estimations.

Regional PEC in agricultural soil (total)	$8.77 \cdot 10^{-5}$	mg/kg wwt
Regional PEC in pore water of agricultural soils	$3.53 \cdot 10^{-6}$	mg/l
Regional PEC in natural soil (total)	$1.26 \cdot 10^{-7}$	mg/kg wwt
Regional PEC in industrial soil (total)	$1.61 \cdot 10^{-5}$	mg/kg wwt
Continental PEC in agricultural soil (total)	$1.76 \cdot 10^{-7}$	mg/kg wwt
Continental PEC in pore water of agricultural soils	$7.09 \cdot 10^{-9}$	mg/l
Continental PEC in natural soil (total)	$1.36 \cdot 10^{-8}$	mg/kg wwt
Continental PEC in industrial soil (total)	$1.64 \cdot 10^{-6}$	mg/kg wwt

Comparison between the measured and the estimated concentration in soil

Sludge

The measured concentration in sludge ranged from <0.001 to 51.2 mg/kg dw and the mean values ranged from 0.006 to 17.9 mg/kg dw. The concentrations estimated by employing EUSES are considerably higher (i.e. two to five orders of magnitude greater). However, the measured

values are mostly taken from municipal sludges and the estimated concentrations in sludges are from STPs receiving wastewater according to the TGD.

Soil

The concentrations in soil without sludge application, representing a soil only exposed to atmospheric deposition were measured to be 0.17 µg/kg (Wang et al., 1995). This value represents 1,2,4-TCB concentration in farmland with unknown - probably large - distance to major emission sources such as major production sites. The estimated 1,2,4-TCB concentrations from deposition alone according to the downstream uses (natural soils, D scenarios) range from 0.1 µg/kg to 0.3 µg/kg which is reasonably in agreement with the measured value. The estimated 1,2,4-TCB concentration in soil near the major production sites indicated 1,2,4-TCB concentrations three orders of magnitude higher.

Measured concentrations in groundwater

In 1976 in the Netherlands when 250 ground water pumping stations were analysed, a maximum concentration of 1.2 µg/l was detected (Zoeteman et al., 1980).

Trichlorobenzenes are persistent in groundwater (Zoeteman et al., 1980). The removal from water from the contaminated River Rhine by mean of bank infiltration or dune infiltration has been studied. Dune infiltration resulted in a better removal, which is due to the higher absorption capacity of the dune subsoil. The concentration in the river was 0.5 µg/l before infiltration and observed to have the average concentration of 0.3 µg/l after bank infiltration (bank infiltration time (ΔT) = 1 to 12 months) and 0.01 µg/l after dune infiltration (ΔT = 2 to 3 months) (Zoeteman et al., 1980).

The leachate from a waste disposal site (Sanitary landfill Georgswerter at Hamburg, Germany) was analysed during 1981-1982. The samples were taken from leachate collecting wells. 1,2,4-TCB concentration in the leachate ranged from below detection limit (not mentioned) to 1,700 µg/l (Götz, 1984).

Estimated concentrations in groundwater

An indication of the potential levels in groundwater is established by the concentration in the pore water of agricultural soil as a worst-case assumption according to the TGD.

Table 3.31 Estimations of concentration in local groundwater

Scenario	$PEC_{soil,agr}$ mg/kg	$PEC_{local,grw}$ mg/l	$PEC_{local,\ grw}$ µg/l
Production			
A*	0.047	0.0019	1.9
B*	0.047	0.0019	1.9
Processing			
D1: intermediate**	3.07	0.122	(<<122)
D2: process solvent**	1.57	0.063	(<<63)
D3: other	0.58	0.024	24
D4: dye carrier	1.05	0.042	42.4

* Based on the main manufacturers' information on emission to atmosphere. The remaining estimations are performed according to theTGD

** Generic scenario including sludge application on soil which according to the main manufacturers is not relevant

Comparison between the measured and the estimated concentrations

The estimated values are in general one to two orders of magnitude lower or higher than the measured values, except for a polluted area (landfill) where the measured concentration in the leachate was up to 1,700 µg/l. Thus, the estimated concentrations are regarded to be in general accordance with the realistic worst-case principle.

The two values based on atmospheric deposition alone (A and B) are estimated to be in the range of measured values. The contribution from sludge application is the main reason for the estimated high groundwater concentration in scenarios D1 to D4. Moreover, 1,2,4-TCB has been measured in sludge from municipal STPs, although at lower levels than estimated by employing EUSES.

3.1.7 Secondary poisoning

3.1.7.1 Measured concentrations

1,2,4-TCB has been measured in a variety of biota from several sources. The maximum measured concentration in fish was 7.19 mg/kg fat (BUA, 1987).

Table 3.32 Measured concentrations in biota

Species		Tissue	Range	Mean	Reference
Benthos					
Lake Ontario, Canada:	1981		5.7-330 ppb dw		Fox et al. (1983)
Amphipods			nd-81 ppb dw		
Oligochaetes					
Mussel					
Slovenia, Gulf of Trieste:	1978				Jan and Malneršic (1980)
Date shell, *Lithophaga lithophaga*				910 ppb F	
Fish					
Slovenia, Gulf of Trieste:					
Trout *Salmo trutta*	1978	muscle		1 ppb F	Jan and Malneršic (1980)
Nase *Chondrostoma nasus*	1978	muscle	2-5 ppb F		"
Whiting *Leuciscus cephalus*	1978	muscle		15 ppb F	"
Mullet *Mugillidae sp.*	1978	muscle		10 ppb F	"
Pilchard *Sardina pilchardus*	1978	muscle		7 ppb F	"
Japan:					Seto and Kanoh (1987)
Sea bass	1985	muscle	2-4 ppb ww	3 ppb ww	
USA:					
Sand dab *Cith. xanthostigma*		liver		28 ppb ww	
Sole *Microstomus pacificus*		liver		7 ppb ww	
Birds					
Herring Gull, Great lakes	1979	eggs		0.02 ±0.02 ppm ww	Struger et al. (1985)
Black-tailed gull, Japan	1985	muscle	0.003-0.005 ppm ww	0.004 ppm ww	Seto and Kanoh (1987)

ww: wet weight. F: fat. dw: dry weight

The concentration of 1,2,4-TCB in superficial sediments in Lake Ontario (just outside the river) ranged 59 to 220 µg/kg dw (1981). The benthos concentration measured was: amphipods: 5.7-330 µg/kg dw and oligochaetes: nd to 81 µg/kg dw (Fox et al., 1983).

Fish and mussels from rivers in Slovenia and the gulf of Trieste (former Yugoslavia), sampled in 1978, were analysed. The freshwater fish were 4-7 years of age. The results in the table are presented on fat basis (Jan and Malneršic, 1980).

The level of 1,2,4-TCB in Japanese seabass (*Lataolabrax japonica*) and black-tailed gull (*Larus crassirostris*) collected from Tokyo bay in 1985 was determined (**Table 3.32**). 1,2,4-TCB was only detected in samples from the Tokyo bay and no other sea areas in Japan (Seto and Kanoh, 1987).

These reported ranges of concentrations measured in marine fish seem generally to fit well with the ranges of concentrations measured in the sea taking the bioaccumulative potential of 1,2,4-TCB into account (cf. **Table 3.14**). This comparison should however only be regarded as indicative, because the marine areas from which monitoring of water and fish originate are different, and because the monitoring was performed at different points of time in the past.

Sediments (0-2 cm) and animals collected near the discharge zone of the Los Angeles County STP were analysed for TCB (1,2,4- and 1,3,5-TCB). The effluents contained 0.77 µg/l 1,2,4-TCB and 0.035 µg/l 1,3,5-TCB. The sediment (0-2 cm) contained 9 µg/kg dry weight. The tissues from the California halibut (*Paralichthys californicus*) contained <1 µg/kg wet weight (ww) in the liver, Pacific sand dab (*Citharichthys xanthostigma*) 28 µg/kg ww in the liver, Dover sole (*Microstomus pacificus*) 7 µg/kg ww in the liver, scorpion fish (*Scorpaena guttata*) 15 µg/kg ww in the liver, white croaker (*Genyonemus lineatus*) <1 µg/kg in the liver, ridgeback

prawn (*Sicyonia ingentus*) <1 µg/kg ww in the muscle, and red pointer crap (*Mursia gaudichaudii*) 8 µg/kg ww in the digestive gland (Gossett et al., 1983).

In 1979 in Japan, the monitoring programme has observed 1,2,4-TCBs in water in 8 out of 111 samples at 0.01-0.13 µg/l (DL 0.01 µg/l). In 1975 in sediments, 3 out of 95 samples contained 2-22 µg/kg (DL 2) and in 1979, 33 out of 111 samples contained 0.5-30 µg/kg (DL 0.1 mg/kg). In fish, 2 out of 75 samples contained 100-200 µg/kg (DL 0.5 µg/kg) in 1975 and 7 out of 93 samples in 1979 contained 0.3-8 µg/kg (DL 0.1 µg/kg) (Japan, 1985).

Eggs from the herring gull (*Larus argentatus*) have been collected around the Great Lakes in Canada during 1978-1982. The herring gull was chosen as indicator species because it is a top predator. Herring gulls eggs readily bioaccumulate lipophilic organochlorines because of the high lipid content (Struger et al., 1985).

3.1.7.2 Estimation of $PEC_{oral, fish}$

The level in food (fish), $PEC_{oral, fish}$, is estimated according to the TGD as 50% $PEC_{water, regional}$ and 50% $PEC_{water, local annual}$ multiplied with BCF_{fish}:

Table 3.33 Estimations of concentration in the food chain ($PEC_{oral, fish}$)

Scenario	$PEC_{water, emission episode}$ mg/l	$PEC_{water, annual}$ mg/l	$PEC_{oral, fish}$ (mg/kg)
Production			
A	0.0000096	0.0000096	0.019
B	0.0000532	0.0000454	0.055
Processing			
D1: intermediate	0.000018	0.000012	0.021
D2: process solvent	0.00147	0.00121	1.22
D3: other	0.038	0.00209	2.09
D4: dye carrier	0.068	0.00187	1.88

$PEC_{regional}$ for surface water: 0.0000095 mg/l

Secondary poisoning via the terrestrial food chain may be estimated in the same way according to the TGD. However, BCF_{worm} was estimated to be 1 and the resulting $PEC_{oral, worm}$ is 50% of the $PEC_{local, soil}$ and $PEC_{regional, soil}$.

Table 3.34 Estimations of concentration in the food chain ($PEC_{oral, worm}$)

Scenario	$PEC_{local, soil}$ mg/kg	$PEC_{oral, worm}$ (mg/kg)
Production		
A	0.047	0.024
B	0.047	0.024
Processing		
D1: intermediate	3.03	1.52
D2: process solvent	1.57	0.79
D3: other	0.58	0.29
D4: dye carrier	1.05	0.53

$PEC_{regional, soil}$: 0.000088 mg/kg ww

3.1.7.3 Comparison between measured and estimated concentrations

According to monitoring data, the measured concentrations in marine fish were 3 to 300 µg/kg. The estimated concentration in fish based on the BCF(fish) and the estimated $PEC_{local, water}$ is between 20 µg/kg and 2 µmg/kg, whereas the same estimated regional concentration is 20 µg/kg. Thus the reported range of concentrations in marine fish monitored in three different locations between one and two decades ago generally fit well with the estimated regional concentration in fish according to the TGD.

3.2 EFFECTS ASSESSMENT

3.2.1 Aquatic compartment

3.2.1.1 Acute toxicity to fish

Valid short-term toxicity studies for fish are summarised in **Table 3.35**.

Table 3.35 Short-term toxicity to fish according to valid studies

Species	Duration (hours)	LC_{50} (mg/l)	Method, conditions	Ref.
Lepomis macrochirus Bluegill sunfish	96	3.02	Flow through, lake water, 17°C, 45 mg $CaCO_3$/l, pH 7.4, measured conc.	Holcombe et al. (1987)
Pimephales promelas Fathead minnow	96	3.01	Flow through, lake water, 17°C, 45 mg $CaCO_3$/l, pH 7.4, measured conc.	Holcombe et al. (1987)
Pimephales promelas Fathead minnow (fry)	96	2.76	Flow through, lake water, 25°C, 44 mg $CaCO_3$/l, pH 7.6, ASTM 1980	Broderius and Kahl (1985)
Pimephales promelas Fathead minnow (fry)	96	2.8	Flow through, lake water, 25°C, 45 mg $CaCO_3$/l, pH 7.5, ASTM 1975	Carlson and Kosian (1987)
Pimephales promelas Fathead minnow	96	2.99	Flow through, lake water, 45.5 mg $CaCO_3$, pH 7.5, 25°C, measured conc.	Geiger et al. (1990), Veith et al. (1983)
*Salmo gairdneri** Rainbow trout	24/48*	1.95	Static (closed), 15°C, 320 mg $CaCO_3$ pH 7.4, OECD TG 203	Calamari et al. (1983)
*Salmo gairdneri** Rainbow trout	96	1.32	Flow through, lake water, 17°C, 45 mg $CaCO_3$/l, pH 7.4, measured conc.	Holcombe et al. (1987)
Jordanella floridae American flagfish	96	1.217	Flow through, lake water, 25°C, 48 mg $CaCO_3$, US EPA 1975, measured conc.	Smith et al. (1991)
Brachydanio rerio Zebra fish	24/48**	6.3	Static (closed), 23°C, pH 7.3, OECD TG 203	Calamari et al. (1983)
Leuciscus idus Golden ide	48	0.7	Static, DIN 38412-15, measured conc.	Knie et al. (1983)
Oryzias latipes Orange red killifish	48	12.3	static, 20°C. ***	MITI (1992)

* Now Oncorhynchos mykiss

** In the study method is mentioned that 24-h LC_{50} is used due to the volatility of the substance but 48-h is stated in the tables of the study

*** MITI (1992) does not clearly specify whether the values represent measured or nominal concentrations

Several short-term studies on fish have been performed. Generally, the results from static tests have been excluded due to the nature of the chemical (volatilisation) unless measured data are present or closed systems have been used. The problem is illustrated in the study by Smith et al. (1991), which observed the EC_{50} (96 h) of 4.0 mg/l in a static test and 1.2 mg/l in a flow through test using measured concentrations. Other reasons for excluding certain studies are observations of undissolved test substance in test medium (e.g. Buccafuco et al., 1981).

1,2,4-TCB has an acute non-specific toxic effect via narcosis (Veith et al., 1983).

Regarding the acute toxicity to fish, a value from the lower end of tests with measured concentrations is used in the risk assessment: LC_{50} (96 h) of 1.0 mg/l.

This value is in general agreement with QSAR estimation according to the TGD (1996) which results in a fish (96 h) LC_{50} of 2.7 mg/l for non-polar narcotic acting substances and QTOXMIN (Pedersen et al., 1995) estimation which result in LC_{50} (96 h) of 2.5 mg/l. The ECOSAR model, which is a computer program for estimating the ecotoxicity of industrial chemicals based on structure activity relationships, estimates a freshwater fish LC_{50} (96 h) to be 1.6 mg/l (US EPA, 1994). The QSAR predictions fit well with the experimental data.

The proposal for classification for N; R50-53 was based on the fact that whilst many of the measured data points lie in the R51 (1-10 mg/l range), there are sufficient data from both fish, crustaceans and other aquatic organisms below 1 mg/l to justify suggesting this classification. It should also be noted that 1,2-dichlorobenzene is classified as N; R50-53 in Annex I of Directive 67/548/EEC, and that the same classification has been proposed for 1,4-dichlorobenzene. For classification, see Section 1.

3.2.1.2 Short-term toxicity to crustaceans

Several studies have been performed. Most studies have not considered the problems with evaporation and in most studies concentrations have not been measured during the study. Results from such studies are not regarded valid and not presented below.

Table 3.36 Short-term toxicity to crustaceans according to valid studies

Species	Duration (hours)	L(E)C_{50} (mg/l)	Method, conditions	Ref.
Daphnia magna	48	3.39	Flow through, lake water, 20°C, 45 mg $CaCO_3$/l, measured conc.	Holcombe et al. (1987)
		2.68 [1)] 1.55 [2)]	Semi-static, Daphnids <2 days old, 22ºC, pH 7, NEN6502	Hermens et al. (1984)
		2.72	Static (closed system), Daphnids 4-6 days old, 23°C, pH 7, US EPA 1975. Nominal conc.	Bobra et al. (1983)
		1.7 2.1	Static (closed), ASTM 1980, measured conc. Results from fed and unfed daphnids	Richter et al. (1983), US EPA (1984)
	24	1.2	Static, closed systems, measured conc. AFNOR	Calamari et al. (1983)
		2.0-2.4	Static, OECD TG 202-I, measured (EC_0: 0.3-0.3, EC_{100}: 6.5-7.5)	Broecker et al. (1984)
Orconectes immunis crayfish	96	3.02	Flow through, lake water, 20°C, 45 mg $CaCO_3$/l, measured conc.	Holcombe et al. (1987)
Palaemonetes pugio (Mature grass shrimp)	96	0.54	Flow through, seawater, pH 8, 22°C, APHA (1985), nominal conc (75-95% of actual)	Clark et al. (1987)
Mysidopsis bahia (shrimp)	96	0.45	Static, US EPA	Clark et al. (1987)
	96	0.49	Flow-through, measured concentrations, (US EPA standard CFR797.1930). NOEC= 0.19 mg/l, LC_{100} = 0.99 mg/l	US EPA (1988)
Nitocra spinipes (copepod)	96	2.6	Static, 21°C, 0,7% salinity, pH 7.8 initial conc.	Bengtsson and Tarkpea (1983)

[1)]: based on nominal concentration. [2)]: based on measured concentrations

In a study by Hermens et al. (1984), the acute toxicity to *Daphnia magna* was an EC_{50} of 2.68 mg/l. The results are not corrected for the measured concentrations. Assuming the average concentration to be the same as in an identical experiment by Hermens et al. (1985), the acute EC_{50} in this study was 1.55 mg/l.

In the study by Calamari et al. (1983), nominal concentrations were used in the estimation of the effect concentration, however, the concentration at the beginning and the end of the study was measured. The deviation between nominal and measured concentrations were < 10% except in the long-term daphnia study. The tests were modified to take in account the volatility and this may explain the low deviation to nominal values observed in these studies (cf. the relevant tables on daphnids and algae).

1,2,4-TCB is apparently more toxic to species living in salt water but the TGD does not include an assessment for marine environment and therefore effect concentrations with these organisms are not included. The geometric mean of the accepted studies on *Daphnia magna* is an EC_{50} (48 h) of 2.1 mg/l, which is used in the risk assessment.

This value is in general agreement with the QSAR estimation according to the TGD (1996) which results in a Daphnia (48 h) EC_{50} of 1.2 mg/l for non-polar narcotic acting substances and the QTOXMIN (Pedersen et al., 1995) estimation, which results in an EC_{50} (48 h) of 1.6 mg/l. The ECOSAR model estimates the Daphnia LC_{50} (48 h) to 2.0 mg/l (US EPA, 1994). The QSARs predicted values fit well with the experimental data. (US EPA, 1994).

3.2.1.3 Toxicity to algae

Table 3.37 Toxicity to algae

Species	Duration	EC_{50} (mg/l)	NOEC (mg/l)	Method, conditions	Ref.	Valid
Selenastrum capricornutum	96 h	1.4	0.37	Static, closed system, US EPA, measured conc.	Calamari et al. (1983), Galassi and Vighi (1981)	yes
Scenedesmus subspicatus	96 h	18.9	2.2 (EC_{10})	Static (open system), 22°C, UBA guideline 1982, nominal conc.	Broecker et al. (1984)	no
		8.4	3.0 (EC_{10})	Static (open system), 22°C, UBA guideline 1982, initial conc.	Geyer et al. (1985)	no
Chlorella vulgaris	7 d	5.6		OECD TG 201 *	Yoshioka and Ose (1993)	no
Cyclotella meneghiniana (diatom)	48 h	2.83		Static, 15°C (effects on DNA content reduction)	Figueroa and Simmons (1991)	no

* Stated to be carried out according to OECD guideline. However, OECD recommends 72-h tests to consider the growth inhibition within the exponential growth stage

Some of the tests did not consider the volatility of the substance. Thus, the real values are probably lower than most of the mentioned. It may be assumed that results from static and open system tests underestimate the toxicity due to evaporation and photolysis, respectively.

Therefore, the results from the test using a closed system are accepted to be used in the risk assessment procedure: Algae EC_{50} (96 h): 1.4 mg/l and NOEC (96 h): 0.37 mg/l.

This value is in general agreement with the QSAR estimation according to the TGD (1996), which results in an algae (72-96 h) EC_{50} of 0.95 mg/l and the QTOXMIN (Pedersen et al., 1995) estimation, which results in an EC_{50} (72 h) of 0.87 mg/l. The ECOSAR model estimates the green algae EC_{50} (96 h) to 1.37 mg/l and the chronic value (>96 h) to 0.45 (US EPA, 1994). The QSARs predicted values fit well with the experimental data.

3.2.1.4 Toxicity to other aquatic organisms

The toxicity to other aquatic organisms is summarised in **Table 3.38**.

Table 3.38 Short-term toxicity to other aquatic organisms

Species	Duration	EC_{50} (mg/l)	Method, conditions	Ref.
Tetrahymena pyriformis * (freshwater aquatic protozoa)	24 h	0.91	30°C, 2% protease peptone medium, growth inhibition	Yoshioka et al. (1985)
Tanytarsus dissimilis (chironomid midge)	48 h	0.93	Flow through, lake water, 17°C, 43 mg $CaCO_3$/l measured conc.	Holcombe et al. (1987)
Aplexa hypnorum Snail	96 h	3.16	Flow through, lake water, 17°C, 43 mg $CaCO_3$/l measured conc.	Holcombe et al. (1987)

* These ciliate data are also included in the section below because they are regarded representative for ciliate species in sewage treatment plants

3.2.1.5 Short-term toxicity to sludge microorganisms

Table 3.39 Short-term toxicity to sludge microorganisms

Species	Duration	EC_{50} mg/l	NOEC mg/l	Method, conditions	Ref.
Activated sludge	12 h	35		25°C, municipal STP sludge, respiration test	Nirmalakhandan et al. (1994)
Activated sludge	3 h	500		OECD TG 209, respiration	Yoshioka et al. (1986)
Nitrosomonas	24 h	210		equivalent to ISO/DIS 9609	Blum and Speece (1991)
Pseudomonas putida	30 min			EC_{10} > 30 mg/l, closed system	Knie et al. (1983)
Tetrahymena pyriformis	24 h	0.91		30°C, 2% protease peptone medium, growth inhibition	Yoshioka et al. (1985)
Microorganisms			0.2	"harmful effects"	Atri (1986)

Using activated sludge from a municipal STP, the reduction in oxygen uptake for 12 hours was measured. The inhibition of oxygen uptake rate, IC_{50}, was observed to be 35 mg/l during 12 hours. Using the polytox freeze dried culture, IC_{50} (6 h) was 23 mg/l (Nirmalakhandan et al., 1994).

The toxicity to each of the 3 bacterial groups: aerobic heterotrophic bacteria, *Nitrosomonas,* and methanogenic bacteria, was studied by Blum and Speece (1991). All assays were carried out in sealed serum bottles under similar conditions. The aerobic heterotrophs predominate in the

activated sludge systems and natural aerobic environment, converting organic material to CO_2 and water. Methanogenic bacteria convert organic matter to CO_2 and methane in anaerobic environments. The heterotrophs, *Nitrosomonas,* and methanogenic bacteria inoculum were obtained from the mixed liquor of an activated sludge wastewater treatment plant.

The 50% inhibition concentration relative to controls (IC_{50}) was 210 mg/l for *Nitromonas*, 120 mg/l for methanogens. IC_{50} for aerobic heterotrophs was 7,700 mg/l which is limited by the solubility. The value in a Microtox test was cited to be 2.3 mg/l (Blum and Speece, 1991).

In the evaluation of risks to microorganisms in STP, the $PNEC_{STP}$ was calculated using each endpoint:

$PNEC_{STP}$ using activated sludge: 35/100 = 0.35 mg/l
$PNEC_{STP}$ using Tetrahymena: 0.91/10 = 0.09 mg/l

3.2.1.6 Long-term toxicity to aquatic organisms

Long-term studies on fish and daphnia are all based on measured concentrations.

Table 3.40 Long-term toxicity to aquatic organisms according to valid studies

Species	Duration	EC_{50} mg/l	NOEC mg/l	Method, conditions	Ref.
Fish:					
Pimephales promelas	32 d		0.29	Flow-through, ESF-test	US EPA (1985), McCarty et al. (1985) A
Pimephales promelas	32 d		0.50	Lake water, flow-through, ESF-test, EPA	Carlson and Kosian (1987)
Brachydanio rerio	21 d	2.4	0.04	Flow-through, mortality, behaviour	Broecker et al. (1984)
Salmo gairdneri	85 d		0.13	ELS (fry)	Carlson and Kosian (1987)
Poecilia reticulate	14 d		0.11	Semi-static (daily renewal), growth	Könemann (1981)
Cyprinodon variegatus	-			ESF-test, MATC = 0.222 mg/l	Suter and Rosen (1988)
Crustaceans:					
Daphnia magna	14 d	0.45	(0.32)	Semi-static, (closed)	Calamari et al. (1983) (NOEC = EC_{16})
Daphnia magna (mortality)	16 d	0.32 *	0.19 *	Semi-static (3 times a week)	Hermens et al. (1984) (*: refer to text below)
Daphnia magna (repro)	16 d	0.16 *	0.06 *	Semi-static (3 times a week)	Hermens et al. (1984) (*: refer to text below)
Daphnia magna (repro)	21 d		0.4	Semi-static, EEC-Ann.V-c	Broecker et al. (1984)
Daphnia magna	28 d		0.36	Semi-static (closed), ASTM 1980	Richter et al. (1983)
Mysidopsis bahia	28 d		≤0.064	Flow-through, measured, EPA standard	US EPA (1988) (LOEC = 0.033 mg/l)K

Abbreviations: ESF-test (Egg and Sac Fry) embryo-larvae test. ELS: Early Life Stage test

The study on Zebrafish (*Brachydanio rerio*) was performed according to a UBA guideline (1982) in a dynamic system. The fish were 4 to 7 months old. The aquarium contained 36 l and the flow was 1.2 l/h. The concentrations were measured. LOEC was 0.18 mg/l (20% mortality and several behavioural abnormalities) (Broecker et al., 1984).

Suter and Rosen (1988) report the chronic MATC value to the marine fish *Cyprinodon variegatus* to be 0.222 mg/l. NOEC is estimated to be approximately half this value.

The daphnia test by Calamari et al. (1983) was performed under semi-static conditions (test medium changed every other day), in a closed system and the measured concentration did not deviate more than 15% from the initial concentration.

In a study by Hermens et al. (1984) on the sublethal toxicity to *Daphnia magna,* the 16-day LC_{50} on mortality was 0.56 mg/l and the EC_{50} on reproduction was 0.27 mg/l (reported as µmol/l in the reference). In an identical 16-day experiment, measurements of the test concentrations are stated to average 58% of nominal (Hermens et al., 1985) and the 16-day EC_{50} was 0.52 mg/l. The results are not corrected for the measured concentrations. Assuming the average concentration was the same in the two experiments, the 16-day LC_{50} was 0.32 mg/l, EC_{50} 0.16 mg/l and the NOEC on mortality and reproduction 0.19 mg/l and 0.06 mg/l, respectively. The corrected values are reported in the table above.

The lowest NOEC in long-term studies was 0.04 mg/l (mortality and behaviour, Zebra fish).

$PNEC_{aquatic\ organisms}$

The data on aquatic organisms include acute toxicity data on fish, daphnia and algae plus several other aquatic animals. Valid long-term studies on both fish and Daphnia and a NOEC for algae are also present. According to the TGD, an assessment factor of 10 applied to the lowest long-term NOEC may therefore be used. The lowest NOEC (21 d) on Daphnia is 0.06 mg/l and the lowest NOEC (21 d) on fish is 0.04 mg/l, that is within the same long-term toxicity range.

$PNEC_{aquatic\ organisms}$: 0.04/10 = 0.004 mg/l or 4 µg/l

Other assessment reports also include evaluation of short- and long-term aquatic toxicity data on 1,2,4-TCB (cf. footnote[9]).

[9] CSTE (1993) recommends a value of 0.1 µg/l for the three trichlorobenzene isomers (1,2,3-, 1,2,4- and 1,3,5-TCB) as water quality objective (WQO) value defined as a maximum acceptable concentration that should not be exceeded to avoid hazards to the aquatic environment, including the marine environment. Thus, this evaluation also takes into account the difference in characteristics between salt water and fresh water (Council Directive 76/464/EEC, art.6.2). Other differences between the current PNEC and the WQO may be caused by the methods used in calculating WQO and PNEC (i.e. how assessment factors are employed - WQO-values are also concluded based on information on the persistence and bioaccumulation properties of the substance) This may explain the difference in the WQO-value recommended compared to the $PNEC_{aquatic\ organisms}$ estimated in this risk assessment.

The Canadian quality criteria for 1,2,4-TCB based on acute and early life chronic (freshwater) data are 0.5 µg/l (IMO, 1994). Based on acute toxicity, UK has reached a quality criterion for 1,2,4-TCB of 1.0 µg/l (IMO, 1994). Experimentally derived NOEC values based on multiple species systems compared to single species test results resulted in a NOEC of 57 µg/l (Okkerman et al., 1990). A literature search for single species tests of NOECs from reliable chronic toxicity tests used to estimate the 95% protection level at 95% probability levels using the extrapolation method, reached the value 2 µg/l for 1,2,4-TCB (Aldenberg et al., 1990).

3.2.1.7 Toxicity to sediment dwelling / benthic organisms

Clark et al. (1987) studied the waterborne and sediment-source toxicities to grass shrimp and amphioxus. Both species are abundant in estuarine environment and are important in estuarine food webs and detritus processing system. Amphioxus burrow into sediment along estuaries, marine mudflats and sandy bottoms. Grass shrimps ingest detritus and sediment particles and reside above the sediment water interface. The test sediment was 9:1 washed beach sand and sediment dredged from Santa Rosa Sound. The mixture contained 0.5-1% organic matter. The studies used 200 ml sediment in 3.8 l aquaria. The measured concentrations were 75-95% of nominal concentrations in waterborne studies and 60-95% in sediment exposures. Sediments containing 1,2,4-TCB at 10 mg/kg were not lethal to grass shrimp during 10 days of flow-through and no higher concentration were tested (Clark et al., 1987).

For amphioxus (*Branchiostoma caribaeum*), the 96-hour LC_{50} for waterborne 1,2,4-TCB was between 1.5 (0% mortality) and 10 mg/kg sediment (100% mortality). In the 10-day sediment test, LC_{50} was observed to be 200 mg/kg (NOEC: 75 mg/kg). Both tests were performed under flow through conditions and results based on nominal values (Clark et al., 1987).

The effects of 1,2,4-TCB on estuarine macrobenthic communities exposed via water and sediments were studied in laboratory study (Tagatz et al., 1985) using sand-filled aquaria (clean silica sand at 5.5 cm height) under flow-through conditions. In one test, communities established by planktonic larvae entrained in continuously supplied unfiltered seawater for 50 days were exposed to 1,2,4-TCB for 6 days at the nominal concentrations 0.05, 0.5 and 5 mg/l. The lowest measured concentrations that affected the average numbers of individuals exposed via water were 0.04 mg/l for molluscs, 0.4 mg/l for arthropods and 4 mg/l for annelids, and the average number of species was significant lower than the control at 4 mg/l.

In a second test, 1,2,4-TCB was added to the sediment before 8 weeks of colonisation. The concentrations in the sediment fluctuated during the exposure period: The nominal concentrations were 10, 100 and 1,000 mg/kg, the measured ranges were 4.3-<0.01 mg/kg, 97-2.1 mg/kg and 790-519 mg/kg sediment. After 8 weeks, the measured concentrations were <0.01, 6.1 and 519 mg/kg, respectively, for sediment and 0.51, 12 and 74 µg/l, respectively, for water. The lowest nominal concentration that affected the average numbers of individuals was 100 mg/kg for molluscs and echinoderms and 1,000 mg/kg sediment for arthropods and annelids. The average number of species was significantly lower than the control at ≥100 mg/kg sediment. Concentrations that affected community structure were usually two orders of magnitude lower for waterborne 1,2,4-TCB than for sediment-bound 1,2,4-TCB, but the same types of organisms were affected by each route of exposure. Most 1,2,4-TCB persisted in the sediment but some leached into the water throughout the 8-week exposure period (Tagatz et al., 1985).

In the study by Tagatz et al. (1985), the lowest measured concentration influencing the average number of individuals exposed via the water was 0.04 mg/l (this figure is an order of magnitude higher than the estimated $PNEC_{aquatic\ organisms}$). With exposure via the sediment, the lowest nominal concentration affecting the average number of individuals was 100 mg/kg sediment which after 8 weeks was measured to 6 mg/kg in sediment. The concentration in water was measured to be 12 to 74 µg/l at the end of the study.

However, due to the uncertainties in these two studies, data cannot be used directly in the risk assessment for the sediment compartment, although especially the data from Tagatz et al. (1985) may indicatively be compared with the estimated $PNEC_{sed}$ obtained by employing the equilibrium partitioning method of the TGD.

According to the TGD equation 54:
$PNEC_{sed} = (K_{sed\text{-}water}/RHO_{sed}) \cdot PNEC_{water} \cdot 1{,}000 = 0.218$ mg/kg ww, using a Foc_{sed} of 0.1 (as recommended by technical recommendations, Doc. ECB4/TR2/97 based on discussions at TM IV 1997).

The use of an organic fraction (Foc) of 0.05 according to the TGD results in a $PNEC_{sed}$ of 0.11 mg/kg ww (EUSES).

Another method is the use of $K_{susp\text{-}water}$ and RHO_{susp} which results in:
$PNEC_{sed} = (K_{susp\text{-}water}/RHO_{susp}) \cdot PNEC_{water} \cdot 1{,}000 = (35.9/1{,}150) \cdot 0.004 \cdot 1{,}000 =$
0.09 mg/kg ww.

The difference in PNECs according to these two methods is caused by slight differences in the fraction of solids and water.

In the latter method, sediments are more dominated by the superficial layer of suspended matter, i.e. according to this method the sediment has a higher content of water (and thus less content of solids).

There seems to be different viewpoints regarding which method to employ when performing a risk assessment for the sediment compartment. According to the availability of experimental test data for sediment organisms and knowledge regarding their preferred type of sub-compartmental habitat within the sediment, it may be possible to make a justifiable decision on which of the above methods to employ.

In this case where the derivation of PNEC is based on the application of the equilibrium partitioning method and available experimental data on pelagic organisms, the right choice of method seems to be the application of the latter. If this method is used, the PNEC/PEC ratios for sediment will be virtually the same as those for water.

Thus $PNEC_{sediment} = 0.09$ mg/kg ww.

This $PNEC_{sed}$ is three orders of magnitude lower than the lowest reported nominal and around two orders below the lowest reported measured effect concentration in the experimental study by Tagatz et al. (1985) referred to above. Therefore the derived $PNEC_{sediment}$ by employing the equilibrium partitioning method seems to be of a magnitude with a $PNEC_{sediment}$ which would have been obtained based on the more sophisticated experimental data on sediment organisms which however had some limitations and were difficult to evaluate.

3.2.2 Atmosphere

There are no results available to support an effect assessment in the atmosphere.

1,2,4-TCB in relation to POPs with a high potential for long-range atmospheric transport is discussed in the risk characterisation section (Section 3.3.2).

3.2.3 Terrestrial compartment

Table 3.41 Valid data on toxicity to soil organisms

Species	Duration	EC_{50} (mg/kg)	Method, conditions	Ref.
Earthworms:				
Allolobophora tuberculata	14 d	251	OECD TG, nominal conc.	Neuhauser et al. (1986)
Eisenia foetida		197		
Eudrilus eugeniae	28 d	127		
Perionyx excavatus		180		
Eisenia foetida		250	OECD TG, weight reduction, measured conc.	Broecker et al. (1984)
Plants:				
Avena sativa (oats)	14 d	240	OECD TG 4, draft 1981	Broecker et al. (1984)
Brassica rapa (turnip)	14 d	110	OECD TG 4, draft 1981	
Lactuca sativa (lettuce)	7 d	56	Static, OECD TG 208, nominal conc.	Hulzebos et al. (1993)
Lactuca sativa	14 d	48	(initial)	
Soil microorganisms				
respiration test	24 h	50	sandy loam, 20°C, CO_2 evolution	Marinucci and Bartha (1979)
Pseudomonas fluorescens	20 min	18.3 mg/l	Terrestrial bacterium in water solution	Boyd et al. (1998)

The toxicity to earthworms was studied using the OECD artificial soil test. In the same study, contact tests were performed in which LC_{50} values of 23-27 μg/cm^2 were observed (Neuhauser et al., 1986). In a study on *Eisenia foetida* over 14 days, an EC_{50} was observed at 290 mg/kg soil dry weight. The EC_0 was 100 mg/kg. The substance was applied dissolved in acetone and nominal concentrations used in the effect estimations (Ballhorn et al., 1984).

Toxicity tests on higher plants are performed on lettuce, which was chosen because it is sensitive to different organic compounds and easy to handle. A part of the study has been performed in soilless solution, to test the sensitivity during continuous exposure of 1,2,4-TCB in water. For lettuce *Lactuca sativa* exposed in a semi-static test with the roots in water containing 1,2,4-TCB, the EC_{50} (16-21 days) was 0.6 mg/l (Hulzebos et al., 1993).

The study on oats and turnip used a field soil with 1.54% OC. and performed in climate chambers (Ballhorn et al., 1984). Due to volatilisation in the open soil the EC_{50} (294 and 316 mg/kg dry soil) is not correct as a growth reduction was seen in the control plants probably affected by volatile substance or from condense water. The initial concentrations were used in the estimations. In Broecker et al. (1984), the same plants studied according to OECD TG 208 resulted in an EC_{50} of 40 mg/kg (EC_0 of 10 mg/kg) for oats and an EC_{50} of 110 mg/kg (EC_0 of 1) for turnips (Broecker et al., 1984).

1,2,4-TCB was toxic to soil microbiota as CO_2 development was reduced at increasing concentrations. At 50 μg/g sandy soil, the total CO_2 evolution was depressed to approximately 50% of the normal and the turnover optimum measured as percent 1,2,4-TCB degradation was between 10 and 25 μg/g during a 24-hour study period (Marinucci and Bartha, 1979).

The toxicity of 1,2,4-TCB on terrestrial microorganisms was studied on a terrestrial bacterium by insertion of lux genes into the genome of *Pseudominas fluorescens*. The bioluminiscence was determined after 20 minutes of exposure to mono-, di-, tri-, tetra-, penta- and hexachlorobenzene. The toxicity increased with the chlorination. For 1,2,4-TCB, the EC_{50} was 18.3 mg/l (Boyd et al.,

1998). The test was performed with a soil bacteria, but in a short-term test in an aqueous solution.

Estimation of $PNEC_{soil}$

The EC_{50} in the short-term experiment with the *Pseudomonas* is not used for the $PNEC_{soil}$ derivation because of the short duration and exposure to the concentration of the substance in (pore) water.

If no ecotoxicological data were available for soil organisms, the equilibrium partitioning method could be applied ($PNEC_{soil} = Kp(soil) \cdot PNEC_{aquatic\ organisms} = 28 \cdot 0.004 = 0.112$ mg/kg soil).

However, based on the few data presented, an assessment factor of 1,000 may be applied to the lowest value of 50 mg/kg soil (cf. **Table 3.41** showing that bacteria and most sensitive plant species have equal values) resulting in an indicative:

$PNEC_{soil}$ = 0.05 mg/kg soil[10].

3.2.4 Secondary poisoning

A bioaccumulation potential is present and the BCF in fish is approximately 2,000 based on the whole body wet weight. 1,2,4-TCB has potential for bioaccumulation, however due to the rapid depuration from fish (cf. Section 3.1.3.3) and mammals (cf. Section 4.1.2.1) the potential for biomagnification through the food chain may be low. The possibility that 1,2,4-TCB is an animal carcinogen exists however, and therefore assessment of secondary poisoning is warranted. There are no results on bird toxicity and therefore the effect on fish-eating birds cannot be considered. The same argument applies for birds eating earthworms.

As for fish-eating mammals, it is assumed that the available mammalian toxicity data can give an indication on the possible risks of 1,2,4-TCB to fish eating mammals.

NOAEL oral for rat is 100 ppm in the diet (6 mg/kg bw/d) after 2 years of exposure (cf. Section 4.1.2.6 on conclusion of repeated dose toxicity). An assessment factor of 10 should be applied according to the TGD:

$PNEC_{oral}$ = 100/10 ppm = 10 ppm (~0.6 mg/kg bw/d).

[10] Another assessment report (DMU, 1998) has reached a soil quality objective (SQO) value of 0.001 mg/kg soil dw for chlorobenzenes. The SQO value is based on an evaluation of effect data on 1,2,3-TCB (i.e. an EC_{50}-value on plant (Hulzebos et al. (1993)) of 1mg/kg and employment of an application factor of 1,000.

3.3 RISK CHARACTERISATION

This risk characterisation includes quantifiable releases of 1,2,4-TCB from known sources, hence the risk characterisation does not include 1,2,4-TCB releases from processes such as combustion and transformation from other substances. As regards the industrial sources of 1,2,4-TCB they can be divided into two main categories:

- presently manufactured 1,2,4-TCB,
- formerly manufactured 1,2,4-TCB, which consists of the accumulated 1,2,4-TCB in dielectrical fluids in existing electrical equipment.

As regards the latter it has only been possible to make a very rough worst-case estimation of the total regional release to the environment, which seems to be of the same order of magnitude as the total release from the present industrial production and processing. The EU and national regulations on the destruction of PCB and other highly chlorinated compounds in dielectrical fluids in existing electrical equipment have however been established. This means that the contribution to the environmental release, exposure and risk from this source will decrease significantly during the next decade.

An environmental risk characterisation according to the TGD for the relevant scenarios of the industrial production and processing is presented hereafter.

3.3.1 Aquatic compartment

Surface water

The $PNEC_{water}$ was 0.04 / 10 = 0.004 mg/l or 4 µg/l

Table 3.42 Estimations of PEC/PNEC in local surface water

Scenario	PEC_{water} µg/l	PEC/PNEC
Production		
A	0.010	0.002
B	0.053	0.013
Processing		
D1: intermediate	0.018	0.005
D2: process solvent	1.47	0.37
D3: others	38	9.4
D4: dye carrier	68	17

It is concluded that the use of 1,2,4-TCBs may cause local problems for aquatic organisms.

There were no indications of risks at the main manufacturer production and processing sites, but only for downstream industrial uses according to the uses scenarios D3 to D4.

Microorganisms

$PNEC_{microorganisms}$ (based on sludge test): 0.35 mg/l
$PNEC_{microorganisms}$ (based on *Tetrahymena* test): 0.09 mg/l

Table 3.43 Estimations of PEC_{STP}/PNEC in local STPs

Scenario	PEC_{STP} mg/l	PEC/PNEC (STP bacteria)	PEC/PNEC (STP ciliates)
Production			
A	0.028	0.08	0.31
B	0.031	0.11	0.34
Processing			
D1: intermediate	1.96	5.6	21.5
D2: process solvent	1.02	2.9	11.2
D3: others	0.38	1.1	4.2
D4: dye carrier	0.68	2.0	7.5

The PEC/PNEC is >1 indicating risk for STP microorganisms. There were no indications of risks at main manufacturer production and processing sites, but only for downstream industrial uses according to the uses scenarios D1 to D4.

Sediments (equilibrium partition)

$PNEC_{sed}$: 0.1 mg/kg

Table 3.44 Estimations of PEC/PNEC in local sediments

Scenario	PEC_{sed} mg/l	PEC/PNEC
Production		
A	0.0003	0.002
B	0.0017	0.015
Processing		
D1: intermediate	0.00055	0.006
D2: process solvent	0.046	0.4
D3: others	1.18	12
D4: dye carrier	2.12	21

It is concluded that the use of 1,2,4-TCBs may cause local problems for sediment dwelling organisms. There were no indications of risks at main manufacturer production and processing sites, but only for downstream industrial uses according to the uses scenarios D3 to D4.

Results for the aquatic environment

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

This conclusion is relevant for production and processing by the main manufacturers, for use as an intermediate and process solvent (cf. scenarios A, B, D1, D2).

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

Risk reduction measures should be considered for the use of 1,2,4-TCB as a dye carrier and other downstream uses (cf. scenario D3 and D4).

Results for STP

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

This conclusion is relevant for production and processing by the main manufacturers (cf. scenarios A, B).

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 is relevant for all downstream uses of 1,2,4-TCB resulting in environmental release (cf. scenarios D1 to D4).

3.3.2 Atmosphere

The atmospheric compartment is the major compartment for distribution of 1,2,4-TCB. The photodegradation is moderate with a half-life of approximately 30 days. Atmospheric concentrations on a regional scale are in the ng/m^3 level while on local scale at the perimeter of production/processing plants, average levels are estimated to be at µg/m^3 level. No information on the effects of these concentrations is available.

However evaluation of 1,2,4-TCB for being considered as a POP with a high potential of being considered having a significant potential for long range atmospheric transport have been made ((EB.AIR/WG.7/R.3, 1996; AEA/CS/RCEC16419225, 1995; Van Pul et al., 1997).

The atmospheric residence time can be considered as the most indicative parameter in the evaluation of the potential of long- range transport in air of substances. Van Pul et al. (1997) has developed a generic procedure to determine the potential for long-range atmospheric transport of substances by means of the residence time of the substance in air.

Table 3.45 Atmospheric residence time (selected substances from Table 1 in van Pul et al. (1997))

Substance	R_{pg}	$V_{d,\,eff}$	$V_{d,sea}$	W_{eff}	τ_{degr} (h)	τ_a (h)	τ_{as} (h)	X_t (km)	n
DDT *	0.214	-0.09675	0.03942	46,500	89	111	56	2,010	5.09
PCB *	0.013	0.00558	0.20951	3,320	5,500	997	69	7,937	36.04
Toxaphene *	0.017	0.01340	0.36384	11,400	120	93	29	1,691	4.25
Lindane*	0.002	-0.01887	0.38155	35,200	2,040	242	33	2,103	9.97
1,2,4-TCB	<0.001	0.00008	0.01598	16.7	550	547	349	7,717	20.63

* Substances from LRTAP POP protocol. The PCB isomer addressed here as an example is isomer no. 180 (according to the IUPAC numbering nomenclature)

R_{pg}: Particle/gas ratio

$V_{d,eff}$: Effective dry deposition velocity (cm/s)

$V_{d,sea}$: Dry deposition velocity above sea (cm/s)

W_{eff}: Scavenging ratio

τ_{degr}: Photochemical degradation half-time in air (hours)

τ_a: Atmospheric half-life over land (hours)

τ_{as}: Atmospheric half-life over sea (hours)

X_t: Typical travelling distance (km) after which 50% is still airborne with average wind speed 5 m/s

n: Number of deposition/re-emission cycles

1,2,4-TCB fulfils the properties used in the screening procedure developed by the task Force and Preparatory Working Group on POP for the LRTAP: A half-life in air of more than two days and a vapour pressure less than 1,000 Pa indicating a potential of long-range transport. 1,2,4-TCB has a low degradation rate with a half-life estimated in soil to 300 days, in surface water to 150 days and in air to 30 days. The adsorption coefficient Koc in soil ranged from 900 to 2,300 with the average value 1,400. The vapour pressure is measured to 36 Pa and the Henry's Law constant calculated to 181 Pa m^3/mol. The bioaccumulation factor BCF in fish is estimated to average 2,000.

The removal of 1,2,4-TCB in air may be caused by degradation by chemical- or sunlight-catalysed reactions or by absorption onto particles that settle or are removed from the atmosphere by rain. A measure of the effectiveness of these factors is the atmospheric residence time.

In a field study in California and Arizona, air samples during a two-week period included an unspecified trichlorobenzene. By assuming an average daily (24 hour) abundance of OH radicals of 10^6 molecules/cm^3, the daily loss rates calculated for 12 hours was 0.9%. The estimated residence time was calculated to be 116 days (Singh et al., 1981).

Van Pul et al. (1997) estimated an atmospheric residence time to 547 hours over land and 349 hours over sea or a total 428 hours by estimating 0.4 τ_a + 0.6 τ_{as}. Using an average wind speed of 5 m/s van Pul et al. estimates a travelling distance of 7,700 km. In van Pul et al. (1997), several of the estimated values used in the estimation are different from the values used in the risk assessment report on 1,2,4-TCB (e.g. the photochemical half-life in the atmosphere, τ_{degr}, is 23 days in van Pul et al. (1997) and estimated to be 30 days in the risk assessment report). Using the risk assessment report values (cf. above) may change the estimations slightly. Nevertheless 1,2,4-TCB has intrinsic environmental fate related properties for a significant potential of long-range atmospheric transport. This may also be the reason for inclusion of TCB in the European air emission inventory programme (CORINAIR) for POPs (cf. Section 3.1.2).

Conclusion

The properties of 1,2,4-TCB compared with the guiding criteria on environmental fate related properties in the EB Decision of the LRTAP POP protocol indicate that 1,2,4-TCB should be further considered in relation to POPs.

Results for the atmospheric environment

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

However, this risk assessment supports that it may be justified to consider 1,2,4-TCB further in relation to other national and international regulations addressing POPs which may be transported long ranges via the atmospheric compartment.

3.3.3 Terrestrial compartment

The PEC/PNEC (soil) is estimated based on the few data on terrestrial organisms and the partition equilibrium method for comparison.

$PNEC_{soil} = 50/1{,}000 = 0.050$ mg/kg

Table 3.46 Estimations of concentration in local soil

Scenario	$PEC_{soil,agr,\ 30d}$ mg/kg	$PEC_{soil,agr,180d}$ mg/kg	PEC/PNEC (30 d)	PEC/PNEC (180 d)
Production				
A	0.079	0.047	<<(1.6)*	<<(0.9)*
B	0.079	0.047	<<(1.6)*	<<(0.9)*
Processing				
D1: intermediate	5.09	3.03	<<(102)*	<<(61)*
D2: process solvent	2.64	1.57	<<(53)*	<<(31)*
D3: others	0.98	0.58	20	12
D4: dye carrier	1.77	1.05	35	21

* Based on sludge application to agricultural soil, which according to the main manufacturers is *not* relevant

$PEC/PNEC_{terrestrial}$ >1 in all downstream scenarios and thus, a risk is present for terrestrial organisms in these cases. The indicated risk results are based on sludge application. The relatively high concentrations measured in sludge from STPs from several countries in the EU and North America may furthermore indicate releases from unknown sources. The main manufacturers state that residues and sludge from their production and processing sites are incinerated, and thus this problem seems not to be related to the sites of the main manufacturers.

Results for the terrestrial environment

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

This conclusion is relevant for the production and processing sites of the main manufacturers.

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 is relevant for all downstream uses resulting in environmental release (cf. scenarios D1 to D4).

3.3.4 Secondary poisoning

For fish eating mammals, the risk assessment is estimated as:

$PEC_{oral} = PEC_{water} \cdot BCF_{fish}$ (cf. Section 3.2.4)
$PNEC_{oral} = 10$ ppm.

Table 3.47 Estimations of $PEC_{oral, fish}/PNEC_{oral}$

Scenario	$PEC_{oral, fish}$ (mg/kg)	$PEC_{oral, fish}/PNEC_{oral}$
Production		
A	0.019	0.0019
B	0.055	0.0055
Processing		
D1: intermediate	0.021	0.0021
D2: process solvent	1.22	0.122
D3: other	2.09	0.209
D4: dye carrier	1.88	0.188

Results

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

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

4.1.1.1 General discussion

Humans may be exposed to 1,2,4-TCB at the workplace, from the use of consumer products and via the environment.

The industrial use pattern for 1,2,4-TCB has been described in Section 2.2.

The number of people exposed is difficult to estimate without actually counting exposed persons in a representative sub-population. There is no knowledge of surveys where this has been done and where the sub-population can still be regarded as representative. Information provided by Industry suggests that only few workers are exposed in Europe during the production of 1,2,4-TCB, maybe as few as 50 persons. There is no information on the number of people exposed during downstream use of the substance.

4.1.1.2 Occupational exposure

The following institutions report that they have no exposure data on 1,2,4-TCB: BIA, Germany (1998); National Institute of Occupational Health, Hungary (1998); INRS, France (1998); DSM, The Netherlands (1998), TNO, The Netherlands (1998), and the National Institute of Occupational Health, Denmark (1998).

Exposure to 1,2,4-TCB can occur by inhalation of vapours and liquid aerosols, dermal exposure to vapours and liquids and via the gastrointestinal tract. Dermal exposure to vapours is considered to be insignificant and ingestion is disregarded.

Some occupational exposure limits are given in **Table 4.1.**

Table 4.1 Some occupational exposure limits for 1,2,4-TCB

	8 h TWA, ppm	8 h TWA, mg/m^3	STEL, ppm	STEL, mg/m^3	Notes
USA (ACGIH, 1997)			5	37	
EU (1994)	2	15.1	5	37.8	Skin
NL (1997-1998)	2	15.1	5	37.8	Skin
D (MAK, 1997)[1)]	5	38			Skin
UK (1998)	5	38	5	38	
DK (1996)	2	15.1			Skin

TWA: time weighted average. ppm: parts per million (cm^3/m^3). STEL: short-term exposure limit.
[1)]: Germany has withdrawn the MAK value for 1,2,4-TCB and listed it as a carcinogen class IIIb (NL, 1999).

Personal Protective Equipment (PPE)

The air exposure considered in this assessment is the concentration component of available dose, measured as the concentration in the breathing zone of the workers. PPE will not be taken into account in this exposure section because the actual degree of protection cannot be known. PPE protects against air exposure to 1,2,4-TCB between 0-100 %, depending on the type of PPE, the way the equipment is used, and the maintenance of the equipment. During repair work the workers are obliged to wear PPE. Repair work is usually not performed by members of the normal production staff, but done by specialists (Bayer, 1998).

Gloves may protect against dermal exposure to 1,2,4-TCB, depending on the type of gloves, the qualitative and quantitative composition of the product, the way the gloves are used and how often they are replaced. Use of gloves may even increase dermal uptake rate of 1,2,4-TCB above uptake rate through unprotected skin, due to occlusion ("washerwoman's fingers"). No account will be taken of gloves in this exposure section, because the actual degree of protection cannot be known.

Exposure data

Industry has provided data on exposure to 1,2,4-TCB during the production of 1,2,4-TCB and use as a raw material. Some data have been provided by the UK on the exposure to 1,2,4-TCB during dismantling of transformers, production of plastic pellets, wire and cabling (HSE (UK), 1999). Other European databases, which have been consulted, have reported no data on occupational exposure to 1,2,4-TCB.

The data available from industry are scarce and reported as arithmetic mean and range. In the occupational environment, exposures are reported to be log-normally distributed (Esmen, 1979; Rappaport, 1991; Roach, 1992) and the geometric standard deviation may be of the order of 5-10 (Buringh and Lanting, 1991). If this is generally true for exposures to 1,2,4-TCB, the use of the arithmetic mean will over-report the general exposure levels. The size of the over-reporting cannot be very large, judging from the narrow range of most of the data series. Little or no information is available on how the measured data were produced (sampling time, sampling volume, quality control of analysis, method of sampling, and sampling strategy). The work performed by the workers is not described in detail. A process as drumming gives some indications on what was going on during the sampling period. No information on filling rates are given and thereby the rate of vapours entering the workplace is unknown.

A few data points are characterised as being 8-hour values. One reference (Bayer, 1998b) applies a "correction factor", which is unity for all but one measurement. One result of 3.6 mg/m^3 has been calculated to 1.35 mg/m^3, using a "correction factor" of 2.7, corresponding to a sampling time of three hours out of eight. If this is correct, it must be concluded that the rest is 8-hour values. For the rest of the data reported, no information is given on how the 8-hour values have been calculated. It is unclear whether time outside the sampling period has been assigned a concentration of zero or been given the same concentration as found in the sampling periods.

Scenarios

Occupational exposure may occur during:

Q. Production of 1,2,4-TCB, including storage and handling (i.e. transfer from one container to another), sampling and analysis of quality control samples, cleaning, repair and maintenance of the equipment.

R. Use of pure TCB in synthesis (use as an intermediate) and as a dye carrier. Synthesis of compounds based on 1,2,4-TCB includes operations such as storage and handling (i.e. transfer from one container to another), sampling and analysis of quality control samples, cleaning, repair and maintenance of the equipment.

S. Production, storage and handling of 1,2,4-TCB containing products (semi-products as well as products for sale), sampling and analysis of quality control samples, cleaning, and repair and maintenance of equipment.

T. 1,2,4-TCB exposure during the use of 1,2,4-TCB containing products (occupational exposure), cleaning, repair and maintenance of equipment.

For scenarios Q, R, and T, measurements of workplace exposures for workers are available. For some cases it is not reported whether it was personal or area sampling.

The available measured data are scarce and, therefore, it has been decided also to include modelled exposure estimates for those scenarios. For scenario S, no measurements are available and, therefore, the risk characterisation will be based on modelled exposure estimates.

The original DOS version of EASE is used in EUSES (1997), whereas EASE2 is a revised Windows version of EASE. For inhalation exposures, the two versions sometimes give different results. The risk characterisation was based on EASE2 (1997) predictions, unless measurements were available and considered to be of adequate quality. For comparison the results from modelling using EUSES (1997) are included.

Potential dermal exposure has been expressed as mg/cm^2 for the evaluation of local dermal exposure, and as mg/kg bw/day for systemic effects of dermal exposure. The calculations assume that workers do not wash their hands during the working day. Because of low vapour pressure evaporation of 1,2,4-TCB is disregarded.

Exposure concentrations in mg/m^3 have been converted to mg/kg/d by multiplying the air concentration by:

$$\frac{\text{minute volume (l/min)} \cdot \text{work exposure time (minutes/day)} \cdot \text{percentage absorption}}{1{,}000\ \text{l/m}^3 \cdot \text{body weight (kg)}}.$$

The following values have been used:

minute volume:	40 l/min [1)]
work exposure time:	480 min [2)]
body weight:	70 kg
percentage absorption:	100%

1) A standard minute volume has been used for all scenarios. The value chosen for workers is the mean (40 l/min) of values normally accepted for light work (20 l/min) and heavy physical work (60 l/min)

2) A standard exposure time (full 8-hour shift) has been used for all worker exposure scenarios

Total systemic exposure has been calculated as the sum of the values chosen to represent the realistic worst case for full-shift inhalation and dermal exposures assuming 100% dermal absorption. This figure is therefore potentially an overestimate of the total systemic exposure.

4.1.1.2.1 Production of 1,2,4-TCB (Scenario Q)

Production of 1,2,4-TCB is carried out in closed systems and therefore the occupational exposure is expected to be low. Significant exposure may occur during special situations such as material sampling, drumming, repair, and maintenance, and from spills and leaks.

Scenarios Q1-Q3

Scenarios Q1, Q2, and Q3 cover surveillance type of work, where no control samples are taken.

The sources of exposure are taken to be spills from leaks of valves and pumps. The available measured data are presented in **Table 4.2**.

Exposure calculations for scenario Q1, Q2, and Q3 have been carried out.

For air exposures the following parameters were used: liquid temperature was 20°C, no aerosols were formed, use-pattern was closed system which is not breached, and the pattern-of-control was full containment.

For dermal exposures the following parameters were used: use-pattern was a closed system which was not breached, the pattern-of-control was not direct handling. The skin area used in the calculations was 420 cm^2 (both palms) and the body weight used was 70 kg.

Table 4.2 Full-shift exposures (concentrations in air) during the production of 1,2,4-TCB in closed systems.

	Exposure settings	Type of work	n	AM mg/m³	Range mg/m³	EASE 3) air mg/m³	EASE dermal mg/kg/d	EASE dermal mg/cm²	Total systemic dose mg/kg/d
Q1	Production area Outdoors	Surveillance 1)	5	0.12	0.1-0.14	0-0.7 (0-0.8)	Negligible	Negligible	0 – 0.2
Q2	Production area Outdoors	No information 2)	8	<0.1	-	0-0.7 (0-0.8)	Negligible	Negligible	0 – 0.2
Q3	Distillation area Outdoors	No information 2)	2	1.7	0.5–2.9	0-0.7 (0-0.8)	Negligible	Negligible	0 – 0.2

n: number of samples
AM: arithmetic mean
1) Bayer (1998b)
2) Bayer (1998a)
3) Calculations performed in EASE2 (1997). The results from calculations performed in EUSES (1997) are shown in brackets

For these scenarios EUSES (1997) and EASE2 (1997) predict approximately the same air exposure interval. The predictions do not contradict the measured data when comparing with the arithmetic means. However, some of the measurements of 1,2,4-TCB are approximately four times higher than the values predicted.

Scenarios Q4 and Q5

Scenarios Q4 and Q5 cover surveillance type of work in combination with collection of control samples.

The sources of exposure are taken to be spills from leaks of valves and pumps as well as from the production equipment, when control samples are collected.

The available measured data are presented in **Table 4.3**.

Exposure calculations for scenarios Q4 and Q5 have been carried out.

For air exposures the following parameters were used: liquid temperature was 20°C, no aerosols were formed, use-pattern was a closed system which is not breached (except for short moments, when samples were collected), and the pattern-of-control was full containment.

For dermal exposures the following parameters were used: use-pattern was a closed system which sometimes was breached for collection of samples (i.e. non-dispersive use), the pattern-of-control was direct handling, and the contact level was incidental. The skin area used in the calculation was 420 cm^2 (both palms) and the body weight used was 70 kg.

Table 4.3 Full-shift exposures (concentrations in air) during the production of 1,2,4-TCB in closed systems.

	Exposure settings	Type of work	n	AM mg/m³	Range mg/m³	EASE 3) air mg/m³	EASE dermal mg/kg/d	EASE dermal mg/cm²	Total systemic dose mg/kg/d
Q4	Distillation area Outdoors	Collection of samples 1)	6	-	0.1-2.9	0-0.7 (0-0.8)	0 – 0.6	0 – 0.1	0 – 0.8
Q5	Production and distillation area Outdoors	Surveillance and collection of samples 2)	7	0.75	0.15-1.5	0-0.7 (0-0.8)	0 - 0.6	0 – 0.1	0 – 0.8

n: number of samples
AM: arithmetic mean
1) Bayer (1998b). During collection of samples, it is obligatory to wear suitable gloves, but no mask
2) Rhône-Poulenc (1996): 30 workers are working with production and distillation of 1,2,4-TCB
3) Calculations performed in EASE2 (1997). The results from calculations performed in EUSES (1997) are shown in brackets

For these scenarios EUSES (1997) and EASE2 (1997) predict approximately the same air exposure intervals. It is assumed that the short moments, where samples are taken, do not contribute significantly to the air exposure. In contrast, dermal exposure is considered to be due to incidental spills when samples are taken. The few measurements are not in conflict with the results of the modelling. However, some measurements are up to four times higher than the values predicted.

Scenarios Q6-Q8

Scenarios Q6, Q7, and Q8 cover drumming of pure 1,2,4- TCB.

According to one of the producers (Bayer, 1998b) most 1,2,4-TCB is filled into road tankers and only a small part is filled into 200 litres drums. The filling procedure for drums is done semi-automatically with local exhaust ventilation. The workers are obliged to wear gloves. The filling of road tankers is done outside the building in open air, whereas drumming is done indoors. There is no reason to believe that the filling procedure at the other production plants differs significantly.

The available measured data are presented in **Table 4.4**.

Exposure calculations for scenarios Q6, Q7, and Q8 have been carried out.

For air exposures the following parameters were used: liquid temperature was 20°C, no aerosols were formed, the use-pattern was non-dispersive use, and the pattern-of-control was local exhaust ventilation.

For dermal exposures the following parameters were used: the use-pattern was non-dispersive use, the pattern-of-control was direct handling, and the contact level was incidental. The skin area used in the calculation was 420 cm^2 (both palms) and the body weight used was 70 kg.

Table 4.4 Full-shift exposures for filling of containers (personal sampling)

	Type of work	n	AM mg/m³	Range mg/m³	EASE [4] air mg/m³	EASE dermal mg/kg/d	EASE dermal mg/cm²	Total systemic dose mg/kg/d
Q6	Drumming [1]	2	0.7	0.1-1.35	3.7-7.4 (3.8-22.6)	0 – 0.6	0 – 0.1	1 - 2.6 (1 – 6.8)
Q7	Drumming [2]	1	3.6	-	3.7-7.4 (3.8-22.6)	0 – 0.6	0 – 0.1	1 - 2.6 (1 – 6.8)
Q8	Drumming [3]	3	0.68	0.65-0.69	3.7-7.4 (3.8-22.6)	0 – 0.6	0 – 0.1	1 - 2.6 (1 – 6.8)

n: number of samples
AM: arithmetic mean
[1] Bayer (1998b)
[2] Bayer (1998a)
[3] J P Stevens and Co, Inc. USA (1983)
[4] Calculations performed in EASE2 for Windows (1997). The results from calculations performed in EUSES (1997) are shown in brackets

For these scenarios EUSES (1997) and EASE2 (1997) do not predict similar air exposure intervals. It is of note that the EUSES (1997) predictions of air exposure concentrations are up to 6 times higher than the highest measured values, whereas the values calculated using EASE2 (1997) are approximately up to a factor of two higher.

Discussion for scenario Q

Inhalation

In general, the number of measurements is very limited and there is no information on how the data were produced (sampling time, sampling volume, sampling strategy, etc.). For these reasons, the quality of the data is considered to be inadequate for deriving a reliable estimate of the realistic worst-case full-shift exposure level. Consequently, the upper range of the EASE calculations will be used to represent the realistic worst-case full-shift exposure level.

For surveillance (Q1-Q3) and collection of samples (Q4-Q5) the highest measured value will be used to represent the reasonable worst-case short-term exposure level.

For drumming (Q6-Q8) even the upper range of the measured data is considerably lower than the modelled exposure estimates. Considering the low number of measurements this does not necessarily contradict the modelled exposure estimates. For drumming, the realistic worst-case short-term exposure level is assumed to be twice the modelled full-shift exposure level.

Dermal

The upper range of the EASE calculations will be used to represent the realistic worst-case exposure level.

4.1.1.2.2 Use of pure 1,2,4-TCB (Scenario R)

The scenarios considered here are scenarios where the pure 1,2,4-TCB is used as a raw material for synthesis, as a dye carrier in the textile industry, and as a process solvent.

Scenarios R1-R3

Scenarios R1, R2, and R3 cover the use of pure 1,2,4-TCB in synthesis.

The synthesis process is enclosed. Occupational exposure may occur during reactor loading, collecting of quality control samples, repair and maintenance, and from stack emissions, leaks and spills. At one of the plants, five persons are working between 10 and 100 days a year. Another five persons work from 100 to 250 days a year (Rhône-Poulenc, 1996).

The available measured data are presented in **Table 4.5**.

Exposure calculations for scenarios R1, R2, and R3 have been carried out.

For air exposures the following parameters were used: the liquid temperature was 20°C, no aerosols were formed, the use-pattern was a closed system which was not breached (except for short moments where control samples were taken), and the pattern-of-control was full containment.

For dermal exposures the following parameters were used: the use-pattern was a closed system which sometimes was breached for collection of samples (i.e. non-dispersive use), the pattern-of-control was direct handling, and the contact level was incidental. The skin area used in the calculation was 420 cm^2 (both palms) and the body weight used was 70 kg.

For these scenarios EUSES (1997) and EASE2 (1997) predict approximately the same air exposure intervals. It is assumed that the short moments, where samples are taken, do not contribute significantly to the air exposure. In contrast, dermal exposure is considered to be due to incidental spills, when samples are taken. The exposure calculations on air exposure are comparable to the arithmetic mean values of the measured data. However, single measurements are up to six times higher than the EUSES (1997) and EASE2 (1997) calculations.

Scenario R4

There is no information available on the occupational exposure in relation to the use of 1,2,4-TCB as a dye carrier. Due to this total lack of information of this process no modelling has been carried out.

Scenario R5

There is no information available on the occupational exposure in relation to the use of 1,2,4-TCB as a process solvent. Due to this total lack of information of this process no modelling has been carried out.

Table 4.5 Short-term exposures at a synthesis plant (closed system, personal sampling)

	Type of work	n	AM mg/m³	Range mg/m³	EASE 1) air mg/m³	EASE dermal mg/kg/d	EASE dermal mg/cm²	Total systemic dose mg/kg/d
R1	Loading rack operator	2	<0.1	-	0-0.7 (0-0.8)	0 – 0.6	0 – 0.1	0 – 0.8
R2	Plant loading rack	2	0.7	0.03-1.2	0-0.7 (0-0.8)	0 – 0.6	0 – 0.1	0 – 0.8
R3	Collection of control samples	7	1.1	0.2–4.8	0-0.7 (0-0.8)	0 – 0.6	0 – 0.1	0 – 0.8
R4	Dye carrier	no information available						
R5	Process solvent	no information available						

n: number of samples
AM: arithmetic mean. Rhône-Poulenc (1996)
1) Calculations performed in EASE2 for Windows (1997). The results from calculations performed in EUSES (1997) are shown in brackets

Discussion for scenario R

Inhalation

For loading and collection of samples (R1-R3) the number of measurements is very limited and there is no information on how the data were produced (sampling time, sampling volume, sampling strategy, etc.). For these reasons, the quality of the data is considered to be inadequate for deriving a reliable estimate of the realistic worst-case full-shift exposure level. Consequently, the upper range of the EASE calculation will be used to represent the realistic worst-case full-shift exposure level.

Further, the highest measured value will be used to represent the reasonable worst-case short-term exposure level.

For use of 1,2,4-TCB as a dye carrier (R4) and as a process solvent (R5) no information is available and no exposure assessment can be performed.

Dermal

The upper range of the EASE calculations will be used to represent the realistic worst-case exposure level.

4.1.1.2.3 Production of 1,2,4-TCB containing products (Scenario S)

1,2,4-TCB has been used as a constituent in dielectric fluids in transformers. In addition, according to the Nordic Product Registers, certain anticorrosive paints, rust removers, cooling agents, lubricants polishes, and maintenance products contain 1,2,4-TCB.

No information on the work processes or the exposures during production of 1,2,4-TCB containing products is available. Therefore, three EASE scenarios have been included for pre-dispersion, dispersion, and canning of paint. These are considered to be representative for the

production of the known 1,2,4-TCB containing products. When the product contains no pigment, the second process is not needed.

Scenario S1

Mixing and pre-dispersion of pigments in a 1,2,4-TCB containing paint on a high-speed dissolver, equipped with lid and exhaust unit. Liquid components filled into the vessel from stationary pipes or pumped into the vessel from barrels. Pigments are added to the mixture from bags.

Exposure calculations for scenario S1 has been carried out.

For air exposures the following parameters were used: the liquid temperature was 95°C, no aerosols were formed, the use-pattern was a closed system which was breached (i.e. non-dispersive use), and the pattern-of-control was local exhaust ventilation. It is assumed that the 1,2,4-TCB content is 10% w/w, corresponding to the highest value found in the Nordic Product Registers. The result has therefore been divided by 10.

For dermal exposures the following parameters were used: the use-pattern was inclusion onto matrix, the pattern-of-control was direct handling, and the contact level was incidental. The skin area used in the calculation was 420 cm^2 (both palms) and the body weight used was 70 kg. In addition, the worker operating the high-speed dissolver may occasionally disconnect loading pipes. Skin exposure arising from direct contact with pure 1,2,4-TCB during this type of operation was modelled with the parameters: pattern of control was direct handling and contact level was incidental contact with 1,2,4-TCB. The same skin area and body weight was used for this calculation.

Scenario S2

Dispersion of pigments in a pearl mill. The pre-dispersed paint is pumped into the pearl mill through a hose connected to bottom outlet of the pre-dispersion vessel. From the pearl mill, the finished paint is collected in a vessel equipped with lid, and local exhaust ventilation.

Exposure calculations for scenario S2 has been carried out.

For air exposures the following parameters were used: the liquid temperature was 60°C, no aerosols were formed, the use-pattern was closed system which is sometimes breached (i.e. non-dispersive use), and the pattern-of-control was local exhaust ventilation.

For dermal exposures the following parameters were used: the use-pattern was inclusion onto matrix, the pattern-of-control was direct handling, and the contact level was incidental. The skin area used in the calculation was 420 cm^2 (both palms) and the body weight used was 70 kg.

It is assumed that the 1,2,4-TCB content is 10% w/w, corresponding to the highest value found in the Nordic Product Registers. The result has therefore been divided by 10.

Scenario S3

Canning of paint in an automatic tapping machine. The dispersed paint is pumped into the tapping machine through a hose connected to bottom outlet of the vessel containing the finished paint. The tapping machine is equipped with local exhaust ventilation.

Exposure calculation for scenarios S3 has been carried out.

For air exposures the following parameters were used: the liquid temperature was 20°C, no aerosols were formed, the use-pattern was a closed system, sometimes breached (i.e. non-dispersive use), and the pattern-of-control was local exhaust ventilation.

For dermal exposures the following parameters were used: the use-pattern was inclusion onto matrix, the pattern-of-control was direct handling, and the contact level was incidental. The skin area used in the calculation was 420 cm^2 (both palms) and the body weight used was 70 kg.

It is assumed that the 1,2,4-TCB content is 10% w/w, corresponding to the highest value found in the Nordic Product Registers. The result has therefore been divided by 10.

Scenario S4

Information on the use of 1,2,4-TCB in dielectric fluids has been supplied by the industry in addition to other information available. The 1981 US EPA Exposure and Risk Assessment for 1,2,4-TCB contains information about this use of the substance, which at the time represented a significant use of the substance. In the absence of any specific information concerning production of dielectric fluids, no exposure assessment can be performed.

Table 4.6 Full-shift exposures during the production of 1,2,4-TCB containing products.

	Type of work	EASE [1] air mg/m³	EASE dermal [2] mg/kg/d	EASE dermal [2] mg/cm²	Total systemic dose mg/kg/day
S1	Pre-dispersion on high speed dissolver	7.4-14.8 (7.6-37.7)	0 - 0.6 [3]	0 – 0.1 [3]	2.6 – 5.7 (2.6 – 13.4)
S2	Dispersion on pearl mill	0.4-0.7 (0.4-2.3)	0 - 0.06	0 – 0.01	0.1– 0.3 (0.1 – 0.8)
S3	Canning of paint	0.4-0.7 (0.4-2.3)	0 - 0.06	0 – 0.01	– 0.3 (0.1 – 0.8)
S4	Production of dielectric fluids	No information			

1) Calculations performed in EASE2 for Windows (1997). The results from calculations performed in EUSES (1997) are shown in brackets

2) The dermal exposure in S1 is exposure to pure 1,2,4-TCB, whereas the dermal exposure in S2 and S3 is to paint containing 10% 1,2,4-TCB

3) Skin exposure arising from direct contact with pure 1,2,4-TCB during disconnecting loading pipes

Discussion for scenario S

Inhalation

For production of 1,2,4-TCB containing products no measured data were available. For scenarios S1, S2 and S3 (Pre-dispersion on high speed dissolver, Dispersion on pearl mill, Canning of paint) exposure has been modelled.

For these scenarios, the upper range of the EASE calculation will be used to represent the realistic worst-case full-shift exposure level. Reasonable worst-case short-term exposure levels are assumed to be twice the full-shift exposure levels.

For scenario S4 (production of dielectric fluids) information is so scarce that no exposure assessment can be performed.

Dermal

For scenarios S1, S2 and S3 (pre-dispersion on high speed dissolver, dispersion on pearl mill, canning of paint) exposure has been modelled.

The upper range of the EASE calculations will be used to represent the realistic worst-case exposure level.

For scenario S4 (production of dielectric fluids) information is so scarce that no exposure assessment can be performed.

4.1.1.2.4 Occupational use of 1,2,4-TCB containing products (Scenario T)

Little information is available on the occupational use of 1,2,4-TCB containing products. Exceptions are the use of 1,2,4-TCB containing dielectric fluids in transformers and the production of plastic pellets. Furthermore, there is anecdotal information available on the occupational use of 1,2,4-TCB containing products during production of wire and cabling (HSE (UK), 1999).

Scenario T1

Dismantling of transformers. Dismantling transformers is not likely to involve many workers, nor is it likely that any of the individual workers will be frequently involved in this type of work.

Exposure to 1,2,4-TCB can occur when draining dielectric fluid during dismantling of transformers. A few data are available, from the UK industry, on exposure during the dismantling of transformers containing 1,2,4-TCB. Of the seven results available, the highest was a personal sample from the probable highest exposure area. This value was 0.68 mg/m^3 and was obtained during transformer washing when there is a risk of a localised concentration of residual 1,2,4-TCB being forced out of the hole cut in the transformer top.

Furthermore, there is anecdotal evidence to support the view that 1,2,4-TCB concentrations are generally low during transformer dismantling. At a UK company, in the summer of 1991, several cores from PCB-containing transformers were stored under plastic for several hours. Sampling under the plastic revealed concentrations of 1,2,4-TCB well below 10 ppm, even under these extreme conditions (HSE (UK), 1999).

It is assumed by the UK industry that the greater volatility of 1,2,4-TCB will produce air concentrations in an order of magnitude above those found for PCBs. PCB levels during transformer dismantling, with good occupational hygiene, do not exceed 100 μg/m^3. This value, given the above assumptions, suggests that 1,2,4-TCB levels should not normally exceed 1 mg/m^3 (0.13 ppm). The small number of measured exposures is in line with this.

Dermal exposure to 1,2,4-TCB during transformer dismantling can be described as non-dispersive use, direct handling using both hands (840 cm^2) with intermittent exposure (HSE (UK), 1999). The bodyweight was set to 70 kg. It is assumed that the concentration of 1,2,4-TCB in the transformer fluid is 50% w/w. The result has therefore been divided by two.

Scenario T2

Spray painting. No measured data are available.

Exposure calculations for scenario T2 has been carried out.

For air exposures the following parameters were used: the liquid temperature was 20°C, aerosols were formed, the use-pattern was non-dispersive use, and the pattern-of-control was local exhaust ventilation.

For dermal exposures the following parameters were used: the se-pattern was non-dispersive use, the pattern-of-control was direct handling, and the contact level was extensive. The skin area used in the calculation was 1,300 cm^2 (hands and face) and the body weight used was 70 kg.

The predictions of air exposure were 74-151 mg/m^3 (EUSES, 1997) and 74-148 mg/m^3 (EASE2, 1997) to 1,2,4-TCB using paint with a content of 1,2,4-TCB of 10% by weight.

It has been pointed out that EASE calculation in a scenario in which aerosols are formed overestimates the actual exposure (NL, 1999). An alternative approach is to predict 1,2,4-TCB exposure based on measured data on isocyanate exposure during spraying (de Pater et al., 1999):

$$\text{Exposure}(1,2,4-\text{TCB}) = \text{Exposure}(\text{isocyanates})\frac{C_{1,2,4-\text{TCB}}}{C_{\text{isocyanate}}},$$

where $C_{1,2,4\text{-TCB}}$ and $C_{\text{isocyanate}}$ are the concentrations of 1,2,4-TCB and isocyanate, respectively, in the products sprayed.

A value of Exposure(isocyanates) of 10 mg/m^3 and a value of $C_{\text{isocyanate}}$ of 30% have been suggested (NL, 1999). Using these figures, the expected exposure will be:

$$\text{Exposure}(1,2,4-\text{TCB}) = 10\frac{10}{30} = 3.3\ \text{mg/m}^3$$ for a 1,2,4-TCB concentration of 10%.

Concerning potential dermal exposure the prediction of EASE was 2-9 mg 1,2,4-TCB/kg bw/d for a 70 kg person, who is exposed on hands and face (approximately 1,300 cm^2). A study done by TNO (NL) shows that the reasonable worst-case exposure level of hands and face (1,300 cm^2) during spray painting is 4.1 mg product/cm^2/d (Marquart et al., 1999; Lansink et al., 1998). Using these values, the potential dermal exposure becomes 8 mg 1,2,4-TCB/kg/d for a 70 kg person using paint containing 10% 1,2,4-TCB for a full 8-hour shift. This result is in accordance with the potential dermal exposure predicted by EASE.

Scenario T3

Production of plastic pellets. Thirteen results are available of concentrations during production of plastic pellets ranging from 0.08 mg/m^3 up to 15.2 mg/m^3. One value was as high as 57 mg/m^3 but for this value the vapours were sampled just above the freshly produced pellets and would not be in the breathing zone of any worker. For that reason this measurement has been disregarded. Though, with a single measurement being this high, exposure to an air concentration of 15.2 mg/m^3 does not seem to be unrealistic. Therefore, the value of 15.2 mg/m^3 is chosen to represent the "realistic worst-case" and will be used in the risk characterisation.

Usually, production of plastic pellets is carried out in such a way that the workers do not need to have direct contact with the material produced. Dermal exposure, therefore, can be considered to be negligible.

Scenario T4

Production of wire and cabling. A value of 1.9 mg/m^3 has been given for exposure during production of wire and cabling (HSE (UK), 1999). This value was the highest of 8. No information is available on how the production took place during sampling or about possible engineering controls. These data, therefore, will not be used in the risk assessment and no modelling will be performed.

Scenario T5

Polishing, e.g. a car or a truck in a workplace equipped with local exhaust ventilation. No measured data are available.

Exposure calculation for scenario T5 has been carried out.

For air exposures the following parameters were used: the liquid temperature was 20°C, no aerosols were formed, the use-pattern was inclusion onto matrix, and the pattern-of-control was local exhaust ventilation.

For dermal exposures the following parameters were used: the use-pattern was inclusion onto matrix, the pattern-of-control was direct handling, and the contact level was extensive. The skin area used in the calculation was 420 cm^2 (both palms) and the body weight used was 70 kg.

The concentration of 1,2,4-TCB in the products is chosen to be 10% for all these scenarios corresponding to the maximum concentration reported for a former product in the Nordic Product Registers. The results calculated have, therefore, been reduced by a factor of 10.

Table 4.7 Full-shift exposures for the use of 1,2,4-TCB containing products.

	Type of work	Air mg/m^3	dermal mg/kg/d	dermal mg/cm^2	Total systemic dose mg/kg/d
T1	Dismantling transformers	0.68 [1]	0.6-6 [2]	0.05 – 0.5	0.8 – 6.2
T2	Spray painting	3.3 [3]	8 [4]	0.4	9.1
T3	Production of plastic pellets	<0.08-15.2 [1]	Negligible	Negligible	<0.1 – 5.2
T4	Production of wire and cabling	1.9 [1]	No information	No information	0.7
T5	Polishing	0.4-0.7 [2] (0.4-2.3)	0.6-3.0 [2]	0.1 – 0.5	0.7 – 3.2 (0.7 – 3.8)

[1] Measured values provided by HSE (UK) (1999)
[2] Calculations performed in EASE2 for Windows (1997). The results from calculations performed in EUSES (1997) are shown in brackets.
[3] Based on exposure data on isocyanates (de Pater et al., 1999)
[4] Based on Marquart et al. (1999) and Lansink et al. (1998)

Discussion for scenario T

Inhalation

For dismantling of transformers (T1) a few measured data are available. The data are of poor quality, but are in accordance with anecdotal evidence. The highest measured value is taken to represent the realistic worst-case full-shift exposure level. The realistic worst-case short-term exposure level is assumed to be twice the full-shift value.

For spray painting (T2) no measured data were available, and exposure levels have been modelled. It has been pointed out that EASE tends to overestimate exposure where aerosols are formed. Therefore an exposure has been predicted based on measured data on isocyanate exposure during spraying. This value is taken to represent realistic worst-case full-shift exposure level. The realistic worst-case short-term exposure level is assumed to be twice the full-shift value.

For production of plastic pellets (T3) a few measured data are available. The highest value was sampled just above the freshly produced pellets and would not be in the breathing zone of any worker. Therefore, the second highest value is taken to represent the realistic worst-case full-shift exposure level. The realistic worst-case short-term exposure level is assumed to be twice the full-shift value.

For production of wire and cabling (T4) a single top range value has been given. There is no further information on how this value was obtained or how the production took place and the scenario will be disregarded. No exposure assessment can be performed.

For car polishing (T5) no measured data were available, and exposure levels have been modelled. Reasonable worst-case short-term exposure levels are expected to be twice the full-shift exposure levels.

Dermal

Potential dermal exposure for scenario T1 was modelled. For scenario T2 potential dermal exposure was predicted based on a Dutch study estimating the reasonable worst-case exposure level of hands and face during spray painting. For scenario T3 potential dermal exposure can be considered negligible. For scenario T4 no information was available and no exposure assessment can be performed. Potential dermal exposure for scenario T5 was modelled.

4.1.1.2.5 Summary of occupational exposure assessment

Table 4.8 provides an overview of the realistic worst-case exposure for each scenario which is brought forward to the risk characterisation. Some sub-scenarios have been grouped together since they describe similar activities.

This table also includes values for the total systemic exposure from both full-shift inhalation and dermal uptake.

Table 4.8 Realistic worst-case exposure values for each sub-scenario

	Type of work	Exposure, inhalation, Full shift mg/m³	Exposure, inhalation, Short-term mg/m³	Exposure, dermal mg/kg/d	Exposure, dermal mg/cm²	Total systemic dose mg/kg/d
Q1-Q3	Surveillance / no information	0.7	2.9[1)]	Negligible	Negligible	0.2
Q4-Q5	Collection of samples	0.7	2.9[1)]	0.6	0.1	0.8
Q6-Q8	Drumming	7.4	15	0.6	0.1	2.6
R1-R3	Loading and collection of samples	0.7	4.8[1)]	0.6	0.1	0.8
R4	Dye carrier	No information				
R5	Process solvent	No information				
S1	Pre-dispersion on high speed dissolver	14.8	30	0.6	0.1	4.7
S2	Dispersion on pearl mill	0.7	1.4	0.1	0.01	0.3
S3	Canning of paint	0.7	1.4	0.1	0.01	0.3
S4	Production of dielectric fluids	No information				
T1	Dismantling transformers	0.68[1)]	1.4	6	0.5	6.2
T2	Spray painting	3.3	6.6	8	0.4	8.9
T3	Production of plastic pellets	15.2[1)]	30	Negligible	Negligible	4.2
T4	Production of wire and cabling	Lack of information				
T5	Polishing	0.7	1.4	3.0	0.5	3.2

1) Measured values. When disagreements were found between the results obtained using EUSES (1997) and EASE2 (1997), the value obtained by using EASE2 (1997) has been chosen for the risk characterisation. The reason for this choice is that this program will be incorporated in the revised version of the TGD (HSE (UK), 2000)

4.1.1.3 Consumer exposure

According to the Nordic Product Registers, 1,2,4-TCB containing products have been available in the EU market recently.

There is no information available concerning consumer use and no specifications as to how these products were used (e.g. product application). Considering the type of products that were previously in the market, there is no reason to believe that these products were only available to professionals. Consumer exposure is however likely to be limited since there are relatively few products containing 1,2,4-TCB.

Three scenarios have been modelled for consumers. It is assumed that the product application during consumer use and occupational use are comparable, whilst the exposure situation differs. The three scenarios are:

U1: Spray painting items using 1,2,4-TCB containing paint,
U2: Polishing a bicycle using 1,2,4-TCB containing polish,
U3: Polishing a car using 1,2,4-TCB containing polish.

Exposure has been estimated based on the following assumptions:

- The concentration of 1,2,4-TCB in the products used is assumed to be 10 w/w %. This is the highest concentration reported in the Nordic Product Registers (1998).
- Exposure takes place indoors. The room size is assumed to be 20 m^3.
- The bodyweight is set to 70 kg.
- A standard value for inhalation minute volume for light work has been chosen (20 l/min).
- In scenario U1 (spray painting) it is assumed that hands and face (1,300 cm^2) will be exposed while for scenarios U2 and U3 (polishing) it is assumed that only hands (840 cm^2) will be exposed.

The exposure is estimated as per event for the evaluation of risk of acute effects and as per day for the evaluation of risk for chronic effects assuming the following pattern of use:

U1: One event per week of 0.5 hr duration,
U2: One event per week of 0.5 hr duration,
U3: One event per two weeks of 1 hr duration.

For the evaluation of risk of acute effects exposure is estimated as:
Inhalation: mg/m^3
Dermal: mg/kg bw/event and maximal concentration on the skin (mg/cm^2).
Total systemic dose: mg/kg bw/event

For the evaluation of risk of chronic effects exposure is estimated as:
Inhalation: mg/kg bw/d.
Dermal: mg/kg bw/d and average concentration on the skin (mg/cm^2).
Total systemic dose: mg/kg bw/d.

In order to calculate inhalation exposure as mg/kg bw/d exposure concentrations in mg/m^3 have been converted to mg/kg/d by multiplying the air concentration by:

$$\frac{\text{minute volume (l/min)} \cdot \text{event exposure time (minutes/day)} \cdot \text{percentage absorption}}{1{,}000\ \text{l/m}^3 \cdot \text{body weight (kg)}}.$$

Total systemic exposure has been calculated as the sum of the inhalation and dermal exposures assuming 100% dermal absorption. This may lead to an overestimation of the total systemic dose.

Scenario U1

U1 is a spray painting scenario using 1 kg paint per event.

Exposure for the evaluation of acute effects

It has been pointed out that EASE calculations on scenarios in which aerosols are formed overestimate the actual exposure (TNO, 1999). An alternative approach is to predict 1,2,4-TCB exposure based on measured data on isocyanate exposure during spraying (de Pater et al., 1999):

$$\text{Exposure}(1,2,4-\text{TCB}) = \text{Exposure}(\text{isocyanates})\frac{C_{1,2,4-\text{TCB}}}{C_{\text{isocyanate}}}$$

where $C_{1,2,4\text{-TCB}}$ and $C_{\text{isocyanate}}$ are the concentrations of 1,2,4-TCB and isocyanate, respectively in the products sprayed.

A value of Exposure(isocyanates) of 10 mg/m^3 and a value of $C_{isocyanate}$ of 30% have been suggested (TNO, 1999). Using these figures, the expected exposure will be:

$$\text{Exposure}(1,2,4-\text{TCB}) = 10\frac{10}{30} = 3.3 \text{ mg/ m}^3$$ for a 1,2,4-TCB concentration of 10%.

The isocyanate measurements were carried out in industrial settings equipped with local exhaust ventilation, whereas this type of equipment is not normally available in private homes. Furthermore, the size of rooms in industrial settings is usually larger than 20 m^3.

The calculated result, therefore, should be corrected for that no local exhaust ventilation is present in the private home and for the smaller room size.

It is assumed that the EASE2 (1997) overestimation of exposures for spray painting scenarios is due to the parameter: aerosol formed, i.e. that the parameters for the use pattern and pattern of control applied to the process are not responsible for the overestimation. A calculation in EASE2 (1997) on the same scenario without local exhaust ventilation predicts a five times higher exposure concentration than with local ventilation present. The exposure in scenario U1, therefore, can be expected to be 5 times higher than it would have been if local exhaust ventilation were present. The corrected result, therefore, becomes 16.5 mg/m^3.

No information on room size is available in the study of de Pater et al. (1999). If the average room size in industrial settings is 100 m^3, then the predicted value of 16.5 mg/m^3 should be multiplied by a factor of five for a 20 m^3 room, giving a predicted exposure concentration of 83 mg/m^3.

The inhalation uptake is then:
83 mg/m^3 · 20 l/min · 30 min/event · 1/(1,000 l/m^3) · 1/(70 kg bw) = 0.7 mg/kg bw/event.

A study done by TNO shows that the reasonable worst-case exposure level of hands and face (1,300 cm^2) during spray painting is 4.1 mg product/cm^2/d (Marquart et al., 1999; Lansink et al., 1998) calculated for a full 8-hour work shift.

Using these values, the maximum concentration on the skin becomes:
4.1 mg/cm^2/d · 10 % · 0.5 h/event · 1/(8 h/d) = 0.03 mg/cm^2/event.

The potential dermal exposure becomes:
0.03 mg/cm^2/event · 1,300 cm^2 · 1/(70 kg bw) = 0.5 mg/kg bw/event.

The above estimated exposures give a total systemic dose of:
0.7 + 0.5 mg/kg bw/event = 1.2 mg/kg bw/event.

Exposure for the evaluation of chronic effects

The predicted exposure concentration is as estimated above 83 mg/m^3.

The inhalation uptake is 0.7 mg/kg bw/event which for the suggested use pattern of 1 event per week corresponds to an uptake of:

0.7 mg/kg bw/event · 1/(7 days/event) = 0.1 mg/kg bw/d.

The potential dermal uptake for the suggested use pattern of 1 event per week is estimated to be 0.5 mg/kg bw/event, which for the suggested use pattern of 1 event per week corresponds to an average dermal uptake of: 0.5 mg/kg bw/event · 1/(7 days/event) = 0.08 mg/kg bw/d.

The above estimated exposure gives a total systemic dose of:
0.1 + 0.08 mg/kg bw/d = 0.18 mg/kg bw/d.

Scenario U2

U2 is a bicycle maintenance scenario, using 1 g of polish per event.

Exposure for the evaluation of acute effects

Using EUSES (ver. 1.0) the air concentration is estimated to be 5 mg/m^3, corresponding to an inhalation uptake of:

5 mg/m^3 · 20 l/min · 30 min/event · 1/(1,000 l/m^3) · 1/(70 kg bw) = 0.04 mg/kg bw/event.

Assuming that 1 cm^3 of product is in contact with the skin during one event, potential dermal uptake is estimated (EUSES ver. 1.0) to be 1.4 mg/kg bw/event, corresponding to a maximum concentration on the skin of 0.1 mg/cm^2.

The above estimated exposures give a total systemic dose of:
0.04 + 1.4 mg/kg bw/event = 1.4 mg/kg bw/event.

Exposure for the evaluation of chronic effects

The air concentration was estimated to be 5 mg/m^3 and the inhalation uptake to be 0.04 mg/kg bw/event. For the suggested use pattern of 1 event per week this corresponds to an uptake of: 0.04 mg/kg bw/event · 1/(7 days/event) = 0.005 mg/kg bw/d.

Assuming that 1 cm^3 of product is in contact with the skin during one event, potential dermal uptake for the suggested use pattern of 1 event per week is estimated (EUSES ver. 1.0) to be 0.2 mg/kg bw/d.

The above estimated exposures gives a total systemic dose of:
0.005 + 0.2 mg/kg bw/d = 0.2 mg/kg bw/d.

Scenario U3

U3 is a car maintenance scenario, using 4 g of polish per event.

Exposure for the evaluation of acute effects

Using EUSES (ver. 1.0) the air concentration is estimated to be 20 mg/m^3, corresponding to an inhalation uptake of:

20 mg/m^3 · 20 l/min · 60 min/event · 1/(1,000 l/m^3) · 1/(70 kg bw) = 0.3 mg/kg bw/event.

Assuming that 2 cm^3 of product is in contact with the skin during one event, potential dermal uptake is estimated (EUSES ver. 1.0) to be 2.9 mg/kg bw/event, corresponding to a maximum concentration on the skin of 0.2 mg/cm^2.

The above estimated exposures give a total systemic dose of:
0.3 + 2.9 mg/kg bw/event = 3.2 mg/kg bw/event.

Exposure for the evaluation of chronic effects

The air concentration was estimated to be 20 mg/m^3 and the inhalation uptake to be 0.3 mg/kg bw/event. For the suggested use pattern of 1 event per 2 weeks this corresponds to an uptake of: 0.3 mg/kg bw/event · 0.5/(7 days/event) = 0.02 mg/kg bw/d.

Assuming that 2 cm^3 of product is contacting the skin during one event, potential dermal uptake for the suggested use pattern of 1 event per 2 weeks is estimated (EUSES ver. 1.0) to be 0.2 mg/kg bw/d.

The above estimated exposures give a total systemic dose of:
0.02 + 0.2 mg/kg bw/d = 0.2 mg/kg bw/d.

Conclusion on consumer exposure

No data are available on consumer exposure. Consumer exposure cannot however, be fully excluded. Three scenarios for consumers have therefore been calculated based on the Product Register information on former products.

Table 4.9 Calculated consumer exposure for the evaluation of risk for acute effects

	Type of work	Air mg/m^3	Dermal mg/kg bw/event	Dermal mg/cm^2	Total systemic dose mg/kg bw/event
U1	Spray painting items	83 [1)]	0.5 [3)]	0.03 [3)]	1.2
U2	Polishing a bicycle	5 [2)]	1.4 [2)]	0.1 [2)]	1.4
U3	Polishing a car	20 [2)]	2.9 [2)]	0.2 [2)]	3.2

1) based on de Pater et al. (1999)
2) EUSES (1997)
3) based on Marquart et al. (1999) and Lansink et al. (1998)

Table 4.10 Calculated consumer exposure for the evaluation of risk for chronic effects

	Type of work	Air mg/m^3	Inhalation mg/kg/d	Dermal mg/kg bw/day	Total systemic dose mg/kg bw/day
U1	Spray painting items	83 [1)]	0.1 [1)]	0.08 [3)]	0.18
U2	Polishing a bicycle	5 [2)]	0.005 [2)]	0.2 [2)]	0.2
U3	Polishing a car	20 [2)]	0.02 [2)]	0.2 [2)]	0.2

1) based on de Pater et al. (1999)
2) EUSES (1997)
3) based on Marquart et al. (1999) and Lansink et al. (1998)

4.1.1.4 Humans exposed via the environment

The human intake from indirect exposure in local and regional scenarios is presented in **Table 4.11**. The estimations were performed according to EUSES (ver. 1.0).

The values for the local scenario are shown as examples below from three different release scenarios.

The first scenario shown is where 1,2,4-TCB is used as an industrial intermediate in the processing phase (scenario D1). This scenario is chosen because this is the scenario which gives the highest estimated total daily intake for humans for a local scenario. It is also an example of a scenario where 1,2,4-TCB occurs largely in root crops. The scenario includes sludge application to agricultural soil. According to the main manufacturer, the sludge is incinerated or kept at controlled landfills and thus the actual intake would be expected to be significantly lower.

The second and third scenario shown is where 1,2,4-TCB is used in scenario D3 (others) and D4 (dye carrier). These scenarios give a somewhat lower estimated total daily intake for humans than scenario D1. They have been chosen because these are examples of scenarios where 1,2,4-TCB also occurs in fish.

Table 4.11 Estimated human intake of 1,2,4-TCB from local and regional scenarios of EUSES.

Route	Local (mg/kg bw/d)			Regional (mg/kg bw/d)
	Industrial Intermediate (processing) (Scenario D1)	Others (Scenario D3)	Dye carrier (Scenario D4)	
Drinking water	$3.49 \cdot 10^{-3}$	$6.72 \cdot 10^{-4}$	$1.21 \cdot 10^{-3}$	$1.01 \cdot 10^{-7}$
Fish	$3.93 \cdot 10^{-5}$	$6.82 \cdot 10^{-3}$	$6.15 \cdot 10^{-3}$	$3.12 \cdot 10^{-5}$
Leaf crops	$5.37 \cdot 10^{-7}$	$1.42 \cdot 10^{-6}$	$9.00 \cdot 10^{-7}$	$9.55 \cdot 10^{-9}$
Root crops	0.068	0.0131	0.0236	$1.97 \cdot 10^{-6}$
Meat	$8.60 \cdot 10^{-6}$	$1.67 \cdot 10^{-6}$	$2.99 \cdot 10^{-6}$	$4.11 \cdot 10^{-10}$
Milk	$5.07 \cdot 10^{-6}$	$9.86 \cdot 10^{-7}$	$1.77 \cdot 10^{-6}$	$2.42 \cdot 10^{-10}$
Air	$8.37 \cdot 10^{-7}$	$1.63 \cdot 10^{-5}$	$9.04 \cdot 10^{-6}$	$1.17 \cdot 10^{-7}$
Total intake	0.0715	0.0206	0.031	$3.34 \cdot 10^{-5}$

The estimates show that the most important human intake routes are via root crops, fish and drinking water. None of the other potential sources of exposure exceed 1% of the total exposure for the particular scenario, and can be considered as negligible. In the scenarios, the main exposure is from consumption of root crops (>50%).

According to the EUSES estimations (cf. Appendix on EUSES estimations), the values for the total human intake of 1,2,4-TCB for the local scenario range from 0.00118 mg/kg bw/d to 0.0715 mg/kg bw/d depending on the release/use category. All the different local scenarios will be considered further in the human risk characterisation (cf. **Table 4.36**).

In a study of 108 human autopsy fat samples collected in 1985 in Canada, 1,2,4-TCB was found in a mean concentration of 103 ng/g wet tissue of the positive samples. The maximum concentration was 358 ng/g wet tissue. In samples from Eastern Canada, 1,2,4-TCB was below the limit of detection, whereas in Quebec, Ontario and Western Canada the levels were 112, 93,

and 110 ng/g wet tissue, respectively. The concentration of 1,2,4-TCB seemed to be independent of sex and age (Mes et al., 1990). Other studies have also been carried out earlier to measure organochlorine residues in human adipose tissue autopsy samples in Canada (Williams et al., 1984).

In a study of human breast milk samples also collected in Canada, 1,2,4-TCB was found in samples at concentrations from below the minimum detectable limit (4 μg/kg) to 17.4 μg/kg (Mes et al., 1993). Other earlier studies have also examined the levels of organochlorine residues in human breast milk in Canada (Mes et al., 1986; Davies and Mes, 1987). WHO (1996) quotes a level of 1 μg 1,2,4-TCB/kg (Jan, 1983a).

1,2,4-TCB has also been measured in Slovenia in fish (Jan and Malneršic, 1980) and in market meat and milk (Jan, 1983b).

The concentrations found in meat (beef) are in the order of $1 \cdot 10^{-3}$ mg/kg. This can be compared with the values calculated in EUSES for meat in the regional scenario of $1 \cdot 10^{-7}$ mg/kg and in the local scenarios ranging from $2 \cdot 10^{-3}$ to $3 \cdot 10^{-5}$ mg/kg.

The concentrations found in milk (cow) are in the order of $0.7 \cdot 10^{-3}$ mg/kg. This can be compared with the values calculated in EUSES for milk in the regional scenario of $3 \cdot 10^{-8}$ mg/kg and in the local scenarios ranging from 0-$3.6 \cdot 10^{-4}$ mg/kg.

Concentrations found in marine fish in monitoring studies one to two decades ago were in the order of 3-300 μg/kg (see Section 3.1.5.). This can be compared with the values calculated for fish in the regional scenario of 20 μg/kg and in the local scenarios ranging from 20 μg/kg to 2 mg/kg wet fish (cf. Section 3.1.7).

The concentrations measured above in meat correspond roughly to the values calculated in EUSES for a local scenario, and are well above those calculated for a regional scenario. The concentrations measured in fish are lower than those calculated for a local scenario. However, these figures are not easy to interpret as there is no suggestion by the authors that these measured levels are necessarily associated with the production or use of 1,2,4-TCB, but may rather be the result of indirect exposure following the use of lindane, combustion, or other sources, or by metabolism of other chlorinated compounds (see Section 4.1.2.1). 1,2,4-TCB is found in hen eggs after intramuscular administration to the hen. Between 2.5 and 6.1% of the administered dose was transferred to the yolk. Little was found in the albumin, and the transfer occurred without chemical change (Kazama et al., 1971).

TCB has been detected in dried vegetables grown under controlled conditions with no pesticide application, indicating that the origin of TCB was probably environmental contamination (Lovegren et al., 1979, cited by WHO, 1991). In a Dutch compilation of chemicals occurring in food 1,2,4,-TCB was only reported in vinegar, Swiss cheese and green tea (3.1 ppm).

1,2,4-TCB has also been measured in a variety of vegetables collected from supermarkets in the UK (Wang and Jones, 1994c). Concentrations were measured in root crops (carrots, potatoes, onions) and other vegetables (cabbages, cauliflowers, lettuce, beans, peas and tomatoes). Concentration of 1,2,4-TCB in potato peel was 0.0320 μg/kg fresh weight. No figures are given for potato core, onions or carrots. For other vegetables, concentrations ranged from 0.007 (lettuce) to 0.0469 (cauliflower flower) μg/kg fresh weight. The corresponding regional values for root crops and plant leaves are 0.4 and $5 \cdot 10^{-4}$ μg/kg. Calculated local concentrations for root crops range from 0.2 to 12.4 mg/kg; for plant leaves from 0.03-2 μg/kg. The measured concentrations for the only root crop measured (potato peel) were ten times lower than the predicted regional concentrations.

The most recent data on 1,2,4-TCB concentrations in foods are in a report from the UK (UK MAFF, 1998). This study, undertaken in 1995, measured concentrations of 11 chlorobenzenes in a wide range of food products. 1,2,4-TCB was one of the five of the 11 chlorobenzenes studied which was detected at concentrations above the analytical detection limit. The analytical detection limit for each chlorobenzene was 2 μg/kg fat for samples with a fat content of less than 10 percent, and a limit of 10 μg/kg fat for samples with a fat content of more than 10 percent.

Clorobenzenes were detected in animal and milk products, fish, vegetables and cereal products. 1,2,4-TCB however was found in only some of these products. These were pork carcass (40 μg/kg fat basis), canned pork (30 μg/kg fat basis), milk (2 μg/kg fresh weight), butter (10 μg/kg fat basis), cream (10-50 μg/kg fat basis) and cheese (50 μg/kg fat basis). The concentrations of 1,2,4-TCB found in meat and milk are comparable to the figures reported above for Slovenia (Jan, 1983b).

No 1,2,4-TCB was found at concentrations above the detection limit in marine fish, vegetables, or cereals. It is noted that this recent monitoring data of marine fish do not confirm the concentration levels of older monitoring studies on fish mentioned above. Furthermore the absence of detectable concentrations of 1,2,4-TCB in fish, vegetables and cereals is significant in view of the EUSES calculations which suggest that concentrations of 1,2,4-TCB would be higher in these types of food compared to those where 1,2,4-TCB is actually found.

Drinking water

Drinking water is produced from surface water or groundwater. Complete removal of suspended particles from surface water and groundwater is assumed. The effects of the treatment processes used for purification of groundwater, which are generally not intended for purification of groundwater is neglected. Surface water treatment can be estimated according to EUSES. The maximum concentration in drinking water from each of the two methods ($C_{groundwater}$ or $C_{surface\ water}$ · purification factor) is used as $C_{drinking\ water}$.

The concentration in groundwater is calculated for indirect human exposure of 1,2,4-TCB through drinking water. The concentration in pore water of agricultural soil (180 d) is taken as an indication of potential groundwater levels. It should be noted that this is a worst-case assumption, neglecting transformation and dilution in deeper soil layers.

Table 4.12 Calculated concentrations of 1,2,4-TCB in drinking water (EUSES)

Scenario	Concentration (μg/l)
Regional	0.0035
Production (Site A)	1.9
Production (Site B)	1.9
Industrial Intermediate (scenario D1): processing *	122
Process solvent (scenario D2): formulation *	63.4
Minor uses (scenario D3): processing	23.5
Dye carrier (scenario D4): processing	42.4

* The concentration in drinking water is based on estimated concentration in groundwater. The concentration in the generic scenarios D1 and D2 includes sludge application, which according to manufacturers does not take place, cf. Section 3.1.2

Data from the US samples (US EPA, 1977, quoted in US EPA, 1981) were collected between March and April 1976. 1,2,4-TCB was found in 1/112 sample at a concentration of 10 μg/l. The maximum value for all TCB isomers found in a groundwater study from the Netherlands was 1.2 μg/l (Zoeteman et al., 1980, quoted in WHO, 1996). In 1998, 75 drinking water samples have been analysed in two French departments, Alpes de Haute-Provence and Alpes Maritimes. In all these samples, the concentration of 1,2,4-TCB was below the detection limit of 1 μg/l (Bintein, 1999). No information is available for other EU countries.

WHO (1993) reports an odour threshold for 5-30 μg 1,2,4-TCB/l and a taste threshold of 30 μg 1,2,4-TCB/l. These figures can be compared with the calculated concentrations shown in **Table 4.12**. The calculated local concentrations for scenarios D1 to D4 all exceed the taste and odour thresholds reported by WHO (1993).

Conclusion

These studies illustrate that indirect human exposure to 1,2,4-TCB may occur. The presence of 1,2,4-TCB in the food chain may however in many cases be due to other sources of environmental release of 1,2,4-TCB than the result of a specific industrial use of this particular substance.

4.1.1.5 Combined exposure

No estimates of combined exposure have been made. Many of the examples of workplace or consumer exposure are limited either to relatively few exposed individuals or taken as examples of clearly "worst-case" situations. Combination of these examples is not considered to add any additional information to the risk assessment.

4.1.2 Effects assessment: Hazard identification and Dose (concentration) - response (effect) assessment

A number of reviews of the health effects of the substance have been prepared. These include reviews by IPCS (WHO, 1991), BUA, (1987), US EPA (1981,1987, 1992) and the Swedish Criteria Group for Occupational Standards (1993).

4.1.2.1 Toxicokinetics, metabolism and distribution

1,2,4-TCB is well absorbed by the oral route as the following studies show.

In groups of five rats given single doses of ^{14}C-labelled 1,2,4-TCB (10 mg/kg bw) by gavage, radioactivity was measured at 0.5, 1, 2 and 4 hours, 1, 2, 7, 14, 28 and 56 days. Radioactivity was found in the blood and tissues after 0.5 hours (the first sampling time) and peaked around 2-4 hours after dosing (Chu et al., 1987). Radioactivity was measured in the different organs sampled, and reported as mean ppm equivalent of 1,2,4-TCB. 0.5 hours after dosing, radioactivity was found in (in decreasing order of concentration) the gastro-intestinal tract (173 ppm), bladder (12.9 ppm), kidney (9.7 ppm), adrenal (9.6 ppm), fat (8.9 ppm), liver (7.1 ppm), pancreas (5.7 ppm), and lung (4.4 ppm) with roughly equal levels of radioactivity (4-1 ppm) being found in the other organs. The testes showed the lowest concentration of radioactivity (0.6 ppm). At later sampling points the relative concentrations of radioactivity

decreased in the gastro-intestinal tract and increased in skin, liver, kidney, adrenal, fat, and bladder. In general, the levels of radioactivity in the body peaked around 4 h, and then gradually decreased. The excretion of 1,2,4-TCB from the body was biphasic with half-lives of 12 and 93 hours, respectively.

No specific studies of the ^{14}C excretion following administration of ^{14}C-1,2,4-TCB was made, although the excretion was measured for the two other isomers (1,2,3- and 1,3,5-TCB) studied at the same time. For these two isomers, 89-95% of the administered radioactivity was excreted in the urine and faeces in 48 hours. It may be deduced from the data on kidney and bladder radioactivity that 1,2,4-TCB or its metabolites are excreted via urine, though some may be excreted via faeces.

In a tissue distribution study (Kato et al., 1993) groups of rats were given 1.36 mmol 1,2,4-TCB/kg intraperitoneally and animals were killed at intervals up to 120 hours after dosing. The estimated half-lives of 1,2,4-TCB in blood, liver and kidney were 5.8, 5.2, and 6.2 hours, respectively. The 1,2,4-TCB levels were much higher in adipose tissue than in blood and other tissues.

In another study from Tanaka et al. (1986) groups of five rats were dosed with ^{14}C-labelled 1,2,4-TCB with by gavage at 50 mg/kg in order to study the distribution, metabolism and excretion of the substance. In the analysis of radioactivity in organs a fairly even distribution was found except for higher amounts of radioactivity in adipose tissue throughout the seven-day observation period. During the seven days, excretion of radioactivity in urine and faeces accounted for 66% and 17%, respectively. In expired air, 2.1% of the radioactivity was found as 1,2,4-TCB and dehalogenated derivatives, no $^{14}CO_2$ was found. Nearly all (80%) was excreted within the first three days.

In a separate experiment with two rats a biliary excretion of 45% was found. With an excretion of 20% of the radioactivity in faeces, this suggests the existence of an enterohepatic circulation for 1,2,4-TCB. The major metabolites found in faeces and urine were conjugated and free 2,3,5-trichlorophenol and 2,4,5-trichlorophenol. In faeces some unchanged 1,2,4-TCB was found.

Smith et al. (1985) studied the distribution of 1,2,4-TCB in rats and monkeys by gavage and by intravenous administration.

Seven groups of four male Charles River rats were dosed with 10 mg 1,2,4-TCB/kg by gavage, the 1,2,4-TCB was carbon-14 labelled. At the periods of 3, 6, 12, 24, 48, 72, and 96 hours after dosing animals from one group were killed. Urine and faeces were collected at 24 hours intervals or at sacrifice. Whole blood, plasma, liver, spleen, kidneys, lungs, heart, testes, brain, fat, muscle, and skin were assayed for radiolabel, and in addition the gastrointestinal tract was divided into the sections: stomach, small intestine, caecum, and large intestine. Each section together with its contents was analysed for total radiolabel.

About 80-90% of the radiolabel was recovered in urine and 10-20% was recovered in faeces. The excretion of radiolabel was almost complete (96%) by 24 hours and complete (101%) by 48 hours. The $T_{½}$ of 1,2,4-TCB in rats range from four to six hours in the first phase. This phase is followed by a much longer second phase (no $T_{½}$ estimated).

The highest tissue concentrations were observed at three hours. By 24 hours most tissues except the gastrointestinal tract contained less than 2µg ^{14}C/g. In the stomach there was very little ^{14}C but about 3.5% in the rest of the gastrointestinal tract, and only 1% in all other tissues.

Smith et al. (1985) also dosed seven groups of four male Charles River rats with 10 mg 1,2,4-TCB/kg by intravenous injection to the femoral vein, the 1,2,4-TCB was carbon-14

labelled. At the periods of 3, 6, 12, 24, 48, 72, and 96 hours after dosing animals from one group were killed. Urine and faeces were collected at 24 hours intervals or at sacrifice. Whole blood, plasma, liver, spleen, kidneys, lungs, heart, testes, brain, fat, muscle, and skin were assayed for radiolabel, and in addition the gastrointestinal tract was divided into the sections: stomach, small intestine, caecum, and large intestine; each section together with its contents was analysed for total radiolabel.

Excretion of radiolabel was primary via the urine (83 -86%), with about 12% being found in faeces. The excretion was 90% complete by 24 hours and virtually 100% complete by 48 hours. Maximum tissue levels of radiolabel occurred in blood, plasma, liver, and kidney after six hours, while in the other tissues the peak occurred at three hours or the three and six hour values were equal. Concentrations of radioactivity were higher in fat than in other tissues analysed. After 24 hours the concentration of radioactivity was higher than 1 µg/g in fat, kidney, and liver. Levels of ^{14}C were most persistent in the fat (0.8 µg/g at 96 hours) but at 96 hours it was still appreciable in kidney and liver (approximately 0.5 µg/g). In the small intestine, caecum, and large intestine appreciable amounts of radioactivity occurred and peaked at 12 hours post dosing. This suggests the existence of an enterohepatic circulation of 1,2,4-TCB or its metabolites.

Groups of two female rhesus monkeys received a single oral or intravenous dose of 10 mg ^{14}C-1,2,4-TCB. Blood samples were taken prior to dosing and at 1, 2, 4, 6, 8, 12, 24, 48, 72, and 96 hours post-treatment. Urine samples were collected at 6, 12, 24, 48, 72, and 96 hours post-treatment; faeces were collected at 24-hour intervals for seven days (Smith et al., 1985).

When ^{14}C-1,2,4-TCB was administered intravenously there was a dramatic drop in the ^{14}C content of whole blood from an estimated zero time level of about 112 µg/ml to a level of 2.0-2.9 µg/ml one hour post-treatment. From this time on there was a slow decline over the next four days to levels of 0.2 µg/ml. The plasma concentrations of ^{14}C-1,2,4-TCB were higher than the respective whole blood concentrations ranging from 3.1 to 4.9 µg/ml at one hour and declining bi-phasically to 0.24 µg/ml at 96 hours.

In one orally dosed monkey the blood level peaked at one hour (3.9 µg/ml in blood, 4.6 µg/ml in plasma), in the other the peak was at two hours post-treatment (2.3 µg/ml in blood, 3.6 µg/ml in plasma). During the remaining of the period of observation, there were no significant differences in the blood and plasma levels of the intravenous and orally treated animals.

Urinary excretion following intravenous administration accounted for about 38% of the dose in four days; 22% was excreted during the first 24 hours. In the monkeys receiving 1,2,4-TCB orally, urinary excretion accounted for a significantly greater amount of the dose, 36 to 40% was recovered during the first 24 hours and 56 to 73% of the dose in four days.

The difference in the amount of substance being excreted after oral and intravenous dosing, can be explained due to the fact that 1,2,4-TCB is very lipid soluble and is rapidly deposited in fat depots following intravenous administration. When the compound is administered orally, it is transported to the liver where it can be stored and metabolised before entering the systemic circulation.

Faecal excretion of ^{14}C-1,2,4-TCB by rhesus monkeys following either oral or intravenous treatment is insignificant, accounting for less that 4% of the total dose. This suggests that the compound is readily and completely absorbed from the gastrointestinal tract and quite readily metabolised to products easily excreted in the urine.

In order to elucidate the possible enterohepatic circulation of 1,2,4-TCB metabolites Bakke et al. (1992) dosed 23 mg ^{14}C-1,2,4-TCB/kg orally to both intact and bile-duct cannulated rats. It was found that in normal rats, 70% of the dose was excreted via urine and 9% via faeces. In the bile duct cannulated rats 61% of the dose was excreted via the bile, 21% via urine and 2% via faeces. These data suggest that most of the urinary metabolites excreted by normal rats had undergone enterohepatic circulation, in this case 85% of the dose. Using various proposed metabolites of 1,2,4-TCB the authors were able to justify the occurrence of an arene epoxide in the metabolism of 1,2,4-TCB and confirmed the pattern of metabolites found by Lingg et al. (1982).

From subchronic and chronic exposures via inhalation, it can be deduced that 1,2,4-TCB can be taken up via the airways (Coate et al., 1977; Kociba et al., 1981; Watanabe et al., 1978) but no precise data exist on the uptake after single inhalation exposures.

The dermal absorption potential of 1,2,4-TCB defined by flux predicted from physico-chemical properties has been calculated (Fiserova-Bergarova et al., 1990) in an attempt to develop criteria for skin notation. The substance has also been assessed by the Commission Scientific Committee on Occupational Exposure Limits (SCOEL, 1993) and skin notation has been recommended. No specific information on dermal uptake of 1,2,4-TCB was found, however, data from both acute and chronic dermal application suggest that 1,2,4-TCB can be taken up via the skin.

The metabolism of 1,2,4-TCB differs from species to species (see **Figure 4.1**).

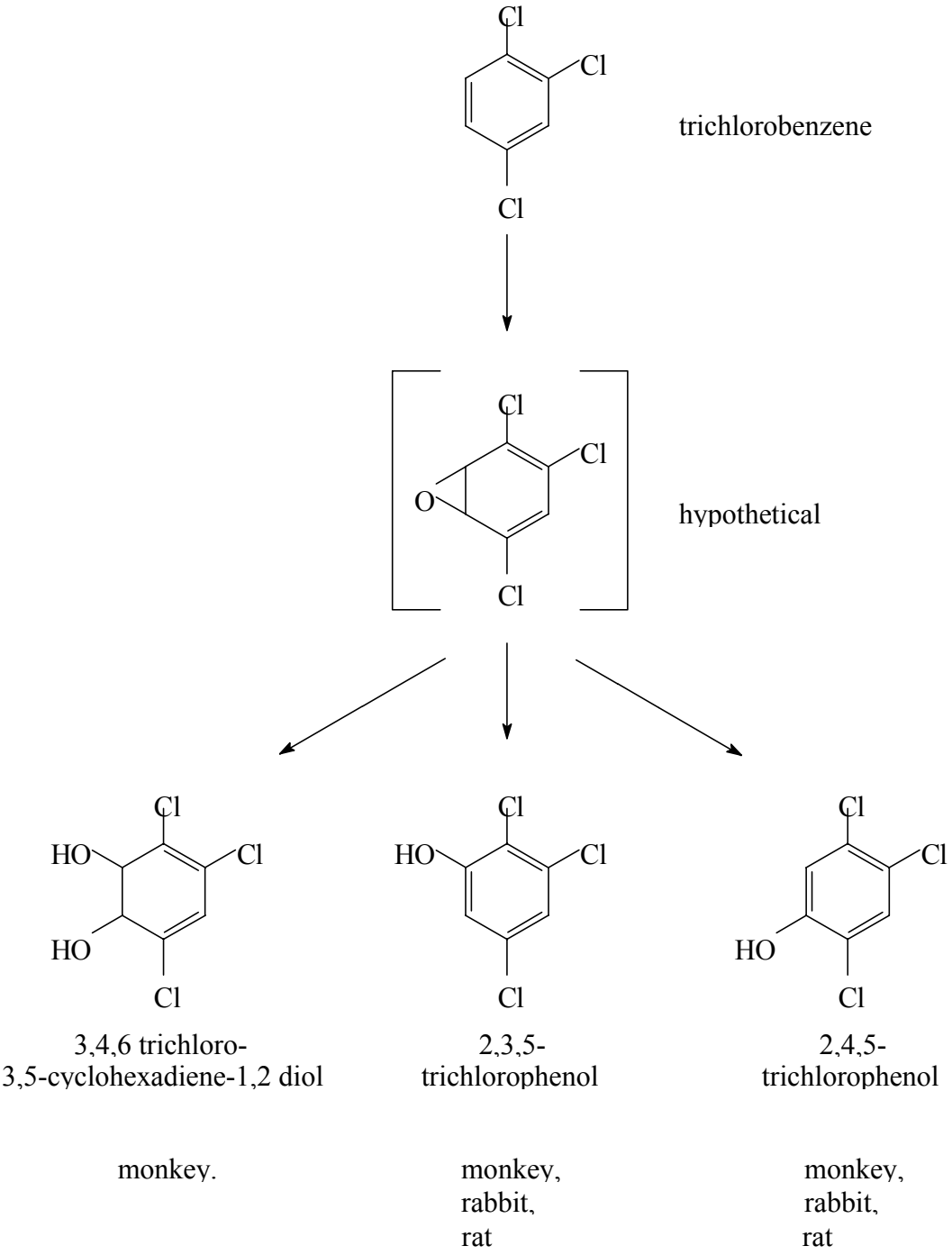


Figure 4.1 Metabolism of 1,2,4-TCB in laboratory animals

As shown by the following studies, the main difference between rat and monkey in the metabolism of 1,2,4-TCB is in the sequence of steps following initial formation of an arene oxide. In the rat, conjugation with glutathione occurs, whereas in the monkey hydrolysis of the arene oxide occurs and the resulting dihydrodiol is excreted as a glucuronide. In the rabbit two major phenols, small amounts of trichlorocatechol and of two mercapturic acids are excreted.

Radiolabelled 1,2,4-TCB was administered orally (10 mg/kg) and intravenously (10 mg/kg) to rats and rhesus monkeys. By 24 hours, the rat had excreted 95% (84% in urine, 11% in faeces) after oral administration and 85% (78% in urine, 7% in faeces) after intravenous administration. After 24 hours, monkeys had only excreted about 40% in urine and less than 1% in faeces after oral administration, and 22% in urine and less than 1% in faeces after iv administration. The HPLC pattern of radiolabelled urinary metabolites was strikingly different between the two species with three equally important metabolites in the monkey and one major out of four metabolites in the rat. In the monkey the metabolites were glucuronides of 3,4,6-trichloro-3,5-cyclohexadiene-1,2-diol or of 2,3,5- and 2,4,5-trichlorophenol. In the rat 60% of the metabolites were a mixture of 2,4,5- and 2,3,5-isomers of N-acetyl-S-(trichlorophenyl)-L-cystein, and free 2,4,5- and 2,3,5-isomers of trichlorothiophenyl amounted to 33% of the urinary metabolites after oral dosing (Lingg et al., 1982).

During and after seven days of dosing to rats with 181 mg (1 mmol) 1,2,4-TCB/kg bw/d containing a total of 6,660,000 dpm radioactivity, urinary and faecal radioactivity was followed until day 21 post dosing. Urine contained throughout the observation period the highest amount of radioactivity. In urine the peak of activity during dosing was 1,000,000 dpm whereas faeces contained 50,000 dpm. In faeces the radioactivity declined to background levels on day 15 post dosing, whereas urine on day 21 still contained about 1,100 dpm (Smith and Carlson, 1980). In the same study, abdominal fat retained radioactivity at least until day 16 post dosing (2,033 dpm/g day 1 and 408 dpm/g day 16).

Jondorf et al. (1955) fed 1,2,4-TCB at 0.5 g/kg to three rabbits and analysed the urine for metabolites in the form of glucuronides, etheral sulphate, and mercapturic acid conjugates plus free trichlorophenols. It was found that glucuronides of trichlorophenols amounted to 18-33% of the dose and etheral sulphates amounted to 10-12% of the dose. In total 33-51% of the dose was excreted in the form of trichlorophenols or conjugates of this substance.

Similar results were obtained qualitatively by Kohli et al. (1976) in the rabbit and it was suggested that the formation of trichlorobenzene oxides could account for the metabolites found.

Formation of 1,2,4-TCB as a metabolite of other chlorinated compounds

1,2,4-TCB is formed *in vivo* by metabolism of a number of other chlorinated compounds. This is mentioned briefly here, as this route of formation may be relevant for the 1,2,4-TCB found in animals and in humans (see Section 4.1.1.4)

Most reports relate to hexachlorocyclohexane or pentachlorocyclohexane. 1,2,4-TCB has been seen in the adipose tissue of pigs treated with γ-HCH after either oral administration or by spraying (Mottram et al., 1983). 1,2,4-TCB has been seen in the urine of rats treated with α-HCH in the diet (Macholz et al., 1982). 1,2,4-TCB is formed from lindane and other related compounds *in vitro* after incubation with liver enzyme preparations or liver microsomes (Foster and Saha, 1978; Kurihara et al., 1979a, 1979b; Tanaka et al., 1979; Fitzloff and Pan, 1984,).

Conclusions for toxicokinetics

1,2,4-TCB is taken up in the body after oral, dermal, and inhalation exposure. Quantitative data on the absorption only exist for the oral route, where it seems that the absorption is high (70-90%). No quantitative estimate of absorption following inhalation or dermal administration has been made.

Due to the high excretion of 1,2,4-TCB via the bile and the low excretion via faeces an enterohepatic circulation of 1,2,4-TCB exists.

The metabolism of 1,2,4-TCB differs between species (see **Figure 4.1**), as can be seen from the profiles of the metabolites excreted in the urine from rat, monkey and rabbit. The first common step is supposed to be the formation of a probable trichlorobenzene epoxide. However this intermediate has never been observed experimentally. The benzene metabolism in humans also involves the formation of an epoxide (estimated half-life in rat blood: 8-10 minutes (Lindstrøm et al., 1997). Based on chemical reasoning, an inductive effect of the chlorine in the molecule, the 1,2,4-TCB epoxide may be considered to have a longer $T_{½}$. In rhesus monkeys the 1,2,4-TCB epoxide is converted into a cyclohexadienediol compound and into trichlorophenols, which after conjugation are excreted as glucuronides (glucoronidation). In rats and possibly also rabbits the trichlorobenzene oxide is converted into trichlorophenols, which upon GSH-conjugation are mainly excreted as N-acetyl-S-(trichlorophenyl)-L-cysteine.

After oral administration the major route of excretion is via urine with 84% of the administered dose being excreted within 24 hours in rats and 40% in monkeys. In faeces 11% and 1% are excreted in rats and monkeys, respectively.

1,2,4-TCB is a metabolite of a number of higher chlorinated compounds.

4.1.2.2 Acute toxicity

Acute oral toxicity

The only study according to OECD TG 401 (draft, OECD, 1979), using 98% pure 1,2,4-TCB, gave an LD_{50} of 0.76 ml/kg (1,107 mg/kg) for male rats and 0.70 ml/kg (1,019 mg/kg) for female rats (Korte and Greim, 1981). Detailed test results are not available.

Groups of four rats of each sex weighing between 150 and 250 g were given 98% pure 1,2,4-TCB by gavage. Information regarding doses and vehicle is not given. An LD_{50} of 756 mg 1,2,4-TCB/kg (556-939 mg/kg, 95% confidence limits) was estimated (Brown et al., 1969). The signs of intoxication described in the study were depression of activity at low doses and pre-death extensor convulsions at lethal dose levels.

Groups of 5 rats of each sex with starting weights between 159 g and 173 g were given 1,2,4-TCB by gavage. The LD_{50} was 0.93 g/kg (Bayer, 1982).

Groups of 5 rats of each sex with a mean starting weight of 169 g were given Trichlorbenzol S (containing 83-91% of a mixture of 1,2,4-TCB and 1,2,3-TCB) by gavage. The LD_{50} was 0.98 ml/kg (1,421 mg/kg) (Bayer, 1980).

A number of other values for the oral LD_{50} are available, but for which the available data on numbers of animals, dose, vehicle, symptoms and pathology are limited. These studies are included for the sake of completeness.

In a range-finding study for a subchronic study Côté et al. (1988) have given an oral LD_{50} for rats of 0.88 g/kg. Dow Chemical (1958) found an LD_{50} (1/2 animals) of 1,000 mg/kg. In a study of the comparative toxicity of 1,2,4-TCB and *o*-dichlorobenzene, Du Pont de Nemours (1982) found an "Approximate Lethal dose" (the lowest dose which killed) of 2,250 mg 1,2,4-TCB/kg. The report concludes that the toxicity of the two substances is roughly equivalent.

LD_{50} values are also available for other species.

Groups of four mice of each sex weighing between 18 and 23 g were given 98% pure 1,2,4-TCB by gavage. An LD_{50} of 766 mg 1,2,4-TCB/kg (601-979 mg/kg, 95% confidence limits) was estimated (Brown et al., 1969).

The LD_{50} for guinea pigs is between 1,600 mg/kg (LD_0) and 2,000 mg/kg (LD_{100}) (Dow Chemical, 1938).

Groups of three female Wistar rats were given a single oral dose of 0, 125, 250, 500, 750, 1,000, or 1,500 mg 1,2,4-TCB/kg. Body weight, liver weight and various biochemical parameters were assessed in liver extracts 24 hours after dosing. From the dose 250 mg/kg an induction of the drug-metabolising enzymes aniline hydroxylase and amino pyrine demethylase and cytochrome P-450 occurred. The activity of d-ALA synthetase, which is the rate limiting enzyme in the porphyrine biosynthetic pathway, was enhanced at all dose levels (Ariyoshi et al., 1975).

In groups of four rats given a single oral dose of 0 or 500 mg 1,2,4-TCB/kg, the time course of the parameters studied above was assessed with sampling at 3 hr, 6 hr, 12 hr, 24 hr, 48 hr, 5 days, and 15 days. The activities of aniline hydroxylase and cytochrome P-450 were significantly raised from 24 hr to 5 days. The activity of aminopyrine demethylase also raised at 24 hours and was still significantly above controls at 15 days. The activity of d-ALA synthetase decreased in the first 3-6 hours and were above the control value at 24 hr (Ariyoshi et al., 1975).

Acute inhalation toxicity

No data on LC_{50} 4-hour, rats are available.

The only study in rats with a 4-hour exposure time was carried out in 1982 by Du Pont de Nemours (1971a). No fatalities were seen at a single level of 418 ppm (3.1 mg/litre/4 hr).

Kociba et al. (1981) briefly mention two studies. In the first study rats were exposed via inhalation to approx. 330 ppm (2.5 mg/litre) 1,2,4-TCB for 7.5 hours without any symptoms and signs of toxicity at autopsy. In the second study rats were exposed via inhalation to 1,800 ppm (13.6 mg/litre) for 7 hours to the vapours evolved by heating 1,2,4-TCB at 100°C. This resulted in no adverse effects during exposure. Pathological examination of one rat on day 1 post exposure revealed congestion of the lungs and kidneys, and mottled liver. Pathological examination of three rats on day 14 post exposure revealed no gross pathological changes.

ACGIH (1991) quotes Treon (1950) for reporting that the target organs from non-lethal exposures of cats, dogs, rats, rabbits and guinea pigs included the liver, kidney, ganglion cells of the brain, and irritation of mucous membranes.

Acute dermal toxicity

The only study according to OECD TG 402 (draft, OECD 1979), using 98% pure 1,2,4-TCB, gave an LD_{50} of 7.8 ml/kg (11,356 mg/kg) after 14 days in both species of rats (Korte and Greim, 1981). Detailed test results are not available.

Four rats of each sex were exposed for 24 hours with undiluted 98% pure 1,2,4-TCB in an occlusive bandage on the dorso-lumbar region. An LD_{50} of 6,139 mg 1,2,4-TCB/kg (4,299-9,056 mg/kg, 95% confidence limits) was estimated. The signs of intoxication were depression of activity at low doses and pre-death extensor convulsions at lethal dose levels. All deaths occurred within 5 days of exposure. Autopsies of the animals that died and those killed

after the 10-day observation period revealed no pathological lesions attributable to the compound (Brown et al., 1969).

The acute dermal LD_{50} in rabbits for pure 1,2,4-TCB is approximately 5,000 mg/kg (Dow Chemical, 1982) and >5,000 mg/kg for technical 1,2,4-TCB (Dow Chemical, 1980).

A study in ddY mice using 10 animals of each sex per group reporting the acute dermal toxicity gave values of 300 mg/kg (243-369 mg/kg, 95% confidence limits) for males and 305 mg/kg (247-375 mg/kg, 95% confidence limits) for females (Yamamoto et al., 1978). There is no obvious explanation for the very low value for the LD_{50} found in this study.

Other routes of administration

An LD_{50} of 1,223 mg/kg after i.p. administration in rats has been reported (Mohtashamipur et al., 1987). No experimental details are given.

Table 4.13 Data on acute toxicity of 1,2,4-TCB

Application	Species	Effect	Value	Reference
Oral	Rat	LD_{50}	1,107 mg/kg (male) - 1,019 mg/kg (female)	Korte and Greim, 1981
			756 mg/kg	Brown et al. (1969)
			930 mg/kg	Bayer (1982)
			1,421 mg/kg [1)]	Bayer (1980)
			880 g/kg	Côté et al. (1988)
			ca. 1,000 mg/kg	Dow Chemical (1958)
		LD_{LO}	2,250 mg/kg	Du Pont de Nemours (1982)
	Mouse	LD_{50}	766 mg/kg	Brown et al. (1969)
	Guinea pig	LD_0 LD_{100}	1,600 mg/kg 2,000 mg/kg	Dow Chemical (1938)
Inhalation	Rat	LC_0	3.1 mg/litre/4 hr	Du Pont de Nemours (1971a)
			2.5 mg/litre/7½ hr - 13.6 mg/litre/7 hr	Kociba et al. (1981)
Dermal	Rat	LD_{50}	11,356 mg/kg	Korte and Greim, (1981)
			6,139 mg/kg	Brown et al. (1969)
	Rabbit	LD_{50}	5,000 mg/kg	Dow Chemical (1982)
			>5,000 mg/kg [2)]	Dow Chemical (1980)
	Mouse	LD_{50}	300 mg/kg (male) - 305 mg/(kg (female)	Yamamoto et al. (1978)
i.p	Mouse	LD_{50}	1,223 mg/kg	Mohtashamipur et al. (1987)

1) Test performed on trichlorbenzol S
2) Test performed on technical trichlorobenzene

Conclusion for acute toxicity

In the rat, the range of the oral LD_{50} values of pure 1,2,4-TCB is between 756 and 1,107 mg/kg. A value of 750 mg/kg has been used in EUSES for the risk characterisation.

No data on LC_{50} (4 hour) are available. In one study using 7 hours of exposure the LC_{50} of 1,2,4-TCB was more than 1,800 ppm (13.6 mg/litre). An arbitrary value of 20 mg/l (the limit for classification as Xn; R20) has been used in EUSES for the risk characterisation.

The acute dermal toxicity of 1,2,4-TCB is low. The dermal LD_{50} in the rat is more than 6,000 mg/kg. A value of 6,000 mg/kg has been used in EUSES for the risk characterisation.

Most of the studies on acute toxicity have either not been available for detailed study or were performed prior to establishment of OECD test guidelines. However, in view of the uniformity of the LD_{50} values given for each species and route of exposure, the data set is considered valid for the purpose of the risk assessment of 1,2,4-TCB.

1,2,4-TCB is classified as Xn; R22 (harmful by ingestion). For classification, see Section 1.

4.1.2.3 Irritation and corrosivity

Skin irritation/corrosivity

The only study according to OECD TG 404 (draft, OECD 1979), using 98% pure 1,2,4-TCB, resulted in slight irritation. Detailed test results are not available. The substance caused slight redness and slight oedema. Thus no classification is indicated according to the EU classification criteria for effects after a single exposure (Korte and Greim, 1981).

Range finding studies carried out by Dow Chemical (1958) showed that undiluted 1,2,4-TCB is slightly to moderately irritating to intact and abraded skin.

Schreiber (1980a) tested the skin irritating potential of Trichlorbenzol S (containing 83-91% of a mixture of 1,2,4-TCB and 1,2,3-TCB) in New Zealand white rabbits according to US Code of Federal Regulations, Title 16, Section 1500.41 and obtained a score of 7.1 for primary skin irritation. The test substance was applied for 24 hours under an occlusive bandage. The substance was classified as strongly irritating and corrosive according to the criteria used. The use of an occlusive dressing for as long a period as 24 hours makes the interpretation of this study according to the test method B.4 in Annex V of Directive 67/548/EEC difficult.

Tested in guinea pigs by Haskell Laboratories at concentrations of 75% and 95% 1,2,4-TCB produced no to mild irritation on young guinea pig skin but moderate to severe skin irritation on older guinea pigs (Du Pont de Nemours, 1971b).

100% 1,2,4-TCB was tested in mice by Yamamoto et al. (1978) and erythema was observed in 4 out of 8 mice.

Brown et al. (1969) tested 98% pure 1,2,4-TCB for skin irritation in rabbits (4 of each sex) by placing lint patches soaked in 1 ml 1,2,4-TCB on shaven skin for 6 hr/d for 3 days under occlusion. In addition 1,2,4-TCB was tested by direct application to the backs of rabbits (1 male, 1 female) and guinea pigs (5 of each sex) 5 days/week for 3 weeks. Some inflammation of the superficial dermis was present in rabbits exposed daily for 3 weeks. The authors conclude that

skin contact is unlikely to cause dermatitis unless the contact is repetitive or prolonged, in which case degreasing action may be troublesome.

Powers et al. (1975) evaluated the acnegenic potential of 1,2,4-TCB. Three times weekly groups of rabbits received a dose of either solvent control, either positive control or 1,2,4-TCB solutions (5, 25 or 100% in petroleum ether) on the inner surface of the ear for 13 weeks. No evidence of chloracne was seen in the 1,2,4-TCB dosed animals, but irritation ranging from slight to severe was observed. The dermal irritation was probably due to the degreasing effect and directly related to the concentration of test material.

Groups of five male and five female New Zealand rabbits were treated by skin application with either 0 (distilled water control), 30, 150, or 450 mg undiluted 1,2,4-TCB/kg for five days/week for four weeks on an area of approximately 4·4 inches (ca. 100 cm^2) without occlusion (Rao et al., 1982). The 1,2,4-TCB used was a technical grade consisting of 70% 1,2,4-TCB and 30% 1,2,3-TCB. Skin lesions consistent with a degreasing action of 1,2,4-TCB were observed at the sites of application. The size of the affected area increased with increasing doses.

Groups of 75 male and 75 female Slc:ddY mice were painted on the skin with a 0.03 ml drop of 60 or 30% 1,2,4-TCB (18 or 9 mg 1,2,4-TCB) in acetone twice a week for two years. In the control group of 50 male and 50 female mice, painting was carried out with acetone alone (Yamamoto et al., 1982). At the site of painting with 1,2,4-TCB a thickening and keratinization of the epidermis was seen, followed by inflammation. Painting with acetone alone did not cause any dermal lesions.

Eye irritation

The only study according to OECD TG 405 (draft, OECD 1979), using 98% pure 1,2,4-TCB, resulted in a slight irritation. There were no effects on the cornea or iris; test scores for conjunctiva redness and oedema were 1 and 0-2, respectively. Detailed test results are not available.

Following the method described in the US Federal Register (US FDA, 1964) Brown et al. (1969) concluded that 98% pure 1,2,4-TCB was irritating to the eyes of rabbits. The test method is very similar to the test B.5 in Annex V of Directive 67/548/EEC. Pain was apparent, with severe conjunctivitis, chemosis and discharge but without corneal involvement. The lids became very swollen. The conjunctiva was inflamed for at least 48 hours. Irrigation of the eye with water was helpful but only if done immediately following exposure. No details of the study results are available.

Range finding studies carried out by Dow Chemical (1958) showed that undiluted 1,2,4-TCB and a 10% solution in propylene glycol are both slightly irritating to the eye.

Schreiber (1980b) tested the eye irritating potential of Trichlorbenzol S (containing 83-91% of a mixture of 1,2,4-TCB and 1,2,3-TCB) in New Zealand white rabbits according to US Code of Federal Regulations, Title 16, Section 1500.42 and obtained a mean score of 0.7 for primary eye irritation. No effects were seen on the cornea and iris. In the conjunctiva redness was seen in two rabbits after 24 and 48 hours. Other readings were zero at 24, 48 and 72 hours and after 8 days. The authors concluded that the substance was not eye irritating.

The only human data available are anecdotal (see below under lung irritation).

Lung irritation

Industrial data quoted by ACGIH (1991) report minimal eye and throat irritation at 3–5 ppm (23-37 mg/m^3) in certain people (Rowe, 1975).

Local irritation of the lungs and functional changes in respiration e.g. dyspnea was noted in animals later dying from inhalation exposure in an unpublished study of acute and subacute inhalation toxicity (Treon, 1950, quoted in ACGIH, 1991).

Coate et al. (1977) exposed groups of 9 male cynomolgus monkeys 0, 25, 50, or 100 ppm 99.1% pure 1,2,4-TCB for 7 hours/day 5 days/week for 26 weeks by inhalation. Pulmonary function was tested at 1, 3, and 6 months, and the values obtained in the exposure groups were comparable to those seen in the controls, and no dose-related changes were observed.

No treatment related irritant effects on the lung were seen in rats, rabbits or dogs by Kociba et al. (1981).

Industrial data quoted by ACGIH (1991) report an odour threshold of approximately 3 ppm in certain people (Rowe, 1975). The odour threshold for this substance has been reported to be as low as 1.4 ppm (Amoore and Hautala, 1983).

Conclusion for corrosivity and irritation

1,2,4-TCB is not corrosive according to the EU classification criteria.

1,2,4-TCB is provisionally classified by several producers as Xi; R38 (IUCLID). Although results following single exposure generally lead only to mild inflammation, there is clear evidence of inflammation after repeated contact. 1,2,4-TCB is classified as Xi; R38. For classification, see Section 1.

Whilst there is some suggestion of respiratory irritation in humans at relatively low levels there is little evidence for this effect. However, the ACGIH TLV limit is based on the irritant properties of the substance. Chronic exposure studies in monkeys show no effects on lung function.

Concerning eye irritation the picture is less clear. In the Korte and Greim (1981) draft OECD guideline study, 1,2,4-TCB was found to be non-irritating to the eye according to the EU criteria. This is supported by the results of the Schreiber (1980) study, although the test substance was not pure 1,2,4-TCB. The study of Brown et al. (1969) shows that 1,2,4-TCB causes moderate to severe eye irritation, but detailed scores are not available to evaluate this study according to the EU criteria. Whilst US and EU test methods are similar and both use the Draize scoring system, the interpretation of the scores is different, and the use of the US criteria will in general lead to a more severe classification. The substance appears to have some irritating effects on the eye, but these effects are not considered to fulfil the criteria for classification as Xi; R36.

4.1.2.4 Sensitisation

Skin sensitisation

A guinea-pig maximisation study according to OECD TG 406 (draft, OECD 1979) using 98% pure 1,2,4-TCB resulted in a positive reaction in ≤10% of the animals. Detailed test results are not available. There is no information on any negative control group, on the results of the pilot

study used to determine whether the doses used caused irritation, or the concentration of 1,2,4-TCB used in the actual study. In general, substances were tested in this study at concentrations of 0.5-10%. According to the criteria used, this incidence of response is considered as weakly sensitising (Korte and Greim, 1981).

In another study (Brown et al., 1969) guinea pigs were exposed subcutaneously and open epicutaneously to 0.1% w/v of 98% pure 1,2,4-TCB in light liquid paraffin to the shorn skin on the back of the guinea pigs on 3 days in each of three successive weeks. The animals then received no treatment for 10 days and a "challenge" dose of the same solution on the right flank and of solvent on the left flank on the eleventh day. Following the "challenge" the animals were examined at 1 hour, 24 hours and 48 hours for signs of sensitisation reaction. The test result was negative. The test was repeated with the same animals and also gave a negative result.

Tested in guinea pigs by Haskell Laboratories by applying 1,2,4-TCB either topically 9 times over a three week period, or by intradermal injection 4 times over the same period, and challenged by dermal application after a two-week rest period, the animals showed no sign of sensitisation (Du Pont de Nemours, 1971b). However (as described above under skin irritation) both treated and control animals showed signs of skin irritation after the challenge.

Conclusion for skin sensitisation

All the studies available suffer from various forms of deficiencies and as a result, the database for this effect is limited. However, these results indicate only a weak sensitisation potential and the classification of 1,2,4-TCB for skin sensitisation is not required according to the EU classification criteria.

In spite of these deficiencies, further testing is not considered necessary.

Respiratory sensitisation

No data are available on respiratory sensitisation.

4.1.2.5 Repeated dose toxicity

There are several studies on repeated dose toxicity of 1,2,4-TCB using the three major routes of dosing.

Oral administration

Groups of five male and five female rats received a diet containing 0, 600, 1,200, 2,400, 4,800, or 9,600 ppm 1,2,4-TCB for 15 days (Bio/dynamics, 1987). Mean substance intake were 57-71, 117-141, 237-277, 466-542, and 853-939 mg/kg bw/d for the 600, 1,200, 2,400, 4,800, and 9,600 ppm groups, respectively.

Physical observations and body weight and food consumption measurements were carried out prior to and during dosing. At sacrifice selected organs were weighed and organ to body weight ratios estimated.

All animals survived throughout the study. Observations during the study included yellow staining of the anogenital area in one high-dose male during week 2, two high-dose females during week 1 and all high-dose females during week 2. In the 9,600 ppm group mean body

weights were significantly lower for both males and females than control animals for weeks 1 and 2.

Males in all treated groups and females in the 2,400, 4,800 and 9,600 ppm groups had statistically significant ($p < 0.01$) increases in liver weights and liver-to-body weight ratios. The liver-to-body weight ratio was also increased ($p < 0.05$) in the 1,200 ppm females. In all treated groups of males the kidney-to-body weights were significantly ($p < 0.01$) higher than control values, although no clear dose-related pattern was apparent. Absolute kidney weights for males in the 1,200, 2,400, and 4,800 ppm groups were also statistically significantly higher than control weights. Mean kidney weight for 9,600 ppm males was comparable to the mean control weight, although based on a significantly low body weight in this group, it would have been expected to be lower than the control mean. In the females, the only difference noted was a low mean kidney weight in the 9,600 ppm females.

The target organs were liver and kidneys. For male rats the LOAEL was 600 ppm 1,2,4-TCB in the diet corresponding to 57-71 mg/kg bw/d. For female rats the LOAEL was 1,200 ppm (117-141 mg/kg bw/d) and the NOAEL was 600 ppm (57-71 mg/kg bw/d).

In a study similar to OECD TG 408 groups of ten male and ten female weanling Sprague Dawley rats were fed diets containing 1, 10, 100 or 1,000 ppm 99% pure 1,2,4-TCB for 13 weeks (Côté et al., 1988).

The dose of 1,2,4-TCB ingested was calculated to be 0.07, 0.78, 7.8, and 82 mg/kg bw/day for males and 0.11, 1.4, 15, and 101 mg/kg bw/day for females.

During the dosing no signs of toxicity were observed. At the terminal sacrifice body weights of male rats were similar in all groups, and relative liver weights, kidney weights and relative kidney weights showed increases which were statistically significant at the high dose level. No specific data for female body and organ weights were given. This might be taken to indicate that no statistically significant effects were observed. The activities of aniline hydroxylase and aminopyrine demethylase of the liver were significantly increased in males at the dose of 1,000 ppm, and the latter enzyme was also increased in females at 1,000 ppm. At the histopathological examination, treatment-related changes were seen in the livers, thyroids, and kidneys but significantly only at the highest dose level. In general the changes were more severe in males than in females.

The livers had marked changes characterised by aggregated basophilia as well as midzonal vacuolation due to fatty infiltration. Histopathological examination of the kidney failed to reveal any abnormal changes, neither did the urinalysis. Changes in the thyroid were characterised by reduction in follicular size, increased epithelial height from flattened cuboidal cells to columnar shape, and reduced colloid density.

The target organs were liver, kidneys, and thyroid. A NOAEL of 100 ppm for both sexes (7.8 mg/kg bw/d for males and 15 mg/kg bw/d for females) can be derived from the study. A LOAEL of 1,000 ppm (82 mg/kg bw/d) for male rats can be derived from this study. For female rats a LOAEL cannot be derived due to the lack of information.

Groups of 10 male and 10 female Fischer F344 rats received 0, 200, 600, or 1,800 ppm 1,2,4-TCB in the diet for three months (Bio/dynamics, 1989). The calculated ranges for the test substance intake in mg/kg bw/day for males is 27-10 (200 ppm), 96-32 (600 ppm) and 242-96 (1,800 ppm) and for females 33-13 (200 ppm), 108-40 (600 ppm) and 276-108 (1,800 ppm). The

study does not specify any guideline or GLP. However, the observations performed very closely resemble those made in an OECD TG 408 study.

Physical observations revealed a greater frequency of lachrymation and chromodacryorrhea in the treated animals but no dose-effect relation could be observed.

No ocular abnormalities or differences in body weight were observed among the groups.

The weekly mean food consumption was significantly higher in the 600 and 1,800 ppm groups during three and five weeks of the study period, respectively.

The clinical laboratory studies revealed a significant decrease in mean erythrocyte count, haemoglobin, and haematocrit values in the 1,800 ppm males at termination of the study. In the 1,800 ppm females a similar trend was seen, though statistical significance was seen for low mean haemoglobin and haematocrit values, only. In 1,800 ppm males the mean platelet count was significantly increased. The blood urea nitrogen (BUN) was elevated in both males and females of the 1,800 ppm group; elevated total protein, albumin and calcium were seen in the 1,800 ppm males; and low serum aspartate aminotransferase values for 600 and 1,800 ppm males were seen. The elevated BUN for both sexes in the high dose group suggests an effect of 1,2,4-TCB on kidney function and was consistent with the microscopic findings in male animals.

At necropsy, mean liver weights and liver/body and liver/brain weights ratios for the 200, 600, and 1,800 ppm male dose groups and for females in the 600 and 1,800 ppm groups were statistically significantly higher than the control values. Dose-related increases in mean kidney weight indices were also evident in treated males with statistically significant differences between control and treated groups limited to an elevated mean kidney/body weight ratio for the 600 ppm males and an elevation in all these indices seen in the 1,800 ppm males. Mean kidney/body weight ratios for the 600 and 1,800 ppm females were also statistically significantly higher than the control values. The mean testes weight for the 1,800 ppm males was statistically significantly higher than the control value.

In pathology, treatment-related changes were evident in kidneys of the 1,800 ppm males, and to a lesser extent of the 600 ppm males. The changes were dilated tubules, granular casts, hyaline droplets, and papillary mineral deposition. There was also an increased incidence or degree of severity of interstitial nephritis and regenerative tubular epithelium. There was an equivocal increase in the degree of tubular mineral deposition in the 1,800 ppm females. In livers centrolobular hepatocyte hypertrophy was present in the 1,800 and to a lesser extent in the 600 ppm males and the 1,800 ppm females. The liver changes were more prominent in male than in female rats.

Based on elevations noted in liver weights and the kidney pathology, the LOAEL and the NOAEL for females were 600 ppm (40 mg/kg bw/day) and 200 ppm (13 mg/kg bw/day) 1,2,4-TCB in the diet, respectively. A LOAEL of 200 ppm (11 mg/kg bw/day) 1,2,4-TCB in the diet can be established for male rats but a NOAEL cannot be derived.

Groups of 50 male and 50 female F-344 rats were given 0, 100, 350 or 1,200 ppm 1,2,4-TCB in the diet for 104 weeks (Moore, 1994b). The study was carried out according to GLP and the US test guideline 40 CFR 798.3300 (similar to OECD TG 451).

The mean consumed dose of 1,2,4-TCB during the 104 weeks was 0, 5.5, 18.9, and 66.7 mg/kg bw/d, respectively in the males; and 0, 6.7, 22.9, and 79.3 mg/kg bw/d, respectively, in the females.

The main target organs affected in this study were the liver and kidney.

Table 4.14 Incidence of specific liver changes in the rat after chronic oral administration of 1,2,4-TCB (Moore, 1994b)

		1,2,4-TCB (ppm)			
		0	100	350	1200
Enlargement of centrilobular hepatocytes	males females	2/50 6/50	1/50 5/50	5/50 5/50	30/50 37/50
Diffuse fatty liver changes	males females	5/50 15/50	3/50 6/50	5/50 21/50	14/50 30/50
Liver focal cystic degeneration	males females	9/50 0/50	3/50 0/50	4/50 0/50	19/50 0/50
Renal papillary mineralisation	males females	34/50 39/50	14/50 18/50	44/50 47/50	49/50 48/50
Renal transitional cell hyperplasia	males females	2/50 0/50	0/50 0/50	2/50 0/50	34/50 0/50

The high-dose (1,200 ppm) dietary concentration produced a significant decrease in survival of the males, and a significant depression of the mean body weight gain for weeks 1 through 24 in males and females. Significantly increased mean absolute and relative liver weights were seen in males and females. Mean absolute and relative kidney weights were increased (not statistically significant) in males and females. The severity of chronic progressive nephropathy was increased in males.

In the 350 ppm groups there was a slight increase in incidence and severity of renal papillary mineralisation and a slight increase in diffuse fatty liver changes in females.

The 100 ppm dietary concentration produced no treatment related effects.

For systemic toxicity, the dietary concentration of 350 ppm, corresponding to a daily dose of 19-23 mg/kg bw/d, can be considered a LOAEL based on the slightly increased incidence of renal papillary mineralisation and the fatty changes in the liver. The dietary concentration of 100 ppm, corresponding to a daily dose of 5.5-6.7 mg/kg bw/d, can be considered a NOAEL for 104 weeks feeding studies in F-344 rats. The conclusions of this study for carcinogenicity are shown in Section 4.1.2.7.

Groups of 10 male and 10 female B6C3F1/CrlBR mice were given 0, 220, 3,850 or 7,700 ppm 1,2,4-TCB (99.48% pure) in the diet for 13 weeks in a guideline study carried out according to GLP (Hiles, 1989).

The problem of evaporation of 1,2,4-TCB from the feed was properly addressed i.e. the practical doses were in general 10% less than the theoretical given above. The calculated ranges for the test substance intake (uncorrected for loss) in mg/kg bw/day for males is 58-76 (220 ppm), 651-1,112 (3,850 ppm) and 1,064-1,341 (7,700 ppm) and for females 80-92 (220 ppm), 933-1,337 (3,850 ppm) and 1,192-1,531 (7,700 ppm).

There were no treatment-related clinical signs of toxicity.

The body weights for males and females fed 220 ppm 1,2,4-TCB tended to be lower throughout the study. A statistically significant lower body weight was observed for males and females fed 7,700 ppm 1,2,4-TCB during weeks 1 and 5 through 13 and weeks 4 through 13, respectively.

Body weights were significantly lower for males fed 3,850 ppm 1,2,4-TCB during weeks 8, 11, and 12 and for males fed 220 ppm during weeks 11 and 12.

The cumulative body weight gain was significantly lower in males fed 220, 3,850, and 7,700 ppm 1,2,4-TCB from week 1 except in the 220 ppm group where significance was attained from week 2. In the females the cumulative body weight gain was significantly lower in the 7,700 ppm group from week 3 to 13, and in the 3,850 ppm group in weeks 4 and 5.

Food consumption was significantly lower in the 7,700 ppm males and females through weeks 1 to 13. In the 3,850 ppm group food consumption was lower for males in weeks 1 through 7 and in females in weeks 1 through 6 and in week 10.

In clinical pathology carried out at sacrifice, treatment-related effects were higher total protein in males given 3,850 and 7,700 ppm and in females given 7,700 ppm; higher albumin and globulin in males and females given 7,700 ppm; higher ALT (alanine aminotransferase) in males given 3,850 and 7,700 ppm and in females given 7,700 ppm; and higher SDH (sorbitol dehydrogenase) in males and females given 3,850 or 7,700 ppm 1,2,4-TCB.

In anatomical pathology the following observations were made: significantly lower absolute brain weights in males and females fed 3,850 or 7,700 ppm; absolute liver weights, liver-to-body weight percentages, and liver-to-brain weight ratios were significantly higher in males and females given 3,850 or 7,700 ppm. These weight differences correlated with microscopic liver changes characterised by hepatocellular cytomegaly with karyomegaly and multinucleation vascular degeneration, and necrosis.

A NOAEL for 1,2,4-TCB in the diet of 220 ppm (80 mg/kg bw/day) theoretical, 195 ppm practical for female B6C3F1/CrlBR mice was found. The LOAEL was 3,850 ppm (ca. 1,000 mg/kg bw/day). For males of the same strain a NOAEL could not be established as effect of dosing (reduction in body weight) was seen at the lower dose level (220 ppm, 62 mg/kg bw/day), which is the LOAEL.

Groups of 50 male and 50 female B6C3F1 mice were given 0, 150, 700, or 3,200 ppm 1,2,4-TCB in the diet for 104 weeks (Moore, 1994a). The study was carried out following GLP and the test guideline 40 CFR 798.3300 (similar to OECD TG 451).

The mean consumed dose of 1,2,4-TCB during the 104 weeks was 0, 20.9, 100,5, and 522 mg/kg bw/d for males and 0, 26.2, 127.2, and 574.9 mg/kg bw/d for females in the 0, 150, 700, and 3,200 ppm groups, respectively.

In the high-dose group there was a decrease in survival from week 52 and onwards. For the 3,200 ppm group males and females survival at the end of the study was significantly decreased when 100% females and 90% males were dead. The mortality rate at 700 ppm was 18 % in males and 16 % in females, at 150 ppm 12% in males and 24 % in females and in the control group 10 % in males and 22 % in females.

Compared to control mean values significantly lower weekly mean body weights were noted in the 3,200 ppm dose group males and females. Conversely, weekly mean body weights were greater (frequently statistically significant) in the 150 and 700 ppm dose group males and females.

Table 4.15 Incidence of specific liver changes in the mouse after chronic oral administration of 1,2,4-TCB (Moore, 1994a)

Results measured at 104 weeks		1,2,4-TCB (ppm)			
		0	150	700	3200
Surviving animals	males females	45/50 39/50	44/49 37/49	41/50 42/50	5/50 0/50
Absolute liver weight in g	males females	1.6±0.6 1.4±0.2	1.8±0.4 1.9±0.4	3.0±1.7 4.0±2.3	7.4±1.8 no data
Relative liver weight	males females	5.0±2.3 5.1±0.5	5.0±1.4 6.0±0.9	9.5±5.5 12±6.8	27±5.7 no data
Enlargement of centrolobular hepatocytes.	males females	0/50 0/50	0/50 0/50	27/50 1/50	20/50 8/50

The main target organ for 1,2,4-TCB in this study is the liver. Evaluation of the results at the end of the study is strongly influenced by the very high mortality in the 3,200 ppm group. Evaluation of organ weight data revealed statistically increased absolute liver weights for the 150 and 700 ppm animals and for the remaining 3,200 ppm males and increased relative liver weight ratio for 150 ppm females, 700 ppm animals, and 3,200 ppm males. The increases in liver weight are confirmed by the histopathology which shows that the centrilobular hepatocytes were enlarged. This is interpreted as being a result of the 1,2,4-TCB treatment.

The tumours seen in this study are described in Section 4.1.2.7 and the effects on testis in Section 4.1.2.8.

For this study, for systemic toxicity it seems appropriate to consider 150 ppm (21-26 mg/kg bw/d) as a LOAEL based on changes in liver weights.

Carlson and Tardiff (1976) dosed groups of six adult male albino rats by gavage with 0, 150, 300 or 600 mg reagent grade 1,2,4-TCB/kg bw/d or 0, 10, 20, and 40 mg reagent grade 1,2,4-TCB/kg bw/d in corn oil for 14 days and the effects of dosing on the liver, some liver enzymes, and hexobarbital sleeping time were studied.

There was a statistically significant decrease in the activity of glucose-6-phosphatase in rats dosed with 300 and 600 mg 1,2,4-TCB/kg bw/d. The hexobarbital sleeping time was only determined in the control and the high dose groups (600 mg 1,2,4-TCB/kg bw/d) and in the high-dose group the sleeping time was significantly decreased. In activities of the various enzymes determined after dosing with 0, 10, 20, and 40 mg 1,2,4-TCB/kg bw/d the activity of cytochrome c reductase, cytochrome P-450, glucuronyltransferase and azoreductase increased with increasing doses of 1,2,4-TCB, as did the EPN detoxification. The relative liver to body weight was also increased at the dose levels used (Carlson and Tardiff, 1976).

From this study a LOAEL of 10 mg 1,2,4-TCB/kg bw/d for 14 days can be established for rats based on effects on the liver. A NOAEL cannot be established.

Carlson and Tardiff (1976) also dosed groups of 12 male rats by gavage with 0, 10, 20 and 40 mg 1,2,4-TCB/kg bw/d orally for 90 days. Half of the rats were given a 30-day recovery period post dosing.

The liver to body weight ratio increased in a dose-related manner, and this increase was still found after 30 days recovery in the high dose group. No differences could be found in haemoglobin concentration and haematocrit values after the 90 days of dosing.

In parameters for xenobiotic metabolism, cytochrome c reductase, cytochrome P-450, EPN detoxification, benzpyrene hydroxylase and azoreductase showed statistically significant dose-related increases and glucuronyltransferase showed a statistically significant dose-related decrease after 90 days. After the 30-day recovery period the liver to body weight ratio was still increased in the 40 mg/kg group and the parameters for xenobiotic metabolism, which showed increases after 90 days, were still increased in the 40 mg/kg group (Carlson and Tardiff, 1976).

From this study a LOAEL of 10 mg 1,2,4-TCB/kg bw/d for 90 days can be established for rats based on effects on the liver. The liver effects seen at this dose were however no longer significant at the end of the 30-day recovery period. A LOAEL of 40 mg 1,2,4-TCB/kg bw/d for 90 days can be established based on effects on the liver that were not reversible at the end of the 30-day recovery period. A NOAEL cannot be established.

Groups of four female rhesus monkeys were given 0, 1, 5, 25, in one study, followed by a second study where 0, 90, 125 or 174 mg 1,2,4-TCB/kg by gavage 7 days/week for three months (Smith et al., 1985). Body weight was determined weekly. Once a month blood samples were taken for clinical chemistry, and the chlorguanide metabolite profile was determined at 30 days intervals (this is a method to determine the relative ratio between the P-448 and P-450 systems).

In the 125 mg/kg animals serum LDH and GOT were clearly lowered at two and three months. In the 1, 5, and 25 mg/kg animals no effects of dosing were seen and these animals were used for a further dosing with 90, 125, and 174 mg/kg for 10 weeks.

In the 90 mg/kg group one animal died in week 7, in the 125 mg/kg group one animal died in week three, and in the 174 mg/kg group three animals died, two in week 4, and one in week 6.

In general this study is poorly reported. It may be inferred from the data that 90 mg 1,2,4-TCB/kg is a LOAEL and 25 mg 1,2,4-TCB/kg is a NOAEL for rhesus monkeys in a three-month gavage study.

In a two-generation study Robinson et al. (1981) dosed groups of rats with 0, 25, 100 and 400 ppm 1,2,4-TCB in 0.125% Tween 20 in drinking water. Groups of 10 male and 10 female rats were sacrificed at 37 and 95 days after birth in both the F_0- and F_1-generations. The liver, lungs, heart, kidneys, adrenals, and gonads, as well as the seminal vesicles in the males were removed and weighed. Blood was collected by cardiac puncture, and the serum was analysed for 20 different parameters.

In the F_0-generation, the dose given was 3.7, 14.8, and 53.6 and 2.5, 8.9, and 33.0 mg 1,2,4-TCB/kg bw/d for females and males, respectively, at 83 days of age in the different dose groups. In the 400 ppm group significant increases of adrenal weights were seen in both sexes and generations.

In this study the only observed effects in the parental animals was on a single organ weight, increase in adrenal weight at 400 ppm (33 to 55 mg/kg bw/d). A NOAEL of 100 ppm (9-15 mg/kg bw/d) can be established.

Dermal administration

Groups of five male and five female New Zealand rabbits weighing approximately 3 kg were treated by skin application with either 0 (distilled water control), 30, 150, or 450 mg undiluted 1,2,4-TCB/kg for five days/week for four weeks on an area of approximately 4·4 inches (ca. 100 cm^2) without occulsion (Rao et al., 1982). The 1,2,4-TCB used was a technical grade consisting of 70% 1,2,4-TCB and 30% 1,2,3-TCB.

Animals were weighed twice weekly. Ten days prior to exposure and during the last week of dosing basic haematological and clinical chemistry parameters were determined from all rabbits. Twenty-four hour urine specimens were collected from three rabbits/sex/dose group prior to exposure, after approximately two weeks of treatment, and immediately prior to termination. Urine volume was recorded and analysis for coproporphyrin, uroporphyrin, and creatinine was carried out.

After killing the rabbits, a complete external and internal gross necropsy examination was conducted. The brain, heart, liver, kidneys, and testes (males only) were weighed. Sections of 44 organs were preserved and a histopathological examination was carried out on these organs in the control and high dose groups. Additionally histopathological examination was carried out on skin, liver, kidneys, spleen, thymus, vertebral bone with bone marrow, and pertinent gross lesions in the 30 and 150 mg/kg groups.

No significant alterations were observed among males in any of the haematology parameters evaluated. In females a dose-related decrease in total red cells, haemoglobin, and packed cell volume was observed on day 25 of the study, which was significant for the high dose group. For the intermediate dose group (150 mg/kg bw/d) only the total red cell count was decreased. However, on day 31 at termination none of these decreases were statistically significant.

No treatment-related changes were observed in any of the clinical chemistry parameters evaluated.

In the urinary parameters evaluated, a slight and significant increase in coproporphyrin excretion was observed in male rabbits at the high dose level (450 mg/kg bw/d) at day 25 of study.

In the pathology study, skin lesions consistent with a degreasing action of 1,2,4-TCB was observed at the sites of application. The size of the affected area was increasing with increasing doses (0.9, 4.5 and 13.5 mg/cm^2). Treated rabbits showed histological changes characterised as subacute inflammation with reactive epidermal changes. All treated rabbits showed some effects considered to be treatment-related at the site of application. The skin reaction was considered light at the two lower dose levels and moderate at the high dose level.

At necropsy a slight generalised pallor of the liver was observed in animals receiving 450 mg 1,2,4-TCB/kg. This change was not associated with any consistent histological changes.

Based on the effects seen in the Rao et al., (1982) study on the liver and coproporpyrin excretion the systemic LOAEL was 450 mg 1,2,4-TCB/kg bw/d and the systemic NOAEL was 150 mg 1,2,4-TCB/kg bw/d for dermal exposure during four weeks. The changes seen in the total red cell count in the intermediate (150 mg/kg bw/d) group are not considered to be related to treatment.

For local effects on the skin, only a LOAEC of 0.9 mg/cm^2 could be determined.

Groups of 75 male and 75 female Slc:ddY mice were painted on the skin with a 0.03 ml drop of 60 or 30% 1,2,4-TCB (approximately 500 or 250 mg/kg 1,2,4-TCB) in acetone twice a week for two years. In the control group of 50 male and 50 female mice painting was carried out with acetone alone (Yamamoto et al., 1982).

General signs of toxicity were recorded, and histological analysis was carried out on all animals of the three dose groups.

General signs of toxicity included excitement, acceleration of spontaneous activity and panting. The survival rate at the end of the study was low, and mortality was higher in the dosed groups. Skin inflammation was also seen in this study (see Section 4.1.2.3).

Amyloidosis, which mainly affected the liver, spleen, kidney, and adrenal, was more frequent in the dosed groups. Inflammation of the liver, kidney and adrenal was also clearly more frequent in the dosed groups.

This type of study is not in general well suited to establish a NOAEL, particularly when the application is made by two weekly administrations. It should also be noted that the unusually low LD_{50} reported in Section 4.1.2.2 was seen in a study by this author in this strain of mice.

Inhalation administration

Gage (1970) studied the subacute inhalation toxicity of 109 industrial chemicals. The details of each study are limited. Groups of 2 male and 2 female rats were exposed to 15 6-hour exposures with 70 and 200 ppm. Lethargy and retarded weight gain were seen at both dose levels. A "gross examination" of the organs was carried out; the following organs were taken for histological examination: lungs, liver, kidneys, spleen and adrenals. At autopsy, the organs were normal in all treated animals.

A LOAEC of 70 ppm (520 mg/m^3) is uncertain due to the limited number of animals and the limited data reported.

Coate et al. (1977) exposed groups of 30 male rats, 16 male rabbits and 9 male cynomolgus monkeys 0, 25 ppm (188 mg/m^3), 50 ppm (377 mg/m^3), or 100 ppm (754 mg/m^3) 99.1% pure 1,2,4-TCB for 7 hours/day 5 days/week for 26 weeks by inhalation.

During the exposure animals were observed daily for signs of toxicity, and they were weighed weekly for the first four weeks, biweekly for the next 8 weeks, and at 4-week intervals thereafter.

In the monkey study, blood urea nitrogen, total bilirubin, serum glutamate-oxaloacetate transaminase, serum glutamate-pyruvate transaminase, alkaline phosphatase, and lactate dehydrogenase was determined after 5 days, and after 4, 13, and 26 weeks of exposure. CBC's (presumably clinical blood chemistry) were performed on all monkeys.

All monkeys had ophthalmoscopic and gross eye examinations and a series of lung function tests at 4, 13, and 26 weeks.

A complete necropsy with gross pathological examination was performed on all animals. The brain, lungs, heart, liver, kidneys, spleen, eyes, spinal cord, bone marrow, and a section of abdominal skin from each animal were fixed and after staining subjected to histopathological examination.

There were no effects of dosing upon survival, body weight, ophthalmoscopic, haematological and serum biochemical, and pulmonary function parameters.

No treatment-related histopathological changes were observed after 26 weeks.

In these studies, rabbits were examined for the same effects as monkeys with the exception of lung function tests.

There were no effects on dosing upon survival, body weight, ophthalmoscopic, haematological and serum biochemical parameters. No treatment-related histopathological changes were observed after 26 weeks.

In monkeys and rabbits the inhalation NOAEC is greater than 100 ppm 1,2,4-TCB (754 mg/m^3).

For rats examined in the same study as the rabbits and monkeys, blood biochemistry and CBC's were performed on sacrificed rats after 4, 13 and 26 weeks of exposure. A complete necropsy was carried out and the same organs examined as described above.

There were no effects on dosing upon survival, body weight, haematological and serum biochemical parameters. In the rats, histopathological changes were seen at the three dose levels in livers (hepatocytomegaly) and kidneys (hyaline degeneration) at weeks 4 and 13, but after 26 weeks of exposure these changes had disappeared.

Based on the effects seen at weeks 4 and 13 on the livers and kidneys of rats an inhalation LOAEC can be set at 25 ppm 1,2,4-TCB (188 mg/m^3) from the Coate et al. (1977) studies.

Kociba et al. (1981) exposed groups of 20 male rats, 4 male rabbits, and 2 male dogs to 0, 30 ppm (226 mg/m^3) or 100 (754 mg/m^3) ppm of 99.4% pure 1,2,4-TCB vapour for 7 hours/day, 5 days/week for 30 exposures in 44 days.

The animals were observed daily, and weighed 3 times weekly. Between exposure days 28 and 30 basic haematological parameters such as total red blood cells, total differential white blood cells, packed cell volume, and haemoglobin concentration were done on 10 rats per group and on all rabbits and dogs. In addition, standard biochemical parameters including blood urea nitrogen, serum glutamic pyruvic transaminase, and alkaline phosphatase activities were determined in the same animals. Twenty-four hour urine samples from 5 rats of the high-dose group and the control group were collected immediately after the last exposure. The urine samples were analysed for coproporphyrin and uroporphyrin concentrations.

Pathology examinations included weight of liver, kidneys, spleen, adrenal glands (dogs and rabbits only), heart, brain, thymus (rat only), and testes. Thirty different organs from all animals were removed and fixed. Most of the fixed tissues from 2 dogs, 4 rabbits, and 5 rats per control and 100 ppm exposure groups were examined histopathologically.

At 100 ppm dogs had statistically significant increased liver weights.

In rabbits a statistical decrease of relative liver-to-body weight was observed at both 30 and 100 ppm. 1,2,4-TCB, and the absolute and relative testes weight was statistically higher at 100 ppm.

At 100 ppm rats had statistically significant increased liver weights and statistically significant increased relative kidney weights. Urinary excretion of porphyrins was increased in rats exposed to 30 or 100 ppm.

In the pathology there were no clear substance-related changes, but in all three species some pulmonary changes were ascribed to "a low grade chronic infectious process".

An inhalation LOAEC of 30 ppm 1,2,4-TCB (226 mg/m3) and no NOAEC can be derived for rats from the Kociba et al. (1981) study based on effects on liver and kidney.

For rabbits and dogs the experimental groups seem too small to establish a LOAEC and a NOAEC.

In a follow-up study, Watanabe et al. (1977) studied the level which would not increase the excretion of urinary porphyrins in rats. Sprague Dawley rats were exposed to 10 ppm (75 mg/m^3), 3 ppm (23 mg/m^3) or 0 ppm of 1,2,4-TCB 6 hr/day, 5 days/week for a total 65-66 exposures for three months. Exposure to 10 ppm of 1,2,4- TCB resulted in a slightly increased urinary uroporphyrin excretion over the 90-day period. This effect was reversible and no increase was observed 2 or 4 months following termination of exposure. Exposure to 3 ppm

(23 mg/m^3) did not cause any increase in urinary porphyrin excretion, and thus, under the conditions of this study can be considered a NOAEC for rats.

Porphyria

A number of the studies described above refer to effects associated with porphyria (Rao, 1982; Kociba et al., 1981; Watanabe et al., 1977). A number of additional studies addressing the question of porphyria have been carried out with 1,2,4-TCB. This effect was of particular interest following an occurrence of human cutaneous porphyria in Turkey after exposure to the fungicide hexachlorobenzene.

A number of chlorobenzene derivatives were studied for effects on urinary and liver porphyrins after oral administration to rats (Rimington and Ziegler, 1963). Effects on urinary coproporphyrin and uroporphyrin were seen after doses of up to 730 mg/kg bw/d 1,2,4-TCB for 15 days. 1,4-dichlorobenzene showed even greater effects at similar dose levels. A dose of 500 mg/kg 1,2,4-TCB caused decreases in the levels of liver glutathione content. The porphyrinogenic effects of 1,2,4-TCB could be prevented by simultaneous administration of i.p. reduced glutathione.

No effects on porphyrin excretion were seen after oral dosing with up to 200 mg/kg bw/d 1,2,4-TCB suspended in corn oil, although liver weight did increase (Carlson, 1977). 1,4-dichlorobenzene was tested at the same time and had a higher (though still low) potential for causing porphyria.

The effect of oral administration of a number of chlorobenzenes on the porphyrin content in the Harderian gland of rats was studied (Eida et al., 1977). An increase was seen 1, 3, and 5 days after the administration of 500 mg/kg bw/d 1,2,4-TCB. The effects of 1,4-dichlorobenzene were very different, and showed a fall in porphyrin levels in the gland. The difference in effects to those seen in the liver is attributed to a lack of responsiveness of ALA-synthetase in the Harderian gland. This in turn is believed to be related to the deficiency of cytochrome P 450 levels in this gland.

The porphyrinogenic effect of 1,2,4-TCB was examined in chickens and in quail (Miranda, 1983). The quail was found to be the most sensitive species, whilst the chick embryo was non-responsive.

An unusual occurrence of pink fluorescent bones in sheep in Victoria, Australia is attributed to the accumulation of porphyrins. 1,2,4-TCB was found in the sheep bone fat at concentrations of 120 μmoles/kg. There had been no exposure to 1,2,4-TCB and the presence of both the 1,2,4-TCB in sheep bone fat and to the presence of the porphyrins in the bone was attributed to lindane exposure (Nicol et al., 1981).

Conclusion for repeated dose toxicity

The target organs for chronic 1,2,4-TCB toxicity appear to be the liver (increased liver weight histopathological changes and significant changes in activity of liver enzymes), kidney and adrenals. In general the male rat seems more susceptible to 1,2,4-TCB toxicity than the female rat.

Table 4.16 shows the dose-response relationship from some the oral studies reported above.

Table 4.16 Relationship between exposure and effect in some rat studies after oral administration of 1,2,4-TCB

Dose (mg/kg bw/day)	Length of exposure (days)	Effects	Reference
8	90	No significant effects	Côtè et al. (1988)
10-20	14	Induction of liver enzymes	Carlson and Tardiff (1976)
45-133	30-120	Elevated adrenal weights, elevated relative liver and kidney weight, histological changes in liver and thyroid, porphyria	Robinson et al. (1981) Côtè et al. (1988) Carlson (1977)

The NOAELs and LOAELs from different repeated dose toxicity studies are presented in the Tables below. Where sex differences occur, values for the sex showing the lowest effect are shown.

Table 4.17 Subchronic and chronic systemic toxicity of 1,2,4-TCB: Oral administration

Species	Route	Doses	Duration	LOAEL	NOAEL	Ref.
Rat	diet	0, 600, 1,200, 2,400, 4,800, 9,600 ppm	2 weeks	600 ppm ≈ 60 males (60 mg/kg bw/d)	600 ppm females (67 mg/kg bw/d)	Bio/Dynamics, (1987)
Rat		0, 1, 10, 100, 1,000 ppm	13 weeks	1000 ppm (82 males (82 mg/kg bw/d)	100 ppm males (7.8mg/kg bw/d	Côté et al. (1988)
Rat		0, 200, 600, 1,800 ppm	13 weeks	200 ppm males (11 mg/kg bw/d)	200 ppm females (13 mg/kg bw/d)	Bio/Dynamics (1989)
Rat		0, 100, 350, 1,200 ppm	2 years	350 ppm (19-23 mg/kg bw/d)	100 ppm (5.5-6.7 mg/kg bw/d)	Moore (1994b)
Mice		0, 220, 3,850, 7,700 ppm	13 weeks	220 ppm males (62 mg/kgbw/d)	220 ppm females (80 mg/kg bw/d)	Hiles (1989)
Mice		0, 150, 700, 3,200 ppm	2 years	150 ppm (21-26 mg/kg bw/d)	-	Moore (1994a)
Rat	gavage	0, 10, 20, 40 mg/kg bw/d	2 weeks	10 mg/kg bw/d	-	Carlson and Tardiff (1976)
Rat		0, 10, 20, 40 mg/kg bw/d	13 weeks (+ 30 day recovery)	10 mg/kg bw/d 40 mg/kg bw/d (for non-reversible effects)	-	Carlson and Tardiff (1976)
Monkey		0, 1, 5, 25, 90, 125, 174 1 – 173 mg/kg bw/d	13 weeks	90 mg/kg bw/d	25 mg/kg bw/d	Smith et al. (1985)
Rat	drinking water	0, 25, 100, 400 ppm	10 to 12 weeks	400 ppm (33-53 mg/kg bw/d)	100 ppm (9-15 mg/kg bw/d)	Robinson et al. (1981)

Table 4.18 Subchronic and chronic systemic toxicity of 1,2,4-TCB: Dermal and inhalation exposure

Species	Route	Doses	Duration	LOAEL/LOAEC	NOAEL/NOAEC	Ref.
Rabbit	dermal	0, 30, 150, 450 mg/kg bw/d	4 weeks	450 mg/kg bw/d	150 mg/kg bw/d	Rao et al. (1982)
Mice		9, 18 mg 1,2,4-TCB	two years (twice weekly)	-	-	Yamamoto et al. (1982)
Rat	inhalation	70, 200 ppm 520, 1,500 mg/m^3	3 weeks 15 exposures	70 ppm 520 mg/m^3		Gage (1970)
Rat		0, 30, 100 ppm 0, 226, 754 mg/m^3	44 days 30 exposures,	30 ppm 226 mg/m^3	-	Kociba et al. (1981)
Rat		0, 3, 10 ppm 0, 23, 75 mg/m^3	3 months	10 ppm 75 mg/m^3	3 ppm 23 mg/m^3	Watanabe et al. (1977)
Rat		0, 25, 50, 100 ppm 0, 188, 377, 754 mg/m^3	26 weeks	25 ppm 188 mg/m^3	-	Coate et al. (1977)
Rabbit		0, 25, 50, 100 ppm 0, 188, 377, 754 mg/m^3	26 weeks		$\geq$ 100 ppm 754 mg/m^3	Coate et al. (1977)
Monkey		0, 25, 50, 100 ppm 0, 188, 377, 754 mg/m^3	26 weeks		$\geq$ 100 ppm 754 mg/m^3	Coate et al. (1977)

The oral NOAEL is taken as 6 mg/kg bw/d and LOAEL is 20 mg/kg bw/d based on the Moore (1994b) 2-year carcinogenicity study in rats. This is consistent with the NOAEL of 8 mg/kg bw/d from the Côté et al. (1988) 13-week rat diet study and 9-15 mg/kg bw/d from the Robinson et al. (1981) drinking-water study. It should be noted that reversible effects can be seen at doses which are only slightly higher (Carlson and Tardiff, 1976).

For dermal application the LOAEL is 450 mg/kg bw/d and the NOAEL is 150 mg/kg bw/d based on a four-week rabbit study.

The LOAEC (rat) is 25 ppm (188 mg/m3) for organ changes in a 26-week study and 10 ppm (75 mg/m3) for increased excretion of porphyrins in a 90-day study. The corresponding NOAECs are 20 ppm (150 mg/m3) and 3 ppm (23 mg/m3), respectively.

The effects seen after long-term exposure to 1,2,4-TCB (e.g. increased liver weights and liver serum enzyme levels, increased adrenal and kidney weights and excretion of porphyrins) have been seen at dose levels below the limits for classification for chronic effects of 50 mg/kg bw/day after oral exposure, and below 0.25 mg/l, 6 hr/day after inhalation exposure. However the effects seen at these dose levels are not sufficiently severe to warrant classification with R48/22 or R48/20 according to the EU classification criteria.

For the purposes of the risk assessment, the following values have been used:

Table 4.19 Summary of systemic NOAEL/NOAEC values used for the risk characterisation

Route	NOAEL/NOAEC	LOAEL/LOAEC	Duration of exposure	Reference
Oral	6 mg/kg bw/day	20 mg/kg bw/d	2 years	Moore et al. (1994b)
Dermal	150 mg/kg bw/day	450 mg/kg bw/day	4 weeks	Rao et al. (1982)
Inhalation	23 mg/m^3, 6 hr/d, 5 days/week	75 mg/m^3, 6 hr/d, 5 days/week	3 months	Watanabe et al. (1977)

For local effects on the skin, only a LOAEC of 0.9 mg/cm^2 could be determined (Rao et al., 1982).

4.1.2.6 Mutagenicity

Genetic toxicity *in vitro*

Simmon (1975) tested 1,2,4-TCB in *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100 at concentrations of 1, 10, 50, 100, 500, 1,000 and 5,000 μg/plate with and without metabolic activation with rat liver microsomes. Toxicity was seen at 500 μg/plate and above, but the compound was not mutagenic. The substance was also tested in *Saccharomyces cerevisiae* D3 at two concentrations (0.02 and 0.2%). Again, the substance was toxic, but did not increase mitotic recombination.

Schoeny et al. (1979) evaluated the mutagenic potential of 1,2,4-TCB in the *Salmonella*/microsomal assay with the strains TA1535, TA1537, TA98 or TA100 at 8 doses in the range of 102-1.4 · 10^5 μg 1,2,4-TCB/plate with and without metabolic activation using rat liver microsomes induced with PCB or 1,2,4-TCB. Toxicity was seen at doses above 1,599 μg/plate. No mutagenicity was seen for 1,2,4-TCB in the range of 102-2914 μg/plate.

Ames test was performed with the *Salmonella typhimurium* strains TA1535, TA1537, TA98 and TA100 at 0, 3.3, 10, 33.3, 100, and 333.3 μg 1,2,4-TCB/plate with and without S-9 from Arachlor 1254 induced rat and hamster livers using the preincubation procedure. This study was carried out on 250 chemicals using coded samples. Test doses were chosen following checks for toxicity: in the absence of toxicity a maximum of 10 mg/plate was used. The result was negative (Haworth et al., 1983).

Nohmi et al. (1985) tested 1,2,4-TCB in concentrations of 0.03, 0.1, 0.3, 1.0, and 3.0 mg/plate in the Ames test with strains TA100, TA2637, and TA98 with and without metabolic activation. No details of the S-9 mix used are available. The result of the test was negative.

Matsui et al. (1989) tested 1,2,4-TCB for its effect on DNA repair in a *Bacillus subtilis rec* assay. 1,2,4-TCB showed activity that was described as strongly DNA damaging potential after S9 activation.

Ono et al. (1991) tested 1,2,4-TCB in the *umu*-test with and without microsomal activation using S9 prepared from rat livers pre-treated with phenobarbitone and 5,6-benzoflavione. The test showed a positive effect in the absence of S9. The effect seen was greater with increasing time of incubation with the test strain from the normal 2 hour incubation period up to periods of 20 hours incubation. Tested in the presence of microsomal activation toxicity was seen and the effects were negative. In a second study, Ono et al. (1992) confirmed these results when 1,2,4-TCB was tested at

a concentration of 100 μg/ml: 1,2,4-TCB did not induce DNA repair in the *umu*-test with microsomal activation but a positive effect was seen without microsomal activation.

Sofuni et al. (1985) studied the clastogenic potential of 1,2,4-TCB in cultured Chinese hamster cells at concentrations of 0, 0.0313, 0.0625, and 0.125 mg/ml 1,2,4-TCB in DMSO with treatment periods of 24 or 48 hours. The test was carried out without metabolic activation. The concentration of 0.125 mg/ml proved toxic to the cells. At none of the concentrations clastogenic activity was observed in the form of chromosome aberrations.

Ishidate (1987) tested the clastogenic potential 1,2,4-TCB in Chinese hamster lung cell line (CHL) cells without metabolic activation at 62.5 mg/l (0.34 mM) with a negative result (quoted in Ishidate et al., 1988).

Shimada et al. (1983) studied the effects of 1,2,4-TCB on DNA repair in hepatocytes from adult F344 rats *in vitro*. The substance was tested in the hepatocyte primary culture (HPC) DNA repair assay in concentrations from 10^{-5} % (v/v) (0.15 μg/ml) to 1 % (v/v) (14560 μg/ml). DNA repair was quantified by the detection of ^{3}H -thymidine incorporation in nuclear DNA, observed as nuclear grains by autoradiography. Test compounds were reported positive, if the net grain count per cell nucleus was 5 or more. Concentrations of 10^{-2} % (v/v) (146 μg/ml) and above were cytotoxic. 1,2,4-TCB was negative at concentrations of 10^{-3} (15 μg/ml) and 10^{-4} % (v/v) (1.5 μg/ml). The results at 15 μg/ml were 0.6 grains per nucleus in one study and 0 in a second study. The positive controls, 2-AF and B(a)P are clearly positive with from 69 to 218 grains per nucleus. The negative controls, fluorene and DMSO were clearly negative with from 0 to 1.7 grains per nucleus.

Williams et al. (1989) evaluated 1,2,4-TCB in the rat hepatocyte/DNA-repair test in a study of 300 chemicals. 1,2,4-TCB was negative and induced 0.9 grains per nucleus at $8.1 \cdot 10^{-5}$ M (15 μg/ml). The compound did not induce DNA repair.

Microsomal metabolism of 1,2,4-TCB was studied with emphasis on binding to protein and DNA (den Besten et al., 1991). 1,2,4-TCB was metabolised to 2,3,6- and 2,4,5-trichlorophenol, and to a lesser extent to 2,4,6- and 2,3,5-trichlorophenol and trichlorohydroquinone. About 10% of all metabolites became covalently bound to proteins. Protein binding was completely inhibited by ascorbic acid, indicating that the quinone species are the sole reactive species involved. 1,2,4-TCB alkylated DNA, but to a much smaller extent than protein (0.5% of all metabolites). The possibility of ^{14}C-labelled proteins having contaminated the isolated DNA subsequent to incubation cannot be excluded.

Genetic toxicity *in vivo*

By intraperitoneal injection to groups of five NMRI mice of 2 doses of 105, 210, 315, or 420 mg 1,2,4-TCB/kg 24 hours apart and scoring for micronuclei in 1,000 polychromatic erythrocytes 30 hours after the first injection a clastogenic effect in the form of an increased frequency of micronucleated polychromatic erythrocytes was seen (Mohtashamipur, 1987). This study reported the results for 9 different substances, for which only one vehicle control was used. The number of animals/group (5) is less than the number recommended by the OECD guideline (10/group), except when there is no reason to expect any differences between sexes. There is no information about the ratio of polychromatic to normochromatic erythrocytes. All nine examined substances (mostly chlorobenzenes, including 1,4-dichlorobenzene) caused a dose-dependant increase in micronuclei.

Table 4.20 Micronucleus test with 1,2,4-TCB (study 1) (Mohtashamipur et al., 1987)

Treatment	Vehicle (corn oil)	1,2,4-TCB dose (mg/kg bw)			
		210 (2 · 105)	420 (2 · 210)	630 (2 · 315)	840 (2 · 420)
Micronuclei /1000 PCE	1.80 ± 0.748	3.50 ± 0.806 *	4.50 ± 0.806 *	5.80 ± 0.871 *	7.40 ± 0.916 *

* $p < 0.01$ (Student's *t* test).

By intraperitoneal injection to groups of three Swiss CD1 mice of 2 doses of 0 or 500 mg 1,2,4-TCB/kg in a dimethylsulfoxide/olive oil suspension 24 hours apart and scoring for micronuclei in 3,000 polychromatic erythrocytes 30 hours after the first injection a clastogenic effect in the form of a doubling of the frequency of micronucleated erythrocytes was seen (Parrini et al., 1990). The performance of the test does not appear to be carried out according to recommended guidelines. Only three animals were used instead of 10 animals/dose group as the OECD guideline recommends, and there is no information about the toxic effects of the test substance on the animals at the administered dose level.

Table 4.21 Micronucleus test with 1,2,4-TCB (study 2) (Parrini et al., 1990)

Treatment	Vehicle (DMSO/olive oil)	Negative control	1,2,4-TCB dose (mg/kg bw)
			1,000 (2 · 500)
Micronuclei/1000 PCE	1.88 ± 1.28	1.16 ± 0.98	3.66 ± 1.73 *

* significant difference compared to vehicle (Mann-Whitney).

In a micronucleus test carried out according to GLP and the OECD guideline 474 Lehn (1990) tested 1,2,4-TCB at single doses of 0, 100, 330, and 1,000 mg/kg dissolved in polyethylene glycol given orally with smears being made at 24, 48 and 72 hours after dosing. The highest dose level showed clear signs of toxicity (see **Table 4.22**). This test proved negative though significant results were obtained for the 72-hour smears at 330 and 1,000 mg/kg. The significance is considered due to a very low control value measured at this time point.

Table 4.22 Micronucleus test with 1,2,4-TCB (study 3) (Lehn, 1990)

	Sample time:	Vehicle	1,2,4-TCB (mg/kg)			Cyclophos phamide
			100	330	1,000	40
Micronuclei /1000 PCE	24 h	0.7	0.5	1.2	0.3	10.4 *
PCE/NCE		1,000/792	1,000/878	1,000/814	1,000/986	1,000/841
Micronuclei /1000 PCE	48 h	0.9	0.5	0.1	0.22	-
PCE/NCE		1,000/925	1,000/921	1,000/1081	1,000/1246	-
Micronuclei /1000 PCE	72 h	0.1	0.1	0.7 *	0.71 *	-
PCE/NCE		1,000/871	1,000/953	1,000/858	1,000/909	-

* $p \leq 0.05$ compared to vehicle (Mann-Whitney).

Conclusion for mutagenicity

Three independent Ames tests were negative. Two bacterial assays for DNA repair were available: one was equivocal and one was positive. Furthermore two clastogenicity studies with mammalian cells *in vitro* were negative, but no metabolic activation was used in these studies.

For the *in vivo* genetic toxicity, marginally positive tests and one negative micronucleus test have been carried out.

The test which showed a negative result was carried out after oral application and performed according to the OECD guideline 474 and according to GLP. A toxic dose was applied, and cytotoxic effects were seen in bone marrow. In the two other tests, which showed marginally positive results, the test substance was administered intraperitoneally. In both these studies, the experimental protocol was less adequate than specified by the OECD Guideline. This brings into question the validity of the positive results.

The database for genotoxicity is complicated and does not lead to a clear conclusion. There is some evidence of DNA-damage, and there are weakly positive results from two inadequately performed *in vivo* micronucleus assays. The negative Ames test results do not provide strong evidence of a lack of genotoxicity, and the negative clastogenicity studies suffer from a lack of metabolic activation. However, there are no effects on DNA repair in primary hepatocytes and a well conducted *in vivo* micronucleus test was negative.

On balance, 1,2,4-TCB is not considered to express systemic genotoxic effects *in vivo*.

4.1.2.7 Carcinogenicity

In vitro study.

Shimada et al. (1983) studied the effects of 1,2,4-TCB in hepatocytes from adult F344 rats *in vitro*. In the adult rat liver epithelial (ARL) cell transformation assay, 1,2,4-TCB was tested at concentrations of 15 and 73 µg/ml. Transformation occurred at doses which caused severe cell toxicity. 1,2,4-TCB induced a low but definite anchorage dependency in these cells.

In vivo studies.

Groups of 75 male and 75 female Slc:ddy mice were painted on the skin with a 0.03 ml drop of 60 or 30% 1,2,4-TCB (18 or 9 mg 1,2,4-TCB) in acetone twice a week for two years. In the control group of 50 male and 50 female mice painting was carried out with acetone alone (Yamamoto et al., 1982).

Histological analysis was carried out on all animals of the three dose groups.

At the site of painting with 1,2,4-TCB, cell infiltration, and thickening and keratinization of the epidermis were seen. 2 (2.7%) of the high-dose males and 1 (2%) female control showed papillomas, 1 (1.3%) of the high-dose females showed a squamous cell carcinoma. There was no increase in the rate of systemic tumours.

This study does not show increase in tumour incidence in Slc:ddy mice.

Groups of 50 male and 50 female B6C3F1 mice were given 0, 150, 700, or 3,200 ppm 1,2,4-TCB in the diet for 104 weeks (Moore, 1994a). The study was carried out following GLP and the test guideline 40 CFR 798.3300 (similar to OECD TG 451). See **Table 4.23**.

The mean consumed dose of 1,2,4-TCB during the 104 weeks was 0, 20.9, 100,5, and 522 mg/kg bw/d for males and 0, 26.2, 127.2, and 574.9 mg/kg bw/d for females in the 0, 150, 700, and 3,200 ppm groups, respectively.

In the high-dose group there was a decrease in survival from week 52 and onwards. For the 3,200 ppm group males and females survival at the end of the study was significantly decreased when 100% females and 90% males were dead. The mortality rate at 700 ppm was 18 % in males and 16 % in females, at 150 ppm 12% in males and 24 % in females and in the control group 10 % in males and 22 % in females.

Compared to control mean values significantly lower weekly mean body weights were noted in the 3,200 ppm dose group males and females through most of the study. Terminal body weights of the 3,200 ppm females could not be assessed due to no survivors at week 104. Conversely, weekly mean body weights were greater (frequently statistically significant) in the 150 and 700 ppm dose group males and females. Histopathology revealed that liver tumours were seen in all three treatment groups as well as in the concurrent control group (**Table 4.23**).

Table 4.23 Liver tumour incidences in the mouse after chronic oral administration of 1,2,4-TCB (Moore, 1994a)

		1,2,4-TCB (ppm)			
		0	150	700	3,200
Surviving animals (104th week)	Male female	45/50 39/50	44/49 37/49	41/50 42/50	5/50 0/50
Hepatocellular adenomas	Male female	4/50 3/50	7/50 4/50	16/50 16/50	2/50 8/50
Hepatocellular carcinomas	Male female	8/50 1/50	5/50 1/50	27/50 28/50	50/50 46/50

There was a significantly increased incidence of hepatocellular carcinoma in the high- and mid-dose group.

Adenomas were also increased in incidence in the two highest groups except 3,200 ppm males.

The long-term feeding study with mice has deficiencies. The mortality rate at the high dose (3,200 ppm) for both males and females is high, complicating interpretation of the results from this group. However, hepatocellular carcinomas were seen in almost all animals in the high-dose group. At 700 ppm there is a tumour rate which is significantly increased compared to the concurrent control. The use of the mouse strain B6C3F1 in the carcinogenicity study is complicated by the fact that this strain of mice is known to produce a high incidence of hepatocellular carcinomas, when exposed to a substance which has a toxic effect on the liver. However, the results of this study show a positive carcinogenic effect of 1,2,4-TCB in this mouse strain.

The NOAEL of 1,2,4-TCB for carcinogenicity was 150 ppm in the feed equal to 21-26 mg 1,2,4-TCB/kg bw/d for B6C3F1 mice.

Groups of 50 male and 50 female F-344 rats were given 0, 100, 350 or 1,200 ppm 1,2,4-TCB in the diet for 104 weeks (Moore, 1994b). The study was carried out according to GLP and the US test guideline 40 CFR 798.3300 (similar to OECD TG 451). See **Table 4.24**.

The mean consumed dose of 1,2,4-TCB during the 104 weeks was 0, 5.5, 18.9, and 66.7 mg/kg bw/d, respectively in the males; and 0, 6.7, 22.9, and 79.3 mg/kg bw/d, respectively, in the females.

Survival at the end of the study in the high dose group was 60% (30/50) for the males and 72% (36/50) for the females. The major cause of unscheduled death in all groups was neoplasia, which included mononuclear cell leukaemia and tumours in the pituitary and Zymbal's gland.

Table 4.24 Incidences of the predominant tumours in the rat after chronic oral administration of 1,2,4-TCB (Moore, 1994b)

		1,2,4-TCB (ppm)			
		0	**100 ***	**350 ***	**1,200**
Surviving animals (104th week)	male female	41/50 38/50	39/49 37/49	42/50 36/50	30/50 36/50
Mononuclear cell leukaemia	male female	15/50 10/50	13/49 10/49	18/50 13/50	21/50 10/50
Pituitary gland tumours (carcinomas/adenomas)	male female	19/50 19/50	13/49 22/49	8/50 19/50	12/50 21/50
Zymbal's gland * tumours (carcinomas/adenomas)	male female	1/50 0/50	0/49 2/49 **	1/50 0/50	4/50 2/50

* Histological examination carried out only on indication

** 1 of these tumours was reported as an adenoma. All remaining Zymbal's gland tumours were carcinomas. On re-examination (Moore, 2000) all tumours were classified as carcinomas

Mononuclear leukaemia and pituitary gland tumours are common findings in old Fischer F344 rats, and no significant difference between control and high-dose animals is seen. With respect to the Zymbal's gland tumours, a non-significant increase is seen in high-dose animals. The incidence of Zymbal's gland tumours (carcinomas and adenomas) is however normally less than 1% (Seely, 1991). Further, from the NTP Historical Control Information Service, Environmental Health Information Service (EHIS, 2000) it appears that the incidence does not exceed 4% and in most cases is 2% or lower.

Since the histological examination of these tumours had only been carried out on indication, a supplementary histopathological examination of all the Zymbal's glands from the study was carried out (Moore, 2000).

Table 4.25 Incidences of Zymbal gland tumours in the rat after chronic oral administration of 1,2,4-TCB (Moore, 2000)

	1,2,4-TCB (ppm)			
Incidence	**0**	**100**	**350**	**1,200**
Male	1/50	0/50	1/50	4/50
Female	0/50	3/50	0/50	2/50
Combined	1/100	3/100	1/100	6/100

There is no statistically significant increase when the incidence in the test groups is compared to the controls (p from 0.21 to 0.32). For males, the significance of a trend test just fails to achieve 5% probability (p = 0.0547). A Fischer's exact test of the combined incidence shows p = 0.056.

In the rat-liver foci bioassay, an indicator of initiating and/or promoting activity in rat liver, i.p. application of 1,2,4-TCB after prior initiation with diethylnitrosamine did not lead to an increased incidence of γ-glutamine transferase (GGT) foci in female Sprague-Dawley rats (Herren-Freund and Pereira, 1986).

Conclusion on carcinogenicity

An *in vitro* cell transformation test was positive, but the levels of cytotoxicity were very high.

After dermal application 1,2,4-TCB did not show carcinogenicity in Slc:ddy mice.

Administration of 1,2,4-TCB via the feed for two years produced carcinogenicity in B6C3F1 mice. It is found that hepatocellular tumours are produced in B6C3F1 mice by a number of substances which have a toxic effect on the liver. The relevance of these tumours for humans is an issue of considerable discussion. The finding that 150 ppm 1,2,4-TCB in the feed (21-26 mg/kg bw/d) did not induce liver tumours in the B6C3F1 mice indicates a threshold for liver tumours and supports the view that the liver tumours are the result of a general toxic effect on the liver. This is further supported by the finding that 1,2,4-TCB did not produce tumours in other organs in the mouse.

Administration of 1,2,4-TCB via the feed for two years in F344 rats produced an increase in Zymbal's gland tumours that was close to statistical significance. The probability in the trend test in male rats was p = 0.0547. The Fischer's exact test on the combined incidence in males and females was p = 0.056. The incidence in three of the treated groups (100 ppm females and 1,200 ppm males and females) is in excess of most of the published control data for carcinomas in this strain of rats. Genotoxic carcinogens typically induce Zymbal's gland tumours. This gland is not found in man, but tumours seen in this organ can be related to tumours found in sebaceous glands in man. It cannot be excluded that the observed increase in frequency in males is due to the administration of 1,2,4-TCB.

1,2,4-TCB is on balance not considered to be genotoxic *in vivo* and binding studies of 1,2,4-TCB indicate no or only marginal adduct formation with DNA. The 1,2,4-TCB induced liver tumours in the B6C3F1 mice strain is not in itself considered to be relevant for humans. The Zymbal's gland tumours in the F344 rat are of concern. Whilst the incidence reported here is not statistically significantly increased, in several groups the incidence of carcinomas is substantially higher than the levels normally seen.

Substances that produce Zymbals's gland tumours are often associated with genotoxicity. Nine chemicals which were identified as causing Zymbal's gland neoplasms in rats from a survey of 222 chemicals evaluated for carcinogenicity by NCI/NTP were also mutagenic for Salmonella typhimurium. Reactive metabolites of chemicals carcinogens may be formed in Zymbal's gland since homogenates of the gland contain cytochrome P-450 dependant enzyme activity (reviewed in Seely (1991)).

However, the results presented above are not considered to fulfil the criteria for classification for carcinogenicity according to the EU classification criteria.

4.1.2.8 Toxicity for reproduction

Toxic effects on reproductive organs seen in subchronic and chronic studies

Post-mortem examination of reproductive organs have been performed in oral subchronic toxicity studies (Côté et al., 1988; Hiles, 1989; Bio/Dynamics, 1989) and histopathological examination was performed in carcinogenicity studies (Moore, 1994a; 1994b).

In a study similar to OECD TG 408 groups of ten male and ten female weanling Sprague-Dawley rats were fed diets containing 1, 10, 100 or 1,000 ppm 99% pure 1,2,4-TCB for 13 weeks (Côté et al., 1988). The dose of 1,2,4-TCB ingested was calculated to be 0.07, 0.78, 7.8, and 82 mg/kg bw/day for males and 0.11, 1.4, 15, and 101 mg/kg bw/day for females. No effects were seen on organ weights and no histological effects wereseen on the reproductive organs.

Groups of 10 male and 10 female B6C3F1/CrlBR mice were given 0, 220, 3,850 or 7,700 ppm 1,2,4-TCB (99.48% pure) in the diet for 13 weeks in a guideline study carried out according to GLP (Hiles, 1989). Absolute weights of left and right testis/epidiymis were significantly lower in all groups of treated males. Relative testis/epididymis to brain weights were significantly lower in groups dosed with 220 or 3,850 ppm. These differences were not accompanied by macroscopic or microscopic changes in the testes or epididymides. The cause of the differences may be related to depletion of fat stores.

Groups of 10 male and 10 female Fischer F344 rats received 0, 200, 600, or 1,800 ppm 1,2,4-TCB in the diet for three months (Bio/dynamics, 1989). The study does not specify any guideline or GLP. However, the observations performed very closely resemble those made in an OECD TG 408 study. The mean testes weight for 1,800 ppm males was statistically significantly higher than the control value.

Groups of 50 male and 50 female B6C3F1 mice were given 0, 150, 700, or 3,200 ppm 1,2,4-TCB in the diet for 104 weeks (Moore, 1994a, for study details see previous sections). The testes and seminal vesicles were examined microscopically from control, 700 and 3,200 ppm dose groups. The percentage of males exhibiting degeneration (either uni- or bilateral) of the testes were 2, 6 and 20%, respectively. The percentage exhibiting decreased secretion (bilateral) in the seminal vesicles was 0, 2 and 53% respectively. The authors conclude that the degenerative changes seen in the high dose males are a secondary effect.

This study provides little evidence on which a NOAEL could be based.

Groups of 50 male and 50 female F-344 rats were given 0, 100, 350 or 1,200 ppm 1,2,4-TCB in the diet for 104 weeks (Moore, 1994b, for study details see previous sections). No treatment related effects were seen in reproductive organs.

Developmental toxicity and fertility: 2-generation reproductive toxicity study

In a 2-generation reproductive toxicity study with 1,2,4-TCB in Charles River rats (Robinson et al., 1981), dosage groups received 0, 25, 100, or 400 ppm 1,2,4-TCB in the drinking water, beginning with birth of the F0 generation and continuing through weaning of the F2 generation. An additional vehicle control group received 0.125% Tween 20 in the drinking water. In all generations, each treatment group consisted of 17-23 litters. The estimated 1,2,4-TCB doses were 2.5, 8.9 and 33 mg/kg bw/d (males) and 3.7, 14.8 and 53.6 mg/kg bw/d (females) for adult animals.

The treatment did not affect fertility, growth, viability, locomotor activity, or blood chemical analyses. No histological changes were seen in the kidney or liver.

At 400 ppm, corresponding to 53 mg/kg bw/d and 33 mg/kg bw/d for females and males, respectively, statistically significantly increased absolute and relative adrenal weight was observed in both sexes in the F0 and F1 animals at 95 days of age. Only the left adrenals were dissected. The adrenals were not examined histologically.

In order to examine the reasons for the adrenal enlargement, an acute study in pre-weanling rats was carried out. Groups of 9-10 females were dosed i.p. with 0, 250 or 500 mg/kg 1,2,4-TCB at 22, 23 and 24 days of age. At 25 days of age, body weights were recorded, the animals decapitated, and the uterus, ovaries, liver, kidneys and adrenals were removed and weighed. Dose-related changes were seen in decrease in body weight and in uterus weight, and increases in liver and adrenal weight. The relative uterus weight was not reported. However, the mean values reported for the three groups suggest that the relative weight was unchanged. The fall might therefore be a reflection of systematic toxicity produced by the relatively high intraperitoneal doses. Whilst the authors do not provide an explanation for the rise in adrenal weight, they exclude the possibility that the effect is due to estrogenic properties, as no rise in uterus weight was seen in this study. They also claim to exclude the possibility of some form of long-term stress, since the adrenal enlargement can be produced with acute doses of 1,2,4-TCB.

It should be noted that adrenal enlargement was seen in the Robinson et al. (1981) studies. These are the only studies in which pre-weanling animals are exposed. It cannot be excluded that this effect occurs only after dosing at this age, and is therefore not exclusively an expression of maternal toxicity.

1,2,4-TCB does not seem to affect fertility of rats at doses up to 400 ppm in the drinking water. However body weights of the parental animals were not affected and the only effects seen were on the adrenal weight. From this study, it can be concluded that the NOAEL for developmental toxicity and fertility is 400 ppm. This is equal to 33 mg/kg bw/day for males and 53 mg/kg bw/day for females.

Developmental toxicity studies

13-14 pregnant Sprague-Dawley rats/dose group were given 0, 75, 150 and 300 mg/kg 1,2,4-TCB dissolved in corn oil by gavage from day 6 to 15 day of gestation (Black et al., 1988). Of these, 10-12 rats/group produced litters. In a prior range-finding study, mortalities in the dams were seen at a dose of 600 mg/kg bw/d. The maternal toxicity seen in this study was most apparent for 1,2,4-TCB compared to 1,3,5- and 1,2,3-TCB studied at the same time. The doses chosen for the 1,2,4-isomer were 75, 150 and 300 mg/kg, and for the other two isomers, the doses were 150, 300 and 600 mg/kg. Maternal body weight was decreased in the high-level 1,2,4-TCB dose group, but this decrease was not significant. Other external signs of maternal toxicity were not determined.

Post-mortem examination showed slight liver changes (increased periportal cytoplasmic eosinophilia and slight anisokeryosis of the cell nuclei of the hepatocytes) in dams dosed with 150 mg/kg bw/d. In addition to these effects, a significant 5.7% increase in relative liver weight was seen in the 300 mg/kg dose group; the absolute liver weight was also significantly increased, but the weights of other organs were statistically normal. Changes in the thyroid gland were also observed in the 300 mg/kg 1,2,4-TCB group. These effects are considered to be an adequate expression of maternal toxicity.

Haematological and clinical chemistry investigations showed significantly reduced hemoglobin and haematocrit values as well as a significant increase in the protein content and in the aminopyrine-N-demethylase activity in the liver at 150 mg/kg bw/d and above.

Histological lesions occurred in the lenses of eyes of foetuses from the intermediate dosage group. These effects were not seen in the other two treatment groups. The ocular changes consisted of central areas of cellular disorientation and disaggregation with ballooning and granular degeneration. This finding is interpreted by the authors as possibly indicating early cataract development. However, no data on the incidence or severity of these findings are given. (Similar effects were also seen with all three groups treated with 1,3,5-TCB, when tested in the same study.) The authors draw attention to the fact that the histopathological examination of the other foetal tissues was made more difficult as a result of autolysis and insufficient conservation. This brings into question the validity of the findings in the eye.

The authors conclude that "none of the trichlorobenzene isomers tested in this study produced teratogenic or fetotoxic effects."

The NOAEL for the dams is 75 mg/kg bw/d in this study. For the foetuses, the NOAEL depends on the significance attributed to the eye lesions seen in the foetuses in the middle dose group. The effects seen in the eye are not considered substance related, and therefore the NOAEL for the foetuses is 300 mg/kg bw/d. However, it cannot be entirely excluded that the effects seen in the foetal eye could be substance-related, in spite of the lack of dose dependency, and that the effect is seen in the intermediate dose only. On this basis, a NOAEL of 75mg/kg bw/d can be established for both the dams and the foetuses.

Groups of six or more pregnant Sprague-Dawley rats received 0, 36, 120, 360, or 1,200 mg 1,2,4-TCB/kg bw/d by gavage on days 9-13 of pregnancy (Kitchin and Ebron, 1983). The animals were sacrificed on day 14 of pregnancy, and the possible maternal hepatic and reproductive effects were assessed.

The first signs of maternal toxicity (liver enzyme induction) were observed at 120 mg/kg /day. At 360 mg/kg bw/d the body weight gain of the dams was reduced and mortality was slightly increased (2/9). All dams dosed with 1,200 mg/kg bw/d died during the study.

The only teratogenicity data presented in the paper are those of the control group and the 360 mg 1,2,4-TCB/kg bw/d group represented each by 12 dams. Treatment with 360 mg 1,2,4-TCB/kg resulted in delayed embryonic development in the form of reduced head length, reduced crown-rump length, reduced somite number and reduced protein content. Resorption rates, the number of live foetuses and the incidence of malformations did not differ from the controls.

The effects on foetuses at a dose level of 360 mg/kg /day indicates foetotoxicity of 1,2,4-TCB at a dose level showing maternal toxicity.

From the results of this study a NOAEL of 36 mg/kg bw/d for the dams can be established.

Chernoff and Kavlock (1983) tested 0 and 130 mg 1,2,4-TCB/kg in groups of 25 CD-1 pregnant mice as part of the validation of a teratology test system. 1,2,4-TCB was administered by gavage dissolved in corn-oil from the 8^{th} to the 12^{th} day of pregnancy. 1,2,4-TCB did not give rise to any discernible foetal effects. In this study, compounds were administered at or near the maternally minimally toxic dose (MTD).

Endocrine disrupting activity

During metabolism of 1,2,4-TCB, 2,4-dichlorophenol may be formed. The latter is suspected to be an environmental endocrine disrupter. According to an OECD proposal (1996), the potential endocrine disrupting potential of chemicals and their decomposition products should be investigated.

QSARs have been developed to predict endocrine disrupting effects of chemicals. Mekenyan et al. (1998) have developed an algorithm to identify potential estrogen receptor ligands. 1,2,4-TCB is not expected to bind to the estrogenic receptor, and therefore not to show estrogenic activity (Mekenyan, 1998).

Walker (1998a) has developed a tool to rapidly sort and prioritise chemicals for endocrine disrupter screening and testing. This includes data on HQSAR (Hologram QSAR) (Tong et al., 1998; Waller, 1998). 1,2,4-TCB has a HQSAR of -1.84, indicating low potential binding affinity to an estrogen receptor. Estradiol has a HQSAR of 2.41 (Walker, 1998b).

The evidence from the Robinson et al. (1981) study reported above which shows that i.p. administration of 1,2,4-TCB to pre-weanling rats does not result in an increase in uterus weight suggests that the substance does not have any specific estrogenic activity. However, the absence of any explanation for the increase in adrenal weight in these animals, changes in other endocrine hormones may be possible.

1,2,4-trichlorobenzene has also been tested for androgenic, anti-androgenic and cytotoxic activity *in vitro* (Vinggaard, 1999).

The androgen receptor assay was performed essentially as described by Vinggaard et al. (1999). Chinese Hamster Ovary cells were seeded at a density of 5,000 cells per well and incubated the following day in the presence of 0.5, 2.5, 5, 25 and 50 µM 1,2,4-TCB. For testing of an anti-androgenic activity the androgen R1881 (0.1 nM) was added. Shortly after addition of test compounds, each well was transfected with a total of 50 ng DNA consisting of the expression vector for the human androgen receptor (pSVAR0) and a luciferase reporter gene (MMTV-LUC) using the non-liposomal transfection reagent FuGene. After an incubation period of 24 hours, the cells were lysed and luciferase activity was determined.

Cytotoxicity was also tested using AlamarBlue. After incubation of the CHO cells for 24 hours with compounds at the indicated concentrations, the cell number was determined by measuring the reduction of AlamarBlue as described (Vinggaard et al., 1999). The assay is based on metabolic reduction of the AlamarBlue dye into a fluorescent species, which is detected after excitation of the reduced dye at 560 nm and subsequent emission at 590 nm.

No effects of 1,2,4-TCB up to 50 µM were observed in the above mentioned assays.

Conclusion on toxicity for reproduction

The findings on the reproductive organs in the subchronic and chronic toxicity studies are inconsistent, but do not however exclude the possibility that 1,2,4-TCB may adversely effect fertility.

The available studies on fertility and developmental toxicity do not fulfil requirements of the existing OECD TGs. The following deficiencies of the studies can be identified:

The dose level in the two-generation Robinson et al. (1981) study is too low, since no effects were observed on parental body weights. However, the NOAEL for reproductive effects was equal or greater than 33 to 53 mg/kg /day, but a LOAEL for possible reproductive effects cannot be established based on the available information.

The teratology study from Black et al. (1988) used 10-12 animals per group. The decrease in body weight gain of the dams in the 300 mg/kg bw/d dose group was only slight, but all dams died at 600 mg/kg bw/d. Some effects (slight liver changes and haematology) were seen in the dams in the 150 mg/kg bw/d group. Effects on the eyes were seen in the foetuses in this group only, and the effect does not show dose dependency. For the dams, a NOAEL of 75 mg/kg bw/d can be established. If the above effect on foetuses of the middle dose group are regarded as substance related the NOAEL is 75 mg/kg /day; if not the NOAEL is 300 mg/kg /day according to this study.

In the study by Kitchin and Ebron (1983), the dosing period was only days 9-13 (compared to days 6-15 in the OECD TG 414) and the animals were sacrificed on day 14 of pregnancy instead of day 21. The dose levels induced decreased body weight gain of the dams, but malformations cannot be properly assessed due to the shorter dosing period and the early time of sacrifice. Therefore only a LOAEL of ≤360 mg/kg bw/d can be established based on this study.

The Chernoff and Kavlock study did not demonstrate any discernible foetal effects. This study is however only a screening study based on a single dose.

The data presented here do not indicate that classification for reproductive toxicity is necessary. However, it is possible that an effect on the reproduction (fertility and development) would have been observed if a higher dose had been studied. It cannot be discounted that an effect would have been seen that even in the presence of slight maternal toxicity might have lead to classification for reproductive toxicity.

The available studies for reproductive toxicity also suffer from various forms of deficiencies in establishing a LOAEL or a NOAEL.

None of the sub-chronic or chronic toxicity studies provide a good basis for setting a NOAEL. A NOAEL for effects on the foetus based on the 2-generation (Robinson) study is equal or greater than 33 mg/kg bw/d, as no LOAEL could be established. For developmental effects, a NOAEL of 75 mg/kg bw/d for the foetus can be calculated, based on an effect seen in the eye. This effect is not however considered to be substance related, and if this is ignored, the relevant NOAEL is 300 mg/kg.

In spite of the deficiencies in the studies reported here, further testing for reproductive toxicity is not considered necessary.

1,2,4-TCB does not show oestrogenic or anti-androgenic activity.

4.1.3 Risk characterisation

4.1.3.1 General aspects

1,2,4-TCB is absorbed well and rapidly after oral exposure. The relative amount absorbed after inhalation exposure has not been measured, but subchronic and chronic exposures show that the substance is well absorbed by this route. It is assumed that similar amounts are absorbed after inhalation as are after oral administration. There is also evidence that 1,2,4-TCB is absorbed through the skin, although both the acute and systemic effects seen after dermal administration appear at higher doses than those seen after oral or inhalation administration. This would suggest that absorption by the dermal route is lower.

The substance shows acute toxicity in the "Harmful" range after oral administration.

The substance has traditionally been regarded as irritant to eyes, skin and respiratory tract. The substance shows some eye irritation, but this is not enough to fulfil the classification criteria. Whilst some skin irritation is seen after acute dermal application, irritation is mainly the result of repeated dosing. Evidence for respiratory tract irritation is largely anecdotal.

The substance appears to have weak sensitising properties, which are not considered significant for either classification or risk characterisation.

There are several assays to assess the repeated dose and chronic toxicity. For the purpose of the risk characterisation of total systemic dose, the oral NOAEL is taken as 6 mg/kg bw/d based on the Moore (1994b) 2-year carcinogenicity study in rats. This is consistent with the NOAEL of 8 mg/kg bw/d from the Côté et al. (1988) 13-week rat study. This figure is close to the level at which effects on liver enzymes and relative organ weights can be seen. At higher doses, elevated adrenal weights, elevated relative liver and kidney weights, histological changes in the liver and thyroid and porphyria are seen.

For chronic inhalation exposure, a NOAEC of 3 ppm (23 mg/m^3) has been used in the risk assessment. The effects seen in this study are very similar to those seen in oral studies. The equivalent oral dose for the rat has been calculated (US Chlorobenzene Producers Association, 1996) as 3.2 mg/kg bw/d. Whilst slightly lower than the oral value, this is not considered to be unreasonable.

For dermal application the systemic LOAEL is 450 mg/kg bw/d and the NOAEL is 150 mg/kg bw/d based on a four-week rabbit study. These levels are higher than comparable figures for the oral or the inhalation route.

For local effects on the skin, only a LOAEL of 0.9 mg/cm^2 could be determined.

The effects seen after long term exposure to 1,2,4-TCB (e.g. increased liver weights and liver serum enzyme levels, increased adrenal and kidney weights and excretion of porphyrins) have been seen at dose levels below the limits for classification for chronic effects of 50 mg/kg bw/day after oral exposure and 0.25 mg/l, 6 hr/day after inhalation exposure. However, the effects seen at these dose levels are not sufficiently severe to warrant classification with R48/22 or R48/20 according to the EU classification criteria.

The database for genotoxicity is complicated and does not lead to a clear conclusion. On balance, 1,2,4-TCB is not considered to express systemic genotoxic effects *in vivo*.

1,2,4-TCB produced a significant increase in hepatocellular carcinomas in B6C3F1 mice, and an increase, however not statistically significant, in the tumours of the Zymbal's gland in F-344 rats after oral administration. No carcinogenic effect was seen in mice after dermal application. The use of the mouse strain B6C3F1 in the carcinogenicity study is complicated by the fact that this strain of mice is known to produce a high incidence of hepatocellular carcinomas when exposed to substances which have a toxic effect on the liver. The 1,2,4-TCB induced liver tumours in the B6C3F1 mice strain is not in itself considered to be relevant for humans. The Zymbal's gland tumours in the F344 rat are of some concern. Whilst the incidence reported here is not statistically significantly increased, in several groups the incidence of carcinomas is substantially higher than the levels normally seen.

In spite of the uncertainties associated with the evaluation of both the genotoxicity and the carcinogenicity of the substance, it is considered unlikely that additional guideline testing would provide further information that would lead to either a change in the conclusion for the mutagenicity or the carcinogenicity of the substance. An investigation of the capability of 1,2,4-TCB for covalent binding to DNA in the Zymbal's gland could be of interest.

Based upon the present data, classification as either a category 3 carcinogen or a category 3 mutagen is not considered appropriate.

Since the concern for a carcinogenic effect in the mouse liver is associated with the potential of the substance to cause changes in this organ, a NOAEL that is based on an absence of effects on the liver, i.e. the NOAEL for repeated dose toxicity, is considered to be adequate for the purposes of this risk assessment.

The data on the effects of 1,2,4-TCB are inadequate to properly evaluate the possible effects on reproductive toxicity. The data on the effects of 1,2,4-TCB are inadequate to establish a LOAEL for reproductive effects. A NOAEL for effects on the foetus based on a 2-generation study can be established as greater or equal to 33 mg/kg bw/d for males and 53 mg/kg bw/day for females, which is at a level of 5 to 10 times the NOAEL chosen for repeated dose toxicity. It is considered unlikely that further testing will lead to a lower NOAEL/NOAEC for reproduction. The data presented here do not suggest that classification for reproductive toxicity is appropriate.

Overall confidence in the database

The findings of the studies are sufficiently coherent that appropriate judgements can be based on the database. The conclusions drawn in this Risk Assessment are in general in agreement with evaluations carried out by other Authorities.

Uncertainty in NOAEL arising from the variability in the experimental data

Oral administration

The studies cited above allow a NOAEL based on liver toxicity to be determined from 2 repeated dose studies. The US EPA (US EPA, 1991) sets a long-term water quality standard on the basis of the NOAEL from the Robinson (1981) 2-generation study. From the above study a LOAEL for the parental animals of 400 ppm (33-53 mg/kg bw/d) and a NOAEL of 100 ppm (9-15 mg/kg bw/d) 1,2,4-TCB in drinking water for 95 days may be established with the target organ being adrenals (increased weight). This is consistent with the NOAEL of 6 mg/kg bw/d established above. The NOAEL from the Moore (1994b) 2-year carcinogenicity study is consistent with the NOAEL of 8 mg/kg bw/d from the shorter Côté et al. (1988) 13-week rat study.

Inhalation exposure

The estimates for a NOAEC following exposure by inhalation are derived from a 26-week and a 3-month rat study. The corresponding NOAECs were 150 and 23 mg/m^3. The calculated equivalent oral doses correspond closely to the level seen after oral administration, and suggest that the extent of absorption after inhalation exposure is similar to that after oral absorption.

There are no reasons to assume a special extent of uncertainty which has to be taken into account.

Dermal exposure

The estimate for a NOAEL for dermal exposure (150 mg/kg bw/d) is substantially higher than for oral exposure, and based on a single 4-week rabbit study. A chronic NOAEL could be expected to be lower than this, and often a conventional factor of 3 to convert from a 28-day study to a three-month study is used (cf. classification criteria for R48 in Annex VI of Directive 67/548/EEC). Even taking this into account, the figure would still be higher than the oral NOAEL. A higher figure is however consistent with the lower acute toxicity seen after administration by this route.

Evaluation of the MOS for systemic dermal exposure should reflect the shorter exposure time (4 weeks) on which this NOAEL is based, compared to the other two routes of exposure.

The substance causes irritation after repeated exposure. For this effect only a LOAEL of 0.9 mg/cm^2 has been measured.

Intra- and interspecies variation

Data on the metabolism of 1,2,4-TCB suggest qualitative differences between monkeys and rodents. The uncertainty of possible interspecies variation could justify an increased MOS.

Nature and severity of the effect

The effect described at the "lowest-observed-adverse-effect level" is an effect on liver weight and enzyme induction. Whilst these effects are considered to be potentially reversible, the possibility that the substance could be considered as possibly carcinogenic to humans cannot be excluded. There are also deficiencies in the mutagenicity and the reproductive toxicity tests. There is therefore some concern for the effects caused by the substance, which could justify an increased MOS.

Dose-response relationship

There is no reason to suggest that concerns for a special dose response relationship for this substance should be reflected in the magnitude of the MOS.

Differences in exposure (route, duration, frequency and pattern)

Data are available for setting a NOAEL following oral, dermal and inhalation routes of exposure. The levels at which acute and chronic effects are seen after dermal exposure suggest that the NOAEL following dermal exposure is indeed higher than after the other routes of exposure, even though the study length is shorter than that available for the other two routes of administration.

There is also evidence to suggest that absorption after dermal exposure is lower than after inhalation exposure. The total systemic dose calculated by adding the realistic worst-case inhalation exposure and the realistic worst-case dermal exposure is therefore likely to be an overestimate.

General conclusions for the risk characterisation

The following conclusions are drawn for all the following scenarios considered for both worker and consumer exposures.

Sensitisation

1,2,4-TCB appears to have weak sensitising properties, but is not considered to be a skin sensitiser according to EU classification criteria. In all cases considered below, there is no need for further information or testing or risk reduction measures beyond those which are being applied already **(conclusion (ii)).**

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

Mutagenicity

1,2,4-TCB is not considered to express systemic genotoxic effects *in vivo*. In all cases considered below, there is no need for further information or testing or risk reduction measures beyond those which are being applied already **(conclusion (ii)).**

Carcinogenicity

The substance is not considered to be carcinogenic to humans. However, tumours have been seen in mouse liver and the rat Zymbal gland. It is recognised that it is difficult to draw unequivocal conclusions on the carcinogenicity database, not least due to the increase in tumour incidence in Zymbal's gland tumours in the rat study. However, the data do not support a proposal for classification as a carcinogen. In addition, it is considered unlikely that further testing will lead to a revision of the conclusions for either carcinogenicity or mutagenicity. Since the primary possible concern for a carcinogenic effect is associated with the potential of the substance to cause changes in the liver, the NOAEL for repeated dose toxicity based on an absence of effects on the liver is considered adequate for assessing this end point. For the purposes of this report, a **conclusion (ii)** for this endpoint is made for all scenarios.

Reproductive toxicity

The substance is not considered to be toxic to reproduction. The data on the effects of 1,2,4-TCB is inadequate to establish a LOAEL for reproductive effects. There is therefore no reliable basis on which to establish a MOS. However, a NOAEL for effects on the foetus based on a conservative evaluation is at a level of at least 5 to 10 times the NOAEL chosen for repeated dose toxicity. In all cases considered below, there is no need for further information or testing or risk reduction measures beyond those which are being applied already **(conclusion (ii)).**

4.1.3.2 Workers

General considerations

The exposure conditions that are considered in this risk characterisation have all been described and discussed in Section 4.1.1.2. The exposure routes considered are inhalation and dermal exposure, and the MOS for exposure by each route is considered separately.

In addition, for scenarios with conclusion (ii) for both these exposure routes, the significance of the MOS for total systemic exposure is also considered. The significance of the MOS for total systemic exposure is not however considered where conclusion (iii) has been drawn for either or both of the exposure routes separately, as the possible concerns have already been identified.

4.1.3.2.1 Risk characterisation for the production of 1,2,4-TCB (Scenario Q)

(Scenario Q: Production of 1,2,4-TCB, including storage and handling (i.e. transfer from one container to another), sampling and analysis of quality control samples, cleaning, repair and maintenance of the equipment).

The exposure data for this scenario have been described in Section 4.1.1.2.1. The realistic worst-case values used for the MOS calculations shown below are taken from **Table 4.8**.

Acute toxicity

The acute toxicity data used for the following MOS calculations is taken from Section 4.1.2.2.

Table 4.26 Risk characterisation for the production of 1,2,4-TCB with regard to acute toxicity

Type of work		Inhalation				Dermal			
		Exposure, short-term Mg/m³	LC_{50} mg/m³	MOS	Concl.	Exposure mg/kg/d	LD_{50} mg/kg/d	MOS	Concl.
Q1-Q3	Surveillance	2.9	20,000	$7 \cdot 10^3$	ii	Negligible	6000	-	ii
Q4-Q5	Collection of samples	2.9	20,000	$7 \cdot 10^3$	ii	0.6	6000	$1 \cdot 10^4$	ii
Q6-Q8	Drumming	15	20,000	$1.3 \cdot 10^4$	ii	0.6	6000	$1 \cdot 10^4$	ii

There is no concern for acute toxic effects by inhalation or dermal exposure **(conclusion (ii))**.

Irritation

Eye and respiratory tract, vapours

For scenarios Q1-Q5 the short-term exposure levels are below the levels of 23-37 mg/m³ reported for minimal eye and throat irritation. This endpoint is not of concern **(conclusion (ii))**.

For scenarios Q6-Q8 the short-term exposure levels are about half the levels of 23-37 mg/m³ reported for minimal eye and throat irritation. Although the potential for eye or respiratory tract

irritation cannot be excluded, the evidence for an effect is largely anecdotal. This endpoint is not of concern **(conclusion (ii))**.

Eye, liquid

For scenarios Q1-Q3 there is no significant potential for eye contact. This endpoint is not of concern **(conclusion (ii))**.

For scenarios Q4-Q8, there is a potential for eye contact. Although the substance is not classified as an eye irritant according to the EU criteria, it can have an irritating effect and the use of appropriate PPE is recommended. This endpoint is not of concern **(conclusion (ii))**.

Skin, liquid

For scenarios Q1 to Q3, the potential for skin contact is negligible. This endpoint is not of concern **(conclusion (ii))**.

For scenarios Q4-Q8, the dermal exposure has been calculated to be 0.1 mg/cm^2. The LOAEC for chronic exposure is 0.9. Whilst there is a potential for skin irritation from direct contact during these scenarios, the effect of concern is seen primarily after repeated exposure. The substance is classified as a skin irritant, and the use of appropriate PPE is recommended. This endpoint is not of concern **(conclusion (ii))**.

Repeated dose toxicity

The repeated dose toxicity data used for the following MOS calculations are taken from Section 4.1.2.5 and shown in **Table 4.19**.

Table 4.27 Risk characterisation for the production of 1,2,4-TCB with regard to repeated dose toxicity

Type of work		Inhalation				Dermal, systemic effects			
		Exposure, full shift mg/m^3	NOAEC mg/m^3	MOS	Concl.	Exposure mg/kg/d	NOAEL mg/kg/d	MOS	Concl.
Q1-Q3	Surveillance	0.7	23	33	ii	Negligible	150	-	ii
Q4-Q5	Collection of samples	0.7	23	33	ii	0.6	150	250	ii
Q6-Q8	Drumming	7.4	23	3	iii	0.6	150	250	ii
Type of work		**Total systemic dose**				**Dermal, local effects**			
		Exposure, full shift mg/kg/d	NOAEC Mg/kg/d	MOS	Concl.	Exposure mg/cm^2	LOAEC mg/cm^2	MOS	Concl.
Q1-Q3	Surveillance	0.2	6	30	ii	Negligible	0.9	-	ii
Q4-Q5	Collection of samples	0.8	6	7.5	ii	0.1	0.9	9	ii
Q6-Q8	Drumming	2.6	6	2	iii	0.1	0.9	9	ii

The MOS for inhalation exposure for scenarios Q1 to Q5 is 33. This endpoint is not of concern (**conclusion (ii)**).

The MOS for inhalation exposure for scenarios Q6-Q8 is 3. This endpoint is of concern (**conclusion (iii)**).

The MOS for the scenarios for systemic dermal effects where exposure is not negligible is 250. Even though the actual chronic NOAEL may be lower than the figure used in the calculation of the MOS, this MOS value is considered to be acceptable. This endpoint is not of concern (**conclusion (ii)**).

The MOS for total systemic exposure for scenarios Q1 to Q3 is 30. This endpoint is not of concern (**conclusion (ii)**).

The MOS for total systemic exposure for scenarios Q4-Q5 is 7.5. Since this MOS is based on a total dose calculated by adding the realistic worst-case values for the two exposure routes considered, this value is conservative. The total exposure is largely determined by the dermal exposure, and there is reason to believe that the dermal absorption will be less than 100%. Uncertainties in the evaluation of the MOS are considered to be more related to the estimate of dermal absorption. It is recognised that this MOS is borderline, but is sufficiently conservative to be acceptable. This endpoint is not of concern **(conclusion (ii))**.

For scenarios Q1 to Q3 there is no concern for local dermal effects (**conclusion (ii)**).

The MOS for local dermal effects for scenarios Q4-Q8 is 9. The substance is classified as a skin irritant, and the use of appropriate PPE is recommended. This endpoint is not of concern **(conclusion (ii))**.

Conclusion for the production of 1,2,4 TCB (Scenario Q)

No concerns have been identified for scenarios Q1-Q5 **(conclusion (ii))**.

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.

Concerns have been identified for repeated dose toxicity after inhalation exposure during drumming (scenarios Q6- Q8) **(conclusion (iii))**.

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

4.1.3.2.2 Risk characterisation for the use of 1,2,4-TCB as a pure substance (Scenario R)

The pure substance is used as an intermediate in chemical synthesis, as a dye carrier in the textile industry and a process solvent.

Risk characterisation for the use of 1,2,4-TCB as an intermediate in chemical synthesis (R1-R3)

The exposure data for these scenarios have been described in Section 4.1.1.2.2. The realistic worst-case exposure values used for the MOS calculations shown below are taken from **Table 4.8**.

Acute toxicity

The acute toxicity data used for the following MOS calculations are taken from Section 4.1.2.2.

Table 4.28 Risk characterisation for the use of 1,2,4-TCB as an intermediate in chemical synthesis with regard to acute toxicity

Type of work		Inhalation				Dermal			
		Exposure, short-term mg/m³	LC_{50} mg/m³	MOS	Concl.	Exposure mg/kg/d	LD_{50} mg/kg/d	MOS	Concl.
R1-R3	Loading and collection of samples	4.8	20,000	$4 \cdot 10^3$	ii	0.6	6,000	$1 \cdot 10^4$	ii

There is no concern for acute toxic effects by inhalation or dermal exposure **(conclusion (ii))**.

Irritation

- Eye and respiratory tract, vapours

For scenarios R1-R3 the short-term exposure levels are below the levels of 23-37 mg/m^3 reported for minimal eye and throat irritation. This endpoint is not of concern **(conclusion (ii))**.

- Eye, liquid

There is a potential for eye contact in these scenarios. Although the substance is not classified as an eye irritant according to the EU criteria, it can have an irritating effect and the use of appropriate PPE is recommended. This endpoint is not of concern **(conclusion (ii))**.

- Skin, liquid

For scenarios R1-R3, the dermal exposure has been calculated to be 0.1 mg/cm^2. The LOAEC for chronic exposure is 0.9. Whilst there is a potential for skin irritation from direct contact during these scenarios, this is seen primarily after repeated exposure. The substance is classified as a skin irritant, and the use of appropriate PPE is recommended. This endpoint is not of concern **(conclusion (ii))**.

Repeated dose toxicity

The repeated dose toxicity data used for the following MOS calculations are taken from Section 4.1.2.5 (shown in **Table 4.19**).

Table 4.29 Risk characterisation for the use of 1,2,4-TCB as an intermediate in chemical synthesis with regard to repeated dose toxicity

Type of work		Inhalation				Dermal, systemic effects			
		Exposure, full shift mg/m³	NOEAC mg/m³	MOS	Concl.	Exposure mg/kg/d	NOEAL mg/kg/d	MOS	Concl.
R1-R3	Loading and collection of samples	0.7	23	33	ii	0.6	150	250	ii
Type of work		**Total systemic dose**				**Dermal, local effects**			
		Exposure, full shift mg/kg/d	**NOEAC mg/kg/d**	**MOS**	**Concl.**	**Exposure mg/cm²**	**LOEAC mg/cm²**	**MOS**	**Concl.**
R1-R3	Loading and collection of samples	0.8	6	7.5	ii	0.1	0.9	9	ii

The MOS for inhalation exposure is 33. This endpoint is not of concern (**conclusion (ii)**).

The MOS for systemic dermal effects is 250. Even though the actual chronic NOAEL may be lower than the figure used in the calculation of the MOS, these scenarios are not considered to be of concern (**conclusion (ii)**).

The MOS for total systemic dose is 7.5. Since this MOS is based on a total dose calculated by adding the realistic worst-case values for the two exposure routes considered, this value is conservative. The total exposure is largely determined by the dermal exposure, and there is reason to believe that the dermal absorption will be less than 100%. Uncertainties in the evaluation of the MOS are considered to be more related to the estimate of dermal absorption. Whilst the value for this MOS is borderline, for these scenarios the MOS is not considered to be of concern **(conclusion (ii))**.

The MOS for local dermal effects is 9. The substance is classified as a skin irritant, and the use of appropriate PPE is recommended. This endpoint is not of concern **(conclusion (ii))**.

Risk characterisation for the use of 1,2,4-TCB as a dye carrier (R4) and as a process solvent (R5)

No information has been provided by Industry on the use of 1,2,4-TCB as a dye carrier or as a process solvent. However, exposures may occur during filling of 1,2,4-TCB or 1,2,4-TCB containing dyes into a closed system. A risk characterisation of this type of work has been described above in the sections on the use of 1,2,4-TCB as an intermediate in chemical synthesis (R1-R3), for which no concerns have been identified.

Other related operations (e.g. further processing of textiles) are not necessarily carried out in closed systems and may lead to considerable exposures, but no information is available describing these operations. No useful risk characterisation can be carried out for these additional processes, since further information is necessary to estimate the occupational exposure **(conclusion (i))**.

Conclusion for the use of 1,2,4 TCB (Scenario R)

No concerns have been identified for scenarios R1 to R3 **(conclusion (ii))**.

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.

No information is available for the use of 1,2,4-TCB as a dye carrier (scenario R4) or as a process solvent (scenario R5), and no risk characterisation has been carried out for these processes. Further information is necessary to estimate the occupational exposure during these operations **(conclusion (i))**.

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

4.1.3.2.3 Risk characterisation for the production of products containing 1,2,4-TCB (Scenario S)

1,2,4-TCB has been used as a constituent in dielectric fluids in transformers. In addition, certain anticorrosive paints, rust removers, cooling agents, lubricants polishes and maintenance products contain 1,2,4-TCB according to the Nordic Product Registers.

Risk characterisation for the production of products containing 1,2,4-TCB (S1-S3)

The exposure data for these scenarios has been described in Section 4.1.1.2.3. The realistic worst-case exposure values used for the MOS calculations shown below are taken from **Table 4.8**.

Acute toxicity

The acute toxicity data used for the following MOS calculations are taken from Section 4.1.2.2.

Table 4.30 Risk characterisation for the production of 1,2,4-TCB containing products with regard to acute toxicity

Type of work		Inhalation				Dermal			
		Exposure, short-term mg/m³	LC_{50} mg/m³	MOS	Concl.	Exposure mg/kg	LD_{50} mg/kg	MOS	Concl.
S1	Pre-dispersion on high speed dissolver	30	20,000	667	ii	0.6	6,000	$1 \cdot 10^4$	ii
S2	Dispersion on pearl mill	1.4	20,000	$1.4 \cdot 10^4$	ii	0.1	6,000	$6 \cdot 10^4$	ii
S3	Canning of paint	1.4	20,000	$1.4 \cdot 10^4$	ii	0.1	6,000	$6 \cdot 10^4$	ii
S4	Production of dielectric fluids	No information				No information			

There is no concern for acute toxic effects by inhalation or dermal exposure **(conclusion (ii))**.

Irritation

- Eye and respiratory tract, vapours

For scenario S1, the calculated short-term exposure levels are roughly the same as the levels of 23-37 mg/m^3 reported for minimal eye and throat irritation. The potential for eye or respiratory tract irritation cannot be excluded, and, even though the evidence for an effect is largely anecdotal, this endpoint is considered to be of concern **(conclusion (iii))**.

For scenarios S2 and S3 (dispersion on pearl mill and canning of paint) the short-term exposure levels are below the levels of 23-37 mg/m^3 reported for minimal eye and throat irritation. This endpoint is not of concern **(conclusion (ii))**.

- Eye, liquid

There is a potential for eye contact in these scenarios. Although the substance is not classified as an eye irritant according to the EU criteria, it can have an irritating effect and the use of appropriate PPE is recommended. This endpoint is not of concern **(conclusion (ii))**.

- Skin, liquid

For scenario S1, the dermal exposure has been calculated to be 0.1 mg/cm^2. The LOAEC for chronic exposure is 0.9. Whilst there is a potential for skin irritation from direct contact during these scenarios, this is seen primarily after repeated exposure. The substance is classified as a skin irritant, and the use of appropriate PPE is recommended. This endpoint is not of concern **(conclusion (ii))**.

For scenarios S2 and S3, the dermal exposure has been calculated to be 0.01 mg/cm^2. This endpoint is not of concern **(conclusion (ii))**.

Repeated dose toxicity

The repeated dose toxicity data used for the following MOS calculations are taken from Section 4.1.2.5 and shown in **Table 4.19**.

Table 4.31 Risk assessment for the production of 1,2,4-TCB containing products with regard to repeated dose toxicity

Type of work		Inhalation				Dermal, systemic effects			
		Exposure, full shift mg/m³	NOAEC mg/m³	MOS	Concl.	Exposure mg/kg/d	NOAEL mg/kg/d	MOS	Concl.
S1	Pre-dispersion on high speed dissolver	14.8	23	1.5	**iii**	0.6	150	250	ii
S2	Dispersion on pearl mill	0.7	23	33	ii	0.1	150	1,500	ii
S3	Canning of paint	0.7	23	33	ii	0.1	150	1,500	ii
Type of work		**Total systemic dose**				**Dermal, local effects**			
		Exposure, full shift mg/kg/d	**NOAEC mg/kg/d**	**MOS**	**Concl.**	**Exposure mg/cm²**	**LOAEC mg/cm²**	**MOS**	**Concl.**
S1	Pre-dispersion on high speed dissolver	4.7	6	1.3	**iii**	0.1	0.9	9	ii
S2	Dispersion on pearl mill	0.3	6	20	ii	0.01	0.9	90	ii
S3	Canning of paint	0.3	6	20	ii	0.01	0.9	90	ii

The MOS for inhalation exposure for scenario S1 is 1.5. The endpoint is of concern (**conclusion (iii)**).

The MOS for inhalation exposure for scenarios S2 and S3 is 33. The endpoint is not of concern (**conclusion (ii)**).

The MOS for systemic dermal effects for scenario S1 is 250. Even though the actual chronic NOAEL may be lower than the figure used in the calculation of the MOS, these scenarios are not considered to be of concern (**conclusion (ii)**).

The MOS for systemic dermal effects for scenarios S2 and S3 is 1,500. The endpoint is not of concern (**conclusion (ii)**).

The MOS for total systemic dose for scenarios S2 and S3 is 20. The endpoint is not considered to be of concern (**conclusion (ii)**).

The MOS for local dermal effects for scenario S1 is 9. The substance is classified as a skin irritant, and the use of appropriate PPE is recommended. This endpoint is not of concern **(conclusion (ii))**.

The MOS for local dermal effects for scenarios S2 and S3 is 90. The endpoint is not considered to be of concern (**conclusion (ii)**).

Risk characterisation for the production of dielectric fluids (S4)

Information on the use of 1,2,4-TCB in dielectric fluids has been supplied by the industry in addition to other information available. The 1981 US EPA Exposure and Risk Assessment for 1,2,4-TCB contains information about this use of the substance, which at the time represented a significant use of the substance. Because of present EU and national legislation regarding

destruction of PCB and other chlorinated compounds in dielectrical fluids in electrical equipment it can be foreseen that the future level of environmental release of 1,2,4-TCB from this source will decrease significantly in the EU.

However, in order to make a formal evaluation of risk, further information on occupational exposure during the production of dielectric fluids is necessary **(conclusion (i)).**

Conclusion for the production of products containing 1,2,4 TCB (Scenario S)

Concerns have been identified for repeated dose toxicity for inhalation exposure and for eye and respiratory tract irritation for scenario S1 (Pre-dispersion on high speed dissolver) **(conclusion (iii))**.

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

No concerns have been identified for scenarios S2 and S3 (Dispersion on pearl mill and canning of paint) **(conclusion (ii))**.

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.

In order to make a formal evaluation of risk, further information on occupational exposure during the production of dielectric fluids is necessary **(conclusion (i)).**

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

4.1.3.2.4 Risk characterisation for the use of 1,2,4-TCB containing products (Scenario T)

(Scenario T: 1,2,4-TCB exposure during the use of 1,2,4-TCB containing products (occupational exposure), cleaning, repair and maintenance of equipment).

In order to make a formal evaluation of the risk, further information on occupational exposure during the production of dielectric fluids is necessary **(conclusion (i)).** The exposure data for these scenarios have been described in Section 4.1.1.2.4. The realistic worst-case exposure values used for the MOS calculations shown below are taken from **Table 4.8**.

For scenario T4 (Production of wire and cabling) only very limited information is available on occupational exposure and further information is necessary in order to make a formal risk characterisation **(conclusion (i))**.

Acute toxicity

The acute toxicity data used for the following MOS calculations are taken from Section 4.1.2.2.

Table 4.32 Risk characterisation for the occupational use of 1,2,4-TCB containing products with regard to acute toxicity

Type of work		Inhalation				Dermal			
		Exposure, short-term mg/m³	LC_{50} mg/m³	MOS	Concl.	Exposure mg/kg	LD_{50} mg/kg	MOS	Concl.
T1	Dismantling transformers	1.4	20,000	$1.4 \cdot 10^4$	ii	6	6,000	$1 \cdot 10^3$	ii
T2	Spray painting	6.6	20,000	$3 \cdot 10^3$	ii	8	6,000	750	ii
T3	Production of plastic pellets	30	20,000	667	ii	Negligible	6,000		ii
T4	Production of wire and cabling	Lack of information				Lack of information			
T5	Polishing	1.4	20,000	$1.4 \cdot 10^4$	ii	3	6,000	$2 \cdot 10^3$	ii

There is no concern for acute toxic effects by inhalation or dermal exposure **(conclusion (ii))**.

Irritation

Eye and respiratory tract, vapours

For scenarios T1, T2 and T5 the short-term exposure levels are below the levels of 23-37 mg/m^3 reported for minimal eye and throat irritation. This endpoint is not of concern **(conclusion (ii))**.

For scenario T3, the short-term exposure levels are roughly the same as the levels of 23-37 mg/m^3 reported for minimal eye and throat irritation. The potential for eye or respiratory tract irritation cannot be excluded, and, even though the evidence for an effect is largely anecdotal, this endpoint is considered to be of concern **(conclusion (iii))**.

Eye, liquid

There is a potential for eye contact in these scenarios. Although the substance is not classified as an eye irritant according to the EU criteria, it can have an irritating effect and the use of appropriate PPE is recommended. This endpoint is not of concern **(conclusion (ii))**.

Skin, liquid

For scenarios T1, T2 and T5 the dermal exposure has been calculated to be 0.4-0.5 mg/cm^2, which is about half the LOAEC for chronic exposure (0.9 mg/cm^2). Whilst there is a potential for skin irritation from direct contact during these scenarios, this is seen primarily after repeated exposure. The substance is classified as a skin irritant, and the use of appropriate PPE is recommended. This endpoint is not of concern **(conclusion (ii))**.

Repeated dose toxicity

The repeated dose toxicity data used for the following MOS calculations are taken from Section 4.1.2.5 and shown in **Table 4.19**.

Table 4.33 Risk assessment for the occupational use of 1,2,4-TCB containing products with regard to repeated dose toxicity

Type of work		Inhalation				Dermal, systemic effects			
		Exposure, full shift mg/m³	NOAEC mg/m³	MOS	Concl.	Exposure mg/kg/d	NOAEL mg/kg/d	MOS	Concl.
T1	Dismantling transformers	0.68	23	34	ii	6	150	25	**iii**
T2	Spray painting	3.3	23	7	**iii**	8	150	19	**iii**
T3	Production of plastic pellets	15.2	23	1.5	**iii**	negligible	150	-	ii
T4	Production of wire and cabling	No information				No information			
T5	Polishing	0.7	23	33	ii	3	150	50	**iii**
Type of work		**Total systemic dose**				**Dermal, local effects**			
		Exposure, full shift mg/kg/d	**NOAEC mg/kg/d**	**MOS**	**Concl.**	**Exposure mg/cm²**	**LOAEC mg/cm²**	**MOS**	**Concl.**
T1	Dismantling transformers	6.2	6	< 1	**iii**	0.5	0.9	1.8	**iii**
T2	Spray painting	8.9	6	< 1	**iii**	0.4	0.9	2.3	**iii**
T3	Production of plastic pellets	4.2	6	1.4	**iii**	Negligible	0.9	-	ii
T4	Production of wire and cabling	No information				No information			
T5	Polishing	3.2	6	1.9	**iii**	0.5	0.9	1.8	**iii**

The MOS for inhalation exposure for scenario T1 and for scenario T5 are 34 and 33, respectively. These endpoints are not of concern (**conclusion (ii)).**

The MOS for inhalation exposure for scenarios T2 and T3 is 7 and 1.5, respectively. These endpoints are of concern (**conclusion (iii)**).

The MOS for systemic dermal exposure for scenarios T1 and T2 are 25 and 19 respectively. The uncertainty concerning the NOAEL for this effect suggests these MOS values may be overestimated. This endpoint is of concern (**conclusion (iii)**).

The potential for dermal exposure for scenario T3 is negligible. The endpoint is not of concern (**conclusion (ii)**).

The MOS for systemic dermal exposure for scenario T5 is 50. The uncertainty concerning the NOAEL for this effect suggests this MOS value may be overestimated, and considered on its own, this could perhaps be considered as acceptable. However, when the total systemic dose is calculated, a low MOS (1.9) is obtained. This MOS is based on a total dose calculated by adding

the realistic worst-case values for the two exposure routes considered, and is a conservative value. The total exposure here is almost exclusively determined by the dermal exposure, and there is reason to believe that the dermal absorption will be less than 100%. Uncertainties in the evaluation of the MOS are considered to be more related to the estimate of dermal absorption. Taking all these factors into account, this endpoint (systemic effects due to dermal exposure) is considered to be of concern (**conclusion (iii)**).

The MOS for local dermal effects for scenario T1, T2 and T5 is close to 2. Irritation is mainly caused by repeated exposure, and the use of appropriate PPE is recommended. However, a MOS of two is considered to be too low which means that this endpoint is of concern **(conclusion (iii))**.

The potential for dermal exposure for scenario T3 is negligible. The endpoint is not of concern (**conclusion (ii)**).

Conclusion for the use of products containing 1,2,4 TCB (Scenarios T1-T5)

Concerns have been identified for repeated dose toxicity for dermal systemic effects and for local dermal effects for scenario T1 (dismantling transformers) **(conclusion (iii))**.

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

Concerns have been identified for repeated dose toxicity for inhalation and for dermal systemic effects and for local dermal effects for scenario T2 (spray painting) **(conclusion (iii))**.

Concerns have been identified for eye and respiratory tract irritation and for repeated dose toxicity for inhalation for scenario T3 (production of plastic pellets) (**conclusion (iii))**.

For scenario T4 (Production of wire and cabling) only very limited information is available on occupational exposure and further information is necessary in order to make a formal risk characterisation **(conclusion (i))**.

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

Concerns have been identified for repeated dose toxicity for dermal systemic effects and for local dermal effects for scenario T5 (polishing) **(conclusion (iii))**.

4.1.3.2.5 Results of the risk characterisation for workers

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

This conclusion is reached in order to make formal risk characterisation for the scenarios R4 (Use of 1,2,4-TCB as a dye carrier), R5 (Use of 1,2,4-TCB as a process solvent), S4 (Production of dielectric fluids), and T4 (Production of wire and cabling) as further information on occupational exposure is necessary.

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.

This conclusion applied for scenarios Q1 – Q5, for scenarios R1 to R3, and for scenarios S2 and S3 (Dispersion on pearl mill and canning of paint).

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 for:

- repeated dose toxicity after inhalation exposure for the production of 1,2,4-TCB (drumming, scenarios Q6-Q8);
- repeated dose toxicity for inhalation exposure and for eye and respiratory tract irritation for the production of products containing 1,2,4-TCB (scenario S1, Pre-dispersion on high speed dissolver);
- repeated dose toxicity for dermal systemic effects and for local dermal effects for scenario T1 (dismantling transformers);
- repeated dose toxicity for inhalation and for dermal systemic effects and for local dermal effects for scenario T2 (spray painting);
- eye and respiratory tract irritation and for repeated dose toxicity for inhalation for scenario T3 (production of plastic pellets);
- repeated dose toxicity for dermal systemic effects and for local dermal effects for scenario T5 (polishing);

4.1.3.3 Consumers

The exposure conditions that are considered in this risk characterisation have all been described and discussed in Section 4.1.1.3.

The exposure routes considered are inhalation and dermal exposure, and the MOS for exposure by each route is considered separately.

Table 4.34 Consumer exposure per event (from Table 4.9)

Type of work		Air mg/m³	Dermal mg/kg bw/event	Dermal mg/cm²	Total systemic dose mg/kg bw/event
U1	Spray painting items	83 [1)]	0.5 [3)]	0.03 [3)]	1.2
U2	Polishing a bicycle	5 [2)]	1.4 [2)]	0.1 [2)]	1.4
U3	Polishing a car	20 [2)]	2.9 [2)]	0.2 [2)]	3.2

1) based on de Pater et al. (1999)
2) USES (1997)
3) based on Marquart et al. (1999) and Lansink et al. (1998)

Acute toxicity

There is no concern for acute toxic effects by inhalation (LC_{50} > 20 mg/l) or dermal exposure for any of the three scenarios **(conclusion (ii))**.

Irritation

Eye and respiratory tract, vapours

There is a potential for eye/respiratory tract irritation in scenario U1 as the levels of exposure are well above the levels of 23-37 mg/m^3 reported for minimal eye and throat irritation, even though the evidence for the effect is anecdotal. This endpoint is of concern (**conclusion (iii)**).

The potential for eye/respiratory tract irritation in scenario U2 is at least 5 times lower than the levels of 23-37 mg/m^3 reported for minimal eye and throat irritation. The evidence for the effect is anecdotal, and the exposure levels that have been calculated are based on work in a closed area. On this basis, this endpoint is not considered to be of concern (**conclusion (ii)**).

There is a potential for eye/respiratory tract irritation in scenario U3 as the levels of exposure are close to the levels of 23-37 mg/m^3 reported for minimal eye and throat irritation, even though the evidence for the effect is anecdotal. This endpoint is of concern (**conclusion (iii)**).

It should be noted that the risk assessment of professional use leads to a conclusion (iii) for similar scenarios.

Eye and skin, liquid

There is a potential for eye and skin irritation from direct contact. However, this is not of concern due to the fact that the content of 1,2,4-TCB in the products are relatively low (1-10%). Moreover, the concern for skin irritation is primarily after repeated exposure. It is unlikely that single exposures at weekly intervals in practice would lead to skin irritation **(conclusion (ii))**.

Repeated dose toxicity

Table 4.35 Consumer exposure per day for repeated dose exposure (from Table 4.10)

Type of work		Air mg/m^3	Inhalation mg/kg bw/d	Dermal mg/kg bw/day	Total systemic dose mg/kg bw/day
U1	Spray painting items	83 [1)]	0.1 [1)]	0.08 [3)]	0.18
U2	Polishing a bicycle	5 [2)]	0.005 [2)]	0.2 [2)]	0.2
U3	Polishing a car	20 [2)]	0.02 [2)]	0.2 [2)]	0.2

1) based on de Pater et al. (1999)
2) EUSES (1997)
3) based on Marquart et al. (1999) and Lansink et al. (1998)

The table above shows the estimated chronic doses for the three scenarios which have been carried out using the assumptions shown in the section on consumer exposure.

Whilst the dose per event can be calculated with reasonable confidence (see **Table 4.9** and **Table 4.34**), it is difficult to predict the more long-term use patterns for these three scenarios for consumers with any certainty. Whilst for some consumers this type of use may be highly infrequent, for others, the use pattern may more closely resemble that of a professional user.

The predicted doses per event (**Table 4.34**) would lead to an entirely unacceptable MOS (<2-5 for total systemic dose) for consumers if the consumer pattern of use is in any way similar to the

assumed occupational exposure. The MOS calculated for the consumer exposure frequency pattern described in **Table 4.35** range from 60-1,200 for inhalation exposure, 750-1,875 for dermal exposure and 30-33 for total systemic dose.

The acceptability of the MOS for these consumer applications of 1,2,4-TCB containing products depends on the assumptions made about the frequency of use. The basis for the choice of these scenarios is an assumption that 1,2,4-TCB containing products of this type are on the market, and that they are used by consumers as well as by professionals. The conclusion for professional use of these products is conclusion (iii).

The same conclusion is therefore drawn for consumers (**conclusion (iii)**).

Results of the risk characterisation for consumer exposure to products containing 1,2,4-TCB

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

4.1.3.4 Humans exposed via the environment

According to the EUSES estimations (see Section 4.1.1.4) the values for the total human intake of 1,2,4-TCB for the local scenario range from 0.00118 mg/kg bw/d to 0.0715 mg/kg bw/d depending on the release/use category etc.

Table 4.36 Estimated human intake of 1,2,4-TCB in mg/kg bw/d from local scenarios of EUSES

Scenario	Total intake	MOS
Production (Site A)	0.00118	5,084
Production (Site B)	0.00127	4,724
Industrial Intermediate (scenario D1): processing	0.0715	84
Process solvent (scenario D2):formulation	0.0415	145
Minor uses (scenario D3): processing	0.0206	291
Dye carrier (scenario D4): processing	0.031	194

The calculated margin of safety for total exposure of humans via the environment for local production scenarios is approximately 5,000 based on the NOAEL for repeated dose toxicity of 6 mg/kg bw/d. For local use scenarios, the MOS ranges from 84 to 291 for the different scenarios.

The UK MAFF has calculated the estimated dietary intake of 1,2,4-TCB based on the average concentrations measured in the 1995 survey (UK MAFF, 1998). The average dietary intake has an upper bound of 0.48 μg/person/day and a lower bound of 0.04 μg/person/day. For a high level dietary intake the comparable figures are 1.3 and 0.09 μg/person/day. The UK report compares these figures directly with the WHO (WHO, 1991) TDI of 1,200 μg/person/day.

In the TDI set by WHO in 1991, the TDI was based on a NOAEL of 7.8 mg/kg bw/d using an uncertainty factor of 500 (Table 26 in WHO, 1991). In the TDI set by WHO in 1993, an uncertainty factor of 1,000 (100 for inter- and intraspecies variation and 10 for short duration of study) was applied to the NOAEL of 7.7 mg/kg bw/d for liver toxicity identified in the Côté et

al. (1988) 13-week rat study (WHO, 1993). It should be noted that whilst the NOAEL used in this report (6 mg/kg bw/d) is similar to the NOAEL used by WHO (7.7 mg/kg bw/d) the former figure is derived from a two-year study.

The calculated exposures in the local use scenarios range from 1 to 70 μg/kg bw/d. These figures should be compared with the TDI recommended by WHO (1991) of 20 μg/kg bw/d or 7.7 μg/kg bw/d (WHO, 1993).

This conclusion, that there is some concern for indirect exposure from these processes, is largely a result of the predicted intake from, in particular, root crops. It should be noted that in the MOS calculations shown above, much of the intake is assumed to be from fish and root crops, food sources which according to the UK results do not contribute significantly to the intake from food sources. Measured values for meat and milk suggest that these values could be underestimated. In addition, it is unclear whether the presence of 1,2,4-TCB in the environment is a general phenomenon, rather than a result of specific uses of the substance.

In a recent modelling assessment of the environmental fate of chlorobenzenes in Canada employing a Mackay III model of Southern Ontario, it is concluded that for 1,2,4-TCB there is no concern for humans exposed indirectly via the environment (MacLeod and Mackay, 1999). Even though this conclusion may be of general interest it is difficult to compare the monitoring data and model estimations and the concern level for man of MacLeod and Mackay (1999) with the equivalent values in this report because of differences in the employed monitoring values, model input parameters of 1,2,4-TCB, model settings and TDI or NOAEL.

WHO (1993) recommends a TDI for trichlorobenzenes (total, all three isomers) of 7.7 μg/kg body weight by applying an uncertainty factor of 1,000. The guideline value would be 20 μg/l (rounded figure) for each isomer based on an allowance of 10% of the TDI to drinking-water. However, because of the similarity in the toxicity of the TCB isomers, a guideline value of 20 μg/l is proposed for total TCBs. This figure exceeds the lowest reported odour threshold in water.

The drinking-water concentrations (see **Table 4.12**) calculated for all local processing scenarios using EUSES range from 25 to 122 μg/l. These concentrations exceed both the odour threshold of 5-30 μg/l, the taste threshold of 30 μg/l and the recommended WHO guideline value of 20 μg/l.

In drawing the conclusion shown below it is recognised that

- the TDI set by WHO (1993) may be over conservative, in that an extra uncertainty factor of 10 has been included to reflect the short-term nature of the study; this extra factor would not be required on the basis of the database reviewed here,
- the food sources of concern identified by the EUSES calculations are mainly root crops; the available data suggest that these are not likely to be a major source of 1,2,4-TCB intake,
- odour and taste thresholds can vary considerably from individual to individual and that the calculated drinking water concentrations are worst-case assumptions.

However daily exposures that exceed WHO recommended TDI values for dietary intake or drinking water concentrations are not considered acceptable.

Results of the risk characterisation for 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.

There is concern that the TDIs set by WHO (1991, 1993) may be exceeded for indirect exposure via the environment for certain local use scenarios. There is also concern for the concentrations of 1,2,4-TCB in drinking water for these local use scenarios (scenarios D1 to D4).

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

4.2.1 Exposure assessment

See Section 4.1.1.

4.2.2 Effects assessment

Explosivity

1,2,4-TCB has no explosive properties.

Flammability

1,2,4-TCB has a flash point of 110°C, and the auto flammability temperature is >500°C, therefore it is not considered flammable.

Oxidising potential

1,2,4-TCB has no oxidising properties.

4.2.3 Risk characterisation

There is no reason for concern with respect to the physico-chemical properties of 1,2,4-TCB.

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.

5 RESULTS

5.1 ENVIRONMENT

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.

This conclusion applies to production by the main manufacturers and for atmosphere.

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 is reached because of:

- concerns for effects on the aquatic ecosystem and terrestrial ecosystem as a consequence of exposure arising from the use of the substance as a dye carrier and other uses;
- concerns for sewage treatment plants as a consequence of exposure arising from use as an intermediate, as well as from the use sectors of basic chemicals as a solvent, textile industry as dye carrier and other downstream uses.

Risk reduction measures should be considered that will ensure a reduction in the levels of 1,2,4-trichlorobenzene (1,2,4-TCB) found in the environment. Risk reduction measures in relation to downstream open use resulting in environmental exposure is indicated because of risks identified for STP and soil receiving sludge from STPs. This conclusion is supported by the identified risks to the aquatic environment (including the sediment compartment) in relation to use of the substance as a dye carrier and for "other" downstream uses.

The risk indicated above were identified by employing generic release and exposure scenarios because of lack of specific information of the possible open use and subsequent environmental release of the substance. Recent environmental monitoring data however indicate that such uses and environmental releases may still occur in the EU.

The risk assessment indicates that it should be further investigated if the substance should be considered in relation to national or international programmes addressing persistent organic pollutants.

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.

This conclusion is reached because of:

- concerns for general systemic toxicity as a consequence of repeated inhalation exposure arising from drumming activities in the production of the substance, from the production of products containing the substance in the sector of pigment production and from the use of products containing the substance in the sector of spray painting;
- concerns for eye and respiratory tract irritation as a consequence of repeated exposure to the vapour of the substance arising from the production of products containing the substance in the sector of pigment production and from the use of products containing the substance in the sector of production of plastic pellets;
- concerns for general systemic toxicity and local dermal effects as a consequence of repeated dermal exposure arising from the use of the products containing the substance in the sectors of spray painting, dismantling transformers and polishing.

Adverse effects due to eye/respiratory tract irritation and due to repeated dose toxicity after inhalation and dermal exposure cannot be excluded for workers. Risk reduction measures should therefore be considered that will ensure a reduction in the levels of 1,2,4-TCB found in the workplace during the production of 1,2,4-TCB, the production of 1,2,4-TCB containing products, and the use of products containing 1,2,4-TCB.

Irritating effects on skin after repeated dermal exposure cannot be excluded for workers using 1,2,4-TCB containing products. Proper use of personal protective equipment (PPE) should be recommended.

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

This conclusion is reached because of:

- concerns for effects as a consequence of exposure.

The information and/or test requirements are

- information on occupational exposure during the use of the substance as a dye carrier and as a process solvent, during production of products containing the substance in the sector of production of dielectric fluids and during the use of products containing the substance in the sector of production of wire and cabling.

The need to actually obtain the information allowing the performance of the risk characterisation will be considered when the recommended risk reduction strategy is published in the Official Journal.

In order to make a formal risk characterisation for the scenarios R4 (Use of 1,2,4-TCB as a dye carrier), R5 (Use of 1,2,4-TCB as a process solvent), S4 (Production of dielectric fluids) and T4 (Production of wire and cabling) further information on occupational exposure is necessary.

The actual need to obtain this information allowing the performance of the risk characterisation for these scenarios (R4, R5, S4, and T4) will be considered when the risk reduction strategy is addressed. Hence, any formal request for further information on these processes should be seen in the light of other possible risk reduction measures for these scenarios based on concerns identified elsewhere in this report.

5.2.1.2 Consumers

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 is reached because of:

- concerns for eye and respiratory tract irritation as a consequence of repeated exposure to vapours and general systemic toxicity as a consequence of repeated inhalation and dermal exposure arising from spray painting and car polishing.

For consumers, adverse effects due to inhalation and dermal exposure cannot be excluded. Risk reduction measures should therefore be considered that will ensure a reduction in the levels of 1,2,4-TCB found during use of products containing 1,2,4-TCB (anti-corrosive paint and maintenance products). However, this conclusion should be seen in the light of a) the products concerned are almost certainly identical to those used by workers, b) for some consumers the use of these products may be highly infrequent, while for others, the use pattern may more closely resemble that of a professional user, and c) it is uncertain whether these products are in fact used at all by consumers.

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.

This conclusion is reached because:

- concerns for indirect exposure as calculated exposures can exceed WHO TDIs, and WHO guideline values in drinking water for local use scenarios.

5.2.2 Human health (risks from physico-chemical properties)

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

This conclusion is reached because:

- the risk assessment shows that risks are not expected. Risk reduction measures already being applied are considered sufficient.

6 REFERENCES

Aarhus Amt (1998). "Miljøfremmede stoffer i Århus Amt Fase 2 og 3, 1997-98", Århus Amt natur og Miljø, sept. 1998.

ACGIH (1991). Documentation of the threshold values and biological exposure limits. Sixth Edition. American Conference of Governmental Industrial Hygienists Inc. Cincinnati, Ohio.

AEA/CS/RCEC 16419225 Issue 2 (1995). "Selection criteria for prioritising persistent organic pollutants". Report prepared by the Department of the Environment, Air Quality Division, by AERA Technology, UK, May 1995.

AEA/RCEC 16419225/2 Issue 2 (1995). Draft proposal procedure for incorporating new substances into the UNECE protocol on long atmospheric transport of persistent organic pollutants" Report prepared by the Department of the Environment, Air Quality Division, by AERA Technology, UK, May 1995.

Aldenberg T, Slob W, Knoop JM (1990). Three methods for estimating ecotoxicological protection levels from NOEC toxicity data. RIVM, Bilthoven, the Netherlands.

Akermark B, Baeckström P, Westlin UE, Göthe R, Wachtmeister CA (1976). Photochemical dechlorination of 1,2,4-trichlorobenzene. Acta Chem. Scand. B 30, 49-52.

Amoore JE, Hautala E (1983). Odor as an aid to chemical safety: Odor thresholds compared with threshold limits values and volatilities for 214 industrial chemicals in air and water dilution. J. Appl. Toxicol. 3, 272-290.

AOPWIN (1995). Atmospheric oxidation program for Microsoft Windows 3.1 (AOPWIN) prepared by Meylan W and Howard P, Syracuse Research Corporation, Merrill Lane, Syracuse, NY.

Arbeitsgemeinschaft für die Reinhaltung der Elbe (1994). Wassergütedaten der Elbe von Schmilkas bis zur See. Zahlentafel 1993. Arbeitsgemeinschaft für die Reinhaltung der Elbe, Nov. 1994.

Arendt G, Haag F, Pruggmayer D (1977). Mainwasseruntersuchungen. Bericht zum Auftrag 198-13. Batelle Institute, Frankfurt am Main.

Ariyoshi T, Ideguchi K, Iwasaki K, Arakaki M (1975). Relationship between chemical structure and activity. III. Dose-response or time-course of induction in microsomal enzymes following treatment with 1,2,4-trichlorobenzene. Chem. Pharm. Bull. 23, 831-836.

ARW (1984). Organische Spurenstoffe im Rhein und bei der Trinkwasseraufbereitung. Teil 5 in: 41. Bericht der Arbeitsgemeinschaft Rhein-Wasserwerke E.V. p.177-190, Dez. 1984.

ARW (1985). 42. Bericht der Arbeitsgemeinschaft Rhein-Wasserwerke E.V. p.35-37, 115-119, Dez. 1985.

ARW (1986). 43. Bericht der Arbeitsgemeinschaft Rhein-Wasserwerke E.V. p.34-37, 77-90, 1986.

Ashworth RA, Howe GB, Mullins ME, Rogers TN (1988). Air-water partitioning coefficients of organics in dilute aqueous solutions. J. Haz. Mater. 18, 25-36.

Atkinson R et al. (1985). Environ. Sci. Technol. 19, 87-89.

Atri FR (1986). Chlorierte Kohlenwasserstoffe in der Umwelt IV. Schriftenreihe des Vereins für Wasser, Boden- und Lufthygiene 70. Gustav Fischer Verl. Stuttgart, Germany 1986.

Bakke JE, Huwe JK, Mulford DJ, Bergman Å (1992). Metabolism of 1,2,4-trichlorobenzene in rats: examination of thiol formation. Xenobiotica, 22, 199-210.

Ballhorn L, Freitag D, Geyer H, Quast I, Rott B, Scheunert I, Spieser h, Vishwanathan R (1984). Überprüfung der Durchführbarkeit von Prüfungsvorschriften und der Aussagekraft der Stufe I und II des E. Chem. G. Umweltforschungsplan des Bundesministeriums des Innern. Chemikalien, Forschungsbericht 106 04 011/02. 1984.

Banerjee S (1984). Solubility of organic mixtures in water. Environ. Sci. Technol., 18, 587-591.

Banerjee P, Piwoni MD, Ebeid K (1985). Sorption of organic contaminants to a low carbon subsurface core. Chemosphere 14(8), 1057-1067.

Bayer (1980). Löser E. Trichlorbenzol S. Untersuchung zur akuten oralen Toxizität an männlichen und weiblichen Wistar-Ratten, 24.11.1980.

Bayer (1982). Bomhard E, 1,2,4-Trichlorobenzol. Untersuchung zur akuten oralen Toxizität an männlichen und weiblichen Wistar-Ratten. Bayer, Institut für Toxikologie, 26.01.1982.

Bayer (1986). Bayer Interne Messungen 1986.

Bayer (1994). Internal lab. Report,

Bayer (1995). Steffens, Bayer AG, Leverkusen, Germany: letter of 1995-11-15.

Bayer (1996). 1,2,4-Trichlorobenzene (CAS No: 120-82-1). Description of hazard potentials and risks for the North Sea. Bayer, February 1996.

Bayer (1996). Risk assessment report on 1,2,4-trichlorobenzene. Draft June 1996. Bayer AG.

Bayer (1998a). Finzenhagen, M, Bayer AG; letter of 10th August, 1998.

Bayer (1998b). Stock. EU risk assessment on 1,2,4-Trichlorobenzene.

BASF (1966). Fax to the Danish Environmental Protection Agency, 9th October1996.

Bengtsson BE, Tarkpea M (1983). The acute aquatic toxicity of some substances carried by ships. Mar. Pollut. Bull. 14, 213-214.

den Besten C, Smink MCC, de Vries EJ, van Bladeren PJ (1991). Metabolic Activation of 1,2,4-Trichlorobenzene and Pentachlorobenzene by Rat Liver Microsomes: A Major Role for Quinone Metabolites. Toxicol. Appl. Pharmacol., 108, 223-233.

Beurskens JEM, Winkels HJ, de Wolf J, Dekker CGC (1994). Trends of priority pollutants in the Rhine during the last fifty years. Water. Sci. Technol., 29(3), 77-85.

Beyer WN (1996). Accumulation of chlorinated benzenes in earthworms. Bull. Environ. Contam. Toxicol., 57, 729-736.

BIA (1998). Bochman, Germany; personal communication.

Bio/dynamics (1987). Project no. 86-3121. A two week palatability study of 1,2,4-trichlorobenzene in rats. May 1, 1987.

Bio/dynamics (1989). Project no. 86-3122. A three months dietary range-finding study of 1,2,4-trichlorobenzene in rats. January 26, 1989.

Bintein S (1999). French Ministry of the Environment. Personal communication.

Black WD, Vally VEO, Ruddick JA, Villeneuve DC (1988). Assessment of Teratogenic Potential of 1,2,3- 1,2,4- and 1,3,5-Trichlorobenzenes in Rats. Bull. Environ. Contam. Toxicol., 41, 719-726.

Blum DJW, Speece RE (1991). A database of chemical toxicity to environmental bacteria and its use in interspecies comparisons and correlations. J. Water Pollut. Control Fed., 63(3), 198-207.

Bobra AM, Shiu Wy, Mackay D (1983). A predictive correlation for the acute toxicity of hydrocarbons and chlorinated hydrocarbons to the water flea (*Daphnia magna*). Chemosphere, 12(9), 1121-1129.

Borneff J, Hartmetz G, Fischer A (1978). Die Belastung von Oberflächenwasser mit Chlorbenzolen. In: Organohalogenverbindungen in der Umwelt. Projektbericht 1975-1978. Kernforschungsanlage Jülich GmbH, Juli 1979.

Bosma TNP, van der Meer JR, Schraa G, Tros ME, Zehnder AJB (1988). Reductive dechlorination of all trichloro- and dichlorobenzene isomers. Microbiol. Ecol., 53, 223-229.

Boyd EM, Meharg AA, Wright J, Killham K (1998). Toxicity of chlorobenzenes to a *lux*-marked terrestrial bacterium, *Pseudominas fluorescens*. Envir. Toxicol. Chem., 17, 2134-2140.

Brinkman DW, Dickson JR (1995). Contaminants in used lubrication oils and their fate during distillation/hydrotreatment re-refining. Environ. Sci. Technol., 29(1), 81-86.

Broderius S, Kahl M (1985). Acute toxicity of organic chemical mixtures to the Fathead minnow. Aquatic Toxicology, 6, 307-322.

Broecker B, Fischer R, Gerber HG, Markert M, Wellens H (1984). Überprüfung der Durchführbarkeit von Prüfungsvorschriften und der Aussagekraft der Stufe I und II des Chemikaliengesetzes. Umweltforschungsplan des Bundesministeriums des Innern. Umweltchemikalien, Forschungsbericht 106 04 011/07.

Brown VKH, Muir C, Thorpe E (1969). The acute toxicity and skin irritant properties of 1,2,4-Trichlorobenzene. Ann. Occup. Hyg., 12, 209-212.

Bruckmann P, Kersten W, Funcke W, Balfanz E, König J, Theisen J, Ball M, Päpke O (1988). The occurrence of chlorinated and other organic trace compounds in urban air. Chemosphere, 17(12), 2363-2380.

Bruckmann P, Kersten W, Hagedorn B, Ball M, Päpke O, Funcke W, Theisen J (1989). Immissionsmessungen halogenierter organischer Verbindungen in Hamburg. VDI Berichte 745, 209-234.

Bruijn J de, Busser F, Seinen W, Hermens J (1989). Determination of octanol/water partitioning coefficients for hydrophobic organic chemicals with the "slow-stirring" method. Environ. Toxicol. Chem., 8, 499-512.

BUA (1987). 1,2,4-Trichlorobenzene. BUA Report 17. GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance (Beratergremium für Umweltrelevante Altstoffe).

Buccafusco RJ, Ells SJ, Leblanc GA (1981). Acute toxicity of priority pollutants to Bluegill (*Lepomis macrochirus*). Bull. Envir. Contam. Toxicol., 26, 446-452.

Buringh E, Lanting R. (1991). Exposure Variability in the Workplace: Its Implication for the Assessment of Compliance. Am. Ind. Hyg. Assoc. J., 52 (1), 6-13.

Burkhard LP, Sheedy BR, McCauley DJ, DeGraeve GM (1997). Bioaccumulation factors for chlorinated benzenes, chlorinated butadienes and hexachloroethane. Environ. Toxicol. Chem., 16(8), 1677-1686.

Calamari D, Galassi S, Setti F, Vighi M (1983). Toxicity of selected chlorobenzenes to aquatic organisms. Chemosphere, 12(2), 253-262.

Callahan MA, Slimak MW, Gabl NW, May JP, Fowler CW, Freed JR, Jennings P, Durfee RL, Whitmore FC, Maestri B, Mabey WR, Holt BR, Gould C (1979). Water related environmental fate of 129 priority pollutants. US Environmental Protection Agency, Dec 1979, EPA 440/4-79-029.

Carlson AR, Kosian PA (1987). Toxicity of chlorinated benzenes to Fathead minnow (*Pimephales promelas*). Arch. Environ. Toxicol., 16, 129-135.

Carlson GP, Tardiff RG (1976). Effect of Chlorinated Benzenes on the Metabolism of Foreign Organic Compounds. Toxicol. Appl. Pharmacol., 36, 383-394.

Carlson GP (1977), Chlorinated benzene induction of porphyria, Experientia (Basel), 33, 1627-1629.

CDN (1993). Priority substances list assessment report. Canadian Government Ottawa/CDN. Ottawa/CDN Publishing Centre Supply and Services Canada, Vol. o.A., VI, 39 p.

CEN (1995). EN 689. European Committee for Standardization. Central Secretariat: Brussels.

Chernoff N, Kavlock RJ (1983). A teratology test system which utilises postnatal growth and viability in the mouse. Environ. Sci. Res., 27, 417-427.

Chessells M, Hawker DW, Connell DW (1991). Critical evaluation of the measurement of the 1-octanol/water partition coefficient of hydrophobic compounds. Chemosphere, 22(12), 1175-1190.

Chiou CT (1985). Partition coefficients of organic compounds in lipid-water systems and correlations with fish bioconcentration factors. Environ. Sci. Technol., 19, 57-62.

Chiou CT, Porter PE, Schmedding DW (1983). Partitioning equilibria of nonionic organic compounds between soil organic matter and water. Environ. Sci. Technol., 17, 227.

Chu I, Murdoch DJ, Villeneuve DC, Viau A (1987). Tissue distribution and elimination of Trichlorobenzenes in the rat. J Environ. Sci. Health, B22, 439-453.

Clark JR, Patrick JM, Moore JC, Lores EM (1987). Waterborne and sediment-source toxicities of six organic chemicals to Grass shrimp (*Palaemonetes pugio*) and amphioxus (*Branchiostoma caribaeum*). Arch. Environ. Contam. Toxicol., 16, 401-407.

Coate WB, Schoenfisch WH, Lewis TR, Busey WM (1977). Chronic, Inhalation Exposure of Rats, Rabbits and Monkeys to 1,2,4-Trichlorobenzene. Arch. Environ. Health, 32, 249-255.

Côté M, Chu I, Villeneuve DC, Secours VE, Valli VE (1988). Trichlorobenzenes: Results of a thirteen week feeding study in the rat. Drug Chem. Toxicol., 11(1), 11-28.

CSTE (1993). The setting of water quality objectives for chemicals dangerous to the aquatic environment - List 1 chemicals - in accordance with European Council Directive 76/464/EEC. EEC Scientific Advisory Committee to Examine the Toxicity and Ecotoxicity of Chemical Compounds (Ecotoxicology Section), CSTE 93/03 XI - Final, December 1993.

Danish EPA (1990). Danmarks udledning af industrielt spildevand. (Danish emission of wastewater.) (In Danish). Miljørapport Nr. 153, Danish Environmental Protection Agency, Copenhagen.

Danish EPA (1998). Results from screening programmes on hazardous substances in the aquatic environment. Examination of 76 organic substances in water from rivers and sediments from lakes, rivers and marine locations in the county of Aarhus in 1997. Examination of 113 organic substances in marine sediments from the South-western part of the inner Danish waters (Little Belt and around Funen) (Summary results by the Danish EPA, Marine Division based on county reports (In Danish). Pers. comm.

Davies D, Mes J (1987). Comparison of the residue levels of some organochlorine compounds in breast milk of the general and indigenous Canadian populations. Bull. Environ. Contam. Toxicol., 39, 743-749.

Deutsche Kommission zur Reinhaltung des Rheins (DKR) (1995). Zahlentafeln der physikalisch-chemischen Untersuchungen 1992. Deutsche Kommission zur Reinhaltung des Rheins, April 1995.

Deutsche Kommission zur Reinhaltung des Rheins (DKR) (1996). Zahlentafeln der physikalisch-chemischen Untersuchungen 1994. Deutsche Kommission zur Reinhaltung des Rheins.

DIPPR (1998). Data Compilation of Pure Compound Properties, Version 6.0. US Department of Commerce. National Institute of Standard and Technology, Gaithersburg.

DMU (1998). Kemiske stoffer i landbruget (Chemical substances in agriculture). DMU Temarapport 19/98 (In Danish). National Environmental Research Institute, Denmark.

Dow Chemical Co. (1938). The toxicity of fluoro-chlorobenzenes. 29.7.1938. NTIS/OTS 84003A Doc. ID 878211365.

Dow Chemical Co. (1958). The results of range finding toxicological tests on 1,2,4-trichlorobenzene. February 24, 1958. NTIS/OTS 84003A Doc. ID 878211091.

Dow Chemical Co. (1980). Technical grade trichlorobenzene. Acute percutaneous absorption potential in rabbits. March 18, 1980. NTIS/OTS 84003A Doc. ID 878211366.

Dow Chemical Co. (1982). 1,2,4-trichlorobenzene (99% pure). Acute percutaneous absorption potential in rabbits. December 20, 1982. NTIS/OTS 84003A Doc. ID 878211092.

DSM (1998). The Netherlands. Personal Communication.

Dulin D, Drossman H, Mill T (1986). Products and quantum yields for photolysis of chloroaromatics in water. Environ. Sci. Technol., 20(1), 72-77.

Dunovant VS, Clark CS, Hee SSQ, Hertzberg VS, Trapp JH (1986). Volatile organics in the wastewater and airspaces of three wastewater treatment plants. Journal Water Pollut. Control. Fed., 58(9), 886-895.

Du Pont de Nemours and Co. (1971a). Inhalation four-hour single exposure. 1st. October, 1971. NTIS/OTS 84003A. Doc. ID 878220476.

Du Pont de Nemours and Co. (1971b). Primary skin irritation and sensitization tests on guinea pigs. NTIS/OTS 84003A. Doc. ID 878220477.

Du Pont de Nemours and Co. (1982). Comparative toxicity of ortho dichlorobenzene (ODCB) and trichlorobenzene (TCB) with cover letter. 3rd December, 1982. NTIS/OTS 84003A. Doc. ID 878220475.

Durham RW, Oliver BG (1983). History of Lake Ontario contamination from the Niagara River by sediment radiodating and chlorinated hydrocarbon analysis. J. Great Lakes Res., 9(2), 160-168.

Eadsforth CV (1986). Application of reverse-phase HPLC for the determination of partition coefficients. Pest. Sci., 17, 311-325.

EASE version 2 (1999). Health and Safety Executive, United Kingdom.

EB.AIR/WG.7/R.3 (1996). Review of the Methodology for Selection of the Initial List of persistent Organic Pollutants (POPs´) for the Proposed UN/ECE Protocol, Report submitted by the United Kingdom, UN Economic and Social Council, 18 June 1996.

EC (1996). Council Directive 96/59/EC of 16. September 1996 on the disposal of polychlorinated biphenyls and polychlorinated terphenyls (PCB/PCT). OJ L243, 24. September 1996, p. 31-35.

EC (1998). Commission Directive 98/98/EC of 15 December 1998 adapting to technical progress for the 25. time Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances. OJ L355, 30. December, 1998. p. 1.

EEA (1997). CORINAIR 94. Summary report. Report to the European Environment Agency from the European Topic Centre on Air Emissions. Final report, April 17, 1997, p. 9-16.

EEC (1980). Council Directive 76/464/EEC on pollution caused by certain dangerous substances discharged into the aquatic environment of the Community. OJ L 129 of 18 May, 1976, p.23.

EEC (1993). Council Regulation (EEC) 793/93 of 23 March 1993 on the evaluation and control of the risks of existing substances. OJ L84, 5. April, 1993, p.1.

Eck JMC van, Koelmans AA, Deneer JW (1997). Uptake and elimination of 1,2,4-trichlorobenzene in the guppy (*Poecilia reticulata*) at sublethal and lethal aqueous concentrations. Chemosphere, 34(11), 2259-2270.

EHIS (2000). Environmental Health Information Service: http://ehis.niehs.nih.gov/ntp/docs/ntp_hcrs.html.

Eida K, Hasumi F, Nisimura N, Kikutani, M (1977). Harderian gland. VI. Effect of chlorinated benzenes on porphyrin biosynthesis in the Harderian Gland of Rat. Chem. Pharm. Bull., 25(6), 1209-1214.

EPIWIN (1995). Estimation programs interface for Microsoft Windows 3.1. By Meylan W, Howard P. Syracuse Research Corporation, Syracuse, NY, November 1995.

Esmen NA, Hammad Y (1977). Log-Normality of Environmental Sampling Data. J. Environ. Sci. Health, A12 (1 and 2), 29-41.

EUSES (1997). The European Union System for the Evaluation of Substances, EUSES, Version 1.00. RIVM (NL) for the European Chemicals Bureau, JRC Environment Institute, Ispra, Italy.

Fängmark I, Strömberg B, Berge N, Rappe C (1994). Influence of postcombustion temperature profiles on the formation of PCDDs, PCDFs, PCBzs, and PCBs in a pilot incinerator. Environ. Sci. Technol., 28(4), 624-629.

Fängmark I, Strömberg B, Berge N, Rappe C (1995). The influence of fly ash load and particle size on the formation of PCDD, PCDF, PCBz and PCB in a pilot incinerator. Waste Management and Research, 13(3), 259-272.

Fathepure BZ, Tiedje JM, Boyd SA (1988). Reductive dechlorination of hexachlorobenzene to tri- and dichlorobenzenes in anaerobic sewage sludge. Appl. Environ. Microbiol., 54, 327-330.

Figueroa IC, Simmons MS (1991). Structure-activity relationships of chlorobenzenes using DNA measurement as a toxicity parameter in algae. Environ. Toxicol. Chem., 10, 323-329.

Fiserova-Bergarova V, Pierce JT, Droz PO, (1990). Dermal Absorption Potential of Industrial Chemicals: Criteria for Skin Notation. Am. J. of Industrial Med., 17, 617-635.

Fitzloff JF, Pan JC (1984). Epoxidation of the lindane metabolite, β-PCCH, by human- and rat-liver microsomes. Xenobiotica, 14, 599-604.

Fooken C, Gihr R, Häckl M, Seel P (1997). Orientierende Messungen gefährlicher Stoffe - Landesweite Untersuchungen auf organische Spurenverunreinigungen in hessischen Fließgewässern, Abwässern und Klärschlämmen 1991 - 1996. Hessische Landesanstalt für Umwelt: Umweltplanung, Arbeits- und Umweltschutz. Heft 233. Wiesbaden 1997. ISBN 3-89026-250-3, 189 pp.

Foster TS, Saha JG (1978). The *in vitro* metabolism of lindane by an enzyme preparation from chicken liver. J. Environ. Sci. Health, B13(1), 25-45.

Fox ME, Carey JH, Oliver BG (1983). Compartmental distribution of organochlorine contaminants in the Niagara river and the Western basin of Lake Ontario. J. Great Lakes Res., 9(2), 287-294.

Freitag D, Ballhorn L, Geyer H, Korte F (1985). Environmental hazard profile of organic chemicals. Chemosphere, 14(10), 1589-1616.

Friege H, Bachhausen P, Leuchs W, Alberti J, Jonke B, Klinke I, Reupert R, Plöger E (1989). Belastung von Klärschlämmen mit organischen Schadstoffen - Untersuchungsergebnisse und Konsequenzen. Vom Wasser, 73, 413-427.

Friesel P, Milde G, Steiner B (1984). Interactions of halogenated hydrocarbons with soil. Fresenius Z. Anal. Chem., 319, 160-164.

Froese KL, Hutzinger O (1996). Polychlorinated benzene and polychlorinated phenol in heterogeneous combustion reactions of ethylene and ethane. Environ. Sci. Technol., 30(3), 1009-1013.

Froese KL, Hutzinger O (1997). Mechanisms of the formation of polychlorinated benzenes and phenols by heterogeneous reactions of C_2 aliphatics. Environ. Sci. Technol., 31(2), 542-547.

Gage JC (1970). The subacute inhalation toxicity of 109 industrial chemicals. Br. J. Ind. Med., 27, 1-18.

Galassi S and Vighi M (1981). Testing toxicity of volatile substances with algae. Chemosphere, 10(19), 1123-1126.

Garrison AW, Hill SW (1972). Organic pollutants from mill persist in downstream waters. Am. Dyestuff Reporter, 21-25, Feb. 1972.

Geiger DL, Brooke LT, Call DJ (eds.) (1990). Acute toxicity of organic chemicals to Fathead minnow (*Pimephales promelas*). Vol.V. Centre for Lake Superior Environmental Studies, University of Wisconsin-Superior.

Geyer H, Politzki G, Freitag D (1984). Prediction of ecotoxicological behaviour of chemicals: Relationship between n-octanol/water partition coefficient and bioaccumulation of organic chemicals by alga *Chlorella*. Chemosphere, 13, 269.

Geyer H, Scheunert I, Korte F (1985). The effects of organic environmental chemicals on the growth of the alga *Scenedesmus subspicatus*: A contribution to environmental biology. Chemosphere, 14 (9), 1355-1369.

Giger W, Molnar-Kubica E, Wakehamm S (1978). Volatile chlorinated hydrocarbons in ground and lake waters. In: Hutzinger O. Aquatic pollutants, transformation and biological effects. Pergamon Press, Oxford, pp. 101-123.

Gomez-Belinchon JI, Grimalt JO, Albaigès (1991). Volatile organic compounds in two polluted rivers in Barcelona (Catalonia, Spain). Water Res., 25(5), 577-589.

Gossett RW, Brown DA, Young DR (1983). Predicting the bioaccumulation of marine compounds in marine organisms using octanol/water partitioning coefficients. Marine Pollut. Bull., 14(10), 387-392.

Götz R (1984). Untersuchungen an Sickerwässern der Mülldeponie Georgswerder in Hamburg (Auswertung der Analysenergebnisse bis einschliesslich 1982). Müll und Abfall, 16(12), 349-356.

Götz R (1985). Polychlorierte Dibenzodioxine (PCDD), polychlorierte Dibenzofuranan (PCDF) und andere toxische Organische Substanzen in Sickerflüssigkeiten der Mülldeponie, Georgswerder/Hamburg. Vom Wasser, 65, 215-228.

Götz R, Schumacher E, Roch K, Specht W, Weeren RD (1990). Chlorierte Kohlenwasserstoffe (CKWs) in Hamburger Hafensedimenten. Vom Wasser, 75, 375-392.

Götz R, Bauer OH, Friesel P, Roch K (1998). Organic trace compounds in the water of the river Elbe near Hamburg. Part I. Chemosphere, 36(9), 2085-2101.

Grüttner H, Jacobsen BN (1994). Miljøfremmede stoffer i renseanlæg (Xenobiotic substances in sewage treatment plants) (In Danish). Miljørapport No. 278, Danish Environmental Protection Agency, Copenhagen.

Grüttner H, Vikelsøe J, Pritzl G (1996). Miljøfremmede stoffer i spildevand og slam (Xenobiotic substances in municipal wastewater and sludge) (In Danish). Miljørapport Nr. 325. Danish Environmental Protection Agency, Copenhagen.

GSF (1982). Überprüfung der Durchführbarkeit von Prüfungsvorschriften und der Aussagekraft der Grundprüfung des ChemG. Bericht eines Seminars 25/26.02.1982, Neuherberg. GSF-Bericht Nr. Ö-714. Gesellschaft für Strahlen- und Umweltforschung GmbH, München, Germany.

Guicherit R, Schulting FL (1985). The occurrence of organic chemicals in the atmosphere of the Netherlands. Sci. Tot. Environ., 43, 193-219.

Haberer K, Drews M (1985). Reinigungswirksamkeit der Uferfiltration an einem stärker belasteten Flussabschnitt. Vom Wasser, 64, 243-267.

Haider K, Jagnow G, Kohnen R, Lim SU (1974). Abbau chlorierter Benzole, Phenole und Cyclohexan-derivate durch Benzol und Phenol-verwertende Bodenbakterien unter aerobe Bedingungen. Arch. Microbiol., 96, 183-200.

Hamburger Umweltberichte (1985). Gewässergütebericht '84. Hamburger Umweltberichte 2/85. Freie und Hansestadt Hamburg.

Hansch and Leo (1985). MEDCHEM Project. Issue No. 26. Claremont, CA. Pomona College.

Harper DJ, Ridgeway IM, Leatherland TM (1992). Concentrations of Hexachlorobenzenes, trichlorobenzenes and chloroform in the waters of the Forth estuary, Scotland. Marine Pollut. Bull., 24(5), 244-249.

Haworth S, Lawlor T, Mortelmans K, Speck W, Zeiger E (1983). Salmonella Mutagenicity Test Results for 250 Chemicals. Environ. Mutagen., Suppl. 1, 3-142.

Heitmüller PT, Clark JR (1989). Bioaccumulation of 1,2,4-trichlorobenzene from food and water sources by spot (*Leiostomus xanthurus*). Aquatic Tox. Hazard Assess. Vol. 12, ASTM STP 1027. Cowgill UM, Williams LR (eds.) American Testing and Materials, Philadelphia, pp. 261-269.

Heitmüller PT, Hollister TA, Parrish PR (1981). Acute toxicity of 54 industrial chemicals to sheepshead minnow (*Cyprinodon variegatus*). Bull. Environ. Contam. Toxicol., 27, 596-604.

Hermens J, Canton H, Janssen P, de Jong R (1984). Quantitative structure-activity relationships and toxicity studies of mixtures of chemicals with anaesthetic potency: Acute lethal and sublethal toxicity to *Daphnia magna*. Aquatic Toxicol., 5, 143-154.

Hermens J, Broekhuyzen E, Canton H, Wegman R (1985). Quantitative structure activity relationships and mixture toxicity studies of alcohols and chlorohydrocarbons: Effects on growth of *Daphnia magna*. Aquatic Toxicol., 6, 209-217.

Herrchen M, Müller M (1997). Selection scheme for substances dangerous to surface waters - second level. Final report. Fraunhofer Institute for Environmental Chemistry and Ecotoxicology, Schmallenberg, Germany.

Herren-Freund SL, Pereira MA (1986). Carcinogenicity of by-products of disinfection in mouse and rat liver. Environmental Health Perspectives, 69, 59-65.

Hiles AH (1989). 13-week toxicity study with 1,2,4-trichlorobenzene in mice. Hazleton Laboratories America, Project no. HLA 6221-104. April 5, 1989.

Holcombe GW, Phipps GL, Sulaiman AH, Hoffman AD (1987). Simultaneous multiple species testing: Acute toxicity of 13 chemicals to 12 diverse freshwater amphibian, fish, and invertebrate families. Arch. Environ. Toxicol., 16, 697-710.

Hooftman RN, de Kreuk JF (1982). Investigation of the environmental load of chlorinated benzenes (Literature study). TNO report CL 81/ 153a.

Howard (1989). Handbook of environmental fate and exposure data for organic chemicals. Vol.1: Large production and priority pollutants. Lewis Publ. Inc. Michigan.

HSE (UK) (1999). Comment on the 1,2,4-TCB RAR, com.ecb4/039/98 Add. 8.

Hulzebos EM, Adema DMM, Dirven-van Breemen EM, Henzen L, van Dis WA, Herbold HA, Hoekstra JA, Baerselman R, van Gestel CAM (1993). Phytotoxicity studies with *Lactuca sativa* in soil and nutrient solution. Environ. Toxicol. Chem., 12, 1079-1094.

IKSR (1991). Zahlentafeln der physikalisch-chemischen Untersuchungen des Rheinwassers und des Schwebstoffes. Internationale Kommission zum Schutze des Rheins, Koblenz.

IKSR (1993). Zahlentafeln der physikalisch-chemischen Untersuchungen des Rheinwassers und des Schwebstoffes. Internationale Kommission zum Schutze des Rheins, Koblenz.

IKSR (1996). Zahlentafeln der physikalisch-chemischen Untersuchungen des Rheinwassers und des Schwebstoffes,1994. Internationale Kommission zum Schutze des Rheins.

IMO (1994). Chlorobenzenes in UK sewage sludges. Paper to the 17th meeting of the scientific group. International Maritime Organisation, 5 July 1994.

INERIS (1994). Inventaire des micropolluants dans les entreprises de la région Rhône-Alpes (draft).

INRI (1998). Vincent. INRI, France. Personal communication.

Ishidate MJr (Ed.) (1987). Chromosome aberration test *in vitro*. L.I.C. Inc., Tokyo.

Ishidate MJr, Harnois MC, Sofuni T (1988). A comparative analysis of data on the clastogenicity of 951 chemical substances tested in mammalian cell cultures. Mutation Res., 195, 151-213.

IUCLID (1996). IUCLID Data sheet. Bayer AG. February 29, 1996.

Jacobs LW, Zabik MJ (1983). Importance of sludge-borne organic chemicals for land application programs. Annu. Madison Conf. Appl. Res. Pract. Munic. Ind. Waste, 6th, pp. 418-426.

Jan J, Malneršic S (1980). Chlorinated residues in fish in Slovenia (Yugoslavia). Bull. Environ. Contam. Toxicol.,24, 824-827.

Jan J (1983a). Chlorobenzene residues in human fat and milk. Bull. Environ. Contam. Toxicol., 30, 595-599.

Jan J (1983b). Chlorobenzene residues in market meat and milk. Mitt. Gebiete Lebensm. Hyg., 74, 420-425.

Japan (1985). Chemicals in the environment. Report on environmental survey and wildlife monitoring in F.Y. 1982 and 1983. Office of Health Studies, Department of Environmental Health, Environment Agency Japan, March 1985.

Jay K, Stieglitz L (1995). Identification and quantification of volatile organic components in emissions of waste incineration plants. Chemosphere, 30(7), 1249-1260.

Jensen KA (1969). Organisk kemi.

Jondorf WR, Parke DV, Williams RT (1955). The metabolism of Halogenobenzenes. 1,2,3-, 1,2,4- and 1,3,5-Trichlorobenzenes. Biochem. Journal, 61, 512-521.

Juuti S, Vartiainen T, Ruuskanen J (1996). Formation of organochlorine compounds in kraft pulp bleaching processes. Chemosphere, 33(12), 2431-2440.

Kato Y, Yamada S, Sato M, Kimura R (1993). Role of 2,3,5-trichlorophenyl methyl sulfone, a metabolite of 1,2,4-trichlorobenzene, in the induction of hepatic microsomal drug-metabolizing enzymes by 1,2,4-trichlorobenzene in rats. Toxicol. Appl. Pharmacol., 122, 214-221.

Kazama M, Yamazoe R, Ito K, Mizuishi K, Nakamura Y, Totani T (1971). Chemical hygiene studies on organic halogen compounds. I. Transfer of chlorobenzenes into hen eggs. Eisei Kenkysho, Tokyo, 23, 93-100.

Kitchin KT, Ebron MT (1983). Maternal hepatic and embryonic effects of 1,2,4-trichlorobenzene in the rat. Environ. Res., 31, 362-373.

Kjølholt J, Andersen HV, Poll C (1995). Forekomst og effekter af miljøfremmede organiske stoffer i spildevandsslam (Occurrence and effects of organic xenobiotics in sewage sludge.) (In Danish). Arbejdsrapport Nr. 15, Danish Environmental Protection Agency, Copenhagen.

Klein W, Herrchen M, Müller M, Storm U, Storm A (1997). Hazard ranking of substances relevant for the aqueous environment. Final report. Fraunhofer Institute for Environmental Chemistry and Ecotoxicology, Schmallenberg, Germany. May 1997.

Knie J, Hälke A, Juhnke I, Schiller W (1983). Ergebnisse der Untersuchungen von chemischen Stoffen mit vier Biotests. Deutsche Gewässerkundliche Mitteilungen, 27(3), 77-79.

Kociba RJ, Leong BKJ, Hefner RE Jr (1981). Subchronic toxicity study of 1,2,4-trichlorobenzene in the rat, rabbit and beagle dog. Drug and Chem. Toxicol., 4(3), 229-249.

Kock AC de, Lord DA (1987). A simple procedure for determining octanol-water partition coefficients using reverse phase high performance liquid chromatography (RPHPLC). Chemosphere, 16(1), 133-142.

Kohli J, Jones D, Safe S (1976). The metabolism of higher chlorinated benzene isomers. Can. J. Biochem., 54(3), 203-208.

Kondo M, Nishihara T, Shimamoto T, Ichikawa T, Fujii M (1988). Screening test for degradation of chemicals in water - Degradation test by photoirradiation. Eisei Kagaku, 34, 41-47.

Könemann H (1981). Quantitative structure-activity relationships in fish toxicity studies. Part 1: Relationships for 50 industrial pollutants. Toxicology, 19, 209-221.

Köneman H, Zelle R, Busser F (1979). Determination of log P_{oct} values of chloro-substituted benzenes, toluenes and anilines by high-performance liquid chromatography on ODS-silica. J. Chromatography, 178, 559-565.

Korte F, Greim H (1981). Ûberprüfung der durchführbarkeit von Prüfungsvorschriften und der Aussagekraft der Grundprüfung des E. Chem. G. Umweltforschungsplan des Umweltministeriums des Innern, Chemikalien, Forschungsbericht 107 04 006/01.

Korte F, Freitag D (1986). Kriterien zur Auswahl umweltgefährlicher alter Stoffe: Mobilität einschliesslich Abbaubarkeit und Akkumulation. Umweltforschungsplan des Umweltministeriums des Innern, Chemikalien, Forschungsbericht 106 05 025.

Kotzias D, Parlar H, Korte F (1982). Photoreaktivität organischer Chemikalien in wässrigen Systemen in Gegenwart von Nitraten und Nitriten. Naturwissenschaften, 69, 444-445.

Kraybill HF (1983). Assessment of human exposure and health risk to environmental contaminants in the atmosphere and water with special reference to cancer. J. Environ. Sci. Health, C1, 175.

Kristensen P, Tørsløv J, Samsøe-Petersen L, Rasmussen JO (1996). Anvendelse af affaldsprodukter til jordbrugsformål (Use of organic waste products for application on farmlands) (In Danish). Miljøprojekt Nr. 328. Danish Environmental Protection Agency.

Kröber B, Häckl M (1989). Bericht über orientierende Messungen auf gefährliche, organische Stoffe in Abwassereinleitungen, Abwasserbehandlungsanlagen und Gewässern in Hessen, 1985-1989. Schriftenreihe Umweltplannung, Arbeits- und Umweltschutz. Heft Nr. 96. Hessische Landesanstalt für Umwelt. 1989.

Krogh PH, Holmstrup M, Jensen J, Petersen SO (1996). Økologisk vurdering af spildevandsslam i landbrugsjord. (Ecological risk assessment of sewage sludge applied to agricultural soil) (In Danish). Arbejdsrapport Nr. 43, Danish Environmental Protection Agency, Copenhagen.

Krogh PH, Holmstrup M, Jensen J, Petersen SO (1997). Ecotoxicological assessment of sewage sludge in agricultural soil. Arbejdsrapport Nr. 69, Danish Environmental Protection Agency, Copenhagen.

Kuntz KW, Warry ND (1983). Chlorinated organic contaminants in water and suspended sediments of the Lower Niagara river. J. Great Lakes Res., 9(2), 241-248.

Kurihara N, Tanaka K, Nakajima M (1979a). Anaerobic metabolism of lindane and related compounds by liver microsomes. Advances in Pesticide Sciences. Plenary Lecture Symposium papers: 4th International Congress of Pesticide Chemistry. Vol. 3, 557-561.

Kurihara N, Yamakawa K, Fujita T, Nakajima M (1979b). Anaerobic degradation of tetra-, penta- and hexachlorocyclohexane isomers by rat liver microsomal P-450. J. Pesticide Sci., 5, 93-100.

Lahaniatis ES, Roas R, Bieniek D, Klein W, Korte F (1981). Bildung von chlorierten organischen Verbindungen bei der Verbrennung von Polyäthylen in Gegenwart von Natriumchlorid. Chemosphere, 10(11/12), 1321-1326.

Lansink CJM, van Hengstum C and Brouwer DH (1998). Dermal exposure due to airless spray painting - a semi-experimental study during spray painting of a container. TNO report V97.1057, Zeist, The Netherlands.

Lawrence HK (1997). Environmental endocrine disrupters. John Wiley and Sons, Inc. New York.

Leblanc GA (1980). Acute toxicity of priority pollutants to water flea (*Daphnia magna*). Bull. Environm. Contam. Toxicol., 24, 684-691.

Lehn (1990). Micronucleus assay in the bone marrow cells of the mouse with trichlorbenzol. CCR project 165600, Cytotest Cell Research GmbH, Rossdrof.

Ligocki MP, Leuenberger C, Pankow JF (1985). Trace organic compounds in rain - II. Gas scavenging of neutral organic compounds. Atmos. Environ., 19, 1609-1617.

Linak WP, Kilgroe JD, McSorley JA, Wendt JOL, Dunn JE (1987). On the occurrence of transient puffs in a rotary kiln incinerator simulator - Part I.: Prototype solid plastic wastes. J. Air Pollut. Control Assoc., 37(1), 54-65.

Lindstrøm AB, Yeowell-O'Connell K, Waidyanatha S, Golding BT, Tornero-Velez R, Rappaport SM (1997). Measurement of benzene oxide in the blood of rats following administration of benzene. Carcinogenesis, 18(8), 1637-41.

Lingg RD, Kaylor WH, Pyle SM, Kopfler FC, Smith CC, Wolfe GF, Cragg S (1982). Comparative Metabolism of 1,2,4-Trichlorobenzene in the Rat and Rhesus Monkey. Drug Metabol. Disp., 10(2), 134-141.

Lord KA, Briggs GG, Neale MC, Manlove R (1980). Uptake of pesticides from water and soil by earthworms. Pestic. Sci., 11, 401-408.

LUA NRW (1996). Monitoringdaten für 1,2,4-Trichlorbenzol. Landesumweltamt Nordrhein-Westfalen. Letter to Bayer 24.09.1996.

Macholz RM, Knoll R, Lewerenz H.-J, Petrzika M, Engst R (1982). Metabolism of a-hexachlorocyclohexane in urine and organs of rats. Xenobiotica, 12, 227-231.

Mackay D (1991). Multimedia Environmental Models: The fugacity approach. Lewis Publ., Chelsea, Michigan.

Mackay D, Paterson S (1990). Fugacity models. In: Karcher W and Devillers J (eds.). Practical applications of quantitative structure-activity relationships (QSAR) in environmental chemistry and toxicology. ECSC, EEC, EAEC, Brussels. Kluwer Acad. Publ. The Netherlands, pp. 433-460.

Mackay D, Di Guardo A, Paterson S, Cowan CE (1996). Evaluating the environmental fate of a variety of types of chemicals using the EQC-model. Environ. Toxicol. Chem., 15, 1627-1637.

MacLeod M and Mackay D (1999). An Assessment of the environmental fate and exposure of benzene and the chlorobenzenes in Canada, Chemosphere 38 (8), 1777-1796.

Madsen T (1997). Torben Madsen, The Water Quality Institute, VKI, Denmark. Personal Communication. Sept. 4, 1997.

Mansour M, Feicht E, Méallier P (1989). Improvement of the photostability of selected substances in aqueous medium. Toxicol. Envir. Chem., 20-21, 139-147.

Marchand M, Caprais JC, Pignet P (1988). Hydrocarbons and halogenated hydrocarbons in coastal waters of the Western Mediterranean (France). Marine Environ. Res., 25, 131-159.

Marinucci AC, Bartha R (1979). Biodegradation of 1,2,3- and 1,2,4-trichlorobenzene in soil and in liquid enrichment culture. Appl. Environ. Microbiol., 38(5), 811-817.

Marquart, J, Brouwer DH and van Hemmen JJ (1999) Draft. Updated dermal exposure model. TNO report V98.1216, Zeist, The Netherlands.

Matsui S, Yamamoto R, Yamada H (1989). The Bacillus Subtilis/Microsome Rec-Assay for the detection of DNA damaging substances which may occur in chlorinated and ozonated waters. Water Sci. Technol., 21, 875-887.

McCarty PL, Reinhard M (1980). Trace organics removal by advanced wastewater treatment. J. Water Pollut. Control Fed., 52(7), 1907-1922.

McCarty LS, Hodson PV, Craig GR, Kaiser KLE (1985). The use of quantitative structure-activity relationships to predict the acute and chronic toxicities of organic chemicals to fish. Environ. Toxicol. Chem., 4(5), 595-606.

van de Meent D, den Hollande HA, Pool WG, Vredenbregt MJ, van Oers HAM, de Greef E, Luijten JA (1986). Organic micropollutants in Dutch coastal waters. Water Sci. Technol., 18, 73-81.

Mekenyan O, Bradbury S, Kamenska A, Ankley G (1998). A computationally based identification algorithm for potential estrogen receptor ligands: An exploratory application of COREPA-C. Proceedings of 8th International Workshop on Quantitative Structure Activity Relationships (QSARs) in the Environmental Sciences. 16 - 20 May 1998. Baltimore, MD, USA.

Mekenyan O (1998). Personal communication.

Merck Index (1996). The Merck Index. An encyclopaedia of chemicals, drugs and biologicals. 12th ed. Budavari et al. (eds). Merck and Co. Whitehouse Station, NJ.

Mes J, Davies DJ, Turton D, Sun WF (1986). Levels and trends of chlorinated hydrocarbons in the breast milk of Canadian women. Food Additives and Contaminants, 3, 313-322.

Mes J, Marchand L, Davies DJ (1990). Organochlorine residues in adipose tissue of Canadians. Bull. Environ. Contam. Toxicol., 45, 681-688.

Mes J, Davies DJ, Doucet J, Weber W, McMullen E (1993). Levels of chlorinated hydrocarbon residues in Canadian human milk and their relationship to some characteristics of the donors. Food Additives and Contaminants, 10, 429-441.

Meylan W, Howard P (1994). PCKOC. Soil adsorption coefficient (Koc) program for Microsoft Windows 3.1. Syracuse Research Corporation, Syracuse, NY.

Meylan WM, Howard PH (1995). Atom/fragment contribution method for estimating octanol-water partitioning coefficients. J. Pharm. Sci., 84, 83-92.

Mikkelsen J (1995). Fate model for organic chemicals in sewage treatment plants. Environmental project No. 308, Danish Environmental Protection Agency, Copenhagen.

Miller MM, Ghodbane S, Wasik SP, Tewari YB, Martire DE (1984). Aqueous solubilities, octanol/water partition coefficients, and entropies of melting of chlorinated benzenes and biphenyls. J. Chem. Eng. Data, 29, 184-190.

Miranda CL, Wang JL, Henderson MC, Carpenter HM, Nakaue HSD, Buhler DR (1983). Studies on the porphyrinogenic action of 1,2,4-trichlorobenzene in birds. Toxicology, 28, 83-92.

MITI (1992). Biodegradation and bioaccumulation. Data of existing chemicals based on the CSCL Japan. Chemicals Inspection and Testing Institute (ed). Japan Chemical Industry Ecology-toxicology and Information Centre (publ.), Japan.

Mohtashamipur E, Triebel R, Straeter H, Norpoth K (1987). The bone marrow clastogenicity of eight halogenated benzenes in male NMRI mice. Mutagenesis, 2(2), 111-113.

Moore MR (1994a). 104-week dietary carcinogenicity study with 1,2,4-trichlorobenzene in mice. Study no. HWA 2603-102. Hazleton Washington, Rockville, Maryland.

Moore MR (1994b). 104-week dietary carcinogenicity study with 1,2,4-trichlorobenzene in mice. Study no. HWA 2603-103. Hazleton Washington, Rockville, Maryland.

Moore MR (2000). Supplementary Histopathological examination of Zymbal's gland from 1,2,4-trichlorobenzene carcinogenicity study in rats. Final Report 7085-100 prepared for the Chlorobenzene Producers Association. Covance Laboratories Inc., Vienna, Virginia.

Mottram DS, Psomas IE, Patterson RLS (1983). Chlorinated residues in the adipose tissue of pigs treated with γ-Hexachlorcyclohexane. J. Sci. Food Agric., 34, 378-387.

National Product Control Agency, Finland (1997). Sihvonen K: letter of 1997-10-15.

Nelson CR, Hites RA (1980). Aromatic amines in and near the Buffalo river. Environ. Sci. Technol., 14(9), 1147-1149.

Neuhauser EF, Durkin PR, Malecki MR, Anatra M (1986). Comparative toxicity of ten organic chemicals to four earthworm species. Comparative Biochemistry and Physiology, 83, part C: 197-200.

Nichol AW, Elsbury S, Rousseaux, CG (1981). Porphyrin accumulation in sheep bones associated with 1,2,4-trichlorobenzene. Bull. Environm. Contam. Toxicol., 27, 72-78.

NINCAS (1998). Vickers C, the National Industrial Chemicals Notification and Assessment Scheme. Sydney: letter of 1998-06-04.

NIOH (1998). Miklos, NIOH, Hungary. Personal communication.

Nirmalakhandan N, Sun B, Arulgnanendran VJ, Mohsin M, Wang XH, Prakash J, Hall N (1994). Analysing and modeling toxicity of mixtures of organic chemicals to microorganisms. Water Sci. Technol., 30(10), 87-96.

Nohmi T, Miyata R, Yoshikawa K, Ishidate M (1985). Mutagenicity tests on organic chemical contaminants in city water and related compounds. I. Bacterial mutagenicity tests. Bull. Natl. Inst. Hyg. Sci. (Tokyo), 103, 60-64.

Nowak J, Kirsch NH, Hegemann W, Stan HJ (1996). Total reductive dechlorination of chlorobenzene to benzene by methanogenic mixed culture enriched from Saale rive sediment. Applied Microbiology and Biotechnology, 45(5), 700-709.

NRW (1985). Gewässergütebericht '84. Landesamt für Wasser und Abfall. Nordrhein-Westfalen. Düsseldorf, Maj 1985.

NRW (1987). Results from monitoring the river Rhein 1984-1986. Letter from Landesamt für Wasser und Abfall, Nordrhein-Westfalen to Bayer AG, 19.05.1987.

NRW (1990). Gewässergütebericht '89. Landesamt für Wasser und Abfall. Nordrhein-Westfalen. Düsseldorf, August 1990.

NRW (1991). Gewässergütebericht '90. Landesamt für Wasser und Abfall. Nordrhein-Westfalen. Düsseldorf, August 1991.

NRW (1992). Gewässergütebericht '91. Landesamt für Wasser und Abfall. Nordrhein-Westfalen. Düsseldorf, October 1992.

OECD (1979). Short Term Toxicology Group.

OECD (1996). European Workshop on the impact of endocrine disrupters on human health and wildlife. 2-4 December, Weybridge, UK. Report of the proceedings.

Okkerman PC, van de Plassche EJ, Roghair CJ, Canton JH (1990). Validation of some extrapolation methods with toxicity data derived from multiple species experiments. Report submitted to the OECD workshop on Ecotoxicological Effect Assessment, Arlington USA, December 1990. RIVM, Bilthoven, the Netherlands.

Oliver BG (1985). Desorption of chlorinated hydrocarbons from spiked and anthropogenically contaminated sediments. Chemosphere, 14(8), 1087-1106.

Oliver BG (1987). Bio-uptake of chlorinated hydrocarbons from laboratory-spiked and field sediments by oligochaete worms. Environ. Sci. Technol., 21, 785-790.

Oliver BG, Bourbonniere RA (1985). Chlorinated contaminants in surficial sediments of Lakes Huron, St. Claire and Erie: Implications regarding sources along the St. Clair and Detroit rivers. J. Great Lakes Res., 11(3), 366-372.

Oliver BG, Charlton MN (1984). Chlorinated organic contaminants on settling particulates in the Niagara river vicinity of Lake Ontario. Environ. Sci. Technol., 18, 903-908.

Oliver BG, Niimi AJ (1983). Bioconcentration of chlorobenzenes from water by rainbow trout: Correlations with partition coefficients and environmental residues. Environ. Sci. Technol., 17, 287-291.

Oliver BG, Nicol KD (1982). Chlorobenzenes in sediments, water, and selected fish from Lakes Superior, Huron, Erie and Ontario. Environ. Sci. Technol., 16, 532-536.

Oliver BG, Nicol KD (1984). Chlorinated contaminants in the Niagara River, 1981-1983. Sci. Total Environ., 39, 57-70.

Ono Y, Somiya I, Kawamura M (1991). The evaluation of genotoxicity using DNA repairing test for chemicals produced in chlorination and ozonation processes. Water Sci. Technol., 23, 329-338.

Ono Y, Somiya I, Kawaguchi T (1992). Genotoxic evaluation on aromatic organochlorine compounds by using *umu* test. Water Sci. Technol., 26(1-2), 61-69.

Panagiotou T, Levendis YA, Carlson J, Dunayevskiy YM, Vouros P (1996). Aromatic hydrocarbon emissions from burning poly(styrene), poly(ethylene), and PVC particles at high temperatures. Combust. Sci. and Tech., 116-117 (1-6), 91-128.

Pankow JF, Isabelle LM, Asher WE (1984). Trace organic compounds in rain. 1. Sampler design and analysis by adsorption/thermal desorption (ATD). Environ. Sci. Technol., 18(5), 310-318.

Parrini M, Bolognesi C, Roggieri P (1990). Induzione di micronuclei in eritrociti policromatici di midollo osseo di topo in seguito a somministrazione intraperitoneale di algeno-benzeni. Boll. Soc. Ital. Biol. Sper., 66, 709-16.

de Pater AJ, Marquart J. Inhalation Exposure to Non-volatile Compounds during Spray Painting. TNO draft report V98 (1999). Zeist, The Netherlands.

Pedersen F, Tyle H, Niemelä J R, Guttman B, Lander L, Wedebrand A (1995). Environmental classification - data collection and interpretation guide for substances to be evaluated for classification as dangerous for the environment (2nd edition). Nordic Council of Ministers, TemaNord, 1995: 581, 166 pp.

Peijnenburg WJMG, 't Hart MJ, den Hollander HA, van de Meent D, Verboom HH, Wolfe NL (1992). Reductive transformations of halogenated aromatic hydrocarbons in anaerobic water-sediment systems: Kinetics, mechanisms and products. Environ. Toxicol. Chem., 11, 289-300.

Perry DL et al. (1979). Identification of organic compounds in industrial effluents discharges. Environmental Protection Technology Series, EPA-600/4-79-016 (1979).

Powers MB, Coate WB, Lewis TR (1975). Repeated Topical Applications of 1,2,4-Trichlorobenzene. Arch. Environ Health, 30, 165-167.

Rao KS, Johnson KA, Henck JW (1982). Subchronic dermal toxicity study of trichlorobenzene in the rabbit. Drug Chem. Toxicol., 5(3), 249-263.

Rappaport SM (1991). Assessment of Long-Term Exposures to Toxic Substances in Air. Ann. Occup. Hyg., 35(1), 61-121.

Rhône-Poulenc (1996a). Gard A, Floc'h F: letter of 1996-08-31.

Rhône-Poulenc (1996b). Gard A, Floc'h F: letter of 1996-10-09.

Richter JE, Peterson SF, Klainert CF (1983). Acute and chronic toxicity of some chlorinated benzenes, chlorinated ethanes and tetrachloroethylene to *Daphnia magna*. Arch. Environ. Toxicol., 12, 679-684.

Rimington C, Ziegler G (1963). Experimental porphyria in rats induced by chlorinated benzenes. Biochem. Pharmacol., 12, 1387 - 1397.

Rinke M, Zetzsch C (1984). Rate constants for the reactions of OH radicals with aromatics: Benzene, phenol, aniline and 1,2,4-trichlorobenzene. Ber. Bunsenges. Phys. Chem., 88, 55-62.

Rippen G (ed) (1991). Handbuch Umweltchemikalien. Vol 7, 1-23. Ecomed Verlagsgesellschaft mbH, Landsberg/lech, Germany.

Roach S (1992). Health Risks from Hazardous Substances at Work: Assessment, Evaluation and Control. Oxford: Pergamon Press.

Robinson KS, Kavlock RJ, Chernoff N, Gray LE (1981). Multigeneration study of 1,2,4-Trichlorobenzene in Rats. J. Toxicol. Environ. Health, 8, 489-500.

Rodan BD (1997). Review of screening criteria data for persistent organic pollutants. US-EPA, Office of Research and Development. Presentation to UNECE-LRTAP WGS, October 20, 1997.

Rogers HR, Campbell JA, Crathorne B, Dobbs AJ (1989). The occurrence of chlorobenzenes and permethrin in twelve UK sewage sludges. Water Res., 23(7), 913-921.

Rogers HR, Crathorne B, Leatherland TM (1989). Occurrence of chlorobenzene isomers in the water column of a UK estuary. Mar. Pollut. Bull., 20(6), 276-281.

Rowe VK (1975). Private communication. Cited in ACGIH, (1991) Documentation of TLV for 1,2,4-trichlorobenzene.

Sabljic A, Güsten H, Verhaar H, Hermens J (1995). QSAR modelling of soil sorption. Improvements and systematics of log Koc vs. log Kow correlations. Chemosphere, 31, 4489-4514.

Santiago S, Thomas RL, Larbaigt G, Corvi C, Rossel D, Tarradellas J, Gregor DJ, McCarthy L, Vernet JP (1994). Nutrients, heavy metal and organic pollutant composition of suspended and bed sediments in the Rhône river. Aquatic Sci., 56(3), 220-242.

Schmidt-Bleek F, Haberland W, Klein AW, Caroli S (1982). Steps towards environmental hazard assessment of new chemicals (including a hazard ranking scheme, based upon directive 79/831/EEC). Chemosphere, 11(4), 383-415.

Schoeny RS, Smith CC, Loper JC (1979). Non-mutagenicity for salmonella of the chlorinated hydrocarbons Arochlor 1254, 1,2,4-Trichlorobenzene, Mirex and Kepone. Mutat. Res., 68, 125-132.

Schreiber G (1980a). Bericht über die Prüfung von Trichlorbenzol S auf die primäre Hautrezwirkung. Fraunhofer-Institut für Toxikologie und Aerosolforschung, Schmallenberg.

Schreiber G (1980b). Bericht über die Prüfung von Trichlorbenzol S auf Schleimhautreizwirkung. Fraunhofer-Institut für Toxicologie und Aerosolforschung, Schmallenberg.

SCOEL (1993). Recommendations from Scientific Expert Group on Occupational Exposure Limits for 1,2,4-Trichlorobenzene. Commission of the European Communities, Scientific Committee on Occupational Exposure Limits, DG V. SEG/SUM/35B.

Seely JC (1991). Carcinomas of the Auditory Sebaceous Glands, Rat. In: Monographs on Pathology of Laboratory Animals. The Eye and Ear. Jones TC and Hunt RD (Eds.). Springer-Verlag.

Seto H, Kanoh T (1987). Survey of chemical pollutants in biota from Tokyo Bay (V). Residue levels in Japanese sea bass and gull in 1985 (in Japanese). Ann. Rep. Tokyo Metr. Res. Lab., 38, 286-289.

Shimada T, McQueen CA, Williams GM (1983). Study of effects on cultured liver cells of three chlorinated benzenes. Final report: December 5, 1983. NTIS/OTS 0291. Doc. ID: FYI-AX-0284-0291IN.

Sievers S and Friesel P (1989). Soil contamination patterns of chlorinated organic compounds: Looking for the source, Chemosphere, 19 (1/6), 91-698.

Simmon VF (1975). Stanford Research Institute: *In vitro* microbiological mutagenicity studies of Ethyl Corporation compounds. Ethyl Corporation. NTIS/OTS 0515770. Doc. ID: 86-870001694.

Simmons P, Branson D, Bailey R (1977). 1,2,4-Trichlorobenzene: Biodegradable or not. Textile Chem. Color., 9(9), 211-213.

Singh HB, Salas LJ, Smith AJ, Shigeishi H (1980). Atmospheric measurements of selected toxic organic chemicals. US-EPA, NC EPA 600/3-80-072. NTIS PB80-198989.

Singh HB, Salas LJ, Smith AJ, Shigeishi H (1981). Measurements of some potentially hazardous organic chemicals in urban environments. Atmospheric Environment, 15, 601-612.

Slooff W, Bremmer HJ, Hesse JM, Matthijsen AJCM (eds) (1991). Integrated criteria document Chlorobenzenes. National Institute of Public health and environmental Protection, Bilthoven, The Netherlands. Report No. 710401015.

Smith AD, Bharath A, Mallard C, Orr D, McCarty LS, Ozburn GW (1990). Bioconcentration kinetics of some chlorinated benzenes and chlorinated phenols in American flagfish (*Jordanella floridae*). Chemosphere, 20(3/4), 379-386.

Smith AD, Bharath A, Mallard C, Orr D, Smith K, Sutton JA, Vukmanich J, McCarty LS, Ozburn GW (1991). The acute and chronic toxicity of ten chlorinated organic compounds to the American flagfish (*Jordanella floridae*). Arch. Environ. Contam. Toxicol., 20, 94-102.

Smith CC, Cragg ST, Wolfe GF, Weigel WW (1985). Investigation of the metabolism of chlorinated hydrocarbons in subhuman species. Department of Environmental Health, University of Cincinnati. US EPA report number: EPA-600/1-85-001.

Smith EN, Carlson GP (1980). Various Pharmacokinetic Parameters in relation to Enzyme-inducing abilities of 1,2,4-Trichlorobenzene and 1,2,4-Tribromobenzene. J. Toxicol. Environ. Health, 6, 737-749.

Sofuni T, Hayashi M, Matsuoka A, Sawada M, Hatanaka M, Ishidate M (1985). Mutagenicity tests on organic chemical contaminants in city water and related compounds. II. Chromosome aberration tests in cultured mammalian cells. Bull. Natl. Inst. Hyg. Sci., (Eisei Shikensho Hokoku), 103, 64-75.

Soldner K, Gollmer G (1982). Probleme mit PCB-gefüllten Transformatoren. Elektrizitätwirtschaft, 81 (17/18), 573-583.

Southworth GR, Keller JL (1986). Hydrophobic sorption of polar organics by low organic carbon soils. Water, Air and Soil Pollution, 28, 239-248.

Srour R (1994/89). Aromatic intermediates and derivatives. Rabih Srour, Paris, France (The document contains pages from 1994 and 1989).

Srour R (1996). Trichlorobenzenes and derivatives. Rabih Srour, Paris, France.

Stieglitz L, Zwick J, Beck J, Bautz H, Roth W (1989). Carbonaceous particles in fly ash - a source for the *de-novo* synthesis of organochlorocompounds. Chemosphere, 19(1-6), 283-290.

Struger J, Weseloh DV, Hallett DJ, Mineau P (1985). Organochlorine contaminants in Herring Gull eggs from the Detroit and Niagara Rivers and Saginaw bay (1978-1982): Contaminant discriminants. J. Great Lakes Res., 11(3), 223-230.

Suter GW, Rosen AE (1988). Comparative toxicology for risk assessment of marine fishes and crustaceans. Environ. Sci. Technol., 22(5), 548-556.

Swedish Criteria Group for Occupational Standards (1993). Scientific Basis for Swedish Occupational Standards XIV: Consensus report for Trichlorobenzene. Arbete och Hälsa, 37, 21-30.

Swedish EPA (1992). Slam. Innehåll av organiske miljöfarliga ämnen. (Sludge. Content of organic environmental hazardous substances. In Swedish). Naturvårdsverket, Sweden.

Tabak HH, Quave SA, Mashni CI, Barth EF (1981). Biodegradability studies with organic priority pollutant compounds. J. Water Pollut. Contr. Fed., 53(10), 1503-1518.

Tagatz ME, Plaia GR, Deans CH (1985). Effects of 1,2,4-trichlorobenzene on estuarine macrobenthic communities exposed via water and sediment. Ecotoxicol. Environ. Safety, 10(3), 351-360.

Tanaka K, Kurihara N, Nakajima M (1979). Oxidative Metabolism of tetrachlorocyclohexanes, pentachlorocyclohexanes and hexachlorohexanes with microsomes from rat liver and house fly abdomen. Pesticide Biochemistry and Physiology, 10, 79-95.

Tanaka A, Sato M, Tsuchiya T, Adachi T, Niimura T, Yamaha T (1986). Excretion, distribution and metabolism of 1,2,4-trichlorobenzene in rats. Arch. Toxicol, 59, 82-88.

ten Hulscher TEM, van der Velde LE, Bruggeman WA (1992). Temperature dependence of Henry's Law constants for selected chlorobenzenes, polychlorinated biphenyls and polycyclic aromatic hydrocarbons. Environ. Toxicol. Chem., 11, 1595-1603.

TGD (1996). European Commission: Technical guidance documents in support of Commission Directive 93/67/EEC on risk assessment for new notified substances and Commission Regulation (EC) 1488/94 on risk assessment for existing substances. Parts I to IV. Luxembourg, Office for Official Publications of the European Communities. EC Catalogue Nos. CR-48-96-001-EN-C, CR-48-96-002-EN-C, CR-48-96-003-EN-C, CR-48-96-004-EN-C.

TGD Corrigendum (1997). European Commission: Technical guidance documents in support of Commission Directive 93/67/EEC on risk assessment for new notified substances and Commission Regulation (EC) 1488/94 on risk assessment for existing substances. Luxembourg, Office for Official Publications of the European Communities. Part II. EC Catalogue No. CR-48-96-002-EN-C.

TNO (1998). Marquart H, TNO, The Netherlands. Personal communication.

TNO Nutrition and Food Research (1999). Volatile Compounds in Food - qualitative and quantitative data. Zeist. The Netherlands.

Tong W, Perkins R, Chen Y, Lowis DR, Welsh WJ, Sheehan DM (1998). Evaluation of various QSAR methods for the large scale prediction of estrogenic compounds. Proceedings of 8th International Workshop on Quantitative Structure Activity Relationships (QSARs) in the Environmental Sciences. 16 - 20 May 1998. Baltimore, MD, USA.

Treon J (1950) Unpublished report from the Kettering Laboratory, University of Cincinnati, OH, USA. Cited in ACGIH, (1991) Documentation of TLV for 1,2,4-trichlorobenzene.

UBA (1987). Daten zur Umwelt 1986/87.p310-320. Umweltbundesamt, Germany.

UBA (1989). Daten zur Umwelt 1988/89. Umweltbundesamt, Germany.

UBA (1994). Erprobung von Zielvorhaben für 28 gefärliche Wasserinhaltstoffe an ausgewählten Fliessgewässern 1988-1991. Texte 9/94, Umweltbundesamt, Germany.

UBA (1998). Letter of 27. May 1998 from German Umweltsbundesamt to Danish CA.

Uchimura Y, Shinohara R (1988). Chlorobenzenes in aquatic environment in the Kitakyushu area. Suishitsu Odaku Kenkyu, 11(2), 123-127.

UK-MAFF (1998). Joint Food Safety and Standards Ghroup: Food surveillance Information sheet: Chlorobenzenes in Foods. No. 141. February 1998. (http://www.maff.gov.uk/food/infsheet/1998/no141/141chl.htm).

Ullmann (1986). Chlorinated hydrocarbons. In: Gerharts W (ed): Ullmann's Encyclopedia of Industrial Chemistry. 5th ed., Vol.6. VCH Verl. Weinheim, Germany.

US Chlorobenzene Producers Association (1996). Proposal to Use the Pharmacokinetics, Physical, and Chemical Properties of 12,2,4-Trichlorobenzene to fill Data Gaps. Document supplied by Bayer (1998).

US EPA (1977a). Investigation of selected potential environmental contaminants. Halogenated benzenes. US Environmental Protection Agency, July 1977. Department of Commerce, NTIS, PB-273 206.

US EPA (1977b). The National Organic Monitoring Survey. US Environmental Protection Agency, Office of Water Supply. Washington DC.

US EPA (1980). Ambient water quality criteria for chlorinated benzenes. US-Environmental Protection Agency, Washington DC, Oct. 1980. EPA 440/5-80-028, PB81-117-392.

US EPA (1981). An Exposure and Risk Assessment for 1,2,4-trichlorobenzene. US-Environmental Protection Agency, Washington, DC. August 1981. (Authors: McNamara P, Byrne M, Goyer M, Lucas P, Scow K, Wood D and Wendt S. Report prepared by Arthur D. Little Inc.). NTIS/PB 85-220762.

US EPA (1984). Aquatic toxicity tests to characterize the hazard of volatile organic chemicals in water. A toxicity Data summary. Parts 1 and 2. US-Environmental Protection Agency, Research Lab. Duluth, MN, Jan. 1984. EPA 600/3-84-009, PB84-141-506.

US EPA (1985). Health Assessment Document for chlorinated benzenes. US Environmental Protection Agency, Cincinnati, Ohio. Jan 1985. NTIS, PB 85-150332.

US EPA (1987). Health Effects Assessment for 1,2,4-trichlorobenzene. US Environmental Protection Agency, Cincinnati, Ohio. Jan 1985. NTIS, PB 88-176367.

US EPA (1991). Approaches for developing screening quality estimates of occupational exposure used by the US EPA's Office of Toxic Substances and their applicability to the OECD SIDS Program. US EPA's Office of Toxic Substances, Washington DC.

US EPA (1992). Drinking Water Criteria Document for Trichlorobenzenes. US Environmental Protection Agency, Cincinnati, Ohio. Jan 1992. NTIS, PB 92-173491 (Revises PB-90215336).

US EPA (1994). ECOSAR ver. 1.01. A computer program for estimating the ecotoxicity of industrial chemicals based on structure activity relationships. US EPA, Office of Pollution Prevention and Toxics.

US EPA, Office of Water, Office of Ground Water and Drinking Water: Http://www.epa.gov/OGWDW/dwh/t-voc/124-tric.html.

US FDA (1964). Rules and Regulations. Title 21 - Food and Drugs. Chapter 1 - Food and Drug Administration, Dept. of Health, Education and Welfare. Part 191 - Hazardous Substances: Definitions and procedural and interpretive regulations. F.R. Doc. 64-9242. 29 FR 13009.

Van Pul WAJ, de Leeuw FAAM, van Jaarsveld JA, van der Gaag MA, Sliggers CJ (1997). The potential for long-range transboundary atmospheric transport. RIVM, The Netherlands. Chemosphere, 37(1), 113- 41.

Veith GD, Call DJ, Brooke LT (1983). Structure-toxicity relationships for the Fathead minnow, *Pimephales promelas*: Narcotic Industrial chemicals. Can. J. Fish. Aquat. Sci., 40, 743-748.

Vinggaard AM (1999). Personal communication.

Vinggaard AM, Jørgensen ECB and Larsen JC (1999). Rapid and sensitive reporter gene assays for detection of antiandrogenic and estrogenic environmental chemicals. Toxicol.Appl.Pharmacol., 155(2), 150-160.

Wagner BO, Mücke W, Schenck HP (1989). Umwelt-Monitoring: Umweltkonzentrationen organischer Chemikalien - Literatur-Recherche und -Auswertung. Ecomed Verl., Landsberg am Lech.

Wakeham SG, Davis AC, Karas JL (1983). Mesocosm experiments to determine the fate and persistence of volatile organic compounds in coastal seawater. Environ. Sci. Technol., 17(10), 611-617.

Walker JD (1998a). The endocrine disruptor priority setting database (EDPSD): a tool to rapidly sort and prioritise chemicals for endocrine disruption screening and testing. Proceedings of 8th International Workshop on Quantitative Structure Activity Relationships (QSARs) in the Environmental Sciences. 16 - 20 May 1998. Baltimore, MD, USA.

Walker JD (1998b). Personal communication.

Waller C (1998). A comparison of CoMFA, HQSAR and SKEYS/GFA derived quantitative structure activity relationships for estrogen receptor binding affinities of structurally diverse compounds. Proceedings of 8th International Workshop on Quantitative Structure Activity Relationships (QSARs) in the Environmental Sciences. 16 - 20 May 1998. Baltimore, MD, USA.

Wang MJ, Jones KC (1994a). The chlorobenzene content of contemporary UK sewage sludges. Chemosphere, 28(6), 1201-1210.

Wang MJ, Jones KC (1994b). Behaviour and fate of chlorobenzenes in spiked and sewage sludge-amended soil. Environ. Sci. Technol., 28, 1843-1852.

Wang MJ, Jones KC (1994c). Occurrence of chlorobenzenes in Nine United Kingdom Retail Vegetables. J. Agric. Food Chem., 42, 2322-2328.

Wang MJ, McGrath SP, Jones KC (1995). Chlorobenzenes in field soil with a history of multiple sewage sludge applications. Environ. Sci. Technol., 29, 356-362.

Ware SA, West WL (1977). Investigation of selected potential environmental contaminants: Halogenated benzenes. US-EPA report 560/2-77-004.

Watanabe PG, Yakel HO, Kociba RJ (1977). Subchronic toxicity study of inhaled 1,2,4-trichlorobenzene in rats. R and D report, Dow Chemical USA dated August 29, 1977. NTIS/OTS 84003A Doc. ID 878221105.

Weast RC (1975). Handbook of chemistry and physics. CRC Press.

WHO (1991). Chlorobenzenes other than hexachlorobenzene. International Programme on Chemical safety (IPCS), Environmental Health Criteria 128. World Health Organisation, Geneva.

WHO (1993). Guidelines for Drinking-Water Quality, volume 1: Recommendations. World Health Organisation, Geneva.

WHO (1996). Guidelines for Drinking-Water Quality, volume 2: Health Criteria and other supporting information. World Health Organisation, Geneva.

Williams DT, LeBel GL, Junkins ER (1984). A comparison of organochlorine residues in human adipose tissue samples from two Ontario municipalities. J. Toxicol. Environ. Health, 13, 19-29.

Williams GM, Mori H, McQueen CA (1989). Structure-activity relationships in the rat hepatocyte DNA-repair test for 300 chemicals. Mutat. Res., 221, 263-286.

Wilson JT, Enfield CO, Dunlap WJ, Cosby RL, Foster DA, Baskin LB (1981). Transport and fate of selected organic pollutants in a sandy soil. J. Environ. Qual., 10(4), 501-506.

Wolfgang (1998). BIA, Germany. Personal communication 1998.

Yalkowsky SH, Orr RJ, Valvani SC (1979). Solubility and partitioning. 3. The solubility of halobenzenes in water. Ind. Eng. Chem. Fundam., 18, 351-353.

Yamamoto H, Taniguchi Y, Imai S, Ohno Y, Tsubura Y (1978). Acute toxicity and local irritation tests of Trichlorobenzene (TCB) on DDY mice. J. Nara Med. Ass. (Nara Igaku Zasshi), 29, 569-573.

Yamamoto H, Ohno Y, Nakamori K, Okuyama T, Imai S, Tsubura Y (1982). Chronic toxicity and carcinogenicity test of 1,2,4-trichlorobenzene on mice by dermal painting. J. Nara Med. Ass. (Nara Igaku Zasshi), 33, 132-145.

Yasuhara A, Morita M (1988). Formation of chlorinated aromatic hydrocarbons by thermal decomposition of vinylidenechloride polymer. Environ. Sci. Technol., 22(6), 646-650.

Young DR, Heesen TC (1980). DDT, PCB and chlorinated benzenes in the marine ecosystem of Southern California. In: Jolley et al. (eds): Water chlorination - Environmental impact and health effects. Vol 3. Ann Arbor Sci. Ann Arbor, Mitchigan USA. pp. 267-290.

Young DR, Heesen TC, Gossett RW (1980). Chlorinated benzenes in Southern California municipal wastewaters and submarine discharge zones. In: Jolley et al. (eds): Water chlorination - Environmental impact and health effects. Vol 3. Ann Arbor Sci. Ann Arbor, Mitchigan USA. pp.471-486.

Yoshioka Y, Ose Y (1993). A quantitative structure-activity relationship study and ecotoxicological risk quotient for the protection from chemical pollution. Environ. Toxicol. Water Qual., 8(1), 87-101.

Yoshioka Y, Ose Y, Sato T (1985). Testing for the toxicity of chemicals with *Tetrahymena pyriformis*. Sci. Total Envir., 43, 149-157.

Yoshioka Y, Nagase H, Ose Y, Sato T (1986). Evaluation of the test method "Activated sludge, respiration inhibition test" proposed by OECD. Ecotox. Environ. Safety, 12, 206-212.

Zoeteman BCJ, Harmsen K, Linders JBHJ, Morra CFH, Sloof W (1980). Persistent organic pollutants in river water and groundwater of the Netherlands. Chemosphere, 9, 231-249.

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 III 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 50 percent dissipation / degradation

E	Explosive (Symbols and indications of danger for dangerous substances and preparations according to Annex III 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 III 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 t/a)
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 III 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	Oxidizing (Symbols and indications of danger for dangerous substances and preparations according to Annex III 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 III of Directive 67/548/EEC
SAR	Structure-Activity Relationships
SBR	Standardised birth ratio
SCE	Sister Chromatic Exchange
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 III 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 Organization
WWTP	Waste Water Treatment Plant
Xn	Harmful (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
Xi	Irritant (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)

Appendix A Regulation, international agreements and national laws

EU regulation

In 1976, the EU has adopted a directive, Council Directive 76/464/EEC, (EEC, 1976) about pollution caused by the discharge of certain chemicals dangerous to the aquatic environment. These substances constitute the black list of the substances of the EU. From the black list, on the basis of a general consensus about environmental hazard, a list of currently 132 substances or groups of substances have been selected which are studied more carefully. Trichlorobenzene (technical mixture, no. 117 on the list) and 1,2,4-TCB (no. 118 on the list) were included in the EU list of originally 129 substances which qualified for the black list.

Member States are obliged to take suitable precautions to eliminate pollution of fresh and marine waters from the hazardous substances included on List I in the Council Directive 76/464. For trichlorobenzenes, limit values on emissions and quality objectives have been established.

For trichlorobenzene emission limits have been defined for various branches of industry and apply to cases where waste containing trichlorobenzenes (TCB) leave the industrial grounds. TCB consists of the sum of the isomers 1,2,3-TCB, 1,2,4-TCB and 1,3,5-TCB.

Branch of industry	Limits *		Apply
	Weight	Concentration	from
Production of TCB by dehydrochlorination of HCH and/or conversion of TCB	25 g per ton [1)] 10 g per ton [1)]	2.5 mg/l [2)] 1.0 mg/l [2)]	1. 1. 1993 1. 1. 1995
Production and/or conversion of chlorobenzene by chlorination of benzene [3)]	5 g per ton [1)] 0.5 g per ton [1)]	0.5 mg/l [2)] 0.05 mg/l [2)]	1. 1. 1993 1. 1. 1995

* The limits indicate the highest admissible amount and concentration of TCB which on average may be discharged per month. The highest admissible amount and concentration on one day may not exceed twice the amount in the table

1) For the first branch of industry, the limits for discharge of TCB are given compared to the total production capacity of TCB. For the second branch of industry, the limits for the discharge of TCB are given compared to the total production and conversion capacity of mono- and dichlorobenzenes

2) For the first branch of industry, the limits for concentrations of TCB are given compared to the reference volume of 10 m^3/ton of produced or converted TCB. For the second branch of industry, the limits for concentrations of TCB are given compared to the reference volume of 10 m^3/ton of produced or converted mono- and dichlorobenzenes

3) For existing companies which belong to the second branch of industry and which discharge less than 50 kg/year from January 1, 1995, the limits apply on that date which equals half the limits which apply from January 1, 1993

The European Commission Scientific Advisory Committee on Toxicity and Ecotoxicity of Chemicals (CSTE), recommended the quality objectives for trichlorobenzenes in the aquatic environment in application to article 6(2) of the Council Directive 76/464/EEC taking into account that the three trichlorobenzenes (1,2,3-, 1,2,4- and 1,3,5-TCB) have similar toxicity in aquatic organisms, that they have a potential for bioaccumulation and that they are persistent within the environment, the total concentration of trichlorobenzenes in fresh and salt water should be as low as possible and should not exceed 0.1 µg/l (CSTE, 1984).

Water directive

The ECE list (ECE/CEP/2; 26-3-1994) has been included in a recommendation concerning the prevention, control and limitation of the pollution of surface waters by harmful substances. The

trichlorobenzenes (1,2,4-TCB and 1,3,5-TCB) are included in the indicative list of substances of priority hazard substances (Annex I of the recommendation).

Drinking water directive

The target value for the sum of chlorinated carbonhydrogen substances except pesticides:
1 µg/l (EEC 1980).

CSTE/EEC List 1

The ecotoxicity section of the CSTE (The European Commission Scientific Advisory Committee on Toxicity and Ecotoxicity of Chemicals) has included 1,2,4-TCB in the list of substances (List 1: Bro-Rasmusssen et al., 1994) among the original 129 candidates. The water quality objective referring to the maximum concentration level to be satisfied in the environment outside the point of discharge, for 1,2,4-TCB recommended by the CSTE using assessment factors (extrapolation factors: not specifically reported but after 1985 of the same order as TGD 1996) in June 1984 (CSTE, 1984) and adopted by EEC Council June 1990 was 0.1 µg/l (cf. above).

North Sea list

The international North Sea Action Programme which has as a goal the protection of the North Sea against pollution, has included trichlorobenzenes in the list of hazardous chemicals, on the basis of biodegradability, toxicity and bioaccumulation.

HELCOM

In the context of HELCOM, the isomers of TCB are set on the "List of priority harmful substances other than nutrients for immediate action in order to reach the 50% reduction goal by 1995" in water and air (HELCOM, 1991).

OSPARCOM

The Oslo-Paris Convention (OSPAR) includes trichlorobenzenes in a further list of substances identified as of concern by OSPAR in the period 1991-1996 (OSPAR, 1997).

National laws and regulations

The Netherlands

Trichlorobenzenes are included in the black list of substances drawn up for the environmental compartments air, water and water bottom (sediment). The black list is indicative for the Dutch granting of licences (directed to sources). The substances on the list I are evaluated to form a possible threat to bottom, water and/or air quality. They are selected on the basis of intrinsic properties like toxicity, degradability and bioaccumulation and concerns substances which are found in significant amounts in the environment (Ministry of Housing, Spatial Planning and the Environment, 1997).

Trichlorobenzenes are belonging to the List I which contains substances of which it is not known to what extent they are a threat and/or which are presumed to represent only a local problem.

The target value defines a desired general environmental quality and is indicative for environmental policies concerning emission reductions. The target value for trichlorobenzenes is 0.01 µg/l for water bottom (sediment).

The limit values for newly formed sediments have been derived from the limits for surface waters. Newly formed sediment is the top layer of the water bottom which stands in direct contact with the surface water. The limit values for trichlorobenzenes are 0.4 µg/l for water and 0.3 µg/l for water bottom.

The soil pollution intervention values are mentioned in the ministerial circular (9 May 1994, Stct 96). Where the level in the soil are equivalent to or higher than the intervention value there is an instance of serious soil contamination as meant in the Soil protection Act. For trichlorobenzenes, the target value for soil/sediment is 0.01 mg/kg dw, for groundwater the target value is 0.01 µg/l and the intervention value 10 µg/l (Ministry of Housing, Spatial Planning and the Environment 1994).

Limits for the discharge of trichlorobenzene have been defined in Ministerial Order (3 January 1992, Stbl 24). The limits have been defined for various branches of industry and apply to cases where waste containing the TCB leaves the industrial grounds (refer to the table above) (Ministry of Housing, Spatial Planning and the Environment, 1997):

Declaration of intent for execution of environmental policies by the chemical industry contains the environmental goals for emission reduction to water for the chemical industry. For trichlorobenzenes, the emission in the reference year 1985 were 0.13 ton and the reduction goal was 50% by 1995, 75% in year 2000 and 90% in 2010.

Denmark

Council Directive 76/464 has basically been implemented in Denmark. Trichlorobenzene are included in the Statutory order no. 75, 1992 (Danish EPA, 1992). The emission values adopted are presented in the table above. The target value for watercourses, coastal areas and territorial marine waters is 0.4 µg/l and the quality objective 0.1 µg/l.

Working Environment

In Germany, the maximum concentration in the working environment expressed as a MAK (Maximale Arbeitsplatz Konzentration) value is the highest allowed concentration of a substance in the air in the working environment: MAK-value (1994): 5 ppm, 40 mg/m^3 (DFG, 1994).

In America, the American Conference of Governmental Industrial Hygienists (ACGIH) has established a Threshold Limit Value (TLV) based on time-weighted average:
TLV (TWA): 5 ppm, 40 mg/m^3 (Lewis, 1992).

Recommendations

Germany

In Belgium and Italy, the use of 1,2,4-TCB as dye carrier is discouraged and substitutes are preferred. A study by The German textile association TEGEWA revealed that there was no more use of 1,2,4-TCB as dye carrier in The Netherlands and Switzerland and that German producers of textile auxiliaries do not market trichlorobenzene for use as a dye carrier in Germany (Bayer, 1996).

References

Bayer (1996). Risk assessment report on 1,2,4-trichlorobenzene. Draft June 1996. Bayer AG.

Bro-Rasmussen F, Calow P, Canton JH, Chambers PL, Fernandes AS, Hoffmann L, Jouany JM, Klein W, Persoone G, Scoullos M, Tarazona J, Vighi M (1994). EEC water quality objectives for chemicals dangerous to aquatic environments (List 1). Rev. Environ. Contam. Toxicol., 137, (pre-print).

CSTE (1984). Report of the Commission Scientific Advisory Committee to examine the toxicity and ecotoxicity of chemical compounds. Quality objectives for monochlorobenzene and trichlorobenzenes in the aquatic environment (Article 6- Directive 76/464/EEC). Opinion adopted in June 1984. Luxembourg, Office for Official Publications of the European Communities, 1990. EUR 12964 EN.

Danish EPA (1992). Bekendtgørelse nr. 75 af 30. januar 1992 om grænseværdier for udledning af visse farlige stoffer til vandløb, søer og havet (Liste I stoffer). (Statutory order from the Ministry of the Environment No. 75 of January 30 1992 on limit values for the emission of certain hazardous substances to water courses, lakes and the sea (List I substances). - In Danish). Ministry of the Environment, Danish Environmental protection Agency, Copenhagen.

DFG(1994). MAK- und BAT-Werte-Liste 1994. Deutsche Forschungsgemeinschaft, Senatskommission zur Prüfung gesundheitsschädlicher Arbeitsstoffe. Mitteilung 30. VCH, Weinheim, Germany.

EEC (1976). Council Directive 76/464/EEC on pollution caused by certain dangerous substances discharged into the aquatic environment of the Community. O. J. L 129 of 18 May 1976, p.23.

EEC (1980). Council Directive 80/778/EEC of 15 July 1980 relating to the quality of water intended for human consumption. O. J. L 229 of 30 August 1980. p. 11-29.

HELCOM (1991). Convention on the protection of the marine environment of the Baltic Sea area. Baltic Marine Environment Protection Commission - Helsinki Commission. Twelfth meeting, Helsinki 19-22 February 1991. HELCOM 12/18, Annex 6.

HSE (UK) (2000). Personal communication with John Tickner, HSE 2000-01-06.

OSPAR (1997). Oslo and Paris conventions for the prevention of marine pollution meeting of heads of delegation, London 23-25 June 1997. Draft strategy to implement OSPAR's objective with regard to hazardous substances. HOD(2) 97/13/4 rev 1-E.

Lewis RJ (1992). Sax's dangerous properties of industrial materials. 8th ed. Van Nostrand Reinhold, New York.

Ministry of Housing, Spatial Planning and the Environment (1994). Environmental Quality Objectives in the Netherlands. Risk Assessment and Environmental Quality division Directorate for Chemicals, external safety and Radiation protection. Ministry of Housing, Spatial Planning and the Environment, The Netherlands.

Ministry of Housing, Spatial Planning and the Environment (1997). Inventory of lists of substances and regulations on substances and preparations. Ministry of Housing, Spatial Planning and the Environment, The Netherlands. March 1997.

TGD (1996). European Commission: Technical guidance documents in support of Commission Directive 93/67/EEC on risk assessment for new notified substances and Commission Regulation (EC) 1488/94 on risk assessment for existing substances. Parts I to IV. Luxembourg, Office for Official Publications of the European Communities. EC Catalogue Nos. CR-48-96-001-EN-C, CR-48-96-002-EN-C, CR-48-96-003-EN-C, CR-48-96-004-EN-C.

European Commission

EUR 20540 EN **European Union Risk Assessment Report**
1,2,4-trichlorobenzene, Volume 26

Editors: B.G. Hansen, S.J. Munn, M. Luotamo, C. Musset, S. Pakalin, J. de Bruijn, F. Berthault, S. Vegro, G. Pellegrini, R. Allanou, S. Scheer.

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Environment and quality of life series

The report provides the comprehensive risk assessment of the substance 1,2,4-trichlorobenzene. It has been prepared by Denmark 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.

The evaluation considers the emissions and the resulting exposure to the environment and the human populations in all life cycle steps. Following the exposure assessment, the environmental risk characterisation for each protection goal in the aquatic, terrestrial and atmospheric compartment has been determined. For human health 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 for 1,2,4-trichlorobenzene concludes that there is at present concern for workers, consumers and humans exposed via the environment. The environmental risk assessment for 1,2,4-trichlorobenzene concludes that there is at present concern for the aquatic ecosystem, the terrestrial ecosystem and for microorganisms in the sewage treatment plant and no concern for the atmosphere.

The conclusions of this report will lead to risk reduction measures to be proposed by the Commissions committee on risk reduction strategies set up in support of Council Regulation (EEC) N. 793/93.

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European Union Risk Assessment Report

1,2,4-trichlorobenzene

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