European Chemicals Bureau

Institute for Health and Consumer Protection

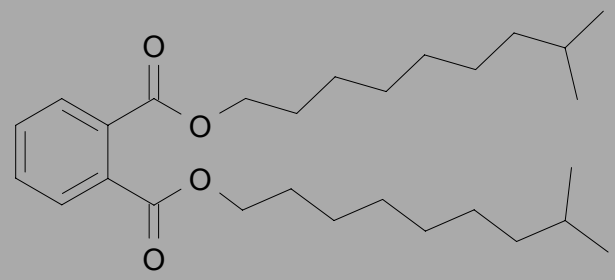
European Chemicals Bureau

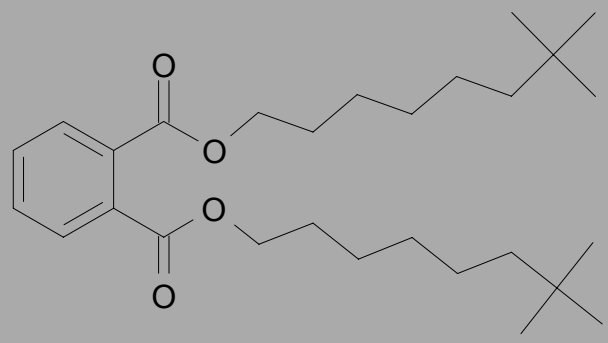
Existing Substances

European Union Risk Assessment Report

CAS Nos: 68515-49-1 26761-40-0	EINECS Nos: 271-091-4 247-977-1

1,2-benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich and di-"isodecyl" phthalate (DIDP)





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European Union Risk Assessment Report
DIDP
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European Union Risk Assessment Report

1,2-BENZENEDICARBOXYLIC ACID, DI-C9-11-BRANCHED ALKYL ESTERS, C10-RICH

AND

DI-"ISODECYL" PHTHALATE

(DIDP)

CAS Nos: 68515-49-1 and 26761-40-0

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RISK ASSESSMENT

Cataloguing data can be found at the end of this publication
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RISK ASSESSMENT

Final Report, 2003

France

The French rapporteur for the risk evaluation of 1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich and di-"isodecyl" phthalate, is the Ministry of the Environment and the Ministry of Employment and Solidarity.

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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-Nos:	68515-49-1 and 26761-40-0
EINECS-Nos:	271-091-4 and 247-977-1
IUPAC name:	1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich and di-"isodecyl"phthalate

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 reached for the aquatic compartment, the terrestrial compartment, the atmosphere, microorganisms in the sewage treatment plant as well as for secondary poisoning.

Human health

Human health (toxicity)

Workers

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

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 applies in case DIDP should be used as a substitute for other phthalates in toys because of concerns for hepatic toxicity as a consequence of repeated exposure of infants and newborn babies arising mainly by the oral route from mouthing and sucking toys and baby equipment.

Pertaining to reduced offspring survival, due to the uncertainty related to the relevance of this end point for newborns and infants and to the lack of experience in this particular field of trans-generational effect, no formal conclusion could be drawn.

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 for all other scenarios.

Humans exposed via the 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.

Combined exposure

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 in case DIDP should be used as a substitute for other phthalates in toys because of concerns for hepatic toxicity as a consequence of repeated exposure of infants.

Pertaining to reduced offspring survival, due to the uncertainty related to the relevance of this end point for infants and to the lack of experience in this particular field of trans-generational effect, no formal conclusion could be drawn.

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.

Human health (risks from physico-chemical properties)

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.

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

In this risk assessment report two di "isodecyl" phthalate products (hereafter referred to as DIDP) are evaluated. There are two different CAS numbers. Following specific information from ECPI (1996) these two products are prepared essentially from the same feed, through an identical olefin oligomerisation process and through similar oxo alcohol manufacturing and phthalate esterification processes (see Section 2.1.1).

The two phthalates are considered fully interchangeable within their whole range of the market end uses.

Remark: In the "oxo" Industry, the term "iso" is used for designating a mixture and does not refer to the IUPAC definition.

1.1 IDENTIFICATION OF THE SUBSTANCE

The following data have been gathered from IUCLID and specific industry information on their products.

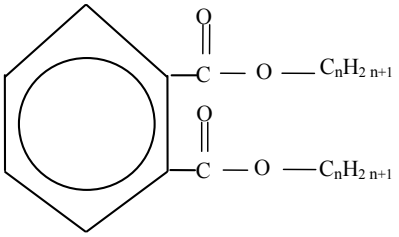
Table 1.1 Identification of the substance

CAS	68515-49-1	26761-40-0
EINECS-Nr	271-091-4	247-977-1
Substance name (IUPAC Name)	1,2-benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich	di-"isodecyl" phthalate
Molecular formula	$C_{28}H_{46}O_4$ (average)	
Molecular weight	446.68 (assuming the above average molecular formula)	

Commercial names

Jayflex DIDP; Palatinol Z; Vestinol DZ; Emkarate 1020.

Structural formula



n = 9 to 11

1.2 PURITY/IMPURITIES, ADDITIVES

DIDP is a complex mixture containing mainly C_{10}-branched isomers, with a mean formula $C_{28}H_{46}O_4$ and mean molecular weight M = 446.68 $g \cdot mol^{-1}$.

The report from Exxon Biomedical Sciences (1996a), studying water solubility of DINP (diisononyl phthalate) and DIDP, confirms that these phthalates contain a number of constituents, of which many might be common to both (gas chromatography retention times 13.5 to 16.5 minutes for DINP and 14 to 18 minutes for DIDP). The reconstituted chromatogram for a DIDP sample extracted from water shows ca. 29 different peaks.

Howard et al. (1985) studied by gas chromatography the composition of a DIDP sample provided by the Chemicals Manufacturers' Association (CMA), with no clear indication on its identity. They found a mixture of unresolved compounds with 19 - 20 alkyl chain length.

Rastogi (1998) analysed the phthalate esters present in plastic toys, and presented gas chromatograms of DINP and DIDP provided as reference samples and analysed by Fluka. Both are complex mixtures and may have common constituents (retention times from 22.9 to 25.7 minutes for DINP, and from 25.2 to 27.0 for DIDP).

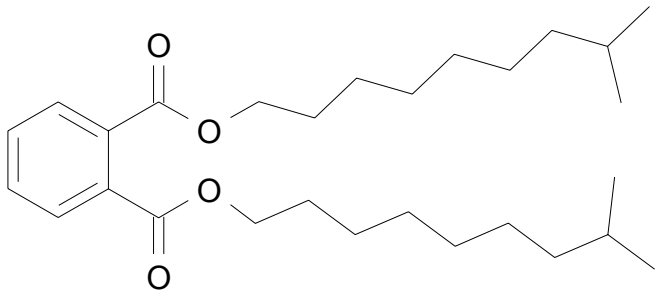
These data have been completed by a personal communication from the author, summarised in **Table 1.2**.

Table 1.2 Retention times (RT, minutes) and area percentages of the main (> 5%) gas chromatography peaks from DINP and DIDP samples analysed in the same conditions (from the integrator output)

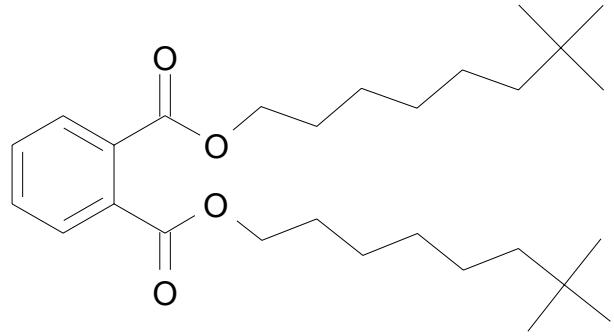
DINP	**RT**	24.195	24.295	24.551	24.640	24.741	24.904	25.007
(22 peaks)	**%**	8.17	9.89	9.83	12.30	6.89	7.13	9.22
DIDP	RT	25.289	25.474	25.715	26.119	26.127	26.275	26.532
(18 peaks)	%	5.95	5.31	14.60	8.61	10.10	7.01	9.23

The detailed chemical structure and the isomeric composition of both DIDP and its precursor, the isodecylalcohol (CAS 93821-11-5) are not available due to the complexity of the isomers mixture (see also production process in Section 2).

The following molecular structures are recovered when searching under the used CAS numbers:



CAS 68515-49-1



CAS 26761-40-0

The correct structures can only be estimated. Based on nonene (CAS 97593-01-6) isomer distribution analysis and 1H-NMR analysis of isodecyl alcohol, an estimation of key isomeric structures of isodecylalcohol - hence of DIDP were provided by ECPI (1998a) (cf. **Table1.3**).

Table 1.3 Best estimates of the different chemical structures of DIDP

Longest chain (estimates)	DIDP (CAS 68515-49-1 & CAS 26761-40-0)	Best estimated content (%)
C7	tri-methyl heptanols	0-10
C8	di-methyl octanols	70-80
C9	methyl nonanols	0-10
C10	n-decanol	0

Phthalates are produced with a high degree of purity (>99.5%) in terms of ester content. Trace impurities have been summarised from producers data in **Table 1.4**.

Table 1.4 Impurities of DIDP according to manufacturers

Diisodecyl ether and Isodecyl benzoate (0.02 - 0.1% w/w)
Isodecyl alcohol (0.01 - 0.05% w/w)
Traces of other phthalates
Water (max. 0.1% w/w)

Note: Bisphenol A may be included upon request by customer

1.3 PHYSICO-CHEMICAL PROPERTIES

1.3.1 Physical state

DIDP is an oily, viscous liquid at normal temperature and pressure.

1.3.2 Melting point

Representative data have been collected below (**Table 1.5)**.

Table 1.5 Melting point (MP) of DIDP

MP (°C)	Method	References
-50	ASTM D 97 (pour point)	Exxon Chemical Europe (1994). Typical value
-35	ASTM D 97 (pour point)	ICI (1996)
ca. -42	DIN 51 583	Hüls (1986)
-41	DIN-ISO 3016 ("Pour point")	BASF (1996)
ca. -45	DIN-ISO 3016	Hoechst (1990)

Measurements seem difficult and poorly reproducible. A rough value is ca. -45 °C.

1.3.3 Boiling point

Selected data of boiling points at reduced pressure are summarised in **Table 1.6**.

Table 1.6 Boiling point of DIDP

Boiling point, °C	Reference
250-267°C at 5 hPa	Hoechst (1990)
250-267°C at 7 hPa	BASF (1992)
257°C at 10 hPa	Haertel (1985)

Using the linear regressions relating vapour pressure to temperature (cf. below), a theoretical boiling point of > 400°C at atmospheric pressure can be obtained.

1.3.4 Density

Collected data are presented in **Table 1.7**.

Table 1.7 Density of DIDP at 20°C

Density ($g.cm^{-3}$)	Method	Reference
≥ 0.964, ≤ 0.968	ASTM D 4052	Exxon Chemical Europe (1994)
≥ 0.964, ≤ 0.970	ASTM D 1298	ICI (1996)
0.964 - 0.968	DIN 51 757	Hoechst (1990)
0.966 - 0.969	DIN 51 757	Hüls (1986)
0.960 - 0.968	DIN 51 757	BASF (1996)
0.963	-	Haertel (1985)
0.9695 (calc.)	Continuous measurements from 100°C to 230°C and extrapolation	BASF (1991b)

Density at 20°C is most often given as between 0.964 (min) - 0.968 (max) (e.g. Hoechst, 1990). The range may be due to measurement uncertainties and to the presence of additives, impurities and water. Water has probably the largest influence. Producers indicate water contents of 0.02% and ≤ 0.1%. If density is measured by weighing a 10 ml picnometer, 0.1% of water corresponds to a mass of 0.01g. So, for instance, if there is 0.02% of water in DIDP with a "true" density of 0.965, the result would be given as 0.967.

A value of 0.966 may be taken as representative.

1.3.5 Vapour pressure

Various values of vapour pressure for commercial DIDP-type mixtures have been reported (BASF, 1983; 1987a; 1991a; Hüls, 1996). The determinations have been mostly carried out in the temperature range of 180-340°C. Nevertheless, with extrapolation by linear regression using the Clausius-Clapeyron equation, estimates of vapour pressure values in the temperature range of greatest interest for environmental modelling (20°C to 30° C) can be obtained.

The extrapolation of four data series of DIDP is shown in **Figure 1** and **Table 1.8**. The plot suggests that there are no significant differences between the different DIDP samples examined. The small differences are presumably caused by insignificant impurities or different composition of isomers of the tested substance. The extrapolation of data series of **Figure 1** to a temperature of 20°C suggests vapour pressure values in-between $7.03 \cdot 10^{-6}$ - $9.3 \cdot 10^{-5}$ Pa for DIDP.

Individual data from other sources are also shown in **Table 1.8**. A relatively high value has been calculated by Sears (1982). No further explication about the calculation method or measurement explication is given (Russom et al., 1991). The original report for the QSAR (Quantitative Structure-Activity Relationship) data (lowest value) is not available.

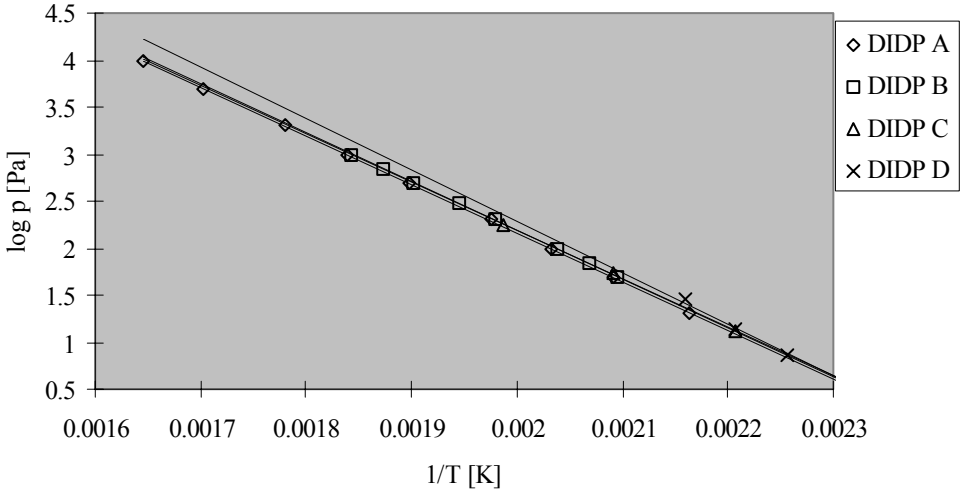


Figure 1 Plot of several data series obtained from DIDP producers, calculation of linear regression

Table 1.8 Vapour pressure values obtained by extrapolation of linear regression, individual values from IUCLID are included

DIDP	20°C	25°C	30°C	100°C
DIDP A	$7.2 \cdot 10^{-6}$ Pa	$1.4 \cdot 10^{-5}$ Pa	$2.7 \cdot 10^{-5}$ Pa	0.044 Pa
DIDP B	$8.45 \cdot 10^{-6}$ Pa	$1.67 \cdot 10^{-5}$ Pa	$3.2 \cdot 10^{-5}$ Pa	0.049 Pa
DIDP C	$7.03 \cdot 10^{-6}$ Pa	$1.4 \cdot 10^{-5}$ Pa	$2.7 \cdot 10^{-5}$ Pa	0.045 Pa
DIDP D	$9.3 \cdot 10^{-5}$ Pa	$1.6 \cdot 10^{-4}$ Pa	$2.7 \cdot 10^{-4}$ Pa	0.1 Pa
Mean value:	$2.8 \cdot 10^{-5}$ Pa	$5.1 \cdot 10^{-5}$ Pa	$8.9 \cdot 10^{-5}$ Pa	0.059 Pa
QSAR data		$3.1 \cdot 10^{-10}$ Pa		
Sears (1982)		$8 \cdot 10^{-6}$ Pa		

In conclusion, by comparison of regression lines obtained from measurements with different DIDP products, it was attempted to determine differences between the samples. Apparently, the differences are not important, the resulting different regression lines (**Figure 1**) are very similar. Only DIDP product D differs from the other three. Product D is indeed the only product for which the vapour pressure has been measured over a temperature range of 30 to 190°C with a vapour pressure balance, while the other products have been tested in the range of 180-335°C. While results at low temperatures are available with one product only, these results are to be considered with care as the limits of the method are reached at low temperatures. On the other hand considerable error can be attributed to the extrapolated values due to the large difference in temperature.

Using the data by Howard et al. (1985) (excluding butylbenzyl phthalate, which is not homologous with the other "alkyl" phthalates), the following relationship may be drawn between vapour pressure and molecular weight:

$$\log VP = -0.0145\ M.W. + 2.2147 \qquad (r^2 = 0.9543)$$

Extrapolation to DIDP gives a vapour pressure of $7.44 \cdot 10^{-5}$ Pa at 25°C. This value is clearly in agreement with the above estimated values.

For the risk assessment a vapour pressure of $2.8 \cdot 10^{-5}$ Pa at 20°C and of $5.1 \cdot 10^{-5}$ Pa at 25°C will be retained. The value of 0.059 Pa at 100°C will be used to estimate release factors during processing which is carried out at this range of temperature.

1.3.6 Surface tension

No experimental data on surface tension are available**.** Due to the low solubility of DIDP a test on surface tension is not feasible.

1.3.7 Water solubility

An estimation of DIDP water solubility (Sw) has been made by Hollifield (1979), using a nephelometric technique. This author emphasises the inherent limitations of this technique, especially for its "uncertain accuracy for impure chemicals or mixture of isomers and/or similar substances" (and he clearly recognises DIDP as such), but finds generally acceptable agreement with more expensive (e.g. radiotracer) techniques (within an order of magnitude). With practical grade materials, he estimates precision as ± 20%. He gives DIDP water solubility as 280 $\mu g \cdot l^{-1}$; so, solubility would lie in the 220-340 $\mu g \cdot l^{-1}$ range. This result is of interest because it is obtained by a technique not used by others.

Using ^{14}C phthalates (labeled in the carbonyl position) pre-dissolved in acetone, Brown and Thompson (1982a) checked the stability of aqueous solutions (0.5 ml of spiked acetone in 1 l water) of DIDP. According to these authors, measured concentrations of DIDP in distilled water are stable for concentrations lower than 180 $\mu g \cdot l^{-1}$. In fact, their data show stability on 5 days of labeled DIDP in distilled water at 154 $\mu g \cdot l^{-1}$. The next higher concentration (447 $\mu g \cdot l^{-1}$ at day 0) clearly shows instability (with a regular decrease down 412 $\mu g \cdot l^{-1}$ at day 5). So Sw = 160 $\mu g \cdot l^{-1}$ may represent the highest value acceptable in distilled water.

In BASF (1987b) the solubility of water in DIDP and of DIDP in water are studied. DIDP is soluble at 0.0089% in water (w/w) at 20°C, i.e. Sw is 89 $\mu g \cdot l^{-1}$, with an incertitude estimated as 28%. So Sw would be in the range 50 to 110 $\mu g \cdot l^{-1}$.

In a further study performed by BASF (1990), water solubility was determined to be < 0.5 mg/l. 10 litre of deionized water were spiked with 5 mg DIDP and most of the substance remained undissolved after several hours of stirring.

Since water solubility is a key physiological property, a critical review of the available data is necessary. A number of problems were identified with the experimental methods used in earlier studies. First, most experiments involved vigorous mixing during equilibration of the test material with the aqueous phase. Due to the nature of high molecular weight phthalates, which have a density similar to that of water, high energy mixing produces quasi-stable emulsions of free product microdroplets. Consequently, the apparent water solubility obtained from such test systems can significantly exceed the true water solubility. Second, in some studies a pipette was passed through the air-water interphase to sample the aqueous phase. Since undissolved material floats, this sampling technique may include neat phthalate at the surface. Third, in a number of the previous studies, analytical quantification relied upon non-specific techniques. Thus trace amounts of water soluble impurities (e.g. unreacted alcohols) that are present in commercial

products could confound the interpretation of experiments which relied upon radiotracer or nephelometric methods for analytical quantification.

A study by Exxon Biomedical Sciences (1996a) was designed to circumvent the deficiencies of early experiments. In order to minimise the formation of emulsions of undissolved test material, a slow-stir procedure was used as proposed by the US EPA (Environmental Protection Agency) (Ellington and Floyd, 1997). To avoid potential contamination with neat test material as a result of sampling through the surface layer, samples were withdrawn by gravity from a port at the bottom of an all glass test system. To ensure highly selective and sensitive analytical quantification, GC-MS in selected ion mode was employed. A water solubility of <0.00003 to < 0.00013 mg/l at 20°C was measured. The water solubility of DIDP could not be determined in this test with a practical quantification limit of 0.13 µg/l and is therefore reported as less than 0.13 µg/l. Some specific criticism may nevertheless be addressed towards this study:

1. strong adsorption of the dissolved phthalate on glass walls. Williams et al. (1995) measured an adsorption of 92.0% to glass vessels at 7 days for DIDP, in the absence of sediment. In this Exxon experiment "the entire test systems were glass", and "samples were collected directly in the all-glass extraction disk apparatus" (Exxon Biomedical Sciences, 1996a). To minimise the potential for glass sorption, all glass components were deactivated with isooctanol as recommended by Furtmann (1993). The delay between rinsing and the beginning of the test is unknown. A loading of 1 mg/l was used to ensure that excess undissolved test material was present to maintain a saturated aqueous phase and throughout the experiment droplets of DIDP were observed on the water surface;

2. possibly poor retention of the dissolved DIDP on the solid phase extraction cartridges in the presence of a large excess of water (3 liter water samples were extracted using C_{18} extraction disks). Hendriks et al. (1993) state that very lipophilic organics (log Pow > 5) are not extracted from water by XAD. Furtmann (1993) uses 250 mg of an octadecyl phase, too, but estimates recovery at 91-108%. He selects the quantity of water to be treated (250 ml) to avoid phthalate losses (a breakthrough of dimethyl phthalate is observed after 400 ml of test sample, but no breakthrough is observed for other phthalates - up to dioctyl phthalate - within 1,000 ml). The report by Exxon Biomedical Sciences (1996a) does not mention having checked the possibility of breakthrough after 3 litre samples. However spike recovery experiments with carbon treated water demonstrated good recoveries using this extraction procedure, even though the time elapsed between spiking and extraction is not stated, but is probably much shorter than for samples (3 to 9 days);

3. the above data may be indicative of a strong dependency of the water solubility on water quality (hardness, pH, presence of sediments). The experiment by Exxon Biomedical Sciences (1996a) did not use distilled water, but "unbuffered carbon treated water". Organic matter possibly present in the carbon treated well water could have complexed DIDP. The total organic carbon content was < 1 mg/l and therefore complexation is not expected to be significant. Since an excess of DIDP was present in the test system, the aqueous phase would still be saturated with dissolved phase chemical even if significant organic matter were present.

Some evidence exists nevertheless to support the result by Exxon Biochemical Sciences (1996a):

- results of quantitative structure property relationships estimating Sw from the molecular weight or the Kow (0.0014-0.0421 µg/l; Scherf (1995)),
- results of quantitative structure property relationships estimating Sw from the logKow, the molecular weight as well as the melting point (0.103 µg/l; SRC, (1994)) measured logKow values which are very high and therefore inconsistent with the reported water solubilities,

- results of water solubility experiments with DEHP (di-ethylhexyl phthalate) using a generator column technique (Boese et al., 1986).

More recent studies confirmed the results found by Exxon Biomedical Sciences (1996a).

Letinski et al. (1999) studied the water solubility of DIDP in a slow-stir apparatus. The loading of the substances was 1 mg/l. Test vessels were stirred at 20-22°C in a manner that prevented the formation of a vortex in the water column. The equilibration period lasted up to 16 days. Samples were taken in triplicate from the bottom port of the vessels and extracted using an all glass extraction-filtering apparatus (HPLC mobile phase filter flask) fitted with an extraction disk. The solubility was found to be 0.17 ± 0.02 µg/l.

The solubility of di-n-decyl phthalate (DnDP) was determined by Ellington (1999) in a slow-stir apparatus. 100 µl of DnDP was added to the surface of 6 litres of water and the stirring rate was adjusted to move the droplet of phthalate on the surface of the water at approximately 10 cm/min. 0.5 l samples were extracted at different time intervals for analysis. Equilibrium was established within the first 18 hours of stirring and little change was observed at sampling times 120, 150 and 753 hours. The mean result of 4 measurements was 0.22 µg/l. Furthermore, "No-stirring" water solubility experiments were conducted in a manner identical to the "slow-stirring" experiments except the stirrer motor remained "off". Equilibrium was attained within 353 hours. The mean water solubility was determined to be 0.16 µg/l.

Based upon the above results, it can be considered that the "true" water solubility of DIDP is approximately 0.2 µg/l. This value will be used in the risk assessment. Nevertheless, it has to be kept in mind that the substance forms stable emulsions and that apparent water solubilities up to a maximum of 1 mg/l can be observed. This explains the diverging results found in the "older" studies and also how many of the aquatic toxicity tests could be performed.

1.3.8 Henry's law constant

A Henry's law constant of 3.7 $Pa \cdot m^3$/mole (at 25°C) has been calculated with the QSAR programme developed at the Syracuse Research Corporation (SRC, 1994). According to the Technical Guidance Document (EC, 1996), hereafter referred to as TGD, this QSAR method only applies to highly soluble substances.

Therefore, the Henry's law constant (H) is estimated as follows (TGD):

$$H = (\text{vapour pressure} \cdot \text{molecular weight})/\text{solubility}$$

The Henry's constant for DIDP is approximately 114 $Pa \cdot m^3$/mol and the deduced log H = 2 will be used in the risk assessment.

1.3.9 Partition coefficient octanol water

A logKow = 9.3 has been determined experimentally by HPLC retention time (Scherf, 1995). The reliability of this value may be discussed as the method is only reliable for logKow values in the range of 0 to 6. The test substance is not specified and the purity not known.

The Kow of di-n-decyl phthalate (DnDP) was determined in a slow-stir apparatus (Ellington, 1999). DnDP was dissolved in 50 ml of octanol at a concentration of 35-75 mg/ml and added to the surface of 10 litres of water. The stirring rate was adjusted to create a vortex of approximately 1 cm at the octanol/water interface. 1 l water samples were extracted at different

time intervals for analysis. Equilibrium was established within the first 20 hours of stirring and little change was observed at different sampling times up to 336 hours. The mean result of 4 measurements is logKow = 8.83. Furthermore, "No-stirring" experiments were conducted in a manner identical to the "slow-stirring" experiments except the stirrer motor remained "off". Equilibrium was attained within 39 hours. Measurement continued up to 263 hours. The mean logKow was determined to be 9.27. After the 263 hours, the "slow-stirring" was started and continued for 118 hours. The aqueous layer was sampled 1 hour after stirring was stopped and a logKow of 8.45 was determined. The aqueous layer was sampled again at 24 and 144 hours and logKow-values of 8.92 and 8.93 were determined respectively.

The calculated partition coefficients with the QSAR programme LOGKOW (SRC, 1994) are at maximum 10.5 (di-n-decyl phthalate). The calculated logKow value diminishes slightly with the degree of ramification. The main components of DIDP as estimated by ECPI (1998a) (cf. **Table 1.3**) can be estimated by QSARs:

Chain structure	logPow
- Trimethylheptyl	10.13
- Dimethyl octyl	10.28
- Methylnonyl	10.35
- n-Decyl	10.50

The measured value with the HPLC-method is outside the validation range of the method used. The measurement of partition coefficients of highly lipophilic substances is problematic and the currently available OECD methods are not adapted for such compounds. The result from the « slow-stir » method is therefore to be preferred. As can be seen in the above table, the chain structure has an influence on the result. The expected Kow value for DIDP is therefore probably slightly lower than for DnDP. For risk assessment purposes, the measured value of logKow = 8.8 will be used in the risk assessment.

More specific data are nevertheless available for estimating the environmental partitioning behavior and these will be used preferentially (cf. Section 3.1.1).

1.3.10 Flash point

Table 1.9 Flash point of DIDP

Data (°C)	Method	Reference
> 200	ASTM D93	Exxon Chemical Europe (1994)
≥ 215	ASTM D92	ICI (1996)
240	DIN 51 758	BASF (1996)
ca. 218	DIN 51 758	Hüls (1986)
217	Pensky Martens	BASF (1972)
>200	DIN 51 758	Hoechst (1990)

Flash point measurement may strongly depend on the presence of lighter components, the proportion of which may vary.

1.3.11 Auto flammability

Auto-flammability temperatures have been measured in the range from 365°C (BASF, 1972) to ca. 400°C (Hüls, 1986). A representative value is ca. 380°C.

1.3.12 Viscosity

Selected values are indicated in **Table 1.10**.

Table 1.10 Selected values of viscosity of DIDPs at 20°C

Value (mPa.s)	Method	Reference
≥ 120, ≤ 130	ASTM D 445	Exxon Chemicals Europe (1994)
120 - 150	DIN 53 015	Hüls (1986)
125 - 135	DIN 51 562	Hoechst (1990)
105 – 140 (106, measured)	DIN 51 562	BASF (1996)

A representative value would be approximately 130 mPa · s.

1.3.13 Summary of physico-chemical properties

Table 1.11 Summary of physico-chemical properties

Property	Value
Melting point	-53 to -39°C (av. -45°C)
Boiling point	> 400°C
Density	0.966 at 20°C
Vapour pressure	$5.1 \cdot 10^{-5}$ Pa at 25°C
Water solubility	0.2 µg/l at 20°C
Henry's law constant	114 Pa · m^3/mol
Log Kow	8.8
Flash point	> 200°C
Autoflammability	ca. 380°C
Viscosity	ca. 130 mPa · s

1.4 CLASSIFICATION

There is no entry in Annex I to Directive 67/548/EEC for DIDP.

Proposal: not classified as dangerous for the environment.

2 GENERAL INFORMATION ON EXPOSURE

2.1 PRODUCTION, IMPORT, EXPORT AND CONSUMPTION VOLUMES

Data from producers/importers are included in the IUCLID database. These are listed in the following table:

Table 2.1 List of producers/importers having submitted a HEDSET diskette

BASF, Germany
Hüls AG, Germany
Exxon Chemical, Holland
ICI C&P, France
Alusuisse / Lonza / Enichem, Italy

Furthermore, production at Neste in Finland ceased in 1991 and limited production at CEPSA/PDL in Spain and Gas de Portugal/PDL stopped in 1995 or 1996.

In 1994 the production volume of DIDP in the European Community was estimated to be ca. 279,450 t/a. Ranges are given in the IUCLID database and have been taken when no specific information on production volumes was reported by Industry. Apparently, 5 major production sites are located in Europe.

Three companies have provided export data (outside Europe) corresponding to ca. 38,000 t/a. No import of DIDP was reported for Europe in 1994. A mean DIDP plasticiser consumption in Western Europe has been reported by ECPI (1996) to be ca. 200,000 t/a (within a range of 193,000-220,000 t/a). An EU DIDP consumption of approx. 200,000 t/a is considered in this risk assessment.

Based on estimations by the producers, the evolution of the consumption volumes of DIDP (t/a) in Western Europe over the last decades is (Exxon Biomedical Sciences, 1999):

Year:	1964	1970	1975	1980	1985	1990	1994
Volume (t/a):	50,000	50,000	60,000	90,000	120,000	140,000	200,000

A further increase of the consumption of DIDP is to be expected over the following years.

2.2 PRODUCTION PROCESS

DIDP is prepared from propylene and butenes through an oligomerisation process forming hydrocarbons with 8 to 15 carbon atoms. After distillation (in view of obtaining nonene), oxonation forms aldehydes with one more carbon atom ("isodecanal"). The latter are hydrogenated and distilled to form monohydric alcohols (mainly C10). These are reacted with phthalic anhydride (PA). The first reaction step, alcoholysis of PA to give the monoester, is rapid and goes to completion. By charging in excess alcohol and by removing the water which is formed, the equilibrium can be shifted almost completely towards the products side. The reaction rate is accelerated by using a catalyst and high temperature.

Depending on the used catalyst the temperature range is in between 140°C and 250°C. For an acid catalyst, neutralisation with aqueous caustic soda or sodium carbonate is necessary. However, traces of alkali remain in the organic phase, and therefore a washing step is included. After distillation of remaining water and alcohol the catalyst is removed by filtration.

In order to minimise the emissions into the different compartments the reaction water is used in the neutralisation step and the distilled alcohol is recycled.

The following figure illustrates the production procedure.

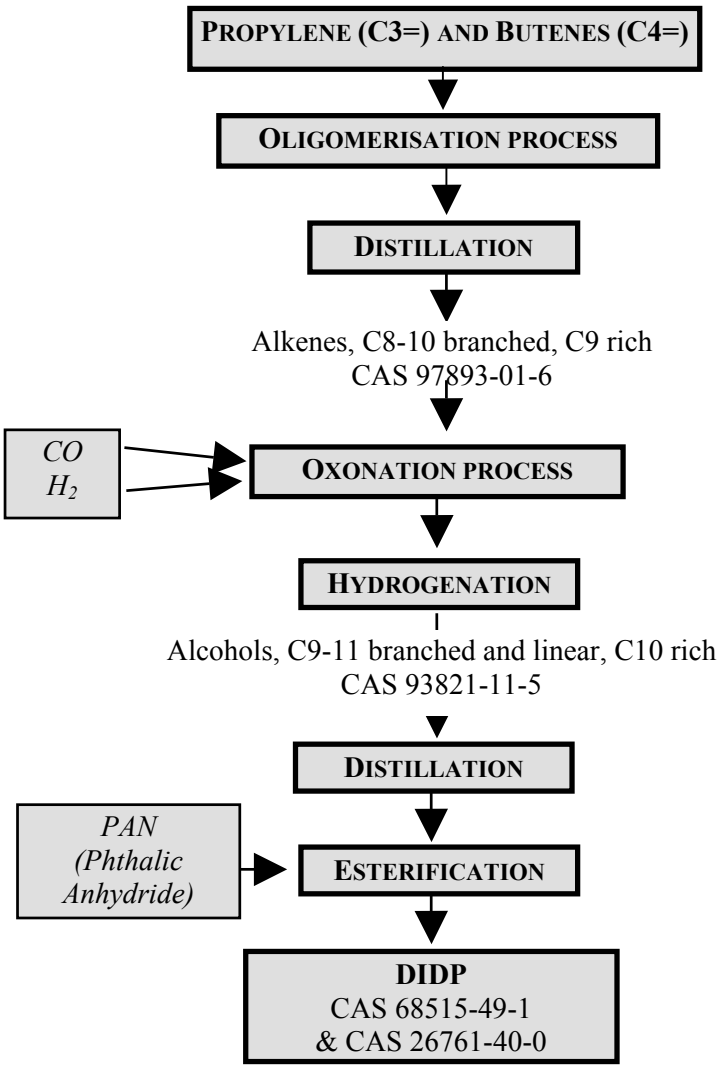


Figure 2.1 Production procedure of DIDP

2.3 USES

DIDP is mainly used as plasticiser in PVC. The DIDP consumption corresponds to 22% of the total European phthalate consumption used as plasticisers. The plasticiser consumption of phthalates in Europe is about 970,000 t/a.

According to Cadogan (personal communication, 1997), DIDP consumption in PVC amounts to 191,000 t/a. The PVC end use split for all phthalates according to Cadogan et al. (1994) as well as an estimation for DIDP is shown in **Table 2.2**.

Table 2.2 PVC end use split for all phthalates and estimation for DIDP Cadogan et al. (1994)

Application	Consumption of phthalates [t/a]	Consumption of DIDP [t/a]	Percentage
Total consumption in PVC	**877,000**	**191,000**	
Calendering			
Film, sheet and coated products	138,000	29,987	15.7
Flooring, roofing, wall covering	31,000	6,685	3.5
Total		36,672	
Extrusion			
Hose and profile	47,000	10,123	5.3
Wire and cable	251,800	54,807	28.7
Clear, medical, film	62,400	13,580	7.1
Total		78,510	
Injection Moulding			
Footwear and miscellaneous	72,800	15,843	8.3
Plastisol spread coating			
Flooring	92,000	20,055	10.5
General (coated fabric, wall covering, etc.)	100,000	21,774	11.4
Total		41,829	
Other plastisol applications			
Car undercoating and sealants	67,000	14,516	7.6
Slush/rotational moulding etc.	17,000	3,629	1.9
Total		18,145	

The typical content of DIDP in flexible PVC products is between 25 and 50%.

Approximately 9,000 t/a of DIDP are consumed in Europe in non-PVC applications. The non-PVC applications of phthalates are very small when compared to the PVC application. Non-PVC applications are in other vinyl resins than PVC, cellulose ester plastics and other polymer containing products, such as pressure sensitive adhesives and printing inks. Otherwise DIDP is applied in non-polymer applications, such as anti-corrosion and anti-fouling paints (Norwegian Pollution Control Authority, 1997).

Accurate information on consumption of phthalates in non-PVC end uses was available only from the USA (Neste, 1996). In this risk assessment it is supposed that the structure of consumption is quite similar in Europe.

Table 2.3 shows the breakdown of the consumption of phthalates in the USA in non-PVC products and the estimated tonnages for DIDP used in these applications in Europe.

Table 2.3 Estimated non-PVC end use split for DIDP

End use	Consumption [Phthalates]-USA [t/a]	Share of non-PVC [Phthalates]-USA	Consumption [DIDP] in Europe [t/a]
PVC	533,000		191,000
Non-PVC	85,000	100%	9,000
Other vinyl resins	48,000	56%	5,040
Cellulose ester plastics	13,000	15%	1,350
Paints & inks & sealing compounds	10,000	12%	1,080
Non-polymer uses	15,000	17%	1,530

The application of vinyl resins other than PVC, consists most likely of acrylic plastic resins, which are basically polymethyl methacrylate (Neste, 1996).

The application "paints & inks & sealing compounds" includes pressure-sensitive adhesives and printing inks. In printing inks, phthalates, mostly dioctyl phthalates, are used as softeners especially for inks used in the textile industry.

According to INRS (1998), the products in the French product register contain between 3 and 30% DIDP. Paints contain at maximum 13% DIDP. Higher contents are found for sealing compounds.

In elastomers, phthalates are not used, but aliphatic and polymeric plasticisers are preferred.

The use of DIDP for the production of ceramics was investigated. Plasticisers can be used as additives for ceramics to improve their processability. They work in combination with binders to give formed, unfired parts the flexibility or deformability required for subsequent handling and processing. They may also be added to spray dried or granulated powders so that the granules crush easily during pressing. Common materials include polyethylene glycol, polypropylene glycol, propylene glycol and several phthalates (SRI International, 1993). According to a market study performed in Germany, only very small amounts of phthalates are used in the processing of ceramics. Only DEHP was identified and a total consumption of 29 t/a of DEHP are estimated for the whole EU (Verband der keramischen Industrie e.V., 2000). Neither DINP nor DIDP are used in the EU for the processing of ceramics.

Compared to the use pattern derived by Neste (1996) for the market in the USA, the quantities allocated for ceramics will be ignored in the use pattern for the EU (cf. **Table 2.4**).

Summary

In **Table 2.4** the use pattern of DIDP as considered in the environmental risk assessment is presented:

Table 2.4 Estimated amount of DIDP used in various PVC and non-PVC applications

Application	Industry category	Quantity in EU (t/a)
PVC end uses	Polymer industry (IC = 11)	191,000
Non-PVC end uses		8,480
Polymer related	Polymer industry (IC = 11)	6,390
Non-polymer related		2,090
anti-corrosion paint	Paints and Varnishes industry (IC = 14)	520
anti-fouling paint	Paints and Varnishes industry (IC = 14)	520
sealing compounds	Paints and Varnishes industry (IC = 14)	520
textile inks	Textile industry (IC = 13)	520
Total Consumption		**199,480**

The 2,090 t/a estimated to be used in paints, inks and sealing compounds as well as the other non-polymer applications (cf. **Table 2.4**) are supposed to be equally distributed among anti-corrosion paints, anti-fouling paints, sealing compounds and textile inks, i.e. 520 t/a for each application. The initially estimated market share for ceramics was removed from the overall total, after it became apparent that DIDP was not used for this purpose in the EU. Based on the data from the French product register, a mean content of 15% DIDP in these products will be assumed.

Type of PVC products and lifetimes

For the estimation of the releases to the environment through articles containing DIDP, it is necessary to estimate the amount of substance included in articles being used outdoors or indoors. Based on the values reported in **Table 2.2**, some products can be recognised for outdoor or indoor use. The flooring is supposed to be used indoors. Car undercoating (14,516 t/a) is used outdoors. Footwear and miscellaneous (15,843 t/a) is assumed to be used outdoors. The use of wires and cables is supposed to be distributed evenly to outdoor (27,400 t/a) and indoor (27,400 t/a) use. For the other types of products, an industry survey for DEHP was performed. 78% of the phthalate containing PVC products are used in indoor applications and the remaining 22% in outdoor applications (BASF, 1999a). The approximate amounts of DEHP used in PVC for different outdoor applications are found in **Table 2.5**, based on figures provided by BASF (1999a). The respective amounts of DIDP can be estimated based on phthalate market shares of 51% for DEHP and 22% for DIDP (Cadogan et al., 1994).

The Danish EPA (Miljöstyrelsen, 1996) reported technical lifetimes for different product groups. For PVC in cars the lifetime was estimated to be 16 years, for different building materials 10-20 years, and for roof coating 20 years. For roofing material BASF AG (1999a) give a lifetime of 20 years. For coil coating a lifetime of 10 years is used (ECPI, 1998b). In this assessment 25 years is used for both roof and wall coating. For cables and wires the lifetime was estimated to be 10-50 years. In this assessment the average, 30 years, is selected. The technical lifetime for a building is assumed to be 100 years (no reference). No lifetime is available for fabric coating. However, it is assumed to be 10 years. According to ECPI (1998b), the lifetime for flooring is 10 years. However, according to a producer (Tarkett-Sommer, 1999) a more realistic lifetime is 20 years. The different lifetimes reported and the values used in this risk assessment are summarised in **Table 2.5**.

Table 2.5 Volumes of DEHP and DIDP in different applications of PVC products and their respective lifetimes

Application	Tonnage DEHP t/a	Tonnage DIDP t/a	Technical lifetime				
			ECPI (1996)	BASF (1999a)	Miljöstyrelsen (1996)	Other	Used in the RAR
Indoor application							
Coated products			7	-	-	-	7
Film & sheet			7	-	1-5 [2]	-	7
Wires & cables		27,400		10-30	30-50	-	30
Hoses & Profiles			10 [1]	-	1-10	20 [3]	20
Floor		20,055	10	-	-	20 [3]	20
Outdoor application							
Roofing material	1,000	430 [4]	-	20	-	-	20
Roofing (coil coating)	5,000	2,150 [4]	-	10	-	-	10
Wires & cables		27,400	-	10-30	30-50	-	30
Coated fabric	21,000	9,060 [4]	-	10	-	-	10
Hoses & Profiles	6,000	2,590 [4]	-	10	-	-	10
Car under-coating		14,516	-	12	16	-	14
Shoe soles		15,843	-	5	-	-	5
Sealings		520					20
Paints & lacquers		1,040					7

1) Assumed to be the same as for flooring
2) PVC-foils
3) Tarkett-Sommer (1999)
4) Estimated from DEHP, based on market shares

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

3.1.1 Environmental fate

As DIDP is an isomeric mixture, the fate and behaviour of the substance cannot be determined with accuracy. Each component of the mixture would tend to have different characteristics concerning its fate and behaviour in the environment. Nevertheless, an overall picture can be drawn, as presented below. As it has been shown above with e.g. the estimations of the Kow, the differences in behaviour between the different components should be rather limited and it can therefore be considered that it is possible to perform a risk assessment by using overall average properties of the substance.

3.1.1.1 Degradation

Hydrolysis

No experimental data on hydrolysis are available. Due to the low solubility of DIDP a test on hydrolysis is not feasible. The EUSES defaults will be used for this assessment.

Photodegradation in air

No measured data are available for DIDP. Assuming an atmospheric hydroxyl concentration of $5 \cdot 10^5$ molecules/cm^3, a half-life of 0.6 day can be calculated (SRC, 1994; Meylan and Howard, 1993).

Biodegradation

Several results from standard test systems, where mineralisation is determined, are available.

- Sugatt et al. (1984) tested 20 mg/l of a test substance in a Shake flask test for inherent biodegradability. 39% was degraded after 9 days whereas 53% was biodegraded after 21 days. The inoculum was preadapted to the compound over a period of 14 days prior to the test.
- O'Grady et al. (1985) also tested DIDP (at 3 mg/l) for inherent biodegradation in a Semi-Continuous Activated Sludge (SCAS). 68% was biodegraded after 24 hours. These results were achieved after a 21-day draw and fill procedure.
- A concentration of 35 mg/l was tested by Exxon Biomedical Sciences (1995a) in a Manometric Respiratory test. (OECD guideline 301 F), 67.1% was degraded after 28 days. The 10-day window criterion was not achieved.
- In an OECD guideline test (301 C), biodegradation by determination of $^{14}CO_2$ evolution was 88% after 28 days, but only 54% determined by BOD. The discrepancy between these 2 results could not be explained (ICI, 1984).
- In a further test with OECD guideline 301C, biodegradation was 42% after 21 days (CITI, 1992), based on BOD. At the end of 21 days, the degradation curve was still on the upward

trend. As no results are available for 28 days, it cannot be concluded whether the criteria for ready biodegradation are met in this test.

Furthermore:

- In treated wastewater, di-n-decyl phthalate was degraded at 82% after 7 days. The initial concentration was 7.8 µg/l. The DT50 was < 1 day. The test was performed at 25°C. Only the disappearance of the parent compound was determined and the degradation products were unknown (Furtmann, 1993).
- In Rhine river water di-n-decyl phthalate was totally degraded after 7 days. The initial concentration was 1.1 µg/l related to the test substance. The DT50 was < 1 day and the DT90 was < 3 days. The test was performed at 25°C. Only the disappearance of the parent compound was determined and the degradation products were unknown (Furtmann, 1993).

One test result on biodegradation under anaerobic conditions is available (Mersiowsky et al., 1999). Solid waste samples from full-scale landfills and from lysimeters with municipal solid waste simulating the conditions in landfills were used as sources of microorganisms. The experimental vessels were incubated in the dark at 30°C. Methane analyses were carried out regularly and compared with the amount in the corresponding control vessels. 9 vessels were incubated with waste samples from full-scale landfills and 20 vessels were incubated with waste samples from lysimeters. The concentration of DIDP was not significantly reduced in 7 of the vessels inoculated with waste from landfills after 147-296 days. Significant reductions of 20 and 50% were observed in 2 vessels after 244 and 296 days, respectively. However, no excess of methane above control level was observed, indicating only primary degradation. Furthermore, the concentration of DIDP was not significantly reduced in 17 of the vessels inoculated with waste from simulation lysimeters after 127-358 days. Significant reductions of 20, 20 and 40% were observed in 3 vessels after 127, 127 and 358 days, respectively. However, no excess of methane above control level was observed, indicating only primary degradation. It can therefore be concluded that the biodegradation potential of DIDP under anaerobic conditions is very low.

Based on results with DEHP (EC, 2001), it can be assumed that the most relevant intermediate metabolite is monoisodecyl phthalate. As this compound is less hydrophobic and therefore more bioavailable than the parent compound, it would be important to consider it in the risk assessment. But, as no effects data are available, it can only indirectly be taken into consideration. The assessment will therefore be performed with the parent compound. The biodegradation rates are derived for mineralisation, thereby including the degradation of the monoester. For bioaccumulation, special care is taken to include if possible the monoester in the estimations.

DIDP failed the 10-day window criterion in the only full-validated test on ready biodegradability.

DIDP can therefore be considered as readily biodegradable without a 10-day window criterion. Based on the fact that DIDP is an isomeric mixture, it could be argued that there are some components of DIDP that are resistant to biodegradation. In the study by Exxon Biomedical Sciences (1995a) in which 67.1% was degraded after 28 days, the biodegradation-curve was still on the upward trend after 28 days. Further results were obtained with the corresponding isomeric alcohols. Exxon Biomedical Sciences (1997 a;b) performed biodegradation tests with isomeric C8-alcohols (CAS 91994-92-2) and C10-alcohols (CAS 93821-11-5) in the manometric respirometry test (OECD guideline 301F). The degradation of the C8-alcohol reached 82% after 28 days and the C10-alcohol reached 71% after 28 days. While the degradation-curve for the C8-alcohol had reached a plateau, the curve for the C10-alcohol was still on the upward trend.

Therefore, the probability that some components of DIDP are resistant to biodegradation is very low.

According to the TGD, based on the OECD screening tests, a rate constant of 0.3 h^{-1} can be extrapolated for sewage treatment plants (STP).

For surface water, a half-life of 50 days could be extrapolated according to the TGD. The simulation test on biodegradation of DIDP in surface water of Furtmann (1993) cannot be considered in this risk assessment as the test was performed at 25°C and only primary biodegradation was determined. A realistic biodegradation rate constant cannot be deduced from this test result. The results indicate though that the substance continues to degrade at low i.e. environmentally relevant concentrations. Based on a limited amount of results from surface water simulation tests, a mineralisation half-life of 50 days was derived for DEHP taking account of temperature adjustment (EC, 2001). In a first approach, the same half-life in surface water of 50 days will be used for DIDP.

For soil and sediment, no results are available. For soil, the extensive database from DEHP could be used to extrapolate a biodegradation rate constant for DIDP. A realistic worst-case half-life for mineralisation of 300 days has been assumed in the risk assessment for DEHP (EC, 2001).

This very conservative value is furthermore confirmed by a study available for DINP. Seven cultured soils from the area of Roskilde in Denmark were investigated for phthalate concentrations (Vikelsoe et al., 1999). At each location two soil cores 50 cm in depth were taken, each profile being divided into 5 subsamples of each 10 cm. One location, which was heavily amended with sewage sludge, was sampled two years after the first analysis. No sludge had been used on this site in the meantime. Di-n-nonyl phthalate as well as diisononyl phthalate were determined:

Table 3.1 Phthalate concentrations in cultured soils in Denmark

	Depth (cm)	DnNP (µg/kg dw)	DINP (µg/kg dw)
Sludge amended with high amounts for 25 years, changed to artificial fertiliser 6 years before sampling, cattle grazing	0-10	160	130
	10-20	200	220
	20-30	200	200
	30-40	180	96
	40-50	120	93
Same location sampled 2 years later	0-10	120	410
	10-20	160	540
	20-30	210	670
	30-40	290	910
	40-50	210	280
	50-60	84	63

No significant decrease in the concentrations could be observed. The same trend was observed for DEHP which was also included in this study. This could be explained by a non-homogeneous distribution of the substances in the soil. Furthermore, it is possible that a high proportion of the phthalates is present in the form of PVC particles (see Section 3.1.2.1 on waste remaining in the environment) and that further leaching out of these particles maintains a high level of extractable compounds in soil over a longer period of time. Other factors may influence the availability of the compounds to biodegradation though. In a first approach, it is therefore proposed to use the same half-life of 300 days in soil for DIDP in this risk assessment.

The same half-life can be used for aerobic sediment. For anaerobic sediment a degradation rate constant of 0 d^{-1} will be used. This is confirmed by the test results from Mersiowsky et al. (1999) as well as the findings of Furtmann (1993) in datable sediment profiles suggesting that DEHP is only broken down very slowly in an anaerobically sealed stratified sediment and that high levels are still detectable years later.

A total half-life of 3,000 days (i.e. k_{sed} = 0.00023 d^{-1}) can therefore be derived for DIDP in the whole sediment column.

Table 3.2 Estimation of biodegradation rate constants in the different compartments

Compartment / medium	Biodegradation rate	Half-lives [day]
Surface water	$k_{sw} = 1.4 \cdot 10^{-2}$ d^{-1}	50
Sediment	k_{sed} = 0.00023 d^{-1}	3 000
Soil	k_{soil} = 0.0023 d^{-1}	300

Elimination in sewage treatment plants (STPs)

Based on the above-cited physical chemical properties (log H = 2, logKow = 9.3, Koc = 286,000 l/kg, see below) as well as the biodegradation rate of 0.3 h^{-1} in a STP, the elimination through biodegradation and distribution can be estimated with the model SIMPLETREAT included in the program EUSES:

Table 3.3 Estimation of removal of DIDP in a STP according to SIMPLETREAT

% to air	3.2
% to water	8.1
% to sludge	84.8
% degraded	3.9
% removal	91.9

These values are retained for the calculation of PEClocal in water and soil through sludge application, as no simulation test and no monitoring data in STPs are available.

3.1.1.2 Distribution

Adsorption-Accumulation in soil

Only one test has been performed for DIDP in sediment (Williams et al., 1995). The experimental conditions have been described in detail. A Koc value of 286,000 l/kg is the mean obtained from experiments with three different sediments and radiolabeled ^{14}C-DIDP.

The three sediment types are the following:

	OC [%]	Sand [%]	Silt [%]	Clay [%]	CEC * [meq/100g]	pH	Koc [l/kg]
EPA 8	0.15	82.4	6.8	10.7	3.72	8.32	111,000
EPA 18	0.66	34.6	39.5	25.8	15.43	7.76	601,000
EPA 21	1.88	50.2	7.1	42.7	8.33	7.60	145,000

*Cation exchange capacity

The lowest result was obtained with a low organic carbon content (the OECD guideline 106 suggests an organic carbon content of 0.6-3.5%). In this test, the coefficient of variation for Koc was similar to that observed for Kd despite a tenfold difference in organic carbon content between the sediments investigated. This suggests that factors in addition to sediment organic carbon are influencing partitioning behaviour.

However the mean value of 286,000 l/kg will be used in the risk assessment as this is the only data set available.

For the different media, using the standard organic carbon contents proposed in the TGD, the water - solids and total compartments - water partition coefficient can be estimated. The results are presented in the following table.

Table 3.4 Partition coefficients between different compartments

Compartments	OC content (%) of solid phase	Solid water partition coefficient	Total compartment - water part. coefficient
Soil - water	2	Kp_soil = 5,720 l/kg	Ksoil_water = 8,580 m^3/m^3
Sediment - water	5	Kp_sed = 14,300 l/kg	Ksed_water = 7,150 m^3/m^3
Suspended matter - water	10	Kp_susp = 28,600 l/kg	Ksusp_water = 7,150 m^3/m^3

3.1.1.3 Bioaccumulation

Bioaccumulation in aquatic organisms

Only one test has been performed with DIDP, where the parent compound is measured in biota and the water phase (CITI, 1992). A BCF of < 14.4 for fish (*Cyprinus carpio*) has been determined according to the OECD guideline 305 C in a flow-through system after an equilibration phase of 8 weeks at a nominal water concentration of 0.1 mg/l. In the same test system, a BCF of 1.3-29.7 was determined for DEHP. Much higher BCFs have been determined with DEHP in fish in other assays (see EC, 2001). A BCF of 840 for fish was retained in the risk assessment for DEHP (see also below).

In a preliminary monitoring study in the Seine estuary in France, water samples and mussel samples were analysed from the same locations (Elf Atochem, 1997). At none of the locations, the content of DIDP could be quantified simultaneously in water and mussels. At one location, a concentration of 1.1 µg/l in water and of < 23 µg/kg wwt in mussels was determined. This would indicate a BAF of <21. As only one sample was taken per location, it is not possible to determine whether these values are representative over a longer period of time.

BCF values of 90 to 147 in Daphnids have been measured by Brown and Thompson (1982a), based on total radioactivity. The concentration in the water phase (mean values of 2.9, 9.6, 32.5 and 100.3 µg/l) was also determined by measuring radioactivity.

In mussels (*Mytilus edulis*), high BCF values of 3,000-4,000 were measured by Brown and Thompson (1982b) in a flow-through system over 28 days. Steady state concentrations were achieved after 14 days. The concentration in the water phase (4.4 and 41.7 µg/l) as well as in mussels were determined by measuring total radioactivity.

As the exposure concentrations were clearly above water solubility, the organisms were probably simultaneously exposed through the water phase as well as through undissolved particles of DIDP and DIDP adsorbed to algae which were added as food to the test system.

In a different test system, a BCF = 0.6 was determined in sediment organisms, also based on total radioactivity (Brown et al., 1996). This value is not comparable to the above results though, as the BCF is related to the total sediment concentration and because the concentration in midges was determined in the emerging animals (the concentration in the shells was therefore not taken into consideration).

The use of BCF values based on total radioactivity may give an overestimation of the BCF due to the fact that the metabolism of DIDP was not taken into account as both ^{14}C-DIDP and any ^{14}C-labeled metabolites of DIDP were measured (including ^{14}C built into the tissue of the organism in e.g. fatty acids). On the other hand, in the test system with mussels reported above, the concentration in the water phase was also determined by radioactivity. As the measured concentrations were far above the water solubility, the bioavailability of the compound in the test system may have been much lower and therefore the bioaccumulation might be underestimated.

Furthermore, it has to be recognised, that by basing the results on the respective concentration of the parent compound, the major metabolite, i.e. the monoester MIDP, is neglected. A BCF that would include the monoester could be somewhat higher, but could be expected to be lower than the BCF values measured with ^{14}C-labeled material.

One bioaccumulation study is available with DEHP, in which also the metabolites were determined. The bioaccumulation of carbonyl-^{14}C-labeled DEHP in adult fathead minnows (*Pimephales promelas*, mean fwt 1.24±0.31 g) was investigated in a flow-through study (Mehrle and Mayer, 1976; Mayer et al., 1977). Test concentrations of DEHP were 1.9, 2.5, 4.6, 8.1, 14, 30 and 62 µg/l (mean measured). The fish were exposed to DEHP for 56 days at 25°C, followed by a depuration phase of 28 days.

Besides the parent compound, the major metabolite found in the fish tissues was MEHP, accounting for 12-50% of the recovered residues after the exposure period. The proportion of MEHP increased with the exposure concentration. The data presented in **Table 3.5** represent the level of residues in fish after 56 days of exposure in a flow-through study. The composition of residues in water was not reported in the study, since the concentrations were measured radiometrically only.

Table 3.5 Level of residues in fish after 56 days of exposure in a flow-through study

	Residue composition in fish after 56 days (% of total recovered)					
Conc. in water (µg/l)	DEHP	MEHP	Phthalic acid	MEHP conjugate	Phtalic acid conjugate	Other
1.9	79	12	2.5	4.1	1.2	1.2
2.5	70	24	1.7	2.2	1.1	1.0
4.6	69	23	4.1	1.2	0.6	2.1
8.1	70	21	5.4	1.0	1.2	1.4
14	60	30	3.6	0.6	5.1	0.7
30	42	40	11	0.4	6.6	0.3
62	33	50	5.7	0.4	9.8	1.1

Bioaccumulation factors based on total residues, DEHP+MEHP, and DEHP in fish, respectively, with exposure concentration in the water given as total ^{14}C are given in **Table 3.6**.

Table 3.6 Bioaccumulation factors after 56 days

Mean exposure conc. (µg/l)	BCF total ^{14}C	BCF DEHP+MEHP	BCF DEHP
1.9	737	670	582
2.5	880	827	616
4.6	891	820	614
8.1	444	404	311
14	357	321	214
30	287	235	121
62	155	129	51

At concentrations higher than ca. 5 µg/l, BCF was inversely correlated with the test concentrations. However, in the two highest test concentrations, steady state does not seem to have been reached during the 56 days of exposure.

As can be seen from the above results, the BCF based on ^{14}C and the BCF based on total DEHP + MEHP concentrations are not significantly different.

Conclusion

As shown above, the results based on total radioactivity can be used to determine a BCF of DIDP in aquatic organisms. The BCF value for DIDP for mussels of 4,000 based on ^{14}C measurements can therefore be used in the risk assessment for secondary poisoning.

For indirect exposure to humans via the environment, the assessment should preferably be based on a BCF for fish as the latter is more representative regarding the food consumption in the EU. The only BCF result for DIDP with fish is very low compared with the results available for DEHP (see EC, 2000). In a first approach, the BCF for fish of 840 retained for the risk assessment for DEHP will also be used for the assessment of the exposure of humans via the environment.

Bioaccumulation in soil organisms

A very low bioaccumulation was observed with earthworms (*Eisenia Foetida*). A BCF of ca. 0.01-0.02 was observed in a 14-day toxicity test (Exxon Biomedical Sciences, 1996b). But the test concentrations in soil were very high (up to 10,000 mg/kg) and it is not clear whether a steady state was achieved.

In a further test with DEHP a low bioaccumulation factor was also observed with *Eisenia foetida* in a 14-day test. Based on dry weights, the highest measured BCF was 0.2 (Hüls, 1998). Assuming a typical dry to wet weight conversion factor of 0.15 for earthworms and of 0.88 for soil, a BCF of 0.034 based on wet weights can be derived. In this second test the concentration in soil was somewhat lower (1,000 mg/kg) than in the test with DINP, but also in this test it is not clear whether a steady state was achieved.

A very low-depuration rate of DEHP from earthworms of 0.04 d^{-1} has indeed been reported by Staples et al. (1997). Based on this first order depuration rate, it would appear that approximately 50% of the steady state tissue concentration is achieved in this time period. EUSES calculates a BCF worm of 25.1 kg/kg. As there is a difference of about three orders of magnitude between the measured and the estimated BCF value, it appears that the higher value is clearly an overestimation. In a first approach, based on the experimental results and the low measured depuration rate, a reasonable worst-case BCF of 1 will be used in the risk assessment.

Bioaccumulation in plants

No results are available regarding bioaccumulation of DIDP in plants. According to the TGD, a plant-water partition coefficient can estimated with:

$$K_{plant\text{-}water} = Fwater_{plant} + Flipid_{plant} \cdot Kow^{b}$$

with:	$Fwater_{plant}$	volume fraction water in plant tissue	0.65 m^3/m^3
	$Flipid_{plant}$	volume fraction lipids in plant tissue	0.01 m^3/m^3
	b	correction for differences between plant lipids and octanol	0.95

i.e. $K_{plant\text{-}water} = 2.3 \cdot 10^6$ $(mg/m_{plant}^3)/(mg/m_{water}^3)$

Several studies were performed with other long-chain phthalate esters.

Overcash et al. (1986) studied the uptake of DEHP and di-n-octyl phthalate (DOP) in fescue, corn, soybeans and wheat under greenhouse conditions. Plants were grown at different substance concentrations ranging between 0.044 and 4.4 ppm for DEHP, respectively 0.022 and 2.2 ppm for DOP. The uptake was monitored by measuring ^{14}C in the plants, assuming that the ^{14}C detected is the parent compound. The highest uptake was recorded with fescue and corn harvested respectively 34 and 17 days after planting while lower uptake were observed in mature wheat and soybeans. The final soil concentration of DEHP was on average 25% of the initial applied concentration. The geometric mean between initial and final soil concentration could be used to derive a BCF. The highest uptakes were recorded for the highest soil concentrations.

Based on dry weights, the accumulation with DEHP is shown in **Table 3.7**.

Table 3.7 Bioaccumulation factors in plants for DEHP Overcash et al. (1986)

Plant	Initial soil conc. (mg/kg dw)	Final soil conc. (mg/kg dw)	Average soil conc. (mg/kg dw) *	Final plant conc. (mg/kg dw)	BCF
Fescue	0.044	ca. 0.011	ca. 0.022	0.028	1.3
Fescue	0.44	ca. 0.11	ca. 0.22	0.27	1.2
Fescue	4.4	ca.1.1	ca.2.2	3.2	1.4
Corn	0.044	ca. 0.011	ca. 0.022	0.009	0.4
Corn	0.44	ca. 0.11	ca. 0.22	0.022	0.1
Corn	4.4	ca.1.1	ca.2.2	4.6	2.1
Soybean	0.044	ca. 0.011	ca. 0.022	0.0	0
Soybean	0.44	ca. 0.11	ca. 0.22	0.012	0.05
Soybean	4.4	ca.1.1	ca.2.2	0.011	0.005
Wheat	0.044	ca. 0.011	ca. 0.022	0.0046	0.21
Wheat	0.44	ca. 0.11	ca. 0.22	0.030	0.14
Wheat	4.4	ca. 1.1	ca. 2.2	0.315	0.14

* Geometric mean

The uptake for DOP was ca. 1 to 2 orders of magnitude lower.

Aranda et al. (1989) also tested the uptake of DEHP under greenhouse conditions in lettuce, carrot, chile pepper and fescue using ^{14}C labeled DEHP. Four soil treatments with initial DEHP concentration in soil between 2.65 and 14.02 mg/kg dw were used. Approximatively 32% of the radioactivity initially applied remained in the soil 115 days after planting. Based on dry weight and initial soil concentrations, the average BCFs for lettuce, carrot tops, roots, chile plants, chile fruit and fescue were 0.47, 0.28, 0.13, 0.15, 0.08 and 0.24, respectively. Assuming an average decrease of 68% in soil over the uptake period, BCFs based on average soil concentrations would be approximately increased by a factor of 2 i.e. BCF = 0.16-0.94. The parent DEHP was also measured in plant tissue and not detected. The measured ^{14}C is therefore mainly to be attributed to metabolites and the estimated BCFs represent certainly an overestimation of the bioaccumulation for DEHP.

Schmitzer et al. (1988) studied the uptake of DEHP in barley and potatoes in outdoor experiments. As DEHP had completely disappeared from soil in the barley experiment, the results could not be used to derive a BCF. The initial and final soil concentrations were 1 mg/kg dw and 0.033 mg/kg dw, respectively, based on ^{14}C measurements. The vegetation period was 111 days. For assessment purposes, an average concentration (geometric mean) of 0.18 mg/kg dw can be used for the BCF estimation, as shown in **Table 3.8**.

Table 3.8 Bioaccumulation factors in plants Schmitzer et al. (1988)

Sample	Average soil conc. (mg/kg dw)	Plant conc. (mg/kg fresh w.)	Plant conc. (mg/kg dw.)*	BCF
Potatoes, peeled	0.18	0.077	1.08	6.0
Peel	0.18	0.032	0.45	2.5
Shoots	0.18	0.119	1.67	9.2
Roots	0.18	0.160	2.24	12.4
Plant total	0.18	0.076	1.06	5.9

* calculated based on TGD defaults

These results are also based on ^{14}C measurements, assuming that the ^{14}C detected is the parent compound. The parent DEHP was also measured in plant tissue and not detected. The measured ^{14}C is therefore mainly to be attributed to metabolites and the estimated BCFs represent certainly an overestimation of the bioaccumulation for DEHP. Laboratory experiments performed in parallel have shown that most of the radioactivity detected in shoots is due to $^{14}CO_2$ uptake. It can therefore be considered that the BCF values for shoots are even more overestimated.

Kirchmann and Tengsved (1991) measured the concentration of DEHP in barley grains grown on sludge-amended soil. The application rate of sludge was 5 tonnes dw/ha. The DEHP concentration in sludge was 116 mg/kg dw, and the resulting concentration in grains was 530 µg/kg dw. The DEHP found in the grain amounted to 0.22% of the dose from the sludge. The barley grown on N-fertiliser or pig slurry amended soil also contained DEHP at concentrations of 89-110 µg/kg, while no DEHP was detected in the fertiliser. The experimental area was not exposed for sludge before the experiment. This would indicate that a large portion of the DEHP in grains is due to air deposition (direct uptake and/or via the soil).

Discussion

Due to its high affinity to organic matter only a limited bioaccumulation of DEHP in plants is expected. The experimental studies confirm this with BCFs ranging between 0.005 and 12. The highest BCFs were observed on barley, corn and potatoes. Lower BCF values were obtained for lettuce, carrot (top), chile plant, soybeans and wheat.

The study on potatoes (Schmitzer et al., 1988) shows similar BCF values in the whole plant. This indicates that DEHP was easily distributed from the root to the shoot. Since the BCF in this case is based on ^{14}C the relatively high BCF in shoots may be a result of a transport of degradation products.

The EUSES model calculates separate BCF for roots and leaves for DIDP. The BCF was calculated to 650 in plant roots and 10^{-4} in plant leaves. The model assumes that most of DIDP is physically adsorbed to the root and only to a minor part be transported to the leaves (based on Koc = 286,000 l/kg and logKow = 8.8). A comparison with experimental results indicates that this calculation is an underestimation of the BCF for the leaves and an overestimation of the BCF for the root. The experimentally derived results are rather uneven. It is therefore difficult to select a single value for the model. The highest value of 12 will therefore be used. Considering that the results are based on ^{14}C-distribution considerably overestimates the real BCF as metabolisation is not taken into account.

Using Kp_{soil} and an average bulk density of plant tissue RHO_{plant} of 0.7 kg/l, a $K_{plant\text{-}water}$ value can be estimated:

$$K_{plant\text{-}water} = BCF \cdot RHO_{plant} \cdot Kp_{soil} \cdot CF_{dry\text{-}wet} = 12 \cdot 0.7 \cdot 5{,}720 \cdot 0.07 = 3{,}432$$

with $CF_{dry\text{-}wet}$ being the plant dry to wet weight conversion factor.

This value will be used for the indirect exposure of humans via the environment

3.1.2 Aquatic compartment

The environmental exposure assessment of DIDP will be based on the expected releases of the substance during the following life cycle steps:

I	Production
II	Distribution
IIIa	Processing in PVC polymers
IIIb	Processing in non-PVC polymers
IIIc	Use in anti-corrosion paints
	A/ formulation
	B/ application
IIId	Use in anti-fouling paints
	A/ formulation
	B/ application
IIIe	Use in sealing compounds
	A/ formulation
	B/ application
IIIf	Use in inks for textiles
	A/ formulation
	B/ application
IVa	Exterior and interior use of DIDP-containing PVC products
IVb	use of DIDP-containing non-PVC polymers
IVc	Applied anti-corrosion paints containing DIDP
IVd	Applied anti-fouling paints containing DIDP
IVe	Applied sealings containing DIDP
V	Disposal of end products

For life cycle stages I and III site-specific and/or generic emission scenarios are used for calculating the predicted environmental concentrations (PEC) values in the various compartments.

Stages II, IV and V, can be regarded as diffuse sources of DIDP. The emissions will be considered in PECregional calculations.

Site-specific scenarios are based on actual data from industry on emission patterns etc. whereas generic scenarios are fully based on model calculations for a realistic worst-case situation.

The exposure assessment is based on the TGD (EC, 1996). Regional concentrations are evaluated with the model SIMPLEBOX included in the program EUSES.

3.1.2.1 Releases to surface water

The following release estimates are based on emissions reported by the producers or estimated with emission factors given in the draft Use Category Document on Plastic Additives, hereafter referred to as UCD (BRE, 1998).

For every life stage the input in raw wastewater and a connection rate to wastewater treatment plants will be estimated. The removal will be considered for the continental, regional and local input in the water compartment. At the same time, the indirect input to air and sludge via the depuration step will be calculated and presented.

Production (life cycle step I)

In Section 2.1 it is mentioned that there are five DIDP producers within the EU. For three producers (three production sites) specific production volumes and emission data were submitted.

For the producers not having submitted releases to the surface water, the releases have been calculated with default values given in the TGD (0.3%).

	A	B	C	D	E
Release [t/a]	0.1 *	3 *	150 ***	< 0.06 **	30 ***

* Specific reported release quantities, no precision related to measurement/estimation techniques have been provided (B reported COD and BOD efficiency)

** Release quantity has been estimated based on a DINP/DIDP solubility of 1 mg/l and average flow rate of wastewater of 160 m^3/d

*** No data received: releases are based on the upper limit of the production reported in the IUCLID database

Considering the 5 EU producers, the sum of the estimated and reported releases is considered as the continental release. As the number of production sites is very low, the regional releases due to production are supposed equal to the highest local release.

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	63	150

Most producers indicated that sludge from the STP at the production site is incinerated. Therefore no soil contamination through sludge application for agricultural purposes is considered.

Distribution (life cycle step II)

The next step to consider in the life cycle of DIDP is the distribution (e.g. road transport) of this substance.

Almost all DIDP consumed in the EU is distributed via road tankers or by ship (Cadogan et al., 1994). In the estimate it was considered that 15% of the consumed phthalates are transported by ship and 85% by tank movement, the majority of which are supplied with sophisticated tank cleaning facilities.

Every roadload transports around 20 tonnes, and it was estimated that during one roadload 1 kg is lost (Cardogan et al., 1994). Considering these values for DIDP transport of 200,000 t/a, there

will be 170,000 tonnes transported by road in 8,500 hauliers, therefore 8.5 t/a will be emitted to the water compartment due to cleaning.

30,000 t/a are estimated to be transported by ship. The chemical shipping industry is similar to the trucking industry in that it has very modern equipment and is well regulated. Product losses are estimated to be close to 0.3% (residues on tank walls, in lines and pumps etc.) (Cadogan et al., 1994). These residues are removed by cleaning with water and at most only 10% of them are emitted to the environment:

$$30{,}000 \cdot 0.1 \cdot 0.003 = 9 \text{ t/a}.$$

The total DIDP emission during distribution is 17.5 t/a due to transport. According to the TGD, it is assumed that 10% of the continental production and uses take place in a "regional" area.

The following emissions can be calculated:

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	15.7	1.8

Processing in PVC polymers (life cycle step IIIa)

As mentioned above, 191,000 t/a of DIDP is used in PVC. In this context, a generic exposure scenario has been carried out with default values of the draft Use Category Document on Plastic Additives (BRE, 1998).

The initial losses will be to air inside of the processing facilities, however subsequent condensation will result in losses to liquid waste. Neither BRE (1998), nor industry information specifies the partition to the different environmental compartments. In a first approach, the releases will be evenly distributed to air and wastewater.

The air treatment (percentages per processing step are documented in ECPI (1996)) will conduct to a lower emission of DIDP into the environment, which is taken into account.

The basic processes used by the PVC industry are distinguished. Local emissions will be calculated for PEClocal estimations.

A: Raw materials handling

The handling of raw material from their arrival on site to their addition to polymers is undertaken by a variety of means. These include manual handling of bags and sacks, conveyor belts, etc.

DIDP products are not notably volatile at room temperature, and thus no evaporation should be expected from ambient temperature handling. Minimal loss can therefore be assumed, this being most likely during transfer (e.g. splashing or accidental spillage).

The estimated release is 0.01% (on the basis of incidental losses) of which 50% are supposed to be released to wastewater:

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	8.55	0.95

B: Compounding

Two general methods are used to prepare for the convenient processing of PVC. Dryblending, a process unique to PVC technology is used to prepare blends for extrusion, injection moulding and sometimes calendering. Plastisol blending is used to prepare plastisols, (approximately 30-35% of all plasticisers in PVC is applied in plastisol applications). A third route, rather obsolete but occasionally associated is Banbury blending.

- Dryblending

This method is based on suspension or mass grade PVC and typically consists of mixing all ingredients with a high speed rotating agitator which heats the material by friction. Temperatures of 100-200°C (max.) are reached and the liquid plasticiser is completely absorbed by the fine PVC powder grain. Gelling is carefully avoided by keeping the temperature at this level, so that a free flowing powder results. Residence times in the lidded blender are in the order of fifteen minutes and the hot blend is dropped in a cooling blender (also lidded) for rapid cooling to avoid lumping. During the last minutes the temperature rises fairly rapidly so that the period of temperatures over 100°C only covers a short time span, carefully controlled to conserve a free flowing sandy dry-blend. During dryblending the exposure of hot material to open air is small. On a total charge of typically 150 kg including, say, 50 kg plasticiser and free air space of 100 litres, at 100°C the saturation concentration of DIDP (vapour pressure at 100°C = $5.9 \cdot 10^{-4}$ hPa) is 7.4 mg/m^3. Assuming one air exchange per run, the amount of emitted plasticiser is 0.0037%.

- Plastisol blending

Plastisol blending takes place in stirred vessels at ambient temperatures. To avoid the development of high viscosities by swelling of the PVC particles due to plasticiser uptake, the vessels have to be cooled to remove the heat of friction. Any significant emission of plasticisers at ambient temperatures is excluded (emission = 0%).

- Banbury mixing

Banbury mixing are lidded vessels with a small open vent to the air. The mixing process is a batch process, starting with the raw materials at ambient temperatures and going up to a maximum temperature of 120-140°C. Emissions are comparable to those in dry blending (i.e. 0.0037%).

The plastisol route for DIDP is used for spread coating and car undercoating and sealings as for slush/rotational moulding. This corresponds to 31.4% (see Section 2.1).

The dryblend route is applied therefore for 68.6% of the total DIDP consumption of 191,000 t/a, which is 131,026 t/a, to which an emission factor of 0.0037% applies. 50% of the releases are supposed to end up in wastewater:

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	2.25	0.25

C: Conversion

PVC is processed in many ways:

1. calendering,
2. extrusion,
3. injection moulding,
4. Several plastisol applications including spread coating (with oven fusion / gelation), rotational moulding, spray coating (with closed tunnel ovens) and miscellaneous small to very small applications.

- Calendering

The output of a typical calendering line is 1,000 kg/h (BRE, 1998). The majority of calendered products are relatively inflexible (e.g. stationary products, furniture veneer), consequently the average plasticiser content is relatively low, ca. 25%, and the plasticiser consumption of such a line is 250 kg/h. The rate of air extraction for such a line is typically 25,000 m^3/hr. Assuming that this extracted air contains a mixture of air from the area over the hot calender bowls containing 7.4 mg/m^3, this results in an emission of plasticiser of 185 g/h or 0.075% of the plasticiser consumption.

However it is more and more common to have air purification equipment in place. For calendering, 54% of the plasticiser consumption is treated (ECPI, 1996), reducing the concentration to approximately 0. The emission factor of 0.075% will therefore be reduced to 0.035%.

The DIDP consumption in calendering is 36,672 t/a. 50% of the total emissions will end up in the wastewater:

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	5.85	0.65

- Extrusion

Major different product types of plasticised PVC extrusion are “profiles” such as wire, cable and hose, and blow moulded film. Profiles are the largest outlet of the two types and at the same time give rise to the least emission. There is no exposure resulting from the extruder itself, it is only for moments after leaving the die, that a short exposure of the hot material takes place. In addition the surface to volume factor is much lower than calendering. An emission factor of 0.01% is proposed (BRE, 1998).

For blown film there is somewhat more evaporation potential since the film bubble has a fairly large surface area and is subject to air currents. The situation is comparable to calendering and the same estimate of 0.035% can be assumed.

As no distinction can be made how much of DIDP is used in extrusion processes for blown film and how much in solid articles, the worst-case emission of 0.035% applies to the entire tonnage used in this processing step.

With a DIDP consumption in extrusion of 78,510 t/a (see Section 2.1), the following emissions can be calculated, assuming that 50% of the total emissions are directed to wastewater:

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	12.35	1.4

- Injection moulding

Injection moulding is comparable to extrusion except that even the cooling process takes place in a closed space (mould). It appears that there is practically no potential for evaporation, but a similar factor to that for extrusion (0.01%) could be used (BRE, 1998).

Approximately 15,843 t/a of DIDP (see Section 2.1) are used in this processing step. Assuming 50% distribution to wastewater, the estimated releases to wastewater would be:

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	0.71	0.08

- Plastisol-spread coating

Spread coated products like cushioned flooring, wall covering, tarpaulins etc. are "fused" (gelled) in tunnel ovens heated with a hot air about 180°C. It can be shown that the amount of air used, is 15-25 m^3/kg plasticiser consumed. This figure is remarkably constant and is independent of the type of product being manufactured. It provides therefore a useful means of calculating the total emission of plasticiser to the environment from the whole range of spread coating activities. The extracted air contains typically 200-1,000 mg/m^3, (average 500 mg/m^3)of a plasticiser. Taking the average air consumption to be 20 m^3/kg plasticiser, the total loss from the process is $20 \cdot 500$ mg/kg plasticiser used or 10 grams (1%). This figure is in close agreement with data based on laboratory experiments (BRE, 1998).

Even if there were no treatment of the purged air, not all of this would reach the environment since abundant condensation would take place in cooler pipes, ducts and stacks.

Already by 1989, 75% of all plasticisers in spread coating applications was used in production lines with air treatment (53% with filters, 25% with incineration). This proportion has certainly increased since then and is probably approaching 100% under the influence of national and European regulations. Air filtration removes at least 95% of the fumes, whilst incineration leaves no plasticiser behind. The conclusion is that, depending on the presence of air treatment equipment (75% of all consumption) the emission may fluctuate between 0-0.05% and 0.5% (plant without air treatment).

DIDP consumption is 41,829 t/a. Taking into account an air treatment of 75% (emission 0.05%) and no air treatment (emission 0.5%) an emission factor of 0.1625% can be calculated. The following emissions are estimated to take place, assuming 50% release to wastewater:

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	30.6	3.4

- Other plastisol processes

The processes concern car underbody coating and sealing, rotational coating, dipping and slush moulding. Of these, car underbody coating and sealing is by far the largest volume application. In this process the sprayed coating is "dried" in long air-heated tunnel ovens at relatively low temperatures (130-160°C). The ovens in this industry invariably have integrated their air incinerators since at the same time paint coats containing solvents are dried. The result is practically zero organic output to the environment.

Of the other processes mentioned above, dip coating and slush moulding (both small volume) are comparable to spread coating in terms of process loss; the presence or absence of air treatment really defines the emission of plasticiser (0.05% or 0.5%). In rotational moulding, final fusion takes place in closed moulds with practically no loss of plasticiser.

DIDP consumption is 14,516 t/a for car undercoating, for which no emission will be considered.

3,629 t/a are used in slush, rotational moulding. In taking into account an air treatment of 32% (emission 0.05%) and no air treatment (emission 0.5%) an emission factor of 0.356% is applied. The following emissions can be calculated, assuming 50% release to wastewater:

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	5.85	0.65

Table 3.9 summarises the different total emissions into the environment during the processing of DIDP.

Table 3.9 Continental and regional release of DIDP to the environment during processing with release factors (BRE, 1998)

Application	Consumption of DIDP [t/a]	Release [%]	Continental release [t/a]	Regional release [t/a]
	191,000			
Raw materials handling		0.01	17.1	1.9
Compounding: Plastisol route	59,974	0	0	0
Dry blending	131,026	0.0037	4.5	0.5
Calendering	36,672	0.035	11.7	1.3
Extrusion	78,510	0.035	24.7	2.8
Injection moulding	15,843	0.01	1.42	0.16
Plastisol spread coating	41,829	0.1625	61.2	6.8
Other plastisol applications:				
Car undercoating and sealants	14,516	0	0	0
Slush/rotational moulding etc.	3,629	0.356	11.7	1.3
Total estimated emission [t/a]			**132.3**	**14.7**

The releases to wastewater assuming even distribution to air and wastewater are shown in **Table 3.10**.

Table 3.10 Continental and regional release of DIDP to wastewater during processing of PVC polymers

Application	Continental release [t/a]	Regional release [t/a]
Raw materials handling	8.55	0.95
Dry blending	2.25	0.25
Calendering	5.85	065
Extrusion	12.35	1.4
Injection moulding	0.71	0.08
Plastisol spread coating	30.6	3.4
Other plastisol applications		
Car undercoating and sealants	0	0
Slush/rotational moulding etc.	5.85	0.65
Total estimated emission [t/a]	**66.1**	**7.3**

Another approach has been published by Cadogan et al. (1994). In order to estimate plasticiser emission it has been assumed that all phthalates have the same volatility as DEHP. This assumption is conservative since approximately 50% of all the phthalate plasticisers used is DEHP, whilst the remainder is predominantly the less volatile higher molecular weight phthalates such as DINP and DIDP.

Table 3.11 Total release of DIDP during processing with release factors Cadogan et al. (1994)

Application	Consumption DIDP [t/a]	Release [%]	Total release [t/a]
Total	191,000		
Calendering			
Film, sheet and coated products	29,987	0.2	60
Flooring	6,685	0.03	2
Spread Coating			
Flooring	20,055	0.25	50
General (coated fabric, wall covering, etc.)	21,774	0.25	54
Other plastisol applications			
Car undercoating and sealants	14,516	0	
Slush/rotational moulding etc.	3,629	0.3	11
Hose and Profile	10,123	0.02	2
Wire and Cable	38,964	0.02	8
Other	45,267	0.02	9
Total estimated emission [t/a]			**196**

In the approach by Cadogan et al. (1994) compounding and raw handling have not been taken into account. The estimated tonnages into the environment according to the emission factors given in the UCD are lower than those in the approach by Cadogan et al. (1994).

According to Poppe (personal communication, 1997) the losses due to processing are the following:

Table 3.12 Total release of DIDP during processing with release factors Poppe (1997)

Application	Consumption DIDP [t/a]	Loss percentage		Total release [t/a]
		See footnote	[%]	
Total	191,000			
Calendering				
Film, sheet and coated products	29,987	a+b1+c1	0.035	60
Flooring	6,685	a+b1+c1	0.035	2
Spread Coating				
Flooring	20,055	a+b2+c4	0.11	50
General (coated fabric, wall covering, etc.)	21,774	a+b2+c4	0.11	54
Other plastisol applications				
Car undercoating and sealants	14,516	a+b2+c5	0.01	
Slush/rotational moulding etc.	3,629	a+b2+c6	0.11	11
Hose and Profile	10,123	a+b1+c2	0.025	2
Wire and Cable	38,964	a+b1+c2	0.025	8
Other	45,267	a+b1+c7	0.0215	9
Total estimated emission [t/a]				**196**

a: Raw materials handling (0.01%)
b1: Compounding (dryblend route: 0.005%)
b2: Compounding (plastisol route: 0.000%)
c1: Calendering (0.02%)
c2: Extrusion (0.01%)
c3: Injection moulding (0.000%)
c4: Spread coating (75% air treatment according to Cadogan et al. (1994), thus averaging 0.75 · 0.05% + 0.25 · 0.25% = 0.1%)
c5: Car undercoating and sealants (0.000%)
c6: Slush/rotational moulding (same loss as spread coating: 0.1%)
c7: Other: 65% extrusion+35% injection moulding (0.65 · 0.01+0.35 · 0.000= 0.0065%)

The emissions estimated are higher according to BRE (1998) approach because calendering and extrusion factors have been applied on a worst-case basis (0.035% instead of 0.02% and 0.01% employed by Poppe).

In a first approach the releases estimated according to BRE (1998) will be considered. During the whole processing step of DIDP in PVC, the following emissions into wastewater have been calculated:

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	66.1	7.3

Processing in non-PVC polymers (life cycle step IIIb)

DIDP is used in vinyl resins and cellulose ester plastics at a tonnage of approximately 6,390 t/a (see Section 2). As there are no specific emission data on non-PVC plastic processing, and no more specific break down data have been provided on non-PVC polymer processing, the same emission factors as for the PVC processing techniques are taken. As this is the same branch of use for DIDP as a plasticiser, the companies are supposed to be equipped with the same elimination facilities, i.e. air treatment, as reported in ECPI (1996).

A: Raw materials handling

The estimated release is 0.01% (on the basis of incidental losses). The following emissions can be calculated, assuming an even distribution between air and wastewater:

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	0.29	0.03

B. Compounding

As a breakdown between the different compounding methods cannot be made, the highest emission factor of 0.0037% (as for PVC dry blending) applies to the whole quantity processed.

The following emissions can be calculated, assuming an even distribution between air and wastewater:

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	0.11	0.012

C. Conversion

For PVC the highest emission factor was estimated for other plastisol processes and especially the slush/rotational moulding with an emission factor of 0.356%. The same emission factor is applied here. The following emissions to wastewater are estimated, assuming an even distribution between air and wastewater:

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	10.35	1.15

In conclusion, it is estimated that during the whole stage of DIDP processing in non-PVC polymers the emissions to wastewater are:

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	10.6	1.18

Use in anti-corrosion paints (life cycle step IIIc)

It has been estimated that ca. 520 t/a are used in anti-corrosion paints.

A/ Formulation

In comparison with Tables 3.1-3.20 of the release category document IC14 for paints (Annex I of the TGD), it can be estimated that 1% is released to wastewater during the formulation of anti-corrosion paints. An emission of 5.2 t/a is calculated.

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	4.7	0.52

B/ Application

For the use of the anti-corrosion paint used in buildings and for maintenance, Table A 4.5 of Annex I of the TGD is used with an emission factor is 0.1% (solvent based). An emission of 0.52 t/a is calculated.

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	0.47	0.052

Use in anti-fouling paints (life cycle step IIId)

It has been estimated that ca. 520 t/a are used in anti-fouling paints.

A/ Formulation

For the formulation of the anti-fouling paints, according to the TGD, IC 14 is used to estimate the emissions (Table 3.13 of IC 14, marine coatings, applies). According to this table, at the formulation stage, as DIDP is non volatile and non water soluble, there are no DIDP emissions to the water and air compartment.

B/ Application

For the use of the anti-fouling paint as marine coatings, in the TGD (IC 14, Table 3.13), an emission factor of 5% is given. However, as these emissions are not supposed to enter in a river systems but into the sea, they will not be taken into account in the regional and continental model. Nevertheless, a local estimation will be carried out.

Use in sealing compounds (life cycle step IIIe)

A/ Formulation

It is assumed that 520 t/a DIDP are used in sealing compounds. The same release factor of 1% as for paint can be used for sealing compounds, as the processes are similar. An emission of 5.2 t/a into the raw wastewater is calculated.

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	4.68	0.52

B/ Application

The application will be mostly at construction sites and therefore the releases would be mainly to solid waste. The release to wastewater can probably be neglected.

Use in inks for textiles (life cycle step IIIf)

A/ Formulation

It is assumed that 520 t/a DIDP are used in inks for textiles. The same release factor of 1% as for paint can be used for sealing compounds, as the processes are similar An emission of 5.2 t/a into the raw wastewater is calculated.

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	4.68	0.52

B/ Application

The application procedure is more related to paint application than to wet textile dyeing (for example, DIDP is supposed to be used as a printing agent for coatings on T-shirts and sweaters). Therefore it is supposed that DIDP is used as a coating material and the release estimates are those used for paint application (IC 14 instead of IC 13) with an emission factor of 0.1% i.e. 0.52 t/a.

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	0.47	0.05

Exterior and interior use of DIDP-containing PVC products (life cycle step IVa)

A) Emissions during interior end use of PVC products

DIDP may be lost through extraction by soapy water during cleaning of flooring. Leached amount has been estimated in two different ways.

1. Apply a general emission factor on an unspecified total volume of DIDP (Method 1),
2. Apply a leaching rate/area on the total area of PVC floor (Method 2).

Method 1: A dissipation rate (evaporation + leaching + abrasion) of 0.3%/year is available from a long-term outdoor study (roofing material, see outdoor use). The studied roofing material was 1.5 mm. A normal floor thickness is about 2 mm. A correction of the emission factor is therefore needed and is calculated to be 0.22%/year ($0.3 \cdot (1.5/2)$). With a consumption volume for floor of 26,740 t/a (20,055 t/a by spread coating and 6,685 t/a by calendering, see **Table 3.12**) and a technical lifetime of 20 years (**Table 2.5**) the loss by leaching will be:

$$26{,}740 \cdot (0.22 / 100) \cdot 20 = 1{,}176 \text{ t/a}$$

Method 2: The annual tonnage for release from washing of polymer floors is based on a Swedish experimental study (Forshaga, 1996). A release of 5 μg/dm^2 per cleaning was measured (cleaning interval of 10 days). It should be noted that the experimental design only covers emission by

diffusion. Emission by abrasion is not included. The total area for PVC-flooring is estimated to be $2.3 \cdot 10^9$ m^2 (ECPI, 1998b). This is based on an assumed lifetime of 10 years. However, according to a producer (Tarkett-Sommer, 1999) 20 years is a more realistic lifetime. This gives a doubling of the area to $4.6 \cdot 10^9$ m^2. About 22% of this area is assumed to containing DIDP, i.e. 10^9 m^2. One cleaning per week is assumed. This will give:

$$10^9 \cdot 52 \cdot 5 = 26 \text{ t/a}$$

Discussion: The two methods show considerable different emissions. It is difficult to decide which method is the most realistic. Method 1 is based on a long-term study on roofing materials where the reduction of the phthalate content was measured after several years of outdoor condition. The question is whether the outdoor condition differs considerably from the indoor washing condition. Method 2 instead is based on a short-term study on new floors. One important difference is that Method 2 does not simulate the influence of dirt on the migration rate. It is known that organic material in contact with the PVC surface may increase the diffusion of DIDP out from the polymer material (see "outdoor use" below).

Further, Method 2 does not cover the release caused by abrasion of the surface which is expected to be extensive in places as offices and schools. The abrasion can be estimated by assuming a total loss during the whole lifetime. According to a standard test for abrasion about 0.1-0.15 mm (average 0.125) will be lost during a lifetime (Tarkett-Sommer, 1999). With a thickness of 2 mm (Tarkett-Sommer, 1999) this will give 6.25% per 20 years or 0.312%/year. This abrasion is expected to occur on surfaces exposed to frequent walk here assumed to be half of the area. Based on these assumptions 835 t/a ($0.5 \cdot 26{,}740$ [$0.312/100$]$\cdot 20$) will be released as small particles. The distribution of this is unknown. Wastewater (wet cleaning) and landfill (via e.g. dry cleaner) are realistic recipients. Before cleaning some of the particles may be distributed into the air as an object for human exposure. Assuming 50% loss to wastewater will give 418 t/a ($0.5 \cdot 835$).

Conclusion: Method 1 is not a realistic substitute for indoor leaching. However, it indicates that Method 2 may underestimate the leaching rate. To cover both leaching and abrasion the result from method 2 (26 t/a) is added to the amount released by abrasion: 26 + 418 = 444 t/a. It can be questioned to add particles to leached amount since they occur in different forms. However, the particle size can be expected to be very small and is here assumed to behave in the same way as DIDP.

In summary:

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	400	44

B) Emissions during exterior end use of PVC products

The following end products are identified as important sources for emissions during use:

1. car undercoating,
2. roofing material,
3. coil coating,
4. fabric coating,
5. cables and wires,
6. hoses and profiles,
7. shoe soles.

Volumes and technical lifetimes for these groups are presented in **Table 2.5**.

Emissions can be divided into two periods. Firstly during the technical lifetime of the product and secondly during the waste lifetime period. The emission from waste is assessed separately ("waste remaining in the environment" see below).

In BRE (1998) general emissions factors for outdoor use are recommended. These are, however, too general to fit the calculations needed for DIDP. Firstly they are not considering the influence of volume/area relationship on the emission rate. Secondly, the leaching rate proposed in BRE (1998) is not correctly derived from the cited study. Some recalculations of the leaching rate are therefore needed.

Recalculations: the annual emission by leaching in outdoor use is estimated from studies on roofing material made by Pastuska et al. (1988) and Pastuska and Just (1990). In open air exposure 0.16%/year was released. For surface covered with gravel 0.35%/year was released (the authors show that dirt strongly increases the emission rate). These figures are derived from PVC with a phthalate mix that contains normal C8-C10 and iso-C10 (no more details in the original report). The results can be considered representative for DIDP.

It should be noted that this emission rate refers to a thickness of 1.5 mm where the emission is limited to one side of the sheet (roofing material). This rate will change according to the area/volume relationship. The emission/volume then will increase for thinner dimensions (e.g. coil coating) and decrease for thicker dimensions (e.g. shoe soles). Furthermore the emission/volume will be doubled if both sides of the emitting material are exposed to the environment. Since the emission depends on the surface and not the content of DIDP, the emission rate/area is calculated from the study on roofing material.

The volume of 1 m^2 roofing material (thickness 1.5 mm) is $1{,}000 \cdot 1{,}000 \cdot 1.5 = 1.5 \cdot 10^6$ mm^3. With a density of 1.406 mg/mm^3 (65%) for PVC (ref. Sax) and 0.966 mg/mm^3 for DIDP (35%) this corresponds to: $[(0.65 \cdot 1.406)+(0.35 \cdot 0.966)] \cdot 1.5 \cdot 10^6 = 1.88 \cdot 10^6$ mg = 1,880 g. With a starting concentration of 35 weight% DIDP and a reduction of 0.16 weight%/year for the open air exposure the annual emission rate will be: $0.16/100 \cdot 35/100 \cdot 1{,}880 = 1.05$ g for 1 m^2 (emission only from one side) → 1.05 g/m^2 for open air exposure. The annual emission rate for graveled surface will then be 2.3 g/m^2.

Used emission factors (water and soil): the annual emission rate derived from roofing material, 1.05 g/m^2 for open air exposure and 2.3 g/m^2 for gravelled surface will be used for all products except for soil buried cable. According to BRE (1998) the leached part is assumed to be equally distributed to soil and surface water.

For emissions from end products the emission rates for "open air" is selected except for shoe soles for which the rates from « dirty area » is used. Special emission rates will be used for buried cable.

In summary

Surface water:	open air:	0.525 g/m^2
	dirty area (gravelled):	1.15 g/m^2

Knowing the emitting surface area for the other product groups the total emission can be calculated. This can be estimated by a "surface correction factor" (SCF) which is here defined as the relative change in emitting surface area compared to the roofing material. A factor of 10 gives 10 times larger emitting surface area. In **Table 3.13** SCFs for the different products are estimated.

The leaching rates from PVC-coated roofing material has been estimated by the recalculation presented above. Since the roofing material is the base for the surface correction factor, the SCF will be 1.

The emissions from car undercoating are due to evaporation and leaching. Only the releases due to leaching are taken into account to estimate the releases to water. Vikelsoe et al. (1998) measured the releases of DINP from cars to washwater in car wash centres. Phthalate concentrations were determined in wash water from two car wash stations in Denmark in 1996 and 1997. The samples were taken at the car wash station in the well collecting the washing water in the washing room. 26 Samples were taken, each from the wash water of a different car. Di-n-nonyl phthalate (DnNP) as well as DINP were determined.

DnNP was analysed in all 25 samples. The concentrations varied from <1 to 55 µg/l (mean: 11.1 µg/l). The corresponding emissions per single wash varied from <0.1 to 8 mg/wash (mean 1.5 mg/wash). DINP was analysed in 13 samples. The concentrations varied from <50 to 510 µg/l (mean: 284 µg/l). The corresponding emissions per single wash varied from <7 to 71 mg/wash (mean: 38 mg/wash).

Given the lower solubility and vapour pressure of DIDP compared to DINP, the results from DINP can be used to estimate the releases of DIDP from car undercoatings.

Assuming approximately $120 \cdot 10^6$ cars in Western Europe and two car washes per month and an average release per wash of 38 mg, the release would amount to 109 t/a. Further release would also occur during normal use e.g. driving on wet roads etc. The releases during car washing can nevertheless be considered as worst-case conditions, so that it can be assumed that the additional releases do not exceed those during car washing. The total losses due to leaching to soil and surface water can therefore be approximated at 218 t/a. The primary recipients for the releases is assumed to be soil (50%) and the surface water (50%) (no reference).

No emission data are available for emissions from coil coated sheets. The thickness of coil coating is about 10 times thinner than that of roofing material (0.1-0.18 mm compared to 1.5 mm in the roofing material, Meki (1999)). A correction of the emission factor for the relatively larger surface area is therefore needed. This gives an SCF of 10.

No data are available for emissions from PVC-coated fabric material. However, this material is assumed to be similar to roofing material except that emission will be possible from two sides. This will give an SCF of 2.

No emission data are available for emissions from hoses and profiles. However, this material is assumed to be twice as thick as the roofing material, consequently the surface area is reduced to the half. This will give an SCF of 0.5.

Emissions from cables and wires are expected as evaporation and leaching. The emission rate and recipient are assumed to be different for above-ground use compared to below-ground use. About 20% is estimated to be above-ground (i.e. 5,480 t/a) and 80% is then below-ground use (ECPI, 1999). For both above- and below-ground use the same dimension as for roofing material is assumed. This will give an SCF of 1. For soil buried cable and wires the emission is expected to be to the soil compartment only.

No emission data are available for emissions from shoe soles. However, this material is assumed to be similar to the roofing material except that the material is thicker. No thickness data are available, however, a thickness of 10 mm is assumed. This will give an SCF of 0.15 (1.5/10).

Technical lifetimes and emission factors for polymer end products are also summarised in **Table 3.13**. The primary recipients for the leached amount is assumed to be soil (50%) and the surface water (50%)(no reference) except for polymers buried deep in the soil (100% to soil). The releases to different environmental compartments from outdoor uses are summarised in **Table 3.14**.

Table 3.13 Surface Correction factor (SCF), technical lifetimes and consumed volumes on main groups of outdoor use types (polymer end products)

Type	Average thickness (mm)	Emission sides [1]	SCF	Volumes (t/a)	Emitting surface area [4] (m^2)	Technical lifetime (years)
Roofing material [2]	1.5	single	1	430	227,900	20
Coil coating	0.15	single	10	2,150	1,1438,000	10
Fabric coating	1.5	double	2	9,060	9,639,840	10
Wires and cables [3]	1.5	single	1	5,480	2,915,360	30
Hoses and profiles	3	single	0.5	2,590	688,940	10
Shoe soles	10	single	0.15	15,843	1,264,270	5

1) Polymer applied on a non-diffusible material will only release DIDP from one side
2) Field study available
3) Above-ground use only
4) [DIDP volume of the end product] · [the area of 1 tonne roofing material = 532 m^2] · SCF

Table 3.14 Summary of total releases from outdoor use of PVC end products

Scenario	Emission to surface water [t/a]
Car undercoating	109
Roofing material	2.4
Coil coating	60
Fabric coating	50.6
Wires and cables	45.9
Hoses and profiles	3.6
Shoe soles	8.2
Total	**279.7**
Continental	**251.7**
Regional	**28**

In summary, the releases to wastewater and surface water from interior and exterior use of PVC products are:

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	400	44
Surface water	251.7	28

Use of DIDP containing non-PVC polymers (life cycle step IVb)

In taking into account the same assumptions and breakdown for exterior and interior use of PVC polymers, DIDP loss can be summarised as follows:

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	13.4	1.5
Surface water	8.43	0.94

Applied anti-corrosion paints containing DIDP (life cycle step IVc)

For anti-corrosion paints, the same approach as for PVC coil coating (see above) can be used. With a use volume of 520 t/a, a release factor to surface water of 0.525 g/m^2 due to leaching, an SCF of 10 and a lifetime of 7 years, the release would be:

	Input continental [t/a]	Input regional [t/a]
Surface water	9.2	1.0

Applied anti-fouling paints containing DIDP (life cycle step IVd)

The releases will be mainly diffusely towards the marine environment. It can be estimated that the total amount of 520 t/a will be released. In the absence of agreed assessment procedures for the marine environment, these releases will not further be regarded in this risk assessment. The assessment will be revised once a scheme is developed.

Applied sealings containing DIDP (life cycle step IVe)

For sealings, the same approach as for PVC roofing material (see above) can be used. With a use volume of 520 t/a, a release factor to surface water of 0.525 g/m^2 due to leaching, an SCF of 1 and a lifetime of 20 years, the release would be:

	Input continental [t/a]	Input regional [t/a]
Surface water	2.6	0.29

Use of DIDP treated textiles (life cycle step IVf)

The annual tonnage for release from washing of clothes with phthalate-containing printing is based on a Danish experimental study on T-shirts (4 different clothes, Miljöstyrelsen (1996)). The release of phthalates in Denmark was estimated to be 6.9 t/a (range: 1.3-13). The range in the estimation indicates that the variation between different clothes is large. With a market share of 22% for DIDP, the release of DIDP can be estimated to be about 1.5 t/a (range: 0.27-2.7 t/a). With an assumption that the Danish use of PVC printing clothes is applicable to the rest of EU (realistic worst case) the total EU emission will be:

(350,000,000 inhabitants in EU) / (5,300,000 inhabitants in DK) · 1.50 t/a = 99 t/a (range: 18-180).

	Input continental [t/a]	Input regional [t/a]
Raw wastewater	90	9.9

Disposal of end products (life cycle step V)

Due to lack of information on non-polymer end products the emission scenarios are limited to polymer end products. Four emission sources are identified for the disposal life cycle step:

- car shredding sites,
- municipal incineration stations,
- municipal landfills,
- waste remaining in the environment.

It is known that the waste management strategies vary considerable between different EU countries. However, the total volume is assumed to be equal to the total consumed volume (200,000 t/a). The incineration releases are based on estimations from an average incineration rate within the EU and the municipal landfill releases are based on the estimation from the UK (ECPI, 1996). Releases from waste remaining in the environment are based on the total EU volumes and specific emission factors.

Car shredder waste

Based on data from BASF AG (1999a) shredding of disposed vehicles is defined to be a potential source for release of DIDP (from car-undercoating and cables). This is carried out to separate the non-ferrous from the ferrous metals for recycling purpose. A by-product is the so-called light shredder fraction, which contains most of the rigid, flexible and foamed plastics, elastomers, wood, glass and dirt. This light shredder is landfilled within the EU. The process of dry shredding is the most practised system in Europe. Old cars enter the shredding process after removal of fluids, batteries and converter radiators. The shredding itself takes place through hammering on the scrap until the granulation of the scrap is small enough to be pushed through the gates. The light fraction is separated through an aspiration system. During the shredder process a normal temperature was measured ranging between 30 and 45°C, with exceptionally higher temperature occurring only temporary at compact and large individual items (e.g. crank shafts).

Release to water is not expected from the dry processing. However, some processing sites separate metals by water flotation. The frequency is however, assumed to be low. Uncontrolled releases of particles is also expected to occur to the surroundings, however, this will be included under “waste remaining in the environment” (see below).

Incineration of waste

No data regarding the release of DIDP from incinerators due to the incineration of DIDP-containing products are available. An estimation of the releases of DEHP from incinerators has been performed in the corresponding risk assessment (EC, 2001), based on measurements in smoke, ash and wastewater at one incineration station in Denmark (Miljöstyrelsen, 1996). It was found that 9% of the emissions are directed to the atmosphere, while 91% remain in the slags and the fly ash, which are landfilled. No releases to wastewater occur.

Disposal to landfills

Landfills are identified to emit phthalates mainly through the leakage water (ECPI, 1996). No measurements of DIDP in leachates from landfills are available. On the other hand, studies have been performed regarding the loss of DIDP from plasticised PVC products under soil-buried and landfill conditions (Mersiowsky et al., 1999). Landfill conditions were simulated in lysimeters containing genuine household waste or model waste mixtures. Elution and biodegradation processes were accelerated by leachate recirculation. The landfill simulation reactors were operated for several years and the corresponding period of time in a landfill was estimated to be approximately one decade. Two lysimeters were spiked with sheets of green cable insulation containing an average of 11% DIDP. The loss of DIDP after 28 months of incubation was negligible.

In a first approach, it will therefore be concluded that the releases of DIDP from landfills to wastewater or air is negligible.

Waste remaining in the environment

As well as volatilisation and leaching losses of DIDP from products/articles, DIDP may also enter into the environment as a result of "waste" from the products themselves during their useful lifetime and disposal. Such waste could include erosion/particulate losses of polymeric products, paints and sealants as a result of exposure to wind and rain or may occur as a result of their mode of use (e.g. wear on conveyor belts, flooring etc.). Similarly, when products/articles are dismantled or disposed of at the end of their useful life there is again a potential for this type of particulate release. In either case the end result is that polymeric particles containing DIDP could enter into the environment. As these releases of DIDP are essentially bound within a polymer matrix, the actual bioavailability and environmental behaviour of DIDP is unknown. There are no agreed methods available in the current TGD for dealing with these types of releases in the risk assessment.

Below, a first attempt is made to estimate the releases from waste remaining in the environment. End products used for outdoor purpose is the most obvious source for this waste formation. For this use some data are available to estimate this release. However, for the indoor use (ca. 78% of DIDP) data are missing.

- Outdoor use

Among outdoor use of end products, the following are expected to form waste during use and disposal:

1. car undercoating,
2. roofing material,
3. coil coating,
4. fabric coating,
5. cables and wires,
6. hoses and profiles,
7. shoe soles.

To estimate the emissions from these type of wastes, the waste formation rate (release of PVC+DIDP) from both use and disposal need to be estimated:

1. Car undercoating: approx. 10% is expected to be released as waste due to abrasions during the technical lifetime period (no reference). For the remaining 90% the release during disposal is assumed to be 2% (no reference), or 1.8% of the total amount. Releases are in particular to be expected from car shredder facilities.

2. Roofing material: No data are available on the losses during its technical lifetime and during disposal. A maximum of 5% is however assumed to be released during the technical lifetime period (no reference). For the remaining 95% the release during disposal is assumed to be 2% (no reference), or 1.9% of the total amount.

3. Coil coating: Losses during their technical lifetime has been estimated in a survey on a number of buildings with PVC coil coated roofs in Stockholm in 1998 (Rathleff-Nielsen, 1999; Skog, 1999). This study estimates that about 50% of the coating was lost after 10 years of use. The same loss is used in this assessment. The recipients for this waste loss are assumed to be soil and surface water. For the remaining 50%, the release during disposal is assumed to be 10% (no reference), or 5% of the total amount.

4. Fabric coating: No data are available on the losses during their technical lifetime and during disposal. Due to its more pliable use coated fabric is assumed to form relatively more waste during use than roofing material. Here a double waste formation rate compared to roofing material during use due to abrasions is assumed i.e. 4% (no reference). For the remaining 96%, the release during disposal is assumed to be 2% or 1.92% of the total amount (no reference).

5. Cables and wires: No data are available on the losses during their technical lifetime and during disposal. For above-ground applications, a loss of 2% is assumed (no reference). For the remaining 98% the release during disposal is assumed to be 2% (no data, worst-case assumption) or 1.96% of the total amount of the above-ground use.

For below-ground applications a loss of 2% is assumed. For the remaining 98% the release during disposal is assumed to be 80% (no data, worst-case assumption) or 78.4% ($0.8 \cdot 98$) of the total amount of the over-ground used. These releases are to be treated specifically, as they are to soil only.

6. Hoses and profiles: No data are available on the losses during their technical lifetime and during disposal. A maximum of 2% is however assumed to be released during the technical lifetime period (no reference). For the remaining 98% the release during disposal is assumed to be 2% (no reference), or 1.96% of the total amount.

7. Shoe soles: No data are available on the losses during their technical lifetime and during disposal. 10% is however assumed to be released during the technical lifetime period (no reference). For the remaining 90% the release during disposal is assumed to be 1% (no reference), or 0.9% of the total amount.

In **Table 3.15** the releases from different kinds of waste remaining in the environment is calculated. It is assumed that all DIDP remaining in the waste will be released at steady state.

Table 3.15 Outdoor use: Calculation of emission of DIDP from waste remaining in the environment

Emission sources	Car under-coating	Roofing material	Coil coating	Fabric coating	Cable and wire		Hose and profile	Shoe soles
					above-ground	below-ground		
Annual volume for application [1)]	14,516	430	2,150	9,060	13,700	13,700	2,590	15,843
Technical lifetime (year) [1)]	14	20	10	10	30	30	10	5
Waste formed during use (%)	10	5	50	4	2	2	2	10
Waste formed during disposal (%)	1.8	1.9	5	1.92	1.96	78.4	1.96	0.9
Total waste fraction (%)	11.8	6.9	55	5.9	4.0	80.4	4.0	10.9
Volume DIDP in waste = annual release rate (t/a)	1,712	30	1,182	534	548	11,014	103.6	1,726
Total (t/a)								**16,852**
Total (t/a) (without release from below-ground use of cables and wires)								**5,839**

1) see Table 2.5

There are no data available about the recipient of these emissions. However, since the polymers occur as solids they will end up in the soil and sediment environment. Smaller fractions can be expected to be transported by wind and water to sediments while larger pieces remain in the soil.

Compared to the releases from product use the emission to air and water is expected to decrease and the release to soil increase. In this assessment the release to air and water are assumed to be 0.1% and 25%, respectively and the release to soil is assumed to be to 75% (see **Table 3.16**).

Table 3.16 Environmental distributions of DIDP released from waste remaining in the environment

Primary Recipient	Environmental distribution	
	From waste remaining in the environment (%)	From soil buried cable (use and waste) (%)
Air	0.1	0
Water	25	0
Soil	75	100

The calculations in **Table 3.15** show that the annual releases from different waste types vary between 30 to 11,014 t/a. The contribution from soil buried cables is special. Since this release occurs deep in the ground it cannot be added together with the other more surface oriented releases. In the TGD the urban/industrial soil depth is only 5 cm. The PEC calculations are therefore not able to cover this release. Development of new distribution models is therefore needed (with focus on groundwater exposure). Until better models will be available the contribution from soil buried cables are excluded from the PEC calculations.

The annual releases from the other waste types vary between 30 and 1,726 t/a. Coil coating and shoe soles are the dominating sources.

The uncertainty of these figures is high (several simplifications). The assumption that the emission is constant during the whole waste lifetime can be questioned. The emission rate will probably decrease when the concentration in PVC passes the "glass point". Furthermore, it is unclear when the steady state will be reached for the different waste groups. The waste type with smallest particles will probably reach steady state faster (e.g. shoe soles).

- Indoor use

Indoor use of polymer end products will most probably also cause waste that will remain in the environment. The abrasion from the floor is already included in the section for end products use. One other obvious scenario is demolishing of buildings that contain products like electrical cable, hose profiles, polymer wall paper and floor (Sten, 1998). Since such demolishing material may be used for landfilling groundwater can be assumed to be the primary recipient. More data and/or new calculation methods are, however, needed before such a scenario can be introduced in the assessment.

For surface water, the total releases from disposal of end products would therefore be:

	Input continental [t/a]	Input regional [t/a]
Surface water	1,314	146

In order to generate these figures, a large number of "worst-case" assumptions have had to be made. This leads to a large uncertainty in the figures obtained, and the approach taken may grossly overestimate the actual releases.

Summary of the releases to wastewater and surface water

Based on the estimations performed above, the overall releases to wastewater and surface water are summarised in **Table 3.17**.

Table 3.17 Total releases to wastewater and surface water

Life cycle step	Wastewater (t/a)		Surface water (t/a)	
	continental	regional	continental	regional
I: Production	63	150	-	-
II: Distribution	15.7	1.8	-	-
IIIa: Processing in PVC	66.1	7.3	-	-
IIIb: Processing in non-PVC polymers	10.6	1.18	-	-
IIIc: Use in anti-corrosion paints				
Formulation	4.7	0.52	-	-
Application	0.47	0.05	-	-
IIId: Use in anti-fouling paints				
Formulation	-	-	-	-
Application	-	-	-	-
IIIe: Use in sealing compounds				
Formulation	4.68	0.52	-	-
Application	-	-	-	-
IIIf: Use in inks for textiles				
Formulation	4.68	0.52	-	-
Application	0.47	0.05	-	-
IVa: Exterior and interior use of DIDP-containing PVC products	400	44	251.7	28
IVb: Use of DIDP-containing non-PVC products	13.4	1.5	8.43	0.94
IVc: Applied anti-corrosion paints containing DIDP	-	-	9.2	1.0
IVd: Applied anti-fouling paints containing DIDP	-	-	-	-
IVe: Applied sealings containing DIDP	-	-	2.6	0.29
IVf: Use of DIDP-treated textiles	90	9.9	-	-
V: Disposal of end products	-	-	1,314	146
Total	**674**	**217.3**	**1,585**	**176.2**

3.1.2.2 Estimation of local aquatic concentrations

Production (life cycle step I)

Daily releases have been obtained by dividing the reported amounts of emission to water with the number of working days (300 days in continuous working systems). The concentration of DIDP in the influent of the STP is calculated in taking the following formula:

$$Clocal_{inf} = \frac{Elocal_{water} \cdot 10^6}{EFFLUENT_{stp}}$$

Explanation of symbols:

$Elocal_{water}$ local emission rate to (waste) water during emission period [kg/d]
$EFFLUENT_{stp}$ effluent discharge of the STP [l/d]
$Clocal_{inf}$ concentration in untreated water [mg/l]

The concentration of DIDP in the effluent ($Clocal_{eff}$) of a STP is calculated with the formula:

$$Clocal_{eff} = Clocal_{inf} \cdot \% \text{ not removed STP (8.3\%)}$$

For DIDP it is assumed that 91.7% elimination occurs in a STP according to SIMPLETREAT (see above).

From the effluent concentration in the STP, the local concentration in the receiving surface water can be calculated with the equation:

$$Clocal_{water} = Clocal_{eff} / [(1 + Kp\_susp \cdot SUSP \cdot 10^{-6}) \cdot D]$$

Where Kp_susp = 28,600 l/kg (see above)
SUSP = 15 mg/l (concentration of suspended matter in river)
D = dilution factor

The default values have been taken from the TGD. Information given in IUCLID for production sites C and E was available. A generic approach was applied to the higher value of the production tonnage range (emission factor: 0.3% = default).

	A	B	C	D	E
Number of operation days [d/a]	300	300	300	300	300
Release to water [%]				0.3	0.3
Amounts released to STP [kg/d]	0.33	10	500	0.2 (DIDP+DINP)	100
Dilution	156	3.74	2,593 *	2,334	2,593 *
Influent STP $Clocal_{inf}$ [mg/l]	0.0008	2.8	250	0.0077	50
Effluent STP $Clocal_{eff}$ [µg/l]	0.07	237	20,750	0.6	4,150
$Clocal_{water}$ [µg/l]	0.0004	44	6	0.0002	1

* based on a default river flow of 60 m^3/s

The concentration of freshly deposited sediment is used in the risk characterisation for sediment, therefore, the properties of suspended matter are used:

$$Clocal_{sediment} = Ksusp_{water}/RHOsusp \cdot Clocal_{water} \cdot 1{,}000 \text{ (wet weight)}$$

The following $Clocal_{sediment}$ can be derived:

	A	B	C	D	E
$Clocal_{sed}$ wet weight [µg/kg]	2.6	275,670	34,820	1	6,960
$Clocal_{sed}$ dry weight [µg/kg]	6.9	716,740	90,530	2.6	18,100

Monitoring results in sediment are available for sites B and E. For site B, a first measurement yielded an upstream concentration of 42,280 µg/kg dw and a downstream concentration of 1,075 µg/kg dw. Because of these inconsistent results, follow-up work to better characterise sediment exposure at this site is expected. At site E, both concentrations upstream and downstream were below 200 µg/kg dw. This value will be used in the risk characterisation.

Processing in PVC polymers (life cycle step IIIa)

Emissions for each processing step have been estimated. For the local scale, each processing technique is considered to take place in a separate factory. This is confirmed by a proprietary market analysis performed by the main producers (Parkerton and Bowes, 1999). Of the 281 processing sites included in the survey, only two sites were identified that had more than one business segment at the same site. Local emissions due to raw material handling and compounding are included with the releases from conversion. Different generic scenarios based on the conversion technique have been derived from the quantities given in ECPI (1996).

Parkerton and Bowes (1999) could establish the consumption of DIDP at processing sites throughout Western Europe. The study covered 95% of the consumption of DIDP in Western Europe. Based on a summary statistical evaluation the 90 percentile consumption of DIDP per site for different business segments could be derived, as presented in **Table 3.18**.

Table 3.18 90 percentile consumption of DIDP per site according to application

Application	Conversion technique	DIdP consumption (90%ile) [t/a]
Wire and Cable	Extrusion	2,740
Film and Sheet	Calendering	2,000
Underbody Coating, Sealants, Mastics	Plastisol application	1,856
Coated Fabric	Plastisol spread coating	1,870
Floor and Wall Covering	Plastisol spread coating	800 *
Compounding	-	1,600
Other	-	1,700 **

* maximum as less than 9 sites involved
** maximum, 90 percentile not determined

The data from **Table 3.18** are considered to be realistic worst-case values and will be used for the Clocal derivation. In the absence of a DIDP consumption value for injection moulding, a consumption of 1,700 t/a per site will be used. For “other plastisol applications”, no distinction is made between car underbody processes and slush or rotational moulding. While no releases occur during car underbody coating, this is by far the largest volume application. Higher releases have been estimated for slush or rotational moulding, but this application concerns only 3,629 t/a of DIDP. For the estimation of the per site consumption, the average per site consumption of 406 t/a is more realistic than the 90 percentile of 1,856 t/a.

	Calendering	Extrusion	Injection moulding	Plastisol spread coating	Other Plastisol applications *
DIDP consumption per site [t/a]	2,000	2,740	1,700	1,870	2406
Release% raw handling	0.005	0.005	0.005	0.005	0.005
Release% compounding	0.00185	0.00185	0.00185	0	0
Release% conversion	0.0175	0.00175	0.005	0.0812	0.178
Release% [total]	**0.024**	**0.024**	**0.012**	**0.086**	**0.183**
Release [t/a]	0.5	0.66	0.20	1.61	0.74
Number of days	300	300	300	300	300
Local release to water [kg/d]	1.62	2.2	0.68	5.36	2.48
Influent STP $Clocal_{inf}$ [mg/l]	0.81	1.1	0.34	2.7	1.2
Effluent STP $Clocal_{eff}$ [µg/l]	65.7	88.8	27.5	21.7	100
Clocal [µg/l]	**4.6**	**6.21**	**1.93**	**15.2**	**7.02**

* Slush or rotational moulding only as the releases are negligible for car underbody coating

For the sediment the following results are obtained:

	Calendering	Extrusion	Injection moulding	Plastisol spread coating	Other Plastisol applications *
$Clocal_{sediment}$ wet weight [µg/kg]	28,600	38,630	12,000	94,500	43,600
$Clocal_{sediment}$ dry weight [µg/kg]	74,370	100,400	31,200	245,600	111,500

* Slush or rotational moulding only as the releases are negligible for car underbody coating

Processing in non-PVC polymers (life cycle step IIIb)

The study by Parkerton and Bowes (1999) includes data on the size of processing sites of DIDP in non-PVC polymers in France. The largest consumption at one site was found to be 450 t/a. A 90 percentile value could not be determined, as less than 9 sites were identified. The maximum value will therefore be used for the derivation of the Clocal. Assuming that for processing in non-PVC polymers exactly the same emission factors as for processing in PVC polymers applies, the following PEClocal estimations can be carried out:

Tonnage DIDP per site [t/a]	450
Release% raw handling	0.005
Release% compounding	0.00185
Release% conversion	0.178
Release% [total]	**0.185**
Local release to water [t/a]	0.83
Number of days	300
Release to water [kg/d]	2.77
Water flow [m^3/d]	2,000
Dilution	10
Influent STP $Clocal_{inf}$ [mg/l]	1.39
Effluent STP $Clocal_{eff}$ [µg/l]	112
Clocal [µg/l]	**7.9**

For the sediment the following result is obtained:

$Clocal_{sediment}$ wet weight [µg/kg]	48,900
$Clocal_{sediment}$ dry weight [µg/kg]	127,100

Use in anti-corrosion paints (life cycle step IIIc)

As described above, 520 t/a DIDP are used in anti-corrosion. There is one scenario (I) with default values for the formulation step and one scenario for application of anti-corrosion paints.

Given the important number of different products registered in the differed product registers (Sweden, Norway, France), it can be assumed that the 10% rule applies and that the fraction of main source for the derivation of the local release is derived from the regional volume i.e. 52 t/a. As stated above, the average DIDP content of the products is supposed to be 15%.

	I [formulation]	**II [application]**
Tonnage DIDP [t/a]	52	52
Corresponding volume of paint [t/a]	350	350
Release % [total]	**1**	**0.1 (Table A4.5)**
Release to water [t/a]	0.52	0.052
Fraction of main source	1 (Table B2.10)	0.00002 (Table B4.5)
Number of days	300 (Table B2.10)	200 (Table B4.5)
Release to water [kg/d]	1.7	0.0000052
Water flow [m^3/d]	2000	2000
Dilution	10	10
Influent STP $Clocal_{inf}$ [mg/l]	0.85	0.0000026
Effluent STP $Clocal_{eff}$ [µg/l]	68.8	0.00021
Clocal [µg/l]	**4.8**	**0.000015**

For the sediment the following result is obtained:

	I [formulation]	II [application]
$Clocal_{sediment}$ wet weight [µg/kg]	29,850	0.09
$Clocal_{sediment}$ dry weight [µg/kg]	77,600	0.25

Use in anti-fouling paints (life cycle step IIId)

As described above, 520 t/a DIDP are used in anti-fouling paints. As seen above, the release at formulation is considered to be negligible. There is one scenario with default values for application of anti-fouling paints.

Given the important number of different products registered in the differed product registers (Sweden, Norway, France), it can be assumed that the 10% rule applies and that the fraction of main source for the derivation of the local release is derived from the regional volume i.e. 52 t/a. As stated above, the average DIDP content of the products is supposed to be 15%.

	II [application]
Tonnage [t/a]	52
Corresponding volume of paint [t/a]	350
Release % [total]	**5 (table 3.13, IC14)**
Release to water [t/a]	2.6
Fraction of main source	0.15
Number of days	300
Release to water [kg/d]	1.3
Water flow [m^3/d]	2000
Dilution	10
Influent STP $Clocal_{inf}$ [mg/l]	0.65
Effluent STP $Clocal_{eff}$ [µg/l]	53
Clocal [µg/l]	**3.7**

For the sediment the following result is obtained:

	II [application]
$Clocal_{sediment}$ wet weight [µg/kg]	22,900
$Clocal_{sediment}$ dry weight [µg/kg]	59,500

Use in sealing compounds (life cycle step IIIe)

As described above, 520 t/a DIDP are used in sealing compounds. Local releases are only considered during formulation, as release to wastewater during use is unlikely. Releases would be primarily to solid waste.

Given the important number of different products registered in the differed product registers (Sweden, Norway, France), it can be assumed that the 10% rule applies and that the fraction of main source for the derivation of the local release is derived from the regional volume i.e. 52 t/a. As stated above, the average DIDP content of the products is supposed to be 15%.

	I [formulation]
Tonnage [t/a]	52
Corresponding volume of sealant [t/a]	350
Release % [total]	**1**
Release to water [t/a]	0.52
Fraction of main source	1
Number of days	300
Release to water [kg/d]	1.7
Water flow [m^3/d]	2,000
Dilution	10
Influent STP $Clocal_{inf}$ [mg/l]	0.85
Effluent STP $Clocal_{eff}$ [µg/l]	69
Clocal [µg/l]	**4.8**

For the sediment the following result is obtained:

	I [formulation]
$Clocal_{sediment}$ wet weight [µg/kg]	29,950
$Clocal_{sediment}$ dry weight [µg/kg]	77,900

Use in inks for textiles (life cycle step IIIf)

A 1% emission is estimated for the formulation step for use in inks for textiles and 0.1% during application. As above, it is supposed that the 10% rule applies.

	I [formulation]	II [application]
Tonnage [t/a]	52	52
Corresponding volume of ink [t/a]	350	350
Release %	1	0.1
Release to water [t/a]	0.52	0.052
Fraction of main source	1	0.15
Number of days	300	300
Release to water [kg/d]	1.7	0.026
Water flow [m^3/d]	2,000	2,000
Dilution	10	10
influent STP $Clocal_{inf}$ [mg/l]	0.85	0.013
effluent STP $Clocal_{eff}$ [µg/l]	69	1.05
Clocal [µg/l]	**4.8**	**0.07**

For the sediment the following result is obtained:

	I	II
$Clocal_{sediment}$ wet weight [µg/kg]	29,950	450
$Clocal_{sediment}$ dry weight [µg/kg]	77,900	1,200

Other life cycle steps

No local estimations are performed for life cycles IVa, IVb, IVc,IVd, IVe, IVf, and V as these are diffuse emissions, which are taken into account in the regional model.

3.1.3 Atmosphere

3.1.3.1 Releases to the atmosphere

Production (life cycle step I)

Emissions to the air compartment (resp. < 0.25 t/a and < 0.025 t/a) are reported by two European producers, whereas the TGD gives an emission factor of 0. Direct deposition fluxes through atmosphere can be neglected as they may not be important at all.

A release of 0.25 t/a is considered in the regional model.

	Input continental [t/a]	Input regional [t/a]
Air	-	0.25

Distribution (life cycle step II)

Only DIDP release to liquid waste due to cleaning of transport facilities is considered in this risk assessment.

Processing in PVC polymers (life cycle step IIIa)

As described in Section 3.1.3, the releases estimated during processing of DIDP in PVC polymers are assumed to be equally distributed to air and wastewater. The total releases to air are therefore:

Table 3.19 Continental and regional release of DIDP to air during processing in PVC polymers

Application	Continental release [t/a]	Regional release [t/a]
Raw materials handling	8.55	0.96
Compounding: Plastisol route	0	0
Dry blending	2.25	0.25
Calendering:	5.85	0.65
Extrusion	12.35	1.4
Injection moulding	0.71	0.08
Plastisol spread coating	30.6	3.4
Other plastisol applications		
Car undercoating and sealants	0	0
Slush/rotational moulding etc.	5.85	0.65
Total estimated emission [t/a]	**66.1**	**7.3**

Processing in non-PVC polymers (life cycle step IIIb)

As for DIDP in PVC polymers it is estimated that emissions are equally distributed to air and wastewater. The total releases to air are therefore:

	Input continental [t/a]	Input regional [t/a]
Air	10.6	1.18

Use in anti-corrosion and anti-fouling paints (life cycle steps IIIc & IIId)

According to the TGD, IC 14 Table 3.13, no air emission takes place at the formulation and application step. In regard to anti-corrosion paints and compared with Tables 3.1 - 3.20 of the release category document IC14 for paints, it can be estimated that there is also no air emission during formulation and use.

Use in sealing compounds (life cycle step IIIe)

The same assumptions as for paints can be assumed here. No air emissions during formulation and processing.

Use in inks for textiles (life cycle step IIIf)

It is assumed that 520 t/a DIDP are used for textiles. Taking into account the emission factor of 0.0025 (MC = 3) for formulation, a total emission of 1.3 t/a can be calculated.

	Input continental [t/a]	Input regional [t/a]
Air	1.17	0.13

As the application procedure is more related to paint application, it is assumed that no direct air emission is taking place due to the application of DIDP in textile processing.

Exterior and interior use of DIDP-containing PVC products (life cycle step IVa)

A) Emissions during interior end use of PVC products

The majority of flexible PVC is used indoors in applications such as floorings, wall coverings, upholstery, wires and cables etc. The total volume for interior use of DIDP in polymer products is approximately 149,000 t/a (78% of the total consumption, BASF (1999a)).

There are two ways to estimate the evaporated amount.

1. Apply a general emission factor to an unspecified total volume of DIDP (Method 1). This gives 74.5 t/a (see below).
2. Apply an evaporation rate/m^2 to the emitting area of different articles (Method 2). This gives 54.4 t/a (see below).

The more detailed Method 2 should be preferred. However, the data on the different uses of the products indoor are not detailed enough to calculate the emission from each product group and to summarise the total emission. Until more detailed information will be available (e.g. better estimate of surface areas for hoses and profiles) Method 1 is decided to represent a realistic worst-case scenario. Thus, 74.5 t/a of DIDP is expected to evaporate from indoor use of products containing DIDP.

Method 1: a general yearly emission factor of 0.05% is proposed in BRE (1998). The total emission from indoor PVC products would then be 74.5 t/a.

Method 2: If the surface area of the products is known, an emission factor of 5.7-9.5 mg/m^2/a can be used as determined for DEHP (Environ Corporation, 1988).

The total area for PVC-flooring is estimated to be $2.3 \cdot 10^8$ m^2 (ECPI, 1998b). With a technical lifetime of 20 years, the total area will be $4.6 \cdot 10^9$. With a market share of 22% of total phthalates for DIDP, the release would be 18.8 t/a.

Vinyl wall covering is a typical product for which statistics are available. The total production in Western Europe in 1988 is estimated to be approx. $400 \cdot 10^6$ m^2 (Cadogan et al., 1994). With a market share of 22% of total phthalates for DIDP, and assuming that the life of this product is 7 years, the release would be 5.85 t/a.

Western European statistics for coated products, film and sheet, such as upholstery, packaging, stationary products, luggage, clothing etc. are not available. Cadogan et al. (1994) propose a

worst-case release for phthalates of 40 t/a (assuming a product lifetime of 7 years). With a market share of 22% of total phthalates for DIDP, the release would be 8.8 t/a.

About 50% of the DIDP-containing cables and wires are used outdoors (ECPI, 1999). Based on the release rates determined by Environ Corporation (1988), a release rate of 86.5 t/a for all phthalates was derived by ECPI (1999). This would correspond to a release for DIDP of 19 t/a.

Assuming that hose and profile (DIDP consumption 10,123 t/a, technical lifetime 10 years) has a similar surface to volume ratio and conditions of use to flooring (DIDP consumption 26,740 t/a), the DIDP emissions from these products are estimated to be 1.8 t/a.

B) Emissions during exterior end use of PVC products

The same lifetimes and break-up of the different products as described in Section 3.2.1 are used to estimate the releases into air.

In BRE (1998) 0.05% is assumed to be evaporated for outdoor use products during its whole lifetime. There is no information on the dimension and technical lifetime lying behind this value. It is therefore not possible to recalculate this figure to emission/area. Instead the emission rate used for indoor use, 9.5 mg/m^2/a (see above) is used. The same specific surfaces as for leaching to surface water and soil is used for the estimation of the evaporation to air.

Technical lifetimes and emission factors for polymer end products are also summarised in **Table 3.20**. The releases to air from outdoor uses are summarised in **Table 3.21**.

Table 3.20 Surface Correction factor (SCF), technical lifetimes and consumed volumes on main groups of outdoor use types (polymer end products)

Type	Average thickness (mm)	Emission sides [1]	SCF	Volumes (t/a)	Emitting surface area [3] (m^2)	Technical lifetime (years)
Car under-coating	1.5	single	1	14,516	7,722,500	14
Roofing material	1.5	single	1	430	227,900	20
Coil coating	0.15	single	10	2,150	11,438,000	10
Fabric coating	1.5	double	2	9,060	9,639,840	10
Wires and cables [2]	1.5	single	1	5,480	2,915,360	30
Hoses and profiles	3	single	0.5	2,590	688,940	10
Shoe soles	10	single	0.15	15,843	1,264,270	5

1) Polymer applied on a non-diffusable material will only release DIDP from one side.
2) Above-ground use only
3) [DIDP volume of the end product] · [the area of 1 ton roofing material = 532 m^2] · SCF

Table 3.21 Summary of total releases from outdoor use of PVC end products to air

Scenario	Emission to air t/a
Car undercoating	1.03
Roofing material	0.04
Coil coating	1.09
Fabric coating	0.91
Wires and cables	0.83
Hoses and profiles	0.06
Shoe soles	0.06
Total	**4.03**

In summary, the total release to air from indoor and outdoor use of PVC products is 74.5 + 4 = 78.5 t/a i.e.:

	Input continental [t/a]	Input regional [t/a]
Air	70.6	7.85

Use of DIDP-containing non-PVC polymers (life cycle step IVb)

In taking into account the same assumptions and breakdown for exterior and interior use of PVC polymers, DIDP loss to air can be summarised as follows:

	Input continental [t/a]	Input regional [t/a]
Air	2.36	0.26

Release from applied anti-corrosion paints containing DIDP (life cycle step IVc)

For anti-corrosion paints, the same approach as for PVC coil coating (see above) can be used. With a use volume of 520 t/a, a release factor to air of 9.5 mg/m^2 due to evaporation, an SCF of 10 and a lifetime of 7 years, the release would be:

	Input continental [t/a]	Input regional [t/a]
Air	0.17	0.018

Applied anti-fouling paints containing DIDP (life cycle step IVd)

The releases will be mainly diffusely towards the marine environment. For this assessment it is assume that no releases occur to air.

Release from applied sealings containing DIDP (life cycle step IVe)

For sealings, the same approach as for PVC roofing material (see above) can be used. With a use volume of 520 t/a, a release factor to air of 9.5 mg/m^2 due to evaporation, an SCF of 1 and a lifetime of 20 years, the release would be:

	Input continental [t/a]	Input regional [t/a]
Air	0.047	0.005

Use of DIDP treated textiles (life cycle step IVf)

For treated textiles, the same approach as for PVC fabric coating (see above) can be used. With a use volume of 520 t/a, a release factor to air of 9.5 mg/m^2 due to evaporation, an SCF of 2 and a lifetime of 10 years, the release would be:

	Input continental [t/a]	Input regional [t/a]
Air	0.047	0.005

Disposal of end products (life cycle step V)

Due to lack of information on non-polymer end products the emission scenarios are limited to polymer end products. Four emission sources are identified for the disposal life cycle step:

- car shredding sites,
- municipal incineration stations,
- municipal landfills,
- waste remaining in the environment.

Car shredder waste

Based on data from BASF (1999a) shredding of disposed vehicles is defined to be a potential source for release of DIDP (from car-undercoating and cables). This is carried out to separate the non-ferrous from the ferrous metals for recycling purposes. A by-product is the so-called light shredder fraction, which contains most of the rigid, flexible and foamed plastics, elastomers, wood, glass and dirt. This light shredder is landfilled within the EU. The process of dry shredding is the most practised system in Europe. Old cars enter the shredding process after removal of fluids, batteries and converter radiators. The shredding itself takes place through hammering on the scraps until the granulation of the scraps is small enough to be pushed through the gates. The light fraction is separated through an aspiration system. During the shredder process a normal temperature was measured ranging between 30 and 45°C, with exceptionally higher temperature occurring only temporary at compact and large individual items (e.g. crank shafts).

Releases will be mainly to air. The following calculation for the dry process can be made (BASF, 1999a):

Car processed in Denmark and Germany:	3.850,000
Shredder sites in EU:	252
Car processed in EU:	10,600,000
PVC per car:	16 kg (source APME)
Plasticiser per car:	5.4 kg (average of 35% soft PVC) (ECPI)
DIDP per car:	1.2 kg (market share of 22% for DIDP)
Total EU input of DIDP in shredder:	12,000 t/a

As a worst-case emission factor for the air the same release factors for "plastisol processing", i.e. 0.356% was assumed:

Total release of DIDP into air $12{,}000 \cdot 0.00356 = 42.7$ t/a

	Input continental [t/a]	Input regional [t/a]
Air	38.5	4.3

Incineration of waste

No data regarding the release of DIDP from incinerators due to the incineration of DIDP-containing products are available. An estimation of the releases of DEHP from incinerators has been performed in the corresponding risk assessment (EC, 2001), based on measurements in smoke, ash and wastewater at one incineration station in Denmark (Miljöstyrelsen, 1996). It was found that 9% of the emissions are directed to the atmosphere, while 91% remain in the slags and the fly ash, which are landfilled. The total releases to the atmosphere for DEHP are estimated to be 5.7 t/a. In a first approach the same releases will be assumed for DIDP:

	Input continental [t/a]	Input regional [t/a]
Air	5.1	0.57

Disposal to landfills

Based on the results by Mersiowsky et al. (1999) (cf. Section 3.1.2.1), it is assumed that no emissions occur to the atmosphere.

Waste remaining in the environment

As presented in Section 3.1.2.1, releases due to waste remaining in the environment is possible. The total release of DIDP was estimated to be 5,839 t/a. The fraction released to air is approximated at 0.1%. The releases would be:

	Input continental [t/a]	Input regional [t/a]
Air	5.25	0.58

The total releases to air due to disposal of end products are therefore:

	Input continental [t/a]	Input regional [t/a]
Air	48.8	5.45

Summary of releases to air

Based on the estimations performed above, the overall releases to air are summarised in **Table 3.22.**

Table 3.22 Total releases to air

Life cycle step	Air (t/a)	
	Continental	**Regional**
I: Production	-	0.25
II: Distribution	-	-
IIIa: Processing in PVC	66.1	7.3
IIIb: Processing in non-PVC polymers	10.6	1.18
IIIc & IIId: Use in anti-corrosion paints and anti-fouling paints Formulation Application	 - -	 - -
IIIe: Use in sealing compounds Formulation Application	 - -	 - -
IIIf: Use in inks for textiles Formulation Application	 1.17 -	 0.13 -
IVa: Exterior and interior use of DIDP-containing PVC products	70.6	7.84
IVb: Use of DIDP-containing non-PVC products	2.36	0.26
IVc: Applied anti-corrosion paints containing DIDP	0.17	0.018
IVd: Applied anti-fouling paints containing DIDP	-	-
IVe: Applied sealings containing DIDP	0.047	0.005
IVf: Use of DIDP-treated textiles	0.047	0.005
V: Disposal of end products	48.8	5.45
Total	**200**	**22.4**

3.1.3.2 Estimation of local air concentrations and deposition rates

The concentration in air at 100 m from a point source can be estimated as follows:

$$Clocal_{air}\ (mg/m^3) = Elocal_{air} \cdot Cstd_{air}$$

where $Elocal_{air}$ (kg/d) = local (max.) emission rate to air
$Cstd_{air}$ = standard concentration in air at source strength of 1 kg/d
= $2.78\ 10^{-4}$ mg/m^3.

Based on its vapour pressure and - 2 < log HENRY < 2, the annual deposition over a radius of 1,000 m around the source can be estimated as:

$DEPtotal_{ann}=(Elocal_{air} + Estp_{air}) \cdot (Fass_{aer} \cdot DEPstd_{aer} + (1-Fass_{aer}) \cdot DEPstd_{gas}$

where: $Estp_{air}$ (kg/d) = local indirect emission to air from the STP

$DEPstd_{gas}$ = deposition flux of gaseous compounds (- 2 < log HENRY < 2) at source strength of 1 kg/d=$4 \cdot 10^{-4}$ mg/m^2/d.

$Fass_{aer}$ = fraction of the chemical bound to aerosol = 1 (measurements at the workplace have shown that 100% of the substance is bound to the aerosol)

$DEPstd_{aer}$ = standard deposition flux of aerosol-bound compounds at a source strength of 1 kg/d=$1 \cdot 10^{-2}$ mg/m^2/d.

Production (life cycle step I)

Emission to air is negligible according to the TGD. Therefore, no local concentrations are estimated.

Processing in PVC polymers (life cycle step IIIa)

The same assumption as for the aquatic environment is taken. The same release fractions as for wastewater are assumed.

Details of $Clocal_{air}$ formula see above.

	Calendering	Extrusion	Injection moulding	Plastisol spread coating	Other Plastisol applications *
DIDP consumption per site [t/a]	2,000	2,740	1,700	1,870	406
Release % raw handling	0.005	0.005	0.005	0.005	0.005
Release % compounding	0.00185	0.00185	0.00185	0	0
Release % conversion	0.0175	0.0175	0.005	0.0812	0.178
Release % [total]	**0.024**	**0.024**	**0.012**	**0.086**	**0.183**
Release per site [t/a]	0.5	0.66	0.20	1.61	0.74
Number of days	300	300	300	300	300
Local release to air [kg/d]	1.62	2.2	0.68	5.36	2.48
Local release to air, indirect [kg/d]	0.052	0.07	0.021	0.171	0.079
DEPtotal [mg/m² · d]	0.016	0.023	0.007	0.055	0.026
$Clocal_{air}$ [µg/m³]	**0.45**	**0.61**	**0.19**	**1.49**	**0.69**

* Slush or rotational moulding only as the releases are negligible for car underbody coating

Processing in non-PVC polymers (life cycle step IIIb)

As for the water emission scenario, the same emission factor as for PVC applications is taken for non-PVC polymer applications.

Tonnage DIDP per site [t/a]	450
Number of days	300
Emission factor %	0.185
Release to air, direct [kg/d]	2.77
Release to air, indirect [kg/d]	0.08
DEPtotal [mg/m² · d]	**0.029**
$Clocal_{air}$ [µg/m³]	**0.77**

Use in anti-corrosion paints (life cycle step IIIc)

There are no direct air emissions due to formulation and application according to the TGD.

Nevertheless, as it was estimated above that 1.7 kg/d are released into the water compartment at the formulation step, indirect releases of 0.054 kg/d can be derived. The local indirect releases during processing can be neglected.

	I [formulation]
Tonnage	52
Release to air, indirect [kg/d]	0.054
DEPtotal [mg/m² · d]	**0.0005**
$Clocal_{air}$ [µg/m³]	**0.015**

Use in anti-fouling paints (life cycle step IIId)

There are no direct air emissions due to formulation and application according to the TGD.

Nevertheless, as it was estimated above that 1.3 kg/d are released into the water compartment at the application step, indirect releases of 0.042 kg/d can be derived respectively.

	II [application]
Tonnage	52
Release to air, indirect [kg/d]	0.042
DEPtotal [mg/m² · d]	**0.0004**
$Clocal_{air}$ [µg/m³]	**0.01**

Use in sealing compounds (life cycle step IIIe)

There are no direct air emissions due to formulation and application according to the TGD.

Nevertheless, as it was estimated above that 1.7 kg/d are released into the water compartment at the formulation step, indirect releases of 0.054 kg/d can be derived.

	I [formulation]
Tonnage	52
Release to air, indirect [kg/d]	0.054
DEPtotal [mg/m² d]	**0.0005**
$Clocal_{air}$ [µg/m³]	**0.015**

Use in inks for textiles (life cycle step IIIf)

During formulation an emission factor of 0.0025 (MC 3) applies. As above, it is supposed that the 10% rule also applies.

In regard to application of DIDP containing inks, no direct emission takes place and an indirect air emission of 0.0008 kg/d is considered negligible to derive a deposition rate.

	I [formulation]
Tonnage	52
Number of days	300
Fraction of main source	1
Emission factor [%]	0.25
Release to air, direct [kg/d]	0.43
Release to air, indirect [kg/d]	0.054
DEPtotal [mg/m² · d]	**0.0048**
$Clocal_{air}$ [µg/m³]	**0.12**

Other life cycle steps

No local estimations are performed for life cycles IVa, IVb, IVc, IVd, IVe, IVf, and V, as these are diffuse emissions, which are taken into account in the regional model.

3.1.4 Terrestrial compartment

3.1.4.1 Releases to soil and estimation of soil concentrations

3.1.4.1.1 Agricultural soil

DIDP can reach agricultural soil through two exposure routes:

- application of sewage sludge in agriculture,
- dry and wet deposition from the atmosphere.

For the calculation of the regional and continental concentrations, the total release through sludge application needs to be determined. The fraction of the DIDP in the STP influent being adsorbed onto sewage sludge is 84.8%. A connection rate of 70% to a STP is considered for all life cycle steps.

The contributions from production have been neglected as most producers have indicated that the sludge from their on-site STP is incinerated. Deposition rates from air have not been calculated as emission due to production is considered to be negligible.

The resulting local concentrations in soil at the different life stages are summarised in the following table. The intermediate calculation results are listed in the EUSES calculations (see Appendix C).

Table 3.23 Local concentrations in soil

Life cycle	$Clocal_{soil}$ [µg/kg dw]	180-d average soil porewater conc. [µg/l]
Processing in PVC (life cycle step IIIa) (highest release)	16,300	2.42
Processing in non-PVC polymers (life cycle step IIIb)	8,400	1.24
Formulation of anti-corrosion paints (life cycle step IIIc)	5,260	0.78
Use in anti-corrosion paints (life cycle step IIIc)	negligible	negligible
Formulation in anti-fouling paints (life cycle step IIId)	negligible	negligible
Use in anti-fouling paints (life cycle step IIId)	3,930	0.58
Formulation of sealing compounds (life cycle step IIIe)	5,260	0.78
Use of sealing compounds (life cycle step IIIe)	negligible	negligible
Formulation of inks for textiles (life cycle step IIIf)	5,260	0.78
Use of inks for textiles (life cycle step IIIf)	78	0.01

Diffuse releases are taken into consideration for estimating the concentration in urban / industrial soil (see below).

It should be noted that in most of the PEC calculations, the porewater concentration is higher than the water solubility of the substance (0.2 µg/l). This throws some doubt over the estimation methods used. The soil porewater concentration is used for the estimation of the exposure of man via the environment, particularly from root crops. For assessment purposes, the soil porewater concentration is set equal to the water solubility of the substance.

Groundwater

Given the high adsorption potential of DIDP, it could be argued that the substance does not leach though the soil column and that the concentration in groundwater would be negligible. Nevertheless, DINP has been detected in agricultural soil, heavily amended with sewage sludge for 25 years, down to a depth of 60 cm in a monitoring study by Vikelsoe et al. (1999). Di-n-nonyl phthalate (DnNP) as well as diisononyl phthalate were determined. The results are presented in **Table 3.24**.

Table 3.24 Local concentrations in groundwater

	Depth (cm)	DnNP (µg/kg dw)	DINP (µg/kg dw)
Agricultural soil, amended with	0-10	160	130
high amounts of sewage sludge	10-20	200	220
for 25 years, changed to	20-30	200	200
artificial fertiliser 6 years	30-40	180	96
before sampling, cattle grazing	40-50	120	93
Same location, sampled 2 years later	0-10	120	410
	10-20	160	540
	20-30	210	670
	30-40	290	910
	40-50	210	280
	50-60	84	63

These results would indicate that also DIDP can migrate to deeper soil layers. This phenomenon might be explained by leaching of particulate matter.

In a first approach, the results obtained with EUSES for soil porewater concentration will be used as groundwater concentrations (corrected for water solubility if necessary).

3.1.4.1.2 Industrial / urban soil

In addition to the releases to agricultural soil due to sludge application and atmospheric deposition, diffuse releases to urban and industrial soil occur. In **Table 3.25**, the estimated DIDP releases to urban / industrial soil are summarised, based on the overall releases as estimated in Section 3.1.2.1.

Table 3.25 Estimated diffuse DIDP-releases to industrial / urban soil

Life cycle step		Emission [t/a]
Exterior and interior use of DIDP-containing PVC products[1] (life cycle step IVa)		
car undercoating		109
roofing material		2.4
coil coating		60
coated fabric		50.6
cables and wires		45.9
hoses and profiles		3.6
shoes soles		8.2
	total	279.7
	continental	251.7
	regional	28
Use of DIDP-containing non-PVC polymers [2] (life cycle step IVb)	total	9.4
	continental	8.43
	regional	0.94
Disposal of end products [3] (life cycle step V)	total	4,379
	continental	3,941
	regional	438
	total	**4,668**
	continental	**4,201**
	regional	**467**

1) It is assumed that the amount released through leaching is equally distributed to urban/industrial soil and surface water (see Section 3.1.2.1)
2) With the same assumptions and breakdown for exterior and interior use of PVC products
3) The fraction released to soil is approximated at 75% (see Section 3.1.2.1)

These releases contribute to the regional concentrations. No local concentrations are derived.

The releases from under-ground use of cables and wire need to be considered separately. Field studies are available for the leaching of DEHP (De Coste, 1968; 1971). The techniques used and locations are almost identical in the two studies. 0.76 mm sheet samples where buried in soil in Georgia, US (humid climate, pH 5.2) at two different depths mounted on polyethene tubes. After 32 or 48 months the concentration of DEHP in the exposed PVC sheets was measured. The following decreases in concentration were observed:

Table 3.26 DEHP loss from cable material after 32 months in soil (Georgia sites, original conc. 37.2%)

	Study I			**Study II**		
Exposure duration	48 month			32 month		
Original conc. DEHP	30.6%			37.2%		
Soil depth	15 cm	45 cm	average	25 cm	60 cm	average
Total % DEHP loss	4.7	3.1	3.9	0.90	2.50	1.70
% loss / year	1.18	0.78	0.98	0.34	0.94	0.64

These studies did not show any clear correlation between emission rate and depth. The observed variation may depend on uncertainty in the chemical analysis. However, it may also depend on heterogeneity in the soil compartment. The relative low pH in the studied soil should be considered. It is unclear if pH influence the emission/degradation of DEHP. An identical study was also carried out in another region (Study I, New Mexico) with higher pH (8.2). The dissipation of phthalates was not measured in this study. However, the change in mechanical

properties (tensile stress) of the plastics was measured. Since elongation for this type of materials is sensitive to small changes in plasticiser concentration (according to the author) this parameter can be used as an indication of phthalate dissipation. By comparing the changes in elongation it clearly indicates that the phthalate dissipation is higher in the basic soil. The level of dissipation of DEHP in **Table 3.26** may therefore be underestimated compared to neutral and basic soils. Due to these uncertainties the highest estimated emission rate in **Table 3.26,** i.e. 1.2%, is assumed in this risk assessment report (worst-case assumption). The primary recipient is assumed to be 100% to the soil environment.

A hypothesis proposed by the industry is that all DEHP diffused to the surface of PVC will directly be degraded by microorganisms. This is based on landfill studies (Mersiowsky et al., 1999) where the authors suggest that the microorganisms by degrading DEHP on the surface of PVC increase the diffusion of new DEHP to the surface. However, a laboratory study has shown that dirt abiotically very effectively increases the diffusion of DEHP to the surface (Pastuska et al., 1988). Further, the environmental conditions in a landfill are considerably different from a mineral soil. Also the microorganism metabolisation/adaptation capacity probably differs between these two environments.

The contribution from soil buried cables is special though. Since this release occurs deep in the ground it cannot be added together with the other more surface oriented releases. In the TGD the urban/industrial soil depth is only 5 cm. The PEC calculations are therefore not able to cover this release. Development of new distribution models is therefore needed (with focus on groundwater exposure). Until better model will be available the contribution from soil buried cables are excluded from the PEC calculations.

3.1.5 Secondary poisoning

As described in Section 3.1.1, the bioaccumulation potential of DIDP is difficult to interpret. For secondary poisoning, BCF values of 4,000 for aquatic organisms and 1 for terrestrial organisms have been chosen. In **Table 3.27**, the exposure to predators through aquatic organisms and earthworms is presented.

Table 3.27 Exposure of top predators through food

Life cycle	$PECoral_{aquatic}$ [mg/kg ww] *	$PECoral_{worm}$ [mg/kg ww]
Production (life cycle step I)	15.4	0.12
Processing in PVC (life cycle step IIIa) (highest release)	31.4	6.1
Processing in non-PVC polymers (life cycle step IIIb)	19.3	3.2
Formulation of anti-corrosion paints (life cycle step IIIc)	14.5	2.0
Use in anti-corrosion paints (life cycle step IIIc)	6.34	0.03
Formulation in anti-fouling paints (life cycle step IIId)	negligible	negligible
Use in anti-fouling paints (life cycle step IIId)	12.4	1.5
Formulation of sealing compounds (life cycle step IIIe)	14.5	2.0
Use of sealing compounds (life cycle step IIIe)	negligible	negligible
Formulation of inks for textiles (life cycle step IIIf)	14.5	2.0
Use of inks for textiles (life cycle step IIIf)	6.46	0.06

* Values corrected for a higher BCF value compared to the EUSES results, based on BCF for fish only

3.1.6 Regional and continental concentrations

The calculations of PECs at a regional and continental scale were carried out using the SIMPLEBOX model, integrated in EUSES.

The resulting regional concentrations (PECregional) are (see Appendix C):

Surface water:	1.8 µg/l
Sediment:	32 mg/kg dw
Air:	0.0007 µg/m^3
Agricultural soil:	0.068 mg/kg dw
Urban / industrial soil	1.84 mg/kg dw
Groundwater:	0.01 µg/l

3.1.7 Monitoring data

The amount of measured concentrations of DIDP in the environment is very limited. A comparison is therefore not opportune. Significantly more information is available regarding the presence di(2-ethylhexyl) phthalate (DEHP) in the environment. The quantities of DEHP used in Western Europe are more than twice the amount of DIDP used (486,000 t/a DEHP compared with 200,000 t/a DIDP), for approximately the same use pattern. Furthermore, DEHP is more volatile, so that a higher release to the environment has to be expected.

An indicative comparison can be made by comparing the DIDP concentrations with the DEHP concentrations measured in the same studies (**Table 3.28**).

Table 3.28 Comparison of DIDP and DEHP concentrations measured at the same locations

Compartment	DIDP	DEHP	Reference
Surface water [µg/l]	1.08, 1.00	0.68, 0.66	Elf Atochem (1997)
Sediment [µg/kg dw]	<100, 130, 115, 190	365, 560, 865, 570	Elf Atochem (1997)
Sediment [µg/kg dw]	< 15 –1109 (median: < 15)	< 25 – 2,089 (median: 150)	ALcontrol (1999)
Mussels [µg/kg dw]	<200, < 500, 1,240	1,500, 1,390, 1,850	Elf Atochem (1997)
Algae [µg/kg dw]	270	650	Elf Atochem (1997)
Sewage sludge [µg/kg dw]	8,030, 5,200, 4,110, 3,800, 5,870	18,300, 17,500, 14,500, 13,400, 17,900	Kolb et al. (1997)
Soil [µg/kg dw]	< 15 (n = 34)	< 25 – 205 (median: 110)	ALcontrol (1999)

These very limited data would suggest that the environmental concentrations of DIDP is of the same order of magnitude or lower than those of DEHP.

The monitoring data of DEHP can therefore be used in this risk assessment.

3.1.7.1 Wastewater

No results regarding the presence of DIDP in municipal or industrial wastewater could be found.

In **Table 3.29**, the most relevant monitoring data for DEHP in wastewater are presented, as reported in the EU risk assessment for DEHP (EC, 2001):

Table 3.29 Monitoring of DEHP in wastewater

Location	Conc. (µg/l) Influent	Effluent	Year	Remarks and References *
Municipal				
Sweden, Stockholm (Henriksdal)	weekdays: 6-11 weekend: 4 - 6	weekdays: <1 weekend: <1	1989	Stockholm vatten (1990) Samples from 2 inlet tubes, 24-hour mixing samples
Sweden, Stockholm (Henriksdal)	w: 39 and 47 we: 34 and 46	w: 28 we: 15	1991	Stockholm vatten (1991a) Samples from 2 inlet tubes
Sweden, Stockholm (Bromma) Three different influent streams to the same STP	23, 34, 38 mean 31.6	1.8	1990	Stockholm vatten (1991b)
Denmark, (Skaevinge). Low industrial load	247 33 14	5,2 4 4	1992 1995	Grüttner and Jacobsen (1994) Grüttner et al. (1995) Two different laboratories
Denmark, (Avedøre). Significant ind. load	122 49 35	23 28 10	1992 1995	Grüttner and Jacobsen 1994 Grüttner et al. (1995) Two different laboratories
Denmark, (Marselisborg). Significant ind. load	223 39 26 28	12 0.5 <2.5 <7	1992 1995	Grüttner and Jacobsen 1994 Grüttner et al. (1995) Three different laboratories
Denmark, Søholt, inlet outlet Viby inlet outlet	Mean 33.3 (n=3) Mean 35 (n=3)	Mean 2.4 (n=3) Mean 1 (n=3)	1996	Boutrup et al. (1998)
Norway, Bekkelaget, Oslo Fugelvik VEAS, Slemmestad, Oslo	6.3 12.8 15.0	0.075 0.127 0.068	1996	Braaten (1996) PVC foil producer in the area
Germany, sewage treatment plant Mainly house hold influent Germany, sewage treatment plant Mainly industrial influent	25 - 71	0.54 0.70 0.90	1992	Furtmann (1996)
Industrial				
Sweden, Neste Oxo		57	1990	Källqvist et al. (1991)
Sweden, Neste Oxo		0.08	1997	Solyom and Ekengren (1997)
Sweden, Stockholm. (Bromma). Wastewater from three industrial areas	1,800, 28, 55	-	1990	Stockholm vatten (1991b)
Canada, Ontario, organic chemical industry (9 sites)	-	0.4 - 19	1989 / 1990	OAEI (1996)
Canada, Ontario, inorganic chemical industry	-	0.22 – 65.1	1989 / 1991	
Canada, Ontario, Petroleum refining (7 refineries)		1.4 – 11 mean: 1.9	1988 / 1989	

* Full references are found in EC (2001)

Summary

In monitoring studies on different municipal STPs in Sweden, Denmark, Norway, and Germany, measured concentrations in untreated wastewater (influent) varied between 4-250 µg/l. The

variation may depend on different contributions from household and industrial wastewater, different methods of analysis and possibly many other factors.

In the treated wastewater (effluent) the DEHP concentrations varies between 0.07 and 28 µg/l. There are very few data on concentrations of DEHP in purely industrial wastewater. There is one example of very high DEHP concentrations (1,800 µg/l) in a tube that connects wastewater from an industrial area to the main inlet tube to a Swedish municipal STP. In effluent wastewater from industries and industrial areas, measured concentrations varied between 0.08 and 65 µg/l.

3.1.7.2 Surface water

Only one study reports measurements of DIDP in surface water (Elf Atochem, 1997). Six locations in the Seine estuary in France were sampled and analysed at a detection limit of 0.5 µg/l. Only two samples were positive at concentrations around 1 µg/l.

In **Table 3.30**, the most relevant monitoring data for DEHP in inland surface water are presented, as reported in EC (2001):

Table 3.30 Monitoring of DEHP in surface water

Location	Pollution status	Date of sampling	n	Concentration (µg/l	Remarks and references *
Riverwater					
The Netherlands, Rhine and Meuse. Sample every month in three years.	Not specified	1988 –1990	36 36	Rhine: <0.1-1.0 Meuse: <0.1-4.2	Random peak values. DetectionLimit: 0.1 µg/l Bodar (1996)
Germany, Rhine: Bad Honnef	Village, industrial region	1991-1992	21	0.14-10.27 (mean: 1.54)	Furtmann (1993)
Germany, Rhine: Dusseldorf-Flehe	Town, industrial region	1991-1992	20	0.11-3.12 (mean: 0.55)	
Germany, Rhine: Götterswickerhamm	Town, industrial region	1991-1992	21	0.23-3.10 (mean: 0.61)	
Germany, Ruhr, Frödenberg	Town, industrial region	1991-1992	8	0.21-0.49 (mean: 0.33)	
Germany, Rhine: Kleve Bimmen	Industrial region	1991-1992	21	0.14-1.94 (mean: 0.64)	
Germany, Sieg, at the mouth to the river Rhine	Industrial region	1991-1992	21	0.08-1.03 (mean: 0.40)	
Germany, Wupper, at the mouth to the river Rhine	Industrial region	1991-1992	21	0.16-6.54 (mean: 0.96)	
Germany, Erft, mouth to the river Rhine	Industrial region	1991-1992	20	0.15-1.06 (mean: 0.36)	
Germany, Ruhr, at the mouth to the river Rhine	Industrial region	1991-1992	21	0.18-1.12 (mean: 0.60)	
Germany, Emsher, at the mouth to the river Rhine	Industrial region	1991-1992	21	0.57-9.58 (mean: 2.36)	
Germany, Lippe, at the mouth to the river Rhine	Industrial region	1991-1992	21	0.151-1.8 (mean: 0.67)	
Sweden, River Fyrisån, Uppsala	Town	Apr 1996	3	0.120, 0.133, 0.326	Parkman and Remberger
Sweden, River Motala ström, Norrköping	Town, down-stream municipal STP.	Mar 1996	3	0.006, 0.011, 0.037	(1996)
Sweden, River Svartån, Örebro	Town	Mar 1996	1	0.022	

Table 3.30 continued overleaf

Table 3.30 continued Monitoring of DEHP in surface water

Location	Pollution status	Date of sampling	n	Concentration (µg/l)	Remarks and references *
Denmark. Giber Å	"spildevandsbelastet"	1998	1 serie 1	<0.2 <0.2 increased flow 0.55	Boutrup et al (1998)
Denmark. Möddebro baek.	"spildevandsbelastet"	1998	1 serie 1	<0.2 <0.2 increased flow 0.87	
Denmark, Hove Å Maglemose Å		1996/1997	2 2	0.14, 0.12 0.73, 0.19	Vikelsoe et al. (1998)
UK River Humber, Ouse	Largely agricultural	1995/1996	4	0.74 / 0.90 / 21 / 8.57	Long et al. (1998)
UK River Humber, Aire	Urban and industrial		4	0.36 / 0.43 / 21 / 13	
UK River Humber, Swale	Upland agricultural		3	1.02 / 1.24 / 3.55	
UK River Humber, Calder	Urban and industrial		4	0.84 / 0.63 / 4.26 / 5.38	
UK River Humber, Don	Urban and industrial		4	1.36 / 1.30 / 8.38 / 8.85	
UK River Humber, Trent	Urban and industrial		3	0.74 / 15 / 18	
Lake water					
Sweden, Lake Riddarfjärden, Stockholm	Town	Apr 1996	1	under ice 0.015 icebreak 0.072	Parkman and Remberger (1996)
Sweden, Lake Orrholmsviken, Karlstad	Town	Mar 1996	3	0.051, 0.061, 0.114	
Sweden, Lake Härsvatten, SW.	Unpolluted area	Mar 1996	3	0.010, 0.011, 0.013	
Sweden, Lake Fräcksjön, SW.	Unpolluted area	Mar 1996	3	0, 0.008, 0.012	
Norway, Lake Femunden.	Non-polluted area	1996	1	<0.060	Braaten et al. (1996)
Norway, Lake Heddalsvatn	Industry and dense population nearby.		1	<0.060	
Norway, Hamar, Lake Mjösa.	Industry and dense population nearby.		1	0	
Norway, Furnesfj., Lake Mjösa.	Industry and dense population nearby.		1	<0.060	
Norway, Gjövik, Lake Mjösa.	Industry and dense population nearby.		1	0.182	
Norway, Lake Lundevatn.	"Effected by long range pollution".		1	0.144	

* Full references are found in EC (2001)

Summary and comparison with estimated concentrations:

Most measured DEHP levels in surface water over the last 10 years are below 1 µg/l. Peak values reach up to 10 µg/l in German rivers. Consistently higher values were measured in rivers in the UK with average concentrations of ca. 6 µg/l and peak values up to 21 µg/l. The only measured results for DIDP lie around 1 µg/l.

Most estimated local concentrations are between 1 and 10 µg/l with peak values at 15 and 44 µg/l. The regional concentration reaches 0.59 µg/l.

It can be concluded that the measured and estimated concentrations fully correlate. The estimated concentrations are therefore used in the risk characterisation.

3.1.7.3 Suspended matter and sediment

Alberti et al. (2000) analysed DIDP in three suspended matter samples in the river Rhine and Wupper in Germany. Concentrations of 6, 9.2 and 10 mg/kg dw were measured.

In **Table 3.31**, the most relevant monitoring data for DEHP in suspended matter are presented, as reported in EC (2001).

Table 3.31 Monitoring of DEHP in suspended matter of surface water

Location	Pollution status	Year	n	Conc. (mg/kg dw)	Reference *
Germany, Rhine: Bad Honnef	Village, industrial region	1991-1992	14	2.9-83.0 (mean: 29.6)	Furtmann (1993)
Germany, Rhine: Dusseldorf-Flehe	Town, industrial region	1991-1992	14	3.6-36.1 (mean: 14.3)	
Germany, Rhine: Götterswickerhamm	Town, industrial region	1991-1992	14	2.4-35.8 (mean: 16.7)	
Germany, Rhine: Kleve Bimmen	Town, industrial region	1991-1992	14	10.8-37.1 (mean: 18.4)	
Germany, Sieg, at the mouth to the river Rhine	Industrial region	1991-1992	12	8.2-56.7 (mean: 23.1)	
Germany, Wupper, at the mouth to the river Rhine	Industrial region	1991-1992	12	18.8-155.0 (mean: 57.0)	
Germany, Erft, mouth to the river Rhine	Industrial region	1991-1992	14	2.8-60.0 (mean: 21.6)	
Germany, Ruhr, at the mouth to the river Rhine	Industrial region	1991-1992	13	4.4-73.4 (mean: 33.2)	
Germany, Ruhr, Frödenberg	Industrial region	1991-1992	7	0.0-89.2 (mean: 26.1)	
Germany, Emsher, at the mouth to the river Rhine	Industrial region	1991-1992	14	48.1-175.0 (mean: 101.3	
Germany, Lippe, at the mouth to the river Rhine	Industrial region	1991-1992	14	4.8-281.8 (mean: 75.6)	
UK, Humber rivers, Ouse	Largely agricultural	1995-1996	4	22.8 / 22.6 / 21.7 / 3.81	Long et al. (1998)
UK, Humber rivers, Aire	Urban and industrial		4	115 / 15.3 / 20.4 / 13.8	
UK, Humber rivers, Swale	Upland agricultural		4	69.7 / 102 / 27.3 / 29.3	
UK, Humber rivers, Calder	Urban and industrial		4	32.3 / 32.3 / 39.1 / 55.4	
UK, Humber rivers, Don	Urban and industrial		4	17.7 / 18.1 / 18.1 / 47.2	

* Full references are found in EC (1999a)

Sediment samples were also analysed from the same locations in the Seine estuaries as described above for surface water. 3 samples contained DIDP concentrations above the detection limit (0.1 mg/kg dw) at 0.115, 0.13 and 0.19 mg/kg dw.

A further study reported measured DIDP concentrations in sediments (Parkman and Remberger, 1995). A problem to overcome in phthalate analysis is a contamination by these substances in laboratory material. This was carefully avoided. Sediments from 8 lakes in Sweden and 10 sample locations in Swedish river systems, which provided a gradient of anthropogenic influence, were analysed for DIDP in 1994. A total of 54 sediment analyses were performed. DIDP was not detected in any sample (detection limit: 0.01 mg/kg dw; Remberger (2000)).

In the same study sediment samples were collected downstream of two point source discharges (processing sites) in 1994. DIDP was only found below one point source: 0.02 mg/kg dw

(sd ± 0.012). Taking into account the relation to organic matter, a concentration of 0.078 mg/kg dw (sd ± 0.028) can be derived.

Phthalates were monitored in sediment samples from the Netherlands in 1999 (ALcontrol, 1999). 30 samples from 21 locations were analysed. 32% of the samples revealed DIDP concentrations above the limit of determination of 0.015 mg/kg dw. The median value was <0.015 mg/kg dw and the maximum measured concentration was 1.11 mg/kg dw. The detailed results are described in **Table 3.32**.

Table 3.32 Monitoring of DIDP in sediment samples in the Netherlands

Sample code	Description of site sampled	% Dry matter	% Organic carbon	% Mineral particles	DIDP (µg/kg dw)
1	Opeinder canal, no known point sources nearby, regional	77.6	1.9	7.5	150
2	Hantummervaart canal, no known point sources nearby, regional	64.6	2	19	93
3	Ool, River Maas, highly industrialised area, uncertain if represents local or regional	56.4	5.1	21	1,135
4	"	58.7	5.4	19	1,152
5	Landgraaf, stagnant pond next to castle, sample contains leaf material, no known point source inputs, regional	62.6	4.3	12	<25
6	Landgraaf, another pond used soley for fishing, no point source inputs, regional	73.3	2.5	6.5	234
7	Assendelft, small river, no known point sources, regional	41.7	8.3	26	<25
8	Wormerveer, small river, phthalate processing plant nearby, local	42.2	14	8.8	6,161
9	Alkmaar, Hoornse/Hoevaart canal with heavy boating activity, no know point source inputs, regional	39.8	6.1	25	1,046
10	"	58.3	5	26	<25
11	Alkmaar, Noord-Hollands canal with heavy boating activity, no know point source inputs, regional	78.5	0.5	2.2	73
12	"	79.8	0.5	2	<25
13	Haarlem, canal, no known point source inputs, regional	73.2	1.9	2.9	<25
14	"	75.4	1.4	3.1	237
15	Noordwijk, canal, sample taken near location where pesticides are heavily used, no known point inputs, regional	74.1	0.8	1.7	<25
16	Leidse, canal, no known point inputs, regional	78.4	0.9	2.7	107
17	Apledoorns, canal, residential neighborhood in the Heerde district, no known point inputs, regional	40.8	7.7	16	2566
18	Enschede, stagnant pond near city centre used by fishing club, no known point inputs, regional	66.2	9.1	7.6	<25
19	Doetchem, river IJssel, harbor used by small boats, no known point inputs, regional	62.3	5.3	10	<25
20	Oud-beijerland, stagnant pond near center of small town, no known point inputs, regional	75.5	<0.5	3.3	<25

Table 3.32 continued overleaf

Table 3.32 continued Monitoring of DIDP in sediment samples in the Netherlands

Sample code	Description of site sampled	% Dry matter	% Organic carbon	% Mineral particles	DIDP (µg/kg dw)
21	Hendrik Ido Ambacht, used by fishing club, no known point inputs, regional	73.7	6.9	11	214
22	Vught, river Dommel,, slow moving river, sample taken at crossing of major Dutch motorway (A2), no known point inputs, regional	49.2	7	12	428
23	Rosmalen, small stream, no known point inputs, regional	73.9	0.8	4.5	<25
24	"	74.9	1	3	<25
25	Woudenberg, small pond, no known point inputs, regional	41	5.2	16	331
26	"	48.2	5.4	17	273
27	Almere, small stream flowing through densely populated city, uncertain if represents local or regional	67.5	6.3	17	173
28	"	51.7	4.6	14	263
29	Voorschoten, small stream, no known point inputs, regional	77.9	0.8	3.8	43
30	"	78.3	0.6	3.5	<25

Concentrations of 650 and 1,150 mg/kg dw weight were measured for DIDP in the sediments of rain retention basins from motorways in Germany. A concentration of 14 mg/kg dw was measured in the sediment of an industrial harbour (Alberti et al., 2000).

In **Table 3.33**, the most relevant monitoring data for DEHP in sediment are presented, as reported in EC (2001).

Table 3.33 Monitoring of DEHP in sediment

Location	Pollution status	Sediment layer (cm)	Date of sampling	n	Concentration (mg/kg dw)	Reference *
River sediment						
Germany, Rhine, 13 sites	Industrial region	-	1991	13	8.9 / 9.2 / 18.3 / 13.8 / 6.8 / 7.8 / 1.8 / 5.0 / 2.2 / 20.8 / 0.35 / 2.5 / 3.0	Furtmann (1993)
Germany, Weser, 5 sites	Industrial region	-	1992	5	4.9-8.9	
Germany, Diemel, mouth of Weser	Industrial region	-	1992	1	1.3	
Germany, Aller, mouth of Weser	Industrial region	-	1992	1	2.7	
Germany, Lower Weser, 3 sites	Industrial region	-	1992	3	0.1-6.3	
Germany, Dortmund-Ems canal, 3 sites	Industrial region	-	1991	3	0.22 / 1.1 / 0.48	
Germany, 4 canals, 9 sites	Limited discharges anticipated	-	1991	9	0.95 / 0.15 / 2.5 / 2.5 / 1.8 / 0.28 / 3.4 / 0.85 / 2.4	

Table 3.33 continued overleaf

Table 3.33 continued Monitoring of DEHP in sediment

Location	Pollution status	Sediment layer (cm)	Date of sampling	n	Concentration (mg/kg dw)	Reference *
Sweden, Svartån	Near DEHP processing, (PVC flooring)	0-5 cm 0-2 cm	1983 1994	2 3	1480 47	Thurén (1986); Parkman and Remberger (1995)
Sweden, Ronnebyån	Near DEHP processing, (PVC flooring)	0-5 cm 0-2 cm	1983 1994	2 3	628 33	
Sweden, Gullspångsälven-Göta älv river system	Ten sampling sites in lakes, rivers and archipelago of Göteborg	0-2 cm	1994	1-3	0.071-0.79	Parkman and Remberger (1995)
Sweden. River Motala ström, Norrköping	Town, downstream municipal STP	0-2 cm 14-16 cm	Mar 1996	3	1.22 1.59	Parkman and Remberger (1996)
Sweden. River Svartån, Örebro.	Town	0-2 cm 6-8 cm	Mar 1996	3	0.95 0.31	
Sweden. River Fyrisån, Uppsala.	Town, downstream municipal STP	0-2 cm 8-10 cm	Apr 1996	3	0.65 0.25	
Denmark	Downstream STPs	0-2 cm	1997 / 1998	18 5 >10	6.5 6.9 1.1	Boutrup et al. (1998)
	Agricultural area			5 >10	0.063 0.075	
The Netherlands. Small rivers.	Unknown pollution status	_	1992	10	<0.5-0.5	Bodar (1996)
The Netherlands. Large rivers.		_	199.2/1993	5	1-4 (mean 2.2)	
The Netherlands. Rivers.		_	1992	5	3-4 (mean 3.7)	
The Netherlands	Unknown pollution status		1999	30	< 0.025 - 2.09 (median: 0.15)	ALcontrol (1999)
UK, Humber rivers, Ouse	Largely agricultural		1995 / 1996	4	3.58/ 2.30 / 6.49 / 6.08	Long et al. (1998)
UK, Humber rivers, Aire	Urban and industrial			4	10.3/ 7.89 / 13.5 / 16.7	
UK, Humber rivers, Swale	Upland agricultural			4	6.47/ 0.23 / 17.9 / 5.72	
UK, Humber rivers, Calder	Urban and industrial			4	5.73/ 5.73 / 4.26 / 19.4	
UK, Humber rivers, Don	Urban and industrial			3	3.43 / 3.43 / 3.97	
UK, Humber rivers, Trent	Urban and industrial			3	0.84 / 1.91 / 12.0	
Lake sediment						
Sweden. Lake Härsvatten. Stratified sample.	Non-polluted area	0-1 cm 1-2 cm 2-3 cm 3-4 cm 5-6 cm 7-8 cm 9-10 cm 12-13 cm 15-15.5 cm	Sep 1994	1	0.599 0.394 0.157 0.147 0.083 0.067 0.046 0.083 0.177	1 cm appr. 10 years of deposition - highest conc. during the last 20 years. Higher levels in the deepest layers probably due to contamination of samples (Parkman and Remberger (1995)

Table 3.33 continued overleaf

Table 3.33 continued Monitoring of DEHP in sediment

Location	Pollution status	Sediment layer (cm)	Date of sampling	n	Concentration (mg/kg dw)	Reference *
Sweden. Lake Riddarfjärden, Stockholm.	Town	0-2 cm	1994	3	2.49	Parkman and Remberger (1995 and 1996)
Sweden. Lake Riddarfjärden, Stockholm	Town.	0-2 cm 14-16 cm	Apr 1996	3	0.76 N.D.	
Sweden. Lake Orrholmsviken, Karlstad	Town.	0-2 cm 8-10 cm	Mar 1996	3	0.28 0.002	
Sweden. Lake Härsvatten	Non-polluted area.	0-2 cm 12-13 cm	Sep 1994		0.39 0.08	
Sweden. Lake Härsvatten	Non-polluted area.	0-2 cm 14-16 cm	Mar 1996		0.102 N.D.	
Sweden. Lake Fräcksjön.	Non-polluted area	0-2 cm	Sep 1994		0.37	
Sweden. Lake Fräcksjön.	Non-polluted area	0-2 cm 14-16 cm	Mar 1996		0.065 0.004	
Abiskojaure	Non-polluted area	0-2 cm	Sep 1994	3	0.008	
Jutsajaure	Non-polluted area	0-2 cm	Sep 1994	3	0.118	
Stensjön	Non-polluted area	0-2 cm	Sep 1994	3	0.059	
Brunnsjön	Non-polluted area	0-2 cm	Sep 1994	3	0.168	
Krageholmssjön	Non-polluted area	0-2 cm	Sep 1994	3	0.208	
Denmark. Braband Sö	Near STP.	0-2 cm	1996	12	2.2	Boutrup et al. (1998)
Denmark. Agri Sö	Agricultural area	0-2 cm	1996	12	0.64	
Denmark. Almind Sö	Rural area	0-2 cm	1997	12	0.31	
Denmark. Silkeborg Langsö	500 m downstream STP of paper industry. 100 m downstream municipal STP	0-2 cm	1998	4 4	2.5 1.8	
Norway, Lake Femunden.	Non-polluted area	0-2 cm 18-20 cm	Feb 1996	1	0.050 0.042	Ice cover at sampling time (Braaten et al., 1996)
Norway, Lake Heddalsvatn	Industry and dense population nearby.	0-2 cm 18-20 cm	May 1996	1	0.080 0.038	
Norway, Hamar, Lake Mjösa.	Industry and dense population nearby.	0-2 cm 18-20 cm	Feb-Mar 1996	1	0.042 N.D.	
Norway, Furnesfj., Lake Mjösa.	Industry and dense population nearby.	0-2 cm 18-20 cm	Feb-Mar 1996	1	0.080 N.D.	
Norway, Gjövik, Lake Mjösa.	Industry and dense population nearby.	0-2 cm 18-20 cm	Feb-Mar 1996	1	0.085 0.128	
Norway, Lake Lundevatn.	"Effected by long range pollution".	0-2 cm 18-20 cm	May 1996	1	0.800 0.058	

* Full references are found in EC (2001)

Summary and comparison with estimated concentrations

Average DEHP concentrations measured in suspended matter in highly industrialised areas vary from 14.3 to 101.3 mg/kg dw. Peak values up to 282 mg/kg dw have been measured.

The highest DEHP concentrations in sediment have been measured in 1983 downstream of DEHP processing sites (628-1,488 mg/kg dw). By 1994, these concentrations were reduced to 33-47 mg/kg due to emission reduction measures. In highly industrialised regions, concentrations are usually above 1 mg/kg dw. Concentrations above 10 mg/kg dw were rarely measured in the river Rhine in Germany and in the Humber rivers in the UK. The highest measured value not related directly to a point source amounts to 20.8 mg/kg dw. The concentrations in unpolluted lakes are significantly below 1 mg/kg dw.

All measured DIDP concentrations not directly related to a point source are below 1 mg/kg dw. Only in rain water retention basins along motorways have high concentrations up to 1,150 mg/kg dw been measured. These high concentrations can be attributed to releases from car underbody coatings and can therefore be related to some kind of "local" release.

Most estimated local DIDP concentrations are between 15 and 150 mg/kg dw with peak values around 250 mg/kg dw. The estimated regional concentration reaches 33 mg/kg dw.

The available monitoring results for DIDP do not allow an estimation of concentrations due to local sources. Only few measurements could be related to local releases. On the other hand, the difference between the measured data and the estimated regional concentration is very high. As results from samples out of rivers from heavily industrialised areas are available, a realistic worst-case concentration can be estimated for the regional situation based on the monitoring results with DIDP. As all measured DIDP-concentrations not directly related to a point source are below 1 mg/kg dw, a value of 1 mg/kg dw can be used to override the calculated regional concentration of 33 mg/kg dw:

$$PECregional_{sed}=1{,}000\ \mu g/kg\ dw$$

3.1.7.4 Sewage sludge

The concentration of phthalates was determined in sewage sludge sampled from the fermenting tanks of 5 STPs. Concentrations of 3.8, 4.11, 5.2, 5.87, and 8.03 mg/kg dw were determined (Kolb et al., 1997).

Somewhat higher concentrations were measured in raw and digested sewage sludge from STPs in Germany (Weisser, 1992). DIDP was measured in sewage sludge of 10 sewage treatment plants between 1987 and 1990. Furthermore, the influence of an aerobic pre-treatment of the raw sewage sludge was investigated in one of the STPs. 80 treatment cycles were sampled over 7 days and daily mixing samples were established. The influence of anaerobic fermentation was also investigated on another one of the STPs. 118 treatment cycles were sampled over 70 days. 24 3-day mixing samples were established.

The concentrations in sewage sludge were between 13 and 83 mg/kg dw (average 28 mg/kg dw). The concentrations in the sludge undergoing aerobic pre-treatment were 12-16 mg/kg dw in raw sludge and 12-14 mg/kg dw in treated sludge. The concentrations from sludge undergoing anaerobic fermentation were 29-44 mg/kg dw in raw sewage and 55-64 mg/kg dw treated sludge.

Further results are available with DEHP (**Table 3.34**), as reported in EC (2001).

Table 3.34 Monitoring of DEHP in municipal STP sludge

Location	Concentration (mg/kg dw)		Year	Remarks and reference*
Sweden, 8 different sites	74 – 661	mean: 247	1987	Swedish EPA (1988)
Sweden, 6 different sites. Sweden, 11 different sites.	76-285 25-462	mean: 144 mean: 174	1988 1989-91	Swedish EPA (1992)
Sweden, Stockholm (Henriksdal)	67		1989	Stockholm vatten (1990)
Sweden, Stockholm (Henriksdal)	93		1991	Stockholm vatten (1991a)
Sweden, Stockholm (Bromma)	116		1991	Stockholm vatten (1991b)
Sweden, Malmö (Klagshamn)	0 – 240 18 –116	mean: 105 mean: 49	1991-1996 1991-1996	Henriksson (1997) Two different laboratories
Denmark Avedøre (significant industrial load) Skaevinge (low industrial load) Marselisborg (significant industrial load)	 48 45 47		1992	Grüttner and Vikelsøe (1996)
Denmark Avedøre Skaevinge Marselisborg	 2.347 and 0.9 43, 1.7 and 189		1995	Grüttner et al. (1995) Same sample two different labs. Same sample two different labs. Same sample three different labs.
Denmark, Herning Skaevinge Marselisborg	Winter 120 17 41	Summer 38 18 37	1994	Kjølholt et al. (1995)
Denmark, 2 sites	23 / 14		1995	Krogh et al. (1996)
Denmark, 19 different sites	3.9 - 170	mean: 37.8 median: 24.5	1994	Kristensen et al. (1996)
Denmark, 6 different sites	9 – 49	mean: 25	1996-1997	Boutrup et. al. (1998)
Denmark, 5 different sites	0.003 - 117	mean: 18.9	1996-1997	Vikelsoe et al. (1999)
Norway, 3 different sites, dry sludge	96.0 / 113.0 / 78.5		1996	Braaten (1996)
Netherlands, 5 different STP, primary sludge	Range: <5 to 185		1992-1993	Bodar (1997)
Germany, predominantly industrial effluent Germany, predominantly household effluent	Fresh / Activated / Dewatered 40 / 21 / 85 225 / 163 / - Raw / Processed / Dewatered 194 / 153 / 74		 1992 1992 1992	Furtmann (1996)
Germany, 5 different sites	13.4 - 1 8.3	mean: 16.3	1997	Kolb et al. (1997)
Canada Winnipeg, digested sludge Winnipeg, raw sludge Hamilton, digested sludge Hamilton, raw sludge	 21 – 176 3 and 29 68 26 - 137	 mean: 89 (n = 4) mean: 85 (n=3)	 1981 – 85 1981 Dec 1981 1982 – 83	Webber and Lesage (1989)
15 different sites incl. Winnipeg and Hamilton	3 – 215	median: 80	1980 - 85	Detected in 93% of samples
Canada, 11 different sites	33 – 440	mean: 163	1993 – 94	Webber and Nicols (1995)

* Full references are found in EC (2001)

Consistently high values of up to 661 mg/kg dw have been measured for DEHP. Many mean or median values vary around 100 and up to 200 mg/kg dw.

3.1.7.5 Soil

Phthalates were monitored in soil samples from the Netherlands in 1999 (ALcontrol, 1999). 35 samples from 19 locations were analysed. All DIDP concentrations were below the limit of determination of 15 µg/kg dw.

In **Table 3.35**, the most relevant monitoring data for DEHP in soil are presented, as reported in EC (2001).

Table 3.35 Monitoring data of DEHP in soil

Description	Concentration (µg/kg dw)	Year	Reference *
Agricultural soils			
Agricultural land (Switzerland), After sludge application.	Direct after appl.: 120-190 After 1 month: N:D: (<0.02)	≤1987	Bergkvist and Kirchmann (1989); Naturvårdsverket (1992)
Agricultural soil, Canada, 10 soils.	Range: 80-2,700 Mean: 420*	Nov. 1992	0-15 cm soil depth. From national benchmark sites. (Webber and Wang 1995)
Agricultural soil, High dose of STP application. West Germany.	Slightly more than 5,000 Background: 24 Dose: 333 tonnes dw /annum:	1986	Kampe (1987) cited in Bergkvist and Kirchmann (1989)
Agricultural soils in Denmark (at 5 depth 0-50 cm) - preserved, uncultivated for more than 50 years - ecologically cultured for 40 years - manured for 5 years, cultured - conventionally cultured, artificially fertilised - sludge amended, medium amounts, cultivated - sludge amended, low amounts, cultivated - heavily amended with sludge (17 t/ha/y), changed to artificial fertiliser 6 y before sampling - same as above, sampled 2 years later - meadow in run-off zone from sludge storage	 8, 6, 27, 4, 0 16, 15, 32, 14, 20 16, 18, 8, 18, 1 9, 12, 9, 15, 20 18, 13, 9, 6, 15 22, 18, 17, 23, 21 990, 1,700, 1,400, 880, 590 1,400, 1,700, 1,800, 3,400, 1,200 670, 76, 9, 26, 5	1996	Vikelsoe et al. (1999)
Other			
The Netherlands	< 25 - 205 (median: 110)	1999	ALcontrol (1999)

* Full references are found in EC (2001)

Summary and comparison with estimated concentrations

Consistently high concentrations have been found where agricultural soil was amended with high amounts of sewage sludge (up to 5,000 µg/kg dw). With medium amended soils, the concentrations drop to a maximum of 23 µg/kg d.

Most estimated local DIDP-concentrations are between 5,000 and 10,000 µg/kg dw with peak values around 15,000 µg/kg dw. The regional concentration reaches 59 µg/kg dw.

Comparable measured and estimated concentrations have only been found in heavily sludge-amended soils. On the other hand, it cannot be assured that the available data are representative for local situations. Nevertheless, based on the results by ALcontrol (1999), the estimated regional concentration of 59 µg/kg dw can be overruled. As a conservative value, a PECregional for agricultural soil of 15 µg/kg dw can be proposed.

3.1.7.6 Biota

In the study by Elf Atochem (1997), DINP was measured in 3 mussel samples and 1 algae sample. The detection limit varied between 200 and 500 µg/kg dw. DIDP was detected in one mussel sample at 1,240 µg/kg dw as well as in the algae sample at 270 µg/kg dw.

In a further limited study by the Research Institute for Chromatography (2001), 3 samples of molluscs from 3 locations in the Netherlands showed concentrations of a maximum of 0.011 mg/kg ww.

In a more extensive study by the Research Institute for Chromatography (2001), 25 fish samples from 23 locations in the Netherlands were analysed. Collected fish were bream and roach with fat contents of 0.2 – 5.1%. No DIDP was detected at a detection limit of 10 µg/kg wet fish.

For DEHP, predominantly older data from the seventies and eighties are available. In **Table 3.36**, the most relevant monitoring data for DEHP in biota are presented, as reported in EC (2001):

Table 3.36 Monitoring of DEHP in biota

Organism	Location	n	Concentration (µg/kg dw) *	Year	Reference *
Plants					
Enteromorpha sp, green algae,	Seine estuary, France		650	1997	Elf Atochem (1997)
Plankton	Japan		63,000 (dw?)	<1981	Environment Agency, Japan (1981)
Plankton	Industrialised area, Finland		0	≤1978	Persson et al. (1978)
Reed: "above-ground"-parts straw leaves Grass Grass	River Elbe Germany	6 4 5	2,300-7,500 2,800 11,300 7,100-10,200 3,200-5,500	1986	Jacobs and Mofid (1988)
Grass	Niedersachsen, Germany		1,200-2,500	ca. 1985	Umweltbundesamt (1987)
Invertebrates					
Aquatic					
Dragonfly larvae (naiads)	Iowa, USA, fish hatchery	1	200 (dw?)	ca. 1971	Mayer et al. (1972)
Arthropods, freshwater	Finland, industrial area		100	≤1978	Persson et al. (1978)
Various aquatic invertebrates	Ronnebyån river, Sweden,		310-14,000 (ww)	1986	Thurén (1986)
	Svartå river, Sweden,		110-5,300 (ww)		
Gammarids	River Elbe, Germany, 2 sites	2	300 (ww)	1986	Jacobs and Mofid (1988)
		6	800-1,100 (ww)		
Molluscs, freshwater	Finland, industrial area		100	≤1978	Persson et al. (1978)
Molluscs	River Elbe, Germany	2	2,300 and 4,300 (ww)	1986	Jacobs and Mofid (1988)
Molluscs, digestive gland, 2 species	River Crouch, Essex, UK		9.2-214 (ww)	≤1983	Waldock (1983)
Mussels	River Seine estuary, France	3	1,390-1,850	≤1997	Elf Atochem (1997)

Table 3.36 continued overleaf

Table 3.37 continued Monitoring of DEHP in biota

Organism	Location	n	Concentration (µg/kg dw) *	Year	Reference *
Tubifids	River Elbe, Germany, 2 sites	2 4	200 and 300 (ww) 500-900 (ww)	1986	Jacobs and Mofid (1988)
Terrestrial					
Soil arthropods	Finland, industrial area		2,800	≤1978	Persson et al. (1978)
Vertebrates					
Aquatic					
Tadpole	Iowa, USA, fish hatchery	1	300 (dw?)	ca 1971	Mayer et al. (1972)
Fish					
Walleye Channel Catfish Channel Catfish,	Black Bay, Lake Superior, CDN Mississippi, Arkansas; USA Iowa, USA, fish hatchery		800 (dw?) 3,200 (dw?) 400 (dw?)	ca 1971 ca 1971 ca 1971	Mayer et al. (1972)
Eel	Canada		104 (ww)	ca 1972	Williams (1973)
Atlantic salmon, juvenile	Canada, fish hatchery	2	12,900 and 16,400 (lw)	≤1973	Zitko (1973)
Various fish species	Lake Michigan, USA		nd-1,300 (dw?)	≤1974	Schacht (1974)
Various species of biota, mainly fish	Gulf of Mexico, USA		1-135 (ww) average 4.5	≤1975	Giam et al. (1978)
Various fish species	Japan		70-450 (dw?)	≤1974	Kodama and Takai (1974)
Various fish species	Japan, various cities		40-720 (dw?)	1974	Goto (1979)
Various fish species	Japan		100-19,000 (dw?) (mean 290)	ca 1977	Kubota (1979); Tomita et al. (1979); Env. Agency, Japan (1981)
Various fish species	Japan		<50-1,800 (dw?)	≤1978	Kamata et al. (1978)
Fry and sticklebacks Pearch Bream Roach, muscle Pike, liver	Finland, industrial area		100 100 500 1,100 2,300	≤1978	Persson et al. (1978)
Shark			max. 7,100	<1980	Sittig (1980)
Plaice, muscle Redfish, muscle Mackerel, muscle Cod, muscle Herring, muscle Herring, muscle Eel	Gulf of St.Lawrence, Can Bay of Fundy, Canada Canada		<1 (ww) <1 (ww) 6,500 (ww) 5,200 (ww) 4,700 (ww) 7,200 (ww) 220 and 370 (ww)	<1980	Burns et al. (1981)
Dab, plaice and whiting, liver Dab, plaice and whiting, muscle Dab, liver Dab, muscle	Tees Bay, UK Crouch estuary, Essex, UK 		43-85.9 (ww) 13-51.3 (ww) 2.0-2.4 (ww) 13.8 (ww)	≤1983	Waldock (1983)
Pike-perch, roach, perch, bream, eel	Rees, Niederrhein, River Rhein, Germany	9	17-70 (ww)	<1981	Malisch (1981)
Bream	Hueckenlock, Süderelbe, River Elbe, Germany	5+5	300 and 500 (ww) average	1986	Jacobs and Mofid (1988)
Coalfish, "rotbarsch", cod, herring, mackerel, "flounder"	Germany		<500 (ww) (mixed samples)	1987	Anon. (1987)
Carp, rainbow trout, brown trout, char, eel	Austria, 58 locations	180	max. 2,600 (ww) 8 fish > 1,000 (ww)	1997	Pfannhauser et al. (1997)
Mammals					
Common seal (*Phoca vitulina*), pup, blubber	Canada		10,600 (lw)	<1973	Zitko (1973)

* Full references are found in EC (2001)

Summary and comparison with estimated concentrations

Measurements of DEHP in plants in the eighties revealed high concentrations up to 11,300 µg/kg dw. Concentrations in plankton are difficult to interpret and vary in single measurements from 0 to 63,000 µg/kg (dw?).

In aquatic invertebrates, consistent concentrations above 1,000 µg/kg ww, up to 14,000 µg/kg (ww) were measured.

For fish, the most relevant study has been performed in Austria in 1997. A total of 180 fish were collected at 58 locations (Pfannhauser et al., 1997). Samples of dorsal muscle free of skin and bones were taken for the determinations. DEHP was found in 71 samples. The highest level of DEHP found was 2,600 µg/kg (ww) in carp. At five sites, DEHP levels in a total of eight fish samples exceeded 1,000 µg/kg (ww).

For DIDP, the measured concentrations in fish in a more limited study (25 samples from 21 locations) were below the detection limit of 10 µg/kg ww.

Most estimated local DIDP-concentrations in fish are between 1,000 and 10,000 µg/kg ww with peak values around 27,000 µg/kg ww.

It can be concluded that the measured concentrations are consistently one or several orders of magnitude below the estimated concentrations. It cannot be assured though that the available data are representative for local situations. The results would suggest though, that the bioaccumulation potential of DIDP is lower than initially assumed. This will be taken into consideration in the risk characterisation.

3.1.8 Overall accumulation of DIDP

Large amounts of DIDP in polymers can build up in:

- end products with long technical lifetimes (e.g. building material),
- landfills,
- waste remaining in the environment (pieces of polymer).

Large amount of polymer end products can accumulate in landfills. The content of DIDP will sooner or later emit from the polymer matrix. Emitted DIDP may then be degraded in the landfill or leave it. The amount of DIDP released from a landfill today is assumed to be small (Mersiowsky et al., 1999).

Compared to landfills DIDP in “waste remaining in the environment” is much more out of technical control. Due to persistency of the DIDP/polymer complex this amount could also be expected to still increase in the technosphere. Some polymer end products with technical lifetimes of several decades still in use are also accumulating in the technosphere.

As a consequence the amount of DIDP in the technosphere (incl. the waste) is still increasing. Increasing amounts may also cause increasing emissions. With constant consumption and waste management the DIDP levels (and emissions) will after a while reach steady state (when consumed amount = emitted amount + incinerated amount + amount degraded in landfills).

The emissions calculated in this assessment are in some cases dominated by emitting materials with long lifetimes. This means that estimated PECs that are dominated by such diffuse sources may to some extent reflect a future hypothetical emission. In other words, the emissions we can

expect in the future if we continue to handle DIDP in the same ways as today. This future perspective may cause difficulties in comparing generated diffuse emissions (regional PEC values) with monitoring data.

On the other hand, the estimated PECregional, which already reflects a steady state, is very consistent with the measured values. For sediment, where the highest discrepancies between measured and estimated values are observed, the chosen PECregional based on monitoring data is less than one order of magnitude lower than the estimated PECregional. Given the fact that the estimated releases, especially from "waste remaining in the environment" might be grossly overestimated, the estimated results would suggest that a major increase of concentrations of DIDP in the environment is not to be expected over the coming years if the consumption volume and use pattern stay stable.

3.2 EFFECTS ASSESSMENT: HAZARD IDENTIFICATION AND DOSE (CONCENTRATION) - RESPONSE (EFFECT) ASSESSMENT

3.2.1 Aquatic compartment

Results have been obtained with various fish species. In general, DIDP toxicity measurements are limited by low solubility of these products. Analytical monitoring has been usually carried out and if not, it is indicated.

3.2.1.1 Toxicity test results

3.2.1.1.1 Fish

Acute toxicity

No acute study is revealing a definite LC50 value for DIDP products, only limit values could be determined. No effect was demonstrated at these values (**Table 3.37**).

Table 3.37 Acute toxicity to fish with DIDP

Species	LC50 (96 h)	Remarks	Reference
Pimephales promelas	≥ 0.66 mg/l	static, direct addition of tests substance to test system, mixed for 2 minutes with homogeniser, measured concentrations	CMA (1983a)
	≥ 1 mg/l	flow through, stock solution of maximum test concentration prepared by mixing and ultrasonification and pumped to predilution chamber, presence of undissolved particles, measured concentrations	CMA (1983b)
Lepomis macrochirus	≥ 0.55 mg/l	static, direct addition of tests substance to test system, mixed for 2 minutes with homogeniser, measured concentrations	CMA (1983c)
Oncorhynchus mykiss	≥ 0.62 mg/l	flow through, stock solution of maximum test concentration prepared by mixing and ultrasonification and pumped to predilution chamber, presence of undissolved particles, measured concentrations	CMA (1983d)
Cyprinodon variegatus	≥ 0.47 mg/l	flow through, stock solution of maximum test concentration prepared by mixing and pumped to predilution chamber, presence of undissolved particles, measured concentrations	CMA (1984a)

In summary, no acute effects have been reported in fish with DIDP at its limit of solubility in the test system.

Results from BASF (1989a), ICI (1989) and CITI (1992) showing no acute toxicity at ≥ 10,000 mg/l, ≥ 1 mg/l and ≥ 3,000 mg/l, respectively, have not been considered valid as documentation was insufficient.

Chronic toxicity

No studies on chronic effects on fish exposed to DIDP via the water phase have been carried out.

A two-generation feeding study has been carried out though with *Oryzias latipes* (Patyna et al., 1999). DIDP was added to dry flake food at 20 mg/kg. DIDP, control (no treatment and acetone control were divided into five replicate tanks (N=50) per treatment. In the F0 generation 14 days old fish were fed at 5% body weight per day. The F0 adults were terminated at day 123. There were no statistically significant changes in mortality or fecundity between the treatment groups. There was no reduced egg production. Evaluation of F_1 and F_2 embryos showed normal development except for a transient decrease in red blood cell pigmentation. This effect was observed in both the DIDP treatment and the acetone control group. The only histopathological change observed in the F0 adults was a minor alteration in hepatocellular staining around the central vein. The male to female ratios (3:1) in all groups were similar. Phenotypic gender classification of male and female fish were histopathologically confirmed to be 100% correct. Ale somatic gonadal index and liver somatic index were not significantly different in any group.

Regarding exposure via the water phase, the large body of existing literature for closely related phthalates can be used as read across data for DIDP. Several individual chronic fish toxicity tests are available (see **Table 3.38**).

These studies include data for C6 to C11 dialkyl phthalate esters across nine fish species. It is important to note that even longer chain phthalates than DIDP do not reveal any chronic toxicity.

Collectively, these studies indicate no effect at the maximum concentration that could be maintained as a stable emulsion in the test system employed.

Table 3.38 Summary of chronic aquatic toxicity tests for C6 - C11 phthalate esters

Species	Phthalate ester	Measured/ Nominal?	Exposure duration (days)	End points considered	LOEC (μg/l)	NOEC (μg/l)	Reference
Rainbow Trout (*Oncorhynchus mykiss)*	DHP [Dihexyl phthalate]	M	143	Egg hatchability and survival; Fry growth and survival	----	220 *	Rhodes et al. (1995)
	DEHP [Di-2-ethylhexyl phthalate]	M	34 100	Sac fry mortality Fry growth	14 ----	5 54*	Mayer et al. (1977); Mehrle and Mayer (1976)
	DEHP	M	90	Egg hatchability and survival; Fry growth and survival	----	502 *	De Foe et al. (1990)
	711P [di(heptyl,nonyl, undecyl phthalate]	M	152	Egg hatchability and survival; Fry growth and survival	----	410 *	Rhodes et al. (1995)
	DUP [Diundecyl phthalate]	M	155	Egg hatchability and survival; Fry growth and survival	----	300 *	Rhodes et al. (1995)
Brook Trout (*Salvelinus fontinalis*)	DEHP	M	150	Adult growth	----	52 *	Mayer et al. (1977)
	DEHP	M	229	Embryo survival; survival and growth of sac fry and yearlings	----	3,730 *	Cary et al. (1976)
Fathead Minnow (*Pimephales promelas)*	DEHP	M?	127	Fry growth	----	100 *	Mayer et al. (1977)
	DEHP	M	56	Adult growth and survival	----	62 *	Mehrle and Mayer (1976)
	DEHP	M	32	Fry growth and survival	42,400	23,800	Horne et al. (1983)
	DOP [Di-n-octyl phthalate]	M	28	Embryo hatching and survival; Fry survival	10,000*	3,200	McCarthy and Whitmore (1989)
Bluegill Sunfish (*Lepomis macrochirus*)	DEHP	M	371	Embryo survival; growth and survival of fry and adults	----	1,920 *	Cary et al. (1976)

Table 3.39 continued overleaf

Table 3.38 continued Summary of chronic aquatic toxicity tests for C6 - C11 phthalate esters

Species	Phthalate ester	Measured/ Nominal	Exposure duration (Days)	End points considered	LOEC (µg/l)	NOEC (µg/l)	Reference
Japanese Medaka (*Oryzias latipes*)	DEHP	M	168	Egg hatchability and survival; Fry growth and survival	554*	----	De Foe et al. (1990)
	DEHP	N	28	Egg survival and development; Fry survival, growth and behaviour	----	320 *	Van den Dikkenberg et al. (1990)
Zebrafish (*Branchydanio rerio*)	DEHP	N	28	Egg survival and development; Fry survival, growth and behaviour	----	320 *	Van den Dikkenberg et al. (1990)
Stickleback (*Gasterosteus aculeatus*)	DEHP	N	28	Egg survival and development; Fry survival, growth and behaviour	----	320 *	Van den Dikkenberg et al. (1990)
Flagfish (*Jordanella floridae*)	DEHP	N	28	Egg survival and development; Fry survival, growth and behaviour	-----	320 *	Van den Dikkenberg et al. (1990)
Guppy (*Poecilia reticulata)*	DEHP	N	28	Egg survival and development; Fry survival, growth and behaviour	----	320 *	Van den Dikkenberg et al. (1990)
Channel Catfish *Ictalurus punctatus*	DINP [Di-isononyl phthalate]	N	7	Mortality at post-hatching	----	30 ***	Birge et al. (1978)
Redear Sunfish *Lepomis microlophus* :	DINP	N	8	Mortality at post-hatching	----	300 ***	Birge et al. (1978)
Fowler's Toad *Bufo fowleri***	DINP	N	8	Mortality at post-hatching	----	300 ***	Birge et al. (1978)
Leopard Frog *Rana pipiens***	DINP	N	8	Mortality at post-hatching	----	300 ***	Birge et al. (1978)

Table 3.38 continued overleaf

Table 3.38 continued Summary of chronic aquatic toxicity tests for C6 - C11 phthalate esters

Species	Phthalate ester	Measured/ Nominal?	Exposure duration (days)	End points considered	LOEC (µg/l)	NOEC (µg/l)	Reference
Channel Catfish *Ictalurus punctatus*	DOP	N	7	Mortality at post-hatching	----	300 ***	Birge et al. (1978)
Redear Sunfish *Lepomis microlophus :*	DOP	N	8	Mortality at post-hatching	----	300 ***	Birge et al. (1978)
Fowler's Toad *Bufo fowleri***	DOP	N	8	Mortality at post-hatching	----	300 ***	Birge et al. (1978)
Leopard Frog *Rana pipiens***	DOP	N	8	Mortality at post-hatching	----	300***	Birge et al. (1978)
Largemouth Bass *Micropterus salmoides*	DOP	M	8	Mortality at post-hatching at two water hardnesses: 50 et 200 mg/l	----	3,730 and 3,260 ***	Birge et al. (1978)
Rainbow Trout *Salmo gairdneri*	DOP	M	26	Mortality at post-hatching at two water hardnesses: 50 et 200 mg/l	----	63,070 and 4,950 ***	Birge et al. (1978)

* Highest concentration (emulsion) tested

** Amphibians

*** NOEC values for the fish and amphibian species have been determined from the concentration-effect values given in the publications. The NOEC value was derived from the geometric mean calculated from the concentration demonstrating a deviation of less than 10% of the control and the first above concentration demonstrating a deviation of more than 10%. For example, if at a concentration of 0.01 mg/l a survival of 98% and at a concentration of 0.1 mg/l a survival of 82% were determined, the derived NOEC corresponds to the geometric mean of 0.03 mg/l.

One early study by Mehrle and Mayer (1976) reported an increase in sac-fry mortality at a concentration of 14 µg/l. This study is considered not valid due to the test conditions employed. Radiolabeled DEHP dissolved in acetone was firstly used to determine the bioaccumulation potential in egg, which was used afterwards for the hatchability and sac fry mortality study. DEHP exposure did not cause egg mortality and did not alter hatchability.

A NOEC of 0.03 mg/l has been determined in a dose effect curve (Birge et al., 1978). However, results are based on nominal concentrations and the exposure period is only 7 to 8 days (the embryos were exposed for 3-4 days until hatching after which larvae were exposed for another 4 days post-hatch). The experiences were conducted in static renewal tests for both diisononyl phthalate (DINP) and dioctyl phthalate (DOP) performed for two species of fish and amphibians. Flow through species were also performed with two fish species (different species than in the static renewal tests) with DOP. Analytical confirmation of test concentration was only performed in the flow through tests with DOP. A comparison of the results is shown in **Table 3.39**.

Table 3.39 Summary of aquatic toxicity data for di-n-octyl phthalate (DOP) and diisononyl phthalate (DINP1) Birge et al. (1978)

Species	Analytical monitoring	Exposure protocol	Exposure duration (d)	DOP LC50 [mg/l]	DINP LC50 [mg/l]
Channel Catfish *Ictalurus punctatus*	No	Static Renewal	3 7 *	1.21 0.69	0.87 0.42
Redear Sunfish *Lepomis microlophus:*	No	Static Renewal	3-4 8 *	77.2 6.18	71.85 4.67
Fowler's Toad *Bufo fowleri* **	No	Static Renewal	3-4 8 *	44.14 3.88	23.51 2.95
Leopard Frog *Rana pipiens* **	No	Static Renewal	3-4 8 *	5.52 4.44	4.94 3.63
Largemouth Bass *Micropterus salmoides*	Yes	Flow-through	3-4 8 *	63.9 42.1	NT NT
Rainbow Trout *Salmo gairdneri*	Yes	Flow-through	22 26 *	139.1 139.5	NT NT

* 4 days post-hatch
** Amphibians
NT = Not Tested

In most experiments five treatment concentrations ranging by a factor of ten from 0.01 to 100 mg/l were targeted. The analytical monitoring in the flow through experiments for DOP was in poor agreement with nominal values. For example, in the largemouth bass test at the nominal treatment concentration of 1 mg/l, mean measured DOP concentrations of 46.3 and 35.5 mg/l were reported at a water hardness of 50 and 200 mg/l, respectively. The inability to confirm nominal concentrations with analytical measurements in flow through tests with DOP causes serious doubts on the validity of toxicity results reported for the static renewal tests. The NOECs derived for DOP in flow through tests (see **Table 3.38**) are exceeding 3,730 µg/l and are in agreement with the values reported in chronic fish studies by Cary et al. (1976) and Horne et al. (1983) (see **Table 3.38**). These concentrations are grossly in excess of water solubility and the effects are most likely attributable to physical influence of the undissolved test substance. This is supported by the observation made by Birge et al. (1978), that larval mortality occurred in the first few days after post-hatch and did not continue after long exposure periods. If chemical toxicity mechanisms were involved, cumulative toxicity would be expected. Moreover, the LC50 for rainbow trout which was based on a much longer test exposure (due to the longer hatching

time for this species) was higher than largemouth bass which was based on only a 7-8-day test duration (see **Table 3.39**).

The chronic fish NOEC for high molecular weight phthalates ranges from 30 to 63,070 µg/l. Not taking into account the results of the studies by Mehrle et Mayer (1976), Mayer et al. (1977), and Birge et al. (1978), the NOEC ranges from 320-23,800 µg/l. The large discrepancies in reported NOEC values between studies reflects the different experimental techniques that were used to obtain maximum exposure concentrations (i.e., emulsions).

Lowest observed effect concentrations (LOECs) were obtained in three studies and range from 554 to 42,400 µg/l (**Table 3.38**). The lowest LOEC of 554 µg/l was reported to cause a 13% reduction in *Oryzias latipes* growth after a 168-day exposure (De Foe et al., 1990). In the same study, no statistically significant effects on rainbow trout growth were observed at 502 µg/l after 90 days. In another study, no effects were observed in *Oryzias latipes* on egg survival and development and fry survival, growth and behaviour up to a concentration of 320 µg/l (Van den Dikkenberg et al., 1990). Since a clear concentration-response was lacking in these studies, it is difficult to determine if the observed effects are artifactual (e.g., physical effects of undissolved test chemical) due to testing at such unrealistically high aqueous concentrations.

Conclusion

In none of the valid tests, a chemical toxic effect could be attributed to the substances tested. Furthermore, a two-generation test with *Oryzias latipes* showed that oral intake of 20 mg/kg had no adverse effect upon reproduction and growth. It can therefore be concluded that based on the available data, DIDP has no adverse effects upon fish and that a NOEC cannot be determined.

3.2.1.1.2 Invertebrates

Acute toxicity

Several studies have been performed determining acute effects on daphnids.

Table 3.40 Toxicity experiments to invertebrates with DIDP

Species	EC50 (48 h)	Remarks	Reference
Daphnia magna	≥ 0.18 mg/l	Test solutions prepared by mixing for 1 h, standing for 24h and siphoned off from the bottom, measured concentrations	CMA (1984e)
	≥ 1 mg/l	*No analytical monitoring;* solubiliser: Castor oil ethoxylate	Brown and Williams (1995)
	≥ 0.32 mg/l	At highest concentration, at 48 h, all Daphnids, although mobile, were floating in surface layer.	Brown and Thompson (1982a)
	≥ 500 mg/l	*No analytical monitoring;* solubiliser Tween 80	BASF (1988)
Paratanytarsus parthenogenetica	≥ 0.96	Stock solution prepared with homogeniser for 2 minutes, measured concentrations	CMA (1984b)
Mysidopsis bahia	≥ 0.15	Stock solution prepared by stirring for 1 hour followed by 0.5 hour no-stirring, measured concentrations	CMA (1984c)

No effect was demonstrated at the limit of solubility.

As no sufficient documentation was available, a value of ≥ 1 mg/l from a test performed by ICI Group Environmental Laboratory (1990) could not be validated.

Chronic toxicity

Table 3.41 Chronic toxicity experiments to invertebrates with DIDP

Species	NOEC (21 d)	Remarks	Reference
Daphnia magna	0.03 mg/l	Physical entrapment (?)	Rhodes et al. (1995)
	≥ 0.1 mg/l	Solubiliser: acetone, higher than 100 mg/l authorised by the guideline	Brown and Thompson (1982)
	≥ 1 mg/l	Solubiliser: castor oil ethoxylate	Croudace et al. (1995)

In one study a definite NOEC value of 0.03 mg/l (Rhodes et al., 1995) was obtained. It is however assumed by the authors of this publication that the effect is due to physical entrapment of daphnids at the surface.

Physical entrapment is not considered as a toxic effect in this risk assessment, (a higher limit value is obtained with a solubiliser), therefore the concentration of 0.03 mg/l is not taken into account in the effect assessment.

In conclusion, no chemical toxic effects of DIDP towards invertebrates could be observed in any of the performed long-term tests and therefore no NOEC can be derived.

3.2.1.1.3 Aquatic plants

Table 3.42 Toxicity experiments to aquatic plants with DIDP

Species	Effects	Remarks	Reference
Selenastrum capricornutum	196 h EC50 ≥ 1.3 mg/l 196 h NOEC ≥ 1.3 mg/l	Test solution prepared by sonication for 1 minute and settling for 4 hours, measured concentration	CMA (1984d)
Scenedesmus subspicatus	72 h EC50 ≥ 500 mg/l 72 h EC20 ≥ 500 mg/l	Solubiliser RH Cremophor was used; *no analytical monitoring*	BASF (1988)

No effect was demonstrated at these limit values. In conclusion, no chemical toxic effects of DIDP towards algae could be observed in any of the performed long-term tests and therefore no NOEC can be derived.

3.2.1.1.4 Microorganisms

Two studies concerning toxicity to microorganisms have been carried out.

Table 3.43 Toxicity experiments to microorganisms with DIDP

Species	EC 0	Remarks	Reference
Activated sludge of predominantly domestic sewage	≥ 85 mg/l	Exposure period 3 h; limit test; analytical monitoring of nominal concentration of 100 mg/l;	Exxon Biomedical Sciences (1997c)
Photobacterium phosphoreum	≥ 85 mg/l	Exposure period 15 min; limit test; analytical monitoring of nominal concentration of 100 mg/l;	Exxon Biomedical Sciences (1997c)

No effect was seen at these limit values. Solution of DIDP was achieved by using a solvent (Tween 20). As analytically monitoring was performed, these results are considered as valid.

A study performed with *Pseudomonas putida* (BASF, 1989b) did not reveal an effect-dose relationship, however a respiration inhibition of 20% for the concentrations 19.5-5,000 mg/l was determined.

In a further study with *Tetrahymena pyriformis* (Yoshizawa et al., 1977), no effect on cell division could be observed over 24 hours at concentrations of 1, 10, 25, 50, 100 or 200 mg/l.

In conclusion, no chemical toxic effects of DIDP towards microorganisms could be observed in any of the performed tests and therefore no NOEC can be derived.

3.2.1.1.5 Potential for endocrine disruption

Several results from *in vitro* and *in vivo* assays to determine the potential of phthalate esters are described in Section 4. Regarding the effects upon ecosystems, the most relevant test result is from the multigeneration study with *Oryzias latipes* by Patyna et al. (1999) as described above.

DIDP was added to dry flake food at 20 mg/kg. There were no statistically significant changes in mortality or fecundity between the treatment groups. There was no reduced egg production. Evaluation of F_1 and F_2 embryos showed normal development except for a transient decrease in red blood cell pigmentation. This effect was observed in both the DIDP treatment and the acetone control group. The male to female ratios (3:1) in all groups were similar. Phenotypic gender classification of male and female fish was histopathologically confirmed to be 100% correct. Ale somatic gonadal index and liver somatic index were not significantly different in any group.

Based on these data there is apparently no impact on any population parameter from chronic exposure to DIDP on fish.

3.2.1.1.6 Sediment dwellers

Several recent studies have been carried out for different sediment dwellers.

Table 3.44 Toxicity experiments to sediment dwellers with DIDP

Test Organism	Test duration (days)	Test end points	NOEC (mg/kg dw)	Reference
Midge (*Chironomus riparius*)	28	Adult emergence, time to emergence, sex ratio	≥10,000 *	Brown et al. (1996)
Midge (*Chironomus tentans*)	10	Survival, growth	≥3,000 *	Call et al. (1997)
Amphipod (*Hyalella azteca*)	10	Survival, growth	≥3,000 *	Call et al. (1997)
Moorfrog (*Rana arvalis*)	28	Egg hatching, tadpole survival	≥600 *	Wennberg et al. (1996)

* Highest concentration tested

No effect was observed at the highest concentrations tested.

3.2.1.2 Calculation of PNEC

Determination of $PNEC_{aqua}$

No chemical toxic effects of DIDP towards fish, invertebrates or algae could be observed in any of the performed long-term tests. No NOECs could be derived. The assessment scheme proposed in EC (1996) can therefore not be used to derive a PNEC for the aquatic compartment. As furthermore, a two-generation study in fish exposed orally was performed, showing no impact on any population parameter, it can tentatively be concluded that DIDP does not cause adverse chemical effects towards the aquatic ecosystem.

Determination of $PNEC_{microorganisms}$

Reliable results were obtained recently by Exxon Biomedical Sciences (1997c) in a test of respiratory inhibition of activated sludge (OECD guideline 209). No effect was observed at a measured limit concentration of 85 mg/l. It can be concluded that the substance does not have any effects upon microorganisms at or above water solubility and that no PNEC can be derived. This would be also supported by the available biodegradability test results.

Determination of $PNEC_{sediment}$

Long-term tests have been performed with vertebrates (moorfrog) and invertebrates (midge). In none of the test systems could any effects be observed. No NOECs could be derived. It can therefore tentatively be concluded, that this compound has no adverse effects towards benthic organisms.

3.2.2 Atmosphere

Some phthalates, especially dibutylphthalate (DBP) have shown to be toxic to plants via the atmosphere (EC, 1999). Hannay and Millar (1986) exposed radish seedlings to an air stream passing over PVC rods plastified with DBP or DIDP. While the growth was inhibited in the experiments involving DBP plastified PVC, no effects were seen in those involving DIDP plastified PVC. The concentrations of DBP or DIDP were not measured though. No conclusion

can unfortunately be drawn from this experiment. As DIDP is much less volatile than DBP, the concentration of DIDP in the "contaminated" air was certainly much lower than the concentration of DBP.

Hardwick et al. (1984) grew cabbage seedlings in a cuvette bioassay in the presence of strips of plastic plasticised with DBP, DEHP or DIDP. Effects were observed with plastics treated with DBP. No effects were observed with DEHP plasticised strips. No effects were observed with small samples of DIDP-plasticised strips. Effects were observed with larger samples of DIDP plasticised strips, but residual concentrations of DBP were measured in the air while no DIDP was detected (limit of determination not indicated).

These experiments do not allow to conclude an absence of toxicity of DIDP to plants via the gas phase. No PNEC can be determined.

3.2.3 Terrestrial compartment

A summary of recent soil toxicity experiments for DIDP are summarised in **Table 3.45**.

Table 3.45 Soil toxicity experiments with DIDP

Test Organism	Test Duration (days)	Test End points	NOEC (mg/kg dw)	Reference
Earthworm (*Eisenia foetida*)	14	Mortality	≥10,000 *	Exxon Biomedical Sciences (1996b)
Lettuce (*Lactuca sativa*)	5	Seed germination	≥10,000 *	Exxon Biomedical Sciences (1996c)
Rye Grass (*Lolium sp.*)	5	Seed germination	≥10,000 *	Exxon Biomedical Sciences (1996c)

* Highest concentration tested

Determination of $PNEC_{soil}$

Only short-term tests have been performed. As no effects have been revealed in results with soil dwelling and consumer organisms, the highest tested concentration of 10,000 mg/kg will be used. An assessment factor of 100 is applied instead of 1,000 as no LOECs could be determined. Therefore:

$$PNEC_{soil} \geq 100 \text{ mg/kg (dry weight)} = 100{,}000 \text{ µg/kg dw}$$

3.2.4 Secondary poisoning

The lowest overall NOAEL of 15 mg/kg bw/d has been determined in a 13-week repeated dose study with dogs. This corresponded to a food concentration of 500 mg/kg. Using an assessment factor of 10, a PNECoral of 50 mg/kg can be estimated for top predators.

3.3 RISK CHARACTERISATION

3.3.1 Aquatic compartment

Sewage treatment plants

The highest value estimated for a STP outlet is 20.75 mg/l (production site C, worst-case scenario with default values). No PNEC could be derived, as no effects at the limit of water solubility could be observed. **Conclusion (ii)**.

Surface waters

In **Table 3.46** the total surface water concentrations for the different exposure scenarios is presented.

Table 3.46 PEClocal for the aquatic compartment

Life cycle step		$PEClocal_{water} = Clocal_{water} + PECregional_{water}$ [µg/l]
Production	A	0.0004 + 1.25
	B	44 + 1. 25
	C	6 + 1. 25
	D	0.0002 + 1. 25
	E	1 + 1. 25
Processing in PVC (*life cycle IIIa*)	1	4.6 + 1. 25
	2	6.21 + 1. 25
	3	1.93 + 1. 25
	4	15.2 + 1. 25
	5	7.02 + 1.25
Processing in non-PVC (*life cycle IIIb*)		7.9 + 1. 25
Use in anti-corrosion paints (*life cycle IIIc*)	I * II **	4.8 + 1. 25 0.000015 + 1. 25
Use in anti-fouling paints (*life cycle IIId*)	II	3.7 + 1. 25
Use in sealing compounds (*life cycle IIIe*)	I	4.8 + 1. 25
Use in inks for textiles (*life cycle IIIf*)	I II	4.8 + 1. 25 0.07 + 1. 25

* I: formulation
** II: processing

No chemical toxic effects of DIDP towards fish, invertebrates or algae could be observed in any of the performed long-term tests. No NOECs could be derived. The assessment scheme proposed in EC (1996) can therefore not be used to derive a PNEC for the aquatic compartment. As furthermore, a two-generation study in fish exposed orally was performed, showing no impact on any population parameter, it can tentatively be concluded that DIDP does not cause adverse chemical effects towards the aquatic ecosystem. **Conclusion (ii)**.

Sediment

In **Table 3.47** the estimated sediment concentrations for the different exposure scenarios are presented.

Table 3.47 PEClocal for the sediment

Life cycle step		$PEClocal_{sed}$ = $Clocal_{sed}$ + $PECregional_{sed}$ [µg/kg dw]
Production	A	6.9 + 1,000
	B	716,740 + 1,000
	C	90,530 + 1,000
	D	2.6 + 1,000
	E	200 + 1,000
Processing in PVC (*life cycle IIIa*)	1	74,370 + 1,000
	2	100,400 + 1,000
	3	31,200 + 1,000
	4	245,600 + 1,000
	5	111,500 + 1,000
Processing in non-PVC (*life cycle IIIb*)		127,100 + 1,000
Use in anti-corrosion paints (*life cycle IIIc*)	I *	77,600 + 1,000
	II **	0.25 + 1,000
Use in anti-fouling paints (*life cycle IIId*)	II	59,500 + 1,000
Use in sealing compounds (*life cycle IIIe*)	I	77,900 + 1,000
Use in inks for textiles (*life cycle IIIf*)	I	77,900 + 1,000
	II	1,200 + 1,000

* I: formulation
** II: processing

Based on an estimated regional background concentration of 33,000 µk/kg dw, the total resulting concentrations would be somewhat higher.

Long-term tests have been performed with vertebrates (moorfrog) and invertebrates (midge). No effects could be observed in any of the test systems. No NOECs could be derived. It can therefore tentatively be concluded, that this compound does not cause adverse effects towards benthic organisms. **Conclusion (ii)**.

3.3.2 Atmosphere

It is so far not possible to realise a biotic assessment in the same way as described for other compartments. No PNEC could be derived from the results available, as no dose response relationship could be established. The absence of adverse effects in the test systems does not give rise for immediate concern though. **Conclusion (ii)**.

3.3.3 Terrestrial compartment

In the following table, the ratios PEC/PNEC$_{soil}$ are shown. Local PECs$_{soil}$ for production sites have not been calculated as most producers dispose of their sewage sludge either through incineration or landfilling.

Table 3.48 PEC/PNEC ratios for agricultural soil

Life cycle step		PEClocal$_{soil}$ = Clocal$_{soil}$ + PECregional$_{soil}$ [µg/kg dw]]	PEC/PNEC
Processing in PVC (*life cycle step IIIa*) (highest release)			
		16,300 + 74	≤ 0.16
Processing in non-PVC (*life cycle step IIIb*)		8,400 + 74	≤ 0.08
Use in anti-corrosion paints (*life cycle step IIIc*)	I *	5,260 + 74	≤ 0.05
	II **	negligible	
Use in anti-fouling paints (*life cycle step IIId*)	I	negligible	
	II	3,930 + 74	≤ 0.03
Use in sealing compounds (*life cycle step IIIe*)	I	5,260 + 74	≤ 0.05
	II	negligible	
Use in inks for textiles (*life cycle step IIIf*)	I	5,260 + 74	≤ 0.05
	II	78 + 74	≤ 0.001

* I: formulation ** II: processing

As all calculated PEC/PNEC ratios are below 1, it can be concluded that there is no risk to soil dwelling organisms through DIDP. **Conclusion (ii)**.

3.3.4 Secondary poisoning

In **Table 3.49**, the PEC/PNEC ratios for top predators are presented.

Table 3.49 PEC/PNEC ratios for predators

Life cycle step	**PECoral$_{aquatic}$ [mg/kg ww]**	**PECoral$_{worm}$ [mg/kg ww]**	**PEC/PNEC fish / worm**
Production (life cycle step I)	15.4	0.11	0.31 / 0.0022
Processing in PVC (life cycle step IIIa) (highest release)	31.4	6.1	0.63 / 0.12
Processing in non-PVC polymers (life cycle step IIIb)	19.3	3.1	0.39 / 0.062
Formulation of anti-corrosion paints (life cycle step IIIc)	14.5	2.0	0.29 / 0.04
Use in anti-corrosion paints (life cycle step IIIc)	6.34	0.02	0.13 / 0.0004
Formulation in anti-fouling paints (life cycle step IIId)	negligible	negligible	/
Use in anti-fouling paints (life cycle step IIId)	12.4	1.5	0.25 / 0.03
Formulation of sealing compounds (life cycle step IIIe)	14.5	2.0	0.29 / 0.04
Use of sealing compounds (life cycle step IIIe)	negligible	negligible	/
Formulation of inks for textiles (life cycle step IIIf)	14.5	2.0	0.29 / 0.04
Use of inks for textiles (life cycle step IIIf)	6.46	0.05	0.13 / 0.001

As for all scenarios PEC/PNEC ratios are below 1, it can be concluded that there is no risk towards top predators from DIDP. **Conclusion (ii)**.

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

4.1.1.1 General discussion

Exposure to DIDP may occur at each stage of its life cycle, from production to waste disposal, including the manufacture or the use of end products containing DIDP. The human populations that may be exposed are:

- workers,
- consumers,
- humans through the environment.

Routes of exposure may be:

- direct skin contact (e. g. manufacture, formulation of products, contact with end products containing DIDP),
- inhalation (e.g. manufacture, processing or use at high temperature of products containing DIDP, aerosol forming activities),
- oral (e.g. toys end use, via food contact materials).

DIDP vapour pressure being so low that it is difficult to measure, its vapour phase concentrations remain always low, even at temperatures used in some industrial conditions (e.g. processing, mixing, calendering). However, in many circumstances aerosols are formed and become a potentially important source of exposure. Pulmonary penetration may be significant if droplets are in the respirable range (e.g. less than 5 μm), as it occurs after recondensation. Pulmonary penetration also occurs when vapours condense on existing respirable airborne particles, as may be the case in the environmental context.

4.1.1.2 Occupational exposure

Occupational exposure to DIDP may occur: 1) by skin contact with pure DIDP, or mixtures (formulations) or end products containing it 2) by inhalation (vapours and aerosols). Oral exposure is not considered to be a significant route of exposure under normal working practices.

Few countries have defined Occupational Exposure Limits for DIDP. In UK, the HSE (1997a) indicates an occupational exposure standard (8-hour TWA) of 5 mg/m^3 for DIDP (CAS 26761-40-0). In Sweden, KEMI (1997) indicates a "level limit value" of 3 mg/m^3 and a "short-term value" of 5 mg/m^3 which apply to phthalates such as DIDP for which no specific limit values have been defined**.**

Workers may be exposed to DIDP at different representative stages of its life cycle. The following exposure scenarios are considered:

1. manufacture of DIDP (reactor opening, drumming, pumping into tanks, cleaning, maintenance, etc),
2. manufacture of products containing DIDP as plasticisers or solvents (adding, mixing, processing e.g. calendering, extruding, injection moulding, etc).
3. use of end products containing DIDP (use of e.g. coatings, adhesives or inks).

In PVC formulations, the typical amount of DIDP is about 20-40% but may go up to 55%. In end products, the amount varies greatly from less than 1% to more than 50% (INRS, 1998).

The use of personal protective equipment is not taken into account in this assessment. Moreover its effectiveness is difficult to estimate in real conditions of use.

4.1.1.2.1 Dermal exposure

Direct or indirect (via contaminated clothes or gloves) skin contact with pure DIDP refers only to some activities during manufacture (drumming, cleaning, maintenance) and handling it at the first step of its industrial use (pumping, emptying containers). Contact is also possible with formulations or end products containing DIDP, especially in the liquid or paste form (e.g. application of coatings, adhesives or inks). Dermal exposure during use of solid finished products is considered to be low because of incorporation of the substance in the polymer matrix.

No measured data are available for dermal exposure.

Exposure assessment does not normally include absorption consideration. However it is useful to discuss the skin penetration of DIDP before proposing predictive external exposure.

Skin absorption of chemicals can be described using a simple model which depends only upon the size of the permeant and its octanol/water partition coefficient (Potts and Guy, 1992). The maximum penetrant flux decreases very rapidly for log P values greater than 2 (Guy and Hadgraft, 1988). The molecular weight is generally considered as presenting less influence (although there was very limited experience with high molecular weight substances), the diffusion coefficient being theoretically inversely proportional to the cube root of molecular weight (ECETOC, 1993). With its very marked lipophilicity and high molecular weight, DIDP may be inferred to have a very low skin penetration. A comprehensive set of experimental data about dermal absorption properties of phthalates presented in Section 4.1.2.1. confirms that skin penetration of DIDP is very low.

Although the potential dermal exposure may change across a wide variety of circumstances encountered in workplaces, it is proposed as a first worst-case approach to use a maximum external exposure in order to calculate the maximum dermal uptake whatever the scenario is.

The maximum daily external exposure is assumed to be 5 mg/cm^2. This value is clearly a maximum because:

- it is qualified as “intermittent contact during wide dispersive use and direct handling” (1-5 mg/cm^2/d) by the EASE model and exposure may be much lower in many circumstances,
- experience with dermato-pharmaceuticals has shown that the skin area-dose during therapeutic use is 2 to 4 mg preparation per cm^2. It was found that the cutaneous penetration rates increased as the dose was increased up to 5 mg/cm^2 of skin, and then remained constant at skin area doses equal to and higher than 5 mg/cm^2. Experience has also shown

that *in vivo* the maximum amount of a compound which can be retained on human skin is around 5 µl/cm^2 of a liquid (ECETOC, 1993).

- DIDP is not always used as a neat substance. Exposure during the use of a formulation is tempered by the percentage of DIDP in the formulation.

4.1.1.2.2 Inhalation exposure

Due to its extremely low vapour pressure, DIDP vapour phase concentrations may not attain high levels, even at the high temperatures used in some industrial conditions (e.g. processing, mixing, calendering). At 20°C DIDP has a vapour pressure of $2.8.10^{-5}$ Pa (best estimated value) and a calculated saturated vapour concentration of 5.1 µg/m^3. If vapours are inhaled up to a temperature of around 35°C (where maximum vapour pressure would be around 8.10^{-5} Pa and prolonged inhalation unlikely), the saturated vapour concentration is ca. 15 µg/m^3. Occupational exposure to vapour will actually be far below these values.

Nielsen et al. (1985) sampled phthalic acid esters (PAEs; mainly DEHP, DIDP and BBP) on glass fibre filters and checked that no vapour passed through the filter. They did not study the aerosol particle size, but estimated it should be in the respirable range, owing to its mechanism of formation. Dirven et al. (1993) also checked that no DEHP was lost when drawing air through mixed cellulose ester membranes spiked with 30 µg DEHP. Recovery was greater than 97%. These data are an experimental confirmation that heavy phthalates have negligible vapour concentrations at ordinary temperature and pressure and that the main source of inhalation exposure originates from aerosol formation.

At high temperatures and mechanical pressures, aerosol formation is observed with DIDP like with other phthalates. Exposure to aerosol is therefore possible in any situation where pure DIDP is heated or materials containing DIDP are heated and under influence of mechanical pressure. This is also the case when mixtures containing DIDP are sprayed.

Few measured data are available for DIDP inhalation exposure. However a significant amount of data is available for other phthalates.

Due to similar physico-chemical mechanisms of aerosol formation, similar aerosol concentrations are likely to be observed with heavy phthalates in similar conditions of use. Then, phthalates considered should not differ too much in molecular weight (hence, in volatility, boiling point, vapour pressure). This allows to consider data available for other phthalates, especially DEHP and heavier phthalates, as a source of information to estimate potential exposure concentrations to DIDP aerosols.

The measured data mentioned in this report are not always presented with sufficient detail to judge their relevance (e.g. no precise information regarding processes, control measures, sampling procedure), some are relatively old and may be associated with less advanced controls than would be expected today. However the total number of measurements is large and most activities that are suspected to lead to relatively high exposure levels are included. Moreover the evolution of controls is not always as fast as expected, especially in small undertakings.

Comparison with modelled data seems difficult. The EASE model is not suitable for substances with very low vapour pressure. Its application is limited to substances with vapour pressures higher than 1 Pa (DIDP vapour pressure is much lower) and estimation of exposure to aerosols is problematic.

Therefore for the initial assessment it is proposed to derive the exposure levels from the available measured data on DIDP and homologous phthalates. Further data would certainly be very useful to refine the assessment.

Scenario 1. Manufacture of DIDP

There are at least five production sites in the EU. "The manufacturing process for DIDP is within a closed system under vacuum. There is little potential for exposure" (ECPI, 1997), except when the lid is opened, at the end of each batch, and fumes are emitted. Other exceptions are cleaning and maintenance work and filling of tanks and drums. Most of the fumes or vapours are generally removed by local exhaust ventilation.

Literature data

Peak values from < 1 mg/m^3 up to as high as 60 mg/m^3 have been reported for production workers, although with little detail on measurement conditions (Gilioli et al., 1978); time-weighted average is reported to be 5 mg/m^3. Liss et al. (1985) presented data on 50 personal exposure measurements (with sampling on 37 mm diameter filter cassettes at 1 l/min) to DEHP for the duration of the workshift; 6 only showed levels above the analytical limit of detection. The maximum measured concentration was 4.1 mg/m^3.

Unpublished data

"Limited monitoring data collected over several years to assess occupational exposure of process operations and maintenance technicians at a plasticiser plant indicate DIDP concentrations in air of less than 2 mg/m^3" (ECPI, 1997). KEMI (1997) indicates an exposure level of 0.1 mg/m^3 during manufacture (closed process). This reflects well controlled procedures, but higher exposures may occur.

King (1996) reported data from different producers and from the HSE (**Table 4.1**). Sampling times are not indicated.

Table 4.1 Exposure to phthalate esters during manufacture King (1996)

Producer/Source	Esters	Personal sample number	Average, mg/m^3	Range, mg/m^3
Producer 1 (EU)	Various DEHP	14 1	0.77 < 0.1	0.2 - 2.3 < 0.1
Producer 2 (EU)	DEHP	4 (production) 2 (tanker filling) 1 (drumming)	< 1.09 < 0.11 0.14	< 0.016 - 4.3 < 0.013 - 0.09 -
Producer 3 (USA) Producer 3 (EU)	Various DINP/DIDP/DIHP Various	12 18 (tanker filling) ?	 ?	< 0.01 - 0.31 <0.05 [1)] < 2.0 [2)]
Producer 4 (EU)	DEHP	28 [3)]	0.36	0.03 - 1.56
HSE data (from ACTS, 1984)	C8 - C13 C9 - C11	10 11		< 0.25 < 0.25

Table 4.1 continued overleaf

Table 4.1 continued Exposure to phthalate esters during manufacture

Producer/Source	Esters	Personal sample number	Average, mg/m^3	Range, mg/m^3
Industry data (from ACTS, 1984)	DIOP DIDP DEHP	86 32 77 [4]		< 5.0 < 5.0 < 5.0

1) Less than the analytical limit of detection. Area monitoring was also performed: of the 29 samples, only 4 taken on top of tank cars exceeded the analytical limit of detection (0.27 mg/m^3 DINP, 0.21 mg/m^3 DIHP, 64.16 mg/m^3 DHP, 53.32 mg/m^3 DIDP). The representative area readings were all < 0.07 mg/m^3 for the phthalates investigated.

2) Limited data: less than the analytical limit of detection.

3) Area measurements - "No cause for concern thus no need for personal monitoring".

4) Of the 77 measurements made, 87% were less than 0.5 mg/m^3, 95% were less than 2 mg/m^3. Similar results are given for DIDP and DIOP.

Exposure to phthalate esters has been estimated in 1996 through measurements of DEHP, when this substance was produced, in a large-scale chemical industry. Of 38 determinations, a median value of 0.18 mg/m^3 appears for routine determinations (meaning on a 8-hour shift duration), with one outlier at 2.8 mg/m^3. Of 12 short-term measurements, the median is 0.6 mg/m^3.

Considering all the data available for this scenario, a reasonable worst-case exposure is estimated at 5 mg/m^3 (8-hour TWA). The typical concentration will be less than 2 mg/m^3, and often still less, DIDP being in general not detected when no aerosol is formed.

Scenario 2. Manufacture of products containing DIDP

Following manufacture, DIDP is incorporated to a polymer (PVC compounding, PVC processing) or to other mixtures (production of inks, adhesives, pigments dispersions, etc). Highest exposure will occur during processing or mixing operations at high temperatures. DIDP being used in PVC formulations at concentrations that may go up to 55% by weight, it may be emitted in sizeable quantities in the course of calendering, extruding, injection moulding.

Literature data

In a study on the health status of workers exposed to phthalate plasticisers in the manufacture of artificial leather and films based on PVC resins, Milkov et al. (1973) reported “ambient levels of vapours or aerosols of the plasticisers (mixed esters) at the working zone of the primers ranging from 10 to 66 mg/m^3. Similar results were obtained at the workstations of the mill operators and calendar operators. In the mixture preparation section, the plasticiser level was found to be 1.7-40 mg/m^3”. The most used phthalates were DBP and higher alkyl phthalates (DAP-789). This paper does not give any indication on measurement conditions (duration, personal or static sampling, sampling technique, method of analysis, specificity).

Nielsen et al. (1985) measured exposure to phthalic acid esters (mainly DEHP, DIDP and BBP) in a PVC processing industry (2-hour sampling times) and found atmospheric concentrations ranging from 0.01 to 2.8 mg/m^3.

Hagmar et al. (1990) give results of the same order of magnitude (0.5 to 3 mg/m^3 among “highly” exposed workers (calendering, mainly exposed to DEHP, DIDP and BBP). They give no detail, however, on sampling techniques.

Vainiotalo and Pfäffli (1990) measured exposures (static, not personal samplings) to DEHP in 9 plants in the range < 0.02 to 1.1 mg/m^3 (this highest single value was measured during

calendering). They sampled on Florisil adsorption tubes at a flow rate of 0.5 l/min, and analysed by HPLC on a reversed phase C_{18} column with a 95:5 acetonitrile-water eluent.

Dirven et al. (1993) measured DEHP concentrations in the ambient air of PVC-processing industries (**Table 4.2**). Two-hour samplings were performed on mixed cellulose ester membranes at 1 l/min. After extraction, analysis was performed with a gas chromatograph.

Table 4.2 Mean concentrations and range of DEHP in ambient air as determined by personal air samplings (Dirven et al., 1993)

Plant	Mixing (mg/m^3)	Extruder (mg/m^3)
Boot	0.26 (0.1 - 1.22), n = 16 *	0.12 (0.05 - 0.28), n = 11 *
Cable	0.18 (0.009 - 0.81), n = 8 *	0.24 (0.01 - 1.27), n = 13 *

Unpublished data

King (1996) reported data collected in the UK by the HSE and by industry. They are of particular interest since they include an idea of data repartition (**Table 4.3**).

Table 4.3 Exposure to phthalates during PVC processing in UK factories King (1996)

Process	Esters	n	Cumulative% results less than (mg/m^3)					
			0.25	0.5	1.0	2.0	5.0	10.0
Manufacture of pigment dispersions	DEHP+ DIAP (total)	8	100					
Recovery of filter DEHP residues	DEHP	11	-	45	100			
Manufacture of floor tiles	DEHP	8	-	100				
Manufacture of flexible floor covering	DEHP BBP	12	100 100					
Manufacture of rubber gloves	BBP D79P	18	100 -	-	100			
Manufacture of PVC	DEHP DIDP	7	100 100					
Manufacture of PVC	DIOP	8	-	-	-	100		
Manufacture of shoes (PVC binding)	DIOP	9	-	-	34	44	67	89
Manufacture of PVC*	Mixed (total)	143	-	-	56	74	93	100
Manufacture of cables*	Mixed (total)	25	-	-	40	80	92	100

RIVM (1997) collected exposure data to various phthalates during processing of polymers. **Table 4.4** summarises the data after selection of phthalates heavier than DBP or BBP (and excluding data already cited from King (1996)). Sampling times are generally not provided.

Table 4.4 DEHP Exposure data during processing of polymers (RIVM, 1997)

Industrial sector	n	Range, mg/m^3	Comments, source
Extrusion, injection, moulding, calendering compounding	34	0.02 - 0.5	At different processing temperatures (120 - 200 C). Personal communication from TNO (1996)
Calendering	3	1.46 - 1.95	BG Chemie (1994)
Calendering	6	0.3 - 2	BG Chemie (1994)
Waste processing	1	1.23	BG Chemie (1994)

KEMI (1997) indicates that exposure to phthalates is in the range of 0.1-0.3 mg/m^3 (8 hours) during manufacture of flooring material (mixture of DEHP, BBP and DIDP) and up to 2 mg/m^3 during calendering of PVC film.

Other data have been collected from databases in the UK (**Table 4.5**), Germany (**Table 4.6**) and France (**Table 4.7**). These data must be interpreted with care as there are a number of possible source of bias, in particular measurements have often been performed in workplaces selected in order to check compliance with occupational exposure standards giving preferential consideration to high levels of exposure.

Table 4.5 Diisooctyl phthalate exposure data (HSE, 1997b)

Plastics processing			
	a	b	c
In primary form	SL	1	0.01
Milling, mixing or coating	SL PL	2 1	< 0.5 0.1
Machine operator	PL or PS	5	< 0.5
Treatment and coating of metals			
	a	b	c
Operator (general)	PL	3	0.01
	PL	1	0.46
	PL	1	0.63
Packing and background	PL SL	2 5 1 1	0.01 0.01 0.02 0.85

a: sampling type (SL: static, long duration; PL: personal, long duration)
b: number of measurements
c: results, in mg/m^3

Table 4.6 Samplings and percentiles of workplace exposure to DEHP collected from 1991 to 1995 (BGAA, 1997)

Industrial activity	Nb. of facilities	n	50th percentile	90th percentile	95th percentile
Transforming:	85	31	0.08	2.45	5.93
- Without control measures	32	14	0.03	0.44	0.57
- With control measures	53	21	0.15	3.65	7.00

(in mg/m^3)

These measurements were performed on membrane filters for 1 hour at least and analysed by high-pressure liquid chromatography.

Table 4.7 Dioctyl phthalate exposure measurements recorded from 1987 to 1996in the COLCHIC database (INRS, 1997)

Industrial sector	n	Global results, mg/m^3	Remarks
Rubber (calendering)	25	Range: 0.04 - 26.7 Mean: 2.48, sd. 5.98	Highest values (with their sampling times, min): 11.7 (60), 2.62 (165), 26.7 (180), 7.77 (197), 2.6 (309), 2.4 (317)
Pharmaceuticals	10	Range: 0.03 - 1.55, Mean: 0.28, sd. 0.54	
Metallic hoses	8	Range: 0.0007 - 0.07 Mean: 0.016, sd. 0.023	

n: sample number
sd: standard deviation

Samplings have been performed principally on filters (81.8%) for "dioctyl phthalate" (very probably DEHP). Analysis is most generally practiced by gas chromatography, sometimes by liquid chromatography.

The very high results found in the COLCHIC database in the rubber industry apply to calendering a rubber containing 4-8% dioctyl phthalate at more than 200°C, at a speed of $12\ m \cdot min^{-1}$. They have been obtained in ambient atmospheres, in places where workers were only present in case of problems or to check processing conditions. The highest measured concentration is referred to a sampling time of 3 hours. The 8-hour TWA is in this case $10\ mg/m^3$, if there is no complementary exposure, and if there is actual personal exposure during this time. These data indicate, however, that short-term concentrations could be as high as $30\ mg/m^3$ or sometimes even more, as already mentioned (Milkov, 1973).

Considering all the data available for this scenario, a reasonable worst-case exposure is estimated to be $10\ mg/m^3$ (8-hour TWA). There are wide variations amongst exposure measurements, depending on circumstances and representativeness of samplings (site, personal or area sampling, duration). The typical concentration would be around $3\ mg/m^3$.

Scenario 3: Use of end products containing DIDP

DIDP may be included in PVC or non-PVC products, such as coatings, rubbers, latexes, mastics and sealants, inks, dyestuffs, lubricants, etc. Other uses indicated are in acrylic resins (most often polymethylmethacrylate), pressure-sensitive adhesives, and creak indicating agents.

Use of end products can be distinguished in aerosol non-forming and aerosol-forming activities. During non aerosol-forming activities (e.g. normal use of paint, adhesive, ink…), inhalation

exposure will be negligible because of the low vapour pressure of DIDP. Significant exposures can occur during aerosol-forming activities when the use of the products involves elevated temperature or spraying technique (e.g. application of hot-melt adhesives, coating using a bath, spray painting or printing, textile spread coating, car underbody spray coating). Actual phthalate concentrations may however be limited due to their low vapour pressure, the range of particle sizes generated (they may not be respirable if not formed by a recondensation mechanism), or their percentage in formulations.

Data collected in the French database COLCHIC are presented in **Table 4.8**.

Table 4.8 Dioctyl phthalate exposure measurements recorded from 1987 to 1996 in the COLCHIC database (INRS,1997)

Industrial sector	n	Global results, mg/m^3
Inks and office equipment	4	Undetected
Commercial vehicles	5	All < 0.1
Boiler making	2	0.083 and 0.046
Carpets	1	< 0.1

n: sample number

Industry (King, 1996) reported some measurements made in 1995 on exposure to DEHP and DIDP during spray coating or spread coating in an automobile factory. Atmospheric concentrations were in the range 0-0.11 mg/m^3.

There are very few exposure data available for this scenario. Although exposure is likely to be very low in many circumstances, there is no clear evidence that worst-case exposure during aerosol forming activities would be lower than for the previous scenario. Therefore, an exposure of 10 mg/m^3 (8-hour TWA) is assumed for this scenario. The typical concentration would be around 1.5 mg/m^3.

4.1.1.2.3 Conclusion of occupational exposure

Dermal

In view of the very low absorption of DIDP by dermal route, a maximum dermal exposure of 5 mg/cm^2 is intentionally assumed for all scenarios. Actual levels of dermal exposure are much lower in most occupational circumstances.

Inhalation

Table 4.9 Conclusion of inhalation occupational exposure

Scenario	Estimated inhalation exposure level (mg/m³ 8-hour TWA)	
	Worst-case	Typical
1- Production of DIDP	5	2
2- Manufacture of products containing DIDP	10	3
3- Use of end products containing DIDP	10	1.5

4.1.1.3 Consumer exposure

4.1.1.3.1 General introduction

DIDP is a plasticiser used in several flexible PVC end products as cables and wires, sheets, film, wall- and roof covering, flooring, coatings and synthetic leather (car seats, home furniture), shoes and boots, outdoor and rainwear, car under-body coating. It has also been found in toys and child-care articles. DIDP is also used in several non-PVC end products as paints, printing inks, rubbers, latex and adhesive. All of these products are available to consumers. However, DIDP is not available to consumers as such.

Consumer exposure may also occur through food and drinking because of contamination from packaging and processing equipment containing DIDP.

Food and drink may also be contaminated via the environment. An assessment of indirect exposure of humans via the environment (including food) is presented in Section 4.1.1.4.

Three categories of consumers have been distinguished:

- newborn baby (0 to 6 months old) [N],
- infant (6 months to 3 years old) [I],
- adult (corresponding to adult and children 3 to 15 years old) [A],

For exposure scenarios, newborn babies and infants were grouped together in the same category (young children) except for food exposure where the diet was different for newborn babies and infants.

Because DIDP is present in several products available to consumers, particularly in soft-PVC, exposure can occur from several sources by different routes (inhalation, dermal, oral) in different situations (**Table 4.10**).

Table 4.10 End products containing DIDP, sources of exposure and categories of consumers exposed

End products/sources	Routes of exposure		
	Inhalation	Dermal exposure	Ingestion
Building materials and furniture	A-I-N	I-N	I-N
Toys and baby equipment	A-I-N	I-N	I-N
Car and public transport interior	A-I-N	A-I-N	
Clothes	A-I-N	A-I-N	
Shoes	A-I-N	A-I	
Gloves	A-I-N	A	
Food and food-related uses			A-I-N

A: Adult
I: Infants (6 months to 3 years old)
N: Newborn babies (0 to 6 months old)

Consumers may be exposed to DIDP released from consumer products. Because plasticisers in flexible PVC and other materials are not chemically bound, they may be released from the end product during its use. The release intensity is not expected to be linear over time. New products would be expected to give a higher exposure than products in which DIDP has reached a steady-state release from product matrix to medium.

All interior end use emissions are to the air compartment via volatilisation mechanisms, except for flooring where abrasion may occur (Exxon Chemical Corporation, 1997).

The following data are used for assessment of DIDP exposure for consumers:

- actual exposure data (food),
- results of migration tests (ingestion from toys),
- results of dermal experiments in rats (dermal exposure),
- results of a mathematical model (inhalation exposure).

Five exposure scenarios are considered referring to the above mentioned uses of DIDP:

1. toys and baby equipment, for young children (infants and newborns) via the oral and dermal routes,
2. food and food related uses, for adults and young children via ingestion,
3. building materials and furniture, for adults and young children via inhalation,
4. car and public transport interior, for adults and young children via inhalation,
5. clothing, gloves and footwear, for adults via skin contact.

Other scenarios, for instance dermal exposure from building materials and furniture may theoretically occur but cannot be easily estimated.

Human internal exposures were calculated taking into account the following bioavailability factors as well as differences in oral and inhalation uptake between children and adults:

- Oral internal exposure: 50% for adults derived from toxicokinetic data in rats (see Section 4.1.2.1 Toxicokinetics, metabolism and distribution), 100% for newborns and infants based on a study from Sjoberg et al. (1985) which seemed to show a greater absorption by oral route of another phthalate DEHP in young Sprague Dawley rats than in

older ones. The 100% bioavailability was also assumed by the CSTEE for calculation of oral exposure in children.

- Inhalation internal exposure: 75% for inhalation exposure in adults estimated upon animal data (see Section 4.1.2.1 Toxicokinetics, metabolism and distribution), 100% assumed for newborns and infants, considered to be in any case a vulnerable sub-population.

Dermal internal exposure is derived from an experiment in rats designed to model the dermal exposure and absorption through direct contact with plastic film containing DEHP (Deisinger et al., 1998). This study is considered more appropriate than dermal absorption studies performed with application of the substance as such. For consumers no correction factor is used to extrapolate from rats to humans. As it has been showed that DIDP is 10 times less absorbed through the skin than DEHP (Elsisi et al., 1989), a factor of 10 is assumed to extrapolate from DEHP to DIDP.

4.1.1.3.2 Scenario 1:Toys and baby equipment

Many soft plastic toys and teethers are composed of PVC plastic that may contain a high concentration of plasticiser e.g. DIDP. Teethers rings, commonly used as a child-care product or as a toy for babies are manufactured especially for chewing/biting by babies when erupting teeth start.

In an investigation published by Greenpeace (1997), DIDP was found in 2 out of 63 toys containing PVC. The two samples were teethers. The first sample was bought in Argentina but had been produced in China and contained 20% of DIDP. The second sample was bought in Philippines but had been produced in USA and contained 15.7% of DIDP (Greenpeace, 1997).

In a study about phthalates in teething rings and animal figures for infants published by the Inspection for Health Protection in Utrecht, the total DIDP content in tested toys was 1.4 to 15% (CSTEE, 1997a).

The UK Government has monitored the content of plasticisers in toys. DIDP was found in 6 out of 18 toys in 1990, 4 out of 27 in 1991 but no DIDP was found in 16 toys in 1992 and in 29 toys in 1996 (CSTEE, 1997b). The rarity or the absence of DIDP in current toys could explain that DIDP was not analysed in many recent studies (CSTEE, 1997c; Vikelsoe et al., 1997; LGC, 1998; RIVM, 1998; Steiner et al., 1998). But DIDP had been used in toys in the past, so it may be considered as an alternative to other phthalates in the future, consequently it may be of value to consider the risks of such possibility.

The young children exposure to DIDP will be assessed in two ways:

- without the toy scenario, regarding the present situation,
- with the toy scenario, considering the foreseeable future use of DIDP as a substitute for other phthalates in toys.

Children may be exposed to DIDP from toys made of plasticised PVC by the oral and dermal routes.

The rate of migration is affected by factors such as the relative solubility of DIDP in the PVC-polymer and in saliva, temperature, the thickness of the polymer and the physical forces acting on the polymer.

Oral exposure

Small children suck, chew and bite toys. Physical "chewing" and the continuous flow of fresh saliva around the article can be a rather effective extraction procedure for DIDP.

There is no method to calculate direct exposure of DIDP from toys. To estimate the exposure level, the leaching values of DIDP found in different studies will be used; the representativeness of these studies in comparison with the real exposure is not known.

There are a number of reported determinations of phthalate leachate from toys. **Table 4.11** presents the available data on leaching of DIDP from materials on the European market. There is at present no standard method available to mimic the actual exposure during chewing. These different investigations represent many different toys; the percentage of DIDP in the toys analysed is never known.

Table 4.11 Reported leaching to saliva of DIDP from toys under static and dynamic experimental conditions

Leaching of DIDP	Unit	Reference
0.9-4.6	µg/cm^2/h	CSTEE (1997d)
nd *-0.084	mg/kg/6 h	Artsana in CSTEE (1997e)
nd*	µg/dm^2/6 h	CSTEE (1997b)
< 0.1	mg/dm^2/h	CEFIC-ECPI in CSTEE (1998a)
0.11	mg/kg/6 h	Artsana in CSTEE (1997f)
5	µg/cm^2/h	Gesondheidsbescherming in CSTEE (1997f)

* nd: not detected

To compare the results given in **Table 4.11**, the maximum emission values are converted to a daily dose for a 8 kg infant mouthing 10 cm^2 of the investigated material for 3 hours every day (CSTEE, 1998b). For the two studies giving the results on a weight basis, these are recalculated using the specific area 15 cm^2/g (CSTEE, 1998b). The resulting doses are presented in **Table 4.12**. These doses are calculated on the fact that 100% of the DIDP leached is absorbed.

Table 4.12 Calculated maximum dose of DIDP for a 8 kg baby mouthing 10 cm^2 of the toy during 3 h per day (CSTEE, 1998b)

Calculated maximum dose of DIDP (µg/kg bw/day)	According to reference
17	CSTEE (1997d)
0.004	Artsana in CSTEE (1997e)
< 4	CEFIC-ECPI in CSTEE (1998a)
0.005	Artsana in CSTEE (1997f)
19	Gesondheidsbescherming in CSTEE (1997f)
7	RIVM in CSTEE (1998b)

In this table, the highest value is roughly 5,000 times more elevated than the lowest value. This difference can be explained by the fact that there are important differences regarding the test methods used to measure phthalate migration (dynamic or static methods) and more specifically between the conditions or assumptions selected (period of exposure, surface contacts, type of stimulant, etc.) to measure such migration. In **Table 4.12**, the lowest results are reported by laboratories using static extraction methods. An Austrian study, where actual sucking of test material has been tested, showed that amounts of phthalates migrated from PVC into saliva by the static method < the agitation method < sucking (CSTEE, 1997b).

To have an idea of the representativeness of these values reported in **Table 4.12**, they have been compared with values reported in a recent *in vivo* study on toys (RIVM, 1998). This study was a human volunteers study to assess release of another similar phthalate DINP from PVC samples to saliva (DINP concentration in toys is about 40%). Maximum level of release was 8.9 µg/min for a toy containing 43% of DINP: this corresponds to an internal exposure of 200 µg/kg bw/day for newborn babies and infants assuming the same criteria as suggested by CSTEE (10 cm^2, 8 kg, 3 hours, 100% bioavailability).

This value is ten times more elevated than the 19 µg/kg bw/day found in study on DIDP (Gesondheidsbescherming in CSTEE, 1997, Add 36). This could be explained by higher quantities of DINP contained in toys tested by RIVM and the difference of methodology (vs. *in vivo/in vitro*).

A maximum internal oral exposure to DIDP in toys of 200 µg/kg bw/day is retained for the risk assessment for newborns and infants. No correction for molecular weight to extrapolate from DINP to DIDP will be made as this would imply a false accuracy in the exposure estimates.

Dermal exposure

DIDP can be transferred to the skin via direct physical contact with infant skin. The amount of DIDP a child is exposed to, is a function of the area of skin in contact with the product, the duration of the contact, the surface availability of DIDP from the product and the penetration of DIDP through the skin.

A study performed by Deisinger et al. (1998) investigated the migration of DEHP contained as a plasticiser in PVC from plastic film and its absorption through rat skin *in vivo*. Sheets of PVC film (15 cm^2) plasticised with DEHP were applied to the shaved backs of 8 male rats in two separate experiments. According to this study, dermal absorption rate for DEHP through rat skin is 0.24 µg/cm^2/h (Deisinger et al., 1998). As it has been shown that DIDP is 10 times less absorbed through skin than DEHP (Elsisi et al., 1989), dermal absorption rate for DIDP is expected to be 0.024 µg/cm^2/h. For consumers no correction factor is used to extrapolate from rats to humans.

For a skin contact area of 100 cm^2 (estimated skin area round the mouth and on the hands in contact with the toy), a contact duration of 3 h/day and a body weight of 8 kg (CSTEE, 1998b), the daily exposure of DIDP would be:

$$\frac{0.024 \cdot 100 \cdot 3}{8} = 1 \text{ µg/kg bw/day}$$

A maximum internal dermal exposure to DIDP in toys of 1 µg/kg bw/day is retained for the risk assessment for newborn babies and infants.

4.1.1.3.3 Scenario 2: Food and food-related uses

Limited data are available to characterise phthalates and particularly DIDP concentrations in food (Sharman et al., 1994; MAFF, 1996a; MAFF, 1996b; MAFF, 1998). In France, DIDP is authorised for food packaging if the release does not exceed 3 mg/kg (Journal Officiel, 1994). DIDP is, actually, only used in a very limited number of such applications. It was never analysed or detected in any food sample tested in these studies.

Adults

In the Sharman study (Sharman et al., 1994), DIDP was not analysed, only DEHP and total phthalate levels were determined. Samples varied considerably in their levels of contamination, the highest being cheese samples containing 17 mg/kg wet of DEHP. However, the majority of samples contained 0.6-3.0 mg/kg wet. The level found in these products was too high to have resulted solely from milk by concentration in the fat phase and must therefore have arisen in other ways.

A recent survey by MAFF estimated the levels of total and individual phthalates in 74 samples of composite fatty foods (MAFF, 1996a). Samples consisted of retail food products including: carcass meat, meat products, offal, poultry, eggs, fish, fats and oils, milk and milk products. DIDP was not detected in any sample in this study (limit of detection = 0.01 mg/kg food).

Total phthalate levels determined in food samples from the Sharman's study (0.04 to 114.4 mg/kg) were more elevated than those from the MAFF (0.1 to 10.2 mg/kg). In the MAFF study, total phthalate levels were determined in food samples from only one European country (UK), while in the Sharman study, total phthalate levels were determined in food samples from three European countries (UK, Norway and Spain). The MAFF results are surely not representative of real levels of total phthalates in the European food market. However, in this study, a wide range of food sample was tested while in the Sharman's study only milk and by-product (cream, butter and cheese) were tested. So, for exposure assessment, the MAFF study will be used.

Considering the detection limit of this study, and assuming a food intake of 1 kg for an adult of 60 kg, the daily intake of DIDP via food would be < 0.17 µg/kg bw/day. The value of 0.2 µg/kg bw/day will be used in the risk assessment. A bioavailability of 50% is considered for oral exposure in adults so the internal exposure will be 0.1 µg/kg bw/d.

Newborns and infants

Another recent MAFF survey estimated the intakes of individual phthalates and total phthalates by infants from infant formulae (MAFF, 1996b). A total of 59 individual samples of 15 different brands of infant formulae were analysed. DIDP was not analysed. The level of DEHP, which was the more abundant phthalate found in samples, ranged from 0.33-0.81 mg/kg wet (casein dominant formulae), 0.38-0.98 mg/kg wet (whey-dominant) and 0.38-0.56 mg/kg wet (soy-based).

The more recent MAFF study estimated the intakes of individual phthalates and total phthalates by infants from infant formulae (MAFF, 1998). A total of 39 individual samples of 14 different infant formulae products (powdered and ready-to-feed) were analysed. But as in 1996, DEHP was the most abundant individual phthalate and the level ranged from 0.05-0.44 mg/kg wet. DIDP was not detected in any sample. Detection limit for DIDP was 0.1 mg/kg dry powder (MAFF, 1998).

For calculation of DIDP intake by food in the present, the highest intake would be 0.1 mg/kg dry powder considering the DIDP detection limit.

The exposure to DIDP through infant formulae at different ages is shown in **Table 4.13**. The daily intake of the infant formulae is based on the recommendations given in the package of the product and information on the declared weight of the formulae per scoop. MAFF (2000) provided manufacturers feeding guides on the packaging of the infant formulae products. The one used to estimate dietary exposure was chosen based on the proper schedule of ages, with declared weight of scoop of 4.4 g powder. A comparable approach than in the DEHP risk assessment report was adopted.

Table 4.13 Infant and newborn exposure to DIDP in infant formulae depending on ages

Age	DIDP conc. (mg/kg dry weight powder) *	Bw (kg)	Daily intake of formulae (g)	Total volume of water used to make up the formulae (ml)	Exposure to DIDP (mg/kg/d)
0-1 week	0.1	3	79	510	0.0026
1-4 weeks	0.1	3.5	88	575	0.0025
1-2 months	0.1	4.5	110	700	0.0024
3 months	0.1	5.5	132	850	0.0024
4 months	0.1	6.5	154	1,000	0.0024
5-6 months	0.1	7.5	176	1,125	0.0023
> 6 months	0.1	8	141	900	0.0018
0-6 months **	0.1	5.5	131	894	0.0024

* 0.1mg/kg dry weight powder: detection limit, used as recommended
** mean for 0-6 months.

For newborns (0-6 months) and for infants (>6 months), the exposure to DIDP derived from infant formulae consumption corresponds respectively to 0.0024 mg/kg/d and 0.0018 mg/kg/d, both will be used for the risk assessment.

Newborn babies

Assuming that a newborn baby takes 0.131 kg (dry weight) of infant formulae per day (MAFF, 1998), the average body weight is 5.5 kg (mean body weight for 0-6 months) and the highest DIDP intake is 0.1 mg/kg dry powder, the daily intake of DIDP by food would be 2.4 µg/kg bw/day. A bioavailability of 100% is considered for oral exposure in newborns so the internal exposure will be 2.4 µg/kg bw/d.

Infants

Assuming that an infant takes 0.141 kg dry powder of infant formulae per day (MAFF, 1998), with an average body weight is 8 kg (OMS, 1994) and the highest DIDP intake by infant formulae is 0.1 mg/kg dry powder, the daily intake of DIDP by infant formulae would be 1.8 µg/kg bw/day.

Infants are in a phase of diversification of their diet. In complement of infant formulae, an infant eats the same type of food as an adult but in a smaller quantity. The high level dietary intake of DIDP was estimated to be 0.2 µg/kg bw/day for adult. This value is equivalent to

12 µg/adult/day. Assuming that an infant eats three times less than an adult does, he eats 4 µg/day, corresponding to 0.5 µg/kg bw/day for an 8 kg infant.

The total DIDP intake (infant formulae and food) for infant would be 2.3 µg/kg bw/day. A bioavailability of 100% is considered for oral exposure in infants so the internal exposure will be 2.3 µg/kg bw/d.

Conclusion for food and food related-uses

For the risk assessment, the values to be used were based on the detection limit for DIDP:

Adults and children	3-15 years old	0.1 µg/kg bw/day
Newborns	(0-6 months old)	2.4 µg/kg bw/day
Infants	(6 months to 3 years old)	2.3 µg/kg bw/day

Food habits of consumers can vary greatly from a country to another and from a social category of consumers to another, leading to the consumption of few or many food packaged in plastic materials with various methods of cooking. So, it could also be of interest to perform further measurements of DIDP in various foodstuffs, including infant formulas, and to relate the results with food habits in Europe to assess the real exposure to DIDP via food.

As DIDP has been widely used as a substitute for DEHP, it may be hypothesised that the same scenario is likely to occur in food packaging. Therefore an hypothetical scenario for replacement of DEHP by DIDP in food contact materials has been included in appendix A for the three categories of consumers.

Other data on the contamination of food by phthalates are mentioned in the "humans exposed via the environment" part.

4.1.1.3.4 Scenario 3: Building materials and furniture

Use of plasticisers in the production of vinyl wall and floor coverings, wire and cable can lead levels of plasticiser vapour being present in room air under normal indoor conditions. The mechanism controlling DIDP emission depends on the shape and surface area of the vinyl product, its DIDP content, the air flow across the product, product usage, etc.

Limited measured data are available to assess phthalates and particularly DIDP concentrations in indoor air:

In a 1996 study, air concentrations of DINP (which is more volatile than DIDP) in a laboratory with DINP coatings were determined to be 0.66 µg/m^3 (Menzel, 1996).

In a more recent survey, few indoor air samples (n = 23) from Belgium were collected and analysed for selected phthalates (Research Institute for Chromatography, 2000). The indoor locations investigated included a sports hall (n = 5), a kindergarten classroom (n = 4), a residential home containing PVC flooring (n = 2), a retail carpet and flooring store (n = 1), a laboratory (n = 5), a greenhouse (n = 1) and an underground park (n = 5). The DIDP concentrations vary from 5 to <20 ng/m^3. The validation of the sampling method and analysis was described in Tienpont et al. (2000). Only a summary of the study was provided, more information about temperature conditions in the rooms and features of these rooms (amount of PVC end products) are necessary to assess the relevance of the results.

A study conducted to determine the amount of DEHP bound to particles in residential air in Norway has been reported (Oie, 1997). The vapour phase exposure was not measured but reference to calculated exposure was made. Based upon vapour phase exposure and their measurements, the authors tentatively suggest that exposure via the particulate phase is 1-3 fold greater than exposure from the vapour phase.

This is supported by the findings that DEHP:

- can migrate from and into different matrices,
- that substances with a low vapour pressure are readily absorbed to particles,
- total air concentrations of DEHP has been shown to exceed the saturated vapour pressure by 100-fold **(**Wams, 1987**)**.

Because there are no data characterising particle-bound DEHP in indoor air, it has been considered reasonable to assume that the amount of DEHP associated with particles is three times more than the amount of DEHP present as vapour in the air.

Given the limited measured data to evaluate residential exposure to DIDP a worst-case exposure can be calculated using DIDP saturated vapour pressure at 20°C: 5 µg/m³ (cf. Section 4.1.1.2). As suggested for DEHP, the amount of DIDP associated with particles may be estimated three times more than the amount of DIDP present as vapour in the air (i.e. 20 µg/m^3). Therefore, it may be assumed that the human indoor exposure represents the vapour exposure in air and three times this value bound to dust particles.

For adults, based upon a daily inhalation volume of 20 m³ (IPCS, 1993), a mean body weight for males and females of 60 kg (IPCS, 1993), the assumption that 20 of 24 hours are spent indoors (IPCS, 1993), and considering 75% of the inhaled dose is absorbed by adults, the internal exposure would be:

$$\frac{5 \cdot 4 \cdot 20 \cdot 20 \cdot 0.75}{60 \cdot 24} = 4.2 \text{ µg/kg bw/day.}$$

For young children, based upon a daily inhalation volume is 9.3 m³ (IPCS, 1993) a mean body weight of 8 kg, the assumption that 22 of 24 h are spent indoors (IPCS, 1993), and considering 100% of the inhaled dose is absorbed by infants, the internal exposure would be:

$$\frac{5 \cdot 4 \cdot 9.3 \cdot 22}{8 \cdot 24} = 21.3 \text{ µg/kg bw/day.}$$

4.1.1.3.5 Scenario 4: Car and public transport interiors

DIDP can be released during fogging (when sheets of PVC as dashboard, doors trim, seats are heated by the sun).

Use of plasticisers, and particularly DIDP, in the material use in interior cars (dashboard, coverings…) can lead levels of plasticiser vapour being present in car air under normal indoor conditions.

Limited measured data are available from a recent survey (Research Institute for Chromatography, 2000). Few inside car samples (n = 3) were collected and analysed for selected phthalates. The concentration of DIDP did not exceed 20 ng/m^3. There is no other measured data about DIDP concentration in the air of public transport or cars.

Given the limited measured data, a worst-case exposure can be calculated using DIDP saturated vapour pressure at 20°C: 5 µg/m³ (cf. Section 4.1.1.2) multiplied by 4 to include particulate bound DIDP (i.e. 20 µg/m³) (cf. Section 4.1.1.3.4).

For adults, based upon a daily inhalation volume for adults of 20 m³ (IPCS, 1993), a mean body weight for males and females of 60 kg (IPCS, 1993), the assumption that 4 hours per day are spent in car and considering 75% of the inhaled dose is absorbed by adults, the internal exposure would be:

$$\frac{5 \cdot 4 \cdot 20 \cdot 4 \cdot 0.75}{60 \cdot 24} = 0.8 \text{ µg/kg bw/day.}$$

For young children, based upon a daily inhalation volume is 9.3 m³ (IPCS, 1993) a mean body weight of 8 kg, the assumption that 2 hours per day are spent in car (IPCS, 1993), and considering 100% of the inhaled dose is absorbed by infants, the internal exposure would be:

$$\frac{5 \cdot 4 \cdot 9.3 \cdot 2}{8 \cdot 24} = 1.9 \text{ µg/kg bw/day}$$

4.1.1.3.6 Scenario 5: Clothing, gloves and footwear

DIDP is used in a variety of products which are in contact with human skin. These products include articles made of fabric coated by flexible PVC containing DIDP (clothing as rain wear, plastic gloves and footwear as high boots). The quantity of human exposure to DIDP is a function of the area of skin in contact with the product, the duration of the contact, the surface availability of DIDP from the product and the percutaneous absorption of DIDP through the skin.

Human exposure to DIDP from gloves is calculated as the maximum dermal uptake of DIDP on the skin area of gloves on both hands. Based on the assumption that dermal absorption rate for DIDP is expected to be 0.024 µg /cm²/h, the skin contact area of the two hands is 840 cm², the duration of contact is 2 hours/day and the body weight of adult 60 kg, the resulting daily exposure to DIDP is:

$$\frac{0.024 \cdot 840 \cdot 2}{60} = 0.7 \text{ µg /kg bw/day}$$

A maximum internal dermal exposure of DIDP via clothing, gloves and footwear of 0.7 µg/kg bw/day is retained for the risk assessment for adults.

4.1.1.3.7 Conclusion of consumer exposure

Combined exposure for adult, infant and newborn consumers by multiple sources is possible. For adults it seems realistic to keep only the combined exposure to all identified sources for risk characterisation purposes. For infants and newborns, two possibilities have been assumed, one without toys (present situation) and the other one with toys (foreseeable use), allowing to assess the part the toys would play in child exposure.

It should be noted that the duration of exposure assumed for the scenario “building materials and furniture” and “car and public transport interior” are very conservative: they imply that an adult or a child is either in a building or in a car, never outdoor.

Table 4.14 Conclusion of consumer exposure

Sources	External and internal exposure					
	Adults		Newborns 0 – 6 months old		Infants 6 months - 3 years old	
	External exposure	Internal exposure (µg/kg/d)	External exposure	Internal exposure (µg/kg/d)	External exposure	Internal exposure (µg/kg/d)
Building materials and furniture	20 µg/m³ *	4.2 a)	20 µg/m³ *	21.3 c)	20 µg/m³ *	21.3 c)
Car and public transport interiors	20 µg/m³ *	0.8 a)	20 µg/m³ *	1.9 c)	20 µg/m³ *	1.9 c)
Clothing, gloves and footwear		0.7	Not estimated			
Food and food-related uses	0.2 µg/kg/d	0.1 b)	2.4 µg/kg/d	2.4	2.3 µg/kg /d	2.3
Total without toys		5.8		25.6		25.5
Toys and teething rings: oral exposure dermal exposure			200	200 c) 1	200	200 c) 1
Total with toys				226.6		226.5

a) A bioavailability of 75% is considered for the inhalation route in adults
b) A bioavailability of 50% is considered for the oral route in adults
c) A bioavailability of 100% is considered for infants 6 months to 3 years old and for newborns 0 to 6 months old for oral and respiratory routes
* Concentration in air

4.1.1.4 Humans exposed via the environment

Exposure for adults (corresponding to adults and children 3-15 years old)

The estimation of the indirect exposure of humans via the environment is presented in the EUSES calculations. It should be noted that in most of the PEC calculations, the porewater concentration is higher than the water solubility of the substance (cf. **Table 3.24**). This throws some doubt over the estimation methods used. The soil porewater concentration is used for the estimation of the exposure of humans via the environment, particularly from root crops. For assessment purposes, the soil porewater concentration is set to be equal to the water solubility of the substance.

The total daily intake based on the local environmental concentrations due to the different uses is presented in **Table 4.15**.

Table 4.15 Total daily intake for adults due to local environmental exposures

Life cycle step	DOSEtot (mg/kg bw/d)
Production	0.010
Use in PVC	0.027
Use in non-PVC polymers	0.017
Formulation of anti-corrosion paints	0.014
Application of anti-corrosion paints	negligible
Formulation of anti-fouling paints	negligible
Application of anti-fouling paints	0.012
Formulation of sealing compounds	0.014
Formulation of textile inks	0.014
Application of textile inks	0.003

Based on the regional concentrations, the total daily intake for humans is 0.002 mg/kg bw/d.

The highest intake is expected through root crops, followed by fish (see Appendix C).

The estimated maximum total daily intakes, as presented in **Table 4.15** will be used in assessing the exposure to adults via the environment.

As shown in Section 4.1.1.3.3, results from monitoring studies in carcass meat, meat products, offal, poultry, eggs, fish, fats and oils, milk and milk products can be used to estimate a maximum exposure of 0.0002 mg/kg bw/d, based on the detection limit for DIDP. This is very much lower than the estimated daily doses based on local exposure but very close to the estimated regional exposure. On the other hand, no monitoring data are available for root crops, which according to the exposure models is one of the main sources of DIDP to humans exposed via the environment. The estimated maximum total daily intakes as shown in **Table 4.15** will therefore also be used in the risk characterisation.

Infants exposure (0.5-3 years old)

As for DEHP an increased sensitivity was observed for young animals, as well as an increased bioavailability, it appears necessary to estimate the exposure to children via the environment.

Children are exposed by multiple pathways. For example, as consumers children are exposed to different sources (indoor air, and car interiors) by different routes and extents of exposure. To determine the combined exposure it is, therefore, necessary to separately determine the extent of exposure via the environment.

The assessment of the exposure to newborns (0-6 months) is probably not relevant, as their diet consists mainly of milk. The contribution through milk in the overall exposure is very low compared to other routes, as shown above for adults. The assessment for children will therefore focus on 0.5-3 year old children who have a more varied diet.

In **Table 4.16** the proposed infant characterisation (0.5-3 years old), with regard to food intake for the estimation of the exposure via the environment is presented (EC, 2001). These values are clearly worst-case values for each food type. The overall food basket is clearly not realistic. But as seen for adults, the exposure is mainly due to one or two exposure routes and therefore a

preliminary exposure assessment can be performed with the food basket below. The risk characterisation will have to be discussed though in the light of the overestimation of the daily food basket.

Table 4.16 Infant characteristics for input in EUSES calculation

	Adult		% of adult	Child	
Daily intake of drinking water	2	l/d	50%	1.0	l/d
Daily intake of fish	0.115	kg/d	73%	0.084	kg/d
Daily intake of leaf crops	1.2	kg/d	50%	0.60	kg/d
Daily intake of root crops	0.384	kg/d	50%	0.192	kg/d
Daily intake of meat	0.301	kg/d	76%	0.229	kg/d
Daily intake of dairy products	1.333	kg/d	126%	1.68	kg/d
Inhalation rate	20	m^3/d	46.5% 1)	9.3	m^3/d
Body weight	70	kg	11.4%	8.0	kg

1) Respiratory volume: 0.5- <3 years human=168 L/h; Times light activity factor for male=2.3; 2.3 · 1.68 · 24=9.3 m^3/d

Based on the food basket proposed above, the exposure to infants for the different exposure scenarios is summarised in **Table 4.17**.

Table 4.17 Total daily intake for infants due to local environmental exposures

Life cycle step	DOSEtot (mg/kg bw/d)
Production	0.063
Use in PVC	0.166
Use in non-PVC polymers	0.102
Formulation of anti-corrosion paints	0.076
Application of anti-corrosion paints	negligible
Formulation of anti-fouling paints	negligible
Application of anti-fouling paints	0.066
Formulation of sealing compounds	0.076
Formulation of textile inks	0.077
Application of textile inks	0.013

Based on the regional concentrations, the total daily intake for infants is 0.013 mg/kg bw/d.

The exposure is almost exclusively due to intake of fish and root crops. The other routes are almost negligible.

As shown in Section 4.1.1.3.3, results from monitoring studies in carcass meat, meat products, offal, poultry, eggs, fish, fats and oils, milk and milk products can be used to estimate a maximum exposure of 0.0002 mg/kg bw/d, based on the detection limit for DIDP. This is very much lower than the estimated daily doses based on local exposure but very close to the estimated regional exposure. On the other hand, no monitoring data are available for root crops,

which according to the exposure models is one of the main sources of DIDP to humans exposed via the environment. The estimated maximum total daily intakes as shown in **Tables 4.15** and **4.17** will therefore also be used in the risk characterisation.

4.1.1.5 Combined exposure

Combined exposure of different populations may occur. The worse cases combined exposure would be:

- an adult exposed from occupational and consumer sources and indirectly via environment,
- a child (3-15 years old) exposed from consumer sources and indirectly via environment,
- an infant (0.5 to 3 years old) exposed from consumer sources (with and without toys) and indirectly via environment.

The newborn (0-6 months) combined exposure is not assessed, because this population is only considered in the consumer part.

The total exposure is the sum of all specific exposure from all sources by all routes.

Table 4.18 Combined exposure

Sources of exposure	Internal exposure (mg/kg bw/d)			
	Adults	Children	Infants	
			Without toys	With toys
Occupational sources	1.10			
Consumer sources	0.01	0.01	0.03	0.23
Via the environment	0.01 a)	0.01 a)	0.17 b)	0.17 b)
Total with occupational exposure **Total without occupational exposure**	**1.12** **0.02**	**0.02**	**0.20**	**0.40**

a) maximum daily intake of 0.027 derived from the use of DIDP in PVC, taking into account 50% bioavailability for adults
b) maximum daily intake of 0.17 derived from the use of DIDP in PVC, taking into account 100% bioavailability for infants

The total combined exposure may be higher because all sources of human exposure have not been quantified. For adults, it should be noted that the exposure durations used for exposure estimation are not always consistent (8 hours for occupational exposure, 20 hours for building and furniture, 2 hours for gloves…) but it is not recognised as a concern because adult combined exposure results mainly from occupational exposure.

4.1.2 Effects assessment: Hazard identification and Dose (concentration) - response (effect) assessment

GLP statements were checked for all studies. When available, the information has been provided. Otherwise, no comment is made.

4.1.2.1 Toxicokinetics, metabolism and distribution

4.1.2.1.1 Oral exposure

In a study (General Motors Research Laboratories, 1983) designed to evaluate the effects of increasing doses of DIDP on disposition and metabolism in Sprague Dawley rats (200 g body weight), radiolabeled DIDP (carboxyl-^{14}C) was administered in corn oil by gavage at doses of 0.1-11.2 and 1,000 mg/kg. Feces were collected over 24-hour periods. Urine was collected over 12-hour periods. Seventy-two hours after exposure, at termination of the collection periods, carcass, brain, lungs, heart, thymus, liver, spleen, kidneys, adrenals, testes, fat and the entire gastrointestinal tract were stored at -10°C to determine the amount of radioactivity.

The radioactivity was determined by liquid scintillation spectrometry. To assess pre-systemic elimination, biliary cannulation was conducted on anaesthetised animals to determine the percentage of administered radioactivity recoverable in the bile. DIDP and its metabolites in tissues, bile and excreta were separated using high-pressure liquid chromatography. Metabolites of DIDP were identified by co-elution with standards.

Absorption

The percentage of the total administered dose (represented by the sum of radioactivity in urine, faeces, carcass, tissues and cage wash) excreted in urine during the 72-hour collection interval was decreased with increasing dose by 41.3% - 32.1% - 12.6% after low, middle, high doses, respectively. The percentage of total administered dose recovered in bile within 72 hours decreased with increasing dose from 0.1 to 1,000 mg/kg (14.3% - 13.8% and 4.7%, respectively). Total absorbed dose may be roughly estimated as the sum of urinary and biliary excretion, leading to 55.6% after 0.1 mg/kg bw, 45.9% after 11.2 mg/kg and 17.3% after 1,000 mg/kg.

Distribution

This study indicated a limited distribution throughout the body. Only 0.5-0.8 and 0.2% of the administered radioactivity was detected in the carcass of low, middle and high-dose animals, respectively. Radioactivity was detected only in liver, kidneys and gastrointestinal tract of animals 72 hours after treatment: 0.49%, 0.77%, 0.17% of the administered radioactivity in gastrointestinal tract, 0.06%, 0.08%, 0.03% in liver and 0.01%, 0.01%, 0.00% in kidneys at 0.1, 11.2 and 1,000 mg/kg, respectively. The content of tissues in µmole equivalents of DIDP increased with increasing dose.

Metabolism

In urine, phthalic acid and the oxidised monoester derivative were detected but not monoisodecyl phthalate (MIDP) or DIDP at any of the doses. The percentage of radioactivity associated with the monoester derivative group increased with increasing dose from 52% after 0.1 mg/kg to 72%

after 1,000 mg/kg. Concurrently, the proportion of radioactivity associated with phthalic acid was observed to decrease from 38 to 18% after 0.1 and 1,000 mg/kg doses, respectively.

In faeces, the monoester oxidative derivative, MIDP and DIDP were detected. Because of potential bacterial degradation of DIDP or its metabolites in faeces, quantification of the data is difficult. It was readily apparent, however, that with increasing dose the percentage of parent compound recovered in faeces increased: 30%, 55% and 60% after 0.1, 11 and 1,000 mg/kg, respectively. The percentage of oxidative derivatives of the monoester and of MIDP were respectively 25 and 30%, 14 and 26%, 13 and 13% after 0.1, 11 and 1,000 mg/kg, respectively.

When bile samples were taken from 0-24 hours following dosing or when liver and kidneys samples were taken 72 hours following dosing, DIDP was not detected in extracts.

The data based on end products suggest a metabolic scheme comparable to the one reported for DEHP: de-esterification to monoester form and an alcohol moiety by apparent non-specific pancreatic lipase and intestinal mucosa esterases prior to absorption; the high content of MIDP in feces is consistent with this proposed mechanism. Further metabolism of the monoester by ω or ω-1 oxidation probably occurred in the liver.

With increasing dose, the percentage of faecal radioactivity associated with the parent compound was increased by a factor of two comparing 0.1 to 1,000 mg/kg doses. Therefore it is probable that esterases capacity has been partially saturated. The parent compound is recoverable from feces even at the lowest dose, which is not the case for DEHP, for which an absorption threshold of 200 mg/kg in a single intake was reported. Below this values, the parent DEHP was not detected. In contrast, even at extremely low doses, DIDP may be less susceptible to the hydrolysis step prerequisite to absorption.

Phthalic acid and apparent oxidative products of MIDP were identified in urine. In bile, it is indicated that only monoester metabolites were detected accounting in part for the content in feces. With increasing dose the metabolite composition in bile was not altered, suggesting that metabolic capacity by that route was not compensated. In urine the percentage of radioactivity associated with phthalic acid decreased with dose while an increase was observed in the oxidative derivatives of the monoester. The percentage of phthalic acid ranged from 38% at 0.1 mg/kg to 18% at 1,000 mg/kg, far exceeding the value of 3% phthalic acid associated with DEHP exposures. The markedly higher production of phthalic acid suggests that DIDP derivatives may be more susceptible to de-esterification within the body perhaps due to destabilisation of the ester bond resulting from the highly branched nature of the ester groups. However, the decrease in phthalic acid content with increasing DIDP dose may suggest partial saturation of metabolite capacity.

Elimination

The primary route of excretion of radioactivity was in feces accounting for 57.5-65.6 and 81.7% of the total body burden after 0.1-11.2 and 1,000 mg/kg, respectively. Biliary excretion accounted in part for the content in feces. Excretion in urine was biphasic and there was no apparent dose-effect relationship on the rates of elimination. The percentage of total administered dose excreted in urine during the 72-hour collection interval decreased with increasing dose from 41.3%-32.1%-12.6% after low, middle, high doses, respectively.

Elimination in urine and feces together represented greater than 99% of the administered dose, whatever the dose.

Transfer through the milk

In a two-generation study (Exxon Biomedical Sciences, 1997d), pups from control group litters were cross-fostered with the high-dose dams. The body weights of pups cross-fostered with high-dose dams were decreased compared with the main study control pups. A decrease of body weight was observed from the PND 1 in both sexes, but the difference between weight of the cross-fostered high-dose pups and the main study control pups reaches a statistical level only at PND 14 and 21. This may indicate that DIDP was transferred through the milk but at a low level, that only led to a low decrease of body weight and that a statistical level of significance was obtained when lactation exposure effects and direct toxicity via feed (solid food is absorbed by pups from PND 14) were combined. In addition, statistically significant increases of some organ weights were observed when pups cross-fostered high-dose dams were compared to pups cross-fostered with control dams. Although pups are also exposed to solid food from day 14, DIDP transfer through the milk cannot be excluded.

4.1.2.1.2 Inhalation exposure

The fate of DIDP was evaluated in 6 male Sprague Dawley rats (mean body weight 200 g) receiving head only exposure to ^{14}C-DIDP aerosol atmosphere nominal concentration: 100 mg/m^3 for 6 hours (General Motors Research Laboratories, 1981). The mass median aerodynamic diameter of DIDP aerosol was 0.98 µm. Three animals were sacrificed immediately following exposure, the remaining animals at the end of the 72-hour collection period. Feces were collected at 24-hour intervals and urine was collected at 12-hour intervals for 72 hours. The radioactivity was determined by liquid scintillation spectrometry.

Absorption

Total body burden following the exposure was 6.75 µmole equivalents or approximately 3 mg. Radioactivity derived from ^{14}C -DIDP was excreted in urine and feces during the 72-hour post-exposure collection period: 45.3% and 41%, respectively, of the total body burden. At the end of the collection period following exposure, 9.4% of the absorbed dose of radioactivity was recovered from carcass and tissues, 2.4% from skin and 1.6% from cage wash.

Distribution

The distribution of radioactivity in rat tissues immediately following the 6-hour inhalation exposure and after 72 hours is shown in **Table 4.19**. Immediately after exposure, the highest concentration of radioactivity was in lung followed by GIT, liver and kidney. The remaining tissues contained far lesser amounts. Radioactivity was below detection limit in brain, spleen and testes.

Elimination

After 72 hours the concentration was decreased in all tissues. The highest level of radioactivity was still found in lung which contained 27% of the content of radioactivity present immediately following exposure. The pulmonary load decreased to a lesser extent than all the tissues except fat which did not appear to change. Radioactivity derived from ^{14}C -DIDP was excreted in urine and feces during the 72-hour post-exposure collection period: 45.3% and 41%, respectively, of the total body burden.

The excretion of radioactivity in urine during the 72-hour collection period following inhalation exposure was best described using first order kinetics. Based on 12-hour interval excretion data,

the half-life (T½) of elimination was 16 hours with an elimination rate constant Ke of 0.042/hour.

Radioactivity derived from ^{14}C -DIDP was excreted in urine (45.3%) and feces (41.3%) during the 72-hour post-exposure collection period. An additional 1.6% was recovered in washings of the metabolic cage collection surfaces and was derived from urine and faecal contamination. From these data 88% of the total absorbed dose of the radioactivity was excreted from the body and the carcass retention data imply that a small fraction of DIDP or metabolites was retained in the body for a longer period of time. Using total recovered radioactivity to represent body content or body burden of ^{14}C immediately following exposure, and given urinary and faecal interval excretion data, an estimate of the disappearance of radioactivity from the whole body with time can be obtained. The decline in body burden was linear and apparent first order with T½ of 26 hours and an elimination rate constant Ke of 0.027/h. Apparently, the elimination half-time included the lung absorption time.

Table 4.19 Distribution of radioactivity in rat tissue following inhalation exposure to [carboxy-^{14}C]-DIDP

Tissue	µMole Equivalents [1]	
	O hr	72 hr
Lung	0.6630 ± 0.2556	0.1822 ±0.0619
GIT	0.0948 ± 0.0080	0.0078 ± 0.0006
Liver	0.0148 ± 0.0012	0.0013 ± 0.0004
Kidney	0.0064 ± 0.0006	0.0006 ± 0.0000
Brain	0.0012 ± 0.0006	ND [2]
Thymus	0.0010 ± 0.0003	0.0004 ± 0.0002
Heart	0.0009 ± 0.0001	Trace [3]
Spleen	0.0007 ± 0.0000	ND
Fat	0.0003 ± 0.0000(4)	0.0004 ± 0.0001 [4]
Testes	0.0004 ± 0.0000	ND

1) Each value represents the mean (±SE) of data from 3 rats
2) Tissue concentration less than detection limits
3) Radioactivity detected in tissue from only 1 of 3 animals
4) µMole Equivalents/g

4.1.2.1.3 Dermal exposure

An overview of data available about phthalate skin penetration, *in vivo* or *in vitro*, in animals or in humans, has been deemed useful to draw the general tendency for the different phthalates in spite of different study protocols.

In vivo

Results specific to [^{14}C]-DIDP (NIEHS, 1988; Elsisi et al., 1989) involved dermal absorption of phthalate diesters (DMP to DIDP) in F 344 rats, *in vivo*. The dose applied to the skin was around 5-8 mg/cm^2. The ring-labeled phthalates were applied dissolved in absolute ethanol, with *in situ* evaporation. The dosed back skin was covered by a circular plastic cap perforated with needle

holes. Total excretion was measured at different times. Results are summarised in **Table 4.20**. This study shows that DIDP is markedly less absorbed (ca. 10 times, when comparing faecal + urinary excretions at day 7) by this route than DEHP.

For DEHP, recovery at 7 days was 86% at the site of application, for a total recovery of 105%. After 5 days, cumulative excretion data indicate that 5% of the dose was recovered.

For DIDP, recovery was 75% at the site of application, for a total recovery of 82% after 7 days. Cumulative excretion data after 7 days indicate that 0.5% of the dose was recovered in feces. No radioactivity was recovered in urine. It is noticeable that only faecal elimination was found. The author implies a preference for biliary excretion when the length of the side chain increases but this is not consistent with the scheme of elimination observed with DINP and the two other routes where radioactivity was shared between urine and feces. High differences in total recovery hinder a quantitative comparison of data. Muscle, adipose tissue and skin contained most of the dose remaining in the body. The total absorbed dose after 7 days can be estimated to be 1%, however this value is possibly underestimated because of the low recovery.

The skin application site was apparently not washed before evaluating DIDP residue. In all cases, dermal uptake decreased when the side chain length increased beyond four carbons. Skin absorption appeared to decrease with branched alkyl side chains.

Table 4.20 Percentage of dose ([^{14}C] equivalents) found in the tissues and the plastic cap that covered the area of application at 7 days following a single application of various phthalate esters to the back skin of male F-344 rats

	Percentage dose (X ± SD)				
Tissue	**DMP**	**DEP**	**DBP**	**DEHP**	**DIDP**
Adipose tissue	0.3 ± 0.3	0.03 ± 0.03	0.41 ± 0.07	0.06 ± 0.02	0.14 ± 0.03
Muscle	0.6 ± 0.7	0.14 ± 0.07	1.1 ± 0.2	1.17 ± 0.22	0.33 ± 0.05
Skin [1)]	0.4 ± 0.4	0.06 ±0.02	1.4 ± 1.0	0.3 ± 0.3	0.10 ± 0.04
Skin of appl. [2)]	19 ± 23	34 ± 24	33 ± 2	86 ± 17	75 ± 1
Other tissues	< 0.5	< 0.5	< 0.5	< 0.5	< 0.5
Plastic cap	5 ± 0.3	4.8 ± 3.2	2.2 ± 2	12 ± 3	5.5 ± 2.7
Total recovery	**66 ± 26**	**74 ± 21**	**100 ± 3**	**105 ± 16**	**82 ± 12**

Total recovery represents the sum of the percentage dose found in urine, feces, tissues and plastic cap in 7 days.
1) Control skin sample removed from a front leg.
2) The skin area of application was digested and analysed, without mention of prior blotting the residual phthalate off the skin surface.

Results specific to [^{14}C]-DINP were obtained *in vivo*, on male F-344 rat back skin (Midwest Research Institute, 1983). They are of interest because, qualitatively, the results are very similar to that obtained for DIDP by Elsisi et al. (1989), but with recoveries compatible with the requirements of the OECD (1996) draft guideline (100% ± 10%). This study was in compliance with GLP. DINP, supplied by Exxon Corporation, was applied as a neat material (0.1 or 0.2 ml per rat) on a 3·4 cm area (i.e. 8.1 or 16.3 mg/cm^2), then the dosed area was occluded.

The [^{14}C] labeled compound was applied on the shaved backs of 3 groups of rats. The first group (non conditioned, 6 rats) received a single dermal application of [^{14}C] DINP (0.2 ml/rat; ~ 1.2 ml/kg) which remained on the skin for the duration of the study (1, 3 or 7 depending on the time for sacrifice of rats). The second group (6 rats) was "conditioned" by pre-treatment with a dermal dose of non-labeled DINP (0.2 ml/rat; ~ 1.2 ml/kg), kept on the skin for 3 days then blotted off prior to single dermal application of the [^{14}C] DINP (0.2 ml/rat; ~ 1.2 ml/kg). The

third group (non-conditioned, 3 rats) received a single lower dermal application of [^{14}C] DINP (0.1 ml/rat; ~ 0.6 ml/kg).

Urine and feces were collected between 0-1, 1-2, 2-3, and 3-7 days following single-application treatment. Two rats from each group receiving the 0.2 ml dose and one rat from the group receiving the 0.1 ml dose were sacrificed at 1, 3 and 7 days following single-application treatment. Levels of radioactivity were determined in excreta, gastrointestinal tracts, blood, skin from non-treated areas (i.e., ears), areas of skin application (and covers) and selected tissues (liver, kidneys, testes, fat and muscle).

Absorption was slow as indicated by the recovery of only ca. 0.3% of applied dose in urine, feces, GI tract, and tissue at 24 hours following treatment. Dermal absorption of DINP (CAS 68515-48-0) in adult male Fischer 344 rats is slow, and low. Under all treatment conditions, most of the applied radioactivity was recovered from the application areas (92-103%) and the total amounts absorbed during the 7-day period ranged from 2 to 4% of the applied doses. The demonstrated radioactivity in feces and GI tract suggests excretion of the absorbed radioactivity by the biliary route. Results are summarised in **Table 4.21**.

Table 4.21 Radioactivity recovery in tissues and excreta of male Fisher 344 rats at 1, 3 or 7 days following dermal application of 0.1 ml per rat of [^{14}C]-DINP

	Percent of applied dose		
	1 day	**3 days**	**7 days**
Fat	0.017	0.024	0.015
Muscle	0.043	0.033	0.089
Skin [1)]	0.124	0.263	0.775
Appl. Area [2)]	95.941	92.744	93.499
Other tissues	0.059	0.056	0.148
Urine + Feces	0.105	0.659	0.028
Total recovery	96.329	93.779	96.554

From MRI (1983, table 3)
1) Control skin sample from untreated areas (ears)
2) Application area, which includes skin and cover, represents non-absorbed radioactivity

^{14}C-carbonyl DEHP plasticised PVC (3 · 5 cm corresponding to about 400 mg DEHP) was held in close contact (24-hour exposure) with the clipped dorsal skin of male Fisher 344 rats (Deisinger et al., 1998). Two studies were realised in order to assess the long-term absorption, short-term absorption and effect of washing skin after exposure. The first study consisted in a 24-hour exposure followed by 6 days of sample collection. The second study consisted in a 24-hour exposure followed by immediate sacrifice of the rats. In this study, dermal exposure area was washed and rinsed 3 times with 40% aqueous solutions of pHistoderm.

For Study 1, total migrated DEHP was 0.06%. Total DEHP absorbed was 0.01% corresponding to urinary elimination (0.003%), faecal elimination (0.002%), cage wash (0.004% assumed to be urinary elimination) and carcass (0.002%). The systemic fraction absorbed from the total DEHP migrated represented 16%. The mean dermal absorption rate was calculated: 0.24 μg/cm^2/h.

For Study 2, total migrated DEHP was 0.13%. Total DEHP absorbed was 0.005% corresponding to urinary elimination (0.0004%), faecal elimination (0.0002%), cage wash (traces) and carcass

(0.004%). The systemic fraction absorbed from the total DEHP migrated represented 3%. The mean dermal absorption rate was calculated: 0.24 μg/cm^2/h.

In vitro

Scott et al. (1987) measured the *in vitro* absorption of some *o*-phthalate diesters (DMP to DEHP) through human abdominal and dorsal rat (Wistar-derived species) skin. In this *in vitro* technique, absorption is directly through the epidermis. The esters were applied directly (0.5 ml; 50 μl for [^{14}C] DEHP) to the epidermal membranes (the epidermis was peeled away from the dermis) as neat liquids, in diffusion cells (of unspecified contact surface) whose donor surface was open to atmosphere. The receptor fluid was 50% aqueous ethanol, and contact time was 30 hours (72 for DEHP). Skin temperature was 30°C. In these conditions, they measured the steady state absorption rate of DEHP (the heaviest phthalate they tested) in human skin (epidermal membranes) as 5.59 ± 1.18 μg/cm^2/h. This study may not be selected as a basis to evaluate the quantity of DINP that could be absorbed through the skin, because the receptor fluid was 50% v/v aqueous ethanol, which strongly increases the penetration rate, as was shown by Pelling et al. (1998).

Other *in vitro* results obtained in well-defined conditions have been presented in more recent papers by Mint and co-workers (Mint and Hotchkiss, 1993; Mint et al., 1994). Neat phthalates were applied in a diffusion cell (contact surface 0.32 cm^2) at doses around 20 mg/cm^2, using either full thickness human breast skin or full thickness male F 344 rat dorsal skin, obtained by surgical separation. The receptor fluid was Hepes (11.9 g) + Hank's balanced salt solution (19.6 g) with additives in order to maintain skin viability; sodium carbonate was also added to obtain a pH of 7.4. Temperature was 32°C, contact time 72 hours, and there was no significant difference between occluded or unoccluded conditions, for human as well as for rat skin. Seven diffusion cells were run concurrently for one single donor, generally 4 occluded and 3 unoccluded. Results are summarised in the **Table 4.22**.

Table 4.22 Skin penetration properties of dimethyl- (DMP), diethyl- (DEP) and dibutyl- (DBP) phthalates (Mint and Hotchkiss, 1993; Mint et al., 1994)

	Recovery (% of applied dose)						S.SAR.		Lag time	
	Receptor fluid		Skin surface		Within skin		μg/cm²/h		h	
	Hmn	Rat	Hmn	Rat	Hmn	Rat	Hmn	Rat	Hmn	Rat
DMP	3.0	20.8	52.4	27.5	4.9	30.5	9.4	66.8	4	4
DEP	4.3	37.0	44.9	19.6	10.8	36.6	12.3	97.9	10	8
DBP	0.6	11.3	54.1	42.4	4.1	20.7	1.8	40.9	0	8

SSAR: steady state absorption rate; Hmn: human.
Total recoveries (i.e. including diffusion cell and teflon cap) range from 97.3% to 106.5%.

Barber et al. (1992) studied *in vitro* percutaneous absorption of eight chemicals, of which DEHP, using full thickness abdominal Sprague-Dawley or F-344 rat skin, and human *stratum corneum* isolated after treating skin samples with warm water (60°C for 45-60 s). [^{14}C]DEHP was tested undiluted (300 μl on a 0.636 or 1.02 cm^2 contact area), contact time was 32 hours and skin temperature 30°C. The receptor fluid was of a physiological type (Dulbecco phosphate-buffered isotonic saline with antibiotics and 60 g/l of a polyethoxyoleate). Measured absorption rates for DEHP were 0.42 ± 0.13 μg/cm^2/h (rat skin, n = 11) and 0.10 ± 0.02 μg/cm^2/h (human skin, n = 4). The ratio of these rates is only 4.2, which may be explained by the fact that the comparison is between full thickness rat skin and *stratum corneum* only. The high concentration

of a surface-active agent may also have modified skin penetration rates. The other studies are summarised in **Table 4.23**.

Table 4.23 Skin penetration properties of DEHP in other publications

Authors Experiment type	Main experimental conditions	(Note) and main results
Melnick et al. (1987) *In vivo* male F-344 rats clipped back skin	30 mg/kg [^{14}C] DBP in ethanol was applied on a 1.33 cm^2 area. After the ethanol evaporated, a perforated plastic cap was glued over the site of application. Urine and feces were collected every 24 hours up to 5 days. Body organs and the skin in the application site were also collected and analysed.	At day 5, the cumulated dose recovered was about 3% in the urine, 2% in the feces (93-95% from the application site). The dermal absorption of DEHP was slightly greater than that of DIDP and much less than that of DMP, DEP, DBP, DIBP, BBP or DNHP.
Ng et al. (1992) *in vitro* - Hairless guinea pig 200 µm thickness skin (dermatome), Membrane integrity assessed with tritiated water	Bronaugh diffusion cell, Receptor fluid: Hepes-buffered Hank's balanced salt solution containing 4% bovine serum albumin, 24 hours contact time, [^{14}C] DEHP applied in acetone, Skin temperature 37 C.	1) 6, 2.4 and 2.5% of the dose permeated into the receptor fluid (low, medium and high-dose groups, respectively). Calculated Ar = 0.27
in vivo: female hairless guinea pigs. Dorsal skin	[^{14}C] DEHP applied in acetone on a 4 cm^2 area (34 nmol/cm^2) + protective non-occlusive pad (24 hours contact time), 6 animals were given 53 µg DEHP, urine and feces were collected for 7 days.	7-day (corrected) cumulative excreta 53.1%, skin wash 30.8%; skin stripping 11.3%. Low recoveries (78 - 90%) may be partly attributed to volatilisation
Pelling et al. (1998) *in vitro* - Male Ola:S-D rats dorsal epidermal membrane and residual dermis (NaBr treatment), Membrane integrity assessed with tritiated water	Bronaugh diffusion cell with perforated PTFE supports for membranes. [14C] DEHP applied in acetone. Contact area 0.64 cm2, Skin temperature 31.5°C, Receptor fluids: phosphate buffered saline or 50% aqueous ethanol.	2) Kp = 1.3.10^{-5} (epidermis); 4.76.10^{-5} (dermis) Less than 1% of the dose was absorbed in 24 hours for both membranes (PBS receptor fluid), Kp = 9.46.10^{-4} (epidermis); 9.83.10^{-5} (dermis) (50% ethanol receptor fluid).

Kp Permeation constant (cm/h); Ar: absorption rate µg/cm^2/h.

1) Data for 7-day cumulative excreta have been corrected for incomplete excretion by the data obtained from the intramuscular mode. Uncorrected data are: 3% (resp. 21%) of the dermally administered dose was absorbed *in vivo* and excreted in 24 hours (resp. 7 days). Note the very limited quantity of substance applied.

2) The skin pre-treatment modified dermis appearance. The epidermis had lost his folded appearance. The appreciably lower results obtained by Scott et al. (1987) are likely due to differences in technique. The use of a non-physiological receptor fluid may alter the permeability of rat skin strata.

Discussion

The various conditions in which skin penetration properties of different phthalates have been studied make a general evaluation difficult, especially for estimating representative values of the different parameters (e.g. percutaneous absorption Kp, absorption rate Ar, phthalate residues at different sites like skin surface, within skin, diffusion cell, excreta, etc.). This is the reason why studies on homologous phthalate series in the same conditions by the same workers have been emphasised. The comparisons made allow the following general conclusions (Scott et al., 1987; Elsisi et al., 1989):

- human skin is markedly (i.e. 4 to 30 times) less permeable than rat skin; this relationship had already been demonstrated (Bartek et al., 1972) or has been confirmed since for a range of phthalates (Barber et al., 1992);
- skin penetration decreases with increasing molecular weight (at least starting from DBP);

- there is a lag time tending to increase with molecular weight, although this relationship was not absolute.

No sure value of skin penetration parameters seems attainable because no standardised procedure was applied. Very low penetration of DIDP through human intact skin is however warranted.

In vivo human data about toxicokinetics, metabolism and distribution are not available.

4.1.2.1.4 Summary of toxicokinetics, metabolism and distribution

Via GIT, absorption of DIDP decreases as dose increases (56% at the low dose of 0.1 mg/kg, 46% at the mid dose of 11.2 mg/kg and 17% at the high dose of 1,000 mg/kg) and seems to be of saturable mechanism, with increasing dose an increasing amount of unabsorbed compound is eliminated (faecal radioactivity associated with parent compound was increased by a factor two between 0.1 and 1,000 mg/kg).

Via dermal route, absorption is very low (most of the unabsorbed dose remained at the skin area at day 7). DIDP showed a very slow excretion, reflecting a slow dermal uptake process: a possible cutaneous tank may be hypothesised, leading to a progressive systemic release, as indicated by the increased amount of radioactivity eliminated in faeces from day 1 to day 7 (Elsisi et al., 1989). The maximum percentage of absorption may be estimated 4% of applied dose in 7 days by analogy with DINP (Midwest Research Institute, 1983). In humans, skin absorption is still lower than in rat as indicated by *in vitro* comparative studies, when SSARs (steady state absorption rate) were compared (Mint and Hotchkiss, 1993).

Inhaled DIDP aerosol seems readily absorbed. It can be assumed that a part of insoluble particles are cleared from the nasopharyngeal region and swallowed. In the same way, in the tracheobronchial tree the mucociliary transport system leads deposited particles upward to the oropharynx where they are swallowed and pass through the GI tract. Thus for the risk characterisation, a 100% absorption may be overestimated and a 75% bioavailability seems realistic.

In tissues, DIDP is mainly recovered in GIT, liver, kidneys, by oral or inhalation route, whereas following dermal exposure, muscle and adipose tissue contain most of the dose remaining in the body. Following inhalation, DIDP content in fat tissue is very low, but remains constant from the end of exposure to the end of the observation period (72 hours).

No parent DIDP or monoisodecyl phthalate (MIDP) but only metabolites (the oxidative monoester derivative and phthalic acid) are excreted in urine. In bile, DIDP was not detected in extracts 24 and 72 hours following dosing. The data on end products suggest a cleavage to the monoester and an alcohol moiety, indicating a metabolic scheme comparable to the one reported for DEHP. In feces the monoester oxidative derivative, MIDP as well as DIDP were detected. It is noticeable that metabolic pathway leading to phthalic acid is saturable, and that consequently monoester elimination is increased.

DIDP is rapidly eliminated and not accumulated in tissues, less than 1% of the radioactivity was recovered in tissues after 72 hours. By oral and inhalation routes, excretion is shared between urine and faeces. By dermal exposure, only faecal elimination was indicated, but considering the low rate of recovery and by analogy with the two other routes and with the DINP behaviour, the same scheme may be anticipated.

In addition, results from the two-generation study suggest a possible transfer of DIDP through the milk when dams are exposed by oral route.

4.1.2.2 Acute toxicity

4.1.2.2.1 Studies in animals

Oral exposure

In a series of acute toxicity tests in rats, no lethality was reported up to 29,100 mg/kg (BASF, 1961; Inveresk Research International, 1981; Krauskopf, 1973). No clinical signs and no macroscopic changes were observed at 15,000 mg/kg (Inveresk Research International, 1981). Diarrhoea and loss of weight were observed at 29,100 mg/kg (Krauskopf, 1973). In a series of LD50 reported by Smyth et al. (1962), the LD50 of DIDP in rats is above 62,080 mg/kg.

In rabbits, a minimum lethal dose of 21,825-29,100 mg/kg has been calculated (Krauskopf, 1973).

Dermal exposure

In a rabbit occlusive study (Industrial Bio-test Laboratories, 1975), two groups of 2 males and 2 females were exposed cutaneously for 24 hours to 200 and 3,160 mg/kg. During the observation period of 14 days, no death occurred, no systemic toxicity was noted, skin changes at 24 hours were characterised by a well-defined erythema and slight desquamation at 7 and 14 days. Necropsy examination did not reveal any gross pathologic alterations except for the local skin changes previously described. The conclusion was that the LD50 was greater than 3,160 mg/kg.

In a briefly reported study (Smyth et al., 1962) 4 male rabbits were exposed to 10 ml DIDP (purity unknown) cutaneously for 24 hours, clinical signs and mortality were not reported and the conclusion was that the LD50 was greater than 10 ml/kg (9,700 mg/kg).

In a 24-hour exposure dermal study (Hazleton Laboratories America, 1978) in rabbits (4 animals, sex not specified), a dose of 3,160 mg/kg was applied on abraded skin and remained in contact with the skin by means of a non-absorbent binding. There was no mortality during the 14-day test period, the dermal LD50 was therefore estimated to be greater than 3,160 mg/kg. Clinical observations reported slight to marked anorexia and slight to moderate depression in all animals; at termination all four rabbits appeared normal. Very slight to well-defined erythema was noted in all rabbits at 24 hours, only two exhibited very slight erythema at day 3. Gross pathology findings noted on day 14 included dark red lungs in 3 rabbits and “raised areas” on all lobes of the lungs in the fourth rabbit.

One group of 8 male and 8 female rats was exposed for 24 hours occlusively to 3 ml/kg (2,910 mg/kg) of Vestinol DZ. None of the rats died during the 14-day post treatment observation period, no clinical signs were noted, and no gross pathological abnormalities were detected at necropsy. Dermal LD50 was therefore estimated to be greater than 3 ml/kg. This study was performed according to GLP procedures (Inveresk Research International, 1981).

Inhalation exposure

In a series of LC50 (Smyth et al, 1962) conducted in 6 male and 6 female rats, no death occurred after 8 hours of concentrated vapour exposure. DIDP was probably administered in aerosol form but no quantitative data are provided and no conclusion can be drawn from this test.

A 6-hour exposure inhalation study (Industrial Bio-test Laboratories, 1975) was conducted in rats, mice and Guinea pigs (5 males and 5 females) at 0.13 mg/l (nominal concentration). DIDP is indicated to be administered as a vapour, but regarding the test conditions the substance was

probably administered as an aerosol. No death occurred, no adverse reactions were noticed following the 14-day observation period, no gross tissue changes attributable to effects of the test material were observed in any of the animals examined.

Four groups of 5 male and 5 female rats were exposed nose-only for 4 hours to 0-5.6-9.72-12.54 mg/l of Vestinol DZ (Inveresk Research International, 1981). The particle size distribution indicated a respirable fraction of 71.1, 59.2, 54.5%, respectively. During the observation period of 14 days, clinical signs were agitation, unkempt appearance on the day after exposure. Animals dosed with 12.54 mg/l showed a body weight loss on day 2 post exposure and resumption of normal body weight gain was observed from day 3 onwards. The only gross pathological findings observed at necropsy were the presence of numerous dark red foci in the lungs, observed more frequently in treated animals (23/30, controls: 2/10). Moreover, treated animals tended to have slightly higher lung/body weight ratio when compared to controls (within normal limits). In conclusion, LC50 was greater than 12.54 mg/l. This study was performed according to GLP procedures.

Other routes of exposure

In a briefly reported study (Lawrence et al., 1973), 100 ml/kg DIDP was administered by *intraperitoneal* route to male ICR mice, the observation period was 7 days, no more details were given. The LD50 was estimated to be greater than 100 ml/kg (97,000 mg/kg).

DIDP was administered via *intraperitoneal* route to mice (number and sex of animals not available) for determination of the approximate mean lethal dose (7 days - ALD50). A total dose of 10 ml undiluted DIDP (9,800 mg/kg) was tolerated without symptoms, there were no particular post-mortem findings (BASF, 1961).

Four, two and two rabbits were dosed via *intravenous* route with undiluted DIDP at different doses: 0.5 - 0.8 and 1.6 ml/kg, respectively (490 mg/kg-784 mg/kg-1,568 mg/kg) (BASF, 1961). Lethality was reported: 2/4-1/2 and 2/2, respectively. Animals died within a few minutes to a few hours after administration of the highest dose. At the lower doses the animals did not die until 2-3 days later. Tonoclonic convulsions and laboured breathing were observed for higher doses. Post mortem examination indicated oedema or haemorrhagic engorgement (more or less pronounced) of the lung. The same effects were observed with olive oil controls and paraffin oil controls.

4.1.2.2.2 Studies in humans

There is no information on acute toxicity in humans.

4.1.2.2.3 Summary of acute toxicity

Most of the animal studies on acute toxicity were either not available as detailed studies or performed prior to establishment of OECD or EU guidelines. However in view of the consistency of the results for all routes of exposure, it can be considered that DIDP has a low acute oral, dermal and inhalation toxicity. No classification is indicated according to the EU criteria for acute toxicity whatever the route of exposure.

4.1.2.3 Irritation

4.1.2.3.1 Studies in animals

Skin irritation

Six male rabbits were exposed to 0.5 ml of the test material during 4 hours, the patch held in contact with the skin by means of a semi-occlusive dressing. Only very slight erythema in one animal was noted at 60 minutes after removal of the patch, no other irritating signs at 24, 48 and 72 hours were observed. This study was performed according to GLP procedures (Exxon Biomedical Sciences, 1996d).

A study conducted in 3 rabbits (2 males and 1 female) according to the OECD guideline 404 using undiluted Palatinol Z under semi-occlusive dressing (about 0.5 ml of the test liquid is absorbed in the dressing) for 4 hours, resulted in a very slight erythema in only one male at 24 and 48-hour post exposure observation time (BASF, 1986a).

Six rabbits (3 males and 3 females) were exposed to Vestinol DZ as supply on both intact and abraded skin for 24 hours under occlusive wrapping. The test site was scored immediately and after 48 hours. The test was carried out according to the FDA recommended method. Vestinol DZ caused very slight-mild reactions at 24 hours only on abraded skin, no irritation was observed on intact skin. At the 72-hour reading, only one abraded site showed a response (Inveresk Research International, 1981).

Palatinol Z stab. (DIDP + 0.5-1% bisphenol A) was applied unmodified on the dorsal skin of 4 rabbits (1 male and 3 females) for 5 minutes and 2 hours with occlusive wrapping. Twenty-four hours after the 5-minute exposure period a very slight erythema (score 1) was observed at 24 and 48 hours in one animal and subsided within 8 days with desquamation. Following the 2-hour exposure period, 3 out of 4 animals exhibited a very slight erythema (score 1) at the 24-hour observation time, 1 out of 4 at the 48-hour observation time. In all cases erythema were reversible but a residual symptom of desquamation was seen at day 8. No oedema was observed in those assays (BASF, 1979b).

Two male and four female rabbits were submitted to 0.5 ml undiluted DIDP for a period of 24 hours on scarified and intact skin under occlusive dressing. Effects were checked at 24, 72 hours and 8 days after application. Immediately after the 24-hour exposure period, there were clear areas of redness on the intact and scarified skin (in 6 out of 6 animals) and in some instance oedema on intact skin was observed as well (in 3 out of 6 animals). The mean score for erythema irritation was 2 at 24 hours on intact and abraded skin. An extensive reaction was observed in one animal (erythema score 3 at 24 hours on intact skin). The mean scores for oedema at 24 hours were 0.8 on intact skin and 1.5 on abraded skin. The symptoms of irritation partially receded during the following 2 days and had completely subsided by the end of the 8-day observation period. As a residual effect, desquamation was observed especially on the scarified skin areas. A primary skin irritancy index of 2.1 was obtained (BASF, 1979c).

In a study reported without any detail, a 24-hour uncovered application of DIDP (mixed isomers) did not produce any irritating effect on rabbit belly (Smyth et al., 1962).

A study using Lawrence's method was conducted in 10 mice: undiluted DIDP produced no sign of irritation via intraperitoneal route (Lawrence et al., 1973).

Dermal irritation observed in sensitisation studies with undiluted DIDP in the Guinea pig is inconsistent and varies from no to well defined erythema.

In conclusion, those studies are indicative of no or moderate irritant reversible effect with desquamation following single skin exposure varying from 5 minutes to 24 hours. When DIDP is applied on skin for 4 hours, no or only very slight irritation is observed. Following 24-hour exposure, irritating reaction are sometimes observed and desquamation is noticed in some cases.

Eye irritation

In a study conducted in 3 rabbits according to the OECD guideline 405, 0.1 ml undiluted Palatinol Z showed redness of the conjunctiva in all animals (score 2) at 1 hour, no reactions were noted at 24, 48 and 72 hours (BASF, 1986b).

0.1 ml of undiluted Vestinol DZ was introduced in the eye of New Zealand white rabbits (3 males and 3 females). Observation times were 1, 24, 48, 72 hours and 7 days. All treated eyes showed a mild-moderate conjunctival redness at 1 hour (mean score 1) and 4/6 eyes mild redness at 24 hours (mean score 0.5). At 1 hour mild chemosis was noted in 2/6 treated eyes, all the eyes were normal at 48, 72 hours and on day 7 (Inveresk Research International, 1981).

In a briefly reported study, eye injury in rabbits was assessed considering the degree of corneal necrosis that results from instillation of various volumes and concentrations of chemicals (method described by Carpenter and Smyth). Grade 1 was obtained for DIDP which indicated, at most, a very small area of necrosis resulting from 0.5 ml of undiluted chemical in the eye (Smyth et al., 1962).

In a shortly reported study, undiluted DIDP did not produce any obvious irritation (Lawrence et al., 1973).

In a study conducted in 6 rabbits (Industrial Bio-test Laboratories, 1975), undiluted DIDP produced only slight signs of irritation on the conjunctiva at 1, 4 and 24-hour observation time (redness score 1 or 2 and discharge at 1 hour, redness score 1 at 4 hours and redness score 1 in 1 animal at 24 hours). All the eyes were normal at 48, 72 and 96 hours.

0.1 ml of Palatinol Z stab (DIDP + 0.5-1% bisphenol A) was applied unmodified to the conjunctival sac of the right eye of 6 albino rabbits. Reactions were assessed after 24, 48 and 72 hours. 24 hours and 48 hours after application, a slight redness of the conjunctiva was observed in 6 out of 6 (maximum score of 2 in one animal at 24 hours). At 72 hours, redness of the conjunctiva (score 1) was still observed in 3 animals. Complete reversibility was not studied. However in view of the score 1 at 72 hours and in regard with the whole studies, a reversibility of the effect can be anticipated. This study was conducted according to FDA test method (BASF, 1979a).

In conclusion, DIDP is slightly irritating for rabbit eyes. The observed effects were redness and chemosis limited to the conjunctiva in a short period after administration.

Respiratory irritation

No indication of upper airways irritation was reported following acute inhalation exposure in animals, and there are no reported effects in humans. Therefore it may be anticipated that DIDP does not induce respiratory irritation, in normal conditions of use.

4.1.2.3.2 Studies in humans

Primary irritation potential of 0.2 ml of undiluted DIDP was evaluated during a single 24-hour application (occluded patch) on 14 female subjects and 1 male subject. Examinations at 30 minutes and 24 hours after patch removal did not reveal any sign of irritation (Hill Top Research, 1995b).

An irritant patch test was conducted by the Finnish Institute of Occupational Health in 144 patients. Only an abstract was available. Two patients exhibited an irritant reaction after application of 5% (w/w) DIDP in petrolatum (Kanerva et al., 1996).

In a repeated insult patch test (modified Draize procedure), no sign of irritation was reported (see Section 4.1.2.5) (Hill Top Research, 1995a; cited in Medeiros et al., 1999).

4.1.2.3.3 Summary of irritation

Results from animal studies following single skin exposure varying from 5 minutes to 24 hours lead to no or moderate effect, reversible with possible desquamation. Effects on eyes are weak and limited to conjunctiva. There is no indication of upper airways irritation in animal. In humans there is no indication of an irritating potential. Thus no classification is indicated according to the EU criteria for those different end points.

4.1.2.4 Corrosivity

From the studies presented in Section 4.1.2.3, it can be concluded that DIDP is not corrosive.

4.1.2.5 Sensitisation

4.1.2.5.1 Studies in animals

In a modified Buehler test (Exxon Biomedical Sciences, 1992) 40 Guinea-pigs (20 treated females and 20 controls) were used for the assessment of dermal sensitisation. Induction phase was performed on days 0, 7 and 14 by occlusive topical application with undiluted DIDP (MRD-92-256) (it is unknown whether the stability, identity and composition or other characteristics which appropriately identify the test material have been determined in a GLP compliance manner, this is a deviation from the GLP standards). DNCB (0.1%) was used as a positive control. Signs of irritation were observed on 18/20 during induction phase. Challenge was performed on day 28 with 5% DIDP in peanut oil. Due to the reactions of irritation noted in the irritation control group, a rechallenge was conducted on day 35 at a lower concentration (1%). Following challenge and rechallenge, one treated animal did not react. Following rechallenge (1%), 4 of 20 treated animals did not react, 8 of 20 were observed with very slight erythema (score 1), 7 of 20 were observed with well-defined erythema (score 2) and very slight oedema was observed in one treated animal (score 1). On day 37, erythema of one treated animal was increased from slight to moderate/severe erythema (score 3). Irritation was noted in one control animal with very slight erythema following rechallenge.

In a Buehler test (Huntingdon Research Centre, 1994) conducted with Jayflex DIDP (composition not available to the laboratory) in 40 Guinea pigs (20 treated and 20 controls),

undiluted substance was applied during induction phases (day 1, 8 and 15) and challenge (day 28), no sign of sensitisation was reported. No sign of irritation was reported during the induction period, this weakens the significance of the test. This study was conducted in compliance with Method B6 of directive 92/69/EEC and performed according to GLP procedures.

In a maximisation test (Inveresk Research International, 1981) conducted according to Magnusson and Kligman, 30 Guinea pigs (20 treated and 10 controls) were treated with Vestinol DZ (as supplied). Induction was done with intradermal injection of 10% DIDP v/v in paraffin oil on day 1 and occlusive patch of 50% (non irritating concentration) DIDP v/v in paraffin oil on day 7 during 48 hours. Challenge was performed on day 23 with 50% DIDP v/v in paraffin oil. It was briefly reported that the control group of adjuvant pre-treated Guinea-pigs did not react positively to topical application of Vestinol DZ at the concentration of 50% v/v in paraffin oil. Similarly there were no positive reactions in the test group which had been subjected to the induction with Vestinol DZ at a concentration of 50% v/v in paraffin oil (unfortunately, tables with scores were not reported in annexes). Although a negative result was achieved, the absence of signs of irritation following dosing during induction period (no application of sodium lauryl sulphate that is normally used to produce an irritant effect) weakens the significance of the test.

4.1.2.5.2 Studies in humans

A repeated insult patch test (modified Draize procedure) (Hill Top Research, 1995a; cited in Medeiros et al., 1999) has been performed on 128 volunteers, 104 completed the study. All exposures were by 24 ± 1 hour contact under occluded patches with undiluted DIDP. Induction applications were made three times per week for three successive weeks. Following a 10 to 17-day rest period, a challenge application of the test article was made to a naive site located away from the original application site. Simultaneous application to a pre-exposed site (i.e. the original site used for induction application) was made concurrently with the challenge at a naive site. Reactions were scored 48 or 72 hours after each induction application (24 or 48 hours after patch removal) and 48 and 96 hours after challenge (24 and 72 hours after patch removal). In induction and challenge phases, no responses were observed to the test article throughout the pilot and main phase of the study. Under the conditions of the study, no evidence of clinical sensitisation or irritation was observed in any of the 104 subjects completing the pilot and the main phase of the study.

In an irritant and allergic patch test (Kanerva et al., 1996) conducted by the Finnish Institute of Occupational Health on 144 patients, only two of them exhibited an irritant reaction after application of 5% (w/w) DIDP in petrolatum. No allergic reactions were reported.

A case of allergic contact dermatitis from DIDP in a polyvinyl chloride identity band has been described (Hills and Ive, 1993). A 64-year-old woman developed a severe vesicular eczema under an identity band on her right wrist. The band was removed and a new one applied on the left wrist. Two days later, eczema developed on the left wrist. Patch tests performed with identity band and 5% DIDP in petrolatum showed positive reactions: testing with other constituents of identity band and with DIDP at 2% and 1% were all negative. Dioctyl phthalate (DOP) and L7-9 phthalates at 5%, 2% and 1% in petrolatum were also negative. DIDP 5% was also negative in 20 controls.

Respiratory sensitisation

Pulmonary sensitising properties have not been demonstrated with any of the phthalates, particularly with DEHP or DBP, and no cases have been reported in humans. Therefore a low potential can be anticipated.

4.1.2.5.3 Summary of sensitisation

One study conducted according to Buehler gives a clear positive response, which should lead to a classification according to the EU criteria. Two other studies conducted either according to Buehler or to Magnusson and Kligman, give negative results with no evidence of irritating effect; these two studies cannot invalidate the previous one since they present some weaknesses in the protocol especially concerning the lack of irritancy at the induction phase. But the marked response obtained in the first Buehler test, normally considered having a low sensibility, is confusing. The strong irritant effect during induction phase, only observed in this assay, is also surprising. In any of the three tests, the DIDP composition is not well established, impurities or additives could explain the discrepancy in results.

No positive reactions were reported in patch test studies conducted in humans. Only one case of dermatitis has been reported in humans. Consequently the evidence that DIDP may cause sensitisation in human is weak.

Moreover sensitising properties have not been demonstrated with any of the phthalates and particularly with DEHP and DBP. A low sensitising potential, if any, can be anticipated.

Overall, the weight of evidence is deemed insufficient to justify a classification.

4.1.2.6 Repeated dose toxicity

4.1.2.6.1 Oral exposure

Rats

28-day sub-acute toxicity test (BASF, 1969a)

In this test, two groups of 20 males and 20 females rats were dosed with 5,000 and 10,000 ppm Palatinol Z in food (600 and 1,250 mg/kg/d for males and 1,100 and 2,100 mg/kg/d for females), 10 males and 10 females were undosed and served as controls. Samples were taken for 10 animals (5 males and 5 females) in each group on day 14 or 15 of the trial and tested for haemoglobin content, red and white blood cell count, hematocrite, differential blood count, blood urea and GPT. On day 23/24, urine was tested for protein, glucose and urobilinogen, urine sediment was examined and the pH value was also determined. At the end of the 28-day treatment period, animals were sacrificed and their liver, kidneys and heart were weighed. Gross abnormalities were noted and histological examination was performed on liver and kidneys.

DIDP was tolerated in concentrations of 5,000 and 10,000 ppm in the 28-day dietary trial by rats without visible toxicity symptoms and without any reduction in food intake. As regard to body weight development, only the male animals from all dosed groups lagged somewhat behind the corresponding animals in control group. The clinical chemistry analyses carried out during the

trial did not detect any deviation from normal in either group. Peroxisome proliferator parameters were not measured.

The absolute and relative liver weight of the rats in each treated group were dose-related increased when compared with those of controls. However the histological tests failed to detect any changes in the liver or kidneys, any fat deposition or adiposis of the organs.

Regarding the only effect observed at 5,000 ppm (600 mg/kg/d), small increase in liver weight, this dose can be considered as the NOAEL in this test.

90-day rat dietary test (BASF, 1969b)

On the basis of the above experimental results, Palatinol Z concentrations of 800, 1,600, 3,200 and 6,400 ppm in the feed were selected for a 90-day rat dietary trial. The doses were equivalent to about 55-100-200-400 mg/kg/d in males and 60-120-250-500 mg/kg/d in females. Forty rats (20 males and 20 females) in each group were dosed daily during 90 days and 20 extra animals (10 males and 10 females) were tested as controls and 6,400 ppm group with a reversibility period of 21 days. Clinical chemistry analyses were carried out on two blood samples (day 32-36 and day 74-78), the following parameters were checked: haemoglobin, red blood cell count, leukocytes count, hematocrite value, differential blood count, blood urea and GPT. Two urine samples (day 33-36 and day 75-78) were tested for: protein, glucose, urobilinogen, sediment and pH value. After sacrifice, macroscopically detectable changes were noted and the liver, kidneys and heart were weighed. For the histological investigation the following organs were fixed in 10% formaldehyde solution and stained with haematoxilin eosin: central nervous system, heart, lung, thyroid glands, trachea, liver, kidneys, adrenal glands, spleen, stomach, intestine, genitals (testis/ovaries), bladder. In addition, a fat stain Sudan III of the liver and kidney was used.

All the rats tolerated administration of DIDP in the stated concentrations over the 90-day period without visible toxicity symptoms. There was no difference in food uptake and body weight development in female rats of any group compared with controls. In male rats, from day 77 onward there was a slight lag in body weight development in the 1,600, 3,200 and 6,400 groups with normal food uptake. This finding was still present after the 21-day reversibility period. Clinical chemistry analysis and urine analysis generally agreed with the normal range of values obtained for the control group.

In males, absolute liver weight was increased in all experimental groups but significantly only at the highest dose (12.19 versus 9.31 g in controls), relative liver weight was significantly higher in all experimental groups but without dose-effect relationship and still statistically significantly elevated at the end of the 21-day post observation period. In female absolute liver weights were significantly increased at the two highest doses (6.04 and 6.94, respectively, versus 5.20 g in controls), and not statistically at 1,600 ppm but by 9.8% (5.71 vs. 5.20 g). However, this increase was dose-related, and relative liver weights significantly increased from 1,600 ppm.

In both sexes absolute kidney weights did not differ from controls. In males relative kidney weights were increased (statistically significant) in all treated group but without dose-effect relationship. In females relative kidney weights were increased only at 1,600 and 3,200 ppm but not at 6,400 ppm.

No pathological changes were observed.

In males, the absolute organ weights were not increased except liver weight at the highest dose (6400 ppm), thus a NOAEL of 3200 ppm (200 mg/kg/d) can be assumed.

In females, a NOAEL of 800 ppm (60 mg/kg/d) can be assumed based on dose-related increase of liver weights: relative liver weights from 1,600 ppm and absolute/relative from 3,200 ppm.

3-month study (Hazleton Laboratories, 1968a)

DIDP-FDA grade was administered to four groups of 10 male and 10 female rats in dietary levels of 0.05%, 0.3% and 1% (approximately 35, 200 and 650 mg/kg/d, respectively). A group of untreated rats served as control. Criteria for evaluation of the compound effect were physical appearance, behaviour, growth, food consumption, survival clinical laboratory values, organ weights, and, gross and microscopic pathology (10% neutral buffered formalin was used as a fixative).

No compound-related effect was demonstrated at any dietary levels with regard to physical appearance, behaviour and survival. Growth in the test rats was not significantly affected. Body weight gains for the two highest levels in males were lower than controls (but not significantly different) and were comparable among the two test groups through the ninth week. Overall, weight gains at 13 weeks for the male test groups showed a dose-related, although slight, decrease. Body weight gains for the high level females were only slightly lower than the controls. Food consumption values were comparable to the controls. The clinical laboratory values for the test groups showed no significant compound-related differences from control values.

Observations at necropsy revealed the liver of the high level animals, particularly the males, to be markedly larger than those of the control rats. Statistical analysis revealed the liver weights and liver/body weight ratios for the high-level males and females to be significantly higher than those for the corresponding controls. No other consistent gross changes were noted in the liver. Histologically, the liver showed no compound-induced alterations. The kidney/body weight ratios but not the absolute weight for the high and intermediate level male group were significantly higher than those for the corresponding controls. Histologically, kidneys showed no compound-induced alterations.

A minimal increase in thyroid activity was observed at the highest-level dose (the activity was judged to be higher when the follicles were more uniform and smaller in size with a lighter colloid along with a tall cuboidal or columnar epithelium).

It can be assumed from this study that the NOAEL is 0.3% (about 200 mg/kg/d) based on the fact that the highest dose leads to liver and thyroid effects. Only relative kidney weight is affected at this intermediate dose, probably due to a lower body weight.

Two-generation study (Exxon Biomedical Sciences, 1997d)

This study is described in detail in Section 4.1.2.9. P_1 males and females received DIDP (0.2-0.4 -0.8%) daily for at least 10 weeks prior to mating and during mating period. Additionally, P_1 females received DIDP during the gestation and post-partum period (day 21). A gross necropsy was performed on all adult animals, selected F_1 and F_2 neonates, and on all animals which died during the study. A full macroscopic examination was performed on these animals and selected organs and tissues were collected, weighed and stained with periodic acid-Schiff hematoxylin.

In females, increases of kidney weight were observed in a non dose-dependant manner from the mid dose in P_1 (8-9%) and from the low dose in P_2 (12-16%) but no correlating histopathology was found. In males, there were statistically significant increases in mean absolute and relative kidney weights from the low dose with microscopic changes included accumulations of dark orange or eosinophilic granular cytoplasmic pigments in the cortical tubules and cortical tubular

degeneration. In the high-dose male rats there was an increase incidence of granular casts in the renal tubules (P_1: 14 versus 2 in controls). There were no differences in incidence or degree of severity of hyaline droplets in cortical tubules in P_1 or in P_2 generation compared to controls. However, hyaline droplets are somewhat difficult to detect with routine haematoxilin staining. Anyway histology was consistent with the hypothesis of male-rat specific nephropathy associated with accumulation of alpha 2u-globulin. Indeed, accumulation of protein droplets occurs rapidly, whereas long-term exposure results in additional histological changes. So, this specific injury is characterised as follows: single cell degeneration and necrosis in the renal proximal tubule. Dead cells are sloughed into the lumen of the nephrons, and while moving through the nephrons contribute to the development of granular casts (IARC, 1999). This hypothesis is emphasised by the fact that no kidney damage was observed in females. No firm conclusion can be addressed; but a strong presumption may be assumed.

Dogs

In a 13-week dietary administration study (Hazleton Laboratories, 1968b), DIDP was put in the diet of three groups of 3 male and 3 female Beagle dogs at levels of 0.05% (about 15 mg/kg/d), 0.3% (about 75 mg/kg/d) and 1% (about 300 mg/kg/d). Comparable animals served as controls. The following parameters were checked:

- haematology: hematocrite and haemoglobin determination, erythrocyte counts and total and differential leukocyte counts;
- biochemistry: determinations of blood urea nitrogen, fasting blood sugar, serum sodium, serum potassium, serum chloride, serum calcium, serum alkaline phosphatase, serum glutamic-oxaloacetic transaminase (AST), serum glutamic-pyruvic transaminase (ALT), total serum bilirubin, carbon dioxide, total serum protein, serum albumin, serum electrophoresis and sulfobromophtalein (BSP) liver function test;
- urine analysis: appearance, specific gravity, pH, protein, glucose, ketones, bilirubin and microscopic examination of the sediment.

All treated groups and controls appeared normal with respect to appearance, behaviour and elimination. Three dogs in the highest diet level showed slight to moderate body weight losses, these findings did not appear to be related to decreased food consumption except for one animal. All clinical laboratory values were generally within accepted limits and comparable between all groups. Gross necropsy examinations did not reveal any consistent compound-related alterations. In regard with liver weights, the individual variations and the small numbers of animals used made assessment of changes difficult (no statistic available). However a dose-related increase in the means weight is observed: 212; 220; 287 versus 190 g in females and 248; 274; 317 versus 253 g in males at 0.05, 0.3 and 1%, respectively. This was accompanied by minor microscopic changes: slight to moderate swelling and vacuolation of hepatocytes revealed by microscopic examination at 0.3% and 1%. There was a lack of a significant dose-response in severity and number of animals affected for these effects: two (out of three) mid-dose males and one high-dose male and two mid-dose females and three high-dose females. These different critical comments limit the significance of the test. Moreover, measurements of ALT and AST activities and BSP clearance were not modified suggesting a minimal, if any, hepatocellular injury.

A NOAEL of 0.05% (15 mg/kg/d) can be assumed for this 13-week study in dogs for hepatic effects observed at 0.3% (75 mg/kg/d) and is considered into the risk characterisation, in spite of the large limitations of the study.

Rabbits

In a sub-acute oral study (BASF, 1961), DIDP was administrated in 10.5% solution in olive oil to 15 rabbits (6 males and 9 females). Duration of the trial was variable and depended on mortality and tolerance of animals. Three animals were dosed with 1,960 mg/kg/d DIDP in olive oil (7, 8 and 10 administrations), 4 animals with 980 mg/kg/d DIDP (5, 7, 8 and 10 administrations), 5 animals with 490 mg/kg/d DIDP (7, 15, 21, 36 and 50 administrations) and 3 animals with 196 mg/kg/d DIDP (each 50 administrations). Two control animals were dosed with 2 ml/kg/d olive oil and two others with 1 ml/kg/d olive oil.

Results in olive oil control are quite similar to those of treated rabbits: death, pathological changes in urine (protein, red blood cells, leukocytes and epithelial cells), strong anaemia pneumonia and/or necrosis of the liver. Kidney damage was only mentioned in some treated rabbits and not found in controls. No firm conclusion can be drawn from this study.

Cats

A similar subacute toxicity test (BASF, 1961) was also performed in 3 cats dosed with 2 ml/kg/d of 50% DIDP (Palatinol Z) in olive oil (980 mg/kg/d). Control animals were administered 2 ml/kg/d olive oil (2 cats), 4 ml/kg/d olive oil (2 cats) and a mixture of 2 ml/kg/d of olive oil with 2 ml/kg/d of paraffin oil (2 cats). Each animal received 60 doses.

All cats survived the 3-month treatment. Palatinol Z induced only loss of appetite, vomiting, diarrhoea, loss of body weight and bronchitis but this was also observed in solvent control. No firm conclusion can be drawn from this test.

Study specifically designed to assess peroxisome proliferation

21-day feeding study (BIBRA, 1986)

In a 21-day feeding study to assess dose-response relationships for the peroxisomal and related effects of DIDP (99.84% purity), a group of 5 male and 5 female young (41-44 days) Fischer 344 rats were fed with DIDP at dietary levels of 0-0.3%-1.2% and 2.5% for 21 days. A further group of 5 rats of each sex was fed with 1.2% DEHP. Daily intake in mg/kg/d was:

- 1,077 mg/kg/d (males) and 1,002 mg/kg/d (females) for 1.2% DEHP,
- 304 mg/kg/d (males) and 264 mg/kg/d (females) for 0.3% DIDP,
- 1,134 mg/kg/d (males) and 1,042 mg/kg/d (females) for 1.2% DIDP,
- 2,100 mg/kg/d (males) and 1,972 mg/kg/d (females) for 2.5% DIDP.

No treatment-related clinical signs were observed. The male rats given 2.5% DIDP lost weight during the first three days of treatment and remained significantly lighter than the controls (69-82% of controls) throughout the treatment period. Males given 1.2% DIDP failed to gain as much weight as the controls but the difference was significant on day 17 only. Females given 2.5% DIDP were significantly lighter than the controls from day 10 onwards (83-87% of controls). Male rats given 1.2% and 2.5% DIDP consumed significantly less diet than the controls during the first three days of treatment, but only in the 2.5% DIDP group was the food intake significantly reduced throughout the treatment period. During the first three days of treatment, only the female rats given 2.5% DIDP consumed significantly less food than the controls.

In both sexes there was a significant increase in the absolute and relative weight of the liver at dose levels of 1.2% and 2.5% DIDP. In males, absolute weights were 186 and 172% of controls for levels of 1.2% and 2.5%, respectively while relative liver weights for these groups were 201

and 254% of controls. In females absolute weights for the same levels were 160 and 192% of control and relative weights were 176 and 238% of controls, respectively. In the males there were also significantly higher liver weights in rats given 0.3% DIDP (121% of controls for absolute and relative weights). There was a reduction in hepatocyte cytoplasmic basophilia in rats fed 1.2 or 2.5% DIDP and in the later group, this was associated with an increase in eosinophilia. Lower periportal lipid levels were seen but not dose-related.

Serum triglycerides and cholesterol levels were only reduced in males given 1.2% or 2.5% DIDP but no dose-relationship was apparent. Cyanide-insensitive palmitoyl-CoA oxidation was significantly increased in all treated animals except those given 0.3% DIDP. There was a significant increase in the 11- and 12-hydroxylation of lauric acid in all treated males but in the females the only significant increase was in the 12-hydroxylase level in those given 2.5% DIDP. Electron microscopy examination of hepatocytes peroxisomes showed in both sexes given 2.5% DIDP a marked but variable increase in number and size, the females showing a greater response.

Males given the two lower doses had heavier kidneys than the controls whilst in both sexes given 2.5% the kidneys weight were lower than the controls (81% and 88% of control weights for the males and females, respectively). Relative kidney weights were significantly higher than the controls in all the treated groups except the females given 0.3% DIDP. No histological changes were observed.

The testis weight from the males given 1.2% of DEHP or DIDP did not differ from the controls. The histology was normal in DIDP group, not conducted in DEHP group. The absolute testis weights of the males given 2.5% DIDP were slightly but significantly lighter than the controls (2.31 g versus 2.59 g in controls). However when expressed relative to the low body weight the value was significantly greater (1.63 versus 1.24 in controls). In histological examination, there was no testicular atrophy (samples preserved in 10% neutral buffered formalin stained with hematoxylin and eosin).

In an identical study reported in DEHP risk assessment (CMA, 1984b), it is indicated that testis weights were significantly reduced in male rats in the 2.5% dose group (2,101 mg/kg/d) and moderate to severe testicular atrophy were noted.

Concerning peroxisome proliferation results summarised in **Table 4.24** allow to compare DIDP, DINP and DEHP. When compared to DEHP at dose level of 1.2%, DIDP exhibited the same characteristic feature of peroxisome proliferator (excepted lauric acid 11- and 12-hydroxylase activities which were not significantly increased in DIDP treated females): increased liver weight, depressed serum triglycerides and cholesterol levels, increased activity of hepatic lipid metabolising enzymes and production of hepatic peroxisome proliferation. DINP and DIDP show comparable responses at comparable dose levels. This study was carried out in compliance with EPA GLP standards.

Similar studies (Lin, 1986)

Similar studies were performed in the same conditions on F-344 rats with 8 phthalate esters (BBP, DBP, 610 P, 711 P, DEHP**,** DINP, DIDP, DUP), each time with a control group fed 1.2% DEHP. For DIDP, 5 males and 5 females per group were fed 0, 0.3, 1.2 and 2.5%, respectively. The effects on hepatic peroxisome proliferation were examined in a total of 132 animals: 2 animals of each sex per group were randomly selected in 33 groups (7 high-dose groups, the 9 negative control groups, the nine 1.2% DEHP control groups, and 4 groups in each DEHP and DEHA). Several end points were selected, the most important of which being the electron microscopy examination of liver centrolobular and periportal peroxisome proliferation. Histological abnormality in the kidneys and testes was not studied.

A peroxisome proliferator index (PPI) was constructed from a linear combination of all usable parameters that yield the best geometric separation among the three peroxisome conditions (low, moderate, and high). It is a weighted average of those parameters that best predict the outcome of the electron microscopic evaluation. It was found by linear discriminant analysis that the best predictive end point is the palmitoyl-CoA (correlation coefficient 0.867), with the relative liver weight performing nearly as well (correlation coefficient 0.861). The analysis also confirmed that females have less peroxisome proliferation than males ($p < 0.001$) after adjusting for body weight.

A ranking of the studied plasticisers was made according to this PPI. This ranking depends on the dosage, the most useful one being considered as this in the low-dose region. So, the statistically predicted dosages that would not induce peroxisome proliferation in 99% of rats were found to be: DEHP (8.8 mg/d), DINP (22.9), DIDP (35.8), DBP (43.7), 610P (64.5), DUP (57.1), BBP (79.2), 711 P (72.8), and DEHA (140.5). Note that the numbers between brackets should be multiplied by a factor of 5, for a 200 g rat, to express the result in mg/kg/d.

Table 4.24 Comparative results of peroxisome proliferation parameters with 1.2% of DEHP, DINP and DIDP BIBRA study (1986)

Effects		Control group		DEHP 1,2%		DINP 1,2%	DIDP 1,2%
		1)	2)	1)	2)		
Liver weights absolute *(relative)*	Male	6.56 *(3.25)*	6.64 *(3.17)*	12.73 *** *(6.88)*	13.10 *** *(6.86)*	9.84 *** *(5.63)*	12.38 *** *(6.37)*
	Female	4.21 *(2.99)*	4.35 *(3.12)*	7.26 *** *(5.62)*	7.41 *** *(5.88)*	6.89 *** *(5.22)*	6.94 *** *(5.48)*
Serum triglycerides (mmole/l)	Male	0.97	0.83	0.48 *	0.50*	0.56 ***	0.55*
	Female	0.35	0.47	0.46	0.52	0.43 *	0.50
Serum cholesterol (mmole/l)	Male	1.96	1.77	1.41 ***	1.44 *	1.34 ***	1.32*
	Female	2.29	2.16	1.94 *	2.08	1.94 *	1.90
Cyanide – insensitive-palmitoyl-CoA oxidation (nmole/min/mg homogenate protein)	Male	6	5.1	41 ***	51 ***	27 ***	51.7 ***
	Female	7	6	37.8 **	33 **	26.3 ***	44.9 ***
Lauric acid 11 hydroxylase activity (nmole/min/mg)	Male	0.8	0.64	3.1 **	2.15 **	2.2 ***	2.12 ***
	Female	0.5	0.53	1.8 **	1.35 **	0.9	0.79
Lauric acid 12 hydroxylase activity (nmole/min/mg)	Male	1	0.84	12.4 ***	10.38 **	7.6 ***	9.13 ***
	Female	0.8	0.81	6.2 **	4.21**	1.3	1.33

Table 4.24 continued overleaf

Table 4.24 continued Comparative results of peroxisome proliferation parameters with 1.2% of DEHP, DINP and DIDP

Effects			Control group		DEHP 1,2%		DINP 1,2%	DIDP 1,2%
			1)	2)	1)	2)		
Total protein (mg/g liver)		Male	207	217	236 ***	239 *	228 *	258 ***
		Female	198	224	237 **	279 **	238 ***	268 ***
Microsomal protein (mg/g liver)		Male	25	26.3	25.1	25.6	26	27.6
		Female	20	21.7	25 *	21.6	23.6 *	23.4
Histological finding: liver	Reduction cytoplasmic basophilia	Male	No	No	Yes	Yes	Yes	Yes
		Female	No	No	Yes	Yes	Yes	Yes
	Increased cytoplasmic eosinophilia	Male	No	No	No	No	No	No
		Female	No	No	No	No	No	No
Peroxisome proliferation (electron microscopic) 3)	Centrilobular	Male	+		++++		++++	++++
		Female	+		++++ / +++		++++	+++++
	Periportal	Male	+		++++		+++++	++++
		Female	+		++++ / +++		++++	+++++

1) Control values for DINP
2) Control values for DIDP
3) DINP-DIDP 2.5% (no evaluation at 1.2%)
\+ few
+++ moderate increase
++++ marked increase
+++++ very marked increase
Differ significantly from the control: * (P< 0.05) - ** (P < 0.01) - *** (P < 0.001)

4 week-study (BIBRA 1990; Lake 1991)

In this study the dose-response relationship for induction of hepatic peroxisome proliferation by DEHP and DIDP was assessed in 42-day-old male Fischer 344 rats. Groups of 5 rats were fed with 1% DEHP (control) and 0.02-0.05-0.1-0.3 and 1% (approximately 25-57-116- 353-1,287 mg/kg/d) DIDP diet. The sample of DIDP used was made up of equal part by weight of Hexaplas (ICI), Jayflex DIDP (Exxon) and Palatinol Z (BASF).

Food consumption and body weight were checked twice weekly, hepatic peroxisome proliferation was assessed by measurement of cyanide-insensitive palmitoyl-CoA oxidation activity. Testicular atrophy was also checked (organ weight and histological changes). This study was performed according to GLP procedures.

Over the course of the study, body weight of animals fed DIDP, at all levels in the diet was not significantly different compared to controls. The two phthalates esters produced dose-related liver enlargement. At 0.1% and higher, there was a statistically significant increase in relative liver weight (3.3158 g/100 g bodyweight vs. 3.0488 g/100 g bodyweight in controls). At 0.3% and higher, this statistically significant increase was also noticed for absolute liver weight (6.6812 g vs. 5.5830g in controls). Biochemical examination of the livers revealed no effect on the whole homogenate of protein content, but an induction of the enzymes of the peroxisomal fatty acid β-oxidation cycle. In this way palmitoyl-CoA oxidation activity was statistically dose-related increased from 0.1% expressed as µmol/min/liver weight/100g bodyweight (4.52 vs. 3.71 in controls), and from 0.3% expressed either as nmol/min/mg protein or as µmol/min/g liver

(respectively 11.82 vs. 5.60 and 2.67 vs. 1.22). These slight increases at 0.1% (increase of relative liver weight and of palmitoyl-CoA activity) could be considered as the trend for peroxisome proliferation effects, clearly confirmed at 0.3% (increase of absolute liver weights and increased enzyme activity whatever the units of expression).

NOELs for food consumption and enzyme activity were reported to be 51.7 mg/kg/d for DEHP.

No testicular atrophy was reported at the highest dose tested: 1,093 mg/kg/d for DEHP and 1,287 mg/kg/d for DIDP.

In vitro study

Bendford et al. (1986) investigated the peroxisome proliferation induction potential of DIDP monoester and DINP monoester (MIDP and MINP, respectively) and DINP in primary monolayer cultures of rat and marmoset monkey hepatocytes. Mono(2-ethylhexyl) phthalate (MEHP) was used as a positive control. The measured parameters were peroxisomal palmitoyl-CoA (PcoA) oxidation, laurate 11-12 hydroxylation (LAH) and the protein content of the homogenate.

In the rat hepatocyte culture, MIDP and MINP were both peroxisome proliferators as indicated by marked dose-related increases in PcoA oxidation. The rank was in order MEHP > MIDP > MINP > DINP. DINP caused much smaller increases as it is poorly converted to the monoester in the culture system. LAH appeared to be more sensitive to induction by MIDP and MINP than by MEHP, the rank was in order MIDP > MINP > MEHP.

In the marmoset hepatocyte culture, only minimal changes in PcoA oxidation activity were observed with MIDP, MINP or DINP with poor dose dependency and showed no changes with MEHP. MIDP and MINP caused up to 4 and 3 fold increases in LAH activity. MEHP has no effect.

Those studies are indicative of a marked species difference in peroxisomal proliferation by phthalates in culture hepatocytes.

Table 4.25 Summary of the oral repeated dose toxicity studies

Species	Treat-ment	Substance Purity/dose	Body Weight	Clinical Signs	Biochemistry/ Haematology	Effects on organs		NOAEL	Reference
						Macroscopy	Microscopy		
Young Rat Fisher 344	21 days in diet	DIDP 99.84% pure 0-0.3-1.2-2.5%	↓ body weight 2.5%	No change	↓ serum triglycerides and cholesterol (1.2 and 2.5% males) ↑ cyanide – insensitive palmitoyl – CoA oxidation 1.2%-2.5% (female and male) ↑ 11 and 12 – hydroxylation of lauric acid 0.3-1.2-2.5% (males) ↑ 12 hydroxylation of lauric acid 2.5% (females)	↑ liver weight from 0.3% (males) from 1.2% (females) Kidney weight ↓ 2.5% Slight ↓ absolute testicular weight 2.5%	↓ hepatocyte cytoplasmic basophilia 1.2 and 2.5% ↑ eosinophilia (2.5%) No testicular change	0.3% (304 mg/kg/d for males) (264 mg/kg/d for females)	BIBRA (1986)
Rat Fisher 344	28 days in diet	0.020-0.05-0.1-0.3-1%	No change	-	↑ cyanide insensitive palmitoyl CoA oxidation from 0.1%	No testicular atrophy	No testicular atrophy	0.05% (57 mg/kg/d)	Lake et al. (1991)
Rat Sprague Dawley	28 days in diet	Palatinol Z 5,000 and 10,000 ppm	Slight ↓ in males	No change	No change	↑ liver weight 5,000 and 10,000 ppm	No change	5,000 ppm (600 mg/kg/d for males) (1,100 mg/kg/d for females)	BASF (1969a)
Rat Sprague Dawley	90 days in diet	Palatinol Z 800-1,600-3,200 & 6,400 ppm	Slight ↓ in male	No change	No change	↑ liver weight (absolute) at 6,400 ppm in males dose-related increase of liver weight from 1,600 ppm in females	No change No change	3,200 ppm (200 mg/kg/d for males) 800 ppm (60 mg/kg/d for females)	BASF (1969b)
Rat	90 days in diet	DIDP-FDA Grade 0.05-0.3-1%	Slight ↓ all doses in males 1% in females	No change	No change	↑ Liver weight 1%	No change	0.3% (200 mg/kg/d)	Hazleton (1968)
Dog (Beagles)	90 days in diet	0.05 - 0.3 - 1%	Slight ↓ 1%	No change	No change	↑ Liver weight 0.3-1%	swollen and vacuolated hepatocytes from 0.3%	0.05% (15 mg/kg/d)	Hazleton (1968)

4.1.2.6.2 Inhalation exposure

Studies in animals

In a 2-week study (General Motors Research Laboratories, 1981) designed to evaluate the fate of DIDP (see Section 4.1.2.1), toxicity was also assessed. DIDP was administered to 8 male rats (6 for control) by inhalation (aerosol) at analytical concentration of 505±7 mg/m^3 (MMAD: 0.98 μm) 6 hours a day, 5 times per week. Rats were observed daily for body weight gain, appearance and gross behaviour. Animals were sacrificed at the end of the observation period (3 weeks) and tissue samples taken for histopathology.

There were no marked outward signs of toxicity during exposure. The rate of body gain was not different between control and exposed animals. Effects in the lungs were: moderate increase in the width alveolar septa with slight interstitial mixed inflammatory reactions, alveolar macrophages and type II pneumocytes were increased in number, peribronchial lymphoid tissue appeared slightly more prominent. In liver, spleen and kidneys, no obvious histologic alterations were noted except for a slight hepatic fatty metamorphosis.

No systemic toxicity, but local irritant effects were observed at the concentration tested, thus a NOAEL of 0.5 mg/l (500 mg/m^3) can be assumed. It should be noted that toxicity assessment is incomplete since no haematological/biochemical parameters were checked.

Studies in humans

In a Swedish survey (Nielsen et al., 1985), no sign of polyneuropathy (clinical assessment) was found among workers in a PVC processing industry where 54 workers (average time of employment: 8 years) were exposed to DEHP, BBP and DIDP in concentrations up to 2 mg/m^3 (though usually below 0.5 mg/m^3).

4.1.2.6.2 Summary of repeated dose toxicity

The target organ for oral sub-acute and sub-chronic DIDP toxicity in animals (rodent and dog) appears to be the liver (increased liver weights and significant changes in liver proliferator peroxisome enzyme activities in rodent). It is clear that NOAELs derived from rat studies are related to peroxisome proliferation liver effects, which are generally considered to be species-specific. Humans are very likely far less sensitive than rats.

In dogs, a NOAEL of 15 mg/kg/d is identified in a 13-week oral study (Hazleton Laboratories, 1968b) for effects in the liver (swollen and vacuolated hepatocytes at higher doses). In spite of the limitations underlined, it is proposed to consider this result in the risk characterisation. Indeed, the dog appears to be, in this case, a more relevant species for human risk assessment: dog is considered not responsive or refractory to peroxisome proliferation. It should be noticed that this study was only considered from a qualitative point of view in the NTP draft monograph (NTP, 1999).

Since the dog study cited above is not very reliable, a NOAEL of 60 mg/kg/d is identified in rats from a standard 90-day study based on increased relative liver weight in female rats at the higher dose (BASF, 1969). Changes in kidney weights are also observed in repeated dose toxicity tests but in a non-consistent way and with no concurrent histopathological changes. Renal damages are only observed in the two-generation study (about 12 weeks) from 100-200 mg/kg/d, but only in male rats and a strong presumption of a specific male rat effect is assumed.

The effects seen in the repeated dose toxicity tests do not justify classification Xn with R48 according to the EU classification criteria.

4.1.2.7 Mutagenicity

4.1.2.7.1 *In vitro* studies

Bacteria

Zeiger et al. (1982; 1985) tested the mutagenic potential of a series of phthalates including DIDP (purity non specified) in 95% ethanol from 100 up to 10,000 µg/plate in *S typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 using a preincubation modification of the Ames test with and without metabolic activation (homogenates of Aroclor 1254-induced Sprague-Dawley rat and Syrian hamster liver S9). No evidence of mutagenic activity was observed.

In a bacterial mutagenicity assay conducted in liquid suspension (Seed, 1982), the mutagenic activity of ten phthalates esters including DIDP was assessed. The bacteria (*Salmonella typhimurium* TA 100) were tested for mutation to azaguanine resistance as well as reversion to histidine prototrophy. Concentrations of DIDP were not reported but the maximal concentration tested was determined by either the limit of solubility or cytotoxicity exceeding more than 90% of the control values. No increase in mutant frequency was observed at any concentration.

Brief results of repair tests conducted by Kurata of twelve samples of phthalate esters on *Bacillus subtilis (recA-)* and *Escherichia coli (uvrA-, PolA-, recA-)* were reported (Omori, 1976). Application of 10 mg and 100 mg/plate (about 0.3 and 3 mg/ml) of DIDP did not produce any bacteriocidal or mutagenic effects.

Mammalian cell studies

In a mouse lymphoma forward mutation assay (Hazleton Biotechnologies Company, 1986), cells line L5178Y TK +/- were exposed for 4 hours to DIDP solutions in acetone. The test material was incompletely soluble and formed oily droplets at all concentrations. Under non-activation conditions, six concentrations of test material, ranging from 2,000 nl/ml to 10,000 nl/ml (namely 2,000; 4,000; 5,000; 6,000; 8,000 and 10,000 nl/ml), were analysed for mutant induction. Moderate to high toxicity was induced (percent relative growth 33.3% to 7.3%). In order for a treatment to be considered as mutagenic, a mutant frequency exceeding $30.2 \cdot 10^{-6}$ was required. In this assay the mutant frequency ranged from $13.2 \cdot 10^{-6}$ to $28.9 \cdot 10^{-6}$. So, the test DIDP was considered non mutagenic under nonactivation conditions.

In the presence of metabolic activation (S9 fraction of rat liver), treatments from 250 nl/ml to 2,000 nl/ml were analysed for mutant induction (namely 250; 500; 1,000; 2,000 nl/ml). Low to high toxicity was induced (percent relative growth 88.6% to 10.3%). The minimum criteria for mutagenesis in this assay was a mutant frequency exceeding $58.4 \cdot 10^{-6}$ and none of the dose induced this level of mutant action. Therefore, this test material was considered non mutagenic with activation.

No increase in mutant frequency was observed in the presence or absence of metabolic activation. This study followed the method 431 FDA modified and was performed according to GLP procedures.

4.1.2.7.2 *In vivo* studies

In a bone marrow micronucleus test (Hazleton Washington, 1994), groups of 10 CD-1 mice were treated by oral route with 1,250, 2,500 and 5,000 mg/kg Jayflex DIDP diluted in corn oil. Animals were sacrificed at 24, 48 and 72 hours. All DIDP dosed groups appeared normal immediately after dosing and remained healthy until the appropriate harvest time. No effect was observed except a slight increase in the percentage of the micronucleated polychromatophile erythrocytes with decreasing of the polychromatophile/normochromatic ratio in male (0.13 ± 0.03 vs. 0.05 ± 0.02 in controls) mice dosed with 1,250 mg/kg at harvest time of 24 hours but not statistically significant. At the other dose levels, no difference in percentages of the micronucleated polychromatophile erythrocytes was observed in male and female mice (0.08 ± 0.02 at 2,500 mg/kg and 0.07 ± 0.02 at 5,000 mg/kg/d vs. 0.05 ± 0.02 in controls). Positive control (cyclophosphamide, at concentration of 80 mg/kg) produced a statistically significant increase in the percentage of the micronucleated polychromatophile erythrocytes (1.91 ± 0.21 vs. 0.05 ± 0.02 in controls). Jayflex DIDP is considered negative in the mouse bone marrow micronucleus assay. This study was performed according to GLP procedures.

4.1.2.7.3 Summary of mutagenicity

DIDP is not mutagenic *in vitro* in bacterial mutation assays (with and without metabolic activation) and is negative in a mouse lymphoma assay. It is not clastogenic in a mouse micronucleus assay *in vivo*. This indicates that DIDP is a non-genotoxic agent.

4.1.2.8 Carcinogenicity

4.1.2.8.1 Cell transformation assays

In an *in vitro* transformation assay (Litton Bionetics, 1985), DIDP suspended in culture medium was tested on clone 1-13 of Balb/c-3T3 mouse cells (subclone C-14). Exposure period was 72 hours and incubation was continued for approximately 4 weeks. The number of foci of transformed cells was determined. The test material was relatively non-toxic at treatment doses below and above the solubility limit in culture medium (1,000 to 5,000 nl/ml) whether the assays were performed in plastic culture flasks or glass bottles. However, DIDP rapidly interacted with the plastic flasks and caused cracks in these vessels at concentration ≥ 20,000 nl/ml. Over the concentration range of 200 to 6,320 nl/ml in plastic flasks and 200 to 2,000 nl/ml in glass bottles, DIDP did not induce statistically significant increases in transforming activity. These ranges of treatments corresponded to approximately 26% to 90% and 51% to 74% survival in simultaneous colony survival assays, respectively. Therefore, DIDP was considered non-toxic and inactive in the BALB/c-3T3 *in vitro* transformation assay. This study was performed according to GLP procedures.

An *in vitro* mammalian cell transformation test (Microbiological Associates, 1981) was performed with the BALB/3T3 Clone A31 mouse embryo cells. Cells were treated for 20-24 hours and incubated 4-6 weeks. DIDP (99.9% purity) in acetone was tested in the absence of metabolic activation at doses of 0.01-0.1 and 1 µl/ml. Relative to the acetone negative control (normalised to 100%), the relative colony-forming efficiency of cells (RCE) exposed to various doses of DIDP ranged from approximately 82% - 91%. The induced transforming frequencies (TF) were not statistically significant at dose levels of 0.01 and 0.1 µl/ml; whereas DIDP at dose

of 1 µl/ml induced 9 type III morphologically transformed foci and relative to negative control, the induced transformation frequency was statistically significant. The negative control fulfilled the requirement for determination of a valid test (relative plating efficiency was greater than 15% of the negative control) as well as the positive MNNG one (N- methyl N'-nitro-N-nitrosoguanidine led to a statistically increased TF relative to negative control and induced 9 type II and 29 type III morphologically transformed foci). The criteria established for the test article was also satisfying: the relative survival of cells was greater than 40%. Therefore under these conditions, DIDP showed a transforming potential (level of transforming activity in 3T3 statistically significant).

One of two cell transformation tests is positive in Balb/3T3 cell line at the highest tested concentration, but those two assays were not conducted in the same experimental conditions. The positive result obtained in the latter cell-transformation test is in accordance with those of well-known peroxisome proliferators.

4.1.2.8.2 Carcinogenicity long-term study

No carcinogenicity long-term study is available for DIDP but an increase in incidence of hepatocellular tumours in rats related to peroxisome proliferation might be anticipated, in regard with the increased incidence in tumour liver cells observed with DEHP and DINP in carcinogenicity studies. Indeed, DINP and DIDP show comparable responses for peroxisome proliferation parameters at comparable dose levels (BIBRA, 1986). However, in response to peroxisome proliferators a marked species difference could be foreseen. The current literature reported that only rats and mice are responsive to the carcinogenic effects of peroxisome proliferators, while dogs, non-human primates and humans are essentially non-responsive or refractory (IARC, 1995; Doull, 1999).

Thus, there is no concern in regard with carcinogenicity. Indeed it is now well-accepted that peroxisome proliferation is specific to rodents. It has been established that peroxisome proliferators exhibit their pleitropic effects due to activation of PPARα and that PPARα is expressed only at low level in humans, explaining the absence of significant response in humans to the action of peroxisome proliferators.

4.1.2.9 Toxicity for reproduction

4.1.2.9.1 Effect on reproductive organs in repeated dose toxicity studies

Some limited information on fertility can be inferred from the 28-day and 90-day repeated dose toxicity studies in rats (BIBRA, 1986, Lake et al., 1991; BASF, 1969b). In these studies, DIDP shows no indication of toxic effect on reproductive organs. It should be noted that a number of testes fixation was conducted in formalin which is generally not considered as the optimal fixative for the testicular tissue. Furthermore the mode of fixation was not specified (immersion or perfusion) and very often the embedding is not specified. It is noteworthy that in a comparative study with DEHP (CMA (1984b) in the DEHP risk assessment report) a testicular atrophy was shown at 2.5% whereas no histological changes were observed with DIDP at the same dose level and under the same conditions.

4.1.2.9.2 Developmental toxicity and fertility

One-generation study in rats (Exxon Biomedical Sciences, 1997e)

A reproduction toxicity range finding study in rats (Exxon Biomedical Sciences, 1997e) was designed to provide general information in order to select dose levels for a two-generation study described underneath. Five groups of Crl:CDBR, VAF Plus rats (10 rats/sex/group) were administered daily in the diet DIDP (assumed 100% pure) at doses of 0 - 0,25 - 0,5 - 0,75 and 1%. P_1 males and females received the test material daily for at least 10 weeks prior to mating and during the mating period. Additionally, P_1 females received the test material during the gestation and postpartum periods, until weaning of the F_1 offspring on postpartum day (PPD) 21. During premating period (10 weeks), these concentrations were as follow: 132 - 264 mg/kg/d, 262 - 521 mg/kg/d, 414 –7 76 mg/kg/d and 542 - 1,014 mg/kg/d in the P_1 generation. During the gestation period, concentrations were most likely similar to week 10, i.e. the lowest of the two values mentioned above. During the postpartum period, mean measured dose rate most likely exceeded the week 10 premating values. Clinical inlife observations, bodyweight and food consumption were recorded for all P_1 animals at least weekly during the premating and mating periods, and for female on gestation day (GD) 0, 7, 14, 21, and on PPD 0, 4, 7, 10, 14, 21. Following birth, the offspring were counted and examined externally daily from postnatal day (PND) 0 to 21 and on PND 28. P_1 males were sacrificed at the end of the mating, while females were sacrificed following weaning of their litters on PPD 21. A gross necropsy was performed on all adults and on all animals which died during the study. A full macroscopic examination was performed on these animals. Organs were not weighed and microscopic evaluations were not performed. This study was conducted in compliance with the EPA GLP standards.

During premating period, signs of toxicity included statistically significant decrease body weight and body weight gain reduction in males at 0.75 and 1% doses. Food consumption was dose-related decreased, but the differences were statistically significant only during weeks 3 (8%), 5 (10%), 9(11%). In the females there were no biologically significant changes in mean body weight between treated and controls. There was statistically significant lower food consumption in the 0.5 (9%), 0.75 (8.5%) and 1% (15%) dose groups during week 7 and in 1% dose group during week 9 compared with controls.

Over the entire gestation period the mean body weight of the 1% dose females was lower than controls (14%) although the difference was not statistically significant. Dose-related decreases in mean food consumption, statistically significant, in the 1% dose group (17%) were observed.

Over the entire postpartum period, statistically significantly body weight reduction and/or body weight loss in the 0.75 and 1% dose females were observed. Dose-related decreases in mean food consumption statistically significant in the 0.5, 0.75, 1% dose groups were observed.

There were no gross postmortem findings and the majority of animals in all groups were free of observable abnormalities at post-mortem examination. There were single incidences of some abnormalities e.g. dilated renal pelves, anogenital staining, but due to the very low incidence, these findings were considered unrelated to the treatment.

There were no statistically differences in mean male mating, male fertility, female fertility, female fecundity, or gestational indices, or percentage of live/dead offspring, between treated and controls.

There were no statistically significant differences in mean offspring survival indices between treated and control animals, no treatment-related clinical findings. However in offspring the mean body weights were statistically significantly lower than controls from 0.5% in a dose-dependent manner. This effect was considered treatment-related. It should be noted that the body weight effect in the offspring in the 0.5% group was at least partially reversible as the pups in this group were not statistically different from controls at day 28.

From this preliminary study a NOAEL for systemic toxicity of 0.5% (about 262 mg/kg bw/d) can be assumed for parents and 0.25% (about 165 mg/kg bw/d) for offspring based on the decrease in body weight at higher doses. At the highest dose tested (1%), no effect was observed on fertility parameters.

Two-generation study in rats (Exxon Biomedical Sciences, 1997d)

In a two-generation study (Exxon Biomedical Sciences, 1997d), four groups of Crl:CDBR, VAF Plus rats (30 rats/sex/group) were administered daily in the diet DIDP (assumed 100% pure) at doses of 0-0.2-0.4 and 0.8%. The doses expressed in mg/kg bw/d are presented in **Table 4.26**. Doses were selected based on results from the previous study.

Table 4.26 Mean actual doses in the two-generation study (Exxon Biomedical Sciences, 1997d)

Concentration in diet	Mean actual dose in mg/kg bw/day during premating			
	P1 males	P1 females	P2 males	P2 females
0.2%	103-198	127-203	117-216	135-218
0.4%	211-405	253-416	229-437	273-433
0.8%	427-787	508-775	494-775	566-927
Concentration in diet	**Mean actual dose in mg/kg bw/day during gestation (G) and postpartum (PP) period**			
	P1 G	**P1 PP**	**P2 G**	**P2 PP**
0.2%	131-149	172-361	135-152	162-379
0.4%	262-287	359-734	262-297	334-761
0.8%	524-551	641-1582	574-611	637-1,424

P_1 males and females received test material daily for at least 10 weeks prior to mating and during the mating period. Additionally P_1 females received test material during the gestation and postpartum periods, until weaning of the F_1 (offspring of the P_1 generation) offspring on PPD 21. P_2 (F_1 generation animals chosen to mate) males were dosed from postnatal day (PND) 21 for at least 10 weeks prior to mating, through the mating period for F_2 (the offspring of the P_2 generation) litters, and until sacrificed. P_2 (F_1) females were dosed from PND 21 for at least 10 weeks prior to mating, during mating, gestation, postpartum and until they were sacrificed following weaning of the F_2 animals on PPD 21.

In addition to the 30 rats/sex/groups, satellite groups of 20 female rats each were treated with the control diet and the high-dose diet during the P_1 generation. Offspring from these animals were utilised in cross-fostering and switched diet experiments to determine if removal of exposure to DIDP would permit recovery from the expected body weight effects. Two groups of 20 males, fed either control or high-dose diets, served as mates for the satellite females.

In the cross fostering study, F_1 generation pups from 10 satellite group 1 (control) litters and 10 satellite group 4 (0,8%) litters were switched on PND 0. In the switched diet satellite study, all the surviving pups of the F_1 generation not selected for the P_2 generation were allowed to become adults. On PND 21, all pups from group 4 were fed control diet and the pups from group 1 were fed group 4 diet. These animals received switched diets for the duration of the P_2 premating period.

Clinical inlife observations, bodyweight and food consumption were recorded for all P_1 and P_2 animals at least weekly during the premating and mating periods, and for females on GD 0, 7, 14, 21, and on PPD 0, 4, 7, 10, 14, 21, and/or at least weekly until sacrificed. Following birth, the offspring were counted and examined externally daily from PND 0 to 21. Offspring were sexed and weighed on PND 0, 1, 4, 7, 14 and 21. Vaginal patency (opening) and preputial separation were evaluated for females and males selected for the second generation. A gross necropsy was performed on all adult animals, selected F_1 and F_2 neonates, and on all animals which died during the study. A full macroscopic examination was performed on these animals and selected organs and tissues were collected and weighed. Tissues from all reproductive organs as well as other key organs were examined microscopically. The right testis was preserved in Bouin's solution and stored in 70% ethyl alcohol. The testes were stained with periodic acid-Schiff hematoxylin.

In females, oestrus cycle length was calculated and the number of primordial oocytes was quantified for all control and high-dose animals. In males, gonadal function was evaluated by counting total cauda epididymal sperm, homogenisation resistant spermatids, and by assessing progressive sperm motility and sperm morphology in both P_1 and P_2 parental males.

This study was conducted in compliance with the EPA GLP standards.

Parental toxicity

Signs were limited to statistically significant reduction of body weight gain and/or decreased food consumption in P_1 and P_2 high-dose females during the postpartum period however there was no statistically significant difference in overall body weight gain during the postpartum period compared with controls and in the P_2 males during the premating period. The statistically significant reduction in body weight gain in the high-dose P_1 females during GD 0/7 interval was not considered biologically significant.

An increased incidence of dilated renal pelves in the high-dose male P_1 (9/30 versus 4/29 in control) was mentioned in post-mortem observations and histopathologically confirmed.

There were statistically significant increases in mean absolute and relative kidney weights in males from the low dose (P_1 and P_2 generations) with microscopic changes included accumulations of dark orange or eosinophilic granular cytoplasmic pigment in the cortical tubules and cortical tubular degeneration. In the high-dose P_1 and P_2 generation male rats there was an increase incidence of granular cast in the renal tubules (P_1: 14 versus 2 in controls). There were a few granular casts seen in the group 2 and 3 in P_2 generation male rats. There were also casts of similar type seen in the control P_1 generation male rats. It is hypothesised that these effects are consistent with male rat-specific nephropathy associated with accumulation of alpha 2u-globulin; but there were no differences in incidence or degree of severity of hyaline droplets in cortical tubules in P_1 or in P_2 generation compared to controls. However, hyaline droplets are somewhat difficult to detect with routine hematoxylin staining. Anyway histology was consistent with the hypothesis of male rat-specific nephropathy. Indeed, accumulation of protein droplets occurs rapidly, whereas long-term exposure results in additional histological changes. So, this

specific injury is characterised as follows: single cell degeneration and necrosis in the renal proximal tubule. Dead cells are sloughed into the lumen of the nephrons, and while moving through the nephrons contribute to the development of granular casts (IARC, 1999). This hypothesis is emphasised by the fact that no kidney damage was observed in females, no firm conclusion can be addressed, but a strong presumption may be assumed.

It is noticeable that in repeated-dose studies, no kidney damage has been observed, but only increase of kidney weight in male rats.

In females, increases of kidney weight were also observed from the mid dose (P_1) from the low dose (P_2) but no correlating histopathology was found.

In P_1 generation females but not in P_2 generation females, there was a dose-related increase in thick and/or discoloured stomach. Microscopic changes consisted of dilatation of mucosal glands in the stomach of female P_1 generation of all dosage groups and high dosage group P_2 generation female rats and mucosal erosions in the stomach of the mid and high-dose P_1 generation female rats.

There were statistically significant increases in the mean absolute and relative liver weights, from the mid dose (P_1) and from the low dose (P_2) in females, and from the low dose (P_1) and from the mid dose (P_2) in males, concurrently microscopic changes were observed and consisted of either centrolobular or diffuse hepatocellular hypertrophy. The affected hepatocytes were enlarged with an increased cytoplasmic eosinophilia, the incidence and severity of the effects increased in a dose-related manner.

There was an increased incidence of thymus atrophy in the high-dose female rats of both generations (P_1 and P_2) (28 versus 6 in controls; 15 versus 0 in controls, respectively). However, this is not considered to be treatment related. Thymus atrophy only occurs at high dose and is associated with body weight depletion. In this case, it is considered that atrophy of thymus is only stress induced (Greaves, 1990).

There were no statistically significant changes to be considered treatment-related in reproductive organ weights as well as in reproductive indices.

Offspring toxicity

There were dose-related decreases in the live birth and Day 4 survival indices (number of live pups at day $4 \cdot 100$/number of live pups at day 0) during the F_1 generation. Additionally, the high-dose group Live bBirth and Day 4 survival indices (94.2% and 88.8%, respectively were statistically significantly decreased compared with controls (98.7% and 93.9%, respectively) and outside the historical control range for this laboratory (cf. **Table 4.27**). In the F_2 offspring, reduced survival was again on day 1 and 4 in several groups. There were statistically significant decreases in the Day 1 and Day 4 survival indices in the high-dose (12% and 17%, respectively) mid-dose (7% and 8%, respectively) and low-dose (5% and 9%, respectively) compared with controls. The Day 7 survival and viability at weaning indices of the high-dose offspring were significantly reduced compared with controls (cf. **Table 4.28**).

Table 4.27 F1 offspring survival indices in the two-generation study

Group	Live birth%	Day 1 survival%	Day 4 survival%	Day 7 survival%	Day 14 survival%	Day 21 survival%	Viability at weaning%
0%	98.7	95.5 h)	93.9	97.8	95.5	100.0	93.4
0.2%	97.6	95.8 h)	93.0	100.0	100.0 **	100.0	100.0 **
0.4%	96.8	94.2 h)	91.5 h)	99.4	99.4 *	100.0	98.9 *
0.8%	94.2 ** h)	92.2 h)	88.8 * h)	98.0	98.4	100.0	96.4
Historical Control	95.2-99.2	96.2-100	92.8-99.7	92.8-100	93.7-100	98.8-100.	86.9-100

* Mean significantly different from control mean ($p \leq 0.05$)
** Mean significantly different from control mean ($p \leq 0.01$)
h) Outside historical control range of this laboratory

Table 4.28 F2 offspring survival indices in the two-generation study

Group	Live birth%	Day 1 survival%	Day 4 survival%	Day 7 survival%	Day 14 survival%	Day 21 survival%	Viability at weaning%
0%	98.5	96.6	94.0	99.3	99.3	100.0	98.7
0.2%	94.7 * h)	92.1 * h)	85.8 ** h)	100.0	100.0.	100.0	100.0
0.4%	98.2	89.6 ** h)	86.7 ** h)	99.3	98.5	100.0	97.8
0.8%	96.8	85.2 ** h)	77.6 ** h)	95.4 *	98.4	98.9	92.9 *
Historical Control	95.2-99.2	96.2-100	92.8-99.7	92.8-100	93.7-100	98.8-100.	86.9-100

* Mean significantly different from control mean ($p \leq 0.05$)
** Mean significantly different from control mean ($p \leq 0.01$)
h) Outside historical control range of this laboratory

It should be noted that no changes in live birth survival indices were reported in the reproduction toxicity range finding study in rats (Exxon Biomedical Sciences, 1997e). However in the two-generation study where the number of animals per group is higher, a decrease in live birth survival indices was observed in F_1 generation and confirmed in F_2 generation. It should be noted that in the follow-up two-generation reproduction toxicity study in rat (Exxon Biomedical Sciences, 2000) conducted at doses of 0, 0.02, 0.06, 0.2, 0.4% DIDP in diet, the decrease in pup survival was confirmed: a decrease in survival indices (day 1 and day 4) was observed at 0.2% and higher and no effect at the lower doses of 0.02% and 0.06%. In F_1 body weights of the high-dose male and female offspring were reduced on PDN 0 (4-6% lower than control); reduced body weight gain continued during the postnatal period (up to 23%) lower than controls, but recovered following weaning (0-7% on day 0 of P_2).

In F_2, body weights of the high-dose male and female offspring were reduced on PDN 0 (6-9% lower than control); reduced body weight gain continued during the postnatal period (up to 22% lower than controls)

In F_1 generation gross post mortem observation showed in one high-dose pup ectodactyly, microcardia and atrial enlargement, and another high-dose pup with multiple malformations including polysyndactyly, craniorachischisis, anencephaly, and protruding tongue. Due to their isolated incidence, all post-mortem observations were considered incidental and unrelated to treatment with the test material.

In F_2, four (out of 123) high-dose male offspring were noted with undescended testes at 21 days.

In F_1 generation, there were statistically significant increases in the mean relative liver weights of the high-dose males and females and mid-dose females compared with controls. In F_2 generation liver weight was not increased, whereas the histopathological observations were identical in F_1 and F_2 generations: hepatocytes were enlarged with an increased cytoplasmic eosinophilia in the mid and high-dose offspring.

There were in F_1 and F_2 high-dose offspring a significant decrease in mean absolute organ weights including reproductive organs and discussed in the next section "Effect on fertility".

Developmental landmarks have been studying in F_1 generation only. There were no statistically significant differences for preputial separation between treated and control males measured in F_1 offspring. The authors considered that the results were not meaningful because the frequency (weekly) of the evaluation was not sufficient to detect an effect. In the females, the mid (33.5 days) and high (34.2 days) dose groups exhibited a statistically significant later maturation for vaginal patency (opening) compared with controls (32.2 days).

Satellite studies

In the cross fostering satellite study, offspring born to high-dose dams and cross-fostered to control dams on PND 0 exhibited body weights which were not different from main study control offspring throughout the postnatal phase. Conversely, the mean body weights of the offspring cross-fostered to the high-dose dams were statistically significant lower (up to 19%) than the main study control offspring of both sexes on PND 14 and 21. This indicates that DIDP may be transferred through the milk but at a low level, evidenced by a low decrease of body weight; a statistical level of significance was obtained when lactation exposure effects and direct toxicity via feed (solid food is absorbed by pups from PND 14) were combined. Following weaning, these animals remained on control or high-dose diet corresponding with their cross-fostering treatment, for the second generation premating phase. The mean body weight of the offspring cross-fostered with high-dose dams continued to be statistically significant lower (9-11% males; 7-10% females) than the mean body weight of the offspring cross-fostered with control dams during premating. In parent equivalents (adult rats stemming from cross-fostered pups), during the premating period there were statistically significant increases in the mean absolute and relative kidney weights of the pups cross fostered with high-dose dams (an increase of respectively 16% and 30% in males, and respectively 9% and 22% in females) compared with pups cross-fostered with control dams. The same trend was observed for liver weights: the mean absolute and relative liver weight of the cross-fostered high-dose group was increased compared with the cross-fostered control group (an increase of respectively 11% and 23% in males and 22% and 35% in females). Pertaining to reproductive organ weight changes in males, mean absolute right and left testis weight of the cross-fostered high-dose group were statistically significantly decreased compared with the cross-fostered control group. Since, relative right and left testis and epididymis weights were increased, this effects is probably due to lower body weight. In females there was an increase of the uterus, right and left ovary weights, only statistically significant when expressed relative to body weights. In absence of histopathology, it could not be determined if changes in tissue structure and function occurred.

In the switched diet phase, weaning from high-dose animals was given control diet, while weaning from control animals was given high-dose diet. The high-dose offspring of both sexes switched to control diet displayed signs of recovery in body weight immediately after weaning and displayed normal growth patterns. However a trend toward lower body weight similar to the main study high-dose males was observed after day 42. The control offspring of both sexes

switched to high-dose diet displayed slight reduction of body weight gain as the study progressed, similar to the main study high-dose animals during the P_1 premating interval. In addition, in the switched diet high-dose P_2 equivalents (adult rats stemming from the switched-diet pups) there were statistically significant increases of the absolute and relative liver weights (an increase of respectively 36% and 34% in males, 31 and 39% in females) and kidney weights (an increase of 27% in males, respectively 15% and 23% in females), right and left testis and epididymis weights compared with the switched diet control P_2 equivalents. The increase of testicular weight observed in males might be related to transient hypothyroidism in early phases of development.

Results from the cross-fostering and switched diet satellite groups indicate that lactation exposure may participate to toxicity of DIDP.

Fertility assessment

In P_1 there were no statistically significant differences in male mating, male fertility, female fertility or female fecundity indices between treated and control animals. In P_2, there were statistically significant increases in male mating, male fertility, female fertility indices in the high-dose group compared with controls. Those indices were above historical control range. Mean days of gestation and mean litter size of the treated and control groups were essentially equivalent in P_1 and P_2. There were no statistically significant differences in the mean sex ratio of the treated offspring compared with controls in P_1 and P_2, except the statistically significant difference in the mean sex ratio M/F in the lowest P_2 dose offspring (41.7/58.3) compared with controls (54.3/45.7). The historical control range for males was 47.3-54.5.

There were some sporadic changes in reproductive organ weights (sporadic increase of right or left testis/epididymis weights in males and sporadic decrease of uterine and left ovary weights in females), but in the absence of correlating histopathology, correlating changes in sperm motility, morphology or cauda epididymal total, and/or a clear consistent pattern of response in both the left and right organs of a paired set, these differences were considered incidental and unrelated to treatment.

In P_1 and P_2 generations, there were no treatment-related microscopic changes in the reproductive organs of either sex (testis was preserved in Bouin's solution and stored in 70% ethyl alcohol).

In P_1 et P_2, there were no statistically significant differences in homogenisation resistant spermatid counts, total cauda sperm counts or progressive sperm motility between the treated and control males.

In P_1, there was a statistically significant decrease in mean percent normal sperm (sperm morphology evidenced by phase contrast microscopy) in all treated groups compared with controls. However, the decrease was not dose-dependent and there were no statistically significant differences in the male fertility index of the treated males compared with controls; in the P_2 generation no statistically significant differences were noted in sperm data. According to the laboratory, these small differences (< 1.4%) were considered incidental and not related to treatment with DIDP.

In P_1, there was a statistically significant decrease in oestrous cycle length in the high-dose females compared with controls. However, this decrease was small (< 6%), within the commonly reported oestrus cycle length of 4-5 days for the rat and did not affect mating or fecundity. Thus, this change was not considered biologically important. It is noteworthy that there were no changes in oestrous cycle length in the P_2 generation.

There were no statistically significant differences in mean oocyte counts between the control and high-dose females (P_1, P_2).

In F_1 and F_2 offspring, there were statistically significant decreases in mean absolute weights of left and right testes (about 25%) in the high-dose males, a concomitant decrease in body weights compared to controls (20-22%) was observed. In F_1 and F_2 there were no changes in relative testes weights thus decreases in mean absolute weights of testes may be attributed to low body weight of pups; no effect was observed in adult following continuous treatment. It should be noted that no histopathology examination has been conducted. In contrast, in absence of changes of body weight gains in pups, testicular damages evidenced by weight decrease and histopathological findings were observed at day-21 following maternal DEHP exposure during pregnancy and suckling at 3-3.5 and 30-35 mg/kg/d (Risk sssessment of DEHP, draft report, November 1998, Arcadi et al., 1998).

In F_2 only, there was statistically significant decrease in both absolute ovary weights in the high-dose offspring compared with controls, but in the absence of similar trend in the relative ovary weights, this decrease was considered as the result of the lower body weights of the high-dose offspring at study termination and not treatment related.

For parental systemic toxicity, based on minor liver changes from the lowest dose, no NOAEL can be determined and a LOAEL of 0.2% (103 to 361 mg/kg bw/d seeing that received doses are widely dependent on the period considered) can be assumed. No overt signs of reproductive toxicity were reported, therefore the NOAEL for parental reproduction toxicity may be considered as 0.8% the highest dose tested.

For offspring survival a decrease in survival indices (day 1 and day 4) from the lowest dose in F_2 generation leads to a LOAEL of 0.2%. For decrease of offspring body weight in F_1 and F_2 generations observed following maternal exposure to 0.8%, a NOAEL of 0.4% (253 to 761 mg/kg bw/d seeing that received doses are widely dependent on the period considered) can be assessed for developmental effects.

Follow up two-generation study in rats (Exxon Biomedical Sciences, 2000)

In the follow up two-generation study (Exxon Biomedical Sciences, 2000), five groups of Crl:CDBR, VAF Plus rats (30 rats/sex/group) were administered daily in the diet DIDP (assumed 100% pure) at doses of 0, 0.02, 0.06, 0.2 and 0.4%. The doses expressed in mg/kg bw/d are presented in **Table 4.29**.

Doses were selected based on results from the previous two generation study.

Table 4.29 Mean actual doses in the two-generation study (Exxon Biomedical Sciences, 2000)

Concentration in diet	Mean actual dose in mg/kg bw/day during premating			
	P1 males	P1 females	P2 males	P2 females
0.02%	12-23	14-20	11-26	14-25
0.06%	33-68	40-58	33-76	41-77
0.2%	114-225	139-191	114-254	137-266
0.4%	233-453	274-380	235-516	271-524
Concentration in diet	**Mean actual dose in mg/kg bw/day during gestation (G) and postpartum (PP) period**			
	P1 G	**P1 PP**	**P2 G**	**P2 PP**
0.02%	13-15	19-37	13-15	19-40
0.06%	39-43	57-112	38-44	52-114
0.2%	127-147	178-377	134-150	166-352
0.4%	254-295	356-744	256-284	356-747

P_1 males and females received test material/diet mixture daily for at least ten weeks prior to mating and during the mating period. Additionally, P_1 female animals received test material during the gestation and postpartum periods, until weaning of the F_1 offspring on Postpartum Day (PPD) 21. P_2 (F_1) males were dosed from Postnatal Day (PND) 21 for at least 10 weeks before mating, through the mating period for F_2 litters, and until sacrificed. The extra F_1 offspring that were not selected for the P_2 generation received test material from PND 21 until sacrificed after reaching vaginal patency or preputial separation.

P_2 (F_1) females were dosed from PND 21 for at least 10 weeks prior to mating, during mating, gestation, postpartum, and until they were sacrificed following weaning of the F_2 animals on PPD 21. The F_2 animals not selected for necropsy received the appropriate test substance/diet mixture until they were sacrificed after reaching vaginal patency (females) or until they were sacrificed on or after PND 56 (males).

Clinical inlife observations, body weight, and food consumption were recorded for all P_1 and P_2 animals at least weekly during the premating and mating periods. Clinical inlife observations and body weight were recorded for all P_1 and P_2 females on Gestation Days (GD) 0, 7, 14, and 21, and on PPD 0, 4, 7, 10, 14, and 21, and/or at least weekly until sacrificed. Food consumption was measured on the same schedule as body weights after Day 0 of each phase. Following their birth, the offspring were counted and examined externally daily from PND 0 to 21. Anogenital distance was measured on PND 0 and nipple retention was assessed on PND 13 or 14 for all offspring of both generations. Offspring were sexed and weighed on PND 0, 1, 4, 7, 14, and 21. Body weights and food consumption were measured on PND 28 and PND 35 for all F_1 animals where these days occurred prior to Day 1 of the P_2 generation. Vaginal patency or preputial separation as appropriate was evaluated for the F_1 animals selected for the P_2 selection pool, and for the F_2 animals not selected for the PND 21 necropsy. Body weights also were recorded for animals on the day vaginal patency or preputial separation occurred.

Each P_1/P_2 male was sacrificed following the end of mating of the satellite animals, while females were sacrificed following weaning of their litters on PPD 21. A gross necropsy was performed on all adult animals, selected F_1 and F_2 neonates (one/sex/litter), and on all animals that succumbed (not euthanised) during the study. A full macroscopic examination was

performed on these animals, liver and kidney weights were taken, and selected organs and tissues were collected. Histopathology was not performed.

This study was conducted in compliance with the EPA GLP standards.

Parental toxicity

In the P_1 generation, there were statistically significant increases in the mean absolute and relative liver weights of the 0.4% dose males (12% and 14%, respectively) and 0.4% dose females (12% and 13%, respectively) compared with controls. These increases were consistent with findings in the previously conducted two-generation reproductive study (Exxon Biomedical Sciences, 1997d), and related to the known capability of DIDP to cause peroxisome proliferation. There were statistically significant increases in mean absolute and relative kidney weights of the 0.4% males (14% and 18%, respectively). These increases were also consistent with findings in the previously conducted two-generation reproductive study (Exxon Biomedical Sciences, 1997d). There also was a statistically significant increase in the 0.4% female mean relative kidney weight (6%) compared with the controls.

In the P_2 generation, there were statistically significant increases in the mean absolute and relative liver weights of the 0.4% males (13% and 14%, respectively), 0.4% females (23% and 20%, respectively), and 0.2% females (17% and 9%, respectively) compared with controls. In the kidneys, there were statistically significant increases in mean absolute and relative weights of the 0.4% dose males (20% and 19%, respectively), and the 0.2% males (10% and 7%, respectively) compared with controls. There was a statistically significant increase in mean absolute kidney weight in the 0.2% females (13%) compared with controls.

There were no treatment-related deaths. There were no gross postmortem observations judged to be related directly to treatment with the test material. The majority of P_1 and P_2 animals throughout the groups were free of observable abnormalities at postmortem examination. In the females, there was an apparent dose-related increase in thick and/or discolored stomachs. This stomach irritation was attributed to ingestion of bedding materials since it was observed only in females and observed in all groups, including controls.

Notable postmortem observations in the P_2 animals surviving to termination were limited to an increased incidence (8/29) of dilated renal pelves in the 0.4% dose males compared with controls. Dilated renal pelves also were observed in the other treated groups (2-5/30), but the incidence generally was similar to controls (3/30). Dilated renal pelves also were noted in several females.

There were no statistically significant differences in the mean body weight between the treated and control males or females during the P_1 or P_2 generation, including the gestation and postpartum intervals.

Offspring toxicity

There were no biologically significant differences in F_1 survivorship between the treated and control offspring and all survival indices were within the historical control range for this laboratory. Statistically significant differences were limited to an increase in the live birth index of the 0.06% and 0.4% dose groups compared with controls. These increases were not considered biologically important (cf. **Table 4.30**).

Table 4.30 F1 offspring survival indices in the two-generation study (Exxon Biomedical Sciences, 2000)

Group	Live birth%	Day 1 survival%	Day 4 survival%	Day 7 survival%	Day 14 survival%	Day 21 survival%	Viability at weaning%
0%	96.6	97.8	96.2	99.5	100.0	100.0	99.5
0.02%	98.5	98.5	97.8	100.0	99.5	99.5	99.0
0.06%	99.2 *	98.4	95.9	99.5	100.0	100.0	99.5
0.2%	95.8	95.9	95.3	100.0	100.0	100.0	100.0
0.4%	99.2 *	97.7	96.9	99.5	100.0	100.0	99.5
Historical Control	95.2-99.2	96.2-100.0	92.8-99.7	92.8-100	93.7-100	98.8-100.0	86.9–100

* significantly different from control mean ($p \leq 0.05$)

Table 4.31 F2 offspring survival indices in the two-generation study (Exxon Biomedical Sciences, 2000)

Group	Live birth%	Day 1 survival%	Day 4 survival%	Day 7 survival%	Day 14 survival%	Day 21 survival%	Viability at weaning%
0%	97.7	99.0	97.7	98.5	95.4	100.0	94.0
0.02%	98.7	98.4	96.8	99.0	99.5 *	100.0	98.5
0.06%	97.4	97.4	96.6	99.0	100.0 *	99.5	98.5
0.2%	99.4	95.2 ** h)	92.3 ** h)	98.8	98.8	98.7 h)	96.3
0.4%	95.5	89.1 ** h)	84.8 ** h)	99.0	98.5	98.5	96.0
Historical Control	95.2-99.2	96.2-100.0	92.8-99.7	92.8-100.0	93.7-100.0	98.8-100.0	86.9-100.0

* Mean significantly different from control mean ($p \leq 0.05$)
** Mean significantly different from control mean ($p \leq 0.01$)
h) Outside historical control range of this laboratory

In the F_2 generation, there was a dose-related decrease in the Day 1 and Day 4 survival indices, with statistically significant decreases being observed in the 0.2% dose group (4% and 10%, respectively) and 0.4% dose group (6% and 13%, respectively) compared with controls. These values were outside the historical control range of this laboratory and were considered treatment-related. These results were consistent with the decreased F_2 survivorship in the previous two-generation study (Exxon Biomedical Sciences, 1997d).

There were no statistically significant differences between the control and treated animals for post-implantation loss. The live birth index for the 0.2% dose group was higher than the historical control and this was not considered biologically important. There were statistically significant increases in Day 14 and viability at weaning indices of the 0.02% and 0.06% dose groups compared with controls. These increases were not considered biologically important. The Day 21 survival indices of the 0.2% and 0.4% dose groups were marginally outside the historical control range for this laboratory, but not statistically significantly different from the control. No biological importance was assigned to these observations (cf. **Table 4.31**).

In the F_1 offspring, there were no statistically significant differences in mean body weights between treated and control animals of either sex up to PND 21 nor statistically significant differences in mean body weight or mean food consumption between treated and control offspring of either sex during the two-week postweaning measurements.

In the F_2 offspring, there were statistically significant lower mean body weights in the 0.4% males on PND 14, the 0.4% females on PND 14 and 21 and the 0.2% females on PND 14 compared with controls. Although, these weights were within the historical control range of the laboratory, these may have been a treatment-related effect. There also was a statistically significant increase in the 0.02% male mean body weight on PND 21. This increase was not considered biologically important. Mean postweaning body weights were significantly decreased compared to controls in the 0.4% dose males during PNDs 28 and 35, and in the 0.2% dose males at PND35 only. At PNDs 42, 49, and 56, an apparent recovery occurred in the 0.2% and 0.4% treated males and their mean body weights were no longer statistically different from controls. There were no statistically significant differences in postweaning body weights between treated and control females on PND 28.

There were no treatment-related clinical signs observed in the F_1 or F_2 offspring of any group and the majority of offspring in all groups were free of observable abnormalities from PND 0-21 and during the post weaning periods. However, there was an increased incidence of cannibalisation of F_2 pups at PND 1 or 2, not sporadically but a few P_2 females in the 0.2 and 0.4% groups were specifically concerned (for instance in the 0.4% treated group one female cannibalised all its litter, e.g. 10 pups/10).

In general, there were no gross postmortem observations in the F_1 or F_2 offspring judged to be related to treatment with the test material. The majority of animals selected for necropsy were free of observable abnormalities at the scheduled terminal sacrifice on PND 21. The majority of animals that died prior to weaning (GD 22 - PND 21) also were free of observable abnormalities.

In the F_1 generation, there were no statistically significant differences in mean absolute or relative organ weights (kidney or liver) between treated and control animals of either sex.

In the F_2 generation, there were no statistically significant differences in mean absolute or relative organ weights (kidney or liver) between treated and control animals of either sex with the exception of the 0.4% dose group female mean relative liver weight. There was a statistically significant increase in the mean relative liver weight of the 0.4% dose group females compared with controls. In the absence of a similar trend in the respective absolute liver weight, this single difference was considered the result of the lower mean body weights of the 0.4% females at study termination and not treatment-related.

There were no statistically significant differences in F_1 or F_2 offspring mean PND 0 anogenital distance between treated and control animals of either sex. Nipple retention was similar between treated and control offspring of both sexes: the majority of females in all groups had six nipples retained on PND 13/14, while all males in all groups had zero.

In the F_1 animals, there were no statistically significant differences in age or weight at preputial separation between treated and control male offspring. There were no statistically significant differences in age or weight at vaginal patency between treated and control female offspring.

In the F_2 animals, there was a statistically significant delay in preputial separation for the 0.4% males when compared to the control male offspring. This delay was small (1.2 days) and preputial separation was still included within the historical data of CD-rats (Bates et al., in Developmental Toxicology Handbook, 1997). There were no statistically significant differences in the mean body weight at which preputial separation occurred between treated and control male offspring. There were no statistically significant differences for age of vaginal patency between treated and control female offspring. However, there was a statistically significant decrease in the mean body weight at the time that the 0.4% females achieved vaginal patency

compared with the control female offspring. This decrease was small (6%) and not considered biologically significant.

Fertility assessment

There were no statistically significant differences in male mating, male fertility, female fertility, female fecundity, or female gestational indices between treated and control animals in the P_1 or P_2 generation. Mean days of gestation and mean litter size and of the treated and control groups were similar. There were no statistically significant differences in the mean sex ratio of the treated offspring compared with controls.

For parental systemic toxicity, based on liver and kidney changes in the P_2 males a NOAEL (0.06%) can be determined (33 to 76 mg/kg bw/d, seeing that received doses are widely dependent on the period considered). Up to the highest dose tested no overt signs of reproductive toxicity were reported and no effect was observed on fertility parameters.

For offspring toxicity, a decrease in survival indices (day 1 and day 4) in F_2 generation leads to a NOAEL of 0.06% (33 mg/kg bw/d, lowest estimated dose for 0.06% DIDP in diet). No effect was observed on development landmarks assessed at any dose tested.

4.1.2.9.3 Developmental toxicity studies

Rats

(Exxon Biomedical Sciences, 1995b; Nikiforov et al., 1995; Waterman et al., 1999)

In a developmental toxicity study, DIDP was administered orally in corn oil at doses of 0, 100, 500 and 1,000 mg/kg/d on days 6-15 of gestation in Crl: CDBR female rats was performed. Twenty-five females (9-week-old) per group were dosed daily and checked for clinical symptoms, food consumption and weight were recorded on gestational days (GD) 0-6-9-12-21. Each animal was sacrificed on GD 21, observed for gross pathologies, uterine weights with ovaries attached were measured, uterine contents were examined and the uterine implantation data were recorded. All live foetuses were weighed, sexed and examined externally for gross malformations. Half of the foetuses were examined for head and visceral abnormalities and the remaining were checked for skeletal malformations and ossification variations. This study was performed according GLP standards.

Maternal effects: all dams survived, no clinical signs were observed during gestation and the majority of dams were free of observable abnormality. At the highest dose level (1,000 mg/kg/d) there was a statistically significant decrease in body weight gain (76 g versus 87 g in control group) and in the mean food consumption during the treatment period GD 6-15. However, mean body weight and mean food consumption of all treated group females were essentially equivalent for the overall gestation period (GD 0-21).

Developmental effects: There were no significant differences in mean fœtal body weight and no statistically significant increases in total or individual external, visceral or skeletal malformations in the treated group when compared with controls. The only visceral variation observed was a single incidence of dilated renal pelves in the mid group. Three controls, one low-dose, three mid-dose, and six high-dose foetuses were stunted. Those observations were considered incidental and unrelated to treatment.

There was a dose-related increase in total foetuses with skeletal variations on both a per fœtus basis (38/196, 35/177, 61/193, 123/196) and a per litter basis (18/25, 17/22, 20/24, 23/24) at a dose of 0-100-500-1,000 mg/kg, respectively. When compared with controls, rudimentary lumbar ribs and cervical ribs were dose-related significantly increased ($p < 0.01$) in the mid and high-dose groups on a per fœtus basis (21%, 52% versus 8.2% in control group and 6.2%, 9.2% versus 1% in control group, respectively; the historical control ranges are 3.7-21.6% and 0.54-4.0%, respectively) and in the high-dose group on a per litter basis (23/24 vs. 10/24 for rudimentary lumbar ribs and 10/24 vs. 2/25 for rudimentary cervical ribs). It is currently admitted that the litter is the preferred unit for developmental toxicity study, in order to avoid exaggeration of the level of significance (Kimmel et al., 1994). Therefore only the effects observed at 1,000 mg/kg/d are considered to set a NOAEL.

The NOAEL for the dams is 500 mg/kg/d; this is the most conservative value, since the maternal toxicity at the higher dose level (1,000 mg/kg/d) is not very significant (decrease in body weight gain is transient and recovery is observed after the end of the treatment). The NOAEL for the conceptus can be assumed to be 500 mg/kg/d based significant increase of skeletal variation on a per litter basis at the high dose of 1,000 mg/kg/d.

(BASF, 1995; Hellwig et al., 1997)

In a screening test (BASF, 1995; Hellwig et al., 1997) performed to assess the prenatal toxicity of DIDP (99.9% purity), 7 to 10 pregnant Wistar rats (Chbb: THOM) were administered daily by gavage at doses of 0, 40, 200 and 1,000 mg/kg/d in olive oil, on day 6 through day 15 post coitum (p.c.). Animals were examined at least once a day for clinical symptoms, evaluation of body weight and food consumption was performed on day 0-1-3-6-8-10-13-15-17-20 p.c. All females were sacrificed at day 20 p.c. and assessed for gross pathology (including determinations of liver and kidney). The foetuses were removed from the uterus, sexed, weighed and further investigations for any external, soft tissue and/or skeletal finding were made.

At 1,000 mg/kg/d, food consumption was slightly but statistically significantly decreased within the first days of the treatment period (day 8-10 p.c.). No body weight change was observed concurrently. Three dams showed vaginal haemorrhage and two showed urine smeared fur during the last days of the treatment period (day 12-15 p.c.). These findings were considered to be treatment-related. Absolute and relative liver weights were also increased.

The substance-related fœtal effect was the following:

- dilatation of the right ventricle of the heart in one fœtus of the high-dose group; this finding is considered as being of spontaneous nature (historical control: 0.02%).
- soft tissue variations: dilated renal pelvis was detected at a higher incidence than in control (26, 33, 22% of fœtal incidence from 40 to 1,000 mg/kg/d versus 6.3% in control group) and outside the historical control range (20.3%). Hydroureter occurred exclusively in the treated group (5.7, 12, 12% of fœtal incidence at 40, 200, 1,000 mg/kg/d, respectively) and outside the historical control range (5.2%). However, there was no significant difference in incidence of hydroureter and dilated renal pelvis on a per litter basis. Moreover a clear dose-effect relationship could not be established for hydroureter (38, 43 and 30% at 40, 200, 1,000 mg/kg/d) and even if it cannot be excluded that it was treatment related, its pathogenicity is uncertain. Several studies provided the evidence that dilatation of the fœtal renal pelvis may be transient and considered as delay in renal development, unlike others who showed no reversal with further development (Kimmel et al., 1994). Besides it was suggested that only postnatal examinations (neonatal rats compared to rats at weaning)

would improve interpretation of the biological significance of dilated renal pelvis (Kavlock et al., 1988). It should be noticed that no renal effect was observed in pups of the two-generation study (Exxon Biomedical Sciences, 1997d). Various malformations of the sternum and the vertebral column were observed but no clear dose-response relationship and no clear difference from control can be established.

- skeletal variations: occurrence of supernumerary ribs (rudimentary cervical and /or 14^{th} ribs) was statistically distinctly increased at 1,000 mg/kg/d on a per litter basis (8/10 vs. 1/10 for surnumerary 14^{th} rib and 6/10 vs. 1/10 for rudimentary cervical ribs).

The study was conducted in accordance with GLP principles.

Administration of 1,000 mg/kg bw/d DIDP to dam rats resulted in increase of liver weight (maternal toxicity is not very marked at this dose) and in significant skeletal variations in foetuses, soft tissue (hydroureter) variations are also observed. Thus a NOAEL of 200 mg/kg can be estimated for fœtus and dams.

This study was conducted also on DEHP and it was reported at 1,000 mg/kg/d a pronounced postimplantation loss, a reduction of numbers of live foetuses per dam and a decrease of mean fœtal body weights. Moreover, DEHP was clearly considered as teratogenic in regard with various malformations not only variations observed at the high-dose of 1,000 mg/kg/d: the rate of malformed foetuses/litter was 70.1%, corresponding to 76% on a per fœtus basis and 100% on a per litter one (Hellwig et al., 1997).

The results of these developmental toxicity studies indicate that DIDP produced slight and transient signs of maternal toxicity at 1,000 mg/kg/d (significant reversible decrease of body weight gain and food consumption) suggesting a conservative NOAEL of 500 mg/kg/d for maternal toxicity.

There was no evidence of severe developmental toxicity only significantly increases of skeletal variations (supernumerary cervical and rudimentary lumbar ribs) on a per litter basis at the high dose. Rudimentary ribs are a common findings in rat foetuses, and should not be regarded as or associated with malformations, but may only be related to transient maternal stress. It should be noticed that supernumerary ribs were located in the cervical region which is less common (Waterman et al., 1999), but the biological significance of cervical supernumerary ribs remains uncertain.

A NOAEL of 500 mg/kg/d may be assumed for skeletal variations.

Mice

An abbreviated developmental toxicity assay (Harding, 1987) according to Chernoff and Kavlock was performed on 60 chemicals by different laboratories. DIDP was tested by Hazleton Laboratories America. Fifty pregnant CD1 mice were dosed orally with 10 ml DIDP undiluted (e.g. 9,650 mg/kg/d) on gestation day 6-13 and were allowed to deliver litters. Litter size, birth weight, neonatal growth and survival to postnatal day 3 were recorded as indices of potential development toxicity. Clinical signs were checked twice daily except on GD 14-17. Females that failed to deliver a litter by the presumed GD 22 were killed and uteri were examined. Neither live nor dead pups were systematically examined for malformations and after weighing on postnatal day 3, dams and pups were discarded. There was no maternal death, no effect on maternal weight, no modification of viable litters compared with controls, no neonatal response changes: live born/litter, survival percentage, birth weight and weight gain of the pups were not affected. DEHP tested concurrently gives rise to decrease in viable litters.

In this preliminary study, conducted with 9,650 mg/kg/d of DIDP in the mouse, no adverse effect was observed. This test was drawn for screening purpose and the negative result does not anticipate an absence of developmental toxicity.

Additional data

In vitro studies

Effects of four phthalate esters, i.e. DEHP, di(2-butoxyethyl) phthalate, DMP and DIDP, were assessed in chick embryos grown *in ovo* and *in vitro* as well as in cultured chick embryonic cells (Lee et al., 1974). Undiluted phthalate esters showed a lethal effect (63% with DIDP versus 18% in controls) on 3-day old embryos *in ovo* but no gross malformations. Undiluted phthalate esters tested on explanted streak stage chick embryos led to lethality in treated embryos significantly higher than that in the controls. Chick Ringer's solution saturated with phthalate esters tested on the development of 3-day-old embryos *in ovo* showed a high death rate and many embryos surviving the first two days died shortly before hatching. In hatched chicks the most common anomaly was twisting or "clubbing" of one or both feet. On explanted streak stage chick embryos of DIDP (0.05 mg/ml) effect on development were comparable to those of 0.05 mg/ml DMP. In all malformed embryos, the brain and neural tube remained either open throughout their length or partially open. Somite formation was often affected. On cultured chick embryonic cells, 0,05 mg/ml DIDP for 10 hours resulted in morphological alterations similar to those in 0.1-0.5 mg/ml DMP treated cells: retraction of protoplasmic processes, formation of additional cytoplasmic vacuoles; cells rounded and numerous sudanophilic granules scattered throughout the cytoplasm after 19 hours of treatment.

4.1.2.9.4 Summary of toxicity for reproduction

In 42-44 day year old (pubertal) or adult rats there is no indication of organ reproductive effects evidenced by histological observation in repeated dose toxicity studies and the two-generation study. In the two-generation study decrease in mean percent normal sperm was observed but of low incidence and only in P_1 generation. In pups (F_1, F_2 and in the cross fostering satellite group) decrease in testes weight and cryptorchidism in F_2 high-dose offspring were observed likely due to the low body weight since no histopathological damages were observed in adult testes. There were no changes in Reproductive Indices. From those assays no adverse effects on fertility may be anticipated.

In regard with reproductive toxicity DIDP is a developmental toxicant since decrease in survival indices was observed consistently in both two-generation studies (Exxon Biomedical Sciences, 1997b; 2000) leading to the NOAEL of 0.06% (Exxon Biomedical Sciences, 2000). The NOAEL of 0.06% (33 mg/kg/d DIDP) is taken into account in the risk characterisation.

In regard with developmental effects, skeletal variations are observed in the developmental studies at 1,000 mg/kg/d concurrently with slight signs of maternal toxicity and lead to a NOAEL of 500 mg/kg/d; in the two-generation rat study (Exxon Biomedical Sciences, 1997b) body weight decrease was observed in offspring partly related to lactation at the highest dose of 0.8% and leads to a NOAEL of 0.4% (253 to 761 mg/kg/d seeing that received doses are widely dependent on the period considered). Those NOAELs are considered for risk characterisation.

No effects were seen on fertility thus no classification according to the EU is needed. With regard to development decrease in survival indices mainly in F_2 (day 1 and day 4) in the

two-generation study as well as skeletal variations in developmental studies are not severe enough to justify a classification.

4.1.2.10 Additional studies

Endocrine disrupter effects

A series of phthalate esters, including DINP and DIDP provided by Exxon, at a 99.9% purity, were screened for estrogenic activity using a recombinant yeast screen (Harris et al., 1997). 4-Nonylphenol, bisphenol A, o,p-DDT and genistein were used in order to demonstrate the activity and potency of some known xenooestrogens. In the recombinant yeast screen a gene for a human oestrogen receptor has been integrated into the main yeast genome and was expressed in a form capable of binding to oestrogen response elements and controlling the expression of the reporter gene *lac-Z* (when receptor is activated, the *lac-Z* is expressed).

These chemicals were tested at concentration ranging from 10^{-3} M to $5 \cdot 10^{-7}$ M compared to 17β-estradiol. Of the six major volume use phthalates, three possessed a very weak estrogenic activity (BBP, DBP and DIBP), two did not (DEHP and DIDP) and one (DINP) behaved unreproducibly in the yeast screen.

A selection of these, including DINP and DIDP, was also tested for their ability to stimulate proliferation of human breast cancer cells (MCF -7 and ZR -75 cells). The results were mostly comparable to those obtained from the yeast screen. However, in the ZR -75 cells, DINP at 10^{-5}, $10^{-6}$and 10^{-7} M induced proliferation to a significantly greater extent than the control, which is in contrast to the findings for this chemical using the yeast screen. All other results were consistent with those obtained using the yeast assay and DEHP and DIDP showed relatively little activity. It should be noted that those *in vitro* assays have investigated one mechanism of action only, that is the ability of phthalates to act as oestrogen agonists.

In order to investigate their estrogenic activity, 8 phthalate esters including DEHP (99% purity), DINP (99.8% purity from Exxon) and DIDP (99.6% purity) were tested in a complementary battery of mechanistically-based *in vitro* and *in vivo* assays (Zacharewski et al., 1999).

In vitro all phthalate esters were examined in the following assays:

- Competitive ligand binding assays: the ability of chemicals to compete with [^{3}H]-E2 for binding to the rat uterine estrogen receptor was investigated 1-1,000 μM of phthalate esters was tested. None of the three phthalate esters effectively competed with [^{3}H]-E2 for binding to the rat uterine estrogen receptor at the concentration tested.
- Transfection and gene transcription assays: the ability of chemicals to induce reporter gene expression in recombinant receptor/reporter gene assays was investigated. MCF-7 human breast cancer estrogen receptor positive cells or HeLa human cervical carcinoma cells transfected with the Gal4-human ER chimera (Gal4-HEGO) and the Gal4-regulated luciferase reporter gene (17m5-G-Luc) were exposed to final concentrations of 0.1, 1, 10 μM of phthalate esters. None of the three phthalate esters exhibited a significant response at the concentrations tested.
- Estrogen receptor-mediated growth of yeast assay: the *Saccharomyces cerevisiae* strain PL 3, transformed with the human estrogen receptor cDNA, was used to examine the ability of phthalate esters to induce estrogen receptor-mediated growth on selective media. None of

the three phthalate esters exhibited estrogen receptor-mediated growth at the tested concentration of 10 μM.

In vivo in the following assays:

- Uterotrophic assay/vaginal cell cornification assay: 20, 200, 2,000 mg/kg/d of the three phthalate esters were administered by oral gavage once daily for a period of 4 days to ovariectomised Sprague-Dawley rats (10 females per dose, two experiments). Ethynyl Estradiol (EE) was used as a positive control. Body weight, uterine wet weight and percentage of vaginal epithelial cell cornification on each day were assessed. Statistically significant decreases in body weight were observed following treatment with DEHP, however these effects were not dose-dependant. In contrast statistically significant increases in body weight were observed with DIDP and DINP in experiment one only.

None of the phthalate esters tested had a reproducible, dose-dependant effect on uterine wet weight relative to vehicle control at any of the dose tested as indicated in **Table 4.32**. Because of the variability of the responses, the value of this test questionable, but in any case, the test is considered negative. None of the phthalate esters tested significantly induced a vaginal cornification response at any of the dose tested.

Table 4.32 Effects of phthalate esters on uterine weight in ovariectomised Sprague-Dawley rats

Treatment	Dose [a] mg/kg	Uterine wet Wt (mg) mean ± SD		Uterine wet Wt (mg/100 g bw) mean ± SD	
		Exp. 1	Exp. 2	Exp. 1	Exp. 2
Sesame	0	13 ± 1	24 ± 6	12 ± 1	0.1 ± 5
EE	1	88 ± 15 **	105± 17 **	85 ± 13	92 ± 14 **
DEHP	20	15 ± 2	22 ± 5	14 ± 2	0.1 ± 4
	200	15 ± 2	17 ± 4 *	14 ± 2	14 ± 3 *
	2,000	20 ± 10	16 ± 4 **	19 ± 10*	13 ± 7 **
Sesame	0	13 ± 1	51 ± 55	12 ± 1	40 ± 46
EE	1 (8) [b]	88 ± 15 **	114± 20 **	85 ± 13	98 ± 16 **
DINP	20	16 ± 3	29 ± 5	14 ± 2	22 ± 4
	200 (9) [b]	14 ± 3	33 ± 5	11 ± 2	24 ±7
	2,000	13 ± 2	20 ± 3 **	11 ± 2*	15 ± 2 **
Sesame	0 (9) [b]	15 ± 3	21 ± 7	14 ± 3	14 ± 5
EE	1 (9) [b]	73 ± 18 **	114± 11 **	73 ± 17**	87 ± 11
DIDP	20	14 ± 2	23 ± 3	12 ± 2	16 ± 2
	200	16 ± 2	28 ± 10	13 ± 1	0.1 ± 6
	2,000	14 ± 2	18 ± 4	11 ± 1*	12 ± 2

a) Ten animals were used per treatment group. However, note that during the course of the experiment some animals died and therefore were not included in the calculation of the mean and standard deviation.
b) Data from animals used in experiment 2 found to possess ovarian stubs were not included in the data set. The number in the brackets indicates the number of animals used to determine the mean ± standard deviation.
* statistically significant difference from control at $p < 0.05$
** statistically significant difference from control at $p < 0.01$

In summary, *in vitro*, DEHP, DINP and DIDP show no activity in assays to test the ability of binding to rodent or human estrogen receptors or to induce estrogen receptors-mediated gene expression. These substances are not able to stimulate cell proliferation, except DINP (this result is not consistent with others, neither with those of its close congeners). *In vivo*, response

obtained with uterine wet weight assay does not allow drawing a firm conclusion but suggests a negative trend. Results of vaginal epithelial cell cornification assay also exhibit an absence of estrogen receptors-mediated estrogenic activity. It should be noticed that those different assays have investigated one mechanism of action only, that is the potential estrogen activity of phthalates and not antiandrogenic effects.

Pertaining to antiandrogenic activity, investigation on possible mechanisms of endocrine disruption are currently ongoing by investigating *in vitro* androgen-receptor binding for a number of phthalates and an adipate including DBP, DEHP, DIDP, DINP, DEHA and DNOP.

In the first two-generation study (Exxon Biomedical Sciences, 1997d), some alterations in male reproductive development might be indicative of a tendency for disturbance of male sexual differentiation through an endocrine-mediated mechanism: sex ratio (male/female) change but only at the lowest dose in P_2 (41.7/58.3% in treated versus 54.3/45.7% in controls), decreases of absolute but not relative testes weight in F_1 and F_2 offspring, cryptorchidism (3.25%) which usually occurred at a lower incidence (0.251%) but delay in body weight gain is considered responsible of the two later effects. In the two-generation study, there were no statistically significant differences for preputial separation between treated and control male measured in F_1 offspring. In the new two-generation DIDP study in rats (Exxon Biomedical Sciences, 2000), there were also no significant differences in developmental landmarks (measurements of anogenital distance, nipple retention and preputial separation for the F_1 and F_2 offspring): no differences were noted in nipple retention and preputial separation for F_1 and F_2 males pups at any dose level (up to 0.4%), no statistically significant differences in age or weight at vaginal patency between treated and control female offspring, nor statistically significant differences in mean PND 0 anogenital distance of F_1 or F_2 offspring between treated and control animals of either sex.

4.1.3 Risk characterisation

4.1.3.1 General aspects

Only few significant human data are available, so the assessment of the hazardous properties of DIDP is based mainly on animal data.

Investigations on toxicokinetic and metabolism behaviour in rats are available by oral, inhalation and dermal route: a significant amount of DIDP (at least 50%) is readily absorbed via the gastro-intestinal tract. Via inhalation, an absorption of 75% may be assumed. By dermal route, absorption is very low in animals and still lower in humans based on *in vitro* or *in vivo* skin penetration studies with various phthalates like DEHP and DINP.

Following absorption, DIDP is rapidly eliminated and not accumulated. In urine, only metabolites are eliminated after oral administration. The data on end products indicate a cleavage to the monoester and an alcohol moiety. The oxidative monoester derivative and phthalic acid are also detected.

Results from a two-generation study (Exxon Biomedical Sciences, 1997d) suggest that DIDP might be transferred through the milk at a low level when dams are exposed by oral route. Such a transfer has been evoked also for DEHP.

DIDP has a low acute oral, dermal and inhalation toxicity.

Animal studies have shown a slight irritation on skin and eye. In humans, there is no indication of irritation. No indication of upper airways irritation is reported following acute inhalation exposure in animals, and there are no reported effects in humans. Therefore it may be anticipated that DIDP does not induce respiratory irritation.

One study (Exxon Biomedical Sciences, 1992) conducted according to Buehler gives a clear positive response. Two other studies, conducted either according to Buehler (Huntington Research Center, 1994) or to Magnusson and Kligman (Inveresk Research International, 1981), give negative results with some weaknesses in the protocol. Data on humans provide weak evidence that DIDP may cause sensitisation (negative patch tests and only one case of dermatitis reported). Moreover sensitising properties have not been demonstrated with any of the phthalates. Therefore, a low sensitising potential can be anticipated despite confusing results in Buehler tests.

The target organ for oral, sub-acute and sub-chronic DIDP toxicity in rats appears to be the liver (increased liver weight and significant changes in liver peroxisome proliferator enzyme activities). It is clear that NOAELs derived from rat studies are related to peroxisome proliferation liver effects, which are generally considered to be species-specific. Humans are very likely far less sensitive than rats.

A NOAEL of 15 mg/kg/d was identified in a 90-day oral study in dogs (Hazleton Laboratories, 1968b), based on liver weight increase accompanied by swollen and vacuolated hepatocytes at higher doses. It is proposed to use this result in the risk characterisation because the dog appears to be a more relevant species for human risk assessment with respect to peroxisome proliferation. However, the poor reliability of the study should be stressed. For this reason, it seems also important to consider the NOAEL of 60 mg/kg/d set up in rat and based on very slight effect consisting of dose-related increase of relative liver weights in females from the LOAEL

(1,600 ppm) in a 3-month study (BASF, 1969b); in male rats, the NOAEL is higher, 200 mg/kg/d (3,200 ppm).

The kidney was also reported as a target organ for phthalates. In the available repeated dose toxicity studies in rats with DIDP, only relative kidney weight was increased in males from 55 mg/kg/d with no concurrent histopathological changes. In a two-generation study, increase in absolute and relative kidney weight with microscopic changes was observed in P_1 males from 103 mg/kg/d. These findings seem consistent with male rat specific nephropathy and relevance for human health is questionable.

A NOAEL of 0.5 mg/l was assessed for systemic toxicity in a 2-week inhalation rat study with limitation (absence of haematological and biochemical parameters) (General Motors Research Laboratories, 1981). The significance of this result is considered too limited for risk assessment.

No study involving repeated dermal exposure has been conducted.

There is no evidence of genotoxic potential of DIDP. The positive result obtained in cell transformation test in BALB/3T3 cell line is consistent with those of well-known peroxisome proliferators.

No carcinogenicity long-term study is available for DIDP. However DIDP is not mutagenic and DINP and DIDP showed comparable responses for peroxisome proliferation parameters at comparable dose levels (BIBRA, 1986). Thus, it can be assumed that hepatocellular tumours related to a peroxisome proliferator mechanism could also occur following long-term exposure to DIDP.

Species difference in response to peroxisome proliferators has been admitted: the current literature reports that only rats and mice are responsive to the carcinogenic effects of peroxisome proliferators, while dogs, non-human primates and humans are essentially non-responsive or refractory. It should be noted that recently IARC gave a ruling on the carcinogenicity of DEHP and concluded that the mechanism (peroxisome proliferation and PPARα activation), by which DEHP increased the incidence of liver tumours in rodents, was not relevant to humans.

For the risk characterisation, on the hypothesis that liver tumours would likely occur as a consequence of peroxisome proliferation and given that DIDP and DINP show comparable responses to peroxisome proliferation, the NOAEL of 112 mg/kg/d determined for increased liver neoplasia in mice in a DINP 2-year chronic / carcinogenicity study (Aristech, 1995) may be used for DIDP since no carcinogenicity study is available.

Therefore the carcinogenic potential of DIDP (and a possible classification) should be discussed in a more general context on the mechanism of action of the peroxisome proliferators, in connection with the conclusions adopted for other phthalates (in particular DEHP, DINP and DBP).

Concerning fertility related to effects on reproductive organs, in 42-44 days old (pubertal) or adult rats, there is no indication of effects evidenced by histological observation in the repeated dose toxicity studies and the two-generation study. No testicular atrophy in adult rats was observed, whereas DEHP induced clear testicular atrophy in comparable studies (Bouin's or Formalin fixation). In the one-generation and in the two-generation studies, fertility parameters are not affected by DIDP treatment.

Concerning reproductive toxicity, decrease in survival indices was observed in both two-generation studies (Exxon Biomedical Sciences, 1997d; 2000) in F_2 generation, leading to a NOAEL of 0.06% in the new one (Exxon Biomedical Sciences, 2000). The NOAEL of 0.06% (33 mg/kg/d DIDP) is used for risk characterisation purposes. Concurrently, parental toxicity noticed from this dose-level consisted of liver changes.

In regard with developmental effects, limited to minor skeletal variations in rats were observed in developmental studies at 1,000 mg/kg/d, concurrently slight signs of maternal toxicity were reported. This allows to derive up a NOAEL of 500 mg/kg/d for dams and fœtus toxicity (Exxon Biomedical Sciences, 1995b). In contrast, at the same high-dose level, DEHP in rats induced malformations.

Furthermore, in rat offspring body weight decreases were observed in the two-generation study (possibly related to lactation), a NOAEL of 253 mg/kg/d (lowest estimated dose for 0.4% in the diet) was achieved for this effect (Exxon Biomedical Sciences, 1997d).

No estrogenic activity was shown in both *in vitro* and *in vivo* tests. Pertaining to antiandrogenic activity, investigation on possible mechanisms of endocrine disruption are currently ongoing by studying *in vitro* androgen-receptor binding for a number of phthalates and an adipate including DBP, DEHP, DIDP, DINP, DEHA and DNOP.

Some alterations indicating a possible effect on male reproductive development were observed in the first two-generation study (Exxon Biomedical Sciences, 1997d): sex ratio (male/female) change (however, the sex ratio varied only at the lowest dose in P_2), absolute testes weight decreases in F_1 and F_2 offspring, cryptorchidism (3.25%) which usually occurred at a lower incidence (0.25%), but delay in body weight gain is considered responsible of the two latter effects. Moreover, in the new two-generation DIDP study in rats (Exxon Biomedical Sciences, 2000), there were no significant differences in developmental landmarks (measurements of anogenital distance, nipple retention, vaginal patency and preputial separation for the F_1 and F_2 offspring of either sex) up to the highest dose of 0.4% DIDP for this study.

On the whole no overt effect related to endocrine disruption of the reproductive system has been observed.

Repeated dose toxicity and reproductive effects are considered to be the critical end-points in the risk assessment of DIDP.

Table 4.33 Studies showing the critical end points

End point	Study	LOAEL Effects observed	NOAEL	Reference
Repeated dose toxicity	90 days, diet, rat	120 mg/kg/d (females) (1,600 ppm) 400 mg/kg/d (males) (6,400 ppm) increased liver weight	60 mg/kg/d (females) (800 ppm)	BASF(1969b)
	13 weeks diet, dog	75 mg/kg/d (0.3%) swollen and vacuolated hepatocytes	15 mg/kg/d (0.05%)	Hazleton Lab. (1968b)
Reproductive toxicity (offspring survival)	2-generation study, diet, rat	117 mg/kg/d (F2) (0.2%) ↘ survival indices	33 mg/kg/d (F2) (0.06%)	Exxon Biomedical Sciences (1997d; 2000)
Developmental toxicity	developmental study, diet, rat	1,000 mg/kg/d Skeletal variations: rudimentary lumbar and cervical ribs	500 mg/kg/d	Exxon Biomedical Sciences (1995b)
	2-generation study, diet, rat	508 mg/kg/d (0.8%) ↘ body weight in F1 and F2	253 mg/kg/ (0.4%)	Exxon Biomedical Sciences (1997d)

Extrapolation of oral toxicity data (route-to-route extrapolation)

Inhalation and dermal routes are relevant occupational and consumer routes of exposure. No adequate NOAEL is available for these routes. Therefore route-to-route extrapolation is necessary using the oral NOAELs.

Difference in bioavailability after oral, dermal and inhalation exposure might result in difference in toxicity between various routes. The following factors have been used to calculate the internal dose:

For oral route, an absorption of 50% was defined for adults derived from the toxicokinetic study in rats (General Motors research Laboratories, 1983). For newborns and infants, an absorption of 100% was set up based on a study from Sjoberg et al. (1985) that seemed to show a greater absorption by oral route of an other phthalate DEHP in young Sprague Dawley rats than in older ones. The 100% bioavailability was also assumed by the CSTEE for calculation of oral exposure in children.

For inhalation route, a bioavailability of 75% for adults is estimated (see Section 4.1.2.1, inhalation*)* and a bioavailability of 100% for newborns and infants, considered to be in any case a vulnerable sub-population.

For dermal route, internal body burden in human has been calculated using an absorption factor derived from experimental studies (MRI, 1983; Deisinger, 1998).

4.1.3.2 Workers

Occupational exposure may occur by dermal or inhalation route during manufacture of DIDP, manufacture of products containing DIDP, use of end products containing DIDP. The maximum potential airborne concentrations are when aerosol formation is possible especially at high temperatures and mechanical pressure.

Dermal route

The worst case for external skin exposure is considered to occur when 5 mg/cm^2 of pure DIDP is applied during 8 hours on a skin surface of 840 cm^2 (for both hands).

From Midwest Research Institute (1983), an *in vivo* GLP study performed with DINP, with very good total recovery a maximum absorption through the rat skin of ca. 4% of the applied dose may be assumed following a single application for a 7-day period with occlusive fittings. This may be transposed to DIDP, because of the high physico-chemical similarities between the two substances. Assuming a quantity of 5 mg/cm^2 applied on 840 cm^2 (4,200 mg), this penetration rate would result in the absorption of 168 mg (4,200 · 0.04) in 7 days.

From comparative experiments, it is estimated that the human skin is between 4 and 30 times less permeable than the rat skin, the difference depending on the chemical. In the work from Mint and coworkers (Mint and Hotchkiss, 1993; Mint et al., 1994; cf. **Table 4.21**), several phthalates are compared on human (full thickness) and rat (full thickness) skins. The factors between steady state absorption rates (rat / human) are, for DMP 6.2, for DEP 8.0, and for DBP 22.7. According to Melnick (1987): “the dermal absorption of DEHP was slightly greater than that of DIDP and much less than that of DMP, DEP, DBP, DIBP, BBP or DNHP.” In this way, it seems realistic to assume that the human skin is at least 10 times less permeable than the rat skin. This would lead to a human dermal intake of ca 16.8 mg (168/10) in 7 days, which represents

2.4 mg per day. It is emphasised that this approach includes full consideration of the reservoir effect *in vivo*, which is certainly at its maximum in this case.

In conclusion, for worst-case situations, it is proposed to take a maximum dermal intake of 2.4 mg/day equivalent to 0.03 mg/kg/day for a 70-kg man.

Inhalation route

Based on available measured data on DIDP and analogous, aerosol occupational worst-case exposure has been evaluated in 3 different scenarios, as: 5 mg/m^3 (DIDP manufacture), 10 mg/m^3 (manufacture of end products containing DIDP), and 10 mg/m^3 (use of end products containing DIDP). However, some uncertainties remain over the reliability of these estimates and there would be a need for a well-conducted survey of occupational exposure during use of DIDP.

The corresponding internal doses are calculated assuming 10 m^3 of air are inhaled in a 8-hour working day by a 70-kg worker and a 75% pulmonary absorption rate.

Combined route

Table 4.34 Worst-case occupational exposure summary

	Route of penetration				Combined routes
	Inhalation		Dermal		
Scenario	**External exposure mg/m^3**	**Internal dose mg/kg/d**	**External exposure mg/cm^2**	**Internal dose mg/kg/d**	**Internal dose mg/kg/d**
DIDP manufacture	5	0.53	5	0.03	0.56
Manufacture of end products containing DIDP	10	1.07	5	0.03	1.10
Use of end products containing DIDP	10	1.07	5	0.03	1.10

In view of the relatively very low penetration by the dermal route, the same worst-case evaluation has been retained for all scenarios. Real quantities penetrating are in fact lower.

For the risk characterisation at the workplace, MOSs have to be determined for route-specific as well as combined inhalation and dermal exposure. Only MOSs derived from combined exposure are presented. As internal exposure by the dermal route is very low, much lower than by the inhalation route, the most significant contribution to the conclusions is via inhalation.

Acute toxicity

Acute dermal and inhalation toxicity is considered to be very low. There was no lethality at doses of 12.54 mg/l in rat inhalation studies and no overt toxic effects were noticed for dermal exposure of 2,910 mg/kg in rats and 9,700 mg/kg in rabbits. Comparison with the highest estimated occupational exposure (scenarios 2 and 3) clearly shows that acute toxicity risks are not of concern: **Conclusion (ii)** for all scenarios.

Irritation / Corrosivity

DIDP showed mild to no skin or eye irritation in rabbits. Effects are not considered of concern. There is no evidence of respiratory irritation after acute or sub-acute exposure. **Conclusion (ii)** for all scenarios.

Sensitisation

Since there were one case of allergic dermatitis reported in humans and a positive Buehler test, the sensitisation risk cannot be completely excluded. But given the wide use and dispersion of DIDP and the only one human case reported, a very low level of risk can be anticipated. **Conclusion (ii)** for all scenarios.

Repeated dose toxicity

Considering the estimated combined internal exposure (cf. **Table 4.34**) and the NOAEL (15 mg/kg/d in dogs and 60 mg/kg/d in rats for hepatic effects), the following MOSs can be calculated:

Table 4.35 MOSs calculated for each scenario and for each RDT critical effect

Scenario	Internal exposure	Internal NOAEL hepatic effects (rat)	Internal NOAEL hepatic effects (dog)	MOS hepatic effects (rat)	MOS hepatic effects (dog)	Conclusion
1	0.56 mg/kg/d	30 mg/kg/d	7.5 mg/kg/d	53	13	ii
2	1.10 mg/kg/d	30 mg/kg/d	7.5 mg/kg/d	27	7	ii
3	1.10 mg/kg/d	30 mg/kg/d	7.5 mg/kg/d	27	7	ii

The MOSs derived from hepatic effects in the 90-day toxicity test via the oral route in dogs are considered sufficient for occupational exposure since effects observed in this study were very slight, and that there was a lack of increase in the number of animals affected, as well as a lack of increase in the severity of the effects. In addition, no changes in biochemical parameters were observed in the study. The poor reliability of the study has also been stressed and for this reason, it seems also important to consider the MOSs derived from the NOAEL set in female rats in the 90-day study. Those MOSs are considered sufficient for occupational exposure since the NOAEL was based on very slight effects (increase of relative liver weights in female rats at the higher dose). The conservative nature of the exposure estimates needs to be also considered. **Conclusion (ii)** for all scenarios.

Mutagenicity

Available data do not reveal a genotoxic potential. Effects are not anticipated to occur. **Conclusion (ii)** for all scenarios.

Toxicity for reproduction

Fertility

Concerning fertility, no indication of overt toxicity was observed in any of the studies provided. **Conclusion (ii)** for all scenarios.

Offspring survival

From the new two-generation study in rats (Exxon Biomedical Sciences, 2000), a NOAEL of 33 mg/kg/d (lowest estimated dose for 0.06% DIDP in diet) was derived based on the confirmed decrease of Survival Indices (days 1 and 4) in the second pup generation (F_2) from 0.2%.

This leads to the following MOSs for workers:

Table 4.36 MOSs calculated for each scenario and for offspring survival

Scenario	Internal exposure	Internal NOAEL ↓ survival Indices	MOS offspring survival (rats)	Conclusion
1	0.56 mg/kg/d	16.5 mg/kg/d	30	ii
2	1.10 mg/kg/d	16.5 mg/kg/d	15	ii
3	1.10 mg/kg/d	16.5mg/kg/d	15	ii

For offspring survival the MOSs are considered sufficient for the occupational exposure especially since the NOAEL of 33 mg/kg/d derived from the new two-generation study (Exxon Biomedical Sciences, 2000) in rats is based on slight decreases in survival indices in the F_2 generation at the higher doses. **Conclusion (ii)** for all scenarios.

Developmental effects

Considering the relevant NOAELs of 500 mg/kg/d (skeletal variations) and 263 mg/kg/d (decrease in body weight), the following MOSs can be calculated:

Table 4.37 MOSs calculated for each scenario and for each development effect

Scenario	Internal exposure	Internal NOAEL skeletal variations	Internal NOAEL ↓ offspring bodyweight	MOS skeletal variations (rat)	MOS ↓ offspring bodyweight	Conclusion
1	0.56 mg/kg/d	250 mg/kg/d	126.5 mg/kg/d	446	226	ii
2	1.10 mg/kg/d	250 mg/kg/d	126.5 mg/kg/d	227	115	ii
3	1.10 mg/kg/d	250 mg/kg/d	126.5 mg/kg/d	227	115	ii

For skeletal variations in rat, the MOSs are considered sufficient for occupational exposure, especially since the minor skeletal variations (supernumerary ribs: rudimentary cervical and/or 14^{th} rib) have been inconsistently interpreted so far and their relevance to humans is questionable. However, a developmental study in mice conducted with DEHP has shown severe effects at quite low doses so a comparable developmental study in mice might be useful to reassure the previous conclusion.

For decrease of offspring bodyweight in rats, the MOSs can be considered of no concern for occupational exposure. **Conclusion (ii)** for all scenarios.

Endocrine effects

No estrogenic activity was shown *in vitro* and *in vivo* tests.

Pertaining to anti-androgenic potency, in the new two-generation study (Exxon Biomedical Sciences, 2000) that addressed landmarks of sexual maturation for male pups (measurements of anogenital distance, nipple retention and preputial separation for the F_1 and F_2 male pups), there were no significant differences between treated and control animals of F_1 and F_2 offspring up to the highest dose of 0.4% DIDP.

Overall no overt effect related to endocrine disruption of the reproductive system has been observed. **Conclusion (ii)** for all scenarios.

Summary of the risk characterisation for workers

Conclusion (ii) for all scenarios.

4.1.3.3 Consumers

Scenarios were built for three sub-populations:

- adults and children 3-15 years old, as these two groups undergo the same sources of exposure,
- infants 6 months to 3 years old, as specific sources of exposure to DIDP are available for this category of consumers (toys and teething rings for example),
- newborns 0 to 6 months old, as their diet is different from this of adults and older children.

The risk characterisation for young children will be assessed in two ways:

- without the toy scenario, regarding the present situation, considering the absence of DIDP in current toys;
- with the toy scenario, considering the foreseeable future use of DIDP as a substitute for other phthalates in toys.

Additional safety factors have been taken into account when determining the conclusions for newborns and infants compared to adults. Indeed, these sub-populations are considered in general as vulnerable sub-populations in respect with differences between adults and children in physiological, biochemical, genetical or anatomical parameters as well as in absorption, metabolism and elimination capacity, which can make children more susceptible to toxicity. Differences in oral and inhalation uptake have been considered through differentiated bioavailabilities: oral internal exposure has been estimated 50% for adults and 100% for newborns and infants and inhalation internal exposure, 75% for adults and 100% for newborns and infants.

The risk characterisation is based on comparison of internal exposure with internal NOAELs derived from animal studies.

The risk characterisation considering the possible use of DIDP as a substitute for DEHP in food packaging has been included in Appendix B.

4.1.3.3.1 Adults and 3-15 years old children

The exposure scenarios considered as important for adults are:

- building materials and furniture,
- clothing, gloves and footwear,
- car and public transport interiors,
- food and food-related uses.

Margins of safety (MOSs) presented below are calculated for exposure from the four above scenarios and for multiple exposure pathways (cf. **Table 4.38**).

Table 4.38 MOSs calculated for adults exposed to DIDP from different matrixes and by multiple pathways

End points	Internal exposure (mg/kg bw/d)	Internal NOAEL (mg/kg bw/d)	MOS Internal NOAEL	Conclusion
RDT/Hepatic	0.0058	7.5 [1)] 30 [2)]	1,293 5,172	ii ii
Offspring survival	0.0058	16.5 [3)]	2,845	ii
Developmental	0.0058 0.0058	126.5 [4)] 250 [5)]	21,810 43,103	ii ii

1) 90-day oral study in dog and based on hepatic effects (Hazleton, 1968b)
2) 90-day oral study in rat and based on hepatic effects (BASF, 1969b)
3) 2-generation study in rat and based on slight decreases in Survival Indices in F_2 generation (Exxon Biomedical Sciences, 2000)
4) 2-generation oral study in rat and based on decrease body weight in F_1 and F_2 (Exxon Biomedical Sciences, 1997d)
5) Development study in rats: skeleton variations leading to the NOAEL of 500 mg/kg/d (Exxon Biomedical Sciences, 1995b)

MOSs are considered sufficient to protect adults. **Conclusion (ii)** for all end points.

4.1.3.3.2 Infants

The exposure scenarios considered as important for infants are:

- toys and baby equipment,
- building materials and furniture,
- food and food related uses,
- car and public transport interiors.

Without toys (present situation)

Table 4.39 MOSs calculated for infants exposed to DIDP from different matrixes and by multiple pathways: without toys (present situation)

End points	Internal exposure (mg/kg bw/d)	Internal NOAEL (mg/kg bw/d)	MOSs	Conclusion
RDT/Hepatic	0.026	7.5 [1)] 30 [2)]	288 1,154	ii ii

1) 90-day oral study in dog and based on hepatic effects (Hazleton, 1968b)
2) 90-day oral study in rat and based on hepatic effects (BASF, 1969b)

For repeated dose toxicity studies, hepatic effects observed in the 90-day dog toxicity test via the oral route lead to a low NOAEL of 7.5 mg/kg/d. Although, these effects were very slight and there was a lack of increase in the number of animals affected, as well as a lack of increase in the severity of the effects and no changes in biochemical parameters were observed. The poor reliability of the study has also been stressed and for this reason, it seems also important to consider the NOAEL derived in female rats in the 90-day study. This NOAEL was based on very slight effects (increase of relative liver weights in female rats at the higher dose). Therefore, the MOSs of 288 and 1,154 are considered sufficient to protect infants. **Conclusion (ii)** applies when taking into account all present sources of exposure without toys.

Pertaining to reduced offspring survival mainly observed in the new two-generation study (Exxon Biomedical Sciences, 2000), a trans-generational effect, for which the sensitive/critical period of exposure is unknown, cannot be ruled out. If it could be conceived that an exposure during early life could lead to an effect on fertility, an internal NOAEL of 16.5 mg/kg/d can be derived. However, it is admitted that there is uncertainty on the relevance of this NOAEL for infant. Considering the internal exposure of 0.026 mg/kg bw/d and the internal NOAEL of 16.5 mg/kg/d in rats, the MOS would be 635; a MOS of such a magnitude would not normally lead to an expression of concern. Nevertheless, in this case owing to the uncertainties on the applicability of the NOAEL for this end point, and hence the significance of the MOS, no formal conclusion could be drawn.

With toys (foreseeable situation)

Table 4.40 MOSs calculated for infants exposed to DIDP from different matrixes and by multiple pathways: with toys (foreseeable situation)

End points	Internal exposure (mg/kg bw/d)	Internal NOAEL (mg/kg bw/d)	MOSs	Conclusion
RDT/Hepatic	0.227	7.5 [1)] 30 [2)]	33 132	**iii** ii

1) 90-day oral study in dog and based on hepatic effects (Hazleton, 1968b)
2) 90-day oral study in rat and based on hepatic effects (BASF, 1969b)

For repeated dose toxicity studies, hepatic effects observed in the 90-day dog toxicity test via the oral route lead to a low NOAEL of 7.5 mg/kg/d. Although, these effects were very slight and there was a lack of increase in the number of animals affected, as well as a lack of increase in the severity of the effects and no changes in biochemical parameters were observed. The MOS of 33 derived from this RDT dog study would not be considered sufficient to protect infants and **conclusion (iii)** would thus apply.

The poor reliability of this study has been stressed and for this reason, it seems also important to consider the NOAEL derived from female rats in the 90-day study. This NOAEL was based on very slight effects (increase of relative liver weights in female rats at the higher dose). The MOS of 132 derived from this RDT rat study would be considered sufficient to protect infants and would lead to a **conclusion (ii)**.

Pertaining to reduced offspring survival mainly observed in the new two-generation study (Exxon Biomedical Sciences, 2000), a trans-generational effect, for which the sensitive/critical period of exposure is unknown, cannot be ruled out. If it could be conceived that an exposure during early life could lead to an effect on fertility, an internal NOAEL of 16.5 mg/kg/d can be derived. However, it is admitted that there is uncertainty on the relevance of this NOAEL for

infants. Considering the internal exposure of 0.227 mg/kg bw/d and the internal NOAEL of 16.5 mg/kg/d in rats, the MOS would be 73; a MOS of such a magnitude would normally lead to an expression of concern. Nevertheless, in this case owing to the uncertainties on the applicability of the NOAEL for this end point, and hence the significance of the MOS, no formal conclusion could be drawn.

4.1.3.3.3 Newborn babies

The exposure scenarios considered as important for newborn consumers are:

- toys and baby equipment,
- building materials and furniture,
- food and food related uses,
- car and public transport interiors.

Without toys (present situation)

Table 4.41 MOSs calculated for newborn babies exposed to DIDP from different matrixes and by multiple pathways: without toys (present situation)

End points	Internal exposure (mg/kg bw/d)	Internal NOAEL (mg/kg bw/d)	MOSs	Conclusion
RDT/Hepatic	0.026	7.5 [1)] 30 [2)]	288 1,154	ii ii

1) 90-day oral study in dog and based on hepatic effects (Hazleton, 1968b)
2) 90-day oral study in rat and based on hepatic effects (BASF, 1969b)

For repeated dose toxicity studies, hepatic effects observed in the 90-day dog toxicity test via the oral route lead to a low NOAEL of 7.5 mg/kg/d. Although, these effects were very slight and there was a lack of increase in the number of animals affected, as well as a lack of increase in the severity of the effects and no changes in biochemical parameters were observed. The poor reliability of the study has also been stressed and for this reason, it seems also important to consider the NOAEL derived from female rats in the 90-day study. This NOAEL was based on very slight effects (increase of relative liver weights in female rats at the higher dose). Therefore, the MOSs of 288 and 1,154 are considered sufficient to protect newborn babies. **Conclusion (ii)** applies when taking into account all sources of exposures.

Pertaining to reduced offspring survival mainly observed in the new two-generation study (Exxon Biomedical Sciences, 2000), a trans-generational effect, for which the sensitive/critical period of exposure is unknown, cannot be ruled out. If it could be conceived that an exposure during early life could lead to an effect on fertility, an internal NOAEL of 16.5 mg/kg/d can be derived. However, it is admitted that there is uncertainty on the relevance of this NOAEL for newborns. Considering the internal exposure of 0.026 mg/kg bw/d and the internal NOAEL of 16.5 mg/kg/d in rats, the MOS would be 635; a MOS of such a magnitude would not normally lead to an expression of concern. Nevertheless, in this case owing to the uncertainties on the applicability of the NOAEL for this end point, and hence the significance of the MOS, no formal conclusion could be drawn.

With toys (foreseeable situation)

Table 4.42 MOSs calculated for newborn babies exposed to DIDP from different matrixes and by multiple pathways: with toys (foreseeable situation)

End points	Internal exposure (mg/kg bw/d)	Internal NOAEL (mg/kg bw/d)	MOSs	Conclusion
RDT/Hepatic	0.227	7.5 [1)] 30 [2)]	33 132	**iii** ii

1) 90-day oral study in dog and based on slight hepatic effects (Hazleton, 1968b)
2) 90-day oral study in rat and based on hepatic effects (BASF, 1969b)

For repeated dose toxicity studies, hepatic effects observed in the 90-day dog toxicity test via the oral route lead to a low NOAEL of 7.5 mg/kg/d. Although, these effects were very slight and there was a lack of increase in the number of animals affected, as well as a lack of increase in the severity of the effects and no changes in biochemical parameters were observed. The MOS of 33 derived from the RDT dog study would not be considered sufficient to protect newborn babies and **conclusion (iii)** would thus apply.

The poor reliability of this study has been stressed and for this reason, it seems also important to consider the NOAEL derived from female rats in the 90-day study. This NOAEL was based on very slight effects (increase of relative liver weights in female rats at the higher dose). The MOS of 132 derived from this RDT rat study would be considered sufficient to protect newborn babies and would lead to a **conclusion (ii)**.

Pertaining to reduced offspring survival mainly observed in the new two-generation study (Exxon Biomedical Sciences, 2000), a trans-generational effect, for which the sensitive/critical period of exposure is unknown, cannot be ruled out. If it could be conceived that an exposure during early life could lead to an effect on fertility, an internal NOAEL of 16.5 mg/kg/d can be derived. However, it is admitted that there was uncertainty on the relevance on this NOAEL for newborns. Considering the internal exposure of 0.227 mg/kg bw/d and the internal NOAEL of 16.5 mg/kg/d in rats, the MOS would be 73; a MOS of such a magnitude would normally lead to an expression of concern. Nevertheless, in this case owing to the uncertainties on the applicability of the NOAEL for this end point, and hence the significance of the MOS, no formal conclusion could be drawn.

4.1.3.3.4 Summary of the risk characterisation for consumers

Adults

Conclusion (ii) applies for all scenarios.

Infants and newborns

Conclusion (iii) applies in case DIDP should be used as a substitute for other phthalates in toys: because of concerns for hepatic toxicity as a consequence of repeated exposure of infants and newborn babies arising mainly by the oral route from mouthing and sucking toys and baby equipment.

Pertaining to reduced offspring survival, due to the uncertainty related to the relevance of this end point for newborns and infants and to the lack of experience in this particular field of trans-generational effect, no formal conclusion could be drawn.

Conclusion (ii) applies in all other scenarios when taking into account all present sources of exposure.

4.1.3.4 Humans exposed via the environment

As seen above, repeated dose toxicity and reproductive effects are considered to be the critical end-points in the risk assessment of DIDP.

4.1.3.4.1 Repeated dose toxicity

Adults (corresponding to adults and children 3-15 years old)

The exposure assessment has shown that the main route of intake is the oral route. In **Table 4.43,** the MOSs are calculated for the lowest NOAELs determined for repeated dose toxicity, the internal NOAEL for hepatic effects in rats being set at 30 mg/kg bw/d and the internal NOAEL for hepatic effects in dogs being set at 7.5 mg/kg bw/d.

Table 4.43 MOSs calculated for adults for repeated dose toxicity

Life cycle step	DOSEtot mg/kg bw/d	Internal dose mg/kg bw/d	MOS hepatic effects (rat)	MOS hepatic effects (dog)	Conclusion
Production	0.010	0.005	6,000	1,500	ii
Use in PVC	0.027	0.014	2,140	535	ii
Use in non-PVC polymers	0.017	0.009	3,330	833	ii
Formulation of anti-corrosion paints	0.014	0.007	4,285	1,070	ii
Application of anti-corrosion paints	negligible	negligible	-	-	ii
Formulation of anti-fouling paints	negligible	negligible	-	-	ii
Application of anti-fouling paints	0.012	0.006	5,000	1,250	ii
Formulation of sealing compounds	0.014	0.007	4,285	1,070	ii
Formulation of textile inks	0.014	0.007	4,285	1,070	ii
Application of textile inks	0.003	0.002	15,000	3,750	ii

The MOS derived from hepatic effects in the 90-day toxicity test via the oral route in dogs is considered sufficient for exposure of this sub-population via the environment since effects observed in this study were very slight, and that there was a lack of increase in the number of animals affected, as well as a lack of increase in the severity of the effects. In addition, no changes in biochemical parameters were observed in the study.

The poor reliability of the study has also been stressed and for this reason, it seems also important to consider the MOSs derived from the NOAEL set in rats in the 90-day study. Those MOSs are considered sufficient for exposure of adults via the environment since the NOAEL

was based on very slight effects (increase of relative liver weights in female rats at the higher dose) and that hepatic effects are mainly addressed to peroxisome proliferation in rodents. Indeed peroxisome-related liver effects are generally considered to be species-specific, in all the cases, humans are far less sensitive than rats (cf. Section 4.1.2.8). The conservative nature of the exposure estimates needs also to be considered. **Conclusion (ii)**.

Infants (0.5-3 years old)

The exposure assessment has shown that the main route of intake is the oral route. As the bioavailability of DIDP in children is assumed to be higher than in adults, an internal dose corresponding to 100% of the external dose will be used. In **Table 4.44**, the MOS are calculated from the lowest NOAELs determined for repeated dose toxicity, the internal NOAEL for hepatic effects in rats being set at 30 mg/kg bw/d and the internal NOAEL for hepatic effects in dogs being set at 7.5 mg/kg bw/d.

Table 4.44 MOSs calculated for infants for repeated dose toxicity

Life cycle step	DOSEtot mg/kg bw/d	Internal dose mg/kg bw/d	MOS hepatic effects (rat)	MOS hepatic effects (dog)	Conclusion
Production	0.063	0.063	476	119	ii
Use in PVC	0.166	0.166	180	45	ii
Use in non-PVC polymers	0.102	0.102	294	73	ii
Formulation of anti-corrosion paints	0.076	0.076	394	99	ii
Application of anti-corrosion paints	negligible	negligible	-	-	ii
Formulation of anti-fouling paints	negligible	negligible	-	-	ii
Application of anti-fouling paints	0.066	0.066	454	114	ii
Formulation of sealing compounds	0.076	0.076	394	99	ii
Formulation of textile inks	0.077	0.077	394	99	ii
Application of textile inks	0.013	0.013	2,307	576	ii

The above derived MOSs are related to local environmental exposure, based on the release estimations for all the scenarios. In addition to the comments regarding the NOAEL from the dog study related above, the conservative nature of the exposure assessment has to be highlighted:

- One of the two main exposure routes is through root crops. The estimation of the accumulation of DIDP in root crops is based on experiments with DEHP. Given the lower bioavailability of DIDP compared to DEHP and the higher adsorption potential in soil, the accumulation of DIDP in root crops is certainly overestimated.
- Regarding the diet chosen for infants (0.5-3 years old), European worst cases have been chosen for each route of exposure. For DIDP, two major routes of exposure through food have been identified: fish and root crops. A combination of worst-case values for the two exposure routes leads to an overestimation of the daily intake.

- Furthermore, for infants, 73% and 50% of the intake for adults have been used, respectively for fish and root crops, as proposed in the risk assessment for DEHP. This would clearly be an overestimation compared to food intake for adults.

Given the considerations above, it can be concluded that the estimated MOSs are sufficient for the exposure of infants via the environment. **Conclusion (ii)**.

4.1.3.4.2 Toxicity for reproduction

Fertility

Concerning fertility, no indication of overt toxicity was observed in any of the studies provided. **Conclusion (ii)**.

Offspring survival

From the new two-generation study in rats (Exxon Biomedical Sciences, 2000), a NOAEL of 33 mg/kg/d (lowest estimated dose for 0.06% DIDP in diet) was derived based on the confirmed decrease of Survival Indices (days 1 and 4) in the second pup generation (F_2) from 0.2%.

Adults

Considering the estimated combined internal exposure (cf. **Table 4.34**) and the internal NOAEL for a decrease in survival indices being set at 16.5 mg/kg bw/d, the following MOSs can be calculated for adults exposed via the environment:

Table 4.45 MOSs calculated for adults for offspring survival

Life cycle step	DOSEtot mg/kg bw/d	Internal dose mg/kg bw/d	MOS offspring survival (rats)	Conclusion
Production	0.010	0.005	3,300	ii
Use in PVC	0.027	0.014	1,180	ii
Use in non-PVC polymers	0.017	0.009	1,833	ii
Formulation of anti-corrosion paints	0.014	0.007	2,360	ii
Application of anti-corrosion paints	negligible	negligible	-	ii
Formulation of anti-fouling paints	negligible	negligible	-	ii
Application of anti-fouling paints	0.012	0.006	2,750	ii
Formulation of sealing compounds	0.014	0.007	2,360	ii
Formulation of textile inks	0.014	0.007	2,360	ii
Application of textile inks	0.003	0.002	8,250	ii

For offspring survival, the MOSs are considered sufficient for exposure of adults via the environment. **Conclusion (ii)**.

Infants

Pertaining to reduced offspring survival mainly observed in the new two-generation study (Exxon Biomedical Sciences, 2000), a trans-generational effect, for which the sensitive/critical period of exposure is unknown, cannot be ruled out. If it could be conceived that an exposure during early life could lead to an effect on fertility, an internal NOAEL of 16.5 mg/kg/d can be derived. However, it is admitted that there is uncertainty on the relevance of this NOAEL for infant. Considering the internal exposure of 0.17 mg/kg bw/d derived from the use of DIDP in PVC and the internal NOAEL of 16.5 mg/kg/d in rats, the MOS would be 93; a MOS of such a magnitude would not normally lead to an expression of concern. Nevertheless, in this case owing to the uncertainties on the applicability of the NOAEL for this end point, and hence the significance of the MOS, no formal conclusion could be drawn.

Developmental effects

Considering the relevant NOAELs of 500 mg/kg/d (skeletal variations) and 253 mg/kg/d (decrease in body weight), the following MOSs can be calculated, setting the internal NOAELs at 250 and 131 mg/kg bw/d:

Adults

For adults exposed via the environment, the following MOSs can be estimated:

Table 4.46 MOSs calculated for adults for each development effect

Life cycle step	DOSEtot mg/kg bw/d	Internal dose mg/kg bw/d	MOS skeletal variations (rat)	MOS decrease of offspring bodyweight	Conclusion
Production	0.010	0.005	50,000	26,200	ii
Use in PVC	0.027	0.014	17,860	9,360	ii
Use in non-PVC polymers	0.017	0.009	27,780	14,555	ii
Formulation of anti-corrosion paints	0.014	0.007	35,710	18,710	ii
Application of anti-corrosion paints	negligible	negligible	-	-	ii
Formulation of anti-fouling paints	negligible	negligible	-	-	ii
Application of anti-fouling paints	0.012	0.006	41,670	21,830	ii
Formulation of sealing compounds	0.014	0.007	35,710	18,710	ii
Formulation of textile inks	0.014	0.007	35,710	18,710	ii
Application of textile inks	0.003	0.002	125,000	65,500	ii

For all scenarios, the MOSs are considered sufficient. **Conclusion (ii)**.

4.1.3.4.3 Summary of the risk characterisation for humans exposed via the environment

For all scenarios, the MOSs are considered sufficient. **Conclusion (ii)**.

4.1.3.5 Combined exposure

Adults

The MOSs calculated for the worst-case combined exposure are presented in **Table 4.47**.

Table 4.47 MOSs calculated for adults for combined exposure without occupational exposure

Effects	Internal exposure mg/kg bw/d	Internal NOAEL mg/kg bw/d	MOSs	Conclusion
RDT (hepatic effects in dog)	0.02	7.5	375	ii
RDT (hepatic effects in rat)	0.02	30	1,500	ii
↓ Survival indices (rat) (day 1-4)	0.02	16.5	825	ii
Decrease of offspring body weight (rat)	0.02	126.5	6,325	ii
Skeletal variations (rat)	0.02	250	12,500	ii

Table 4.48 MOSs calculated for adults for combined exposure considering occupational exposure

Effects	Internal exposure mg/kg bw/d	Internal NOAEL mg/kg bw/d	MOSs	Conclusion
RDT (hepatic effects in dog)	1.12	7.5	6.6	ii
RDT (hepatic effects in rat)	1.12	30	27	ii
↓ Survival indices (rat) (day 1-4)	1.12	16.5	15	ii
Decrease of offspring body weight (rat)	1.12	126.5	112	ii
Skeletal variations (rat)	1.12	250	223	ii

As combined exposure for adults is almost exclusively related to occupational exposure, the MOSs are considered sufficient for adults. **Conclusion (ii)** applies with or without occupational exposure.

Children (3-15 years)

The MOSs calculated for the worst-case combined exposure are presented in **Table 4.49**.

Table 4.49 MOSs calculated for children for combined exposure

Effects	Internal exposure mg/kg bw/d	Internal NOAEL mg/kg bw/d	MOSs	Conclusion
RDT (hepatic effects in dog)	0.02	7.5	375	ii
RDT (hepatic effects in rat)	0.02	30	1,500	ii

For children exposure, the MOSs are considered sufficient. **Conclusion (ii)** applies for all effects for children.

Pertaining to reduced offspring survival mainly observed in the new two-generation study (Exxon Biomedical Sciences, 2000), a trans-generational effect, for which the sensitive/critical period of exposure is unknown, cannot be ruled out. If it could be conceived that an exposure during early life could lead to an effect on fertility, an internal NOAEL of 16.5 mg/kg/d can be derived. However, it is admitted that there is uncertainty of the relevance on this NOAEL for children. Considering the internal exposure of 0.02 mg/kg bw/d and the internal NOAEL of 16.5 mg/kg/d in rats, the MOS would be 825; a MOS of such a magnitude would not normally lead to an expression of concern. Nevertheless, in this case owing to the uncertainties on the applicability of the NOAEL for this end point, and hence the significance of the MOS, no formal conclusion could be drawn.

Infants (0.5-3 years old)

The MOSs calculated for the worst-case combined exposure are presented in **Table 4.50**.

Table 4.50 MOSs calculated for infants for combined exposure

Effects	Internal exposure mg/kg bw/d		Internal NOAEL mg/kg bw/d	MOSs		Conclusion	
	without toys *	with toys **		without toys *	with toys **	without toys *	with toys **
RDT (hepatic effects in dog)	0.20	0.40	7.5	37.6	18.8	ii	**iii**
RDT (hepatic effects in rat)	0.20	0.40	30	150	75	ii	ii

* present situation
** foreseeable situation

As combined infant exposure without toys is almost exclusively related to environmental exposure, the MOSs calculated are considered sufficient (see Section 4.1.3.4, Humans exposed via the environment, Repeated dose toxicity - Infants (0.5-3 years)).

Pertaining to reduced offspring survival mainly observed in the new two-generation study (Exxon Biomedical Sciences, 2000), a trans-generational effect, for which the sensitive/critical period of exposure is unknown, cannot be ruled out. If it could be conceived that an exposure during early life could lead to an effect on fertility, an internal NOAEL of 16.5 mg/kg/d can be derived. However, it is admitted that there is uncertainty on the relevance of this NOAEL for infants. Considering the internal exposure of 0.2 mg/kg bw/d (without toys) or 0.4 mg/kg bw/d (with toys) and the internal NOAEL of 16.5 mg/kg/d in rats, the MOS would be 83 (without toys) or 41 (with toys); a MOS of such a magnitude would not normally lead to an expression of concern. Nevertheless, in this case owing to the uncertainties on the applicability of the NOAEL for this end point, and hence the significance of the MOS, no formal conclusion could be drawn.

In case DIDP should be a substitute for other phthalates in toys in the future, MOS derived from hepatic toxicity in dog would not be considered sufficient to protect infants and **conclusion (iii)** would apply.

Summary of the risk characterisation for combined exposure

Conclusion (iii) applies in case DIDP should be used as a substitute for other phthalates in toys, because of concerns for hepatic toxicity as a consequence of repeated exposure of infants.

Pertaining to reduced offspring survival, due to the uncertainty related to the relevance of this end point for newborns and infants and to the lack of experience in this particular field of trans-generational effect, no formal conclusion could be drawn.

Conclusion (ii) applies in all other scenarios.

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

4.2.1 Exposure assessment

Workers

The exposure assessment, to the extent it is related to physico-chemical properties, has already been discussed. No specific exposure information is available.

4.2.2 Effects assessment: Hazard identification

Explosivity

DIDP has no explosive properties.

Flammability

DIDP has a very low degree of flammability (flash point >200°C).

Oxidising potential

DIDP has no oxidising potential.

4.2.3 Risk characterisation

Workers

DIDP has neither explosive nor oxidising properties. The likelihood of an adverse effect deriving from flammability is very low. **Conclusion (ii)** for all scenarios.

Consumers

Exposure is considered negligible with respect to this section of the risk assessment. **Conclusion (ii)** for all scenarios.

Humans exposed indirectly via the environment

Exposure is considered negligible with respect to this section of the risk assessment. **Conclusion (ii).**

Summary of the risk characterisation for physico-chemical properties

Conclusion (ii).

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 is reached for the aquatic compartment, the terrestrial compartment, the atmosphere, microorganisms in the sewage treatment plant as well as for secondary poisoning.

5.2 HUMAN HEALTH

5.2.1 Human health (Toxicity)

5.2.1.1 Workers

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.

5.2.1.2 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 applies in case DIDP should be used as a substitute for other phthalates in toys because of concerns for hepatic toxicity as a consequence of repeated exposure of infants and newborn babies arising mainly by the oral route from mouthing and sucking toys and baby equipment.

Pertaining to reduced offspring survival, due to the uncertainty related to the relevance of this end point for newborns and infants and to the lack of experience in this particular field of trans-generational effect, no formal conclusion could be drawn.

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 for all other scenarios.

5.2.1.3 Humans exposed via the 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.

5.2.1.4 Combined exposure

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 in case DIDP should be used as a substitute for other phthalates in toys because of concerns for hepatic toxicity as a consequence of repeated exposure of infants.

Pertaining to reduced offspring survival, due to the uncertainty related to the relevance of this end point for infants and to the lack of experience in this particular field of trans-generational effect, no formal conclusion could be drawn.

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 for all other scenarios.

5.2.2 Human health (risks from physico-chemical properties)

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

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ABBREVIATIONS

ACTS	Advisory Committee on Toxic Substances
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
BBP	Butylbenzyl phthalate
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
CMA	Chemicals Manufacturers' Association
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
D79P	Di-alkyl phthalate (C_7 - C_9 alkyl chains)
DBP	Dibutyl phthalate
DEHP	Diethylhexyl phthalate
DG	Directorate General

DIAP	Di-isoamyl phthalate
DIBP	Di-isobutyl phthalate
DIDP	Di-isodecyl phthalate
DIN	Deutsche Industrie Norm (German norm)
DINP	Di-isononyl phthalate
DIOP	Di-isooctyl phthalate
DMP	Dimethyl phthalate
DNA	DeoxyriboNucleic Acid
DNHP	Di-*n*-hexyl phthalate
DOC	Dissolved Organic Carbon
DOP	Di-octyl phthalate
DT50	Degradation half-life or period required for 50 percent dissipation / degradation
DT90	Period required for 90 percent dissipation / degradation
E	Explosive (Symbols and indications of danger for dangerous substances and preparations according to Annex 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
ECPI	European Council for Plasticisers & Intermediates
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)
HSDB	Hazardous Substances Data Bank
HSE	Health and Safety Executive (UK)
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
PAE	Phthalic acid ester
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
PTFE	Polytetrafluoroethylene
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
RDT	Repeated Dose Toxicity
RfC	Reference Concentration
RfD	Reference Dose
RIVM	Rijksintituut voor volksgezondheid en milieu (NL)
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
Sw	Water solubility
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
TWA	Time Weighted Average
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	Wastewater 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 Hypothesis of replacement of DEHP by DIDP in food contact materials (exposure assessment)

As DIDP has been used as a substitute for DEHP, it may be hypothesised that the same scenario is likely to occur in food packaging. Therefore an hypothetical scenario for replacement of DEHP by DIDP in food contact materials has been included for the three categories of consumers.

Adults

Since samples contained 0.3-0.7 mg/kg wet of DEHP (MAFF, 1996a), the high level dietary intake of DEHP was estimated to be 0.7 mg/person/day, which is approximately 12 µg/kg bw/day for a 60 kg adult. So the high level dietary intake of DIDP would be 12 µg/kg bw/day. A bioavailability of 50% is considered for oral exposure in adults so the internal exposure will be 6 µg/kg bw/d.

Newborns and infants

The exposure to DIDP is estimated from the maximum level of DEHP detected in samples in the study from MAFF (1998): 440 µg/kg dry powder. Indeed further arguments have been provided by the MAFF in favour of a decrease of phthalate concentrations in infant formulae since 1996 (MAFF, 2000):

- In 1997, 10 samples of infant formulae based on cows milk or soya protein were analysed in a study organised by the Utrecht Inspectorate for Health Protection. Participating laboratories used analytical methods of their own choice. The total phthalate content of the samples were some 4 to 23 times lower than found in the 1996 MAFF survey.
- Results from the analysis of samples of infant formulae commissioned at CSL in 1997 by two European manufacturers were reported to MAFF. The concentrations of total phthalates were approximately 10-times lower than found in the 1996 MAFF survey. The levels of individual phthalates were about half those found in the 1996 MAFF survey. The levels found were similar to those in the raw ingredients (milk derived ingredients, vegetable oils...) indicating that further contamination does not occur during the powder manufacture or by migration from the packaging materials.
- MAFF-CSL continues (up to and including 2000) to get occasional requests from industry to test formulae and formulae ingredients for phthalates and levels remain low - similar or lower than the 1998 survey data and far lower than the 1996 data.

The Dutch study, the work commissioned by manufacturers, and the 1998 MAFF study, all support the manufacturers contention that concentrations of phthalates in infant formulae are much lower than those found in 1996. [Source a and b. UK Food Advisory Committee paper FdAC/Contaminants/34. 11th December 1997. Phthalates in infant formulae - update.]

Newborns

Assuming the highest estimated exposure to DEHP is 440 µg/kg dry powder, the maximal exposure to DIDP by infant formulae for a 5.5 kg infant taking 0.131 kg/day dry powder each day, corresponds to 10.5 µg/kg bw/day. The absorption by the oral route is considered as 100% in young children.

Infants

Assuming the highest estimated exposure to DEHP is 440 µg/kg dry powder, the maximal exposure to DIDP by infant formulae for an 8 kg infant taking 0.141 kg/day dry powder, corresponding to 7.8 µg/kg bw/day.

Infants are in a phase of diversification of their diet. It can be considered that, in complement of infant formulae, an infant eats the same type of food as an adult but in a smaller quantity. In this assessment, the hypothesis is that he eats three times less than an adult does.

The high level dietary intake of DIDP was estimated to be 12 µg/kg bw/day for adult. This value is equivalent to 720 µg/adult/day. Assuming that an infant eats three times less than an adult does, he eats 240 µg/day, corresponding to 30.0 µg/kg bw/day for an 8-kg infant.

Total DIDP intake (infant formulae and food) for infant is 37.8 µg/kg bw/day.

Summary of exposures for consumers

Table A.1 Summary of internal exposure of multiple route exposure to DIDP for newborns, infants and adults in the hypothesis of replacement of DEHP by DIDP in food

Source	**External and internal exposure**					
	Newborns		**Infants**		**Adults**	
	External exposure	**Internal exposure µg/kg bw/d**	**External exposure**	**Internal exposure µg/kg bw/d**	**External exposure**	**Internal exposure µg/kg bw/d**
Food and food related uses	50.2 µg/kg bw/d	10.5	58.1 µg/kg bw/d	37.8	12 µg/kg bw/d	6
Building materials	20 µg/m^3 *	21.3	20 µg/m^3 *	21.3	20 µg/m^3 *	4.2
Car interior	20 µg/m^3 *	1.9	20 µg/m^3 *	1.9	20 µg/m^3 *	0.8
Clothing, gloves and footwear	Not estimated		Not estimated			0.7
Total without toys		**33.7**		**61**		**11.7**
Toys oral exposure dermal exposure	200	200 1	200	200 1		
Total with toys		**234.7**		**262**		**11.7**

* Concentration in air

References: see Section 6

Appendix B Hypothesis of replacement of DEHP by DIDP in food contact material (risk characterisation)

As DIDP has been widely used as a substitute for DEHP, it may be hypothesised that the same scenario is likely to occur in food packaging. Therefore an hypothetical scenario for replacement of DEHP by DIDP in food has been included for the three categories of consumers.

Adults

Table B.1 MOSs calculated for adults exposed to DIDP from different matrixes and by multiple pathways

End points	Internal exposure (mg/kg bw/d)	Internal NOAEL (mg/kg bw/d)	MOS Internal NOAEL	Conclusion
RDT/Hepatic	0.0117	7.5 [1)] 30 [2)]	641 2,564	ii ii
Offspring survival	0.0117	16.5 [3)]	1,410	ii
Developmental	0.0117	126.5 [4)] 250 [5)]	10,812 21,367	ii ii

1) 90-day oral study in dog and based on hepatic effects (Hazleton Laboratories, 1968b)
2) 90-day oral study in rat and based on hepatic effects (BASF, 1969b)
3) 2-generation study in rat and based on slight decreases in Survival Indices in F_2 generation (Exxon Biomedical Sciences, 2000)
4) 2-generation oral study in rat and based on decrease body weight in F_1 and F_2 (Exxon Biomedical Sciences, 1997d)
5) Developmental study in rats: skeleton variations leading to the NOAEL of 500 mg/kg/d (Exxon Biomedical Sciences, 1995b)

MOSs are considered sufficient to protect adults. The result of the consumer risk characterisation for adults is that **conclusion (ii)** applies for all scenarios.

Infants

Without toys (present situation)

Table B.2 MOSs calculated for infants exposed to DIDP from different matrixes and by multiple pathways, without toys (present situation)

End points	Internal exposure (mg/kg bw/d)	Internal NOAEL (mg/kg bw/d)	MOS Internal NOAEL	Conclusion
RDT/Hepatic	0.061	7.5 [1)] 30 [2)]	123 492	**iii/ii** * ii

1) 90-day oral study in dog and based on hepatic effects (Hazleton, 1968b)
2) 90-day oral study in rat and based on hepatic effects (BASF, 1969b)
* Conclusion not agreed at TM level

Conclusion (iii): For repeated dose toxicity studies, hepatic effects observed in the 90-day dog toxicity test via the oral route lead to a low NOAEL of 7.5 mg/kg/d. These effects were very slight and there was a lack of increase in the number of animals affected, as well as a lack of increase in the severity of the effects and no changes in biochemical parameters were observed. However, the susceptibility to toxicity of this subpopulation needs to be considered. Therefore, the MOS of 123 derived from this RDT dog study would not be considered sufficient to protect

infants and **conclusion (iii)** would thus apply. The poor reliability of this study has been stressed and for this reason, it seems also important to consider the NOAEL derived from female rats in the 90-day study. This NOAEL was based on very slight effects (increase of relative liver weights in female rats at the higher dose). The MOS of 492 derived from this RDT rat study would be considered sufficient to protect infant consumers and would lead to a **conclusion (ii)**.

Conclusion (ii): For repeated dose toxicity studies, hepatic effects observed in the 90-day dog toxicity test via the oral route lead to a low NOAEL of 7.5 mg/kg/d. Given the very slight effects observed, the lack of increase in the number of animals affected, the lack of increase in the severity of the effects, the absence of changes in biochemical parameters and the poor reliability of this study, the MOS of 123 derived from this study would be considered sufficient. Moreover, it seems also important to consider the NOAEL derived from female rats in the 90-day study. This NOAEL was based on very slight effects (increase of relative liver weights in female rats at the higher dose). Therefore, the MOSs of 123 and 492 are considered sufficient to protect infant consumers and would lead to a **conclusion (ii)**.

Pertaining to reduced offspring survival mainly observed in the new two-generation study (Exxon Biomedical Sciences, 2000), a trans-generational effect, for which the sensitive/critical period of exposure is unknown, cannot be ruled out. If it could be conceived that an exposure during early life could lead to an effect on fertility, an internal NOAEL of 16.5 mg/kg/d can be derived. However, it is admitted that there is uncertainty on the relevance of this NOAEL for infant. Considering the internal exposure of 0.061 mg/kg bw/d and the internal NOAEL of 16.5 mg/kg/d in rats, the MOS would be 270; a MOS of such a magnitude would not normally lead to an expression of concern. Nevertheless, in this case owing to the uncertainties on the applicability of the NOAEL for this end point, and hence the significance of the MOS, no formal conclusion could be drawn.

With toys (foreseeable situation)

Table B.3 MOSs calculated for infants exposed to DIDP from different matrixes and by multiple pathways, with toys (foreseeable situation)

End points	Internal exposure (mg/kg bw/d)	Internal NOAEL (mg/kg bw/d)	MOS Internal NOAEL	Conclusion
RDT/Hepatic	0.262	7.5 [1)] 30 [2)]	29 115	**iii** ii

1) 90-day oral study in dog and based on hepatic effects (Hazleton, 1968b)
2) 90-day oral study in rat and based on hepatic effects (BASF, 1969b)

For repeated dose toxicity studies, hepatic effects observed in the 90-day dog toxicity test via the oral route lead to a low NOAEL of 7.5 mg/kg/d. Although, these effects were very slight and there was a lack of increase in the number of animals affected, as well as a lack of increase in the severity of the effects and no changes in biochemical parameters were observed. The MOS of 29 derived from this RDT dog study would not be considered sufficient to protect infants and **conclusion (iii)** would thus apply. The poor reliability of this study has been stressed and for this reason, it seems also important to consider the NOAEL derived from female rats in the 90-day study. This NOAEL was based on very slight effects (increase of relative liver weights in female rats at the higher dose). The MOS of 115 derived from this RDT rat study would be considered sufficient to protect infants and would lead to a **conclusion (ii)**.

Pertaining to reduced offspring survival mainly observed in the new two-generation study (Exxon Biomedical Sciences, 2000)**,** a trans-generational effect, for which the sensitive/critical period of exposure is unknown, cannot be ruled out. If it could be conceived that an exposure during early life could lead to an effect on fertility, an internal NOAEL of 16.5 mg/kg/d can be derived. However, it is admitted that there is uncertainty on the relevance of this NOAEL for infants. Considering the internal exposure of 0.262 mg/kg bw/d and the internal NOAEL of 16.5 mg/kg/d in rats, the MOS would be 63; a MOS of such a magnitude would normally lead to an expression of concern. Nevertheless, in this case owing to the uncertainties on the applicability of the NOAEL for this end point, and hence the significance of the MOS, no formal conclusion could be drawn.

Newborns

Without toys (present situation)

Table B.4 MOSs calculated for newborns exposed to DIDP from different matrixes and by multiple pathways, without toys (present situation)

End points	Internal exposure (mg/kg bw/d)	Internal NOAEL (mg/kg bw/d)	MOS Internal NOAEL	Conclusion
RDT/Hepatic	0.0337	7.5 [1)] 30 [2)]	223 890	ii ii

1) 90-day oral study in dog and based on hepatic effects (Hazleton, 1968b)
2) 90-day oral study in rat and based on hepatic effects (BASF, 1969b)

For repeated dose toxicity studies, hepatic effects observed in the 90-day dog toxicity test via the oral route lead to a low NOAEL of 7.5 mg/kg/d. Although, these effects were very slight and there was a lack of increase in the number of animals affected, as well as a lack of increase in the severity of the effects and no changes in biochemical parameters were observed. The poor reliability of the study has also been stressed and for this reason, it seems also important to consider the NOAEL derived from female rats in the 90-day study. This NOAEL was based on very slight effects (increase of relative liver weights in female rats at the higher dose). The MOSs of 223 and 890 are considered sufficient to protect newborns and would lead to a **conclusion (ii)**.

Pertaining to reduced offspring survival mainly observed in the new two-generation study (Exxon Biomedical Sciences, 2000), a trans-generational effect, for which the sensitive/critical period of exposure is unknown, cannot be ruled out. If it could be conceived that an exposure during early life could lead to an effect on fertility, an internal NOAEL of 16.5 mg/kg/d can be derived. However, it is admitted that there is uncertainty on the relevance of this NOAEL for newborns. Considering the internal exposure of 0.0337 mg/kg bw/d and the internal NOAEL of 16.5 mg/kg/d in rats, the MOS would be 489; a MOS of such a magnitude would not normally lead to an expression of concern. Nevertheless, in this case owing to the uncertainties on the applicability of the NOAEL for this end point, and hence the significance of the MOS, no formal conclusion could be drawn.

With toys (foreseeable situation)

Table B.5 MOSs calculated for newborns exposed to DIDP from different matrixes and by multiple pathways, with toys (foreseeable situation)

End points	Internal exposure (mg/kg bw/d)	Internal NOAEL (mg/kg bw/d)	MOS Internal NOAEL	Conclusion
RDT/Hepatic	0.2347	7.5 [1)] 30 [2)]	32 128	**iii** ii

1) 90-day oral study in dog and based on hepatic effects (Hazleton, 1968b)
2) 90-day oral study in rat and based on hepatic effects (BASF, 1969b)

For repeated dose toxicity studies, hepatic effects observed in the 90-day dog toxicity test via the oral route lead to a low NOAEL of 7.5 mg/kg/d. Although, these effects were very slight and there was a lack of increase in the number of animals affected, as well as a lack of increase in the severity of the effects and no changes in biochemical parameters were observed. The MOS of 32 derived from this RDT dog study would not be considered sufficient to protect newborns and **conclusion (iii)** would thus apply. The poor reliability of this study has been stressed and for this reason, it seems also important to consider the NOAEL derived from female rats in the 90-day study. This NOAEL was based on very slight effects (increase of relative liver weights in female rats at the higher dose). The MOS of 128 derived from this RDT rat study would be considered sufficient to protect newborns and would lead to a **conclusion (ii)**.

Pertaining to reduced offspring survival mainly observed in the new two-generation study (Exxon Biomedical Sciences, 2000)**,** a trans-generational effect, for which the sensitive/critical period of exposure is unknown, cannot be ruled out. If it could be conceived that an exposure during early life could lead to an effect on fertility, thus, an internal NOAEL of 16.5 mg/kg/d can be derived. However, it is admitted that there is uncertainty on the relevance of this NOAEL for newborns. Considering the internal exposure of 0.2347 mg/kg bw/d and the internal NOAEL of 16.5 mg/kg/d in rats, the MOS would be 70; a MOS of such a magnitude would normally lead to an expression of concern. Nevertheless, in this case owing to the uncertainties on the applicability of the NOAEL for this end point, and hence the significance of the MOS, no formal conclusion could be drawn.

References: see Section 6.

Appendix C EUSES Modelling

In the EUSES model the use pattern refer to the following scenarios in the risk assessment:

Use Pattern 1	Use in inks for textiles
Use Pattern 2	Use in sealing compounds
Use Pattern 3	Use in anti-fouling paints
Use Pattern 4	Use in anti-corrosion paint
Use Pattern 5	Use in non-PVC polymers
Use Pattern 6	Use in PVC
Use Pattern 7	Disposal of end products

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

European Commission

EUR 20785EN **European Union Risk Assessment Report**
1,2-benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich and di-"isodecyl" phthalate (DIDP), Volume 36

Editors: S.J. Munn, R. Allanou, K. Aschberger, F. Berthault, J. de Bruijn, C. Musset, S. O'Connor, S. Pakalin, G. Pellegrini, S. Scheer, S. Vegro.

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Environment and quality of life series

The report provides the comprehensive risk assessment of the substances 1,2-benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich and di-"isodecyl"phthalate (DIDP). It has been prepared by France 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 environmental risk assessment for 1,2-benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich and di-"isodecyl" phthalate concludes that there is at present no concern for the aquatic ecosystem, the terrestrial ecosystem, the atmosphere or for microorganisms in the sewage treatment plant as well as for secondary poisoning.

The human health risk assessment for 1,2-benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich and di-"isodecyl" phthalate concludes that there is no concern for workers and humans exposed via the environment. For consumers, there is concern in case DIDP should be used as a substitute for other phthalates in toys as a consequence of repeated exposure of infants and newborn babies arising from mouthing and sucking toys and baby equipment. In addition there is concern for infants in case of combined exposure.

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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