Institute for Health and Consumer Protection
Toxicology and Chemical Substance (TCS)
European Chemicals Bureau
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BIS (2-ETHYLHEXYL) PHTHALATE (DEHP)

CAS No: 117-81-7

EINECS No: 204-211-0

Summary Risk Assessment Report

2008 **EUR 23384 EN/2**

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SUMMARY RISK ASSESSMENT REPORT

Final report, 2008

Sweden

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PREFACE

This report provides a summary, with conclusions, of the risk assessment report of the substance bis (2-ethylhexyl) phthalate (DEHP) that has been prepared by Sweden in the context of Council Regulation (EEC) No. 793/93 on the evaluation and control of existing substances.

For detailed information on the risk assessment principles and procedures followed, the underlying data and the literature references the reader is referred to the comprehensive Final Risk Assessment Report (Final RAR) that can be obtained from the European Chemicals Bureau[1]. The Final RAR should be used for citation purposes rather than this present Summary Report.

[1] European Chemicals Bureau – Existing Chemicals – http://ecb.jrc.it

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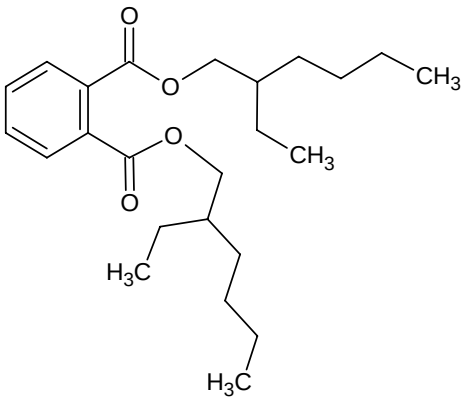
1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS Number:	117-81-7
EINECS Number:	204-211-0
IUPAC Name:	Bis(2-ethylhexyl)phthalate
Synonyms:	DEHP 1,2-Benzenedicarboxylic acid, bis(2-ethylhexyl) ester Bis(2-ethylhexyl) 1,2-benzenedicarboxylate Bis(2-ethylhexyl) o-phthalate Bis(2-ethylhexyl) phthalate Di(2-ethylhexyl) phthalate Dioctyl phthalate DOP (pseudo-synonym, incl. also other isomeric forms of the alcohol part) Phthalic acid dioctyl ester Phthalic acid, bis(2-ethylhexyl) ester
Molecular weight:	390.6
Molecular formula:	$C_{24}H_{38}O_4$
Structural formula:	



The name DEHP is used in this assessment.

1.2 PURITY/IMPURITIES, ADDITIVES

The limited data available on purity indicates a high purity level (99.7%). Impurities found are mainly other phthalates. Some DEHP is, when requested by the user, supplied with "Bisphenol A"; 4,4'-isopropylidenediphenol (CAS No. 80-05-7) as an additive in the range of 0.025 to 0.5%.

1.3 PHYSICO-CHEMICAL PROPERTIES

DEHP is a colorless liquid at room temperature. The vapour pressure is estimated to $3.4 \cdot 10^{-5}$ Pa at 20°C. A wide range of values on the water solubility (0.0006 – 1.3 mg/L at 20-25°C) is available in the literature. The probable explanation is that DEHP readily forms more or less colloidal dispersions in water. Natural constituents in water may influence the solubility. A

non-colloidal solubility of 0.003 mg/L is chosen for the Risk assessment. The Henry´s law constant for DEHP is 4.43 Pa m^3/mol. The octanol-water partition coefficient, log Kow, is 7.5. However, in the model calculations (EUSES 1.0) the highest recommended value of 7.0 is used.

A summary of the physico-chemical properties of DEHP is shown in **Table 1.1**.

Table 1.1 Summary of physico-chemical properties

Property	Value
Physical state	Colourless oily liquid
Melting point	-55°C or -50°C
Boiling point	230°C at 5 mm Hg 385°C at 1013 hPa
Density	0.98 g/cm^3 at 20°C
Vapour pressure	0.000034 Pa at 20°C
Water solubility	3 µg/l at 20°C
Partition coefficient n-octanol/water (log value)	7.5
Conversion factors air	1 ppmv = 16.2 mg/m3 at 20°C and 1013 hPa
Flash point	200°C
Autoflammability, ignition temperature	370°C
Explosive properties explosion limits	0.15 - 0.18 vol.% 0.3 – 49 vol%
Viscosity, dynamic	81 mPa s at 20°C 58 mPa s at 25°C
Henry's constant	4.43 Pa m^3/mol

1.4 CLASSIFICATION

Classification according to Annex I of Council Directive 67/548/EEC:

Human health: Toxic to reproduction, Category 2; R60-61

Environment: None

2 GENERAL INFORMATION ON EXPOSURE

The global production of DEHP in 1994, was estimated to be between 1 and 4 million tonnes/year. The production volume of DEHP in Western Europe was 595,000 tonnes/year in 1997. Recent information from industry (May 2005) shows that the use of DEHP in the EU has decreased to 221,000 in 2004, whilst the use of the phthalates DINP and DIDP have increased during the same period. Some 800 plants in EU use DEHP or preparations with DEHP.

The main use of DEHP is as a plasticizer in polymer products (in EU this is more than 95% of the total use of DEHP), mainly in flexible PVC. The content of DEHP in flexible polymer materials varies but is typically around 30% (w/w). Flexible PVC is used in many different articles e.g. toys, building material such as flooring, cables, profiles and roofs, as well as in medical products such as blood bags and dialysis equipment. DEHP is also used in other polymer products and in non-polymer formulations and products. DEHP is known to migrate slowly from polymer products during their entire lifetime. The main stages identified and considered in the risk assessment include:

- Production of DEHP – DEHP is produced at a handful of chemical plants in EU.
- Formulation of polymers – Mixing DEHP with polymers or other materials to compounds or master-batches. This may take place at the processing site or at a separate site.
- Processing of polymers – A large number of different technologies are used to process polymers with DEHP, for example calendering, extrusion, injection moulding and several plastisol applications including various moulding and coating technologies.
- Formulation of non-polymers – The production of sealants, adhesives, paints, lacquers, printing inks and ceramics.
- Industrial use of non-polymers – The industrial or professional use of sealants, adhesives, paints, lacquers, printing inks and ceramics.
- End-use of products (articles) containing DEHP – The emission of DEHP from products in use, for example from roofing, PVC-coated fabric and car under-coatings.
- Waste management including:
    - Paper recycling – The de-inking of recycled paper is assumed to be a potential local release source.
    - Car shredding – Shredding of disposed vehicles is a potential source for release of DEHP (from car-undercoating and cables).
    - Incineration of DEHP containing products – DEHP can be found in the exhaust air, gas-cleaning residues, slag and fly-ash.
    - Disposal on land fills of DEHP containing products – Municipal landfills are known to emit DEHP (mainly through the leakage water).
- 'Waste remaining in the environment' – This is particles/fragments abraded from end-use products during their service life and during disposal (e.g. particles abraded from car undercoating, coil coating, shoe soles and fragments of plastic bags).

This implies multiple sources of DEHP emissions. The main part of DEHP emissions originates from use and disposal of polymer products. These emissions are widely dispersed, and monitoring data of DEHP in environmental samples confirm a widespread occurrence.

3 ENVIRONMENT

Release of DEHP to the environment occurs during production, transport, storage, formulation and processing of PVC and non-polymers. Furthermore, plasticisers are not chemically bound to the matrix polymer in flexible PVC (or other materials). Therefore the plasticiser will to some extent be lost from the finished article during its use and after its final disposal.

DEHP enters the environment mainly via direct releases to air and waste water, from sewage sludge and from solid waste. In air, DEHP may occur both in vapour phase and as solid particles. The nature of these particles can be either aggregated pure DEHP or polymer particles containing DEHP. Particles formed by weathering of polymer products probably represent an important route of DEHP distribution. It is estimated that around 800 industrial sites in EU use DEHP or preparations containing DEHP. Releases from these sources are expected to cause higher local exposure.

An estimation of the contribution to the total emissions of DEHP from different life-cycle stages is presented in **Table 3.1**.

Table 3.1 Contribution from different life-cycle stages

Source	Emission contribution	Uncertainty in estimate	Emission type
production of DEHP	≈ 2.5%	low	point sources
industrial uses	≈ 2.5%	medium	point sources
end-product uses	≈ 32%	medium	wide dispersive (and point sources)
waste handling*	≈ 63%	high	wide dispersive (and point sources)

* Car shredding, Incineration, Land fills and Waste remaining in the environment

Environmental fate

Photodegradation of DEHP (reaction with OH radicals) is important in the atmosphere ($T_{½}$ = 1 day) but is assumed to be of little importance in water and soil. DEHP does not hydrolyse in water. The biodegradation of DEHP is varying in available studies. Based on the results of standard biodegradation test DEHP is readily biodegradable. Experimental data indicates a biodegradation half-life for DEHP in surface water of 50 days, and 300 days in aerobic sediment. Anaerobic conditions and low temperature further reduce the degradation rate. Results from degradation studies of DEHP in agricultural soil are variable, but indicate moderate to low biodegradation rates. MEHP is the primary biodegradation product of DEHP.

With a log Kow of 7.5, DEHP is expected to be strongly adsorbed to organic matter. DEHP is therefore expected to be found in the solid organic phase in the environment. The log Koc for DEHP is 5.2 L/kg. Hence, DEHP will be strongly adsorbed to the sludge in sewage treatment plants. DEHP has a vapour pressure of $3.4 \cdot 10^{-5}$ Pa (at 20 to 25°C), which indicate a low evaporation rate from its pure state, and a Henry's law constant of 4.4 Pa m^3/mol, indicating a moderate evaporation from a pure water solution ('semi-volatile').

DEHP is found to bioaccumulate in aquatic organisms, and the highest BCF values are observed for invertebrates e.g. 2,700 for Gammarus (BCF_{fish} 840). This indicates that uptake via the food chain might be an important exposure route (secondary poisoning). BCF, as well as monitoring data for different trophic levels, indicate that DEHP does not bio-magnify. This may in part be due to a more effective metabolisation rate in higher organisms.

Due to its high affinity to organic matter only a limited bioaccumulation of DEHP in plants is expected. The environmental studies confirm this with BCF ranging between 0.01 and 5.9. For earthworms a BCF of 1, based on experimental results and modelled (EUSES) data, has been used in the risk assessment.

The large amount of DEHP accumulated in the technosphere indicates a considerable potential for release of DEHP and of subsequent formation and distribution of MEHP. However, the formation rate and fate of MEHP in the environment is not known. MEHP causes reproductive toxicity in studies on mammals. There are no other data on ecotoxicological properties of MEHP available.

Environmental concentrations

The methods in the Technical Guidance Document were used to estimate concentrations in water, sediment, air, soil and biota. In addition a large number of monitoring studies on DEHP are available, with recent studies being much more reliable than earlier ones where contamination often was a problem.

Water

The levels of reported concentrations of DEHP in river waters vary from below the detection limit up to 21 µg/l, with industrial and highly urbanized areas having the higher levels. In lake water, the concentrations were lower. The difference is probably due to the higher levels of suspended matter in flowing waters. In marine surface waters in Norway the concentration of DEHP was below 0.1 µg/l except for one sampling station close to a municipal STP where the concentration was approx. 0.4 µg/l. Measured concentrations of DEHP in surface sediment from rivers and lakes situated in industrial or urban areas where no DEHP using industries were specified, ranged between 0.04 and 21 mg/kg dwt. Close to sites processing materials containing DEHP, much higher concentrations have been found.

The regional PEC in the risk assessment was based on monitoring data from a highly industrialized and densely populated area, and set to 0.8 µg/l. The local PECs were estimated using the EUSES model and are shown in **Table 3.2**.

Table 3.2 PEC surface water and sediment

	Surface water PEC, µg/l	Sediment PEC, mg/kg dwt	
Production sites	0.8 to 219	7.5 to 2045	based on site-specific data
Polymer processing	3.0 to 19	28 to 181	based on default generic data
	0.8 to 1.1	7.5 to 10	based on site-specific data
Non-polymer* formulation/processing	0.8 to 102	11 to 951	based on default generic data
	0.8	7.5	based on site-specific data
Municipal STP	3.2	30	based on default generic data
Waste handling**	0.8 to 3.6	6.0 to 33	based on default generic data

* Sealants, adhesives, paints, lacquers, printing inks, ceramics
** Paper recycling, car shredding, waste incineration

Sewage treatment plants

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. In treated wastewater (effluent) DEHP concentrations varied between 0.07 and 28 µg/l with removal rates mostly in the range 90 – 99%. However, in a few cases removal rates were lower, in one case only 40%. In monitoring studies on DEHP in municipal STP sludge the concentrations vary between 0 and 661 mg/kg dwt in sludge from Sweden, Denmark, Norway, the Netherlands and Germany. There are no measurements available on sludge from industrial STPs.

The local PECs for STP effluent were estimated using the EUSES model and ranged up to 20 mg/l for production and up to 1.3 mg/l for formulation and processing.

Atmosphere

DEHP has been found in gas phase, solid phase (particles), and in water phase (rain water) of air samples. In some of the studies it is not clear which phases that have been analysed. In monitoring studies considered to represent regional scenarios, concentrations of DEHP between 0.3 and 300 ng/m^3 have been measured. The highest values were achieved on sampling sites in urban or unspecified polluted areas.

Soil

The PECs for agricultural soil were estimated using the EUSES model and are shown in **Table 3.3**.

Table 3.3 PEC agricultural soil

	PEC, mg/kg dwt	
Polymer processing	2.0 to 354	based on default generic data
	0.02 to 0.3	based on site-specific data
Non-polymer* formulation/processing	0.5 to 103	based on default generic data
	0.03	based on site-specific data
Municipal STP	2.6	based on default generic data
Waste handling**	3	based on default generic data
Regional	0.07	

* Sealants, adhesives, paints, lacquers, printing inks, ceramics
** Paper recycling, car shredding, waste incineration

In urban/industrial soil the regional PEC was estimated to 3.2 mg/kg dwt using the EUSES model.

Secondary poisoning

The PEC oral-aquatic is calculated by multiplying the bioconcentration factor (BCF) with $PEC_{surface\ water}$ (see **Table 3.2**). The BCF for fish used in this assessment is 840. However, it has been shown that the BCF for fish decreases with increasing DEHP concentrations in water when the water solubility is exceeded. Therefore, the water solubility of 3 µg/l is used as a limit for the calculation of $PEC_{oral\ aquatic\ fish,}$ i.e. when a $PEC_{surface\ water}$ exceeds the water

solubility the water solubility is used for calculating $PEC_{oral\ aquatic.}$ The same approach is used for the calculation of $PEC_{oral\ aquatic\ zooplankton}$ using a wet weight BCF of 2,700. This approach may underestimate the concentration in biota in highly contaminated areas since it can be assumed that in such cases the absorption of DEHP from food becomes increasingly important. The highest measured concentration in fish from an extensive study in Austria was 2.6 mg/kg wwt. This value compares quite well with the concentration derived when multiplying BCF with water solubility. The concentration of DEHP in water was not measured in the Austrian study. For $PEC_{oral\ aquatic\ mussels}$ the calculated $PEC_{surface\ water}$ is used. This is based on a study where no difference in BCF was seen at DEHP concentrations of 4.6 and 46 µg/l respectively. Furthermore, since mussels are filter feeders it is assumed that the non-dissolved and particle bound fractions are bioavailable. Local $PEC_{oral\ worm}$ is not calculated for the production sites since STP sludge from production sites is not used as fertiliser. The calculated PECs are shown in **Table 3.4**.

Table 3.4 PECoral in aquatic and terrestrial biota

	PEC oral-aquatic[3] (mg/kg wwt)			PEC oral-terrestrial (mg/kg wwt)	
	Fish	Mussel	Invertebrates	earthworm	
Production	0.7 to 1.6	2 to 226	2 to 8	-	based on site-specific data
Polymer processing	to 1.6	4 to 38	7 to 8	0.9 to 13.4	based on default generic data
	0.7 to 0.8	2	2 to 3	0.04 to 0.14	based on site-specific data
Non-polymer[1] formulation/processing	0.7 to 1.6	2 to 106	2 to 8	0.2 to 39	based on default generic data
	0.7	2	2	0.04	based on site-specific data
Municipal STP	1.6	4.8	8	1	based on default generic data
Waste handling[2]	0.7 to 1.5	2 to 4.5	2.2 to 7.6	0.04 to 1.2	based on default generic data
Regional	1.6	2	2.2	0.07	

1) Sealants, adhesives, paints, lacquers, printing inks, ceramics
2) Paper recycling, car shredding, waste incineration
3) PEC in food is based on the assumption that 50% of prey is sourced from the local environment and 50% from the regional environment according to TGD. Predator fish are assumed to be stationary and consume all prey locally. Thus, $PEC_{oral\ invertebrates}$ is calculated based only on PEClocal surface water.

3.1 EFFECTS ASSESSMENT

Aquatic compartment (incl. sediment)

Several reliable short-term and long-term studies on effects of DEHP on aquatic organisms exist. There are no studies indicating effects on organisms only exposed to DEHP via water, and at concentrations below the water solubility. However, effects have been shown on fish exposed to DEHP via food. Therefore a NOEC for fish of 160 mg/kg_{food} has been determined.

Studies with sediment organisms showed no effects at 1,000 mg/kg dwt, the highest tested concentration.

Effects on microorganisms

Only one study, on respiration in activated sludge, is considered valid for the risk assessment of DEHP in STPs. No effects were observed at the highest tested concentration, 2,007 mg/L (NOEC).

Atmosphere

No studies exist from which a $PNEC_{atmosphere}$ could be derived.

Terrestrial compartment

There are four valid tests with soil organisms, from three trophic levels, all showing no effects. From these studies a NOEC ≥ 130 mg/kg dwt is obtained.

Secondary poisoning

For exposure via the food a NOEC of 33 mg/kg_{food} for mammalian predators is determined, based on studies showing testicular damage in rats at 4.8mg/kg/d in a three generation reproductive toxicity study. For effects on bird reproduction a NOEC of 1,700 mg/kg_{food} is calculated.

3.2 RISK CHARACTERISATION

As a realistic worst case, the PECs from generic scenarios based on default emission data have been selected except for production where site-specific data has been used. Reliable, relevant and adequate measured data for emissions is only available for a limited number of sites using DEHP (representing less than 5% of the total DEHP use). Where such data is available, it has been used to make local scenarios for the reporting sites, but has not been deemed adequate for extrapolation to all other sites using DEHP (in the order of 800 sites).

Aquatic compartment (incl. sediment)

Due to lack of effects at or below the "apparent" water solubility no PNEC can be specified. The conclusion is that there is no concern for aquatic species exposed via the water phase.

Due to its lipohilic nature and slow degradation under anaerobic conditions DEHP is often found in high concentrations in sediment. The PNEC (> 100 mg/kg dw) is derived from a study where no effects were seen at the highest tested concentration and the other sediment toxicity studies indicates even lower sensitivity. Therefore the actual PNEC may be higher. Repeating the tests at higher test substance concentrations than those used is not proposed because several studies are already available for DEHP and because of the difficulties associated with testing very high concentrations of a substance. Further emission information could be requested to refine the exposure assessment, but since the same scenarios that have PEC/PNEC ratios > 1 for sediment dwelling organisms, also have PEC/PNEC ratios > 1 for the food chains based on aquatic organisms, the risk reduction strategy will have to address the emissions in these scenarios anyway. Further studies are therefore not requested at this point.

Therefore for the use areas with a PEC/PNEC > 1, a **conclusion (i)** "on hold" is reached: There is a need for further information and/or testing, because further refinement of the assessment may remove some concern. However implementation of risk management measures to address the risks identified for other environmental spheres will eliminate the need for further information on sediment dwelling organisms.

This conclusion applies to the processing of polymers containing DEHP and for formulation of lacquers, paints, printing inks, sealants and/or adhesives containing DEHP. The scenarios that give concern are generic scenarios based on default emission data. There is no concern

for the limited number of sites that have reported measured emission data. The production sites with PEC/PNEC ratios above 1 have all ceased production of DEHP.

Atmosphere

There are no data indicating risk for the atmospheric compartment.

Terrestrial compartment

The PNEC (> 13 mg/kg dwt) is derived from a study where no effects were seen at the highest tested concentration and the other soil toxicity studies indicates even lower sensitivity, thus the actual PNEC may be higher. Repeating the tests at higher test substance concentrations than those used is not proposed because several studies are already available for DEHP and because of the difficulties associated with testing very high concentrations of a substance. Further emission information could be requested to refine the exposure assessment, but since the same scenarios that have PEC/PNEC ratios > 1 for soil organisms, also have PEC/PNEC ratios > 1 for the food chains based on terrestrial organisms, the risk reduction strategy will have to address the emissions in these scenarios anyway. Further studies are therefore not requested at this point.

Therefore a conclusion i on hold is reached: There is a need for further information and/or testing, because further refinement of the assessment may remove some concern. However implementation of risk management measures to address the risks identified for other environmental spheres will eliminate the need for further information on soil organisms

This conclusion applies to the processing of polymers containing DEHP and for formulation of printing inks, sealants and/or adhesives containing DEHP. The scenarios that give concern are generic scenarios based on default emission data. There is no concern for the limited number of sites that have reported measured emission data.

Secondary poisoning

The $PNEC_{oral}$ for DEHP in fresh food is 3.3 mg/kg for mammalians, 17 mg/kg for birds, and 16 mg/kg for fish. In this risk assessment we assume that mammalians eat fish, birds eat mussels, and fish eat invertebrates in food chains based on aquatic exposure to DEHP. In the terrestrial food chain mammalians are assumed to eat DEHP exposed earthworms.

Food chains based on aquatic organisms

The PEC/PNEC ratios are below 1 for mammalians eating fish, and for fish eating invertebrates for all scenarios. For birds eating mussels the ratio is above 1 for 6 scenarios, two of which are production sites that have now ceased production of DEHP. The generic, but not the site-specific, local risk characterisation for plastisol spread coating without air cleaning and sealants/adhesives formulation gave PEC/PNEC ratios > 1.

Therefore the conclusion is that releases from sites processing polymers containing DEHP and sites formulating printing ink, sealants and/or adhesives containing DEHP, may cause adverse effects in food chains based on aquatic organisms. The scenarios that give concern are generic scenarios based on default emission data. There is no concern for the limited number of sites that have reported measured emission data.

Food chains based on terrestrial organisms

For mammalians eating earthworms the PEC/PNEC ratios are above 1 for some sites processing polymers containing DEHP and formulating lacquers, paints, printing ink, sealants and/or adhesives containing DEHP. Therefore the conclusion is that releases from these sites may cause adverse effects in food chains based on terrestrial organisms. The scenarios that give concern are generic scenarios based on default emission data. There is no concern for the limited number of sites that have reported measured emission data.

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

Human populations exposed to DEHP are: workers, consumers including patients, and indirect exposure of man via the environment. Also children and babies have been considered in this risk assessment. MOSs have been calculated for single and multiple pathways of exposure. It should be noted that several exposure scenarios have been identified for different human populations. However, there may be other relevant exposure scenarios that have not been identified.

Occupational exposure

Occupational exposure to DEHP, mainly through inhalation but also via the dermal route, occurs in the production of DEHP, industrial use of DEHP as an additive, and at industrial end-use of semi-manufactured products and end-products containing DEHP. For the inhalation exposure, exposure has been assessed based on both measured data and modelled data, whereas dermal exposure solely is assessed using the EASE model. The occupational exposure is shown in **Table 4.1**.

Table 4.1 Occupational exposure

Exposure scenario	Inhalation exposure (mg DEHP/m^3)	Dermal exposure (mg DEHP/day)	Total internal exposure (mg DEHP/kg/day)
Production of DEHP	5	650	1.0
Industrial use of DEHP	10	420	1.4
Industrial end-use of products containing DEHP	10	1,300	2.0

Consumer exposure

The general population can be divided into sub-populations, as the extent of exposure is expected to be different in different sub-populations (e.g. adults, young/children), partly caused by a suspected higher bio-availibility of DEHP in children than in adults. The exposure can be via many different sources, such as indoor air, car interiors, toys, and medical equipment (here defined as consumer exposure), as well as indirectly via the environment (including via breast milk).

Among the consumer exposure scenarios, the highest exposure results from toys and child-care articles (a total child exposure of 0.2 mg/kg/day is estimated) as well as from some of the medical equipments, and these exposure estimates are also based to a large extent on measured data. The exposure scenarios for medical equipment causing high exposure are long-term haemodialysis in adults (3.1 mg/kg/day), long-term blood transfusion in children (0.075 mg/kg/day), transfusions in neonates (1.7 mg/kg/day), and extracorporal oxygenation in children (based on a qualitative assessment). For the other consumer exposure scenarios, exposure is lower and also based to a larger extent on estimated exposure figures.

Humans exposed via the environment

For exposure of man indirectly via the environment, urinary biomonitoring of DEHP and it's metabolites has been used to assess the *regional* exposure to DEHP. This approach resulted in an exposure level of 17 µg/kg/day, and is thought to represent the combined exposure via multiple pathways. *Local* exposure has been assessed using the EUSES model, both for children and adults. Numerous generic scenarios have been assessed, resulting in exposure to 2-67 µg/kg/day for adults and 20-312 µg/kg/day for children. However, when site-specific data has been made available (for approximately 20 out of 800 plants), the estimated exposure is 1-2 orders of magnitude lower than in the generic scenarios.

Data on the concentration of DEHP in breast milk and infant formula has been used to assess exposure of infants (0-3 months of age) and children above 6 months of age. The highest exposure occurs in infants, with an exposure to 6 or 13 µg/kg/day, from breast milk and formula, respectively.

4.1.2 Effects assessment

Toxicokinetics, metabolism and distribution

DEHP is readily absorbed and distributed in the body, but there is no evidence of accumulation. The metabolism of DEHP involves several pathways and yields a variety of metabolites. The major step in the metabolism of DEHP is hydrolysis by lipases to MEHP (mono(2-ethylhexyl)phthalate) and 2-ethylhexanol. The substance is excreted via the urine, mainly as MEHP-metabolites, but some excretion via bile also occurs in rodents. Additionally, there are animal and human data showing that DEHP is transferred to mothers' milk. The relative extent to which different metabolites are produced and excreted is very complex and may depend upon the species, the age of the animal, sex, inter-individual differences, nutrition state, prior exposure to DEHP, the amount of DEHP administered, and the route of administration.

Acute toxicity

Acute toxicity studies indicate a low acute toxicity of DEHP. The oral LD_{50} is > 20,000 mg/kg bw in rats and >10,000 mg/kg bw in mice. An inhalation LC_{50} of about 10,600 mg/m^3 for 4 hours in rats has been reported. Although there are no adequate acute dermal toxicity data, a low acute dermal toxicity is assumed.

Irritation, corrosion and sensitisation

Animal studies performed to current guidelines have shown a slight skin and eye irritation after administration of DEHP, but DEHP is not corrosive to the skin or eyes. DEHP has not been found to induce skin sensitisation in animals.

Repeated dose toxicity

Numerous studies have investigated the toxicity of DEHP following repeated oral administration to experimental animals. Critical organs for DEHP-induced toxicity in laboratory animals are the testis (see below) and the kidney. The effects on the kidneys include increased: absolute and relative kidney weights, incidence and severity of mineralization of the renal papilla, incidence of tubule cell pigments, and incidence and/or

severity of chronic progressive nephropathy. The lowest NOAEL for kidney toxicity is 29 mg/kg/day in the males and 36 mg/kg/day in females, derived from a chronic 2-year study in rats. In the liver, hepatomegaly due to hepatocyte proliferation, peroxisome proliferation and hepatocellular tumours are observed in experimental animals, but the hepatic effects are not believed to be relevant for humans.

Mutagenicity

Concerning the genotoxicity of DEHP, several different short-term tests, comparable to guideline studies and performed according to GLP, are available. The results are negative in the majority of the in vitro and in vivo studies performed with DEHP and its metabolites for detection of gene mutation, DNA damage, and chromosomal effects. The positive results are obtained in the test systems for detection of cell transformation, induction of aneuploidy, and cell proliferation, end-points which are also sensitive to several non-mutagenic substances such as tumour promoters and/or peroxisome proliferators. Taking all data into account, DEHP and its major metabolites can be considered as non-mutagenic.

Carcinogenicity

In rodent studies, liver tumours, Leydig cell tumours, and leukaemia have been observed. The liver tumours are most likely caused by peroxisome proliferation, and are therefore not considered relevant for humans. As to the other two tumours types, a relevance to humans can not be ruled out, although the evidence is inconclusive for this endpoint.

Toxicity for reproduction

A conservative NOAEL value of 4.8 mg/kg/day has been set for testicular toxicity, based on a three-generation reproductive toxicity study, showing a low incidence of small male reproductive organs and minimal testis atrophy at 14 mg/kg/day and complete atrophy and aspermia at doses of 359 mg/kg/day. Developing and prepubertal rats have been found to be more sensitive to the DEHP-induced testicular toxicity than adults, and the NOAEL for testicular toxicity is therefore also used for developmental toxicity (4.8 mg/kg/day). Studies indicate that DEHP may also interfere with the male endocrine function and also influence the male sexual development. Testicular toxicity and developmental toxicity, observed in different animal species and at relatively low dose levels are considered relevant to humans. Effects on fertility has been observed at slightly higher exposure levels in mice and rats, with a NOAEL of 20 mg/kg/day observed in mice.

4.1.3 Risk characterisation

The toxicity to exposure ratio for different human populations and scenarios has been used to derive the MOS. The lowest and most reliable NOAELs established in oral studies in animals have been used. These effects concern: repeated dose toxicity to kidney (NOAEL 29 mg/kg/day) and testes (NOAEL 4.8 mg/kg/day), as well as effects on fertility (NOAEL 20 mg/kg/day) and development (NOAEL 4.8 mg/kg/day). To correct for route-to-route extrapolation, systemic oral NOAELs for kidney and for fertility have been derived from oral NOAELs in rats: this is based on 50% oral bioavailability in adults. This extrapolation has not been necessary for the other end-points, as they are obtained from life-time studies covering phases with different absorption rates (50-100%).

Workers

The exposure scenarios considered for workers in this risk assessment concern exposure to DEHP from production of DEHP, industrial use of DEHP and industrial end-use of preparations or materials containing DEHP.

For the scenarios on production and industrial use, monitored data for inhalation exposure and modelled values for dermal exposure have been used as a realistic worst case. For the scenario industrial end-use of products containing DEHP, it is assumed that relatively high work temperatures, aerosol generation and considerable skin contact occur. There is not enough quantitative and qualitative information available on technical control measures and personal protective equipment used during production and processing to establish their effectiveness.

There is concern for the testicular effects, fertility, toxicity to kidneys, on repeated exposure and developmental toxicity for workers as a consequence of inhalation and dermal exposure during production, processing and industrial end-use of preparations or materials containing DEHP. There is no concern for the acute toxicity, irritation and sensitising effects, carcinogenicity, and mutagenicity.

Consumers

Exposure scenarios considered important for adult consumers concern exposure from indoor air, PVC gloves and car interiors. The information used is based on measurements and modelling of DEHP in indoor air, absorption from gloves and car interiors. Exposure scenarios considered important for children consumers concern exposure from toys and baby equipment, from indoor air and from car interiors. The information used is based on measurements of DEHP in artificial and human saliva for toys and baby equipment and modelled data for indoor air.

The result of the consumer assessment for adults is that: There is no concern for exposure from indoor-air, gloves, car interiors and multiple pathways of exposure for all endpoints studied.

The result of the consumer assessment for children is that: There are concerns with regard to testicular effects, fertility and toxicity to kidneys on repeated exposure as a consequence of oral exposure route to toys and child-care articles, and multiple routes of exposure. No risk is identified for exposure from indoor air or car interiors. There is no concern for the acute toxicity, irritation and sensitising effects, carcinogenicity, and mutagenicity.

Concerning exposure of consumers from medical equipment, there is concern for some or all end points: testicular effects, fertility, and toxicity to kidneys, on repeated exposure and developmental (excluding children) for the exposure scenarios

- long term haemodialysis in adults (testicular, fertility, toxicity to kidneys and developmental)
- long term blood transfusion in children (testicular)
- transfusions in neonates (testicular and fertility)

Calculating the MOS values on data from human lifetime exposure from medical equipment during infusions, there is no concern for the endpoints for haemodialysis, infusion of platelets and autopheresis.

Based on a qualitative risk assessment, there is concern for all end points: testicular effects, fertility, and toxicity to kidneys for extracorporal oxygenation in children

Humans exposed via the environment

Exposure scenarios considered important for adults and children are:

- Environmental exposure of adults
- Environmental exposure of children
- Exposure of babies/infants from infant formulae
- Exposure of babies from breast milk

Environmental exposure has been estimated by two different approaches; by calculation of daily 'regional' intake of DEHP based on the measured excretion of DEHP-metabolites in a general population, and by the EUSES model. Using EUSES, worst-case exposure has been estimated for adults and children. Both environmental monitoring and default values were used in the model. This information was compared with NOAELs derived from oral studies. MOSs for both local and regional exposure have been estimated. The assessment based on measured excretion of DEHP-metabolites is believed to be more reliable (and covering potential contamination of food during handling and processing) than the one based on EUSES, and when it comes to regional exposure, only the conclusion from the former assessment (based on biomonitoring) is presented here. However, the assessment of local exposure is solely based on EUSES.

The result for man exposed indirectly *via* the environment is that for regional exposure of adults and children: There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

In the local exposure scenarios, there is concern for children with regard to testicular effects, fertility, and toxicity to kidneys, on repeated exposure, as a consequence of exposure via food. There is no concern for adults. The scenarios that give concern for children are generic scenarios based on default emission data for children living in the vicinity of sites: processing polymer products; producing sealants/adhesives, lacquers and paints, or printing ink; municipal STP; and recycling paper. For municipal STP and paper recycling the only concern is for testicular effects. There is no concern for the limited number of sites that have reported emission data. Based on the results for local exposure from food, water and air assessment for children the conclusion is that: There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

For exposure of new-born and infants via infant formulae and breast milk, monitoring data have been used. There is no concern for any end-point for new-borns and infants exposed via infant formulae or breast milk.

Combined exposure

Exposure to DEHP apparently occurs during the entire human life time, from different sources. Exposure may therefore be equated with persistent low dose exposure. New-borns are probably the most sensitive sub-population, exposed via many sources, and perhaps at higher levels than the adults. However, combined exposure is considered in setting conclusions for the most sensitive sub-population, i.e. the new-borns, in the section 'Human

exposed via the environment', and no conclusion will therefore be drawn specifically in this section on combined exposure.

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

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

5 RESULTS

5.1 ENVIRONMENT

Atmosphere

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

This conclusion is reached because the risk assessment shows that risks are not expected. Risk reduction measures already being applied are considered sufficient.

Aquatic ecosystem

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

This conclusion is reached because of concern for birds consuming mussels exposed to DEHP near sites processing polymers with DEHP or sites producing printing inks, sealants and/or adhesives with DEHP. The scenarios that give concern are generic scenarios based on default emission data. There is no concern for the limited number of sites that have reported measured emission data.

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

Further refinement of the assessment may remove some concern. This conclusion is reached because of concern for sediment dwelling organisms as a consequence of exposure to DEHP near sites processing polymers with DEHP or sites producing lacquers, paints, printing inks, sealants and/or adhesives with DEHP. The scenarios that give concern are generic scenarios based on default emission data. There is no concern for the limited number of sites that have reported measured emission data.

Further refinement of the assessment may remove some concern. However implementation of risk management measures to address the risks identified for other environmental spheres will eliminate the need for further information on sediment dwelling organisms.

Terrestrial ecosystem

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

This conclusion is reached because of concern for mammals consuming earthworms exposed to DEHP near sites processing polymers with DEHP or sites producing lacquers, paints, printing inks, sealants and/or adhesives with DEHP. The scenarios that give concern are generic scenarios based on default emission data. There is no concern for the limited number of sites that have reported measured emission data.

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

Further refinement of the assessment may remove some concern. However considering that there are other concerns for these scenarios that will require risk management measures, further information will only be requested if needed when risk management measures have

been agreed. This conclusion is reached because of concern for soil organisms exposed to DEHP near sites processing polymers with DEHP or sites producing printing inks, sealants and/or adhesives with DEHP. The scenarios that give concern are generic scenarios based on default emission data. There is no concern for the limited number of sites that have reported measured emission data.

Further refinement of the assessment may remove some concern. However implementation of risk management measures to address the risks identified for other environmental spheres will eliminate the need for further information on soil organisms.

Micro-organisms in the sewage treatment plant

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

This conclusion is reached because the risk assessment shows that risks are not expected. Risk reduction measures already being applied are considered sufficient.

5.2 HUMAN HEALTH

5.2.1 Human health (toxicity)

The conclusion of the assessment of the risks to

Workers

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

This conclusion is reached because of:

- concerns for testicular effects, fertility, toxicity to kidneys, on repeated exposure and developmental toxicity as a consequence of inhalation and dermal exposure during production, processing and industrial end-use of preparations or materials containing DEHP

Consumers

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

This conclusion is reached because of:

- concerns for children in regard to testicular effects, fertility, and toxicity to kidneys, on repeated exposure, as a consequence of oral exposure from toys and child-care articles, and multiple routes of exposure.
- concerns for children undergoing long-term blood transfusion and neonates undergoing transfusions with regard to testicular toxicity and fertility, as a consequence of exposure from materials in medical equipment containing DEHP.

- concerns for adults undergoing long-term haemodialys with regard to repeated dose toxicity to kidney and testis, fertility, and developmental toxicity, as a consequence of exposure from materials in medical equipment containing DEHP.

Humans exposed via the environment

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

This conclusion is reached because of:

- concerns for children with regard to testicular effects, fertility, and toxicity to kidneys, on repeated exposure, as a consequence of exposure via food locally near sites processing polymers with DEHP, or sites producing sealants and/or adhesives, paints and lacquers or printing inks with DEHP. The scenarios that give concern are generic scenarios based on default emission data. There is no concern for the limited number of sites that have reported measured emission data.
- concerns for children with regard to testicular toxicity, as a consequence of exposure via food grown locally near sites recycling paper or municipal sewage treatment plants. The scenarios that give concern are generic scenarios based on default emission data.

5.2.2 Human health (risk from physico-chemical properties)

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

This conclusion is reached because the risk assessment shows that risks are not expected. Risk reduction measures already being applied are considered sufficient.

European Commission

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