Annex XV dossier

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE AS A CMR CAT 1 OR 2, PBT, vPvB OR A SUBSTANCE OF AN EQUIVALENT LEVEL OF CONCERN

Substance Name: Dibutyl phthalate

EC Number: 201-557-4

CAS Number: 84-74-2

- *It is proposed to identify the substance as a CMR according to Article 57(c).*

CONTENTS

TABLES

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE AS A CMR CAT 1 OR 2, PBT, VPVB OR A SUBSTANCE OF AN EQUIVALENT LEVEL OF CONCERN

Substance Name: Dibutyl phthalate

EC Number: 201-557-4

CAS number: 84-74-2

- *It is proposed to identify the substance as a CMR according to Article 57(c).*

Summary of how the substance meets the CMR (Cat 1 or 2), PBT or vPvB criteria, or is considered to be a substance of an equivalent level of concern

Dibutyl phthalate (DBP) is classified according to the 28th ATP of Directive 67/548/EEC as:

Repr. Cat. 2; R61 (May cause harm to the unborn child)
Repr. Cat. 3; R62 (Possible risk of impaired fertility)
N; R50 (Dangerous for the environment: very toxic to aquatic organisms)

Registration number(s) of the substance or of substances containing the substance:

Not available.

JUSTIFICATION

1 IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

1.1 Name and other identifiers of the substance

Chemical Name: Dibutyl phthalate

EC Name: Dibutyl phthalate

CAS Number: 84-74-2

IUPAC Name: Dibutyl phthalate

1.2 **Composition of the substance** (from EU RAR (2004))

For each constituent/ impurity/ additive, fill in the following table (which should be repeated in case of more than one constituent). The information is particularly important for the main constituent(s) and for the constituents (or impurity) which influence the outcome of the dossier.

Chemical Name: Dibutyl phthalate

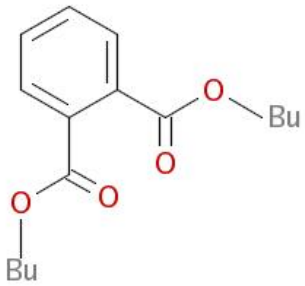
EC Number: 201-557-4

CAS Number: 84-74-2

IUPAC Name: Dibutyl phthalate

Molecular Formula: $C_{16}H_{22}O_4$

Structural Formula:



Molecular Weight: 278.34

Typical concentration (% w/w): Degree of purity ≥ 99% (w/w)

Concentration range (% w/w): -

Impurity: ca. 0.01% (w/w) butal-1-ol (CAS 71-36-3)
ca. 0.01% (w/w) butyl benzoate (CAS 136-60-7)

Additives: none

1.3 Physico-chemical properties

Table 1: Summary of physico- chemical properties, from EU RAR 2004

REACH ref Annex, §	Property	IUCLID section	Value	[enter comment/reference or delete column]
VII, 7.1	Physical state at 20°C and 101.3 kPa	3.1	oily liquid	
VII, 7.2	Melting/freezing point	3.2	-69°C	DIN-ISO 3016 BASF AG Ludwigshafen; Huels AG Marl Sicherheitsdatenblatt Palatinol C 25.4.1994
VII, 7.3	Boiling point	3.3	340°C at 10,013 hPa	BASF AG Ludwigshafen/Kirk-Othmer 1982; Huels AG Marl/*i.a.* Kemppinen & Gogcen 1956
VII, 7.5	Vapour pressure	3.6	$9.7 \pm 3.3 \times 10^{-5}$ Pa at 25°C	BASF AG Ludwigshafen; Huels AG Marl Banerjee & Howard, 1984
VII, 7.7	Water solubility	3.8	10 mg/L at 20°C	
VII, 7.8	Partition coefficient n-octanol/water (log value)	3.7 partition coefficient	log K_{ow} 4.57 at 20°C	measured (Huels AG Marl/Leyder & Boulanger, 1983) and calculated (BASF AG Ludwigshafen/BASF AG, 1987)
IX, 7.16	Dissociation constant	3.21		

2 MANUFACTURE AND USES

Not relevant for this type of dossier.

Information on uses may be useful for prioritisation for inclusion in Annex XIV but this should be summarised under Section 9.2.

3 CLASSIFICATION AND LABELLING

3.1 Classification in Annex I of Directive 67/548/EEC

DBP was inserted into Annex I of Directive 67/548/EEC with the 28th ATP (Commission Directive 2001/59/EC of 6 August 2001) and is classified as follows:

Index: Number: 607-318-00-4

Repr. Cat. 2; R61 (May cause harm to the unborn child)

Repr. Cat. 3; R62 (Possible risk of impaired fertility)

N; R50 (Dangerous for the Environment: Very toxic to aquatic organisms)

Specific concentration limits: none

Labelling:

Symbols: T; N

R-Phrases: 61-62-50

S-Phrases: 53-45-61

3.2 Self classification(s)

This should include the classification, the labelling and the specific concentrations limits. The reason and justification for no classification should be reported here.

It should be stated whether the classification is made according to Directive 67/548/EEC criteria or according to GHS criteria.

4 ENVIRONMENTAL FATE PROPERTIES

4.1 Degradation

4.1.1 Stability

Corresponds to IUCLID 4.1

4.1.2 Biodegradation

4.1.2.1 Biodegradation estimation

4.1.2.2 Screening tests

4.1.2.3 Simulation tests

4.1.3 Summary and discussion of persistence

4.2 Environmental distribution

4.2.1 Adsorption/desorption

Corresponds to IUCLID 4.4.1

4.2.2 Volatilisation

Corresponds to IUCLID 4.4.2

4.2.3 Distribution modelling

4.3 Bioaccumulation

4.3.1 Aquatic bioaccumulation

4.3.1.1 Bioaccumulation estimation

4.3.1.2 Measured bioaccumulation data

4.3.2 Terrestrial bioaccumulation

4.3.3 Summary and discussion of bioaccumulation

4.4 Secondary poisoning

Assessment of the potential for secondary poisoning

5 HUMAN HEALTH HAZARD ASSESSMENT

5.1 Toxicokinetics (absorption, metabolism, distribution and elimination)

5.2 Acute toxicity

5.2.1 Acute toxicity: oral

5.2.2 Acute toxicity: inhalation

5.2.3 Acute toxicity: dermal

5.2.4 Acute toxicity: other routes

5.2.5 Summary and discussion of acute toxicity

C&L including weight-of-evidence considerations.

5.3 Irritation

Not relevant for this type of dossier.

5.4 Corrosivity

Not relevant for this type of dossier.

5.5 Sensitisation

Not relevant for this type of dossier.

5.6 Repeated dose toxicity

5.6.1 Repeated dose toxicity: oral

5.6.2 Repeated dose toxicity: inhalation

5.6.3 Repeated dose toxicity: dermal

5.6.4 Other relevant information

5.6.5 Summary and discussion of repeated dose toxicity:

C&L, dose-response estimation including weight-of-evidence considerations.

5.7 Mutagenicity

5.7.1 In vitro data

5.7.2 In vivo data

5.7.3 Human data

5.7.4 Other relevant information

5.7.5 Summary and discussion of mutagenicity

C&L, dose-response estimation including weight-of-evidence considerations.

5.8 Carcinogenicity

5.8.1 Carcinogenicity: oral

5.8.2 Carcinogenicity: inhalation

5.8.3 Carcinogenicity: dermal

5.8.4 Carcinogenicity: human data

5.8.5 Other relevant information

5.8.6 Summary and discussion of carcinogenicity

C&L, dose-response estimation including weight-of-evidence considerations.

5.9 Toxicity for reproduction

5.9.1 Effects on fertility

5.9.2 Developmental toxicity

5.9.3 Human data

5.9.4 Other relevant information

Estrogenic activity of DBP has been shown in some special *in vitro* assays, however the effects were weak and not confirmed in *in vivo* studies. Therefore the relevance of the estrogenic effects observed in vitro for the in vivo estrogenic toxicity of DBP is questionable. Moreover the results of the developmental studies were indicative of an **antiandrogenic effect** of DBP rather than an estrogenic effect (Mychlreest et al., 1998).

Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Material in Contact with Food (AFC) on a request from the Commission related to Di-Butylphthalate (DBP) for use in food contact materials, Question N° EFSA-Q-2003-192Adopted on 23 June 2005 by written procedure

According to the recent opinion of the Scientific Panel on food additives, flavourings, processing aids and material in contact with food (AFC) on a request from the Commission related to DBP for use in food contact materials (2005) a TDI of 0.01 mg/kg bw based on a LOAEL of 2 mg/kg bw/day (allocating an uncertainty factor of 200) was established. The LOAEL was derived from a recent developmental toxicity study in rats (dietary exposure during late gestation to end of lactation) showing developmental effects at 20 mg/kg bw (Lee et al., 2004 cited in EU RAR).

In vitro assays

The potential estrogenic activity of DBP was demonstrated in an *in vitro* study with human breast cancer MCF-7 cells by induction or repression of endogenous estrogen- regulated marker genes (*pS2, MAO-A, TGFβ3, α1ACT).* Estrogenic activity was demonstrated for DBP, but was much lower than those of Estradiol (E_2), Diethylstilbestrol and Zearalenon. For example the expression level of pS2 was induced almost 25-fold after exposure to 10^{-10}M E2 whereas the induction after exposure to 10-4 M DBP was 10- fold (Jorgensen et al., 2000).

Animal studies

Fenell et al. (2004) investigated pharmacokinetics of DBP in pregnant rats and found Mono-butyl-phthalate to be the major metabolite of DBP. With increasing dose, there was a nonlinear increase in area under curve (AUC) for MBP, with a ten-fold increase in fetal plasma between 50 mg/kg and 250 mg/kg. In amniotic fluid, the major metabolite was MBP glucuronide. This study indicated that MBP, the active metabolite of DBP can cross the placenta in late gestation, and that the metabolism of MBP is saturable.

Findings in humans

Studies in humans, with limited value, due to the small number of subjects (n=85) indicate that prenatal exposure with phthalates (i.e. DBP) at environmental levels may affect male reproductive development in humans. Prenatal exposure to DBP, measured as MBP concentrations in the urine of mothers, was inversely related to the anogenital distance (AGD) in the boys (mean age 12,5 month) (Swan et al, 2005 cited in EU RAR 2004; EU RAR, 2007). According to the RAR of BBP studies with larger sample size are warranted to draw further conclusions (EU RAR, 2007).

In a study by Main et al. (2005) monoester metabolite contamination of human breast milk was investigated on the possible influence on the postnatal surge of reproductive hormones in newborn boys as a sign of testicular dysgenesis (Danish - Finnish cohort study in cryptorchism 1997-2001). The median concentration of MBP in breast milk was 9,6 µg/l. Higher MBP concentrations were positively correlated with SHBG (sex-hormone binding globuline), LH (luteinising hormone)/free testosterone ratio and negatively correlated with free testosterone. No association was found between phthalate monoester levels in breast milk and cryptorchidism.

Duty et al. (2005) investigated the relationship of urinary phthalate levels and serum hormone levels in men. An increase in hormone levels of Inhibin B was found in men with higher urinary metbolites of MBP, whereas according to findings in previous studies a decrease was expected. No increase of FSH levels could be detected. The authors conclude that further analyses with a larger study population are warranted.

Hauser et al., (2006) reported altered semen quality in relation to urinary concentrations of phthalate monoester and oxidative metabolites in humans. Semen from 463 male partners of subfertile couples was investigated and dichotomized according WHO reference values for sperm concentration and motility as well as the Tygberg Kruger Strict criteria for morphology. Results were adjusted for age, abstinence time and smoking status. MBuP (mono-n-butyl-phthalate) was found in 97% of the samples. A dose -response relationship of MBuP with low sperm concentration and motility was found. This result is consistent with studies in laboratory rodents showing testicular toxicity. The study confirms previous results on the relationship of altered semen quality with exposure to MBuP at general population levels. Another study of Jonsson et al. (2005), performed in Swedish young men recruited to medical examination prior to military service found no relationships of MBuP with any of the semen parameters; however there were important differences in study population, study design, analytical methods and statistical analyses.

In studies commissioned by DG Environment of the European Commission a list of 146 substances with endocrine disruption properties has been established (http://ec.europa.eu/environment/docum/pdf/bkh_annex_13.pdf). DBP has been classified as Cat. 3 for wildlife, Cat. 1 for Humans and Combined as Cat. 1 (Cat.1: Evidence for endocrine disruption in living organisms; Cat. 2: Evidence of potential to cause endocrine disruption; Cat.3: No evident scientific basis). DBP is also listed in the list of 66 potentially endocrine substances with classification of high exposure concern (http://ec.europa.eu/environment/docum/pdf/bkh_annex_15.pdf) (EUROPEAN COMMISSION DG ENV, 2000).

5.9.5 Summary and discussion of reproductive toxicity

Based on the available reproduction, fertility and developmental studies and according to EC criteria, DBP is classified in Category 3 for effects on fertility and in Category 2 for effects on developmental toxicity and is labelled with R-phrase 62 (Possible risk of impaired fertility) and R-phrase 61 (May cause harm to the unborn child). A LOAEL of 52 mg/kg bw was established based on embryotoxic effects in rats in the absence of maternal toxicity in a two-generation reproduction study with a continuous breeding protocol including improved sensitive endpoints (such as sperm parameters, estrous cycle characterisation and detailed testicular histopathology) and with exposure of male and female animals. The protocol of this study was supposed to adequately identify compounds with endocrine activity (NTP, 1995; Wine et al., 1997 both cited in EU RAR). Based on the available developmental studies in mice an oral NOAEL of 100 mg/kg bw was derived for teratogenicity, embryotoxicity and maternal toxicity. At the next higher dose-level of 400 mg/kg bw embryotoxic and teratogenic effects were seen in the presence of maternal toxicity (Hamano et al., 1977 cited in EU RAR). In rats developmental studies with exposure during gestation or during gestation and lactation, revealed delayed preputial separation and reproductive tract malformations in male offspring at oral doses ≥ 250 mg/kg bw. Maternal toxicity was seen at doses ≥ 500 mg/kg bw. At the lowest oral dose-level of 100 mg DBP/kg bw, studied in developmental studies in rats, still delayed preputial separation in male progeny was seen. A NOAEL could not be derived from the developmental studies in rats (Mychlreest et al., 1999 cited in EU RAR). No reproduction, fertility or developmental studies with dermal exposure or exposure by inhalation to DBP are available. An epidemiological study on possible reproductive effects in occupationally exposed women is inadequate for assessment of possible reproductive effects caused by DBP in humans in the working environment due to several limitations such as lack of an adequate control group, small study population size, adequate documentation of protocol and results and mixed exposure (Aldyreva et al., 1975 cited in EU RAR).

5.10 Other effects

5.11 Derivation of DNEL(s) or other quantitative or qualitative measure for dose response

5.11.1 Overview of typical dose descriptors for all endpoints

5.11.2 Correction of dose descriptors if needed (for example route-to-route extrapolation)

5.11.3 Application of assessment factors

5.11.4 Selection/ identification of the critical DNEL(s)/ the leading health effect

6 HUMAN HEALTH HAZARD ASSESSMENT OF PHYSICO-CHEMICAL PROPERTIES

Not relevant for this type of dossier.

7 ENVIRONMENTAL HAZARD ASSESSMENT

7.1 Aquatic compartment (including sediment)

7.1.1 Toxicity test results

7.1.1.1 Fish

Short-term toxicity to fish

Long-term toxicity to fish

7.1.1.2 Aquatic invertebrates

Short-term toxicity to aquatic invertebrates

Long-term toxicity to aquatic invertebrates

7.1.1.3 Algae and aquatic plants

7.1.1.4 Sediment organisms

7.1.1.5 Other aquatic organisms

7.1.2 Calculation of Predicted No Effect Concentration (PNEC)

7.1.2.1 PNEC water

7.1.2.2 PNEC sediment

7.2 Terrestrial compartment

7.2.1 Toxicity test results

7.2.1.1 Toxicity to soil macro organisms

7.2.1.2 Toxicity to terrestrial plants

7.2.1.3 Toxicity to soil micro-organisms

7.2.1.4 Toxicity to other terrestrial organisms

Toxicity to birds

Toxicity to other above ground organisms

7.2.2 Calculation of Predicted No Effect Concentration (PNEC_soil)

7.3 Atmospheric compartment

7.4 Microbiological activity in sewage treatment systems

7.4.1 Toxicity to aquatic micro-organisms

7.4.2 PNEC for sewage treatment plant

7.5 Calculation of Predicted No Effect Concentration for secondary poisoning (PNEC_oral)

7.6 Conclusion on the environmental classification and labelling

8 PBT, VPVB AND EQUIVALENT LEVEL OF CONCERN ASSESSMENT

8.1 Comparison with criteria from annex XIII

Not relevant for this dossier.

8.2 Assessment of substances of an equivalent level of concern

Endocrine disrupting effects of DBP have been shown in various studies. These are summarised in Section 5.9.

8.3 Emission characterisation

8.4 Conclusion of PBT and vPvB or equivalent level of concern assessment

Not relevant for this dossier.

INFORMATION ON USE, EXPOSURE, ALTERNATIVES AND RISKS

1 INFORMATION ON EXPOSURE

Production volumes

The RAR (EU RAR, 2004) reports an estimated production volume of DBP in the EU in 1998 of 26,000 tonnes, of which 8,000 tonnes was thought to be exported outside the EU (Industry, 1999 cited in EU RAR). This leads to a use volume of about 18,000 t/a. There is no import of DBP from outside the EU. There is a clear decreasing trend in the production of DBP: 49,000 t/a (1994) - 37,000 t/a (1997) - 26,000 t/a (1998).

The production (> 1000 tonnes) of DBP in 1998 was located at three production sites in the EU.

Table 2: Production sites (> 1000 tonnes) of DBP in 1998.

Company	Location
BASF	Ludwigshafen, Germany
OXENO	Marl, Germany
BP	Hull, United Kingdom*
Lonza	Porto Marghera, Italy*
SISAS	Pioltello, Italy

* Stopped production since 1998

DBP is produced by the reaction of phthalic anhydride with n-butanol in the presence of concentrated sulphuric acid as a catalyst. Excess alcohol is recovered and recycled and the di-n-butyl phthalate is purified by vacuum distillation and/or activated charcoal.

Harris et al. (1997 cited in EU RAR) reported a total volume of 20,000 to 40,000 t/a of European consumption.

Information on uses

Table 3: Industrial and use categories of DBP.

Industrial category	Use category
Polymers Industry	softener (plasticizer in PVC)
Others (adhesives)	softener (paper and packaging, wood building and automobile industry)
Pulp, Paper and Board industry	softener (printing inks)
Others	softener/solvent (e.g. sealants, nitrocellulose paints, film coatings, glass fibres and cosmetics)

The largest usage of DBP in general is as a plasticizer in resins and polymers such as polyvinyl chloride. Plasticizers are materials incorporated into a plastic in order to increase its workability and distend ability. DBP is further used a.o. in printing inks, adhesives, sealants/grouting agents, nitrocellulose paints, film coatings and glass fibres. The ubiquity of DBP in consumer products is demonstrated by its wide usage in cosmetics: a perfume solvent and fixative, a suspension agent for

solids in aerosols, a lubricant for aerosol valves, an antifoamer, a skin emollient and a plasticizer in nail polish and fingernail elongators (IPCS/WHO, 1995 cited in EU RAR).

In Denmark DBP has been found in 1,176 products accounting for 2,848 t/a (Danish Product Register, 1995 cited in EU RAR). In 94 products accounting for 388 t/a the concentration of DBP is 80 - 100%. In Sweden DBP has been found in 343 products, 38 of which are available to consumers (KEMI, 1995 cited in EU RAR). In 1999, still a total number of 230 products (i.a. adhesives, plasticizers, paints) of which 26 are consumer products have been registered in the Swedish Product Register (KEMI, 1999). Furthermore, the Annual Report on Hazardous Substances, produced jointly by the Swedish Chemicals Agency and Statistics Sweden, documents a total substance flow for DBP of 108 tonnes, where 9 tonnes are produced and the remaining 97 tonnes imported into Sweden (KEMI & SCB, 2008). While in 1999 no manufacture of DBP took place this has changed to 9 tonnes in 2006 (KEMI & SCB, 2008).

A number of authors have given estimates of the quantitative usage distribution of DBP (Industry report, 1995; BUA, 1987; RIVM, 1991; Canadian EPA, 1994; Cadogan et al., 1994 all cited in EU RAR). Based on 1997 data, on average around 76% of DBP is used as a plasticizer in polymers, 14% in adhesives, 7% in printing inks and the remaining 3% of DBP is used in miscellaneous other applications.

1.1 Information on exposure

Summary of Human Exposure as described in EU RAR, 2004

The human population can be exposed to DBP via the workplace, through the use of consumer products and indirectly via the environment; human exposure occurs through inhalation and ingestion as well as after dermal contact.

Occupational Exposure:

DBP is or may be produced in the following chemical industries with the mentioned purposes:

- basic chemicals: production of dibutyl phthalate;
- polymer industry:
- plasticizer in Poly Vinyl Alcohol (PVA);
- plasticizer in Poly Vinyl Chloride (PVC);
- plasticizer in rubber industry; polychloroprene rubber acrylonitrile-butadiene copolymer (nitrile) rubber;
- solvents for nitrocellulose esters, colours, oils, natural resins;
- lacquers and varnishes industry: softener;
- printing ink industry: use as a softener;
- additive in textile industry;
- additive in insecticides;
- polymethylmethacrylate for the purpose of pigment- and additive pastes.

Because of its relatively high volatility, compared to other plasticizers, DBP is only used in combination with other plasticizers, mostly high molecular phthalates. DBP has better low temperature flexibility in soft PVC than for example diisobutyl phthalate (DIBP).

Occupational exposure towards DBP takes place during the production of DBP, in the polymer industry and in the paint and printing industry. Exposure data during the production of DBP are summarized below.

Table 4: Conclusions of the occupational exposure assessment

Scenario	Exposure		Estimated inhalation exposure level (mg/m^3)					Estimated skin exposure level (mg/day) [a)]	
	Duration (hr/day)	Frequency (day/year)	Full shift (8-hour time weighted average)			Short term			
			Typical	Method [b)]	Worst Case	Method[b)]	Level	Method[b)]	
1.Production	6-8	100-200	2	Meas.	5	Meas.	10	Expert	420
2. Production of products containing DBP	6-8	100-200	2	Meas.	5	Meas.	10		420
3. Use of products containing DBP - aerosol forming activities	6-8	100-200	2	Expert EASE	10	Expert EASE	20	Expert	975
3. Use of products - non-aerosol forming activities	6-8	100-200	negligible	Expert EASE	negligible	Expert EASE	negligible	Expert EASE	

[a)] Based on EASE dermal exposure model

[b)] Meas. = mostly based on measured data; Expert = derived from measured data or model results largely using expert judgement; EASE = mostly based on results of the EASE model

Consumer Exposure:

DBP has been used in making flexible plastics that are part of many consumer products, including home furnishing, paints, clothing and cosmetic products. In Denmark DBP has been found in 1,176 products accounting for 2,848 t/a (Danish Product Register, 1995 cited in EU RAR). In 94 products accounting for 388 t/a the concentration of DBP was 80-100%. In Sweden DBP has been found in 343 products, 38 of which are available to consumers (KEMI, 1995 cited in EU RAR).

DBP is used in several products, some of which are available to consumers such as cosmetics, adhesives and regenerated cellulose film (cellophane) wrapped food. Attention has to be given to the (un)intentional use of DBP in children's toys, in view of the general public concern on the use of phthalates in PVC toys.

The marketing and use of BBP and preparations containing DBP in toys and childcare articles is prohibited through the 22nd amendment to Directive (76/769/EEC): It shall not be used as substance or as constituent of preparations, at concentrations of greater than 0.1% by mass of the plasticized material, in toys and childcare articles. Such toys and childcare articles containing DBP in a concentration greater than the limit mentioned above shall not be placed on the market.

Four exposure scenarios were considered referring to the above-mentioned uses of DBP: I Nailpolish, II Adhesive, III Cellophane wrapped food and IV Toys for children. The worst-case approach for the intake of DBP from use of nail polish was estimated using CONSEXPO. Whereas the dermal uptake was negligible the inhalatory route results in a total internal dose of 2 x 10^{-9} mg/kg bw/day.

The worst case calculation for the intake of DBP from the use as adhesive through the inhalatory route accounts for 3,43x 10^{-4} mg/kg bw/day.

The intake of DBP through the consumption of cellophane wrapped food. The maximum daily intake of DBP was estimated to be 1,9 mg/day with a calculated average intake of 0,23 mg DBP/day (MAFF, 1987 cited in EU RAR 2004).

DBP is not added intentionally to soft PVC toys and child - care articles, but can be present as impurity or by-product in trace amounts. CSTEE took the maximum reported emission rates (259 µg/dm^2/24h) as a worst-case situation (Rastogi et al., 1997 cited in EU RAR) and converted this value to a daily DBP dose, assuming that an 8-kg infant mouthed 10 cm^2 of a toy for 6 hrs every day. This resulted in a daily DBP dose of 0.81 µg/kg bw/day (CSTEE 1998 cited in EU RAR).

Exposure via the environment:

Because of its diverse uses dibutyl phthalate is widespread in the environment and has been identified in air, water and soil (ATSDR, 1990 cited in EU RAR). Human exposure via the environment may occur through contact with contaminated air, water, soil or food.

Local calculated annual average concentrations in the air range from 0.02 µg/m^3 (Production, Processing of adhesives) to 2.4 µg/m^3 (Processing of polymers).

The total human intake via air, drinking water and food (EUSES) for all emission scenarios at local scale ranges from 7.86 x 10^{-4} mg/kg/d (production) to 0.0925 mg/kg/d (processing of polymers). The regional exposure via air was calculated to be 0.006 µg/m^3, whereas the total human intake was 3.59 x 10^{-4} mg/kg/d.

DBP has been identified in human breast milk in concentrations ranging from 10 to 51 µg/kg (Gruber et al., 1998; Bruns-Weller and Pfordt, 2000 all cited in EU RAR). Whether the DBP in human breast milk originates from direct or from indirect sources is not clear, but given the diffuse use and the diffuse emissions in the environment, the latter is more likely. The exposure to babies is calculated according to the WHO (1998 cited in EU RAR) and varies between 1.2 and 6.0 µg DBP/kg bw/day.

There are several recent studies on intake levels available, which are not included in the EU RAR:

Data on DBP concentration in foods and diets in UK (1993) and Denmark (2003) were used to estimate dietary exposure. In UK intakes of DBP from dietary sources were estimated to be respectively 0.2 and 0.5 µg/kg bw/day for adults. Exposure at high percentiles was estimated as 10.2 µg/kg/day in the Danish study (Petersen and Breindahl, 2000). A more recent Danish study estimated daily intakes to be 1.6 µg/kg bw /day in adults, 3.5µg/kg bw/day in children aged 7-14 years and 8µg/kg bw/day in children aged 1 to 6 years (Müller et al., 2003).

The panel noted that exposure to DBP from food consumption is in the range of the TDI and it has to be considered that there are a number of other sources which contribute to the overall human exposure to DBP (EFSA, 2005).

In a retrospective human biomonitoring study 24h urine samples from the German Environmental Specimen Bank for Human Tissues, which were collected from 634 subjects (predominantly students, age range 20-29 years, 326 females, 308 males) in 9 years between 1988 and 2003 (each n >or= 60) were analysed for the concentrations of primary and/or secondary metabolites of various phthalates, including DBP (Wittassek et al., 2007). The median daily intakes in the subsets between 1988 and 1993 were quite constant for DBP (approx. 7 µg/kg bw/d), but from 1996 the median level decreased continuously until 2003 (DBP 1.9 µg/kg bw/d). Female subjects exhibited significantly higher daily intakes for DBP (p=0.013). Overall, for 14% of the subjects daily DBP intakes were above the tolerable daily intake (TDI) value deduced by the European Food Safety Authority (EFSA) of 10 µg/kg bw/d. The frequency of exceedance decreased during the years and

was beneath 2% in the 2003 subset. Even though transgressions of the exposure limit values of the EFSA and the US Environmental Protection Agency (US EPA) occurred only in a relatively small share of the subjects, the cumulative exposure to all phthalates and possible dose-additive endocrine effects of these phthalates has to be taken into account (Wittassek et al., 2007).

According to the results of the German Environmental Survey in Children TDI values for DBP were exceeded in 37% of the investigated children (Kolossa-Gehring, 2007).

A recent study investigated urinary phthalate metabolite concentrations in 102 German subjects between 6 and 80 years of age and estimated a median daily intake of 2.1µg/kg/day for DBP. Children had higher exposures compared to adults and seem to have a more effective oxidative metabolism of phthalates. Due to the endocrine disrupting properties as shown in animal experiments the authors suggest that a concept of a cumulative TDI value may be more appropriate for the consideration of the overall exposure and the potential human health risks resulting from everyday and simultaneous exposure to several phthalates (Wittasek and Angerer, 2008).

Environmental Exposure

Environmental Monitoring data

The main focus of this section is to present Austrian monitoring data which demonstrate wide distribution of DBP in various environmental compartments. These data are also compared to other European monitoring data. For this purpose the risk assessment report (EU RAR, 2004) and current literature are used. New studies which have not been included in the risk assessment report have been taken into account in this dossier.

Measured concentrations of DBP in surface- , ground-, influent-, effluent water, sewage sludge, biota, articles of daily use (e.g. toys) and house dust are summarized in **Tables 5 - 13**.

As phthalates occur in plastics used in laboratories and sample collectors, contamination may sometimes lead to false positive results. There is only little information available in older reports on how such contamination had been avoided. More recent measurements are less affected by such contamination problems. Data presented within this dossier are of high quality and ensure avoidance of contamination due to various precautionary principals (**Tables 5 - 13**), e.g. using glassware, pre-treatment of glassware using solvents and heating, analysing blank values.

Mean and median values are calculated by the so called minimum approach and more than 50% of individual analysed values need to exceed the limit of quantitation (LOQ) to them. Values below the limit of detection (LOD) were set to zero for the statistical analyses and values below the LOQ were set to LOQ.

Compartments with positive findings of DBP

Measured concentrations of DBP in surface water

DBP concentrations in Austrian surface water are presented in **Table 5.** The number of positive findings was 6%. The maximum concentration was 0.79µg/l.

Table 5: Concentration of DBP [µg/l] in surface water (Austria)

Date	No. measured values	No. of positive findings [%] *	LOD	LOQ	Min.	Max.	Median minimum approach	Mean minimum approach	Ref.
Mar. 99	34	6%	0.25	0.5	<0.5	0.79	-	-	UBA, Band 161

all values in [µg/l]
abbreviations: LOD, limit of detection; LOQ, limit of quantitation; Min., minimum; Max., maximum; Ref., reference; n. d., not detected;
* measured values > LOQ;

The EU RAR (2004) contains a number of measured DBP concentrations in European surface water. The values of most samples are below or slightly higher than 1µg/l. But there are also a few values which are significantly higher than 1 µg/l. From 1987 to 1988 1-6 µg/l DBP were found in water samples in Noord Braband (Zwalijs, 1989 cited in EU RAR). In 1984 concentrations between 12.1 and 33.5 µg/l of DBP were detected in surface waters of the UK (Fatoki and Vernon, 1990 cited in EU RAR). An investigation of 115 surface water samples in Germany revealed DBP concentrations from 0.12 to 8.80 µg/l (median: 0.50 µg/l; only one sample lay below the determination limit) (Fromme et al., 2002). High concentrations may probably be attributed to industrial activities, the small run off and a high population density in an area.

Measured concentrations of DBP in the influent and effluent of wastewater treatment plants

Table 6 presents measured DBP concentrations in the influent of sewage treatment plants (STP); concentrations up to 21.3 µg/l were found. The number of positive findings within a group of measurements was in the range of 50% to 100%. It should be noted, that the DBP concentration in the influent depends on various factors such as the percentage of industrial discharges, weather conditions or population equivalents.

Table 6: Concentration of DBP [µg/l] in the influent of Austrian STPs

Date	No. measured values	No. of positive findings [%] *	LOD	LOQ	Min.	Max.	Median minimum approach	Mean minimum approach	Ref.
Nov. 07	16	50%	0.083 – 6.8	0.29 - 14	n.d.	8.7	2.0	3.7	unpublished data
2000	4	100%	0.04	0.07	0.4	21.3	2.2	6.5	UBA, Band 121
Mar. 99	17	59%	0.25	0.5	<0.5	2.3	0.7	0.8	UBA, Band 151
Dec. 98	6	100%	0.25	0.5	1.1	3.1	2.6	2.3	UBA, Band 141

all values in [µg/l]

abbreviations: LOD, limit of detection; LOQ, limit of quantitation; Min., minimum; Max., maximum; Ref., reference; n. d., not detected;
* measured values > LOQ;

DBP concentrations in the effluent of sewage treatment plants were found in concentrations up to 3.2 µg/l. The number of positive findings varied between 12% and 100% (**Table 7**). This can be partially explained by the fact that improvements in the analytical methodology allowed to achieve lower LOQs in the more recent measurements (LOQs may exhibit a range of values because of the differing characteristics of background composition in different wastewater samples).

Table 7: Concentration of DBP [µg/l] in the effluent of Austrian STPs

Date	No. measured values	No. of positive findings [%] *	LOD	LOQ	Min.	Max.	Median minimum approach	Mean minimum approach	Ref.
Nov. 07	16	50%	0.044 – 4.8	0.15 – 9.6	n.d.	2.4	0.7	1.0	unpublished data
2000	4	100%	0.04	0.07	0.217	0.761	0.39	0.44	UBA, Band 121
Mar. 99	17	12%	0.25	0.5	<0.5	3.2	-	-	UBA, Band 151
Dec.98	6	16.7%	0.25	0.5	<0.5	0.87	-	-	UBA, Band 141

all values in [µg/l]

abbreviations: LOD, limit of detection; LOQ, limit of quantitation; Min., minimum; Max., maximum; Ref., reference; n. d., not detected;
* measured values > LOQ;

Influent and effluent concentrations in sewage treatment plants are available for several European countries (EU RAR, 2004). It is assumed that none of the measurements represent specific local activities in the EU and that much of the reduction of DBP in the effluent is mainly caused by adsorption to activated sludge. The concentrations of DBP in influent and effluent waters are compared in a study by Braun et al. (2001), who reports a reduction of 78% and 92% for two STPs. Measured influent concentrations in various European countries (DK, FR, NO, NL, UK, SE) range up to 200 µg/l (STP in Sweden; Paxéus (1996, cited in EU RAR); max. effluent conc.: 2.0 µg/l). The maximum effluent concentration of DBP measured in these STPs was 4.6µg/l (NL; Belfroid et al. 1998). These data are obviously linked to the still significant use of DBP in households, industry and trade.

Measured concentrations of DBP in sewage sludge

DBP concentrations in sewage sludge are presented in **Table 8.** The aim of the study conducted 2001 (UBA, Band 136) was to investigate the concentration of DBP (based on dry weight/kg) of wet sludge, dried and composted sludge originating from the same STP. No difference between composted and wet sludge was revealed. All sludge samples were taken at the same time, but different charges of sludge might explain the difference. The measured DBP concentrations in sludge of Austrian STPs were in the range of not detected up to 0.69 mg/kg dry weight. No DBP was found in composted sewage sludge. In 2006 more actual data have been measured (http://www.ecn.nl/horizontal) with a significantly improved analytical technique. These data also reveal a very high percentage of positive findings (100%). However, as there were only two samples analysed, the data cannot be assumed as being representative and are, therefore, not explicitly mentioned in Table 8. It is noted that some measurements were made on 2 samples only and, the derived percentage of positive findings may not be representative. It is also noted that the significant increase of the percentage of positive findings between 2002 and 2006 may be mainly due to the decrease of the LOQ.

Table 8: Concentration of DBP [mg/kg dwt] in sewage sludge

Sample type	Date	No. measured values	No. of positive findings [%] *	LOD	LOQ	Min.	Max.	Median minimum approach	Mean minimum approach	Ref.
drained sewage sludge	2002	17	24%	0.1	0.205	n.d.	0.69	-	-	UBA, Band 161
wet sewage sludge	2001	4	75%	0.1	0.205	n.d.	0.31	0.27	0.27	UBA, Band 136
drained sewage sludge	2001	17	24%	0.1	0.205	n.d.	0.69	-	-	UBA, Band 136 UBA, Band 161
composted sewage sludge	2001	4	0%	0.1	0.205	n.d.	n.d.	-	-	UBA, Band 136
not stabilized sludge	2000	4	25%	0.09	0.18	<0,18	0.19	-	-	UBA, Band 121

all values in [mg/kg]

abbreviations: dwt, dry weight**;** LOD, limit of detection; LOQ, limit of quantitation; Min., minimum; Max., maximum; Ref., reference; n. d., not detected; * measured values > LOQ;

DBP concentrations in STP sludge from 135 to 670 µg/kg dwt were reported by Braaten et al. (1996 cited in EU RAR). The samples were taken in three Norwegian STPs. The DBP concentration in the influent water of these STPs ranged between 0.0115-0.827 µg/l. Measurements in two STPs in Denmark reveal a similar range for the sludge concentration from 340 to 350 µg/kg dwt (Krogh and Petersen, 1997 cited in EU RAR). These data are well within the range of data found for the Austrian samples.

Measured concentrations of DBP in soil

Table 9 lists measured DBP concentrations found in soil. The highest value of 43 µg/kg dry weight was detected in topsoil (0-5cm), followed by compost (20 µg/kg dry weight).

Table 9: Concentration of DBP [µg/kg dwt] in soil

Sample type	Date	No. measured values	No. of positive findings [%]*	LOD	LOQ	Min.	Max.	Median minimum approach	Mean minimum approach	Ref.
soil	Feb. 07	4	50%	4.0	8.0	<8	9.0	6.0	6.0	http://www.ecn.nl/horizontal/
compost	Feb. 07	4	100%	4.0	8.0	15.0	20.0	18.0	18.0	http://www.ecn.nl/horizontal/
Surface Soil (0-5cm)	May 05	15	100%	2.5	5	5.0	43	21.0	21.0	in press
Undersur-face Soil (5-10cm)	May 05	14	28.6%	2.5	5	n.d.	9.6	-	-	in press

all values in [µg/kg]

abbreviations: dwt, dry weight; LOD, limit of detection; LOQ, limit of quantitation; Min., minimum; Max., maximum; Ref., reference; n. d., not detected; * measured values > LOQ;

No results of DBP concentration measurements in European soils are described in the EU RAR (2004). Concentrations from < 0.1 to 1.4 mg DBP/kg soil are reported for Port Credit/Oakville (Canada) (Golder Associates 1987 in IPCS/WHO, 1997) and values from 2.75 to 29.37 mg/kg were found in agriculturally used soils of China (Xu et al., 2008).

Measured concentrations of DBP in biota

Measured concentrations of DBP in biota (fish) are presented in **Table 10**. In a study conducted by the Umweltbundesamt, Austria (unpublished data) concentrations in biota in the range up to 29 µg/kg dry weight (105°C) were revealed. DBP was found in 57.1% of the samples above LOQ (n=7).

Table 10: Concentration of DBP [µg/kg dwt 105°C] in biota

Date	No. measured values	No. of positive findings [%] *	LOD	LOQ	Min.	Max.	Median minimum approach	Mean minimum approach	Ref.
Mar. 08	7	57.1%	2.5	5	n.d.	29	12.7	15.0	unpublished data

all values in [µg/kg]

abbreviations: dwt, dry weight; LOD, limit of detection; LOQ, limit of quantitation; Min., minimum; Max., maximum; Ref., reference; n. d., not detected; * measured values > LOQ;

There are only a few European data of DBP concentrations in biota available. Measured concentrations of DBP in biota- aquatic invertebrates (Elbe) 300-800 µg/kg dwt and bream (Elbe) 200-500 µg/dwt are reported by Jacobs and Mofid (1986 cited in EU RAR).

Measured concentrations of DBP in compartment articles of daily use

Dibutylphthalate (DBP) is used in several products and some of them are also available to consumers. Sealants, adhesives, car care products, cosmetics and food wrapping material may contain DBP. It has also been reported that DBP was found in baby equipment and children toys. In contrast to other phthalates DBP is not added intentionally to soft PVC toys and child-care articles. However, DBP may be present in these toys as by-product/impurity, due to the use of technical phthalate mixtures in the production process.

Measured concentrations of DBP in articles of daily use are presented in **Table 11**. Available studies (Umweltbundesamt, unpublished) revealed concentrations in articles of daily use in the range of < LOD to 3300 mg/kg. The highest concentration was found in products for children. DBP was detected in 44% of the tested products for children. The highest number of positive findings was detected in tools (76.9%).

Table 11: Concentration of DBP [mg/kg] in articles of daily use

Article	**Date**	**No. measured values**	**No. of positive findings [%] ***	**LOD**	**LOQ**	**Min.**	**Max.**	**Median** minimum approach	**Mean** minimum approach	**Ref.**
Babydoll	Feb. 08	1	0%	12.5	25	n.d.		-	-	unpublished data
Toy	Nov. 07	5	0%	12.5	25	n.d.	n.d.	-	-	unpublished data
Tool	Aug. 06	13	76.9%	0.5	1	n.d.	180	2.5	17.1	unpublished data
Products for Children	Jun. 06	25	44.0%	1	10	n.d.	3300	-	-	unpublished data

all values in [mg/kg]

abbreviations: LOD, limit of detection; LOQ, limit of quantitation; Min., minimum; Max., maximum; Ref., reference; n. d., not detected;
* measured values > LOQ;

Measured concentrations of DBP in house dust

DBP concentrations in house dust are presented in **Table 12**. The dust samples were taken in urban and rural menages with different sizes and living habits of the inhabitants. The sampling was done by vacuum cleaners and the dust was collected in fresh dust bags. Due to the inhomogeneity of the samples, they were sieved and the fraction < 63 µm was used for analysis. DBP was identified in 100% of analyzed samples in 5 of 6 cases. The highest DBP concentration amounted 530 mg/kg. The median concentration of DBP in house dust was 71.8 mg/kg (summary of all house dust samples).

Table 12: Concentration of DBP [mg/kg] in house dust (h.d.)

Sample type	Date	No. measured values	No. of positive findings [%]*	LOD	LOQ	Min.	Max.	Median minimum approach	Mean minimum approach	Ref.
h.d.	May 07	1	100%	5	10	33		-	-	unpublished data
h.d.	Mar. 07	7	100%	4.6-10	9.3-20	52	530	25	92.6	in press
h.d.	Feb. 07	1	100%	14	28	32		-	-	unpublished data
h.d.	Jul. 05	1	100%	0.18	0,36	170		-	-	unpublished data
h.d.	Nov. 04	2	100%	n.a.	n.a.	7.6	14	24	24	unpublished data
h.d.	2004	23	78%	2.5	5	n.d.	67	38	140	BE 258
Summary of all h.d. samples:	Nov.04-Mai 07	35	85.7%	0.18-14	0.36-28	n.d.	530	71.8	100.5	-

all values in [mg/kg]
abbreviations: LOD, limit of detection; LOQ, limit of quantitation; Min., minimum; Max., maximum; Ref., reference; n. d., not detected; * measured values > LOQ

Similar concentrations of DBP (mg/kg) in house dust are reported by Kersten & Reich (2003) measured in German apartments. Following another study DBP had the highest concentrations among the found phthalates in room air, with median values of 1.083 µg/m^3 in apartments and 1.188 µg/m^3 in kindergartens. A list of found DBP concentrations in dust and in indoor air is given in the document "Umweltmedizinische Hintergrundinformationen zu Phthalaten" (2004). The detected median concentrations for DBP in dust range from 470 to 770 mg/kg and from 77 to 482 ng/m^3 for DBP in air.

Monitoring data in other compartments with low exposure

Measured concentrations of DBP in groundwater

DBP concentrations in groundwater are presented in **Table 13.** The substance could not be detected in these samples (n =5).

Table 13: Concentration of DBP [ng/l] in Austrian groundwater

Date	**No. measured values**	**No. of positive findings [%] ***	**LOD**	**LOQ**	**Min.**	**Max.**	**Median** minimum approach	**Mean** minimum approach	**Ref.**
Apr. 02	5	0%	50	100	n.d.	n.d.	-	-	Stadlbauer et. al (2003)

all values in [ng/l]
abbreviations: LOD, limit of detection; LOQ, limit of quantitation; Min., minimum; Max., maximum; Ref., reference; n. d., not detected;
* measured values > LOQ;

No data for DBP concentrations in European groundwater is available in the risk assessment report (EU RAR, 2004). Braun et al. (2001) reports DBP concentrations smaller than 0.05µg/l detected in two of six wells. No DBP could be detected in the other four samples.

2 INFORMATION ON ALTERNATIVES

The two sub-sections on alternatives should be used as appropriate

2.1 Alternative substances

A number of possible substitutes for DBP as softener in PVC and in other uses have been identified, of which several are listed below. It is important to stress that the availability of toxicological data for these substances varies significantly and is often incomplete. COWI 2001 provides a compendium of - by the time of publishing - available (eco)toxicological data for most substances described here. None of the substances listed below is included in Annex I of Directive 67/548/EEC.

During the last years, chemical industry has partly been replacing DBP with DINP (Di-isononyl-phthalate, CAS No. 58033-90-2) and DIDP (Di-isodecyl-phthalate, CAS No. 68515-19-1). Those two phthalates are not classified as reproductive toxicants. However, they are potentially more bioaccumulative, and are suspected to persist in soils and sediments. As they are structurally similar to DEHP and are used in high production volumes for soft PVCs, a critical distribution in the environment can be expected. The structural similarities may cause toxicological effects in humans and environment (Umweltbundesamt Deutschland 2007). Thus, the following examples concentrate on possible alternatives which are not phthalates.

Citrates (especially O-acetyl tributyl citrate (ATBC), CAS-No. 77-90-7) are esters of citric acid and are used as softeners in PVC products, for printing inks and as softeners for plastic in concrete (COWI 2001). They are being used for cling-films, and for toys for babies and toddlers. Their main advantage is that they are biodegradable and not toxic, and can be derived from renewable primary products. Their disadvantage is the considerably higher cost as compared to phthalates (Windsperger et al. 2007).

Hexamoll®DINCH (Di-(isononyl)-cyclohexan-1,2-dicarboxylate, CAS-No. 166412-78-8) is mainly used for the production of toys, medical products, and other PVC products (Windsperger et al. 2007, Biedermann-Brem et al. 2008). Its technical properties are very similar to that of DEHP (Bis(2-ethylhexyl)phthalate). It has been approved by EFSA under corrigendum 2007/19/EG (4th amendment to directive 2002/72/EG) for its use in plastic materials and articles intended to come into contact with foodstuffs. As it was recently notified as a new substance, sufficient data on toxicity and ecotoxicity should be available (WIndsperger et al. 2007, Umweltbundesamt Deutschland 2003, Umweltbundesamt Deutschland 2007).

Adipates (particularly bis-(2-ethylhexyl)adipate (DEHA), CAS No. 103-23-1 and diisononyladipate (DINA), CAS No. 33703-08-1) are diesters of aliphatic dicarboxylic acids and are produced with varying alcohol groups. They are classified as low temperature plasticizers, and the compounds are relatively sensitive to water (COWI 2001). They are mostly used in PVC, but also in fillers, in paints and lacquers, adhesives, plastic in concrete, and rubber products. DEHA is mostly used in packaging for foodstuffs, DINA mostly for floor covering and wallpapers (Umweltbundesamt Deutschland 2007, Windsperger et al. 2007).

Phosphates (e.g. di(2-ethylhexyl)phosphate, CAS No. 298-07-7, tri(2-ethylhexyl)phosphate, CAS No. 78-42-2) are triesters of phosphoric acid and includes triaryl and trialkylesters. This group of plasticizers is more resistant to ignition and burning than all the other groups of ester plasticizers and is most often used as flame-retardants in products with specific fire resistant demands. The main uses are in PVC-products used in e.g. the hospital sector, packing, cables, profiles and floor

and wall coverings. Tri(2-ethylhexyl)phosphate was not mutagenic and was not found genotoxic in chromosome aberration test and micronuclei assays. Slight evidence of carcinogenicity was observed in mouse, but it has been concluded that the substance is not likely to cause cancer in humans. No data were found on reprotoxicity, embryo toxicity and teratogenicity. There is no data to determine reproductive toxicity or teratogenicity for Di(2-ethylhexyl)phosphate (COWI 2001).

Trimellitates (tri-2-ethylhexyl trimellitate, CAS No. 3319-31-1), pyromellitates and other polycarboxylic acid esters are used for heat resistant plasticized PVC articles due to their exceptional thermal properties. Trimellitates are similar to phthalates with respect to their compatibility and plasticizing effect. They generally have a higher molecular weight and corresponding lower vapour pressure, resulting in a lower migration potential to aqueous solutions compared to phthalates and other plasticizer (COWI 2001).

Alkylsulphonic acid esters (o-toluene sulphonamide (OTSA), CAS No. 88-19-7) are based on phenol, sulphate and an alkyl chain. The sulfonic esters are more resistant with respect to hydrolysis than other ester based plasticizers (COWI 2001). They can be used for PVC exposed to severe weather conditions or strong disinfectants and agents, as well as for toys (Umweltbundesamt Deutschland 2003). O-toluene sulphonamide is reported as teratogenic in rats, but no detailed description of the study design is available. Only weak mutagenic activity is shown. There is limited evidence that OTSA is carcinogenic when administered orally to rats. This has been suggested as the cause of carcinogenicity of saccharin. The available data suggest that OTSA impurities at the levels normally found in commercial saccharin do not contribute to the carcinogenicity of saccharin. Based on very limited data the critical effect has been identified as possible teratogenicity (COWI 2001).

Butane esters (2,2,4-trimethyl-1,3-pentanediole diisobutyrate (TXIB), CAS No. 6846-50-0) is mostly used in PVC-products e.g. in the hospital sector, packaging, cables, profiles, floor and wall coverings, printing ink and paint/lacquer (COWI 2001).

Polyesters (polyadipates) are medium viscous polymeric softeners derived from adipic acid, used for oil and grease resistant uses of PVC, and can be used for the production of packaging foil and floor coverings. They comply with several food law requirements (Windsperger et al. 2007).

Epoxyester and epoxydised oils, of which epoxidised soybean oil (ESBO, CAS No. 8013-07-8), which is produced by epoxidation of soybean oil is the dominant plasticizer. ESBO has a high molecular weight and a spacious molecular structure, which makes it more resistant to migration (COWI 2001).

Benzoates (Dipropylene glycol dibenzoate, CAS No. 27138-31-4) may be mainly used in adhesives and fillers (COWI 2001).

Sebacates (Dioctyl sebacate (DOS), CAS No. 122-62-3) are used to add good low temperature flexibility, and generally have the same plasticizing properties as adipates and azilates (COWI 2001).

2.2 Alternative techniques

An alternative technique is the adding of the “softener” (special monomers, like vinyl acetate and maleic acid) in the stage of polymer production (co-polymerisation). As an example, vinyl chloride (the monomer for PVC production) is co-polymerised with a certain amount of vinyl acetate (up to 20%). Thus, instead of being physically bound to the macromolecules by dipole-dipole interaction, the softening monomer becomes part of the macromolecule (i.e. copolymer). Thereby the plastic becomes permanently soft, and the softener does not migrate. These procedures have been known

for some time, due to the more specific complexity of the production process and the reduced flexibility they have been implemented only on very limited scale (Windsperger et al. 2007).

It should be noted, that in several publications (Umweltbundesamt Deutschland 2003, Umweltbundesamt Deutschland 2007) a complete switch from products containing phthalates to other materials like polyethylene or polypropylene is suggested as another alternative. Obviously, the applicability of this alternative depends on the use of the final product.

3 RISK-RELATED INFORMATION

Information such as PNEC and DNEL values may be useful in priority setting for Annex XIV inclusion.

Summary of environmental effects assessment (EU RAR, 2004)

Information concerning the risk for human health and the environment are summarised from the Risk Assessment Report (EU RAR, 2004).

3.1 Human health

Based on all available studies an overall oral LOAEL of 52 mg/kg bw can be established for dibutyl phthalate. Concerning reproduction, fertility as well as developmental studies a NOAEL of 50 mg/kg bw can be established based on embryo toxicity in a one-generation reproduction study in rats with exposure of females only. However, a LOAEL of 52 mg/kg bw can be established based on embryotoxic effects in rats in the absence of maternal toxicity in a two-generation reproduction study with a continuous breeding protocol including improved sensitive endpoints (such as sperm parameters, oestrous cycle characterisation and detailed testicular histopathology) and with exposure of both male and female animals. The protocol of this study was supposed to adequately identify compounds with endocrine activity.

3.2 Environment

3.2.1 PNEC for the aquatic compartment

The PNEC for the aquatic compartment is derived from a 99-day NOEC of 100 µg/l for *Onchorhynchus mykiss* (Ward and Boerie, 1991 cited in EU RAR). This key study is supported by the *Gammarus pulex* study in which a similar value was found based on a decrease in the locomotor activity. An assessment factor of 10 will be used for the extrapolation. This factor is used because long-term NOECs for three trophic levels are available.

$PNEC_{aquatic}$ = 10 µg/l

3.2.2 PNEC for microorganisms

The test with *Tetrahymena pyriformis* (Yoshioka et al., 1985) can be used to derive a $PNEC_{protozoa}$: applying a factor 10 on the EC_{50} leads to a value of 0.22 mg/l.

$PNEC_{STP}$ =0.22 mg/l

3.2.3 PNEC for terrestrial compartment

The NOEC of 200 mg DBP/kg for *Zea mays* (Shea et al., 1982) can be used for the derivation of the PNEC for the terrestrial compartment. According to the TGD, an assessment factor of 100 should be used:

$PNEC_{terrestrial}$ = 2 mg/kg dwt

3.2.4 PNEC for plants

For the derivation of the PNEC for plants a NOEC of 0.1 µg/m^3 DBP is used and it is an average concentration of several measurements (EU RAR, 2003). The used NOEC seems to be based on a very sensitive species, from a consistency point of view a factor of 10 is applied on the NOEC. This leads to the provisional value given below.

$PNEC_{plants\text{-}air}$ = 0.01 µg/m^3

3.2.5 Secondary poisoning

The effects of a diet of 10 mg DBP/kg on egg shell thickness, breaking strength, permeability and shell structure of ring dove (*Streptophelia risoria*) eggs were examined in a 3-week experiment (Peakall, 1974). Egg shell thickness was found to be decreased (10%), whereas the water permeability increased (23%). A 15% decrease in shell thickness is considered significant for reproductive effects. Rapid recovery occurred upon cessation of exposure.

An ED_{50} of 33 µmol (9.19 mg) per egg was calculated for DBP in a chicken embryo toxicity study (Korhonen et al., 1983). As no more information is available on the effects of DBP on higher organisms other than laboratory mammals, the overall oral LOAEL of 52 mg/kg bw will be used for the derivation of the PNEC for predators (conversion factor = 20, assessment factor = 10), resulting in a:

$PNEC_{oral}$ = 104 mg/kg in food

It has to be borne in mind that this PNEC is derived from a LOAEL. The TGD does not give assessment factors for LOAELs. The assessment factor for NOAELs is used now, but this may have resulted in an underestimation (an extra factor of 3-10) of the $PNEC_{oral}$.

Comparison of European monitoring data and Risk Characterisation EU RAR (2004)

In this section a comparison between monitoring and calculated data from Austria and Europe is made. The risk characterisation is based on the ratio of the determined concentrations of DBP and the corresponding PNEC values.

3.3 Surface water

European samples reveal that the mean regional measured DBP concentrations in surface waters range from 0.1 to 1 µg/l, although higher concentrations can occur. The regional surface water concentration of DBP based on EUSES calculations is 0.4 µg/l.

The PNEC for surface water was set at 10 µg/l. The ratios MEC/PNEC and PEC/PNEC (MEC measured environnmental concentration) were found to be below 1, meaning that the DBP concentrations were smaller than the $PNEC_{aquatic}$ **(conclusion (ii)).**

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

3.4 STP influent

DBP Concentrations in the EU RAR, 2003 reveal 200µg/l in influent water as maximum value measured in Europe. Considering a $PNEC_{microorganism}$ of 220µg/l, the MEC/PNEC ratios of both values is below 1 **(conclusion (ii))**.

3.5 Sewage sludge

In European STPs a maximum concentration of 0.068mg/kg DBP/kg dwt sewage sludge was found (RAR, 2004). Considering the application of sewage sludge for soil (**$PNEC_{terrestrial}$ = 2 mg/kg dwt)** the MEC/PNEC ratio is below 1 **(conclusion (ii))**.

3.6 Biota

There is only one figure that can be used for a comparison: 2-5 mg/kg DBP for bream in the river Elbe. (A conversion factor of 10 is used for extrapolating dry weight to fresh weight data). The calculated regional PEC in fish amounts to 1.8 µg/kg. It would be speculative to discuss the difference. Local monitoring data are lacking. The $PNEC_{Oral}$ is 104mg/kg. Both MEC/PNEC ratios for the Austrian and European samples are far below 1 **(conclusion (ii)).**

3.7 Atmospheric compartment

The provisional PNEC for the atmospheric compartment is 0.01 µg/m^3. A comparison of this PNEC with calculated PECs (production and formulation/processing), including a calculated regional PEC and measured local data, shows that all PEC/PNEC ratios are above 1 **(conclusion (i)).** The same is true for the recent (2000) air monitoring data from the Netherlands. As for the production scenarios the local PECs are already based on site-specific data, a chronic fumigation test with plants has to be conducted.

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

OTHER INFORMATION

Dibutyl phthalate (DBP) is on the 1st priority list under Council Regulation (EEC) No 793/93 on the Control and Evaluation of the Risks of Existing Substances with the Netherlands as Rapporteur. The final risk assessment report was published in 2003 and the Addendum to the Environmental Section of the Report in 2004. The risk reduction strategy was endorsed at the 8th RRS Meeting and published in the Official Journal in 2006 (OJ 2006/C90/04).

Note that no re-evaluation was conducted of those references which are cited in this Annex XV dossier and which were taken from the Risk Assessment Report for Dibutyl phthalate (EU RAR, 2004). The last full literature survey for the RAR was carried out in 1994 with subsequently conducted targeted searches. For the present dossier no comprehensive literature survey was conducted, but focus was given to exposure related data (especially monitoring data) and endocrine effects.

REFERENCES

Aldyreva MV et al. (1975). Effect of plasticizers on reproductive function. Gig. Tr. Prof. Zabol. 12, 25-29. In: IPCS (1997). International Programme on Chemical Safety. Environmental Health Criteria 189 Di-n-butyl Phthalate.

Ankley G et al. (1997). Overview of a workshop on screening methods for detecting potential (anti-) estrogenic/androgenic chemicals in wildlife. Environ. Toxicol. Chem. 17, 68-87.

ATSDR (1990). Toxicological profile for di-n-butylphthalate. US Department of Health & Human Services. Public Health Service Agency for Toxic Substances and Disease Registry.

Belfroid AC, Murk A, de Voogt P, Schafer A, Rijs G, Vethaak AD (1998). Hormoonontregelaars in ons water. Orienterende studie naar de aanwezigheid van oestrogeen-actieve stoffen in watersystemen en afvalwater in Nederland. RWS uitgave. In opdracht van RWS-RIZA/RIKZ. In voorbereiding.

Biedermann-Brem S., Biedermann M., Pfenninger S., Bauer M., Altkofer W., Rieger K., Hauri U., Droz C., Grob K. (2008): Plasticizers in PVC Toys and Childcare Products: What Succeeds the Phthalates? Market Survey 2007, Chromatographia (2008), accepted

Braun G., Brüll U., Alberti J., Furtmann K. (2001). Untersuchungen zu Phthalaten in Abwassereinleitungen und Gewässern. Forschungsbericht 29828245 UBA-FB 000180 ISSN 0722-186X

Bruns-Weller E and Pfordt J (2000). Bestimmung von Phthalsäureestern in Lebensmitteln und Frauenmilch. ERNO 1(1), 25-28.

Braaten B, Berge JA, Berglind L and Baekken T (1996). Occurrence of phthalates and organotins in sediments andwaters in Norway. Norwegian Institute for Water Research, NIVA Report SNO 3552-96.

BUA (1987). German Chemical Society. GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance. Dibutylphthalate, BUA-Report 22, December 1987.

Cadogan DF et al. (1994). An assessment of the release, occurrence and possible effects of plasticisers in the environment. In: Progress in rubber technology and plastics technology. JM Buist (ed.). **10**(1). RAPRA technology Ltd.

Canadian EPA (1994). Priority Substances List. Assessment report: Dibutyl phthalate. Ottawa, Ontario, Environment Canada and Health Canada.

COWI (2001) Environmental and Health Assessment of Alternatives to Phthalates and to flexible PVC, EPA Environmental Project No. 590 2001, COWI Consulting Engineers and Planners AS

CSTEE (1998) Phthalate migration from soft PVC toys and child-care articles. EU Scientific Committee on Toxicity, Ecotoxicity and the Environment - Opinion expressed at the CSTEE third plenary meeting in Brussels, 24 April 1998.

Danish Product Register (1995). Arbejds Miljoin Instituttet Produktregistret. Kopenhagen. Dated May 1992.

Duty MS, Calafat AM, Silva MJ, Ryan L and Hauser R. (2005). Phthalate exposure and reproductive hormones in adult men. Human Reproduction 20(3) 604–610, doi:10.1093/humrep /deh656 Advance Access publication December 9, 2004.

EDSTAC (1998). Endocrine Disruptor Screening and Testing Advisory Committee. Draft Report, July 16, 1998.

EDTA (1998). Draft meeting report of first meeting of the joint NCM/RAAB Working Group on Endocrine Disrupters Testing and Assessment (EDTA Working Group) Paris, 10-11 March 1998.

EFSA (2005) Opinion of the Scientific Panel on Food Additives,Flavourings, Processing Aids and Material in Contact with Food (AFC) on a request from the Commission related to Di-Butylphthalate (DBP) for use in food contact materials Question N° EFSA-Q-2003-192 Adopted on 23 June 2005 by written procedure. http://www.efsa.eu.int/EFSA/Scientific Opinion/ afc_op_ej242_dbp_en2,1.pdf.

EU RAR, 2007: European Union Risk assessment report, Benzyl butylphtalate (BBP) Volume: 76 (ISSN 1018-5593)

Fatoki OS and Vernon F (1990). Phthalate esters in rivers of the Greater Manchester area, UK. Sci. Total Environ. **95**, 227-232.

Fennell T.R, Krol, W. L., Sumner S.c.J., Snyder R.W. (2004) Pharmacokinetics of Dibutylphthalate in pregnant rats. Toxicological Sciences 82, 407-418.

Fromme H., Kuchler T., Otto T.,Pilz K., Muller J.,Wenzel A. (2002). Occurrence of phthalates and bisphenol A and Fin the environment. Water Research 36 (2002) 1429–1438

Fromme H., Lahrz T., Piloty M., Gebhart H., Oddoy A., Riden H. (2004). Occurrence of phthalates and musk fragrances in indoor air and dust from apartments and kindergartens in Berlin (Germany). Indoor Air 2004; 14: 188–195. www.blackwellpublishing.com/ina

Gruber L et al. (1998). Untersuchung von Phthalaten in Baby-Nahrung. Deutsche Lebensmittel-Rundschau 94(6), 177-179.

Hamano Y et al. (1977). Studies on toxicity of phthalic acid esters. First report Teratogenic effects in mice administered orally. Osaka-furitsu Koshu Esei kenkyusho Kenkyu Hokoka Shokukhim Eisei Hen 8, 29-33. In: IPCS (1997) International Programme on Chemical Safety. Environmental Health Criteria 189. Di-n-butyl Phthalate. World Health Organization, Geneva. p. 120.

Harris CA et al. (1997). The estrogenic activity of phthalate esters *in vitro*. Environ. Health Perspect. **105**(8), 802-811.

Hauser R, Meeker JD, Duty S, Silva MJ, Calafat AM (2006) Altered semen quality in relation to urinary concentrations of phthalate monoester and oxidative metabolites. Epidemiolog, 17(6):682-691.

IPCS/WHO (1997). Di-n-butylphthalate. Environmental Health Criteria 189. IPCS/WHO.

Jacobs G and A Mofid (1986). UBA F+E 106 07 054 Zwischenbericht Vorkommen und Verteilung von Phthalsäureestern in der Elbe- Untersuchungen im Susswasserwatt Heuckenlock – Teil 1.

Jobling S et al. (1995). A variety of environmentally persistent chemicals, including some phthalate plasticizers, are weakly estrogenic. Environ. Health Perspect. **103**(6), 582-587.

Jonsson BAG, Richthoff J. Rylander L. (2005) Urinary phthalate metabolites and biomarkers of reproductive function in young men. Epidemiology, 16, 487-493.

Jorgensen M., Vendelbo B., Niels E., Skakkebaek N.E., Leffers H. (2000) Assaying estrogenicity by quantitating the expression levels of endogenous estrogen-regulated genes. Environmental Health Perspectives 108, 5, 403-412.

KEMI (1995). Swedish product register, Solna Sweden.

Kersten W., Reich T. (2003). Schwerflüchtige organische Umweltchemikalien in Hamburger Hausstäuben. Behörde für Umwelt und Gesundheit, Umweltuntersuchungen, Abt. Luftuntersuchungen, Hamburg

Kolossa-Gehring M. (2007): Kinder-Survey- Erfahrungen in Deutschland. Fachgespräch Umwelt und Gesundheit. Der Mensch im Zentrum der Umweltbeobachtung vom 19.9.2007.

Kolossa-Gehring M., Becker K., Conrad A., Ludecke A., Riedel S., Seiwert M., Schulz C., Szewzyk R. (2007): German Environmental Survey for Children (GerES IV)--first results. Int J Hyg.Environ Health 210: 535-540.

Korhonen et al. (1983). Embryotoxic effects of phthalic acid derivatives phosphates and aromatic oils used in the manufacturing of rubber on 3 day chicken embryos. Drug Chem Toxicol **6**(2), 191-208.

Krogh PH and Petersen SO (1997). Ecotoxicological assessment of sewage sludge in agricultural soil. Danish EPA.Working Report No. **69**-1997.

Lee KY, Shibutani M., Takagi H., Kato N., Shu T., Unemaya C. and Hirose M. (2004). Diverse developmental toxicity of di-n-butyl phthalate in both sexes of rat offspring after maternal exposure during the period from late gestation through lactation. Toxicology, 203, 221-238.

Lottrup G, Andersson AM, Leffers H, Mortensen GK, Toppari J, Skakkebaek NE, Main KM.(2006) Possible impact of phthalates on infant reproductive health. Int J Androl. 29(1):172-80; discussion 181-5.

MAFF (1987). Survey of plasticizer levels in food contact material and in food. Food Surveillance paper No 21. Ministry of Agriculture, Fisheries and Food. London, Her Majesty's Stationary Office.

Main KM, Mortensen GK, Kaleva MM, Boisen KA, Damgaard IN, Chellakooty M, Schmidt IM, Suomi AM, Virtanen HE, Petersen DV, Andersson AM, Toppari J, Skakkebaek NE. (2006) Human breast milk contamination with phthalates and alterations of endogenous reproductive hormones in infants three months of age. Environ Health Perspect. 114(2):270-6.

Markman S, Guschina I. A., Barnsley S., Buchanan K. L., Pascoe D., Müller C. T. (2007) Endocrine disrupting chemicals accumulate in earthworms exposed to sewage effluent. Chemosphere 70, 119-125

Mylchreest E et al. (1998). Male reproductive tract malformations in rats following gestational and lactationalexposure to di(n-butyl) phthalate: an antiandrogenic mechanism? Toxicol. Sci. 43, 47-60.

Mylchreest E et al. (1999). Disruption of androgen-regulated male reproductive development by di(n-Butyl) phthalate during late gestation in rats is different from flutamide. Toxicol. Appl. Pharmacol. 156, 81-95.

Mylchreest, E. et al. (2000) Dose-Dependent Alterations in Androgen-Regulated male Reproductive Development in Rats Exposed to Di(n-butyl) Phthalate during late Gestation. Toxicol. Sci. 55, 143-151.

Müller, A.M., Nielsen, A. and Ladefoged, O. (2003), Ministeriet for Fødevarer, Landbrug og Fiskeri Veterinær- og Fødevaredirektoratet. Human exposure to selected phthalates in Denmark, rapport 2003:15.

NTP (1995) National Toxicology Program. Toxicity Report Series Number 30. by D.S. Marsman. NTP Technical Report on Toxicity Studies of Dibutyl Phthalate (CAS No. 84-74-2). Administered in Feed to F344/N Rats and B6C3F1 Mice. NIH Publication 95-3353. US Department of Health and Human Services. Public Health Service. National Institutes of Health. Dated April 1995.

Ohtani H., Miura I., and Ichikawa Y. (2000) Effects of Dibutyl Phthalate as an Environmental Endocrine Disruptor on Gonadal Sex Differentiation of Genetic Males of the Frog Rana rugosa. Environ Health Perspect. 2000 December; 108(12): 1189–1193

OJ 2006/C90/04 Commission Communication and Commission Recommentation for substance Dibutylphthalate CAS: 84-74-2, EINECS: 201-557-4.

Paxéus N (1996). Organic pollutants in the effluents of large wastewater treatment plants in Sweden. Wat. Res. **30**(5), 1115-1122.

Peakall DB (1974). Effects of di-n-butylphthalate and di-2-ethylhexylphthalate on the eggs of ring doves. Bull.Environ. Contam. Toxicol. **12**, 698-702.

Petersen JH. and Breindhal T. (2000). Plasticizers in total diet samples, baby food and infant formulae. Food Addit Contam; 17 (2), 133-41.

PRI (2002). Assessment of chronic effects of di-n-butylphthalate (DBP) on plants. Plant Research International.

Rastogi SC et al. (1997). Migration of phthalates from teethers. Research Notes from NERI No.64. Ministry ofEnvironment and Energy/National Environmental Research Institute, Denmark.

RIVM (1991). Update of the exploratory report phthalates. Report no 7104010 08. National Institute of Public Health and Environmental Protection, Bilthoven, May 1991.

SCHER (2007) Scientific Committee on Health and Environmental Riskss. Opinion on risk assessment on indoor air quality. Internetabfrage vom Jänner 2008: http://ec.europa.eu/health/ph_risk/committees/04_scher/docs/scher_o_055.pdf

Stadlbauer, Heimo et al. Grundwasseruntersuchungen auf ausgewählte Hormone, Xenohormone, Arzneimittelwirkstoffe und Phthalate, Bereich Leibnitzerfeld–Haslacher Au GA 01-03, Amt der Steiermärkischen Landesregierung Fachabteilung 17C, Graz, Jänner 2003.

Swan SH, Main KM, Liu F, Stewart SL, Kruse RL, Calafat AM, Mao CS, Redmon JB, Ternand CL, Sullivan S, Teague JL; Study for Future Families Research Team. (2005) Decrease in anogenital distance among male infants with prenatal phthalate exposure. Environ Health Perspect.; 13(8):1056-61.

UBA (Umweltbundesamt), (1998): Sattelberger R., Scharf S.: Abwasseruntersuchung auf östrogen-wirksame Substanzen. Band 141.

UBA (Umweltbundesamt), (1999): Scharf S., Sattelberger R.: Endokrine Substanzen - Kläranlagen. Band 151.

UBA (Umweltbundesamt), (2000): Abwasser- und Klärschlammuntersuchungen in der Pilotkläranlage Entsorgungsbetriebe Simmering (EbS). Band 121.

UBA (Umweltbundesamt), (2001): Hormonell wirksame Substanzen in Klärschlamm. Band 136

UBA (Umweltbundesamt), (2002) Sattelberger R.: Hormonell wirksame Substanzen in der aquatischen Umwelt - Analytische Ergebnisse und Überblick. Band 161.

Umweltbundesamt Deutschland (2003) Leitfaden zur Anwendung umweltverträglicher Stoffe für die Hersteller und gewerblichen Anwender gewässerrelevanter Chemischer Produkte, Teil Fünf, Hinweise zur Substitution gefährlicher Stoffe; 5.1 Funktion: Weichmacher, Berlin 2003

Umweltbundesamt Deutschland (2007) Phthalate – die nützlichen Weichmacher mit den unerwünschten Eigenschaften, Berlin 2007

Umweltmedizinische Hintergrundinformationen zu Phthalaten (2004). Bayerisches Landesamt für Gesundheit und Lebensmittelsicherheit. http://www.lgl.bayern.de/gesundheit/umwelt-medizin/doc/projekt_phthalate.pdf

Ward TJ and Boerie RL (1991). Early life stage toxicity of di-n-butylphthalate (DnBP) to the rainbow trout (Oncorhynchus mykiss) under flow-through conditions. Hampton, New Hampshire, Resource Analysts, Inc. Environ. Systems Division.

WHO (1998). Food Safety Issues, GEMS/FOOD International dietary survey: Infant exposure to certain organochloric contaminants from breast milk – A risk assessment. WHO/FSF/FOS/98.4, Geneva. Switzerland.

Windsperger A, Windsperger B, Tuschl R (2007). PVC-HEUTE, Die aktuelle Situation des Werkstoffs Weich-PVC in den relevanten Themenbereichen, im Auftrag des Fachverbandes der chemischen Industrie Österreichs (FCIO), Wien 2007

Wine RN et al. (1997). Reproductive toxicity of di-n-butylphthalate in a continuous breeding protocol in Sprague-Dawley Rats. Environ. Health Perspect. 105(1), 102-107.

Wittassek M, Angerer J (2008) Phthalates: metabolism and exposure. Int J Androl. 31(2):131-138.

Wittassek M, Wiesmüller GA, Koch HM, Eckard R, Dobler L, Müller J, Angerer J, Schlüter C.(2007) Internal phthalate exposure over the last two decades--a retrospective human biomonitoring study.

World Health Organisation, Geneva. pp.131-132.Duty SM, Calafat AM, Silva MJ, Ryan L, Hauser R. (2005) Phthalate exposure and reproductive hormones in adult men. Hum Reprod. 2005 Mar;20(3):604-10.

Xu G, Li F and Wang Q (2008). Occurrence and degradation of dibutylphthalate (DBP) and di (2-ethylhexyl) phthalate (DEHP) in typical agricultural soils of China. The science of the total Environment 393(2-3), 333-340.

Yoshioka Y et al. (1986). Ecotox. Environ. Safety 12, 15-21. Cited in Rippen (1986). Handbuch Umweltchemikalien. 13 Add. 1/92.

Zwalijs (1989). Projectgroep ZWALIJS. Zwarte lijststoffen in Noord-Brabant.