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Institute for Health and Consumer Protection
European Chemicals Bureau
I-21020 Ispra (VA) Italy

DIBUTYL PHTHALATE

CAS No: 84-74-2

EINECS No: 201-557-4

Summary Risk Assessment Report

with addendum 2004

2003 **Special Publication I.01.66**

European Union Risk Assessment Report

DIBUTYL PHTHALATE

Addendum to the Environmental Section – 2004

CAS No: 84-74-2

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SUMMARY RISK ASSESSMENT REPORT

EXPLANATORY NOTE

This report is an addendum to the European Risk Assessment Report (RAR) on dibutyl phthalate, that has been prepared by the Netherlands in the context of Council Regulation (EEC) No. 793/93 on the evaluation and control of existing substances and published in 2003 on the European Chemicals Bureau website (European Risk Assessment Report, Vol.29, EUR 19840 EN) [1].

In the frame of this work, the initial environmental risk assessment for dibutyl phthalate was completed with a conclusion (i) for the atmospheric compartment. There was felt to be a need for further long-term plant testing (gas phase). Consequently, a long-term fumigation test has been conducted recently exposing six different plant species to various DBP concentrations. Results are presented in this report.

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).

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

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1 INTRODUCTION

The environmental risk assessment for dibutyl phthalate was completed with a **conclusion (i)** for the atmospheric compartment (EC, 2003a). There was felt to be a need for further long-term plant testing (gas phase). The reason behind was that with the derived $PNEC_{plant-air}$ of 0.01 μg/m^3 atmospheric PEC/PNEC ratios above 1 were found for all exposure scenarios, including recent measured regional concentrations in the Netherlands. This $PNEC_{plant-air}$ of 0.01 μg/m^3 was based on a NOEC estimate of 0.1 μg/m^3 in combination with an (arbitrary) assessment factor of 10. The NOEC estimate was, however, based on rather old experimental data showing a number of inconsistencies and limitations (a.o. analytics, exposure time, co-exposure with other phthalates, etc.). The validity of the derived PNEC was therefore debatable.

A long-term fumigation test has been conducted recently exposing six different plant species to various DBP concentrations for a period of 76 days (PRI, 2002). Mean measured concentrations amounted to 0.14 (control), 0.81, 1.37, 3.07 and 13.67 μg/m^3. The plant species chosen for the laboratory experiment were representative of the European flora and included plant species representative for crops, trees and natural vegetation: *Phaseolus vulgaris* (bean), *Brassica campestris* var. *chinensis* (cabbage), *Picea abies* (Norway spruce), *Trifolium repens* (white clover), *Plantago major* (plantain) and *Holcus lanatus* (common velvet grass). Cabbage was "automatically" selected, because this species was found to be the most sensitive one in the earlier DBP fumigation tests.

2 CHRONIC PLANT STUDY

Results

Visual injury was observed on all species, varying from chlorosis and necrosis, leaf crinkling to a total loss of colour in the leaves and needles. The variation in sensitivity between plant species was quantified on the basis of whole plant biomass (shoot plus root) in order to derive NOEC and EC10 values.

The EC10 values for total biomass, including lower and upper limits, for the six species are presented below:

Plant species	EC10 (µg/m^3)	EC10: lower and upper limit
Phaseolus vulgaris	2.32	1.20-4.48
Brassica campestris	0.77	0.36-1.67
*Picea abies**	-	-
Trifolium repens	0.33	0.12-0.91
Holcus lanatus	8.79	-
Plantago major	2.39	1.53-3.75

* No significant effects were observed even at highest tested concentration.

Interestingly, white clover was found to be more sensitive to DBP than cabbage. Further details can be found in the PRI (2002) report and IUCLID.

PNEC$_{plant-air}$ proposal

The PRI (2002) study is considered acceptable and useful for deriving a PNEC $_{plant-air}$. Two different routes can be used for deriving the PNEC$_{plant-air}$: 1) the standard method (lowest NOEC/EC10 divided by assessment factor, and 2) statistical extrapolation with an additional assessment factor.

Using the lowest EC10 value, i.e. 0.33 µg/m^3, and applying the standard factor of 10 would result in a PNEC$_{plant-air}$ of **0.03 µg/m^3**. Calculating the 5th percentile of the species sensitivity distribution (EC10 values for effects on total biomass) would result in a median (50% confidence interval) value of **0.2 µg/m^3** (ETX, 1993). The 5th percentile estimation meets the statistical goodness-of-fit requirements (Anderson-Darling test for normality). Calculating 5th percentile values for either root or shoot biomass, rather than total biomass, results in nearly the same 5th percentile.

The problem now is that there is no guidance yet on deriving a plant-air PNEC in the Technical Guidance Document (TGD) (EC, 2003b). The TGD focuses on the PNEC derivation for water, sediment and soil, but the assumptions etc. for those compartments may not directly hold for plants (airborne route). A number of considerations can be given here on the PNEC$_{plant-air}$ derivation for DBP:

1. the focus is only on deriving a PNEC air for plants. This means that other taxonomic groups of the atmospheric compartment (e.g. insects) will remain beyond the scope of the PNEC. This implies that assessment factors may cover 'less ecosystem' than normally for water, soil and sediment.

2. the TGD (2003b) criteria for using statistical extrapolation are not all met here (e.g. number of NOECs), but they may also not be relevant here as the focus is only on plants (see

point 1). There is a fairly well coverage of plant diversity in the selected plant species, and, in addition, an acceptable goodness-of-fit is shown. One may speculate then about the introduction of an additional assessment factor. Such additional assessment factor should still cover species diversity (see point 3). It is highly uncertain, however, whether a factor of 2, 3 or 4 should then be used. An arbitrary factor of 3 on the current 5th percentile would, for example, yield a PNEC of 0.07 µg/m^3.

3. the focus in the tiered testing program, of which the PRI (2002) test is the last part, has been on sensitive species (*Brassica* in particular). This is supported by literature data. It should be noted, however, that the PRI (2002) test showed that white clover was even more sensitive than *Brassica*. Some factor is needed therefore for possible other, even more sensitive species than clover.

4. according to plant experts, the conditions in greenhouses, are very unfavourable to plants with respect to their sensitivity to toxicants. This due to optimal light and feeding conditions which optimise the exposure and therefore the toxicity. Therefore the standard factor of 10 for extrapolating from laboratory tests to the field-situation may be argued here (lower factor).

Taking all these points into consideration, it is clear that a quantitative approach on the PNEC derivation would be very difficult in this case. The standard assessment factor of 10 is most probably too high, but should it then be 4, 6 or 7.5? The same is true for the additional assessment factor on the 5th percentile. It is pragmatically proposed therefore to use a **PNEC $_{plant\text{-}air}$ of 0.1 µg/m^3** for DBP in the revised risk assessment.

3 REVISED RISK CHARACTERISATION

The adjusted risk characterisation, based on the change in the $PNEC_{plant\text{-}air}$ from 0.01 µg/m^3 to 0.1 µg/m^3, is presented in **Table 3.1** (production sites) and **Table 3.2** (formulation/processing sites). Please note that the PEC/PNEC ratios for the compartments other than atmosphere remained unchanged.

Table 3.1 Local PEC/PNECs in the various compartments at production

PEC/PNEC	site-spec. A	site-spec. B	site-spec. C
STP	0.3	$3.4 \cdot 10^{-4}$	0.4
Surface water	0.4	0.1	0.6
Sediment	0.4	0.1	0.7
Soil	0.7	$3.3 \cdot 10^{-4}$	$3.2 \cdot 10^{-4}$
Oral, fish	$3.5 \cdot 10^{-5}$	$1.7 \cdot 10^{-5}$	$3 \cdot 10^{-5}$
Oral, worm	0.07	$6 \cdot 10^{-4}$	$6 \cdot 10^{-4}$
Plant (air)	0.2	0.2	0.2

Table 3.2 Local PEC/PNEC ratios at formulation/processing

PEC/PNEC for scenario	III-a	III-b1	III-b2	III-c1	III-c2	III-d	III-e
Type of application	plasticiser / softener in PVC	adhesive		printing inks		fibres	grouting agent
STP	0.08	0.4	0.09	0.05	0.002	0	-.
Surface water	0.3	0.9	0.3	0.2	0.1	0.1	0.7 (A) 0.1 (O)
Sediment	0.3	1	0.3	0.2	0.1	0.11	-
Soil	0.2	0.9	0.2	0.1	$5.9 \cdot 10^{-3}$	0.002	-
Oral, fish	$3 \cdot 10^{-5}$	$7.3 \cdot 10^{-5}$	$3 \cdot 10^{-5}$	$2.5 \cdot 10^{-3}$	$1.8 \cdot 10^{-5}$	$1.7 \cdot 10^{-5}$	-
Oral, worm	0.02	0.1	0.02	0.01	$1.2 \cdot 10^{-3}$	$7.4 \cdot 10^{-4}$	-
Plant (air)	23.6	3.4	0.1	0.5	2.0	10.0	-

On the basis of the new atmospheric PEC/PNEC ratios (>1) a **conclusion (iii*)** is drawn for the local DBP processing scenarios III-a (PVC production), III-b1 (adhesive production), III-c2 (printing ink usage) and III-d (glass fibre production). For the remaining scenarios, including the regional one, a **conclusion (ii)** seems to be most appropriate as the PEC/PNEC ratios are all below 1. The regional scenario also comprises the recent air monitoring data from the Netherlands.

4 RESULTS FOR THE ENVIRONMENT - ADDENDUM

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 anticipated risk for plants (atmospheric exposure) at a local scale for the DBP processing scenarios III-a (PVC production), III-b1 (adhesive production), III-c2 (printing ink usage) and III-d (glass fibre production).

DIBUTYL PHTHALATE

CAS No: 84-74-2

EINECS No: 201-557-4

SUMMARY RISK ASSESSMENT REPORT

Final report, 2003

The Netherlands

Rapporteur for the risk evaluation of dibutyl phthalate is the Ministry of Housing, Spatial Planning and the Environment (VROM) in consultation with the Ministry of Social Affairs and Employment (SZW) and the Ministry of Public Health, Welfare and Sport (VWS). Responsible for the risk evaluation and subsequently for the contents of this report is the rapporteur.

The scientific work on this report has been prepared by the Netherlands Organization for Applied Scientific Research (TNO) and the National Institute of Public Health and the Environment (RIVM).

Contact point:

Chemical Substances Bureau
P.O. Box 1
3720 BA Bilthoven
The Netherlands

Date of Last Literature Search:	**1994**
Review of report by MS Technical Experts finalised:	**1999**
Final report:	**2003**

(The last full literature survey was carried out in 1994 - targeted searches were carried out subsequently).

PREFACE

This report provides a summary, with conclusions, of the risk assessment report of the substance dibutyl phthalate that has been prepared by Germany 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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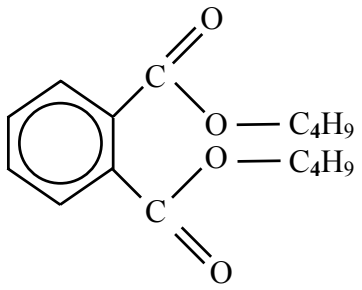
1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS No:	84-74-2
EINECS No:	201-557-4
IUPAC name:	dibutyl phthalate
Synonyms:	di-n-butylphthalat, 1,2-Benzenedicarboxylic acid, dibutyl ester (9CI), Phthalic acid, dibutyl ester (6CI, 8CI), Bis-n-butyl phthalate, Butyl phthalate, DBP, DBP (ester), Dibutyl o-phthalate, Di(n-butyl) 1,2-benzenedicarboxylate, n-Butyl phthalate, Palatinol C, Phthalic acid di-n-butyl ester
Molecular weight:	278.34
Molecular formula:	$C_{16}H_{22}O_4$
Structural formula:	



1.2 PURITY/IMPURITIES, ADDITIVES

Purity:	$\geq$99% (w/w)
Impurity:	ca. 0.01% (w/w) butan-1-ol ca. 0.01% (w/w) butyl benzoate
Additives:	none

1.3 PHYSICO-CHEMICAL PROPERTIES

Physical state:	oily liquid
Melting point:	- 69°C
Boiling point:	340°C at 1,013 hPa
Relative density:	1.045 g/cm^3 at 20°C
Vapour pressure:	$9.7 \pm 3.3 \cdot 10^{-5}$ hPa at 25°C
Water solubility:	10 mg/l at 20°C

Partition coefficient n-octanol/water:	log K_{ow} 4.57
Granulometry:	not applicable
Flammability:	negative
Explosive properties:	negative
Oxidizing properties:	negative

These data are mainly derived from Banerjee and Howard (1984), BASF (corporate data), BUA (1987), Hoyer and Pepperle (1958), Hüls (corporate data); Leyder and Boulanger (1983), Patty (1981). For an extended description see the IUCLID database. [2]

1.4 CLASSIFICATION

Classification and labelling according to the 28th ATP of Directive 67/548/EEC[3]:

Classification:	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
Labelling:	T; N R: 61-50-62 S: 53-45-61	

No Note

Specific concentration limits: none

[2] For references, see the comprehensive Final Risk Assessment Report that can be obtained from the European Chemicals Bureau: http://ecb.jrc.it

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

2 GENERAL INFORMATION ON EXPOSURE

2.1 PRODUCTION

In 1998 the production volume of dibutyl phthalate (hereafter referred to as DBP) in the EU was estimated at 26,000 tonnes, of which 8,000 tonnes was thought to be exported outside the EU. 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 (>1,000 tonnes) of DBP in 1998 was located at three production sites in the EU.

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.

2.2 USE

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 distendability. DBP is further used 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.

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.

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

3.1.1 Environmental fate

DBP may be released into the environment during its production and subsequent life cycle stages, including disposal. Emissions to water and air are expected to be the most important entry routes of DBP. General characteristics of DBP which are relevant for the exposure assessment are given below.

Degradation

The contribution of hydrolysis to the overall environmental degradation of phthalate esters, including DBP, is expected to be low. Photo-oxidation by OH radicals contributes to the elimination of DBP from the atmosphere. An atmospheric half-life of about 1.8 days has been estimated for the photo-oxidation reaction. The metabolic pathway of aerobic and anaerobic biodegradation of phthalates can be summarised as follows. First the di-ester is hydrolysed into the mono-ester by esterases with low substrate specificity. Subsequently the mono-ester is converted into phthalic acid. There is ample evidence that DBP is ready biodegradable under aerobic conditions. The same literature sources indicate that biodegradation of DBP is much slower in the anaerobic environment, e.g. sediments or deeper soil or groundwater layers.

Distribution

The Henry's law constant of 0.27 $Pa \cdot m^3/mol$ indicates that DBP will only slowly volatilize from surface waters, i.e. virtually all of the DBP will remain in the water phase at equilibrium.

The octanol/water partition coefficient (K_{ow}) of DBP is high and consequently the equilibrium between water and organic carbon in soil or sediment will be very much in favour of the soil or sediment. A Koc of 6,340 l/kg can be calculated using the log Kow of 4.57. Despite its low volatility, DBP has been reported as particulate and as a vapour in the atmosphere. In the air DBP is transported and removed by both wet and dry deposition.

Bioaccumulation

The high K_{ow} of DBP indicates that the substance has a potential for bioaccumulation. However, the actual degree of bioaccumulation *in vivo* will be determined by the metabolisation and the elimination rate of the substance. The available BCF data demonstrate a relatively low bioconcentration, but also indicate that higher BCF values are obtained when the BCF is calculated for the total amount of metabolites using ^{14}C-labelled material. The experimental BCF of 1.8 l/kg for DBP from the recent study is used in the further risk assessment for secondary poisoning (aquatic route). In the risk characterisation attention will be paid to the possible consequences of using a higher value. No experimental BCF data are available for terrestrial species. EUSES calculates a BCF worm of 13 kg/kg.

3.1.2 PECs at production and processing

Exposure scenarios

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

I. Production
II. Distribution (e.g. road transport)
IIIa. Processing in polymers
IIIb-1. Formulation in adhesives
IIIb-2. Processing/use of adhesives
IIIc-1. Formulation in printing inks
IIIc-2. Processing/use of printing inks
IIId. Processing of glass fibres
IIIe. Processing of grouting agents
IV. Exterior use of DBP containing products
V. Incineration and disposal of DBP containing products.

For most of these life cycle stages local Predicted Environmental Concentrations (PECs) were calculated based on either generic (TGD defaults) or site-specific scenarios. Results are presented in **Table 3.1** and **Table 3.2** for production and processing, respectively. Regional PECS are calculated to be 0.4 µg/l for water, 89 µg/kg for sediment, 0.006 µg/m^3 for air and 0.01 mg/kg for soil.

In addition to these estimated PECs also a number of EU monitoring data are available for DBP in various environmental compartments (mainly water and sediment).

Table 3.1 Local PECs in the various environmental compartments at production

	Site-spec. A	Site-spec. B	Site-spec. C
$PEC_{effluent, STP}$ (mg/l)	0.06	0.074 *(in µg/l)*	0.09
$PEC_{surface, water}$ (µg/l)	3.6	1	6
PEC_{air} (µg/m^3)	0.02	0.02	0.02
$PEC_{sediment}$ (mg/kg)	0.5	0.1	0.8
PEC_{soil} (mg/kg)	1.1	$0.7 \cdot 10^{-3}$	$0.7 \cdot 10^{-3}$
PEC oral, fish (µg/kg)	3.7	1.8	3.1
PEC oral, worm (mg/kg)	7.6	0.07.	0.06

Table 3.2 Local PECs in the various environmental compartments at formulation/processing

Scenario	IIIa	IIIb-1	III-b2	III-c1	III-c2	III-d
Type of application	Plasticizer in PVC	Adhesive		Printing inks		Fibres
PEC effluent STP (mg/l)	0.02	0.08	0.02	0.01	$4.7 \cdot 10^{-4}$	< 2 µg/l
PEC surface water (µg/l)	2.8	8.9	2.9	2.1	1.1	1
PEC air (µg/m³)	2.4	0.3	0.02	0.05	0.2	1
PEC sediment (mg/kg)	0.4	1.2	0.4	0.3	0.15	0.1
PEC soil (mg/kg)	0.4	1.5	0.4	0.2	0.01	0.003
PEC oral, fish (mg/kg)	0.003	0.008	0.003	0.003	0.002	0.002
PEC oral, worm (mg/kg)	2.5	10.2	2.5	1.5	0.1	0.1

3.2 EFFECTS ASSESSMENT

3.2.1 Aquatic compartment

Both short-term and long-term aquatic toxicity data are available for DBP. The PNEC for the aquatic compartment is derived from the 99-day NOEC of 100 µg/l for *Onchorhynchus mykiss*. 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. The $PNEC_{aquatic}$ amounts to 10 µg/l.

As there are no valid experimental data for the toxicity of DBP to sediment-dwelling organisms, the equilibrium method is used for the derivation of a PNEC in sediment:
$PNEC_{sediment}$ = 1.2 mg/kg wwt.

The test with the protozoan *Tetrahymena pyriformis* can be used to derive a $PNEC_{microorganisms}$. Applying a factor 10 on the EC_{50} of *T. pyriformis* leads to a PNEC value of 0.22 mg/l. It is realised that this PNEC is low compared to the fact that no biodegradation impairment of DBP was found at concentrations far above the water solubility.

3.2.2 Terrestrial compartment

The NOEC of 200 mg DBP/kg for *Zea mays* is used for the derivation of the PNEC for the terrestrial compartment. Applying an assessment factor of 100, results in a $PNEC_{terrestrial}$ of 2 mg/kg dw. For comparison also a $PNEC_{terrestrial}$ is derived based on equilibrium partitioning. This gives a value of 1.24 mg/kg dw, which is in agreement with the $PNEC_{terrestrial}$ derived above.

3.2.3 Atmospheric compartment

There are a number of studies on the airborne toxicity of butyl phthalates to plants. In these studies, plants were exposed in a growth chamber or in a glasshouse to DBP vapour originating from plastics which contained DBP as a plasticizer or from substrates moistened with DBP. The results of the studies show a wide range of effect levels of butyl phthalates, ranging from 1.2 μg/m^3 to 1,000 μg/m^3. An average concentration of about 0.1 μg/m^3 is considered to be a fairly good estimate of the plant NOEC for butyl phthalates. This NOEC of 0.1 μg/m^3 DBP is currently used for the derivation of the PNEC for plants. Although the experiments were carried out under unfavourable greenhouse conditions and, additionally, the 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 a provisional $PNEC_{plant\text{-}air}$ of 0.01 μg/m^3. It was decided that further chronic testing was needed to establish a more reliable PNEC for plants exposed via air. It was agreed to perform a 3-4 months fumigation test with seven plant species (including Brassica).

Following the establishment of criteria for R54 (toxic to flora), application to DBP could also be considered.

3.2.4 Secondary poisoning

The overall oral LOAEL of 52 mg/kg bw for laboratory mammals is used for the derivation of the PNEC for predators (conversion factor = 20, assessment factor = 10), resulting in a $PNEC_{oral}$ of 104 mg/kg in food.

3.3 RISK CHARACTERISATION

3.3.1 General discussion

Table 3.3 and **Table 3.4** present the local PEC/PNEC ratios for, respectively, the production and processing stages of DBP. Details will be discussed in Sections 3.3.2 through 3.3.4.

Table 3.3 Local PEC/PNECs in the various compartments at production

PEC/PNEC	Site-spec. A	Site-spec. B	Site-spec. C
STP	0.3	$3.4 \cdot 10^{-4}$	0.4
Surface water	0.4	0.1	0.6
Sediment	0.4	0.1	0.7
Soil	0.7	$3.3 \cdot 10^{-4}$	$3.2 \cdot 10^{-4}$
Oral, fish	$3.5 \cdot 10^{-5}$	$1.7 \cdot 10^{-5}$	$3 \cdot 10^{-5}$
Oral, worm	0.07	$6 \cdot 10^{-4}$	$6 \cdot 10^{-4}$
Pant (air)	2	2	2

Table 3.4 Local PEC/PNEC ratios at formulation/processing

PEC/PNEC for Scenario	IIIa	IIIb-1	III-b2	III-c1	III-c2	III-d	IIIe
Type of application	Plasticizer softener in PVC	adhesive		printing inks		fibres	grouting agent
STP	0.08	0.4	0.09	0.05	0.002	0	-.
Surface water	0.3	0.9	0.3	0.2	0.1	0.1	0.7 (A) [1)] 0.1 (O)
Sediment	0.3	1	0.3	0.2	0.1	0.11	-
Soil	0.2	0.9	0.2	0.1	$5.9 \cdot 10^{-3}$	0.002	-
Oral, fish	$3 \cdot 10^{-5}$	$7.3 \cdot 10^{-5}$	$3 \cdot 10^{-5}$	$2.5 \cdot 10^{-3}$	$1.8 \cdot 10^{-5}$	$1.7 \cdot 10^{-5}$	-
Oral, worm	0.02	0.1	0.02	0.01	$1.2 \cdot 10^{-3}$	$7.4 \cdot 10^{-4}$	-
Plant (air)	236	34	1	5	20	100	-

1) A= Alna river; O=Oslofjord
PEC/PNEC based on 90-percentile PEC

3.3.2 Aquatic compartment (incl. sediment)

STP

The $PNEC_{microorganisms}$ for DBP was set at 220 µg/l. For the risk characterisation this value is compared with the PEC_{STP} for the various exposure scenarios. For production and processing all PEC/PNEC ratios were found to be below 1 **(conclusion (ii)).**

Surface water

The PNEC for surface water was set at 10 µg/l. For the risk characterisation this value is compared with the PEC in surface water for the various exposure scenarios. For production and processing all aquatic PEC/PNEC ratios were found to be below 1 **(conclusion (ii)).** It should be noted that for scenario IIIe grouting agent the PEC/PNEC based on the maximum (rather than 90 percentile) estimated PEC would amount to 1.5. The current scenario IIIe is based on a Norwegian case and extrapolation to other EU situations is difficult. The general conclusion, however, is that environmental releases of DBP during grouting activities may reach high levels in surface water. Therefore the environmental impact of these kinds of operations should be carefully assessed/monitored. Apart from a few rather old monotoring data (1984) the local and regional measured surface water concentrations were found to be below the PNEC **(conclusion (ii)).** The same is true for the calculated regional water concentration.

Sediment

The PNEC for sediment is 1.2 mg/kg wwt. As both the PNEC and the PEC were calculated with the equilibrium partitioning method from the water data, the same conclusions as for water can be drawn. In addition, most of the available monitoring data are lower than the PNEC for sediment-dwelling organisms. Only the upper limit of the Furtmann data (1993)[4] for the river

[4] For references, see the comprehensive Final Risk Assessment Report that can be obtained from the European Chemicals Bureau: http://ecb.jrc.it

Lippe is higher than the PNEC (PEC/PNEC = 3). Recent marine sediment data (1997) in Denmark indicated that levels (maximum 2.4 mg/kg dwt) very close to the PNEC (fresh water based) can be found. Additional monitoring in marine sediments and identification of emission sources could be relevant. The PEC/PNEC ratio based on a calculated regional PEC sediment is 0.3 **(conclusion (ii))**.

3.3.3 Terrestrial compartment

The PNEC for the terrestrial compartment is 2 mg/kg dw. For the risk characterisation this value is compared with the PEC in soil for the various exposure scenarios. For production and processing all PEC/PNEC ratios were found to be below 1 **(conclusion (ii)).** Measured local data and the calculated regional PEC were also found to be below the PNEC **(conclusion (ii))**.

3.3.4 Atmospheric compartment

The provisional PNEC for the atmospheric compartment is 0.01 µg/m^3. A comparison of this PNEC with the calculated and measured local (production and formulation/processing) and regional PECs, shows that all PEC/PNEC ratios are above 1. A chronic fumigation test with plants has to be conducted **(conclusion (i))**.

3.3.5 Secondary poisoning

The $PNEC_{oral}$ is 104 mg/kg. For the risk characterisation this value is compared with the PECs in fish and worm for the various exposure scenarios. All PEC/PNEC ratios were found to be far below 1 **(conclusion (ii)).** It should be noted that with the application of a higher BCF-value based on tests with ^{14}C-labelled DBP, the risks for secondary poisoning would still be low.

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

4.1.1.1 Occupational exposure

Workplace exposure to DBP is possible due to the production of DBP, the production of products that contain DBP and the use of those products. Occupational exposure levels have been estimated using measured data and modelling by EASE with relevant assumptions.

Production of DBP is done in closed systems. Exposure is mainly due to activities such as filling of tankers and drums, sampling, changing of filters and other maintenance activities. Typical full-shift inhalation exposure levels in production are estimated to be below 2 mg/m^3 with a reasonable worst case of 5 mg/m^3. Short-term inhalation exposure levels of up to 10 mg/m^3 are considered possible. Dermal exposure in production is expected to be highest for drumming of DBP and was estimated by EASE to be up to 420 mg/day.

The formulation of products containing up to 15% of DBP leads to inhalation exposure and dermal exposure mainly due to adding of the substance to mixers, mixing and forming of the products by processes such as extruding and calendering. Mixing and forming processes are done at elevated temperatures (150-210°C). The estimated reasonable worst-case full-shift inhalation exposure level is 5 mg/m^3 (typical: < 2 mg/m^3, short-term 10 mg/m^3). Manual addition of DBP is estimated to lead to a dermal exposure level of 420 mg/day.

The end use of products containing the substance occurs in the polymer industry, the painting industry and the printing industry and can be divided into two subscenarios: aerosol forming techniques, such as spray application, and techniques that do not involve aerosols. Inhalation exposure to DBP in techniques that do not involve aerosols (e.g. application of a product by means of a brush) is estimated to be negligible. The reasonable worst-case full-shift inhalation exposure level is estimated to be 10 mg/m^3 with typical values of 2 mg/m^3 and short-term exposure levels of up to 20 mg/m^3. Dermal exposure during prolonged spay application of products containing DBP is estimated to be up to 975 mg/day. Other activities with products containing DBP are expected to lead to lower dermal exposure levels.

Table 4.1 Summary of the occupational exposure assessment

Scenario	Exposure		Estimated inhalation exposure level (mg/m³)						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]	RWC	Method [b]	Level	Method [b]	
Production	6-8	100-200	2	Meas.	5	Meas.	10	Expert	420
Production of products containing DBP	6-8	100-200	2	Meas.	5	Meas.	10	Expert	420
Use of products containing DBP - aerosol - non-aerosol	 6-8 6-8	 100-200 100-200	 2 negl.	 Expert EASE	 10 negl.	 Expert EASE	 20 negl.	 Expert EASE	975

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
RWC Reasonable worst case
negl. Negligible

4.1.1.2 Consumer exposure

DBP is used in several consumer products. To cover the widespread use of DBP, attention was focussed on products containing a relatively large concentration of DBP such as cosmetics (especially nail polish and enamels), adhesives and regenerated cellulose film (cellophane) wrapped food. Attention was also 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.

Four exposure scenarios have been considered, using measured data or the CONSEXPO model for estimation of the exposure: I Nail polish, II Adhesive, III Cellophane wrapped food, and IV Toys for children. The results are given in **Table 4.2**.

Table 4.2 Summary of consumer exposure

Scenario	Inhalation exposure (mg/m³)	Dermal exposure	Oral exposure	Total internal dose (mg/kg bw/day)
I	$8.59 \cdot 10^{-9}$	negligible		$2 \cdot 10^{-9}$
II	3.18	negligible		$3.43 \cdot 10^{-4}$
III			1.9 mg/person/day	0.027
IV			0.81 μg/kg bw/day	$0.81 \cdot 10^{-3}$

4.1.1.3 Humans exposed via the environment

DBP may be released to the environment through wastewater effluents and air at the sites where it is produced, formulated and/or processed/used. Estimated concentrations (EUSES) in the air near the emission sources for the various exposure scenarios ranged from 0.02 to 2.4 μg/m^3. The calculated total daily human intake via air, drinking water and food for all emission scenarios at local scale (using EUSES) ranged from $7.86 \cdot 10^{-4}$ to 0.0925 mg/kg bw/day for the various exposure scenarios. For the regional scale, the concentration in the air and the total human intake are calculated to be 0.006 μg/m^3 and $3.59 \cdot 10^{-4}$ mg/kg bw/day, respectively.

DBP has been identified in human breast milk in concentrations ranging from 10 to 51 μg/kg. 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. Based on an average daily consumption of 120 g human milk/kg bw for infants, the exposure via breast milk for infants varies between 1.2 and 6 μg DBP/kg bw/day.

4.1.2 Effects assessment

The human population may be exposed by the oral, dermal and inhalation route.

Toxicokinetics, metabolism and distribution

Dibutylphthalate is rapidly absorbed and excreted after oral administration as was demonstrated in studies in laboratory animals. Up to more than 90% of oral doses given to rats or hamsters was excreted in urine within 24-48 hours. Fecal excretion is low (1.0-8.2%).

Also in man oral absorption of DBP takes place.

After dermal exposure of rats to DBP ca. 60% of the dose was excreted in urine within 7 days. In feces ca. 12% of the dose was found. An *in vitro* study revealed slower absorption of DBP by the human skin (2.40 μg/cm^2/hr) than by the rat skin (93.35 μg/cm^2/hr).

Data on absorption after exposure by inhalation are not available.

A substantial fraction of DBP is initially excreted in the bile and subsequently enters the enterohepatic circulation.

No significant accumulation in tissues was observed in laboratory animals after oral as well as dermal exposure; limited inhalation data revealed an indication for some accumulation in tissues.

The major part of DBP is hydrolysed to mono-n-butyl phthalate (MBP) and the corresponding alcohol prior to absorption by the small intestines, but hydrolysis can also occur in liver and kidneys. The metabolites that occur in urine are MBP, MBP-glucuronide, various ω- and ω-1-oxidation products of MBP (more polar ketones, carboxylates) and a small amount of free phthalic acid. Species differences in the excretion of MBP and its glucuronide were observed; rats excreted a larger proportion unconjugated MBP in urine than hamsters.

There are no data on biotransformation after dermal exposure and exposure by inhalation.

Transplacental transfer of DBP and its metabolites was demonstrated in an oral study with ^{14}C-labelled DBP in rats. Radioactivity in embryonic tissues contained less than 0.12-0.15% of the administered dose. MBP accounted for most of the radioactivity in maternal plasma, placenta

and embryo. Unchanged DBP was found in only small amounts. No accumulation of radioactivity was seen in maternal or embryonic tissues.

Acute toxicity

None of the acute toxicity studies have been performed according to current standards. Based on the available data DBP is slightly toxic if swallowed (LD_{50} rat is ≥6,300 mg/kg bw), slightly to moderately toxic by inhalation (LC_{50} rat ≥15.68 mg/L) and slightly toxic in contact with the skin (LD_{50} dermal rabbit >20,000 mg/kg bw).

Irritation

With respect to skin and eye-irritation, studies performed according to current standards were available. DBP appeared to be not irritating for the skin and the eye.

In a 28-day inhalation study in rats adverse local effects in the upper respiratory tract were observed but no signs of inflammation. Hence, DBP is not irritating to the respiratory system.

Sensitisation

Concerning sensitisation one study in animals performed according to current standards and a study performed under GLP conditions were available. DBP did not reveal skin sensitising properties in these animal studies.

The available case studies in man are not appropriate for a definite conclusion with respect to the possible induction of sensitization by DBP.

Repeated dose toxicity

A 90-day study performed according to current standards with repeated oral administration in rats revealed a NOAEL of 152 mg/kg bw. At 752 mg/kg bw, hematological and clinical chemical changes, increased liver and kidney weights and histopathological changes in the liver were seen. However no testicular changes were seen in this study up to and including the highest dose-level of 752 mg/kg bw while in special studies in rats on these effects even the lowest dose-level of 250 mg/kg bw showed an effect (changes in testicular enzymes associated with degeneration of spermatogenic cells). No neurotoxicity was seen in this study.

In addition a NOAEL of 19.9 mg/kg bw in rats with respect to peroxisomal proliferation was found in a special study focused on this effect. However, humans have a low sensitivity for this phenomenon.

Studies with repeated dermal exposure were not appropriate for establishing a NOAEL or LOAEL.

For repeated inhalation exposure a NOAEC of 509 mg DBP/m^3 (the highest concentration tested) for systemic effects including neurotoxic effects can be established based on a 28-day inhalation study in rats performed according to current standards. In this 28-day inhalation study in rats the lowest exposure concentration of 1.18 mg/m^3 is a LOAEC for local effects (histopathological changes in upper respiratory tract).

The epidemiological studies on neurological symptoms in occupationally exposed subjects showed several limitations including lack of an appropriate control group, small size of the exposed population, lack of adequate documentation of protocol and results and mixed exposure

to other compounds than DBP. Therefore these studies are inadequate for the assessment of neurotoxic effects caused by DBP in man in the working environment.

Mutagenicity

With respect to mutagenicity *in vitr*o studies gave an indication for a genotoxic effect in one assay, but in the same experiment, this effect was not seen with other dialkylphthalates (a.o. diethylphthalate). No genotoxic effects for dibutylphthalate were observed in *in vivo* studies detecting chromosomal aberrations.

Based on the data available for dibutylphthalate from a variety of genotoxicity studies as described above and taking into consideration the non-genotoxic properties of other phthalate esters, dibutylphthalate can be considered as a non-genotoxic substance.

Carcinogenicity

No adequate long-term toxicity and/or carcinogenicity studies in animals or man are available. Phthalate esters are known to induce peroxisomal proliferation in the liver of mice and rats. In general the longer chain dialkylphthalates are more potent for the induction of peroxisomal proliferation than the shorter chain ones and branched chain phthalates seemed more potent than straight. Many peroxisome proliferators have been shown to induce hepatocellular tumours when administered at high dose-levels for long periods to mice and rats despite being non-genotoxic. The mechanisms of induction of carcinogenicity by peroxisome proliferators may be complex but are considered to have a threshold. A variety of independent studies have shown that there are marked species differences in the sensitivity to chemicals that cause peroxisome proliferation. Rats and mice are extremely sensitive, hamsters show a less marked response whilst guinea-pigs, primates and man are rather insensitive or non-responsive.

Toxicity for reproduction

Based on the available developmental studies in mice an oral NOAEL of 100 mg/kg bw, can be 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.

In rats, developmental studies with exposure during gestation or during gestation and lactation, revealed preputial separation and reproductive tract malformations in male offspring at oral doses ≥250 mg/kg bw. At the lowest oral dose of 100 mg/kg bw, studied in developmental studies in rats, still delayed preputial separation in male progeny was seen. Maternal toxicity was seen at oral doses ≥500 mg/kg bw. From the developmental studies in rats a NOAEL of 50 mg/kg bw/d could be derived.

Concerning reproduction, fertility as well as developmental studies a NOAEL of 50 mg/kg bw can be established based on embryotoxicity 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, estrous 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.

In some special *in vitro* assays DBP showed weak estrogenic activity. However, the estrogenic effects were not confirmed in *in vivo* studies. Therefore the relevance of the estrogenic effects observed *in vitro* for the *in vivo* estrogenic activity of DBP is questionable. Moreover results of recent developmental studies are indicative of an antiandrogenic effect rather than an estrogenic effect of DBP.

No reproduction, fertility or developmental studies with dermal exposure or exposure by inhalation to DBP are available.

The epidemiological study on possibly reproductive effects in occupationally exposed women is inadequate for assessment of possible reproductive effects caused by DBP in man in the working environment.

Based on all available studies an overall oral LOAEL of 52 mg/kg bw can be established for dibutylphthalate. This figure is derived from a two-generation reproduction study in rats with a continuous breeding protocol and based on embryotoxic effects.

4.1.3 Risk characterisation

4.1.3.1 Workers

Assuming that oral exposure is prevented by personal hygienic measures, the risk characterisation for workers is limited to the dermal and respiratory routes of exposure. Furthermore, it is assumed that adequate risk reduction measures are taken to prevent accidental exposure. If applicable, quantitative risk characterisation is performed by calculation of the MOS (ratio between NOAEL/LOAEL and exposure levels) and comparison of this value with the minimal MOS. The minimal MOS is established via assessment factors, taking into account inter- and intraspecies differences, differences between experimental conditions and the exposure pattern of the worker, type of critical effects, dose-response relationship, confidence of the database and correction for route-to-route extrapolation. A risk is indicated when the MOS is significantly lower than the minimal MOS.

Acute toxicity, irritation and sensitisation

Given the low toxicity observed in the acute oral, inhalation, and dermal studies, the effects observed in the irritation and sensitisation studies and the anticipated occupational exposure levels it is concluded that DBP is of no concern for workers with respect to acute effects, irritation, and skin sensitisation (**conclusion (ii)**). There are no data available on the possible respiratory sensitisation.

Repeated dose toxicity

There are no suitable dermal repeated dose toxicity studies available. The risk assessment for dermal repeated exposure is therefore based on route-to-route extrapolation. Based on the MOSs (10-20) between the NOAEL from the repeated dose study by inhalation in rats (146.6 mg/kg bw/day calculated based on the NOAEC of 509 mg/m^3) and the anticipated dermal exposure levels (420-975 mg/day) it is concluded that for occupational exposure Scenario 3 (use of products containing DBP; subscenario “aerosol forming activities”) adverse systemic health effects due to repeated dermal exposure cannot be excluded (minimal MOS 3.6) (**conclusion (iii)**). No concern for systemic health effects is indicated for other occupational scenarios. There is no

suitable information available to determine the risk for local skin effects after repeated dermal exposure.

Based on the MOSs (51-102) between the NOAEC for systemic effects from the repeated dose study by inhalation in rats (509 mg/m^3) and the anticipated inhalation exposure levels (5-10 mg/m^3) it is concluded that there is no concern for systemic health effects due to repeated inhalation occupational exposure in all scenarios (minimal MOS 90) (**conclusion (ii)**). Based on the MOSs (0.1-0.2) between the NOAEC for local effects from the repeated dose study by inhalation in rats (1.18 mg/m^3) and the anticipated inhalation exposure levels (5-10 mg/m^3) it is concluded that there is concern for local effects due to repeated inhalation occupational exposure in all scenarios (minimal MOS 27) (**conclusion (iii)**).

The conclusions about the risk for systemic health effects derived for the individual routes of exposure are also applicable after combined occupational exposure (i.e. **conclusion (iii)** for Scenario 3 (use of products containing DBP; subscenario "aerosol forming activities") after dermal exposure and **conclusion (ii)** for all other occupational scenarios). A risk assessment for combined exposure is not applicable for local toxicity.

Mutagenicity and carcinogenicity

From the results of the mutagenicity studies it is concluded that DBP may be considered as a non-genotoxic substance (**conclusion (ii)**). No adequate carcinogenicity studies with DBP are available. There are no urgent reasons for concern for workers with regard to carcinogenicity (**conclusion (ii)**).

Toxicity for reproduction

Based on the MOSs (3.7-8.6) between the LOAEL for reproductive toxicity (52 mg/kg bw/day) and the anticipated dermal exposure levels (420-975 mg/day) and the MOSs (36-73) between the LOAEL for reproductive toxicity (52 mg/kg bw/day) and the anticipated inhalation exposure levels (5-10 mg/m^3) it is concluded that there is no concern with respect to reproduction toxicity due to repeated dermal or inhalation exposure for any occupational scenario (minimal MOS 7.2 and 80, respectively) (**conclusion (ii)**).

Occupational limit values

The available current occupational exposure limit values for DBP amount to 5 mg/m^3, and are based on different oral toxicity studies. However, in the present report reference is made to additional oral and inhalation toxicity studies in which among others a LOAEC for local respiratory effects below the present OELs of 5 mg/m^3 was established, based on which there is a need to reconsider the current occupational exposure limits.

4.1.3.2 Consumers

Starting points for the risk assessment for the scenarios with repeated exposure (I, III and IV) are the exposure estimates and the NOAEC of 509 mg/m^3 from the 28-day inhalation study in rats (the highest concentration tested) or the overall oral LOAEL of 52 mg/kg bw/day from the 2-generation reproduction study in rats with a continuous breeding protocol.

The MOS between the inhalation exposure estimate for scenario I and the inhalation NOAEC is $6 \cdot 10^{10}$. The MOSs between the oral exposure estimates and the overall oral LOAEL are 1,925

and 65,00 for scenario III and IV, respectively. These MOSs indicate no concern for consumers (**conclusion (ii)**).

For scenario II the use will be occasionally and exposure is acute. Toxic effects in humans after acute exposure have not been described, in rats the 4h LC_{50} is ≥15,680 mg/m^3. The MOS of 5,000 between this value and the estimated human exposure indicates no concern for consumers (**conclusion (ii)**).

4.1.3.3 Humans exposed via the environment

Inhalation exposure

The MOSs between the inhalation NOAEC of 509 mg/m^3 from the 28-day inhalation study in rats (the highest concentration tested) and the inhalation exposure levels at local as well as at regional scale are all $>2 \cdot 10^5$. From these high MOSs it is concluded that there is no concern for humans indirectly exposed via the environment by inhalation (**conclusion (ii))**.

Total daily intake (from air, drinking water and food)

For the risk characterisation, the estimated total daily intakes for the different scenarios at local scale and for the regional scale are compared with the overall oral LOAEL of 52 mg/kg bw/day. For all local scenarios the MOSs (562-66,000) indicate no concern for humans indirectly exposed via the environment **(conclusion (ii)).**

For the regional scale the MOS of $1.45 \cdot 10^5$ also indicates no concern **(conclusion (ii)).**

Breast milk

Comparing the maximum infant exposure via breast milk (6 µg DBP/kg bw/day) with the overall oral LOAEL of 52 mg/kg bw/day, a MOS of 8,667 can be calculated. This MOS, even when realizing that a LOAEL instead of a NOAEL was used, is considered sufficiently high to conclude that there is no concern for breast-fed babies (**conclusion (ii)**).

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

Flammability, explosive properties and oxidizing properties are not considered to form a hazard. There is no need for further information and/or testing with regard to physico-chemical properties (**conclusion (ii)**).

5 RESULTS

5.1 ENVIRONMENT

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

This conclusion is reached because:

- there is a need for better information to adequately characterise the risks to plants exposed via the atmosphere (the airborne toxicity to plants).

The information requirement is a long-term plant toxicity test.

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

This conclusion applies to effects on the aquatic compartment (including sediment), soil and secondary poisoning.

5.2 HUMAN HEALTH

5.2.1 Human health (toxicity)

5.2.1.1 Workers

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

This conclusion is reached because of:

- concerns for general systemic toxicity as a consequence of repeated dermal exposure arising from aerosol forming activities.
- concerns for adverse local effects in the respiratory tract as a consequence of repeated inhalation exposure in all occupational exposure scenarios.

It is possible that in some industrial premises adequate worker protection measures are already being applied.

5.2.1.2 Consumers

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

5.2.1.3 Humans exposed via the environment

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

5.2.2 Human health (risks from physico-chemical properties)

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