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DIPHENYL ETHER, OCTABROMO DERIVATIVE

CAS No: 32536-52-0

EINECS No: 251-087-9

Summary Risk Assessment Report

2003 **Special Publication I.02.79**

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SUMMARY RISK ASSESSMENT REPORT

Summary report, 2003

France and United Kingdom

This document has been prepared by the French and UK rapporteurs on behalf of the European Union. The scientific work on the environmental part was prepared by the Building Research Establishment Ltd (BRE), under contract to the UK rapporteur.

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PREFACE

This report provides a summary, with conclusions, of the risk assessment report of the substance diphenyl ether, octabromo derivative (octabromodiphenyl ether) that has been prepared by France and the UK in the context of Council Regulation (EEC) No. 793/93 on the evaluation and control of existing substances.

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

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

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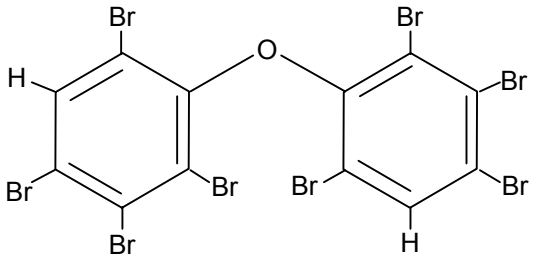
1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS Number: 32536-52-0
EINECS Number: 251-087-9
IUPAC Name: Diphenyl ether, octabromo derivative (octabromodiphenyl ether)
Molecular weight: 801.38
Molecular formula: $C_{12}H_2Br_8O$
Structural formula: (example component)



Synonyms: Octabromobiphenyl ether, OBDPE, OBBE, OBBO, OBDPO, octabromobiphenyl oxide, octabromodiphenyl oxide, octabromo phenoxybenzene and benzene, 1,1'-oxybis-, octabromo derivative

The name octabromodiphenyl ether is used in this assessment.

1.2 PURITY/IMPURITIES, ADDITIVES

There are several components in commercial octabromodiphenyl ether products. The actual composition of the commercial product may vary depending on the manufacturer, however the average number of bromine atoms per molecule in the products is generally around 7.5. Example compositions are given in **Table 1.1**.

Table 1.1 Typical composition of commercial octabromodiphenyl ether flame retardants

Main components	% by weight			
	up to 1994	Composite sample from three suppliers, 1997	Composition reported under the OECD Voluntary Industry Commitment, 2000	Selected production lots, 2000-2001
Pentabromodiphenyl ether	10.5-12.0		1.4-12.0	≤0.5
Hexabromodiphenyl ether		5.5		≤12
Heptabromodiphenyl ether	43.7-44.5	42.3	43.0-58.0	≤45
Octabromodiphenyl ether	31.3-35.3	36.1	26.0-35.0	≤33
Nonabromodiphenyl ether	9.5-11.3	13.9	8.0-14.0	≤10
Decabromodiphenyl ether	0-0.7	2.1	0-3.0	≤0.7

There were no stated additives incorporated into the commercially available forms of this substance.

1.3 PHYSICO-CHEMICAL PROPERTIES

The physico-chemical properties are summarised in **Table 1.2**. Commercial octabromodiphenyl ether is a complex mixture and this means that the measurement and interpretation of some physico-chemical properties is difficult.

Table 1.2 Physico-chemical properties of octabromodiphenyl ether

Property	Value/remark
Physical state (at normal temperature and pressure)	off-white powder or flaked material
Melting point	167-257°C; 130-155°C; 70-150°C (the commercial product has a melting range depending on the composition)
Boiling point	decomposes at elevated temperatures (>~330°C)
Specific gravity	2.9
Vapour pressure	$6.59 \cdot 10^{-6}$ Pa at 21°C
Water solubility	0.5 µg/l at 25°C
Log octanol-water partition coefficient	6.29 (measured by generator column method)
Flammability	not applicable
Autoflammability	not applicable
Explosive properties	none
Oxidising properties	none

1.4 CLASSIFICATION

Octabromodiphenyl ether is not classified for environmental effects.

The proposed classification for human health effects is as follows:

Classification:	Repr. Cat. 2 R61	May cause harm to unborn child
	Repr. Cat. 3 R62	Possible risk of impaired fertility
Labelling:	T R61-62	
	S 53-45	

2 GENERAL INFORMATION ON EXPOSURE

Production

There are no producers of octabromodiphenyl ether in the EU. All of the octabromodiphenyl ether used in the EU is currently imported.

Uses

The main use of octabromodiphenyl ether is as a flame retardant additive for polymers, primarily in acrylonitrile-butadiene-styrene (ABS) polymers at 12-18% loadings in the final product. The main end-use for these polymers is for the housings of office equipment and business machines. The total EU market demand for octabromodiphenyl ether was 450 tonnes/year in 1999, but higher amounts (up to 2,550 tonnes/year) have been estimated to be used in the EU in the recent past. In addition, octabromodiphenyl ether may be imported into the EU in finished or semi-finished products and this was estimated to account for up to a further 1,350 tonnes/year of octabromodiphenyl ether in 1999.

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

Environmental releases

Information from a number of sources has been used to estimate releases from the stages in formulation and use of octabromodiphenyl ether. Emissions from the compounding and processing of plastics have been estimated using information from the plastics industry gathered for a draft Use Category Document in conjunction with the default release factors from the EU Technical Guidance Document. Emissions to the environment during the service life time of the polymer products (e.g. leaching, volatilisation and particulate loss), and at disposal of the products, are also considered. The total EU emissions of octabromodiphenyl ether estimated to occur from use in plastics are 7.55-15.1 tonnes/year to air, 0.16-0.90 tonnes/year to waste water treatment plants, 6.76-14.3 tonnes/year direct to surface water and 20.2-41.8 tonnes/year to urban/industrial soil. The total emissions are dominated by the estimated emissions over the service life of polymers and from disposal of polymers.

Environmental fate

The major characteristics of octabromodiphenyl ether relevant for the exposure assessment are that it is not readily or inherently biodegradable, it has a high log Kow value (6.29) and an estimated atmospheric half-life of 76 days. The high log Kow value indicates that octabromodiphenyl ether will adsorb strongly onto sludge and sediments and is not expected to be mobile in soil. The potential for uptake and accumulation of the substance by fish and other aquatic and terrestrial organisms appears to be low. However, the commercial product contains a significant fraction of hexabromodiphenyl ether components, which may be accumulated. There is also some evidence that octabromodiphenyl ether may (photo)degrade in the environment under certain conditions, possibly forming more toxic and accumulative products, but it is not possible to estimate the extent or rate of these reactions.

The predicted fate of octabromodiphenyl ether in wastewater treatment plants is 91.4% adsorbed onto sewage sludge, 0.14% released to air and 8.46% released to surface water. Thus the major emissions are estimated to occur to water and to land via sewage sludge.

Environmental concentrations

The methods in the Technical Guidance Document were used to estimate concentrations in water, sediment, air, soil and biota (fish and earthworms). In addition to these calculations on the commercial octabromodiphenyl ether product, similar calculations were carried out for the hexabromodiphenyl ether component, which is considered to be the most accumulative component of the commercial product. **Table 3.1** shows the PECs calculated for the various stages of the lifecycle of octabromodiphenyl ether, along with the resulting PEC/PNEC ratios. The predicted air concentrations are very low in all cases (<0.1 $\mu g/m^3$) and so are not shown.

Table 3.1 Summary of PECs and PEC/PNEC ratios estimated for commercial octabromodiphenyl ether

Media	Release source/ comment	PEC		PEC/PNEC	
		Commercial octabromodiphenyl ether	Hexabromodiphenyl ether component	Commercial octabromodiphenyl ether	Hexabromodiphenyl ether component
Surface water	Polymer processing (local)	0.27 µg/l	0.017-0.019 µg/l	≤1.35	0.032-0.033
	Regional sources	3.6-7.5 ng/l	0.15-1.6 ng/l	≤0.018-≤0.038	$2.8 \cdot 10^{-4}$-0.0030
Sediment	Polymer processing (local)	8.0 mg/kg wet wt	0.40-0.43 mg/kg wet wt	≤0.16	≤0.15-≤0.16
	Regional sources	0.19-0.39 mg/kg wet wt	0.0062-0.063 mg/kg wet wt	≤0.004-≤0.008	≤0.0023-≤0.023
Wastewater treatment plant	Polymer processing (local)	8 µg/l	Not applicable	≤0.005	Not applicable
Soil	Polymer processing (local) – agricultural soil	3.25-3.30 mg/kg wet wt	0.19 mg/kg wet wt	≤0.16	≤0.16
	Regional sources – agricultural soil	0.047-0.123 mg/kg wet wt	0.011-0.013 mg/kg wet wt	≤0.002-≤0.006	≤0.011
	Regional sources – industrial/urban soil	4.26-8.82 mg/kg wet wt	0.014-1.11 mg/kg wet wt	≤0.20-≤0.42	≤0.012-≤0.93
Secondary poisoning	Fish - polymer processing	0.057-0.18 µg/kg wet wt	8.6-13.0 µg/kg wet wt	$8.5 \cdot 10^{-6}$-$2.7 \cdot 10^{-5}$	0.015-0.022
	Earthworms - polymer processing	5.34-5.57 mg/kg wet wt	0.67-0.69 mg/kg wet wt	0.8-0.83	1.2

3.2 EFFECTS ASSESSMENT

Aquatic compartment (incl. sediment)

Short-term toxicity test data are available for fish. No effects were seen at concentrations of octabromodiphenyl ether well in excess of its water solubility. For invertebrates, a 21-day reproduction study indicated no effects of the commercial substance at concentrations up to 2 µg/l (the highest concentration tested). No toxicity data are available with algae, but by analogy with another highly brominated diphenyl ether (decabromodiphenyl ether), no effects would be expected to occur in short-term tests with this species at concentrations up to the solubility limit of octabromodiphenyl ether.

Since the commercial octabromodiphenyl ether is a mixture of congeners between hexa- and nonabromodiphenyl ether, consideration has also been given (using the toxicity data for octabromodiphenyl ether and pentabromodiphenyl ether) as to whether the lower brominated

components, particularly hexabromodiphenyl ether, could be more toxic than indicated by the results of the tests with the commercial product.

Based on the currently available toxicity data, a PNEC of >0.2 µg/l has been derived for surface water for the commercial octabromodiphenyl ether product, and a PNEC of 0.11 µg/l has been derived for surface water for the hexabromodiphenyl ether impurity.

The sediment phase is much more relevant for this substance than the water phase, and long-term toxicity data are available for octabromodiphenyl ether with the oligochaete *Lumbriculus variegatus* in two sediment types. No effects were seen in these studies at the highest concentrations tested (1,340 mg/kg dry weight and 1,272 mg/kg dry weight in the two studies respectively). Based on these data, PNECs for the sediment of compartment of ≥49 mg/kg wet wt. and ≥2.7 mg/kg wet weight have been derived for the commercial octabromodiphenyl ether product and the hexabromodiphenyl ether component, respectively.

Octabromodiphenyl ether is of low toxicity to microorganisms. No effects on activated sludge respiration were seen at a concentration of 15 mg/l. Based on these data, a PNEC for wastewater treatment plants of ≥1.5 mg/l can be derived for octabromodiphenyl ether.

Terrestrial compartment

Terrestrial toxicity data are available of octabromodiphenyl ether with plants and earthworms (*Eisenia fetida*). No effects were seen at the highest concentrations tested (1,190 mg/kg dry weight for six species of plants and 1,470 mg/kg dry weight for earthworms). Based on these data, PNECs for the soil compartment of ≥20.9 mg/kg wet weight and ≥1.2 mg/kg wet weight have been derived for the commercial octabromodiphenyl ether product and the hexabromodiphenyl ether component, respectively.

Atmosphere

The predicted atmospheric concentrations of octabromodiphenyl ether are all very low. Neither biotic nor abiotic effects are considered likely because of the limited release and low volatility of the substance.

Secondary poisoning

The information available indicates that although octabromodiphenyl ether has a low potential for bioconcentration and bioaccumulation, some components present in the product are potentially bioaccumulative, and many components have been found to be present in wildlife. The available mammalian toxicity data allow PNECs for secondary poisoning of 6.7 mg/kg food for the commercial octabromodiphenyl ether and 0.58 mg/kg food for the hexabromodiphenyl ether impurity to be derived.

Also of concern with regard to secondary poisoning is the possible formation of lower brominated diphenyl ethers as a result of photolysis/degradation of octabromodiphenyl ether in the environment. The available evidence indicates that more toxic and accumulative lower brominated congeners, if formed, would only be minor products of these reactions, but there is some uncertainty over the actual significance of these processes in the environment, and not all the products from these reactions are known.

3.3 RISK CHARACTERISATION

Aquatic compartment (incl. sediment)

The worst-case PEC/PNEC ratios are summarised in **Table 3.1**. Based on these PEC/PNEC ratios, the risk to the aquatic (surface water) and sediment compartments, and to wastewater treatment plants, from the use of octabromodiphenyl ether can be considered to be low.

Terrestrial compartment

The worst-case PEC/PNEC ratios are summarised in **Table 3.1**. Based on these data, the risk to the terrestrial compartment from the use of octabromodiphenyl ether can be considered to be low.

Atmosphere

Neither biotic nor abiotic effects are considered likely because of limited release and low volatility of octabromodiphenyl ether. The predicted atmospheric concentrations are all very low (<0.1 $\mu g/m^3$).

Secondary poisoning

The PEC/PNEC ratios given in **Table 3.1** indicate that secondary poisoning by octabromodiphenyl ether is not of concern, except when the hexabromodiphenyl ether component is considered in the earthworm scenario. There are considerable uncertainties in the assessment of secondary poisoning for the hexabromodiphenyl ether component, but despite this, it has to be concluded that high levels of hexabromodiphenyl ether component in commercial octabromodiphenyl ether products could lead to a concern for secondary poisoning via the earthworm route. This is supported by the fact that hexabromodiphenyl ether appears to be widespread in biota in the environment, and there is some circumstantial evidence from monitoring data that the concentrations found in organisms may increase through the food chain (concentrations in excess of 1 mg/kg lipid have been measured in some marine mammals). Therefore, based on these findings, there is a need to reduce the risk from the hexabromodiphenyl ether component present in the commercial octabromodiphenyl ether product.

Additional uncertainties

The current approach to risk assessment implies that there is no risk of secondary poisoning (with the exception of the hexabromodiphenyl ether component), and the PEC/PNEC ratios are much less than 1 for the commercial octabromodiphenyl ether product itself. Although it appears to be persistent in the environment, the commercial substance is considered to have a low bioaccumulation potential based on the available laboratory data. It also shows no toxicity towards aquatic organisms up to the limit of water solubility, and effects in other organisms are only observed at relatively high concentrations, based on standard laboratory tests.

Nevertheless, the most recent analytical monitoring surveys indicate that, as well as hexabromodiphenyl ethers, hepta- and octabromodiphenyl ethers (the major components of commercial octabromodiphenyl ether) are present at (relatively) low concentrations in fish, marine mammals and predatory birds' eggs (those of bird-eating Peregrine Falcons and fish-eating Common Terns). The finding of these higher brominated diphenyl ether congeners in some higher mammals and birds' eggs indicates that uptake can occur, possibly via the food chain. The levels of these higher congeners found in fish, etc., are below those that are predicted to cause effects on fish-eating species using the PEC/PNEC approach. However, the sample sizes are small, and the trend in these levels is unknown. It is also possible that higher concentrations

could be found in other organisms. In addition, the available data indicate that some components of the commercial octabromodiphenyl ether products (e.g. hexabromodiphenyl ether congeners) are more bioaccumulative than octabromodiphenyl ether itself and have been found to be widespread in biota in the environment.

It is not possible to assess the effects of the concentrations of these higher brominated components of the commercial product present in, for example, birds' eggs using the current approaches. The mere presence of a chemical in biota is not necessarily a cause for concern, and there is no evidence at this point in time of biomagnification taking place or actual environmental harm arising from this substance at these levels. However, there is some evidence from recent non-standard behavioural tests on mice that neonatal exposure to some of the components of commercial octabromodiphenyl ether (e.g. 2,2',4,4',5,5'-hexabromodiphenyl ether) at doses of 0.45 to 9 mg/kg body weight may cause irreversible behavioural disturbances (as determined by disruption of habituation) in adult mice (such effects have also been seen for decabromodiphenyl ether and so it is likely that other components of the commercial octabromodiphenyl ether product may cause such effects). The toxicological significance of these findings (in terms of population survival) is unclear, and so it is not currently possible to derive a PNEC for the hexabromodiphenyl ether congener based on these endpoints. However, this dose range is below those at which no effects were observed in standard mammalian toxicity tests. In addition, it has recently been shown that some components of commercial octabromodiphenyl ether (2,2',4,4',5,5'- and 2,3,4,4',5,6-hexabromodiphenyl ethers and 2,3,3',4,4',5,6-heptabromodiphenyl ether) show antiestrogenic activity.

In general, a NOAEL has not been established for these types of effects with polybrominated diphenyl ethers. Even if these studies represent a reproducible effect, the interpretation of such an effect in the context of this assessment is unclear, especially in terms of assessment factors and comparison with actual tissue levels (rather than dose). However, they do imply that the standard toxicity tests might not have picked out subtle effects of octabromodiphenyl ether that could be significant at sensitive life stages. This raises some concern about the presence of the substance in birds' eggs. This substance is persistent and so it is also possible that slow uptake may be occurring over extended timescales, so that levels in biota may increase with time. It is therefore possible that the current PEC/PNEC approach for secondary poisoning may not be appropriate for octabromodiphenyl ether in terms of both the PEC and the PNEC, and could underestimate the risk. This issue needs further investigation.

A second aspect of concern is that although the substance is persistent, there is evidence that it can degrade under some conditions. For example, photolysis on solid surfaces has been demonstrated for deca- and tetrabromodiphenyl ether under laboratory conditions, and so octabromodiphenyl ether can be expected to behave similarly. Lower brominated diphenyl ether congeners have been identified among the degradation products from these studies (some products remain unidentified). Limited anaerobic degradation of lower congeners has also been demonstrated in the laboratory. The overall environmental degradation rate has not been determined and the environmental significance of any degradation pathway remains uncertain. There is currently no evidence that significant degradation to lower brominated diphenyl ether congeners is actually occurring in the environment (although it is difficult to state definitively that there is no degradation, since monitoring studies may simply reflect levels of commercial congeners on the market, and this might mask low levels of formation due to degradation). Since some of the products may be more bioaccumulative and toxic than the parent compound, any significant formation would be a cause for concern. The current database in inconclusive on this point, and further work might be needed.

Four possible areas for further work are as follows:

a) A more widespread monitoring project to determine whether the finding in top predators (including birds' eggs) is a widespread or localised phenomenon, and trends (if possible).

b) Further toxicity testing. The existence of a mammalian toxicity data set means that testing could be considered on birds (e.g. an avian reproduction test (OECD 206), with appropriate tissue analysis). Alternatively, a study that administers the substance by injection of eggs could be done to determine whether adverse developmental effects are detectable. Overall, the benefit of further vertebrate testing is open to question due to expected difficulties in achieving sufficiently high exposures. This leaves the toxicity issue with some unresolved uncertainty.

c) An investigation of the rate of formation of degradation products under environmentally relevant conditions over a suitably prolonged time period.

d) Further toxicological work on the non-diphenyl ether degradation products, to determine if they pose a hazard or risk.

There is a high level of uncertainty associated with the suitability of the current risk assessment approach for secondary poisoning and the debromination issue. The combination of uncertainties raises a concern about the possibility of long-term environmental effects that cannot easily be predicted. There is insufficient confidence in the PEC and PNEC estimates to reach either conclusion (ii) or (iii) for this endpoint. In order to be able to reduce the uncertainties to an acceptable level, further research could be attempted. It is noted, however, that much of the information required above would take some considerable time to be generated or gathered, and might not be sufficiently comprehensive to remove all uncertainty. There is evidence that octabromodiphenyl ether is highly persistent, and of particular note, most of the major components of the commercial product have been detected, albeit at relatively low levels and from a limited sample, in predatory birds' eggs and marine mammals. The trend in these levels is unknown. It is not possible to say whether or not on a scientific basis there is a current or future risk to the environment. However, given the persistent nature of the substance, it would be of concern if, once the further information had been gathered, the analysis indicated a risk to predators, since it could then be difficult to reduce exposure.

In summary, although it is concluded that further information should be gathered in order to refine the risk assessment, in light of:

- the persistence of the substance,
- the time it would take to gather the information and
- the fact that there is no guarantee that the studies would provide unequivocal answers,

consideration should be given at a policy level to the need to investigate risk management options now in the absence of adequate scientific knowledge.

[N.B. A number of technical experts from EU member states consider that this uncertainty is sufficient to warrant risk reduction measures directly (conclusion (iii)) based on the information currently provided in this assessment.]

Another area of potential concern for both direct toxicity and secondary poisoning is the possible formation of brominated dibenzo-*p*-dioxins and dibenzofurans from articles containing the substance during combustion or other high temperature processes (e.g. incineration, landfill (where fires could occur), metal recycling or accidental fires). Overall it can be concluded that octabromodiphenyl ether, as a source of bromine, can contribute to the formation of halogenated

dibenzo-*p*-dioxins and dibenzofurans generated during such processes. It is not possible from the available data (and it is beyond the scope of the risk assessment) to quantify the actual contribution that octabromodiphenyl ether makes to the total "toxic" products (fires etc. can generate products other than halogenated dibenzo-*p*-dioxins and dibenzofurans that are considered toxic (e.g. polycyclic aromatic compounds)). Formation of halogenated dibenzo-*p*-dioxins and dibenzofurans in some of these processes is well known and emission control technology is available for incinerators and metal recycling facilities that can reduce emissions to acceptable levels. Although incineration or metal recycling could take place at installations without suitable emission reduction equipment, it should be noted that in most situations octabromodiphenyl ether is unlikely to be the only source of halogenated dioxins/furans. Emission control technology cannot be applied to landfill or other accidental fires. Recycling of plastics containing the substance does not appear to contribute to brominated dibenzo-*p*-dioxin or furan formation.

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

Occupational exposure

Occupational exposure may occur during manufacture, industrial processing in the plastic industry, equipment manufacture and end uses of flame retarded products.

Octabromodiphenyl ether is a solid with a very low vapour pressure. Inhalation of dust and skin contact are the predominant routes of exposure. In situations where exposure to mist may occur as a result of heating (extrusion, moulding), the presence of extraction ventilation is likely to minimise exposure. Exposure is expected to be very low after inclusion in the polymer matrix.

A few dust exposure measurements are available which are not sufficient for the risk assessment. There are no measured data on dermal exposure. Consequently the occupational exposure assessment is based on EASE model estimation and expert judgement. The results for the different scenarios are summarised in **Table 4.1**.

Table 4.1 Summary of occupational exposure

Scenario	External inhalation exposure (mg/m^3)	External dermal exposure ($mg/cm^2/day$)
1 Manufacture (bagging and cleaning activities)	5	1
2 Coumpounding and master batching - bag emptying - extrusion	 5 extremely low	 1 negligible
3 Moulding	extremely low	negligible
4 Equipment manufacture	extremely low	negligible
5 End uses of flame retarded products	negligible	negligible

Consumer exposure

Octabromodiphenyl ether has no direct consumer use but is incorporated as a flame retardant in consumer plastics.

There are no measured data into the indoor environment. Measurements of PBDPE in the air at offices show concentration of at most 97 pg/m^3 and confirm that exposure from the polymer matrix is very low.

In summary, based on scattered pieces of evidence and in agreement with previous risk assessment, it is felt that consumer exposure to octabromodiphenyl ether is likely to be negligible.

Humans exposed via the environment

The maximum total daily human dose of octabromodiphenyl ether is estimated by the EUSES model to be 11 µg/kg bw/day via local sources and 0.42 µg/kg bw/day via regional sources.

4.1.2 Effects assessment

Toxicokinetics, metabolism and distribution

Animal data show an absorption of octabromodiphenyl ether by oral or inhalation route with an accumulation of the parent compound or its metabolites in the liver and also in the adipose tissue and the lung following inhalation administration. The extent of absorption and elimination cannot be assessed from the data available. No information on the metabolism is available. Following oral administration, octabromodiphenyl ether is an inducer of xenobiotic metabolism. There are no measured data on dermal absorption. However based on physicochemical properties and analogy with PCBs, a dermal absorption of 4.5% may be estimated.

Evidence from humans indicates that octa, hexa, hepta and nonabromodiphenyl ethers which are components of commercial octabromodiphenyl ether can be absorbed into the body and distributed into the blood. Distribution to the adipose tissue was evidenced at least for octabromodiphenyl ether and hexabromodiphenyl ether. There are no data available on the rate of elimination or on bioaccumulation of octabromodiphenyl ether from human adipose tissue neither for pentabromodiphenyl ether but given the high lipophilicity of these compounds and the adipose tissue accumulation observed in rats following oral or inhalation routes, it can be assumed that in humans octabromodiphenyl ether might bioaccumulate in these tissues as well. Following pregnancy hexabromodiphenyl ether and others polybrominateddiphenyl ethers such as tetrabromodiphenyl ether and pentabromodiphenyl ethers are excreted in the breast milk. Unfortunately, such measurements were not carried out on octabromodiphenyl ether. However, based on its high lipophilicity, its potential to bioaccumulate in adipose tissues and the breast milk measured data with hexabromodiphenyl ether (one component of commercial octabromodiphenyl ether), excretion of octabromodiphenyl ether in the breast milk may be anticipated.

Acute toxicity

Octabromodiphenyl ether has a low oral, dermal and inhalation acute toxicity in animals. Acute oral toxicity data indicate a rat LD50 greater than 28,000 mg/kg. No deaths, no weight changes or necropsy lesions were reported up to 5,000 mg/kg. At 10,000 mg/kg and 28,000 mg/kg, no deaths were observed but no more information on these studies is available. A dermal LD50 greater than 2,000 mg/kg has been demonstrated in rabbits using octabromodiphenyl ether applied neat under occlusive wraps for 24 hours. No deaths were observed up to 2,000 mg/kg. Local and general signs of toxicity were not reported but necropsies were not performed in this dermal toxicity study. An inhalation LC50 greater than 60 mg/l has been demonstrated in rats exposed during one hour. No deaths and no clinical signs of toxicity were observed up to 60 mg/l.

Irritation / Corrosivity / Sensitisation

Octabromodiphenyl ether is not a dermal or an ocular irritant. There is no indication of skin sensitisation in animals.

Repeated dose toxicity

The only information concerning the effects of repeated oral and inhalation exposure comes from studies in rats involving administration of commercial octabromodiphenyl ether. These studies consistently indicate that the liver is the key target organ within 4 and 13 weeks of repeated oral dosing and within 14 days and 90 days of inhalation exposure. The changes in thyroid status are apparent within 4 and 13 weeks of repeated oral dosing from 1,000 ppm and within 13 weeks of

repeated inhalation dosing from 16 mg/m3 (analytical concentration). The LOAEL is considered to be 100 ppm ≈ 7.2 mg/kg/day in the 90-day dietary study based on the liver changes (increase of liver weight and granular cytoplasmic changes) observed from 100 ppm ≈ 7.2 mg/kg/day. The NOAEC for systemic toxicity is considered to be 1.1 mg/m^3 in the 90-day rat study by inhalation route based on the liver and thyroid status changes observed at the concentration just above: 16 mg/m^3.

Alterations in thyroid homeostasis were reported with organochlorine compounds for many species, including humans and a thyroid hormone like affinity for the serum transport protein transthyretin was shown for hydroxylated PCBs as well as for polybrominated diphenyl ethers congeners such as dibromodiphenyl ether and tetrabromodiphenyl ether. To our knowledge, no studies on transthyretin-T_4 competition have been carried out on octabromodiphenyl ether neither on decabromodiphenyl ether.

Following inhalation exposure, local toxicity was demonstrated with hyperplasia/hypertrophy of the goblet cells within 2 weeks of exposure and with chronic active lung inflammation and alveolar histiocytosis within 13 weeks of exposure. It is obvious that the observed effect at 1.1 mg/m^3 is minimal and reveals only a trend to a chronic inflammation however this value has been taken to set up the LOAEC for local toxicity.

Mutagenicity

Regarding mutagenicity no *in vivo* data are available. However based on the available *in vitro* data, octabromodiphenyl ether is considered as non-genotoxic *in vitro* and no concern for mutagenicity is assumed.

Carcinogenicity

No chronic or carcinogenicity studies in animals are available. Only subchronic studies are available to anticipate carcinogenic potential of the substance, thus no firm conclusion can be drawn on carcinogenicity.

Toxicity for reproduction

No specific fertility study is available. A recent rat inhalation sub-chronic study, well conducted and specifically designed to investigate reproductive organs, did not demonstrate adverse effects on male reproductive organs. Therefore no concern is assumed for male fertility. Regarding female reproductive organs, absence of corpora lutea was shown in this study in 3/10 females at 202 mg/m^3 versus 0/10 in the control group. Since the absence of corpora lutea is considered to be an unusual finding in rats at 20 weeks of age, the 30% incidence in this group was considered treatment-related and therefore a NOAEC for female fertility of 16 mg/m^3 was considered.

Developmental effects are observed in rats in two studies (decrease of fetal body weight from 10 mg/kg/day, increase of post-implantation loss with late resorptions, increase in dead or resorbed conceptuses per litter at 25 mg/kg/day; decrease in the average number of live fetuses per litter and fetal malformation/variation and delayed skeletal ossification at 25 mg/kg/day. Those developmental effects do not seem to be related to maternal toxicity. However, these developmental effects are not confirmed in a third assay in rats conducted with a test article containing a lower percentage of the octabromodiphenyl ether component. In rabbits, the substance produces only slight foetotoxicity from 5 mg/kg/day (slight decrease of the fetal body weight and increase in delayed ossification). The lowest identified NOAEL is considered i.e. 2 mg/kg/day from the rabbit study. Since some of these results are indicative of developmental

effects which are most likely unrelated to maternal toxicity, octabromodiphenyl ether is considered as a developmental toxicant.

Neurotoxicity

With regard to neurotoxicity, recently behavioural disturbances have been reported when mice (10 days old) were exposed to a single oral dose of hexabromodiphenyl ether (0.45, 0.9 and 9 mg/kg bw). Those effects are observed at 2, 4 but also 6 months of age. Nicotinic receptors were also affected in adult mouse in the previous conditions of exposure. The study has certain limitations compared with regulatory guidelines and thus uncertainty as regards interpretation of the results remains. Moreover only an abstract of this study is available with very few details. Therefore, no firm conclusion can be drawn from these data.

4.1.3 Risk characterisation

Workers

For the purpose of the risk characterisation, it is assumed that inhalation of dust and skin exposures are the main routes of exposure. Oral exposure is not considered to be a significant route of exposure under normal working practices.

For inhalation route, assuming a full-shift exposure of 5 mg/m^3, 10 m^3/working day, a 70 kg worker and 100% absorption, the estimated body burden 0.7 mg/kg/day is achieved. For dermal route, assuming maximum skin exposure of 1 mg/cm^2/day, a skin surface exposed of 840 cm^2, a worker's weight of 70 kg and a maximum skin absorption of 4.5 % calculated body burden amounts 0.54 mg/kg/day.

Considering the estimated internal exposure and comparing with the NOAEC of 1 mg/m^3 for systemic toxicity, the LOAEC of 1 mg/m^3 for local toxicity, the NOAEC for female fertility of 16 mg/m^3 by inhalation route, the internal NOAEL of 1 mg/kg/day for developmental toxicity by oral route, MOSs have been calculated. For occupational exposure, these MOSs are of concern.

For dermal exposure, no dermal toxicological data are available for these endpoints. Therefore, on the side of caution, the dermal and oral (inhalation) NOAEL (NOAEC) for repeated doses will be assumed to be the same and a conservative value of 50% for oral absorption and of 100% for inhalation is used to estimate the internal NOAEL(NOAEC). Considering the estimated internal exposure and comparing with the internal LOAEL of 3.6 mg/kg/day for systemic toxicity, the internal NOAEL of 4.6 mg/kg/day for female fertility, the internal NOAEL of 1 mg/kg/day for developmental toxicity, MOSs have been calculated. For occupational exposure, these MOSs are of concern.

Information on the extent of excretion of commercial of octabromodiphenyl ether into the breast milk is recommended as well as information on transthyretin- T_4 competition and effects of prolonged exposure.

Consumers

Consumer exposure to octabromodiphenyl ether is likely to be negligible, with no resulting risk for consumers.

Humans exposed via the environment

The exposure assessment has shown that the main route of intake is by the oral route.

Considering the highest estimated total daily intake of 11 μg/kg/day from local environmental sources and of 0.42 μg/kg/day at a regional level and comparing the LOAEL of 7.2 mg/kg/day derived from the oral subchronic study, the NOAEC for female fertility of 16 mg/m^3, MOSs have been calculated and considered sufficient.

For developmental toxicity, considering a NOAEL of 2 mg/kg/day, the MOS calculated is of insufficient magnitude. In order to refine this estimate, further information is needed either regarding emissions into the environment from use or regarding soil-plant transfer as the exposure is mostly due to high estimated concentrations in root crops.

Information on the extent of excretion of commercial of octabromodiphenyl ether into the breast milk is recommended as well as information on transthyretin- T_4 competition and effects of prolonged exposure.

Combined exposure

Combined environmental exposure and occupational exposure will not influence the characterisation of the risks.

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

Octabromodiphenyl ether gives no reason for concern in relation with its physico-chemical properties. There is no need for further information and/or testing.

5 RESULTS

5.1 INTRODUCTION

Octabromodiphenyl ether is mainly used in the plastics industry as an additive flame retardant for acrylonitrile-butadiene-styrene (ABS) polymers. The commercially supplied product is a mixture of brominated diphenyl ethers typically consisting of 31-36% octabromodiphenyl ether. The other main components are hexabromodiphenyl ether (up to 10.5-12%), heptabromodiphenyl ether (around 44%), nonabromodiphenyl ether (9.5-11.3%) and decabromodiphenyl ether (0-0.7%). The actual composition of the product varies between manufacturers. Recently, a composite sample from three current suppliers of octabromodiphenyl ether to the EU has been used in various physico-chemical and ecotoxicity tests and this had the following composition: 5.5% hexabromodiphenyl ether, 42.3% heptabromodiphenyl ether, 36.1% octabromodiphenyl ether, 13.9% nonabromodiphenyl ether and 2.1% decabromodiphenyl ether. The product is a solid of low water solubility and vapour pressure.

No production of octabromodiphenyl ether currently occurs in the EU. The substance used is imported from outside the EU.

5.2 ENVIRONMENT

Local releases to the environment may occur from polymer processing. In addition, volatilisation of the flame retardant from plastic articles and particulate loss of plastic containing the substance may occur during the lifetime of the article. These releases have been quantified in the assessment and used to calculate PECs for various environmental compartments.

The possible environmental effects of the lower brominated components (e.g. hexabromodiphenyl ether) present in the commercial products are considered in the environmental assessment, along with those of the commercial product as a whole.

For the aquatic compartment, the risk from exposure via surface water is thought to be low. Exposure to organisms via sediment is thought to be much more relevant for this substance and the risk to sediment-dwelling organisms was also found to be low. The risk to wastewater treatment processes was low.

For the terrestrial compartment, no risk was indicated from a worst-case PEC/PNEC comparison.

No adverse effects are expected on the atmosphere from the use of octabromodiphenyl ether.

The available information indicates that the risk of secondary poisoning resulting from the use of octabromodiphenyl ether itself is low using the conventional PEC/PNEC approach. However, when the hexabromodiphenyl ether component present in commercial octabromodiphenyl ether products is considered, a possible risk of secondary poisoning via the earthworm route is indicated. There are considerable uncertainties in the secondary poisoning assessment of octabromodiphenyl ether, and a strict PEC/PNEC approach may not be appropriate for this substance. In addition, the possibility of octabromodiphenyl ether degrading in the environment to give more toxic lower brominated diphenyl ethers cannot be completely ruled out over extended time periods with the available data.

Overall results of the risk assessment

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

This conclusion applies to the risk of secondary poisoning from all sources of octabromodiphenyl ether. It is possible that the current PEC/PNEC approach for secondary poisoning may not be appropriate in terms of both the PEC and the PNEC, and could underestimate the risk. This issue needs further investigation. Two possible areas for further work are as follows:

a) A more widespread monitoring project to determine whether the finding in top predators (including birds' eggs) is a widespread or localised phenomenon, and trends (if possible).

b) Further toxicity testing. The existence of a mammalian toxicity data set means that testing could be considered on birds (e.g. an avian reproduction test (OECD 206), with appropriate tissue analysis). Overall, the benefit of further vertebrate testing is open to question due to expected difficulties in achieving sufficiently high exposures. This leaves the toxicity issue with some unresolved uncertainty.

A second aspect of the concern for secondary poisoning is that although the substance is persistent, there is evidence that it can degrade under some conditions to more toxic and bioaccumulative compounds. The current database in inconclusive on this point, and further work could be done as follows:

c) An investigation of the rate of formation of degradation products under environmentally relevant conditions over a suitably prolonged time period (e.g. years) - for example, an extended monitoring programme to determine trends in degradation product levels in various environmental compartments. This could be coupled with analysis of the parent compound to detect whether it is building up in the environment or has achieved equilibrium. A controlled field study (or studies) might be the way forward, with controlled continuous input of the substance and regular monitoring of other components.

d) Further toxicological work on the non-diphenyl ether degradation products, to determine if they pose a hazard or risk.

There is a high level of uncertainty associated with the suitability of the current risk assessment approach for secondary poisoning and the debromination issue. The combination of uncertainties raises a concern about the possibility of long-term environmental effects that cannot easily be predicted. It is not possible to say whether or not on a scientific basis there is a current or future risk to the environment. However, given the persistent nature of the substance, it would be of concern if, once the further information had been gathered, the analysis indicated a risk to predators, since it could then be difficult to reduce exposure. In summary, although it is concluded that further information should be gathered in order to refine the risk assessment, in light of:

- the persistence of the substance,
- the time it would take to gather the information and
- the fact that there is no guarantee that the studies would provide unequivocal answers,

consideration should be given at a policy level to the need to investigate risk management options now in the absence of adequate scientific knowledge.

[N.B. A number of technical experts from EU member states consider that this uncertainty is sufficient to warrant risk reduction measures directly (conclusion (iii)) based on the information currently provided in this assessment.]

The possible long-term increase in levels as a result of releases from waste sites might need to be considered further in any future revision of this risk assessment report.

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

This conclusion applies to the environmental assessment of risks to the aquatic (surface water, sediment and waste water treatment plants), terrestrial and atmospheric compartments by the conventional PEC/PNEC approach for octabromodiphenyl ether itself from all sources (including the assessment of the hexabromodiphenyl ether component).

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

This conclusion applies to the assessment of secondary poisoning via the earthworm route for the hexabromodiphenyl ether component in the commercial octabromodiphenyl ether product from the use in polymer applications.

5.3 HUMAN HEALTH

5.3.1 Human health (toxicity)

This assessment does not take into account the risks related to the breakdown products formed during processing at elevated temperatures. Repeated dose toxicity, reproductive toxicity, breast milk excretion, endocrine disrupter potential, effects of prolonged exposure are considered to be the critical endpoints in the risk assessment.

Workers

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

This conclusion is reached since information is needed on transthyretin-T4 competition with octabromodiphenyl ether as well as information on the extent of excretion of commercial octabromodiphenyl ether into the breast milk and information on the effects of prolonged exposure**.**

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

This conclusion is reached for manufacture (bagging and cleaning activities) and compounding and master batching (bag emptying), because of:

- systemic effects after inhalation and dermal repeated exposure;
- local effects in the respiratory tract after inhalation repeated exposure;
- developmental effects after repeated dermal and inhalation exposure cannot be excluded at the workplace.

Consumers

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

This conclusion is reached because consumer exposure is considered negligible.

Humans exposed via the environment

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

This conclusion is reached since further information is needed on emissions into the environment from use or on soil-plant transfer; on the extent of excretion of commercial octabromodiphenyl ether into the breast milk and cow's milk. Depending upon the results submitted by Industry on milk excretion further information might be requested. There is a need for exposure information from local and regional sources on the concentration of octabromodiphenyl ether in cows' milk. Information is needed as well on transthyretin-T_4 competition with octabromodiphenyl ether and on the effects of prolonged exposure. This may involve the conduct of a lifetime study in rodents depending upon the way in which the methodology for assessing lifetime exposure is developed and any data requirements that may be indicated for such a methodology.

5.3.2 Human health (risks from physico-chemical properties)

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

Note for all information required under conclusion (i)

It is noted that much of the information required under conclusion (i) would take a long time to be generated or gathered, in particular for breast feeding and effects of prolonged exposure, and that a considerable amount of uncertainty could remain in the risk assessment once the further information had been provided. As a consequence of the environmental and human health (occupational exposure) risk assessment, a risk reduction strategy has been developed for this substance which proposes a restriction of the marketing and use under Directive 76/769/EEC. If this strategy is adopted, then the information requirement should be adjourned.

Results of discussion at the policy level

Following the agreement of the risk assessment conclusions reached on a technical basis as presented in this report, Member States noted the uncertainties expressed regarding the risk characterisation for secondary poisoning and infants exposed to octabromodiphenyl ether from human breast milk. They also noted the conclusion that further information would be required to remove these uncertainties and refine the risk assessment. Member States were concerned that it would take a significant time to gather the information and that the resulting refined risk assessment could then indicate a risk to predators or breast-feeding infants. Furthermore, degradation of some of the components of the substance and the bioaccumulative properties of some of the components and possible degradation products could cause concentrations in biota and breast milk to rise while the data were being gathered. Consequently Member States agreed that risk reduction measures should be considered without delay for the sources of this exposure. In the light of this agreement and as a consequence of the environmental and health risks already identified, a risk reduction strategy for this substance has been developed. This strategy proposes a restriction on the marketing and use of octabromodiphenyl ether under Directive 76/769/EEC. If this strategy is adopted, then the proposed testing requirements listed under the conclusion (i) should be adjourned in the interests of animal welfare and cost versus benefit unless expert advice is provided which indicates that tests may be relevant to the controls which emerge from negotiations under Directive 76/769/EEC.