

クロルデコンの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
<p>【生分解性・加水分解性】 水生環境中であるいは土壤中、生分解又は加水分解するとは予測されない。</p> <p>【光分解性】 大気中で直接的な光分解を受けることは考えられないと結論している。</p> <p>・利用可能な全てのデータに基づき、クロルデコンは環境中で高い残留性を示すと考えられる。</p>	<p>【オクタール/水分配係数】 logKow=4.50-5.41</p> <p>【BCF(経鰓的生物濃縮係数)】 ・藻類: BCF=6000 ・無脊椎生物: BCF=21600 ・魚類: BCF=60200</p> <p>【BMF(経口的生物濃縮係数)】 ・ほとんど又は全く代謝浄化せず、水生の食物連鎖において生物濃縮の可能性がある。 ・食物連鎖の研究において、藻からカキへの移動は非常に低かったが、エビからアミ、アミからスポットへの明白な栄養段階を通じた移動があることが示された。</p>	<p>【反復投与毒性】 ラット(2年): NOAEL 0.05mg/kg/day 0.25mg/kg/day で腎臓影響(蛋白尿、重篤な糸球体硬化)</p> <p>ラット(経口 21ヶ月): LOAEL 0.07mg/kg/day 肝細胞の病理組織学的変化、甲状腺ろ胞サイズ、コロイド含量低下、甲状腺ろ胞上皮細胞の高さの増加</p> <p>ラット(経口 3ヶ月): LOAEL 1.17mg/kg/day 肝の巣状(限局性)壊死、副腎肥大、振戦、多動性、過剰驚愕反応等</p> <p>【生殖毒性】 ラット(3ヶ月): NOAEL 0.25mg/kg/day 精巣萎縮 ラット(90日): LOAEL 0.83mg/kg/day で精子の運動性・生存率低下、精子数減少、1.67mg/kg/day で性嚢、前立腺重量低下 マウス(160日): LOAEL 2mg/kg/day で排卵停止、膻発情持続、ラット妊娠14-20日に母体経由で 15mg/kg/day 投与した雌児動物においても同様の報告</p>	<p>【慢性毒性】 ミジンコ <i>Daphnia magna</i> : 21dNOEC=0.0283 mg/L(繁殖)、 21dNOEC=0.025 mg/L(成長) ミシッドシュリンプ <i>Americamysis bahia</i> : 28dMATC=0.000026-0.00034 mg/L(成長) ユスリカ <i>Chironomus tentans</i> : 14dNOEC=17.9 mg/kg sediment(発達)</p>

		<p>【催奇形性】 ラット(経口): LOAEL 2mg/kg/day で 胎児体重低下、骨化度低下、 10mg/kg/day で脳水腫、停留精巣、腎 盂肥大、脳室肥大</p> <p>【発がん性】 ラット(80週): LOAEL 1.2mg/kg/day 肝細胞がん IARC グループ2B (possibly carcinogenic to human)</p> <p>【その他】 職業ばく露で振戦、情緒不安定、視力 障害、筋力低下、歩行運動失調等、 実験動物で、脾臓、胸腺重量、好中球 数、NK 活性低下、 EU-Strategy for Endocrine Disruptors 優先化学物質(無処置動物の少なくと も一種類において内分泌かく乱活性を 示す科学的根拠がある)に分類</p>	
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**Report of the Persistent Organic Pollutants Review Committee
on the work of its third meeting**

Addendum

Revised risk profile on chlordecone

At its third meeting, the Persistent Organic Pollutants Review Committee revised and adopted the risk profile on chlordecone, on the basis of the draft contained in document UNEP/POPS/POPRC.2/17/Add.2. The text of the risk profile, as amended, is set out below. It has not been formally edited.

CHLORDECONE

RISK PROFILE

Adopted by the Persistent Organic Pollutants Review Committee
at its third meeting

November 2007

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Executive summary

The European Community and its member states being parties to the Stockholm Convention have proposed chlordecone to be listed in the Convention. The Persistent Organic Pollutants Review Committee concluded in its meeting in November 2005 that the substance complies with the screening criteria set out in Annex D of the Convention and that a draft risk profile should be prepared to review the proposal further.

Chlordecone is a synthetic chlorinated organic compound, which has mainly been used as an agricultural insecticide, miticide and fungicide. It was first produced in 1951 and introduced commercially in the United States in 1958 (trade names Kepone® and GC-1189). It was available in the United States until 1976. In France, chlordecone was marketed with a trade name Curlone from 1981 to 1993. Historically, chlordecone has been used in various parts of the world for the control of a wide range of pests. It has been used extensively in banana cultivation against banana root borer, as a fly larvicide, as a fungicide against apple scab and powdery mildew and to control the Colorado potato beetle, rust mite on non-bearing citrus, and potato and tobacco wireworm on gladioli and other plants. Given the specific pesticidal uses of chlordecone, it can be expected that all amounts manufactured are ultimately released to the environment.

Chlordecone is not expected to hydrolyse or biodegrade in aquatic environments, nor in soil. Direct photodegradation is not significant. Therefore, chlordecone is considered to be highly persistent in the environment. With BCF-values in algae up to 6,000, in invertebrates up to 21,600 and in fish up to 60,200 and documented examples of biomagnification, chlordecone is considered to have a high potential for bioaccumulation and biomagnification.

The available data are not conclusive when it comes to long-range atmospheric transport of chlordecone in gaseous form. However, atmospheric transport of particle-bound substances and transport of sediment particles in ocean currents as well as biotic transport could also contribute to long-range environmental transport of chlordecone. Due to lack of monitoring data on chlordecone, the assessment of the potential for long-range transport of chlordecone was based on physico-chemical properties and application of long range transport models.

Chlordecone is readily absorbed into the body and accumulates following prolonged exposure. The pesticide is both acutely and chronically toxic, producing neurotoxicity, immunotoxicity, reproductive, musculoskeletal and liver toxicity at doses between 1 - 10 mg/kg bw/day in experimental animal studies. Liver cancer was induced in rats at a dose of 1 mg/kg body weight per day, and reproductive effects are seen at similar dose levels. The International Agency for Research on Cancer has classified chlordecone as a possible human carcinogen (IARC group 2B). Moreover, chlordecone is very toxic to aquatic organisms, with the most sensitive group being the invertebrates.

Based on the available evidence, chlordecone is likely as a result of its long-range environmental transport to lead to significant adverse human health and environmental effects such that global action is warranted.

1 Introduction

The European Community and its member states being parties to the Stockholm Convention have proposed chlordecone to be listed in Annex A to the Convention (UNEP/POPS/POPRC.1/6).

This risk profile has been prepared following the decision of the Persistent Organic Pollutants Review Committee at its first meeting in November 2005 to establish an ad hoc working group to review the proposal further (UNEP/POPS/POPRC.1/10).

In this document all data are presented according to the International System of Units (SI) and, therefore, many have been recalculated from other units in the data sources. Furthermore, all concentrations are presented based on kg or L (*e. g.* µg/kg or mL/L).

1.1 Chemical Identity of the proposed substance

Chlordecone is a synthetic chlorinated organic compound, which has mainly been used as an agricultural insecticide, miticide and fungicide.

1.1.1 Names and registry numbers

CAS chemical name:

1,1a,3,3a,4,5,5,5a,5b,6-decachloro-octahydro-1,3,4-metheno-2H-cyclobuta-[cd]-pentalen-2-one

Synonyms:

Decachloropentacyclo-[5,2,1,0^{2,6},0^{3,9},O^{5,8}]-decan-4-one,

Decachlorooctahydro-1,3,4-metheno-2H,5H-cyclobuta-[cd]-pentalen-2-one

Decachloroketone

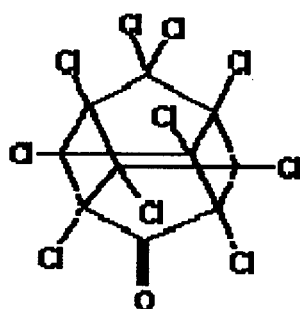
Trade names:

GC 1189, Kepone, Merex, ENT 16391, Curlone

CAS registry number:

143-50-0

1.1.2 Structure



Source: <http://webbook.nist.gov>, as quoted in <http://ecb.jrc.it>

Chlordecone is chemically closely related to mirex, a pesticide which is already listed under the Stockholm Convention. The chemical structure of chlordecone differs from mirex in that the oxygen of the keto group in chlordecone is replaced by two chlorine atoms in mirex.

1.1.3 Physical and chemical properties

The physical and chemical properties of chlordecone are listed in Table 1.1. It demonstrates that the variation is high between data sources for physical properties like vapour pressure and water solubility. This is confirmed by the fact that the Henry's Law Constant varies by one order of magnitude, depending on the type of data used for the calculation. The source of used data are generally considered to be reliable; the data quality have been assessed in the (inter)national consensus documents (IARC, IPCS HSG, IPCS EHC and US ATSDR) and the quality of the data published by Hansch *et. al.* and Howard has been evaluated (Pedersen *et. al.*, 1995).

Table 1.1 Physical and chemical properties of Chlordecone.

Property	Unit	Value	Reference
Molecular formula		C ₁₀ Cl ₁₀ O	
Molecular weight	g/mole	490.6	
Appearance at normal temperature and pressure		Tan-white crystalline solid	IARC, 1979 ¹
Vapour Pressure	Pa	3.0x10 ⁻⁵ (25 °C) < 4.0x10 ⁻⁵ (25 °C) 4.0x10 ⁻⁵ (25 °C)	Kilzer, I <i>et. al.</i> , 1979 ² IARC, 1979 ¹ HSG 41, IPCS, 1990
Water solubility	mg/L	0.35-1.0x 1-2 2.7 (25 °C) 3.0	HSG 41, IPCS, 1990 EHC 43, IPCS, 1990 Kilzer, I <i>et. al.</i> , 1979 ² Kenaga, 1980
Melting point	°C	350; (decomposes)	IARC, 1979 ¹
Boiling point	°C	No data	
Log K _{ow}		4.50 5.41	Howard, 1991 ¹ Hansch <i>et. al.</i> , 1995 ²
Log K _{aw}		-6.69	Scheringer <i>et. al.</i> , 2006
Log K _{oc}		3.38-3.415	Howard, 1991 ¹
Henry's Law Constant	Pa m ³ /mol	5.45x10 ⁻³ , (25 °C) 2.53x10 ⁻³ (20 °C) 4.9x10 ⁻³ 2.0x10 ⁻²	Calculated ² Howard, 1991 ¹ Calculated ³ Calculated ⁴
Atmospheric OH Rate Constant	cm ³ /molecule-sec	≈ 0 (25 °C) ^j	Meylan & Howard, 1993 ²

* It is likely that the 0.35 number is an outlier. The source (HSG 41 by IPCS) did not provide the reference so it is impossible to track where this number came from. The more robust EHC 43 by IPCS did provide a reference and used 1-2 mg/l. This is in the same range with the other values in peer reviewed articles. ATSDR quotes a value of 3 mg/l from Kenaga.

1: Quoted from US ATSDR, 1995

2: Quoted from <http://esc.syrres.com/interkow/webprop.exe>

3: Calculated from maximum water solubility and minimum vapour pressure of this table

4: Calculated from minimum reliable water solubility (1 mg/L) and maximum vapour pressure of this table

1.2 Conclusion of the Persistent Organic Pollutants Review Committee on the Annex D information on Chlordecone

The POP Review Committee applied in its first meeting on 7–11 November 2005¹ the screening criteria specified in Annex D to the Stockholm Convention, and decided, in accordance with paragraph 4 (a) of Article 8 of the Convention, that it was satisfied that the screening criteria have been fulfilled for Chlordecone. It decided furthermore, in accordance with paragraph 6 of Article 8 of the Convention and paragraph 29 of decision SC-1/7 of the Conference of the Parties to the Stockholm Convention, to establish an ad hoc working group to review the proposal further and to prepare a draft risk profile in accordance with Annex E to the Convention. It invited, in accordance with paragraph 4 (a) of Article 8 of the Convention, Parties and Observers to submit to the Secretariat the information specified in Annex E of the Convention before 27 January 2006.

¹ See the meeting report at: www.pops.int/documents/meetings/poprc/

1.3 Data sources

This Risk Profile is mainly based on information from the following review reports:

- Environmental Health Criteria (EHC) 43: Chlordecone. IPCS International Programme on Chemical Safety. United Nations Environment Programme. International Labour Organisation. World Health Organization. Geneva 1990 (available at: <http://www.inchem.org/documents/ehc/ehc/ehc43.htm>)
- Health and Safety Guide No. 41, 1990. IPCS International Programme on Chemical Safety. United Nations Environment Programme. International Labour Organisation. World Health Organization. Geneva 1990 (available at: <http://www.inchem.org/documents/hsg/hsg/hsg041.htm>)
- Toxicological profile for Mirex and Chlordecone. U.S. Department of Health and Human Services, Agency for Toxic Substances and Disease Registry (ATSDR) August 1995 (available at: <http://www.atsdr.cdc.gov/toxprofiles/tp66-p.pdf>).

The above extensive review reports were used as the main source of information on this candidate POP chemical. Prior to the drafting of this risk profile, a detailed literature search was undertaken on Chlordecone which did not uncover any further assessment reports on this chemical, either international or at the level of individual countries. Where the reviews above have been cited, the text quoted (or quoted with modifications) includes the references cited in the original review. These references are not shown individually in the reference list.

Following the request of the POP Review Committee for additional information, as specified in Annex E of the Convention, on Chlordecone, information was provided, which was mainly based on the open literature. However, France provided a report prepared for the Assemblée Nationale describing the history of production and use of Chlordecone in Martinique and Guadeloupe (Beaugendre, 2005).

A search for more recent information included a literature search *via* the Danish Technical University Library and the data base FINDit (search terms: Chlordecone, kepone, merex) as well as a data base search in public data bases. The data bases include "Ecotox" (US-EPA, <http://www.epa.gov/ecotox/>), "NITE" (Japan, National Institute of Technology and Evaluation <http://www.safe.nite.go.jp/english/db.html>) BUA Reports (<http://www.gdch.de/taetigkeiten/bua/berichte.htm>) and Environmental Fate Data Base (<http://www.syrres.com/esc/efdb.htm>). This search was based on the search terms: Chlordecone, Kepone and the CAS number 143-50-0. In addition, the Arctic Monitoring and Assessment Programme² and the UNEP Regionally based assessment of Persistent Toxic Substances Global Report³ were consulted. Most of these gave no further information regarding Chlordecone.

1.4 Status of the chemical under international conventions

Chlordecone is listed in Annex A of the Protocol to the Convention on Long-Range Transboundary Air Pollution (CLRTAP) on Persistent Organic Pollutants. The provisions of the Protocol oblige Parties (currently 25) to phase out all production and uses of Chlordecone. Chlordecone is included in the OSPAR convention as a substance of possible concern⁴.

The proposal to include Chlordecone in the UNEP/FAO Rotterdam Convention was reviewed by the Chemical Review Committee (CRC) at its first meeting in February 2005. The CRC agreed that, on the basis of the information currently available, the notifications from Switzerland and Thailand had met all the criteria of Annex II with the exception of criterion (b) (iii)⁵. Accordingly, the CRC concluded that Chlordecone could not be recommended for inclusion in Annex III of the Rotterdam Convention at the current time.

² <http://www.amap.no/>

³ http://www.chem.unep.ch/pts/gr/Global_Report.pdf

⁴ The chemically related compound mirex is already included in the Stockholm convention. Both mirex and Chlordecone are included in the UNECE 1998 Aarhus Protocol on Persistent Organic Pollutants (POPs). Both are included in OSPAR as substances of possible concern.

⁵ This requires that the documentation supplied demonstrates that the final regulatory action is based on a risk evaluation involving prevailing conditions within the Party taking the action.

2 Summary information relevant for the risk profile

2.1 Sources

2.1.1 Production

Chlordecone has been produced by reacting hexachlorocyclopentadiene and sulfur trioxide under heat and pressure in the presence of antimony pentachloride as a catalyst. The reaction product is hydrolyzed with aqueous alkali and neutralized with acid; Chlordecone is recovered *via* centrifugation or filtration and hot air drying (Epstein 1978) (Quoted from US ATSDR, 1995).

Chlordecone was first produced in 1951, patented in 1952, and introduced commercially in the United States by Allied Chemical in 1958 under the trade names Kepone® and GC-1189 (Epstein 1978; Huff and Gerstner 1978). The technical grade of chlordecone, which typically contained 94.5% chlordecone, was available in the United States until 1976 (IARC 1979). Chlordecone was also found to be present in technical grade mirex at concentrations up to 2.58 mg/kg and in mirex bait formulations at concentrations up to 0.25 mg/kg (EPA 1978b; IARC 1979a) (Quoted from US ATSDR, 1995).

2.1.2 Trade and stockpiles

Between 1951 and 1975, approximately 3.6 million pounds (1.6 million kg) of chlordecone were produced in the United States (Epstein 1978). (Quoted from US ATSDR, 1995) Chlordecone production was discontinued in the USA in 1976. However, a year later it was reported that a French company was considering the establishment of production facilities in France (Anonymous, 1978b), but no further information on this proposal is available. (Modified from EHC 43, (IPCS, 1984)).

No current data are available regarding import volumes of chlordecone. By 1976, technical chlordecone was not exported from the United States and the compound was no longer produced there. Diluted technical grade chlordecone (80% active ingredient) was exported to Europe, particularly Germany, in great quantities from 1951 to 1975 by the Allied Chemical Company (Epstein 1978) where the diluted technical product was converted to an adduct, Kelevan. Kelevan is a derivative of chlordecone and used for the same purposes. In the environment, it oxidizes to Chlordecone and could therefore also be considered with Chlordecone for listing in the Stockholm Convention. Approximately 90-99% of the total volume of Chlordecone produced during this time was exported to Europe, Asia, Latin America, and Africa. (DHHS 1985; EPA 1978b) (Modified from US ATSDR, 1995) There is no information, indicating that Kelevan is being produced or used at present.

Chlordecone was marketed in France as a formulation, Curlone, by De Laguarique from 1981 to 1993. The formulation was used in Martinique and Guadeloupe following hurricane Allen in 1979 and David in 1980 which led to considerable pest infestations. Chlordecone for this formulation was synthesised in Brazil. The authorisation for Curlone was withdrawn by the French Ministry of Agriculture in 1990. Use was continued until September, 1993. (Beaugendre, 2005) In Canada, no product containing Chlordecone has been registered as a pest control product since 2000.

2.1.3 Uses

Chlordecone has been used extensively in the tropics for the control of banana root borer (Anonymous, 1978a; Langford, 1978). This was its only registered food use. It is regarded as an effective insecticide against leaf-cutting insects, but less effective against sucking insects (Information Canada, 1973). Historically, Chlordecone has been used in various parts of the world for the control of a wide range of pests. It can be used as a fly larvicide, as a fungicide against apple scab and powdery mildew (Information Canada, 1973), and to control the Colorado potato beetle (Motl, 1977), rust mite on non-bearing citrus, and potato and tobacco wireworm on gladioli and other plants (Suta, 1978). Chlordecone has also been used in household products such as ant and roach traps at concentrations of approximately 0.125% (IARC 1979a). The concentration used in ant and roach bait was approximately 25%. (Epstein 1978) (Modified from EHC 43 (IPCS, 1984) and US ATSDR, 1995).

2.1.4 Releases to the environment

Given the specific pesticidal uses of Chlordecone, it can be expected that all amounts manufactured are ultimately released to the environment. The use of Chlordecone as a pesticide in Martinique and Guadeloupe until 1993 resulted in severe contamination of soil and surface water, which are being monitored at present. (Bocquene & Franco, 2005, Beaugendre, 2005).

Major releases of Chlordecone occurred to the air, surface waters, and soil surrounding a major American manufacturing site in Hopewell, Virginia. Releases from this plant ultimately contaminated the water, sediment, and biota of the James River, a tributary to the Chesapeake Bay (Quoted from US ATSDR, 1995).

2.2 Environmental fate

The partitioning of Chlordecone in the environment will be governed by its high log K_{ow} (5.41 or 4.50) and relatively low water solubility (1-3.0 mg/L) resulting in sorption to particulate matter (dust, soil and sediment) and organic material (living organisms).

The combination of these properties and the vapour pressure ($3.0-4.0 \times 10^{-5}$ Pa) of Chlordecone, results in a relatively low potential for volatilisation as the Henry's Law Constant is between 2.0×10^{-2} and 5.45×10^{-3} Pa m³/mole (25 °C), depending on the type of data used for the calculation (Table 1.1.).

In the EHC 43 (IPCS, 1984), the volatilisation of Chlordecone is evaluated based on laboratory and field observations that indicate that Chlordecone does not volatilise to any significant extent (Dawson, 1978). However, the release of copious quantities of Chlordecone dust from production facilities has represented a major source of environmental and human contamination. Airborne Chlordecone has been known to spread 60 miles from a point source (Feldmann, 1976), and the potential exists for further dispersion of fine particles (Lewis & Lee, 1976 (Abbreviated from EHC 43 (IPCS, 1984).)

The US ATSDR (1995), concluded that Chlordecone released to the environment partitions to soil and sediment. Small amounts may remain dissolved in water and Chlordecone released to the atmosphere is eventually deposited on soil or surface waters.

2.2.1 Persistence

In the EHC 43 (IPCS, 1984), early reports that did not include any evidence of Chlordecone degradation in the natural environment (Dawson, 1978; Geer, 1978) were quoted as well as a more recent study, in which microbial action had been shown to transform Chlordecone into monohydro- and possibly dihydrochlordecone (Orndorff & Colwell, 1980a).

EHC 43 (IPCS, 1984), concluded that Chlordecone is an extremely stable compound and is not expected to degrade in the environment to any significant extent. However, there have been reports of trace amounts of monohydrochlordecone being found (Carver *et al.*, 1978, Orndorff & Colwell, 1980b), but the mechanism of its formation is not clear. Solar irradiation of Chlordecone in the presence of ethylenediamine results in 78% degradation after 10 days (Dawson, 1978) quoted from EHC 43 (IPCS, 1984). However, ethylenediamine is not usually present in the atmosphere, so at the time, there was no information available regarding the photolytic stability of Chlordecone under environmental conditions.

The more recent review (US ATSDR, 1995), concludes that Chlordecone is not expected to be subject to direct photodegradation in the atmosphere. Furthermore, it is concluded that Chlordecone is resistant to aerobic degradation, although some anaerobic biodegradation does occur and that Chlordecone is very persistent in the environment. Chlordecone will strongly bind to organic matter in water, sediment, and soil. When bound to organic-rich soil, Chlordecone is highly immobile; however, when adsorbed to particulate matter in surface water, Chlordecone can be transported great distances before partitioning out to sediment. The primary process for the degradation of Chlordecone in soil or sediments is anaerobic biodegradation (Abbreviated from US ATSDR, 1995).

Information regarding the persistence of Chlordecone dating after 1995 is scarce, but the use of Chlordecone until 1993 in the Caribbean island of Martinique has resulted in severe contamination and monitoring studies have been initiated. Bocquene & Franco (2005) reported concentrations in samples from 2002 in water (particulate matter) and sediment in rivers of up to 57 µg/kg and 44 µg/kg, respectively. They quoted other investigations for reporting concentrations in river water, sampled in 2000-2001 in the range 1.20 - 2.13 µg/L.

Even though Chlordecone was prohibited from main land France, an exemption was granted that allowed the use of it in the French West Indies until September, 1993. A recent study showed that it is still detected in different ecosystems of Martinique (Coat, S. *et al.*, 2006). Stocks of Chlordecone may have been used in Martinique after 1993, but it is expected that the use ceased several years ago. However, residues are still measurable in both river water and sediment, where the prevailing anaerobic conditions in the latter allow for the only known biotic degradation of Chlordecone. This is all the more remarkable as the climate in this area is optimal not only for crops and pests but also for biodegradation.

Conclusion

Chlordecone is not expected to hydrolyse or biodegrade in aerobic aquatic environments or in soil; however, there is some evidence of degradation under anaerobic condition. Direct photodegradation is not significant. Based on all available data Chlordecone is considered to be highly persistent in the environment.

2.2.2 Bioaccumulation

Because of the lipophilic nature of this compound (high octanol-water partition coefficient ($\log K_{ow}$ 4.50-5.41), Chlordecone has a potential for both bioaccumulation and, with little or no metabolic depuration, also biomagnification in aquatic food chains.

Table 2.1 summarises bioconcentration factors (BCF) selected from the US EPA database Ecotox (US EPA, 2006). The results included are based on measured concentrations and, for organisms different from algae, derived from tests based on flow through exposure. Thereby, the results should reflect the bioconcentration obtained under well defined, constant exposure concentrations. For fish, the results of a series of tests of four days duration were not included, because it is not considered to be likely that equilibrium had been reached⁶. Two additional studies from EHC 43 (IPCS, 1984) are also included.

Table 2.1 BCF values for Chlordecone.

Species	Test Duration	Exposure Concentration $\mu\text{g/L}$	BCF	Reference ¹
Green algae (<i>Chlorococcum sp.</i> , <i>Dunaliella tertiolecta</i>)	24 h	100	230-800	Walsh <i>et al.</i> , 1977
Green alga (<i>Chlorococcum sp.</i>)	48 h	40	6,000	Bahner <i>et al.</i> , 1977
Diatoms (<i>Thalassiosira guillardii</i> , <i>Nitzschia sp.</i>)	24 h	100	410-520	Walsh <i>et al.</i> , 1977
Crustacean (<i>Callinectes sapidus</i>)	96 h	110-210	6.2-10.4	Schimmel, 1977
Crustacean (<i>Palaemonetes pugio</i>)	96 h	12-121	425-933	Schimmel, 1977
Crustacean (<i>Palaemonetes pugio</i> , <i>Americamysis bahia</i>)	21-28 d	0.023-0.4	5,127-13,473	Bahner <i>et al.</i> , 1977
Crustacean (<i>Palaemonetes pugio</i>)	16 d	0.041	12,094	Fisher & Clark, 1990
Oyster (<i>Crassostrea virginica</i>)	19-21 d	0.03-0.39	9,278-9,354	Bahner <i>et al.</i> , 1977
Midge (<i>Chironomus tentans</i>)	14 d	11.8-169.2	21,600	Adams <i>et al.</i> , 1985
Fish (<i>Brevoortia tyrannus</i>)	1-18 d	0.14-1.55	2,300-9,750	Roberts & Fisher, 1985
Fish (<i>Menidia menidia</i>)	1-28 d	0.08-0.8	21,700-60,200	Roberts & Fisher, 1985
Fish (<i>Cyprinodon variegatus</i>)	28 d	< 0.02-1.9	3,100-7,115	Bahner <i>et al.</i> , 1977; Hansen <i>et al.</i> , 1977
Fish (<i>Leiostomus xanthurus</i>)	30 d	0.029-0.4	2,340-3,217	Bahner <i>et al.</i> , 1977
Fish (<i>Pimephales promelas</i>)	56 d	0.004	16,600	Huckins <i>et al.</i> , 1982 ²
Fish (<i>Cyprinodon variegatus</i>)	Life cycle	0.041	1,800-3,900	Goodman <i>et al.</i> , 1982 ²

1: All quoted from the Ecotox database (US EPA, 2006), except for two² quoted from EHC 43 (IPCS, 1984)

The information on bioaccumulation from food is limited, but the EHC 43 (IPCS, 1984) report includes two relevant studies; one on food exposure and the other on an estuarine food chain. When chlordecone was fed to juvenile spot for 28 days, the body burden of chlordecone increased additively and equilibrium was not attained (Stehlik & Merriner, 1983). The estuarine food chain study (Bahner *et al.*, 1977) was composed of green algae, oysters, mysids, grass shrimps, sheepshead minnows and spot. The transfer from algae to oysters was very low; but a clear transfer from shrimp to mysids

⁶ In OECD Test Guideline 305, the prescribed duration of the exposure phase is 28 days.

and from mysids to spot, indicated that much of the chlordecone was being transferred through the trophic levels. Clearance was slow in shrimp and fish, with tissue levels of chlordecone decreasing by 30-50% in 24-28 days.

US ATSDR (1995), described the bioaccumulation of chlordecone together with that of mirex, stating that they are both highly lipophilic and therefore, have a high bioconcentration potential. They bioaccumulate in aquatic food chains with virtually no degradation of the compounds by exposed organisms (de la Cruz and Naqui, 1973; Epstein, 1978; Huckins *et al.*, 1982; Huggett and Bender, 1980; Kenaga, 1980; Lunsford *et al.*, 1987; Naqui and de la Cruz, 1973; Nichols, 1990; Oliver and Niimi, 1985 and 1988; Roberts and Fisher, 1985)⁷.

Only limited information is available on uptake and bioaccumulation of chlordecone in terrestrial food chains (Naqui and de la Cruz, 1973), and little uptake of chlordecone by plants was observed (Topp *et al.*, 1986).

Conclusion

With BCF-values of up to 6,000 in algae, of up to 21,600 in invertebrates and of up to 60,200 in fish, and with documented examples of biomagnification, chlordecone is considered to have a high potential for bioaccumulation and biomagnification.

2.2.3 Potential for Long-Range Environmental Transport

The potential for long-range environmental transport can be documented through monitoring data from remote regions (*e.g.* the Arctic) and/or through physical-chemical characteristics of the molecule, which are promoting such transport. The most well known mechanism of long-range transport is atmospheric transport of substances in the vapour phase. However, atmospheric transport of particle-bound substances and transport of sediment particles in ocean currents as well as biotic transport could also contribute (*e.g.* AMAP 2004).

One prerequisite for long-range atmospheric transport is persistence to degradation, and Chlordecone is considered to be highly persistent in the environment (see Section 2.2.1). Chlordecone does not volatilise to any significant extent (see section 2.2). The partitioning of Chlordecone in the environment will be governed by its high $\log K_{ow}$ (5.41 or 4.50) and relatively low water solubility (1-3.0 mg/L) resulting in sorption to particulate matter (dust, soil and sediment) and organic materials and living organisms. Therefore, the long range transport is expected to take place through these pathways.

The US ATSDR (1995), states that atmospheric transport of dust containing Chlordecone particles was reported during production years based on results from high volume air sample filters from Hopewell: At approximately 200 yards from the Chlordecon production plant, the contents ranged from 3.0-55 micrograms/m³, depending on weather conditions and date of collection. At more distant sites in May 1975, levels ranged from 1.4-21 ng/m³. Specifically, in South Richmond, 15.6 miles north west from Hopewell, the level was 1.41 ng/m³. At Byrd airport, 14.12 miles north of Hopewell, the level was 1.93 ng/m³. In Petersburg, 8.19 miles south west from Hopewell, the level was 20.7 ng/m³. (Epstein, 1978). They conclude further, that airborne Chlordecone has been known to spread 60 miles from a point source (Feldmann, 1976), and that the potential exists for further dispersion of fine particles (Lewis & Lee, 1976) (US ATSDR, 1995).

Transport in aquatic environments is illustrated by results of measurements in clams and oysters from the James River at sampling locations from 8-64 miles from Hopewell, Virginia that contained 0.2-0.8 mg/kg of Chlordecone (Epstein, 1978).

However, no records are available regarding concentrations of Chlordecone in areas at long distances from sites of production or use. Therefore, the assessment of the potential for long-range transport of Chlordecone must be based on physical properties. For this - apart from persistence - the vapour pressure and the Henry's Law Constant are considered to be the most relevant properties. For a comprehensive evaluation of the potential for long-range atmospheric transport, knowledge of the vapour pressure at high as well as at low temperatures (*e.g.* 25 °C and 0 °C) is required. This information is, however, available for only a few substances (AMAP, 2004), so the vapour pressure at 25 °C is used as a measure of the volatility of the substance.

As a rule of thumb, substances with vapour pressures $>1.33 \times 10^{-2}$ Pa will be entirely in the vapour phase and substances with vapour pressures $<1.0 \times 10^{-4}$ Pa will be particulate (US ATSDR, 2004).

A way of evaluating the characteristics and effects of a substance for which not enough information exists is to compare it with better known substances of similar characteristics. This approach (known as "the benchmark approach") was proposed by Scheringer (1997) and Beyer *et al.*, (2000), has been recently used in some recent studies concerning persistence and environmental transport of pollutants (see, *i.e.* Vulykh *et al.*, 2006, and Klasmeier *et al.*, 2006). As a measure of values of properties that would qualify for long-range atmospheric transport, the currently listed POPs are used. However,

⁷ These references describe both Mirex and Chlordecone.

information regarding physical-chemical properties for chemicals often varies widely between sources and the quality of data cannot be compared without specific review of the individual studies. This is demonstrated by the available data on the physical-chemical properties of Chlordecone presented in Table 1.1. The two values for the vapour pressure are rather uniform (0.3 and 0.4×10^5 Pa) but the water solubility found in literature varies by an order of magnitude (0.35 – 3.0 and the lowest value is considered to be unreliable.⁸

The comparison of Chlordecone with already listed POPs is presented in Table 2.2. As a starting point for this comparison, the highest and lowest values for Chlordecone (Table 1.1) were used. For already listed POPs, information was sought on the UNEP-POPs homepage. Among the currently listed POPs, most of the relevant properties were available for aldrin, chlordane, dieldrin, DDT, hexachlorobenzene, mirex, toxaphene, endrin and heptachlor. Missing information (water solubility of mirex) was sought in US ATSDR (1995) and AMAP (2004). The US ATSDR (1995), quotes values of 0.2 and 0.6 mg/L, while the AMAP (2004), quotes Mackay for very low water solubility: 6.5×10^{-5} mg/L. In order to avoid introduction of what seems to be an outlier in the comparison, the value for water solubility of mirex from US ATSDR (1995) was used.

The water solubility and vapour pressure as well as Henry's Law Constants calculated from these values of the currently listed POPs are summarised in Table 2.2 together with information on Chlordecone from Table 1.1.

Table 2.2 Water solubility (WS), vapour pressure (VP) and (calculated) Henry's Law Constant (HLC) (at 25°C) for Chlordecone and currently listed POPs.

Substance	WS mg/L	VP Pa	HLC Pa m ³ /mol
Chlordecone-min	1.0	0.00003	0.0049 ¹
Chlordecone-max	3.0	0.00004	0.02 ²
POP-min	0.0012 (DDT)	0.000025 (DDT)	0.04 (endrin)
POP-max	3.0 (toxaphene)	27 (toxaphene)	3726 (toxaphene)
POP-2 nd max	0.5 (dieldrin)	0.04 (heptachlor)	267 (heptachlor)

1: Calculated from maximum water solubility and minimum vapour pressure

2: Calculated from minimum reliable water solubility and maximum vapour pressure

Table 2.2 shows that the water solubility of Chlordecone is at the level of the most water soluble among the currently listed POPs (toxaphene and dieldrin), while the vapour pressure is comparable to that of DDT. The highest of the two Henry's Law Constants that were calculated for Chlordecone is of the same order of magnitude as that of endrin. It should be noted that in presenting the data in table 2.2 it is not inferred that a chemical (in this case Chlordecone) is considered to meet the long range environmental transport criterion just because it fits within the range of values of currently listed POPs.

Further to this, it should be mentioned that the latest AMAP report on POPs (AMAP, 2004) describes the possibilities of particle borne transport for substances, which have Henry's Law Constants (HLC) close to that of Chlordecone (HLC = 0.0049 or 0.056). Based on HLC-values from AMAP (2004), it is concluded that semi-volatile compounds such as lindane (γ -HCH) (HLC = 0.000149) and chlordane (HLC = 0.342) are distributed between airborne particles and the gaseous phase, depending on the temperature. These can be washed out *via* precipitation and temporarily deposited in seawater or soil and can absorb to water, plant and soil surfaces from the gaseous phase. During favourable warm weather conditions, these compounds evaporate again into the atmosphere and undergo further atmospheric transport. This remobilization is also called the 'grasshopper effect'. The role of stormy weather situations in remobilization of semivolatile compounds into the atmosphere is obvious but still scarcely investigated (AMAP, 2004).

Besides, certain physical-chemical properties of Chlordecone, such as the partition coefficients $\log K_{ow}$ (octanol-water partition coefficient) and $\log K_{aw}$ (air-water partition coefficient), are similar to those of some toxaphene components which, added to its persistence in air and water, would mean that coupled long range transport in atmosphere and oceans may take place (*i. e.* the substance is exchanging between atmospheric gas phase and oceanic dissolved phase and can be

⁸ Availability of high quality data regarding physical-chemical properties could support more firm conclusions.

transported in either phase). (Wania, F. 2006, personal communication). Chlordecone has a very low Henry's law constant and a high mass fraction is found in water, and therefore it can be inferred that transport with ocean currents contributes to the long-range transport of Chlordecone.

In a recent modeling study, Scheringer *et al.*, (2006), investigated the persistence and long range transport potential of these potential POPs, including chlordecone and hexabromobiphenyl, using an OECD screening tool which based the evaluation of overall environmental persistence and transport potential on the results of several of the currently available multimedia environmental fate models (see also Klasmeier *et al.*, 2006, and Fenner *et al.*, 2005 for a more detailed explanation). They concluded that the four POP candidates have persistence and long range transport potential properties similar to those of several known POPs in this evaluation. Furthermore, they included the uncertainty regarding the data quality in an uncertainty analysis, which indicated that the result is valid although there are considerable uncertainties in the chemical properties of the four POP candidates. It should be noted that environmental fate modeling results strongly depend on the assumptions made, specifically when essential data such as environmental half-lives are not known. In addition, results for substances like Chlordecone, which are strongly bound to particles and are of very low volatility, are highly dependent on the medium to which they are emitted, i.e., to air, to water, or to soil. The emission to air scenario always yields the highest transfer efficiency, and that value is displayed in the Scheringer *et al.*, (2006) plots. Transfer efficiency will likely differ by several orders of magnitude when evaluated under soil and water emission scenarios.

Conclusion

In summary, the above discussion shows that the available data on Chlordecone are not conclusive when it comes to long-range atmospheric transport in gaseous form. However, atmospheric transport of particle-bound substances and transport of sediment particles in ocean currents, as well as biotic transport, could also contribute to long-range environmental transport of Chlordecone. Coupled atmosphere-ocean transport also seems quite possible.

Due to a lack of monitoring data on Chlordecone the assessment of the potential for long-range transport of Chlordecone must be based on physico-chemical properties and modelling data. The modelling study of Scheringer *et al.*, 2006, shows clearly that long range environmental transport is possible (and possibly more than actually estimated), even considering the uncertainties surrounding the physico-chemical properties.

In accordance with paragraph 7 (a) of Article 8 of the Convention, and taking into account that a lack of full scientific certainty should not prevent a proposal from proceeding, Chlordecone is likely, as a result of its long-range environmental transport, to lead to significant adverse human health and environmental effects such that global action is warranted.

2.3 Exposure

2.3.1 Environmental concentrations

The available information regarding environmental concentrations of Chlordecone is very limited and includes only areas in the vicinity of production (US) or use (Martinique).

The US ATSDR (1995), illustrates the presence of Chlordecone in the environment following production of the substance. In 1977, 12 years after production of Chlordecone began and 2 years after the production ceased, average concentrations of Chlordecone in estuarine water (dissolved) were <10 ng/L (ppt) (Nichols 1990). In October 1981, 6 years after production ceased, Chlordecone water concentrations ranged from not detectable to 0.02 µg/L (ppb) (Lunsford *et al.*, 1987). Groundwater monitoring data are lacking, but because Chlordecone binds tightly to organic matter in soil, leaching into groundwater is not expected to occur extensively (Abbreviated from US ATSDR, 1995).

Recent monitoring data from the United States demonstrate the persistence of Chlordecone, known as Kepone in the United States. The substance is included in the U.S. EPA National Lake Fish Tissue Study to estimate the national distribution of selected residues in fish tissue from lakes and reservoirs in the lower 48 states. There were a total of 881 samples collected and analyzed between 2000 and 2005. For Chlordecone, there were 152 hits (17.25%), ranging from 12.3 and 2008 ppb. (Jensen, 2006).

In Martinique, the widespread use of Chlordecone until 1993 has resulted in contamination of soils and surface water in most of the island (Bocquené & Franco, 2005). These authors reported an investigation from 2002 of the presence of a series of pesticides in the water at the mouth of seven rivers. They measured Chlordecone in particulate matter or sediment of six of the seven rivers at concentrations up to 57 µg/kg in particulate matter, and up to 44 µg/kg in sediment.

Bocquené & Franco (2005), quoted other investigations in which concentrations of Chlordecone in the range 1.20 to 2.13 µg/L were measured in rivers of Martinique in 2002-2001. They also stated that Chlordecone was "ubiquitous" in river water used for drinking water.

Further to this, the report prepared for L'Assemblée Nationale (Beaugendre, June 2005), described the history of the use of Chlordecone in Guadeloupe and Martinique, and mentioned several monitoring programmes which are expected to result in reports at the end of 2005. However, these reports have not been available when drafting this document.

2.3.2 Human exposure

In the US ATSDR (1995), the experience from production of Chlordecone is summarised as follows: Chlordecone has not been detected in human adipose tissue or in blood samples from the general population, although historically it was detected in human milk samples collected in the south-eastern United States (EPA 1978c). Information is available regarding Chlordecone levels in blood of occupationally exposed workers and their families during 1974-1975 employed at the Hopewell, Virginia site. (Cannon *et al.*, 1978; Epstein 1978; Knishkowsky & Baker 1986; Taylor *et al.*, 1978). (Quoted from US ATSDR, 1995) Further data on human exposure is quoted in section 2.4.1.

Information regarding human exposure resulting from direct use (application) of Chlordecone in the Caribbean Islands is not available. However, monitoring data in agricultural soils, crops, freshwater fish, littoral fish and shellfish indicates that human exposure more than 10 years after the use of chlordecone has ceased in Martinique and Guadeloupe, is still possible. In soils having received Chlordecone, residues in crop are proportional to soil contamination and may exceed the recommended national residues limits (50 µg/kg to 200 µg/kg). This concerns mainly root vegetables such as radish (max. measured concentration: 0.055 µg/kg), sweet potatoes (max. measured concentration: 0.300 µg/kg), taro root (max. measured concentration: 0.230 µg/kg), but also aerial part of plants, such as sugar cane (max. measured concentration: 0.690 µg/kg), or pineapple (max. measured concentration: 0.160 µg/kg). In addition, workers are directly exposed to contaminated soils. Concentrations in fisheries products (freshwater and estuarine water) have also been found to exceed in some occasions national residues limits up by a factor of 100 (max. measured concentration: 20 mg/kg). National provisions have been taken in order to prohibit fisheries activities in contaminated area (Cabidoche *et al.*, 2006).

2.4 Hazard assessment for endpoints of concern

2.4.1 Toxicity

Toxicokinetics in experimental animals and in man

The US ATSDR (1995) and EHS 43 (IPCS, 1984) both record that Chlordecone is well absorbed following oral, dermal and inhalation exposure. Toxicokinetic data are mainly available from studies in experimental animals (*e. g.* Blanke *et al.*, 1978; Boylan *et al.*, 1979; Cohn *et al.*, 1978; Egle *et al.*, 1978; Fujimori *et al.* 1982a; Guzelian *et al.*, 1981; Hall *et al.* 1988; Hewitt *et al.*, 1986b; Kavlock *et al.*, 1980; Plaa *et al.*, 1987; Richter *et al.*, 1979; Shah *et al.*, 1987; Skalsky *et al.*, 1980; as reported in IPCS, 1984). Following absorption, it is widely distributed in the body, with accumulation in the liver and to a lesser extent in fat, brain and kidneys, both in experimental animal studies and in humans (as reported in US ATSDR (1995) and EHS 43 (IPCS, 1984). Following administration of a single oral dose to rats at 40 mg/kg body weight, the highest concentrations were found in the adrenal glands and liver, followed by the fat and lung (Egle *et al.*, 1978, quoted from IPCS, 1984). Chlordecone has been reported to be slowly metabolised *via* reductive biotransformation to Chlordecone alcohol in the rat (Blanke *et al.*, 1978, as reported in EHS 43). Elimination from the body is slow, with a half-life of the order of several months and Chlordecone disappears more slowly from the liver than from other tissues (Egle *et al.*, 1978, quoted from IPCS, 1984). Elimination is mainly *via* the faeces, a total of 66% of the dose in the Egle study being removed in the faeces and 2% in the urine in the 84 days following administration (Egle *et al.*, 1978, quoted from IPCS, 1984).

EHS 43 reports that Chlordecone was detected in high concentrations in the liver (range 13.3-173 mg/kg), whole blood (range 0.6-32 mg/litre), and subcutaneous fat (range 2.2-62 mg/kg) of 32 male workers (Cohn *et al.*, 1976, adapted from IPCS (1984). In occupationally-exposed workers, serum Chlordecone concentrations ranged from 120 to 2109 µg/litre, and dropped to 37 - 486 µg/litre 6-7 months after exposure had ceased (Adir *et al.*, 1978, reported in IPCS (1984). The half-life of Chlordecone in these workers was estimated to be 63-148 days. Reductive biotransformation to Chlordecone alcohol has also been reported in humans (Blanke *et al.*, 1978, as reported in EHS 43). Chlordecone was eliminated, primarily in the faeces, at a mean daily rate of 0.075% of the estimated total store in the body (Cohn *et al.*, 1976, quoted from IPCS, 1984).

Toxicity of Chlordecone in animal studies

Chlordecone is of high acute toxicity in experimental animal studies, with an LD₅₀ of approximately 100 mg/kg in the rat and ranging from 65 mg/kg in the rabbit to 250 mg/kg in the dog (taken from IPCS, 1984, Table 2). Acute toxicity effects include tremors indicative of a neurotoxic effect on the nervous and/or musculoskeletal systems, investigated by many authors as reported in US ATSDR (1995). The neurotoxic effects of Chlordecone have been reported in chickens (Naber & Ware, 1965), quail (McFarland & Lacy, 1969), fish (Couch *et al.*, 1977), hamsters (Martinez *et al.*, 1976), mice (End *et al.*, 1979), rats (Epstein, 1978), and man (Martinez *et al.*, 1978). Acute oral administration of Chlordecone is also associated with reproductive effects (Khera *et al.*, 1976; Uzodinma *et al.*, 1984a; Yarbrough *et al.*, 1981) and hepatotoxicity in some studies (Fujimori *et al.*, 1983; Mehendale 1977b, 1981b; Teo & Vore 1991) (quoted from US ATSDR (1995)).

Repeated exposure to Chlordecone also causes reproductive, neurological, musculoskeletal and liver toxicity at doses as low as 10 mg/kg bw/day, although effects in other organs including kidney, thyroid, adrenals, and testes have also been reported (US ATSDR, 1995, IPCS, 1984). A Lowest-Observed-Adverse-Effect-Level (LOAEL) of 1.17 mg/kg bw/day was recorded in a 3 month feeding study in rats and signs of toxicity included focal necrosis in liver, enlargement of the adrenal gland, tremor, hyperactivity and exaggerated startle response (Cannon and Kimbrough, 1979, as quoted in US ATSDR, 1995). Histopathological changes in the liver, reduction in thyroid follicular size and colloid content and increase in epithelial cell height were reported in a 21-month gavage study in the rat, with a LOAEL of 0.07 mg/kg bw/day in males (Chu *et al.*, 1981, as quoted in US ATSDR, 1995). Renal effects (proteinuria and increased severity of glomerulosclerosis) were seen in a 2-year feeding study in rats, with a NOAEL of 0.05 mg/kg/day (Larson *et al.*, 1979b, as quoted in US ATSDR, 1995). Oral Chlordecone treatment caused decreased spleen and thymus weights, leukocyte counts, natural killer cell activity, and mitogenic responsiveness (EPA 1986c; Smialowicz *et al.*, 1985; Swanson and Wooley, 1982); decreased natural killer cell activity (Smialowicz *et al.*, 1985); and significant increase in plaque-forming cells (Chetty *et al.*, 1993c) (as reported in ATSDR, 1995). The NOAEL was 5 mg/kg bw/day and the LOAEL was 10 mg/kg bw/day.

Hepatocarcinogenicity (hepatocellular carcinoma) of Chlordecone has been demonstrated in rats and mice (males and females) (NCI 1976, Reuber, 1978, 1979, as quoted in IPCS, 1984 and US ATSDR, 1995). Tumours have been observed at doses as low as 1 mg/kg bw/day in the rat and in mice at a dose of 2.6 mg/kg bw/day (NCI, 1976, as quoted in US ATSDR (1995)). The International Agency for Research on Cancer (IARC) concluded in 1987 that there was sufficient evidence that Chlordecone is carcinogenic in mice and rats and possibly carcinogenic to humans (Group 2B). Chlordecone is not genotoxic in *in vitro* microbial and mammalian cell gene mutation assays, in a clastogenicity test and in the dominant lethal assay (Mortelmans *et al.*, 1986; Probst *et al.*, 1981; Schoeny *et al.*, 1979, Tong *et al.* 1981; Williams 1980, Khera *et al.*, 1976; Simon *et al.*, 1986, as reported in ATSDR (1995), although it has been reported to interfere with cell-to-cell communication (Tsushimoto *et al.*, 1982, Caldwell and Loch-Carusio, 1992, as reported in US ATSDR (1995), suggests that it produces liver tumours by an epigenetic, tumour-promoting mechanism involving both hepatic toxicity and hypertrophy, including cytochrome P-450 induction.

Oral administration of Chlordecone to animals causes decreased fertility or fecundity and litter size, reduced sperm count and testicular atrophy (Khera *et al.*, 1976; Linder *et al.* 1983; Uzodinma *et al.*, 1984a; Yarbrough *et al.* 1981, as reported in US ATSDR (1995). A LOAEL of 0.83 mg/kg/day was recorded for sperm effects in a 90 day feeding study in rats, while effects on seminal vesicles and prostate were apparent at 1.67 mg/kg bw/day (Linder *et al.*, 1983) (Quoted from US ATSDR (1995)).

Chlordecone is also a developmental toxicant. As reported in US ATSDR (1995) and EHC 43 (IPCS, 1984), gestational exposure of rats and mice to low doses of Chlordecone resulted in increased stillbirths and decreased postnatal viability, reduced fetal or neonatal weight and/or skeletal ossification and a low incidence of malformations such as renal pelvis dilatation, undescended testes, enlarged cerebral ventricles, clubfoot, fused vertebrae or ribs, and encephalocele. Chlordecone administered at levels of 2, 6, and 10 mg/kg bw/day to rats and 2, 4, 8, and 12 mg/kg body weight per day to mice on days 7 - 16 of gestation caused 19% maternal mortality in rats at the highest dose and fetuses exhibited reduced weight, reduced degree of ossification, oedema, undescended testes, enlarged renal pelvis, and enlarged cerebral ventricles. (Chernoff & Rogers, 1976, as reported in IPCS, 1984). Lower dose levels induced reductions in fetal weight and degree of ossification. Male rats born to treated dams did not show any reproductive impairment. The reproductive performance of mice fed 0, 10, 30, or 37.5 mg Chlordecone/kg diet was impaired in terms of offspring and litter size (Huber, 1965, as reported in IPCS, 1984). No litters were produced by females fed 40 mg/kg, but litter production did resume within 7 weeks following withdrawal of the Chlordecone, although litters were still smaller than those of untreated controls (quoted from IPCS (1984)). Anovulation and persistent vaginal estrus were observed in female mice given Chlordecone at a dose level of 2 mg/kg bw/day (Swartz *et al.*, 1988, as quoted in US ATSDR, 1995), and similar changes were observed in female offspring of maternal rats given 15 mg/kg/day of Chlordecone on gestation days 14-20 (Gellert and Wilson, 1979, as

quoted in US ATSDR, 1995), although no effects on vaginal patency or fertility were observed in female offspring of maternal mice given 20 mg/kg/day during gestation days 8-12 or 14-18 (Gray and Kavlock 1984, as quoted in US ATSDR, 1995).

Toxicity of Chlordecone in humans

Available human data support the conclusion that Chlordecone has a similar toxicity profile in humans to that seen in experimental animal studies. As reported in US ATSDR (1995), a high incidence of nervous system toxicity was seen in a single group of workers exposed to Chlordecone during its manufacture (Cannon *et al.*, 1978; Martinez *et al.*, 1978; Sanbom *et al.*, 1979; Taylor 1982, 1985; Taylor *et al.*, 1978, taken from US ATSDR (1995)). Exposure of this population occurred by a combination of inhalation, oral, and dermal exposures, although the dermal route was suggested to be the predominant route. The toxicity was manifested as tremors, visual difficulties, muscle weakness, gait ataxia, incoordination, headache, and increased cerebrospinal fluid pressure (US ATSDR (1995)). Prolonged exposure to high concentrations of Chlordecone in the workplace has been suggested to cause oligospermia and decreased sperm motility among male workers, although fertility was not impaired (Guzelian 1982a; Taylor 1982, 1985; Taylor *et al.*, 1978, taken from US ATSDR (1995)). A correlation between blood levels, atmospheric levels and sperm effects has however been difficult to prove conclusively (US ATSDR (1995)). Epidemiological evidence for carcinogenicity of Chlordecone in exposed humans following inhalation exposure to Chlordecone is extremely limited (US ATSDR, 1995, IPCS, 1984). Liver biopsy samples taken from 12 workers with hepatomegaly resulting from intermediate- or chronic-duration exposures to high concentrations of Chlordecone showed no evidence of cancer (Guzelian *et al.*, 1980, taken from US ATSDR (1995)). However, conclusions from this study are limited by the very small number of workers sampled (US ATSDR, 1995).

Effects on endocrine systems

The effects of Chlordecone on reproduction indicate that this pesticide has effects on endocrine systems. It has been evaluated under the EU-Strategy for Endocrine Disrupters⁹ and has been placed in category 1 (evidence of endocrine-disrupting activity in at least one species using intact animals), in the priority list of chemicals established under the EU-Strategy. This categorisation is based on evidence of ED activity in a number of experimental systems including the mouse uterotrophic assay, increased uterine weight in rats given multiple injections of Chlordecone postnatally and receptor binding assays, indicative of an oestrogenic effect (as reported in BKH report, 2000, US ATSDR, 1995).

Conclusion on effects assessment and toxicity of Chlordecone

Chlordecone is readily absorbed into the body and accumulates following prolonged exposure. The pesticide is both acutely and chronically toxic, producing neurotoxicity, immunotoxicity, reproductive, musculoskeletal and liver toxicity at doses between 1 - 10 mg/kg bw/day in experimental animal studies. Liver cancer was induced in rats at a dose of 1 mg/kg body weight per day and in mice at a dose of 2.6 mg/kg bw/day, and reproductive effects are seen at similar dose levels. The International Agency for Research on Cancer has classified Chlordecone as a possible human carcinogen (IARC group 2B).

Table 2.3 summarises the outcomes of key toxicological studies on Chlordecone, including the NOAEL/LOAEL derived in each study. The studies included in this Table have been selected from the very large database on toxicological studies on Chlordecone, on the basis of the importance of the endpoint investigated (*e. g.* reproductive toxicity, carcinogenicity, other key target organ toxicity), robustness of the reported studies and the dose level (NOAEL/LOAEL) at which effects were reported. These studies were considered to be particularly relevant for characterisation of the toxicological risks of these compounds, and some of these studies have been used by US ATSDR to define Minimal Risk Levels (MRLs) for Chlordecone (US ATSDR, 1995).

Table 2.3 Summary of key toxicological studies on Chlordecone.

Species	Study type	Effect	LOAEL/NOAEL (mg/kg bw/day)	Reference
Rat Fischer 344	Short-term/acute toxicity 10 day repeat dose gavage study	65% loss in body weight, changes in clinical chemistry parameters	10 mg/kg bw/day (LOAEL) 5 mg/kg bw/day (NOAEL)	EPA, 1986 (as quoted in US ATSDR, 1995).
Rat Fischer 344	Short-term/acute toxicity 10 day repeat dose	Reductions in spleen and thymus weights, numbers of neutrophils, and natural killer cell activity, secondary to generalized toxicity	10 mg/kg bw/day (LOAEL) 5 mg/kg bw/day	EPA, 1986; Smialowicz <i>et al.</i> , 1985, (as quoted in US ATSDR, 1995).

⁹ http://europa.eu.int/comm/environment/endocrine/strategy/substances_en.htm

Species	Study type	Effect	LOAEL/NOAEL (mg/kg bw/day)	Reference
	gavage study		(NOAEL)	
Rat Fischer 344	Short-term/acute toxicity 10 day repeat dose gavage study	Increased startle response	2.5 mg/kg bw/day (LOAEL) 1.25 mg/kg bw/day (NOAEL)	EPA, 1986c (as quoted in US ATSDR, 1995).
Rat (Sherman)	3 month feeding study	Focal necrosis in liver, enlargement of the adrenal gland, hyperplasia and hypertrophy of cortical cells, tremor, hyperactivity, exaggerated startle response	1.17 mg/kg bw/day (LOAEL)	Cannon and Kimbrough 1979 (as quoted in IPCS, 1984 and US ATSDR, 1995).
Rat, Wistar	2 year feeding study	Renal effects (proteinuria and increased severity of glomerulosclerosis)	0.25 mg/kg bw/day. (LOAEL) 0.05 mg/kg bw/day (NOAEL)	Larson <i>et al.</i> , 1979b (as quoted in IPCS, 1984 and US ATSDR, 1995).
Rat Sprague-Dawley	21 month gavage study	Histopathological changes in liver, reduction in follicular size and colloid content and increase in epithelial cell height in thyroid	0.07 mg/kg bw/day (LOAEL), in males	Chu <i>et al.</i> , 1981(as quoted in IPCS, 1984 and US ATSDR, 1995).
Rat, Wistar	3 month feeding study	Testicular atrophy	0.5 mg/kg bw/day. (LOAEL) 0.25 mg/kg bw/day (NOAEL)	Larson <i>et al.</i> , 1979b (as quoted in IPCS, 1984 and US ATSDR, 1995).
Rat (Osborne-Mendel) and mouse (B3C6F1)	80 week feeding study	Hepatocellular adenoma and carcinoma	1.2 mg/kg bw/day. (LOAEL, rat) and 2.6 mg/kg bw/day (LOAEL, mouse)	NCI, 1976, Reuber, 1978, 1979(as quoted in IPCS, 1984 and US ATSDR, 1995).
Rat	Multiple injections of Chlordecone to neonatal rats	Uterotrophic response - uterine weights increased in a dose-related manner	10 mg/kg bw/day (LOAEL, Gellert, 1978) ≤ 6 mg/kg bw/day (LOAEL, Hammond <i>et al.</i> , 1979 ¹)	Gellert 1978 Hammond <i>et al.</i> , 1979 (as quoted in IPCS, 1984 and US ATSDR, 1995).
Rat, Hotzman strain, ovariectomized immature females	Rats injected x 3 with 0 - 45 mg/kg bw/day Chlordecone ± 0.01, 0.1, 1 or 10 mg/kg bw/day estradiol benzoate	Uterotrophic response. Effect was additive to that of estradiol benzoate over the dose range studied	Dose of 20 mg/kg bw/day Chlordecone appeared to be threshold for embryo implantation functions	Johnson, 1996
Rat	90-day feeding study	Decrease in sperm motility and viability, decreased sperm, decrease in the weight of seminal vesicles and prostate	0.83 mg/kg bw/day LOAEL for sperm effects 1.67 mg/kg bw/day LOAEL for effects on seminal vesicles and prostate	Linder <i>et al.</i> , 1983 (as quoted in IPCS, 1984 and US ATSDR, 1995).
Mouse, Balbc	130 day feeding study	8% decrease in litter size and 19% increase in pair-days to litter (constant oestrus)	1.3 mg/kg bw/day. (LOAEL)	Huber, 1965 (as quoted in IPCS, 1984 and US ATSDR, 1995).
Rats and mice	2, 6, and 10 mg/kg bw/day by gavage to rats and 2, 4, 8, and 12 mg/kg bw/day to mice on days 7 - 16 of gestation.	Reduced foetal weight, reduced degree of ossification, oedema, undescended testes, enlarged renal pelvis, and enlarged cerebral ventricles. Reductions in fetal weight and degree of ossification at lower dose levels. Maternal mortality at top dose. In the mouse, fetotoxicity was observed only at the highest dose level and consisted of increased fetal mortality and clubfoot.	2 mg/kg bw/day. (LOAEL, rat)	Chernoff & Rogers, 1976). (as quoted in IPCS, 1984 and US ATSDR, 1995).
Balbc mice	160 day feeding study	Increased ovulation, persistent oestrus	2 mg/kg bw/day. (LOAEL)	Swartz <i>et al.</i> , 1988 (as quoted in IPCS, 1984 and US ATSDR, 1995).
Rat	Reproductive toxicity	Increased ovulation, persistent oestrus in female offspring of maternal rats given Chlordecone on gestation days 14-20	15 mg/kg/day (LOAEL)	Gellert and Wilson, 1979, as quoted in US ATSDR, 1995)

Species	Study type	Effect	LOAEL/NOAEL (mg/kg bw/day)	Reference
Humans	Occupational exposure	Histories of tremors, unfounded nervousness or anxiety, and visual difficulties. Also skin rashes	Mean blood levels of Chlordecone in workers reporting adverse effects were 2.53 ppm Skin rashes reported in workers with blood Chlordecone levels in excess of 2 µg/L	Cannon <i>et al.</i> , 1978 (as quoted in IPCS, 1984 and US ATSDR, 1995).

2.4.2 Ecotoxicity

A summary of results of aquatic ecotoxicity tests with Chlordecone from the Ecotox database (US EPA, 2006) is given in Table 2.4.

In addition to this, the EHC 43 (IPCS, 1984), summarised a series of experiments investigating the bioavailability of Chlordecone, noting that it is strongly adsorbed on sediment. Exposure of aquatic organisms is therefore partly *via* the water phase and partly *via* sediment. D'Asaro & Wilkes (1982) examined the effects of sediments previously exposed to Chlordecone at a known concentration, and of James River sediments contaminated with Chlordecone, on an estuarine community established in aquaria supplied with non-filtered sea water. Mysid shrimps showed a dose-related mortality rate, when exposed to sediments previously equilibrated at 0.1, 1.0, or 10 µg Chlordecone/L. Mysids were not affected by James River sediment. Put concentration in sediments, if available Oysters showed dose-dependent reduced shell growth when exposed to Chlordecone-equilibrated sediments, and also responded adversely to river sediment. Lugworms *Arenicola cristata* died after 28 days of treatment with sediment exposed to 10 µg Chlordecone/L, though numbers were not affected by lower doses. Both lugworms and oysters concentrated Chlordecone from the sediment. (Quoted from EHC 43, (IPCS, 1984)).

Table 2.4 Summary of key ecotoxicological studies on Chlordecone.

Taxonomic group and species	End point	Duration	Result mg/L	Reference ¹
Algae <i>Chlorococcum sp.</i> , <i>Dunaliella tertiolecta</i> , <i>Nitzschia sp.</i> , <i>Thalassiosira pseudonana</i>	EC ₅₀ growth inhibition	7 days	0.35 - 0.60 (formulation)	Walsh <i>et al.</i> , 1977
Algae <i>Chlorococcum sp.</i> , <i>Dunaliella tertiolecta</i> , <i>Nitzschia sp.</i> , <i>Thalassiosira pseudonana</i>	EC ₅₀ growth inhibition	7 days	350 - 600 (formulation)	Hansen <i>et al.</i> , 1977
Crustaceans <i>Daphnia magna</i>	EC ₅₀ immobility	48 hours	0.120 - 0.690	Barera & Adams, 1983; Adams & Heidolph, 1985; Ziegenfuss <i>et al.</i> , 1986
Crustaceans <i>Americamysis bahia</i> , <i>Callinectes sapidus</i> , <i>Palaemonetes pugio</i>	LC ₅₀	96 hours	0.01 - 0.210	Nimmo <i>et al.</i> , 1977, 1981; Hansen <i>et al.</i> , 1977; Schimmel, 1977; US EPA, 1976
Crustacean <i>Daphnia magna</i>	NOEC reproduction	21 days	0.0283	McKee & Knowles, 1986
Crustacean <i>Daphnia magna</i>	NOEC growth	21 days	0.025	Adams & Heidolph, 1985
Crustacean <i>Americamysis bahia</i>	MATC growth	28 days	0.000026 - 0.00034	Nimmo <i>et al.</i> , 1981
Insect <i>Chironomus tentans</i>	LC ₅₀	48 hours	0.17 - 2.3	Adams <i>et al.</i> , 1985; Ziegenfuss <i>et al.</i> , 1986
Fish 9 species	LC ₅₀	96 hours, flow through	0.0066 - 0.512	Roberts & Bendl, 1982; Roberts & Fisher, 1985; Schimmel, 1977; Hansen <i>et al.</i> , 1977; Mallat & Barron, 1988; Buckler <i>et al.</i> , 1981
Insect <i>Chironomus tentans</i>	NOEC development	14 days	17.9 mg/kg sediment	Adams <i>et al.</i> , 1985

¹: All are as quoted in Ecotox, US EPA 2006

In a publication from SETAC a collation of critical tissue residues (CTR) was presented and evaluated (Jarvinen *et. al.*, 1999). The database contains 32 entries for Chlordecone, with data originating from different studies (see Table 2.5). Some of the tissue residues were from studies where no effects were observed, so they may not represent the real CTR. Critical tissue residue values obtained in studies where effects were identified represent 15 CTR values for three fish species. For fathead minnow two studies are available with values of 1.7 and of 3.8-5.4 mg/kg ww. For sheepshead minnow 12 CTRs are available, ranging from 0.13 to 17 mg/kg ww with an average of 5.9 mg/kg ww. Furthermore, one CTR of 2.7 mg/kg ww for spot is available.

Conclusion

In summary, Chlordecone is very toxic to aquatic organisms. The most sensitive group is the invertebrates, which is not surprising for a substance with insecticidal properties. Even if the lowest effect concentration (0.000026 mg/L) was considered to be an outlier, the lowest effect concentrations would be well below 1 mg/L with the results of short term tests (mortality) in the range of 0.01 to 0.69 mg/L and those of long term tests (reproduction and growth) at 0.0025 and 0.0028 mg/L.

Table 2.5 Collation of critical tissue residues (CTR)

Species	Life Stage	Exprte	Expo of Concentration	Results □g/g (wet)	effect
Cladoceran, Daphnia magna (Fw)	1st instar	Water	175 ng/L	0.133	Survival, Reproduction - No effect
Grass shrimp, Palaemonetes pugio (Sw)	0.09g	Water, Diet	0.04 µg/L; 0.118 µg/g (wet wt)	0.147	Growth - No effect
Blue crab, Callinectes sapidus (Sw)	Juvenile	Diet	2.26 - 2.50 µg/g (wet wt)	2.54 - 4.61	Survival, Growth - No effect
Fathead minnow, Pimephales promelas (Fw)	Larvae-Adult	Water	3.1 µg/L	3.8 - 5.4	Survival, Growth - Reduced
Fathead minnow, Pimephales promelas (Fw)	Larvae-Adult	Water	1.2 µg/L	2.6	Survival, Growth - No effect
Fathead minnow, Pimephales promelas (Fw)	Embryo, 2nd generation	Water, Adult fish	0.31 µg/L; 0.21-0.38 µg/g	1.7	Survival (hatchability) - Reduced
Fathead minnow, Pimephales promelas (Fw)	Embryo, 2nd generation	Water, Adult fish	0.17 µg/L; 0.17-0.46 µg/g	0.26	Survival - No effect
Fathead minnow, Pimephales promelas (Fw)	Larvae, 2nd generation	Water, Adult fish	0.31 µg/L; 0.21 - 0.38 µg/g	0.50	Survival, Growth - No effect
Sheepshead minnow, Cyprinodon variegatus (Sw)	Adult	Water	0.8 µg/L	2.5 - 3.6	Survival - Reduced 22%
Sheepshead minnow, Cyprinodon variegatus (Sw)	Adult	Water	1.9 µg/L	11 - 12	Survival - Reduced 80%
Sheepshead minnow, Cyprinodon variegatus (Sw)	Adult	Water	7.8 µg/L	17	Survival - Reduced 100%
Sheepshead minnow, Cyprinodon variegatus (Sw)	Adult	Water	0.16 µg/L	0.65 - 0.90	Survival - No effect
Sheepshead minnow, Cyprinodon variegatus (Sw)	Embryo	Adult fish	11-12 µg/g	11	Survival - Reduced 25%
Sheepshead minnow, Cyprinodon variegatus (Sw)	Embryo	Adult fish	2.5 - 3.6 µg/g	4.7	Survival - No effect
Sheepshead minnow, Cyprinodon variegatus (Sw)	Larvae-Juvenile	Water, Adult fish	1.9 µg/L; 11-12 µg/g	8.4	Survival - Reduced 63%
Sheepshead minnow, Cyprinodon variegatus (Sw)	Larvae-Juvenile	Water	2.0 µg/L	7.8	Survival - Reduced 40%

Species	Life Stage	Exprte	Expo of Concentration	Results $\mu\text{g/g}$ (wet)	effect
Sheepshead minnow, <i>Cyprinodon variegatus</i> (Sw)	Larvae-Juvenile	Water	0.8 $\mu\text{g/L}$	2.0	Survival - No effect
Sheepshead minnow, <i>Cyprinodon variegatus</i> (Sw)	Larvae-Juvenile	Adult fish	11-12 $\mu\text{g/g}$	0.13	Growth - Reduced
Sheepshead minnow, <i>Cyprinodon variegatus</i> (Sw)	Larvae-Juvenile	Water	0.08 $\mu\text{g/L}$	1.1	Growth - Reduced
Sheepshead minnow, <i>Cyprinodon variegatus</i> (Sw)	Embryo-Adult	Water	0.78 $\mu\text{g/L}$	5, 6.8*	Survival - No effect
Sheepshead minnow, <i>Cyprinodon variegatus</i> (Sw)	Embryo-Adult	Water	0.39 $\mu\text{g/L}$	2.2, 3*	Growth - Reduced
Sheepshead minnow, <i>Cyprinodon variegatus</i> (Sw)	Embryo-Adult	Water	0.12 $\mu\text{g/L}$	0.86, 1.2*	Growth - No effect
Sheepshead minnow, <i>Cyprinodon variegatus</i> (Sw)	Embryo-Adult	Water	0.78 $\mu\text{g/L}$	5, 6.8*	Reproduction - Reduced
Sheepshead minnow, <i>Cyprinodon variegatus</i> (Sw)	Embryo-Adult	Water	0.39 $\mu\text{g/L}$	2.2, 3*	Reproduction - No effect
Sheepshead minnow, <i>Cyprinodon variegatus</i> (Sw)	Embryo, 2nd generation	Adult Fish + Water	0.78 $\mu\text{g/L}$	2.3	Survival - Reduced
Sheepshead minnow, <i>Cyprinodon variegatus</i> (Sw)	Embryo, 2nd generation	Adult Fish + Water	0.39 $\mu\text{g/L}$	1.3	Survival - No effect
Sheepshead minnow, <i>Cyprinodon variegatus</i> (Sw)	Fry, 2nd generation	Adult Fish + Water	0.78 $\mu\text{g/L}$	2.3	Survival - No effect
Sheepshead minnow, <i>Cyprinodon variegatus</i> (Sw)	Fry, 2nd generation	Adult Fish + Water	0.12 $\mu\text{g/L}$	0.41	Growth - Reduced
Sheepshead minnow, <i>Cyprinodon variegatus</i> (Sw)	Fry, 2nd generation	Adult Fish + Water	0.074 $\mu\text{g/L}$	0.30	Growth - No effect
Spot, <i>Leiostomus xanthurus</i> (Sw)	Juvenile	Diet	3.3 $\mu\text{g/g}$ (wet wt)	2.7	Survival - Reduced
Spot, <i>Leiostomus xanthurus</i> (Sw)	Juvenile	Diet	3.3 $\mu\text{g/g}$ (wet wt)	0.7	Survival - No effect
Spot, <i>Leiostomus xanthurus</i> (Sw)	Juvenile	Water, Diet	0.04 $\mu\text{g/L}$; 0.101 $\mu\text{g/g}$ (wet wt)	0.144	Growth, No effect

3 Synthesis of the information

Chlordecone is a synthetic chlorinated organic compound, which has mainly been used as an agricultural pesticide. It is closely related chemically to Mirex, a pesticide which is already listed in Annex A of the Stockholm Convention. Chlordecone is already listed in Annex I of the UNECE Protocol on POPs.

According to available data, Chlordecone can be considered to be highly persistent in the environment. Chlordecone is not expected to hydrolyse or biodegrade in aquatic environments, nor in soil. Direct photodegradation is not significant. Chlordecone does not volatilise to any significant extent.

With BCF-values in algae up to 6,000, in invertebrates up to 21,600 and in fish up to 60,200 and documented examples of biomagnification, Chlordecone is considered to have a high potential for bioaccumulation and biomagnification.

Concerning the potential for causing adverse effects, there is a convincing set of data. Chlordecone is readily absorbed into the body and accumulates following prolonged exposure. It is both acutely and chronically toxic, producing neurotoxicity, immunotoxicity, reproductive, musculoskeletal and liver toxicity at doses between 1 - 10 mg/kg bw/day in experimental animal studies. Liver cancer was induced in rats at a dose of 1 mg/kg body weight per day, and reproductive effects are seen at similar dose levels. The International Agency for Research on Cancer has classified Chlordecone as a possible human carcinogen (IARC group 2B). Moreover, Chlordecone is very toxic to aquatic organisms, most sensitive group being the invertebrates.

The available data on Chlordecone are not fully conclusive when it comes to long-range atmospheric transport in gaseous form. It should be noted that atmospheric transport of particle-bound substances and transport of sediment particles in ocean currents as well as biotic transport could also contribute to long-range environmental transport of Chlordecone.

Due to lack of monitoring data on Chlordecone, the assessment of the potential for long-range transport of Chlordecone is based on physico-chemical properties and especially, on modelling data. While the first of these two approaches may seem somehow insufficient, the modelling data state clearly Chlordecone's LRET potential.

Based on the available data, Chlordecone should be considered as a POP warranting global action.

Production and use of Chlordecone has ceased over the last decades in developed countries, but it is assumed that it can still be produced or used as an agricultural pesticide in some developing countries. If it is still used as pesticide, it will be directly released to the environment. Moreover, the high persistency of the substance has caused high contamination of soil and waters in the areas where it has been used and these contaminated sites can serve as a source of pollution for long times.

4 Concluding statement

It has been demonstrated that Chlordecone meets all the criteria laid down in Annex D of the Stockholm Convention. Moreover, it is chemically very similar to Mirex, an organochlorine pesticide which is already listed in the Stockholm Convention. It is very persistent in the environment and has a great potential for bioaccumulation and in addition there is clear evidence of its biomagnification. While there is no monitoring data from areas remote from sources, the physical and chemical properties, as well as the modelling results, suggest that Chlordecone can be transported long distances bound to particles in air and water, and possibly through coupled transport between these two compartments. Chlordecone is associated with a wide range of harmful effects on both mammals and aquatic organisms.

As Chlordecone can travel in the atmosphere far from its sources, neither a single country nor group of countries alone can abate the pollution caused by this substance. Regional action has already been considered necessary and Chlordecone is totally banned under the UNECE Convention on Long-range Transboundary Air Pollution Protocol on Persistent Organic Pollutants. Although the production and use of Chlordecone seems to be ceased in most countries, its reintroduction remains possible. This could lead to increased releases and levels in the environment.

Based on the available evidence, Chlordecone is likely as a result of its long-range environmental transport to lead to significant adverse human health and environmental effects such that global action is warranted.

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ヘキサブロモビフェニルの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
<p>【生分解性】 分解度 4% (OECD TG 301C)</p> <p>【光分解性】 大気中における分解及び変化は、OHラジカルによる光酸化と光分解である。OHラジカルとの反応による推定半減期は182日。</p> <p>【半減期】 ・水中:2ヵ月を超える ・土壌及び底質中:6ヵ月を超える</p>	<p>【BCF(経口的生物濃縮係数)】 ・ファットヘッドミノール:BCF=18100(32日間暴露) ・ファットヘッドミノールの身:BCF=10000 ・コイ:BCF=4700-16000(重量ベース。60日間暴露)</p> <p>【BMF(経口的生物濃縮係数)】 ・餌(ニシン)と捕食者(ハルトアザラシ)を較べた食物連鎖:BMF=175(脂質ベース)(PCBと同レベルの値) ・ホッキョクグマ中の濃度がグリーンランド東部のワモンアザラシの約100倍</p>	<p>【反復投与毒性】 ラット(混餌7ヶ月):0.45mg/kg/dayで血清中T4濃度低下</p> <p>ラット(混餌30日):LOAEL 0.05mg/kg/day 甲状腺ろ胞数・ろ胞容積増加、血清中T3、T4濃度低下</p> <p>アカゲザル(混餌25~50週):LOAEL 0.73mg/kg/day 主な毒性は、体重低下、潰瘍性大腸炎、脱毛、肝臓の変化等</p> <p>【発がん性】 マウス(妊娠0日~生後56日): NOAEL 0.15mg/kg/day 児の肝細胞がん IARCグループ2B(possibly carcinogenic to human)</p> <p>【生殖毒性】 ラット(妊娠0日~14日) 28.6mg/kg/dayで未着床、新生児生存率低値</p> <p>アカゲザル:LOAEL 0.012mg/kg/day 主な毒性は、月経周期遅延、流産、死産等</p>	<p>【慢性毒性】 ニジマス <i>Oncorhynchus mykiss</i> :ELS 試験 LD50=3.910 mg/kg</p>

		<p>【その他】 汚染事故で吐き気、腹痛、食欲減退、 関節痛、倦怠感、皮膚障害、 EU-Strategy for Endocrine Disruptors 優先化学物質(無処置動物の少なくとも も一種類において内分泌かく乱活性を 示す科学的根拠がある)に分類</p>	
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**Stockholm Convention on Persistent Organic Pollutants
Persistent Organic Pollutants Review Committee
Second meeting
Geneva, 6–10 November 2006**

Report of the Persistent Organic Pollutants Review Committee on the work of its second meeting

Addendum

Risk profile on hexabromobiphenyl

At its second meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on hexabromobiphenyl, on the basis of the draft contained in document UNEP/POPS/POPRC.2/9. The text of the risk profile, as amended, is provided below. It has not been formally edited.

HEXABROMOBIPHENYL

RISK PROFILE

Adopted by the Persistent Organic Pollutants Review Committee
at its second meeting

November 2006

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EXECUTIVE SUMMARY

The European Community and its Member States being Parties to the Stockholm Convention have proposed hexabromobiphenyl to be listed in the Convention. The Persistent Organic Pollutants Review Committee concluded in its meeting in November 2005 that the substance comply with the screening criteria set out in Annex D of the Convention and that a draft risk profile should be prepared to review the proposal further.

Hexabromobiphenyl belongs to a wider group of polybrominated biphenyls (PBBs). The term "polybrominated biphenyls" or "polybromobiphenyls" refers to a group of brominated hydrocarbons formed by substituting hydrogen with bromine in biphenyl. The hexabromo congeners exist as 42 possible isomeric forms. According to the available data, production and use of hexabromobiphenyl has ceased in most, if not all, countries. However, it is possible that hexabromobiphenyl is still being produced in some countries.

Hexabromobiphenyl has been used as a fire retardant in acrylonitrile-butadiene-styrene (ABS) thermoplastics for constructing business, machine housings and in industrial and electrical products and in polyurethane foam for auto upholstery. A considerable part of the substance produced will probably reach the environment sooner or later because of the high stability of these compounds.

According to available data, hexabromobiphenyl can be considered to be highly persistent in the environment. There is evidence of low or no degradation in water, soil and sediment, in the laboratory as well as in the field.

Hexabromobiphenyl is less volatile than many of the currently listed POP substances. However, extensive data on monitoring shows that it is found throughout the Arctic wildlife, demonstrating that it does have a high potential for long range environmental transport.

With measured weight-based BCF values in the range 4,700-18,100 and biomagnification factors in the aquatic food chain exceeding 100, hexabromobiphenyl is considered to be highly bioaccumulative and to have a high potential for biomagnification. These properties are demonstrated by several authors to be comparable to those of hexachlorobiphenyl (a PCB compound), for which the bioaccumulative properties are well documented.

Hexabromobiphenyl is readily absorbed into the body and accumulates following prolonged exposure. Although the acute toxicity of hexabromobiphenyl is low, a number of chronic toxic effects including hepatotoxicity have been observed in experimental animals at doses around 1 mg/kg bw/day following long-term exposure, and effects are seen in the rat thyroid at doses as low as 0.05 mg/kg bw/day. The International Agency for Research on Cancer has classified hexabromobiphenyl as a possible human carcinogen (IARC group 2B). The PBBs are endocrine disrupting chemicals, and effects are seen on reproductive capacity in rats, mink and monkeys. There is epidemiological evidence of hypothyroidism in workers exposed to polybrominated biphenyls and of increased incidence of breast cancer in exposed women. Data on toxicity to other species than laboratory mammals is scarce but suggests the environmental toxicity of hexabromobiphenyl is comparable to that of hexachlorobiphenyl.

Based on the available data, hexabromobiphenyl is likely, as result of its long-range environmental transport, to lead to significant adverse human health and environmental effects, such that global action is warranted.

1 INTRODUCTION

The European Community and its Member States being Parties to the Stockholm Convention have proposed hexabromobiphenyl to be listed in Annex A to the Convention. The original proposal is contained in document UNEP/POPS/POPRC.1/7.

The acceptance of the original proposal for further consideration by the Persistent Organic Pollutants Review Committee implies that the properties of the substance comply with the screening criteria set out in Annex D of the Convention. Therefore, the screening criteria are not discussed in this document. This draft risk profile has been prepared following the decision of the Committee, at its first meeting in November 2005, to establish an ad hoc working group to review the proposal further.

In this document all data are presented according to the International System of Units (SI) and, therefore, many have been recalculated from other units in the data sources. Furthermore, all concentrations are presented based on kg or L (*e. g.* µg/kg or mL/L).

1.1 Chemical Identity of the proposed substance

1.1.1 Names and registry numbers

Hexabromobiphenyl belongs to a wider group of polybrominated biphenyls (PBBs). The term “polybrominated biphenyls” or “polybromobiphenyls” refers to a group of brominated hydrocarbons formed by substituting hydrogen with bromine in biphenyl. The hexabromo congeners exist as 42 possible isomeric forms, which are listed with CAS and IUPAC numbers in US ATSDR (2004) and in document INF 2.

CAS chemical name: Hexabromo -1,1'-biphenyl

Synonyms: Hexabromobiphenyl
Biphenyl, hexabromo
1,1'- biphenyl, hexabromo -
HBB

Trade names: FireMaster^(R) BP-6
FireMaster^(R) FF-1

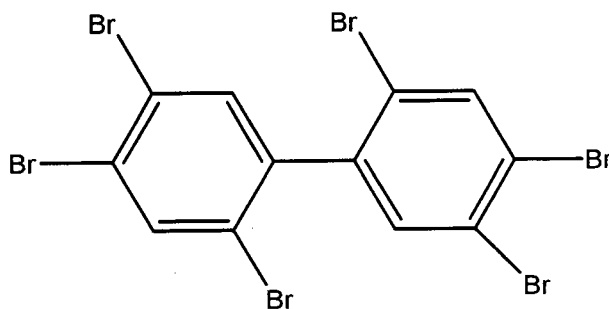
Technical grade PBBs (FireMaster^(R)) contain several PBB compounds, isomers and congeners, hexabromobiphenyl being one of the main components. The composition of FireMaster^(R) BP-6 changes from batch to batch, but its main constituents are 2,2',4,4',5,5'-hexabromobiphenyl (60-80%), and 2,2',3,4,4',5,5'-heptabromobiphenyl (12-25%) together with lower brominated compounds. Mixed bromochlorobiphenyls and polybrominated naphthalenes have also been observed as minor components of FireMaster^(R) (EHC 152 (IPCS, 1994)). FireMaster FF-1 (white powder) is FireMaster BP-6 (brown flakes) to which 2% calcium silicate has been added as an anti-caking agent (EHC 152 (IPCS, 1994)).

Additional data on the composition of identified PBB congeners in FireMaster^(R) BP-6 and FireMaster^(R) FF-1 is given in US ATSDR (2004).

CAS registry number: 36355-01-8¹ (Common CAS number for hexabromobiphenyl isomers)
 59536-65-1 (EHC 192 (IPCS, 1997))²
 67774-32-7 (EHC 192 (IPCS, 1997))³

US ATSDR (2004) provides CAS numbers for a wider number of individual hexabromobiphenyl isomers, as shown in Annex B.

1.1.2 Structure



Structure of 2,2',4,4',5,5'- hexabromobiphenyl (CAS No. 59080-40-9, PBB congener No. 153).
 (Structural formula source: EHC 192 (IPCS, 1997))

1.1.3 Physical chemical properties

The physical and chemical properties of hexabromobiphenyl are listed in Table 1.1.

Table 1.1 Physical and chemical properties of hexabromobiphenyl.

Property	Unit	Value	Reference
Molecular formula'		C ₁₂ H ₄ Br ₆	
Molecular weight'	g/mol	627.58	
Appearance at normal temperature and pressure		White solid	a)
Vapour Pressure	Pa	6.9x10 ⁻⁶ (25° C) 7.5x10 ⁻⁴ (liquid, sub-cooled)	Jacobs <i>et. al.</i> , (1976) ^{a)} Tittlemier <i>et. al.</i> , (2002) ^{a)}
Water solubility	µg/L	11 3	a) Tittlemier <i>et. al.</i> , (2002) ^{a)}
Melting point	°C	72° C	a)
Boiling point		No data	
Log K _{OW}		6.39	Doucette & Andren (1988) ^{a)}
Log K _{OC}		3.33-3.87	Calculated ^{a)}
Henry's Law Constant	Pa m ³ /mol	3.95x10 ⁻¹ 1.40x10 ⁻¹	Waritz <i>et. al.</i> , 1977 ^{a)} Calculated ^{a)}

a): Quoted from US ATSDR, 2004

¹ The CAS registry number 36355-01-8 is given as a generic CAS number for PBBs in the 1988 EU Export-Import Regulation and the UNEP Rotterdam Convention.

² US ATSDR refers to Firemaster^(R) BP-6 as CAS No. 59536-65-1.

³ US ATSDR refers to FireMaster^(R) FF-1 as CAS No. 67774-32-7.

Some of the data for the properties listed in Table 1.1 may not be reliable because products of questionable purity were used by earlier investigators to derive them. Therefore, recent physical and chemical property data that have been reported for hexabromobiphenyl in Tittlemier *et. al.*, (2002) (Quoted from US ATSDR, 2004) are included in Table 1.1.

1.2 Conclusion of the Persistent Organic Pollutants Review Committee on the Annex D information on Hexabromobiphenyl

The POP Review Committee applied at its first meeting on 7–11 November 2005⁴ the screening criteria specified in Annex D to the Stockholm Convention, and decided, in accordance with paragraph 4 (a) of Article 8 of the Convention, that it was satisfied that the screening criteria were fulfilled for hexabromobiphenyl. The Committee decided furthermore, in accordance with paragraph 6 of Article 8 of the Convention and paragraph 29 of decision SC-1/7 of the Conference of the Parties to the Stockholm Convention, to establish an ad hoc working group to review the proposal further and to prepare a draft risk profile in accordance with Annex E to the Convention. It invited, in accordance with paragraph 4 (a) of Article 8 of the Convention, Parties and observers to submit to the Secretariat the information specified in Annex E of the Convention before 27 January 2006.

1.3 Data sources

This Draft Risk Profile is mainly based on information from the following review reports:

- Environmental Health Criteria (EHC) 152: Polybrominated biphenyls. IPCS International Programme on Chemical Safety. United Nations Environment Programme. International Labour Organisation. World Health Organization. Geneva 1994. Available at: <http://www.inchem.org/documents/ehc/ehc/ehc152.htm>.
- Environmental Health Criteria (EHC) 192: Flame Retardants: A General Introduction. IPCS International Programme on Chemical Safety. United Nations Environment Programme. International Labour Organisation. World Health Organization. Geneva 1994. Available at: <http://www.inchem.org/documents/ehc/ehc/ehc192.htm>.
- US ATSDR Toxicological Profile for Polybrominated Biphenyls and Polybrominated Diphenyl Ethers (PBBs and PBDEs). 2004. Available at: <http://www.atsdr.cdc.gov/toxprofiles/tp68.html>

Where the reviews mentioned above have been cited, the text quoted (or quoted with modifications) includes the references cited in the original review. These references are not shown individually in the reference list.

Following the request of the POP Review Committee for additional information, as specified in Annex E of the Convention, information on hexabromobiphenyl was provided by several Parties and observers. This information was mainly based on the open literature or focused on PBDEs.

A search for more recent information included a literature search via the Danish Technical University Library and the data base FINDit (search terms: HBB, hexabromobiphenyl, brominated biphenyls) as well as a data base search in public data bases. The data bases include “Ecotox” (US-EPA, at <http://www.epa.gov/ecotox/>), “NITE” (Japan, National Institute of Technology and Evaluation at <http://www.safe.nite.go.jp/english/db.html>), BUA Reports at <http://www.gdch.de/taetigkeiten/bua/berichte.htm> and Environmental Fate Data Base at <http://esc.syrres.com/efdb.htm>. This search was based on the search terms: hexabromobiphenyl and CAS numbers 77607091, 36355018, 82865892, 82865905, 59261084, 84303479, 120991482,

⁴ See the meeting report at: www.pops.int/documents/meetings/poprc

82865916, 67888997, 84303480, and 60044260. In addition, the Arctic Monitoring and Assessment Programme⁵ was consulted.

1.4 Status of the chemical under international conventions

Hexabromobiphenyl is listed in Annex A of the Protocol to the Convention on Long-range Transboundary Air Pollution (CLRTAP) on Persistent Organic Pollutants. The provisions of the Protocol oblige Parties (currently 25) to phase out all production and uses of hexabromobiphenyl. Hexabromobiphenyl, together with other PBBs, is also included in the UNEP/FAO Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade.

2 SUMMARY INFORMATION RELEVANT FOR THE RISK PROFILE

2.1 Sources

2.1.1 Production

The commercial production of polybrominated biphenyls (PBBs) generally involves bromination of biphenyl, a process involving a much more specific reaction and producing a smaller number of product mixtures than chlorination (Sundstrom *et al.*, 1976a) (Quoted from US ATSDR, 2004).

The process of manufacturing PBBs consists of a Friedel-Crafts type reaction in which biphenyl is reacted with bromine in the presence of chloride in an organic solvent, using aluminium chloride, aluminium bromide, or iron as catalyst (Brinkman & de Kok, 1980) (Quoted from EHC 152 (IPCS, 1994)).

2.1.2 Trade and stockpiles

The commercial production of PBBs began in 1970. Approximately 6 million kg of PBBs were produced in the United States from 1970 to 1976. Only three commercial PBB products were manufactured (*i. e.* hexabromobiphenyl, octabromobiphenyl, and decabromobiphenyl) and these three products were based on a limited number of congeners (Hardy, 2002b). Hexabromobiphenyl constituted about 5.4 million kg (ca 88%) and octa- and decabromobiphenyl constituted ≈ 0.68 million kg together of this total (Neufeld *et al.*, 1977). Michigan Chemical Corporation, St. Louis, Michigan, the sole producer of hexabromobiphenyl in the United States, stopped producing this PBB in 1975. (Quoted from US ATSDR, 2004). Subsequent production of PBBs appears to have been limited to the octa- and decabromobiphenyls.

Production of octa- and decabromobiphenyl continued in the United States until 1979 (IARC 1986; Neufeld *et al.*, 1977). Shortly after the 1973–1974 agriculture contamination accident in Michigan, PBB production in the United States was voluntarily discontinued (Hardy 2000); PBBs are no longer produced in the United States (SRI 2001). Re-initiation of manufacture of PBBs would require approval from the EPA. (Quoted from US ATSDR, 2004)

Two UK companies are reported to have marketed or produced technical-grade decabromobiphenyl in the United Kingdom. In 1977, the production of PBBs in the UK was discontinued. Highly brominated PBBs (Bromkal, 80-9D) were produced in Germany until mid-1985, when the activities concerning bromine-based fire retardants were shifted to the USA. No domestic producer has been identified in the Netherlands. In the early nineties, an Israeli company with two bromine plants in the Netherlands denied the production of PBBs. (Modified from EHC 152 (IPCS, 1994)). There is no information available regarding possible use and production of hexabromobiphenyl in Russia.

⁵ See <http://www.amap.no/>

Until the year 2000, the only PBB in commercial production was decabromobiphenyl, which was manufactured by one company (Atochem) in France (Hardy, 2000). (Modified from US ATSDR, 2004) An author (Darnerud, 2003) has stated that with the closure of the decaBB production in France, the PBB production in the world has ceased.

In the United States, PBBs are not known to be imported or exported anymore except possibly in small quantities for laboratory uses. PBBs have not been imported from other countries into the United States, except in finished products (Neufeld *et al.*, 1977). The two companies that manufactured octa- and decabromobiphenyl in the United States between 1976 (0.805 million pounds) and 1978 exported all of their products to Europe (Neufeld *et al.*, 1977) (Quoted from US ATSDR, 2004).

EXIDIM, the European Database on the Export Import of Dangerous Chemicals under the Rotterdam Convention has registered a total of 6 export applications for PBBs (which do not however include hexabromobiphenyl) in the years 2003–2006 (1 in 2003 and 2004, 2 each in 2005 and 2006). No imports of PBBs to the European Unions are registered in this period.

Information received by 27 January 2006 as a result of the request for information from Stockholm Convention Parties and observers, included response from Brazil, Australia, Japan, Republic of Lebanon and the USA, all stating that there is no production or use of hexabromobiphenyl in these countries.

In summary, according to the information available, production and use of hexabromobiphenyl has ceased in most, if not all, countries. However, it is possible that hexabromobiphenyl is still being produced in some developing countries or in countries with economies in transition.

2.1.3 Uses

In the United States and Canada, hexabromobiphenyl (FireMaster^(R)) was the principal PBB product. It was used as a fire retardant in three main commercial products: acrylonitrile-butadiene-styrene (ABS) thermoplastics for constructing business machine housings and in industrial (e.g. motor housing), and electrical (e.g. radio and TV parts) products: as a fire retardant in coatings and lacquers, and in polyurethane foam for auto upholstery (Neufeld *et al.*, 1977) (Modified from EHC 152 (IPCS, 1994) and US ATSDR, 2004).

Approximately 5 million tonnes of HBB were produced in the USA from 1970 to 1976; 98 per cent was used as FireMaster BP-6 and the rest as FireMaster FF-1 (Hesse and Powers, 1978). Of the estimated 2,200 tonnes hexabromobiphenyl produced in 1974 (IARC, 1978), about 900 tonnes (Mumma & Wallace, 1975; Neufeld *et al.*, 1977; IARC, 1978) were used in ABS plastic products and an even larger amount in cable coatings (Mumma & Wallace, 1975; Neufeld *et al.*, 1977; IARC, 1978). The exact quantity of FireMaster^(R) used in polyurethane foam for automobile upholstery was not published. The two larger consumers ceased using hexabromobiphenyl (one of these in 1972) because PBBs did not decompose in the ultimate incineration of scrapped automobiles (Neufeld *et al.*, 1977) (Quoted from EHC 152 (IPCS, 1994)).

In the EHC 152 (IPCS, 1994), it is stated that at the time, no users of hexabromobiphenyl had been identified (Neufeld *et al.*, 1977; Di Carlo *et al.*, 1978; Brinkman & de Kok, 1980) (Quoted from EHC 152 (IPCS, 1994)).

2.1.4 Releases to the environment

Data for loss into the environment during normal production are published only for the United States. The following information refers to reviews by Neufeld *et al.*, (1977) and Di Carlo *et al.* (1978). Losses of PBBs to the environment at sites of its manufacture can amount to 51 kg/1000 kg of product. These losses occur through:

1) *Emission into the air:*

In 1977, the maximum air losses as particulate matter at production sites were estimated to total 1.1 kg of PBBs/1000 kg manufactured.

2) *Losses in waste waters* resulting from the quenching and washing of the PBBs as they were recovered from the reaction mass. The losses of PBBs to sewers at manufacturing sites were estimated, in 1977, to be 4.6 µg/kg of product.3) *Solid losses to landfills* resulting from drying, handling, shipping and transportation. An estimate of PBB losses as solid waste to landfills was 50 g/kg of product.4) *Losses to the soil*

Soil samples from the bagging and loading areas of the Michigan Chemical Corp. contained PBBs at concentrations of 3500 and 2500 mg/kg, respectively.

(Abbreviated from EHC 152 (IPCS, 1994))

In 1973, an accidental release of PBBs occurred in Michigan (referred to as the "Michigan disaster" in EHC 152), when two products manufactured by the Michigan Chemical Company were inadvertently confused and 250-500 kg (Di Carlo *et al.*, 1978) of FireMaster^(R), instead of NutriMaster^(R), a magnesium oxide-based cattle feed supplement, were added to animal feed and distributed to farms within the state. The compound is believed to have been FireMaster^(R) FF-1 (*e. g.*, Fries, 1985b), even if in some publications the name FireMaster^(R) BP-6 is used (*e. g.*, Neufeld *et al.*, 1977; Di Carlo *et al.*, 1978). This accidental mix up resulted in widespread contamination by PBBs. Chronological reports or reviews of the PBB disaster are given by Carter (1976), Getty *et al.* (1977), Kay (1977), Di Carlo *et al.*, (1978), Damstra *et al.*, (1982), Zabik (1982), and Fries (1985b) (Quoted from EHC 152 (IPCS, 1994)).

Approximately 5350 tonnes of hexabromobiphenyl were used in commercial and consumer products in the United States, most in the production of plastic products with an estimated use life of 5–10 years (Neufeld *et al.*, 1977). Since the cessation of production, all of these products, such as TV cabinet and business machine housings, are expected to have been disposed of by land filling or incineration (Neufeld *et al.*, 1977) (Quoted from US ATSDR, 2004).

Hexabromobiphenyl can enter the environment from the widespread use of flame-retarded products. A considerable part of the substance produced will probably reach the environment sooner or later because of the high stability of these compounds. Furthermore, some of these chemicals may form toxic polybrominated dibenzofurans during combustion processes.

2.2 Environmental fate

2.2.1 Persistence

The EHC review (1994), concludes that polybrominated biphenyls are stable and persistent in the environment. The degradation of PBBs by purely abiotic chemical reactions (excluding photochemical reactions) is considered unlikely.

In air, the two processes that may result in significant degradation or transformation of PBBs are photo-oxidation by hydroxyl (OH) radicals and direct photolysis. Based on a structure-activity relationship for the estimation of half-lives for the gas phase reactions of hydroxyl radicals with organic compounds (Atkinson 1987b), the estimated half-life of hexabromobiphenyl due to reaction with OH radicals is 182 days. The importance of the photochemical reaction under sunlight illumination conditions for the degradation/transformation of PBBs in air cannot be evaluated due to the lack of information. (Abbreviated from US ATSDR, 2004)

The EHC 152 (IPCS, 1994) refers to laboratory experiments in methanol, showing rapid photodegradation of 2,2',4,4',5,5'-hexabromobiphenyl (90% degradation after 9 minutes) and resulting in mainly lower brominated PBBs. However, in the US ATSDR (2004), it is questioned whether this photolysis could take place in water due to the lack of active groups. Therefore it is questionable whether hexabromobiphenyl can be degraded rapidly in air.

Biodegradation in water under aerobic conditions is low, although the lower substituted biphenyls might biodegrade in aerobic water and sediment (Kong and Sayler, 1983; Sugiura, 1992; Yagi, and Sudo, 1980), the higher substituted biphenyls are resistant to aerobic biodegradation (Kawasaki, 1980; Sasaki, 1978; Shelton and Tiedje, 1981) (quoted from US ATSDR, 2004). This is further supported by the measurement (by GC) of negligible biodegradation of hexabromobiphenyl in a four week ready biodegradability test (OECD TG 301C), resulting in 4% reduction in total concentration as measured by GC (Governmental Japanese database NITE, 2006) resulting in an extrapolated half-life in water >2 months.

Under anaerobic conditions, it has been shown that microorganisms in river sediments obtained from populated areas can biodegrade higher substituted PBBs, including FireMaster mixtures (Morris *et al.* 1992) to form lower brominated products (quoted from US ATSDR, 2004). However, the potential of sediment microflora from remote areas has not been investigated, so it cannot be evaluated whether anaerobic debromination may be a considerable cause for degradation under anaerobic conditions.

PBBs have been reported to be persistent under field conditions. The information on the fate of PBBs in soil is limited. Soil samples from a former PBB manufacturing site, analysed several years after accidental release, still contained PBBs. However, the congener composition differed from the original PBB mixture, indicating partial degradation of the PBB residue in the soil samples. According to the 1994 EHC Review, follow-up surveys over a three-year period following the termination of PBB production showed no significant decline in PBB levels in sediments from a river. In laboratory investigations, mixtures of PBBs appear to be fairly resistant to microbial degradation. (Quoted from EHC 152 (IPCS, 1994)) This implies that the degradation half-life in soil and sediment is >6 months.

The US ATSDR (2004), refers to studies in soils with high levels of FireMaster, in which degradation of hexabromobiphenyl was "significant" during a period of several years but it was not complete. However in other soils, in which the concentrations were lower, or to which manure was added, degradation was even slower. The degradation was attributed to photodegradation even if this process will only take place at the soil surface (US ATSDR, 2004).

Conclusion

In spite of photodegradation in methanol, it is questionable whether hexabromobiphenyl can be degraded rapidly in air. There is evidence of low or no degradation in water ($DT_{50} > 2$ months), soil and sediment ($DT_{50} > 6$ months) in the laboratory as well as in the field. Therefore, hexabromobiphenyl is considered to be highly persistent.

2.2.2 Bioaccumulation

The EHC review states that PBBs are lipophilic and able to bioaccumulate. This is also supported by monitoring results from wildlife studies. For example, fathead minnows (*Pimephales promelas*) caged in a river where water levels of PBB remained consistently at less than 0.1 µg/l concentrated these contaminants in their bodies more than 10,000 fold in two weeks of exposure (EHC 152 (IPCS, 1994)).

As expected from their lipophilicity, PBBs show a marked tendency to accumulate in animals. US ATSDR, (2004), states that PBBs may also be transported from water to aquatic organisms in which bioconcentration may take place. Data from different laboratories on the bioconcentration of

PBBs in fish show wide variation. The experimentally determined bioconcentration factor (BCF) for hexabromobiphenyl (mixtures of unspecified congeners) in the whole body of fathead minnows (*Pimephales promelas*) was 18,100 in a 32-day exposure (Veith *et al.*, 1979). In fillet of fathead minnow, the estimated BCF was >10,000 (Hesse and Powers, 1978). Weight-based BCF values in the range 4,700-16,000 were recorded in a 60 day test with the carp *Cyprinus carpio* placed in concentrations of hexabromobiphenyl of 0.1-1 µg/L respectively (Governmental Japanese database NITE, 2006).

Furthermore, a potential for biomagnification has been demonstrated by Jansson *et al.*, (1993), who reported a biomagnification factor (BMF) for 2,2',4,4',5,5'-hexabromobiphenyl (PBB congener 153) of about 175 comparing lipid-based concentrations in prey (herring) and predator (Baltic seal). This BMF was at the same level as that of the PCB congener 153. These findings were supported by Vorkamp *et al.*, (2004)⁶, who found lipid-based concentrations of hexabromobiphenyl (PBB 153) in polar bear to be a factor of about 100 higher than in ringed seal from East Greenland. They conclude further, that the PBBs (and PBDEs) seem to biomagnify along the marine food chain in a manner similar to PCBs and that PBBs show indications of a higher biomagnification potential than PBDEs (Vorkamp *et al.*, 2004).

Conclusion

With measured weight-based BCF values in the range 4,700-18,100 (most of which exceed 5,000) and demonstrated biomagnification in the aquatic food chain, hexabromobiphenyl is considered to be highly bioaccumulative and to have a high potential for biomagnification. These properties are demonstrated by several authors to be comparable to those of hexachlorobiphenyl, for which the bioaccumulative properties are well documented. Evidence appears to be satisfactory to conclude high bioaccumulation and biomagnification.

2.2.3 Potential for Long Range Environmental Transport

The partitioning of hexabromobiphenyl in the environment will be governed by its high log K_{ow} (6.39) and low water solubility (3 µg/L) resulting in sorption to particulate matter (dust, soil and sediment) and organic material (including living organisms). Furthermore, the combination of these properties and the relatively low vapour pressure (6.9×10^{-6} to 7.5×10^{-4} Pa) of hexabromobiphenyl, results in a low potential for volatilisation. The latter is specified in US ATSDR (2004) as follows: Based on an estimated Henry's law constant of 3.95×10^{-1} Pa m³/mol (where Henry's law constant = vapor pressure/water solubility) and an estimation method (Thomas, 1990), the estimated volatilization half-life of hexabromobiphenyl is 23 days. Therefore, the transport of PBBs from water to the atmosphere by volatilization is not expected to be important.

The assessment of the potential for long-range transport of hexabromobiphenyl could be done by comparing the properties of hexabromobiphenyl to those of the currently listed POPs. As a starting point for the assessment of hexabromobiphenyl, the highest and lowest of the values in Table 1.1 were used (for vapour pressure, only the value at 25 °C) and, for comparison, the information on the UNEP-POPs homepage. Among the currently listed POPs, most of the relevant properties were available for aldrin, chlordane, dieldrin, DDT, hexachlorobenzene, mirex, toxaphene, endrin and heptachlor. Missing information (water solubility of mirex) was sought in US ATSDR (1995), so as not to introduce what seems to be an outlier in the comparison by using the value of 6.5×10^{-5} mg/L from AMAP (2004).

⁶ These investigations are part of the Arctic Monitoring and Assessment Programme (AMAP).

The water solubility and vapour pressure as well as Henry's Law Constants calculated from these values of the currently listed POPs are summarised in Table 2.1 together with information on hexabromobiphenyl from Table 2.1.

Table 2.1 Water solubility (WS), vapour pressure (VP) and (calculated) Henry's Law Constant (HLC) (at 25 °C) for hexabromobiphenyl and currently listed POPs.

Substance	WS mg/L	VP Pa	HLC Pa m ³ /mol
Hexabromobiphenyl-min	0.011	6.9x10 ⁻⁶	0.39
Hexabromobiphenyl-max	0.003	6.9x10 ⁻⁶	1.44
POP-min	0.0012 (DDT)	2.5x10 ⁻⁵ (DDT)	0.04 (endrin)
POP-max	3.0 (toxaphene)	27 (toxaphene)	3726 (toxaphene)
POP-2 nd max	0.5 (dieldrin)	0.04 (heptachlor)	267 (heptachlor)

Table 2.1 shows that the water solubility of hexabromobiphenyl is at the level of the least water soluble among the currently listed POPs (DDT), while the vapour pressure of HBB is one order of magnitude lower than that of DDT. The two Henry's Law Constants calculated for hexabromobiphenyl are well inside the range marked by the currently listed POPs, being at least one order of magnitude higher than the lowest (endrin). It should be noted that in presenting the data in table 2.1 it is not inferred that a chemical (in this case hexabromobiphenyl) is considered to meet the long-range environmental transport criterion just because it fits within the range of values of currently listed POPs.

Based on the vapour pressure alone, the potential for long-range airborne transport of hexabromobiphenyl is low compared to most of the currently listed POPs, while a comparison of the Henry's Law Constants places hexabromobiphenyl in a position close to endrin.

The EHC 152 (1994), argues that the vapour pressure of hexabromobiphenyl is 6.9x10⁻⁶ Pa and, thereby the potential for volatilisation is low. There is no information available about measured half-life of hexabromobiphenyl in the atmosphere. In the laboratory photodegradation of 2,2',4,4',5,5'-hexabromobiphenyl was rapid (90% degradation after 9 minutes) mainly resulting in lower brominated PBBs (EHC 152 (IPCS, 1994)). On the other hand, the rates and extent of photolytic reactions of PBBs in the environment have not been determined in detail. The few field observations available indicate a high persistence of the original PBBs or a partial degradation to less brominated, and often more toxic, photoproducts.

In support of the assessment of the potential for long-range environmental transport, monitoring data demonstrate that this substance has managed to reach remote areas like the Barents Sea and Greenland. In the Arctic, hexabromobiphenyl has been measured in samples of animals in several investigations. The results are summarised in Annex A, Table A.1.

In whitefish from Lapland (North Scandinavia) and ringed seal from Svalbard, concentrations of 0.29 and 0.42 µg/kg lipid, respectively, were reported by Jansson *et. al.*, (1993). In another paper, Jansson *et. al.*, (1987) reported concentrations of hexabromobiphenyl (Firemaster BP-6) in ringed seal from Svalbard to be 4 µg/kg lipid and concentrations in guillemot muscle of 50 µg/kg lipid. It is not clear whether these results are from different investigations. For comparison, Krüger (1988), measured 0.8 µg/kg of PBB 153 in unspecified seal samples from the same area (Quoted from US ATSDR, 2004).

In samples of large char collected in 1999-2001 from one of two lakes in Bear Island in the Barents Sea, Evenset *et. al.*, (2005) measured concentrations of 4.11-51.5 µg/kg lipid of hexabromobiphenyl (PBB 153). These figures should be used with some caution since levels of other POPs are always very high in char from this lake, maybe due to a local biotransfer process through neighbouring bird species. These levels are the same as or higher than levels of PBB 153 (0.2-9.4 µg/kg lipid) in lake trout sampled in 1997 from Lakes Ontario, Erie, Huron and Superior, which were measured by Luross *et al.*, (2002) (Table 2.2).

Vorkamp *et. al.* (2004), measured concentrations of PBDEs in samples from Greenland and the Faroe Islands of sediment and seven species of animals representing different trophic levels of the food chain. As a pilot investigation, analyses for five PBBs including PBB 153 were made in selected samples of blubber or fat from ringed seal, mink whale and polar bear from Greenland as well as pilot whale and fulmar from the Faroe Islands. PBBs were detected in all samples, except sediment samples, shorthorn-sculpin samples and samples of ringed seal from West Greenland. In all other samples, PBB 153 was generally the dominant congener. The concentrations measured in samples from (East) Greenland were in the range 0.34-44.26 µg/kg lipid with the lowest values found in the seal and the highest in polar bear. In the Faroese samples, the range of concentrations of PBB 153 was 8.71-25.54 µg/kg lipid weight with the highest values found in fulmar, a fish predator (Vorkamp *et. al.*, 2004).

For comparison, concentrations of PBB 153 in grey seal and osprey from the Baltic Sea were 26 and 22 µg/kg lipid weight, respectively (Jansson *et. al.*, 1993). Thus, concentrations of PBB 153 as µg/kg lipid weight in seals from the Arctic (0.34-0.74) are considerably lower than in seals from the Baltic Sea (26 µg/kg lipid weight), while concentrations in predatory birds from the two areas (fulmar and osprey) are of the same order of magnitude, being 25 and 22 µg/kg lipid weight, respectively.

Vorkamp *et. al.*, (2004), conclude that PBBs and PBDEs seem to biomagnify along the marine food chain in a similar manner to PCBs. PBBs show indications of a higher biomagnification potential than PBDEs. Even though their absolute concentrations are lower than those of PBDEs, the PBDE/PBB ratio increases in the order ringed seal<pilot whale<mink whale<fulmar<polar bear, leading to almost equal concentrations of PBDEs and PBBs in polar bear. Apparently, the compounds follow the same spatial trend as previously observed for organochlorine compounds, with higher concentrations in East Greenland than in West Greenland (Vorkamp *et. al.*, 2004). This indicates that the long-range transport of hexabromobiphenyl may be slow.

Monitoring information on PBBs from areas outside the Arctic, Northern Europe and America is scarce, as only one reference has been found. Hexabromobiphenyl (PBB 153) was not detected (LOD between 0.02 and 0.1 µg/kg wet weights) in samples of muscle and liver from several species of fish from the eastern Mediterranean region of Turkey (Erdogru *et. al.*, 2005).

In summary, the 1994 EHC, review concludes that long-range transport of PBBs in the atmosphere has not been proven, but that the presence of these compounds in Arctic seal samples indicates a wide geographical distribution (EHC 152 (IPCS, 1994)). Several authors report levels of hexabromobiphenyl (and other brominated biphenyls) in arctic animals, especially in fish eating predators and predators at higher trophic levels.

In a recent modelling study, Scheringer *et. al.*, (2006), investigated the persistence and long range transport potential of four potential POPs, including chlordecone and hexabromobiphenyl. They concluded that these POP candidates have persistence and long range transport potential properties similar to those of several known POPs. Furthermore, they included the uncertainty regarding the data quality in a Monte Carlo analysis, which indicated that the result is valid although there are considerable uncertainties in the chemical properties of the four POP candidates.

Conclusion

Although hexabromobiphenyl is less volatile than any of the currently listed POPs, it is found throughout the Arctic wildlife, demonstrating that it does have a high potential for long range environmental transport. The potential for long range environmental transport of hexabromobiphenyl is further supported by the modelling study of Scheringer *et al.*, 2006.

2.3 Exposure

Because production of hexabromobiphenyl is assumed to have ceased (section 2.1.2) the assessment of the exposure will focus on general exposure instead of current production sites.

2.3.1 Concentrations in abiotic environmental media

Recent monitoring data in soil, water and sediments for PBBs are limited. Historical monitoring data from the United States indicate that environmental PBB concentrations are confined to areas near former manufacturing facilities and regions of Michigan affected by the farm accident of the early 1970's (see Section 2.2.3) (US ATSDR, 2004).

The only available data for environmental concentrations of PBBs in areas outside the vicinity of former production sites are those from sediment samples from Greenland (Vorkamp *et al.*, 2004), where PBBs (including PBB 153) were not detected in any sample (the limits of detection/quantification are, however, not well defined in the paper).

2.3.2 Concentrations in biota

In the vicinity of Michigan

Concentrations in biota in the vicinity of the Michigan production and contamination accident sites were measured in a multitude of samples during the decade following the cessation of production. The US ATSDR (2004) includes the following: In the late 1980's, PBBs were detected in the concentration range of 15–15,000 µg/kg (lipid basis) in fish from embayments and tributaries of Lake Huron, but not from Lake Superior. Recently, Luross *et al.* (2002) determined the concentrations of several PBB congeners in lake trout from Lakes Huron, Superior, Erie, and Ontario. 2,2',4,4',5,5'-Hexabromobiphenyl (PBB-153) and 2,2',4,5,5'-pentabromobiphenyl (PBB-101) were found at the highest levels at concentrations ranging from 0.189 to 2.083 µg/kg wet weight and from 0.042 to 0.633 µg/kg wet weight, respectively. Several other congeners were also detected in these lake trout samples (Quoted from US ATSDR, 2004). The concentrations of PBBs in eggs of fish-eating birds (common tern, little gull, herring gull, and red-breasted mergansers) collected during 1975–1980 from nesting islands in northwestern Lake Michigan and Green Bay contained PBBs in the concentration range of 0.02–0.25 mg/kg (µg/g) wet weight (Heinz *et al.* 1983, 1985) (quoted from the US ATSDR, 2004).

Other areas

Monitoring data from areas outside the Arctic (see chapter 2.2.3) and the most exposed region of the US are summarised in Table A.2. in Annex A.

EHC 152 (1994) includes the following investigations on residues of (hexa)bromobiphenyl in biota:

- In Europe, 2,2',4,4',5,5'-hexabromobiphenyl (PBB 153) was found in fish from German and Swedish rivers at concentrations ranging from 0.3 to 0.6 µg/kg lipid (Krüger, 1988; Jansson *et al.*, 1992). A trout sample from a breeding farm contained much lower levels of PBBs than the fish samples from the rivers (Krüger, 1988).

- Swedish reindeers (pooled samples) showed PBB 153 levels as low as 0.04 µg/kg lipid (Jansson *et. al.*, 1992).
- PBBs (as a group) were not found in otters (*Lutra canadensis*) from a region relatively remote from industrial sites in north eastern Alberta (Canada) (Somers *et. al.*, 1987).
- Fish samples (freshwater and marine species) collected in 1983 from an industrial area of Japan (Osaka) did not contain "PBBs" (not specified) (Watanabe & Tatsukawa, 1990).
- In Europe, PBBs have been detected in seals (*Phoca vitulina*; *Pusa hispida*), guillemots (*Uria aalge*; *U. lomvi*), and white-tailed sea eagles (*Haliaeetus albicilla*). The concentrations (estimated by comparison with the technical product Firemaster BP-6) ranged from 3 to 280 µg/kg lipid (Jansson *et. al.*, 1987). The concentrations of PBBs in comparable samples from the Baltic Ocean were all higher than concentrations in samples from the Arctic Ocean. The same was true for polybrominated biphenyl ethers and PCBs (Jansson *et. al.*, 1987).
- Concentrations of PBB 153 determined in marine fish ranged from 0.2 to 2.4 µg/kg lipid (Krüger, 1988; Jansson *et. al.*, 1992). PBB 153 levels of 0.4-26 µg/kg lipid were found in seals (Krüger, 1988; Jansson *et. al.*, 1992).
- Detailed isomer-specific PBB analyses were carried out by Krüger (1988), in fish (several species) from the Baltic and North Seas and from sections of the Lippe and Rur rivers in North Rhine-Westphalia, Germany. Seal samples from Spitsbergen (Norway) were also included in this investigation. All samples contained PBBs. The smallest number of PBB congeners was found in seals (n=5) from an area remote from industrial sites. The main components were different hexabrominated isomers with 2,2',4,4',5,5'-hexabromobiphenyl reaching a mean concentration of 0.8 µg/kg fat. The mean concentrations of several PBB congeners and isomers (penta- to nonabrominated biphenyls) measured in fish (n=35) ranged, mostly, between 0.01 and 2 µg/kg fat. The pattern of PBB congeners found in fish differed in a characteristic manner, depending on the different capture sites. While relatively high amounts of nona- and octabromobiphenyls (besides polybrominated biphenyl ethers) were present in fish from German rivers (n=17; several species), hexabrominated biphenyls were predominant in fish from the North Sea and the Baltic Sea (n = 17; several species). In all samples from the Baltic Sea (n=6), 3,3',4,4',5,5'-hexabromobiphenyl was found in relatively high concentrations (maximum concentration: 36 µg/kg fat), but it was not detected in samples from the North Sea and from rivers. The concentrations of the other hexabrominated biphenyls were mostly higher in fish from the Baltic Sea than in fish from the North Sea.

(Quoted from EHC 152 (IPCS, 1994))

US ATSDR (2004) supplements with:

- Three bottlenose dolphins (*Tursiops truncatus*) collected during 1987–1988 from the U.S. mid-Atlantic contained PBBs at concentrations of 14–20 µg/kg lipid basis (Kuehl *et. al.*, 1991). The source of the PBBs in the dolphins was not given.
- The median concentrations of PBBs in carcass and brain of 10 specimens of bald eagles (*Haliaeetus leucocephalus*) collected from 29 states in 1977 were 0.07 and 0.05 mg/kg (µg/g), respectively (Kaiser *et. al.*, 1980). Twenty-two other specimens did not contain detectable levels (<0.03 mg/kg [µg/g]) of PBBs.
- In whitebeaked dolphins from the North Sea, the concentration of hexa-, penta-, and deca-BBs were 13, 8.3, and <0.9 µg/kg (µg/kg) wet weight, respectively. Tetra-, penta-, and deca-BBs concentration ranges were 1.1–1.9, 0.4–0.9, and <0.5 µg/kg wet weight, respectively, in sperm whales from the Atlantic Ocean (de Boer *et. al.*, 1999).

The German Baltic fish samples (as the only samples in that investigation) also contained PBB 169 at a concentration of 15.16 µg/kg lipid (EHC 152 (IPCS, 1994)).

In the Belgian samples from corpses of birds of prey, the variation in concentrations of hexabromobiphenyl was high. Thus, the maximum concentrations measured in muscle and liver were 150 and 180 µg/kg lipid; respectively (Jaspers *et al.*, 2006).

Jansson *et al.* (1993), measured hexabromobiphenyl (PBB 153) in samples of reindeer (a herbivore) from northern Sweden at a level of 0.037 µg/kg lipid. In two other herbivores (rabbit and moose) from Southern Sweden, PBBs were not detectable (level of detection not well defined).

2.3.3 Concentrations in human tissues and breast milk

Michigan

The human exposure to hexabromobiphenyl subsequent to the Michigan accident is discussed in EHC 152 (1994) as well as in US ATSDR (2004). The general trends of the findings are described as follows in EHC 152 (1994):

- Nearly 100% of the adipose samples randomly selected throughout the state had detectable PBB concentrations. Thus, statewide exposure of Michigan residents to PBBs can be demonstrated.
- Levels of PBBs in serum (Landrigan, 1980; Wolff *et al.*, 1982), breast-milk (Brilliant *et al.*, 1978; Miller *et al.*, 1984), and adipose tissue (Wolff *et al.*, 1982) were highest in the area of the accident (lower peninsula), and lowest in the upper peninsula, farthest from the source.
- Compared with residents of quarantined farms, direct consumers of products from quarantined farms, and PBB production workers, the tissue burdens among the general population of Michigan were 1-3 orders of magnitude lower. Moreover, for example, only 36% of the general population had serum PBB concentrations greater than 1 µg/L, compared with 78% among farmers (Anderson *et al.*, 1979; Wolff *et al.*, 1982).
- PBB levels appear to be higher in males than females (Meester & McCoy, 1976; Landrigan *et al.*, 1979; Landrigan, 1980; Wolff *et al.*, 1978; 1980; Kreiss *et al.*, 1982; Eyster *et al.*, 1983) and higher in children (below the age of 10 years) than in adults (Humphrey & Hayner, 1975; Landrigan *et al.*, 1979; Landrigan, 1980; Barr, 1980; Wolff *et al.*, 1982) (Quoted from EHC 152 (IPCS, 1994)).

The subsequent development is described in EHC 152 (1994):

- In most cases, PBB concentrations did not appear to be decreasing significantly over time. Wolff *et al.* (1979b), did not find any significant variation in the serum PBB levels of nine dairy farm residents during 18 month of observation.
- Paired serum samples, one collected in 1974 and the other in 1977, were also available for 148 members of the Michigan PBB cohort. The data indicate that levels were generally stable over the 3-year period with a mean change of 16 µg/litre (Landrigan *et al.*, 1979). In another study of the Michigan PBB-cohort, the decrements in median serum levels of PBBs between matched pairs over one (1977-78) and two (1977-79) year intervals were both only 1 µg/litre (Kreiss *et al.*, 1982). No significant change in blood plasma PBB levels was observed over a 5-month period in 41 residents of quarantined farms (Humphrey & Hayner, 1975). In contrast, Meester & McCoy (1976) reported a marked decline over 3 years (1974-76) in serum levels of PBBs. These authors also found that the average decrease in PBB concentrations in the fat of 16 individuals was about 40% in a period of 6 months. No changes in PBB levels were seen over an 11-year period (1976-87) in fat samples from a patient with long-term exposure to PBBs from the early 1970s as a result of the Michigan PBBs accident. The average fat level of PBBs was 0.8 mg/kg (Sherman, 1991).

- In 1981, PBBs were found in 13-21% of serum samples from 4-year-old Michigan children. Their mothers belonged to a group that was surveyed either with regard to the consumption of Lake Michigan sport fish (mean PBB level detected in children: 2.4 ng/ml) or with regard to former exposure to quarantined farm products (mean PBB level detected in children: 3.0 ng/ml) (Jacobson *et al.*, 1989) (Quoted from EHC 152 (IPCS, 1994)).

Other areas

The EHC 152 (1994), stresses the lack of available monitoring studies from areas outside Michigan, as few human monitoring data are available for the US population outside of Michigan. One study deals with the population in the vicinity of industrial areas involved in PBB production or use (Stratton & Whitlock, 1979), the other with farmers of the state of Wisconsin who were examined as control group in connection with the Michigan PBB studies (Wolff *et al.*, 1978).

PBBs were found in all studies, but, because of the limited data, the significance is unclear. The highest PBB levels were found in the hair of humans living near PBB industry. Of the nine samples analysed, five had detectable PBB levels. Both male and female hair samples contained PBBs (Stratton & Whitlock, 1979).

There is very little human monitoring data on PBBs in the populations of countries other than the United States. Krüger *et al.*, (1988) reported PBB contamination of breast-milk from women in Europe in a survey from North Rhine-Westphalia, Germany. The milk samples (n=25) contained a typical pattern of certain PBB congeners. It included penta- to octabromobiphenyls in concentrations ranging from 0.002 to 28 µg/kg, based on milk fat. The most abundant component was 2,2',4,4',5,5'-hexabromobiphenyl (PBB 153) followed by a peak consisting of two heptabromobiphenyl isomers (2,2',3,4',5,5',6- and 2,2',3,4',4',5,6'-heptabromobiphenyl, PBB 187 and 182 respectively). Differences in the pattern were only found in the milk given by a Chinese woman and in that given by a woman having been exposed to several fires in industry.

Concentrations of PBB 153 in human and cow's milk, both collected from the same region (North Rhine-Westphalia), were 1 µg/kg and 0.03 µg/kg, respectively, measured on a lipid basis (Krüger, 1988). (Quoted from EHC 152 (IPCS, 1994))

2.3.4 Human exposure

The US ATSDR (2004), considers the current human exposure to PBBs to be very low, because PBBs are no longer produced or used. Thus, the general population exposure to PBBs will only be from historical releases. For people residing in the lower peninsula of Michigan, especially in the immediate vicinity of the PBB contaminated areas of this region, exposure to PBBs may still be occurring today. However, environmental levels have decreased since the 1970s and current exposure, if any, will be at low levels. For other regions of the United States, the levels of exposure will either be very low or none (Quoted from US ATSDR, 2004).

In Arctic and North Atlantic regions, where the traditional diet includes top predators (*e. g.* seal in Greenland and pilot whale in the Faroe Islands), exposure has not ceased. Especially the level of PBBs in pilot whale blubber of up to 17 µg/kg lipid indicate the presence of hexabromobiphenyl in food. Pilot whale blubber is consumed as a delicacy in the Faroe Islands.

2.4 Hazard assessment for endpoints of concern

2.4.1 Toxicity

As described in Section 1.1.1, the descriptor "hexabromobiphenyl" covers 42 different hexabrominated biphenyls or congeners, as individually listed in Annex B. The EHC review (IPCS, 1994) indicates that the hexabrominated biphenyls are the most toxic of the chemical class

of polybrominated biphenyls (PBBs) and that the higher homologues (hepta-, octa-, nona- and decabrominated biphenyls) are of progressively lower toxicity. Toxicological studies on hexabromobiphenyl have been carried out mainly on the congener 2,2',4,4',5,5'-hexabromobiphenyl (PBB 153), which is the major component of the PBB mixture FireMaster[®], and on FireMaster[®] itself. The toxicity of FireMaster[®] appears to be primarily associated with the minor components 2,3,3',4,4',5-hexabromobiphenyl, 2,3',4,4',5,5'-hexabromobiphenyl, 3,3',4,4',5,5'-hexabromobiphenyl (PBB 169) and 2,3',4,4',5-pentabromobiphenyl (IPCS, 1994). The predominant congeners in FireMaster[®] (2,2',4,4',5,5'-hexabromobiphenyl and 2,2',3,4,4',5,5'-heptabromobiphenyl), are less toxic (IPCS, 1994). Other toxic contaminants in technical PBB mixtures include the polybrominated naphthalenes (HBNs). Hexabromonaphthalene has been identified as a toxic contaminant of Firemaster BP-6 or FF-1 at levels of approximately 150 ppm (Birnbaum *et al.*, 1983, as reported in US ATSDR, 2004). The toxicological effects of the PBBs in humans and in animal studies, as described in the scientific literature, are considered to be attributable mainly to exposure to hexabromobiphenyl congeners (EHC 152 (IPCS, 1994) and US ATSDR, 2004)), although a possible contribution of the HBNs to toxicity cannot be ignored.

Mechanism of action

Hexabromobiphenyl, in common with all PBBs, is a potent inducer of hepatic cytochrome P-450 metabolizing enzymes in the liver. The mechanism of action underlying a number of the toxicological effects of some of these compounds, including induction of metabolising enzymes, immunotoxicity, hepatotoxicity and reproductive toxicity, is considered to be due to interaction with the cellular Ah receptor (also the target of the polychlorinated dioxins, furans and dioxin-like PCBs), causing altered gene expression (Poland & Glover, 1977, 1980; Poland *et al.*, 1979; Goldstein, 1980; Moore *et al.*, 1980; McKinney & Singh, 1981; Parkinson & Safe, 1981; Bandiera *et al.*, 1982, 1983; McKinney & McConnell, 1982; Nebert *et al.*, 1982; Poland & Knutson, 1982; Robertson *et al.*, 1982b, 1984c,d; Safe *et al.*, 1982, 1985; Aust *et al.*, 1983; Dannan *et al.*, 1983; Lai, 1984; Safe, 1984, as quoted in IPCS, 1994).

Toxicokinetics

Hexabromobiphenyl is readily absorbed into the body, the primary route of human exposure being via food, due to accumulation and biomagnification in the food chain (IPCS, 1994; US ATSDR, 2004). The majority of animal toxicology studies have used the oral route of exposure and little information is available on exposure via the inhalation and dermal routes, although worker exposure is likely to occur mainly via these routes (Wolff *et al.*, 1979a, as quoted in IPCS, 1994). Following absorption, hexabromobiphenyl is widely distributed in the body and accumulates, with the highest concentrations found in adipose tissue and to a lesser extent the liver (IPCS, 1994).

Exposure *in utero* occurs via transfer of PBBs to offspring by placental transfer and infants are also exposed via milk. Human milk has been found to contain levels of 2,2',4,4',5,5'-hexabromobiphenyl 100 times higher than those found in maternal blood (Brilliant *et al.*, 1978; Landrigan *et al.* 1979; Eyster, 1983, as reported in IPCS, 1994).

Metabolism and excretion of the hexabromobiphenyls is low (IPCS, 1994; US ATSDR, 2004), and the compounds therefore show marked bioaccumulation and persistence in all species. Average half-lives for 2,2',4,4',5,5'-hexabromobiphenyl in humans have been estimated to be between 8 and 12 years (IPCS, 1994), while shorter half-lives have been reported in rats, monkeys, and other species (see Table 68 in IPCS, 1994). It has been suggested that humans may retain certain congeners to a greater degree than experimental animals (*e. g.* Fries (1985b, as quoted in IPCS, 1994), a phenomenon that is also found with the polychlorinated dioxins and furans.

Darnerud (2003), argues that the pattern of toxicity of PBBs should be similar to that of PCBs apart from the change in effects brought about by the chlorine-bromine substitution. Consequently, the planar PBBs are expected to be most toxic (as they bind to the Ah receptor) and toxicity to decrease through mono-ortho congeners to di-ortho congeners. This should be supported by experimental evidence, as 3,3',4,4',5,5' hexabromobiphenyl was found to be the most toxic PBB congener in several systems (Darnerud, 2003).

Toxicity of hexabromobiphenyl in animal studies

In experimental animal studies, hexabromobiphenyl shows relatively low acute toxicity ($LD_{50} > 1$ g/kg body weight) (see Table 70, IPCS, 1994). Toxicity is higher following repeated exposure (IPCS, 1994), due to progressive accumulation of the compounds and a characteristic delay in lethality after exposure is seen (Di Carlo *et al.*, 1978; Gupta & Moore, 1979, (as quoted in IPCS, 1994). At lethal doses, death is reported to be due to a "wasting syndrome" with marked loss in body weight rather than to specific organ pathology (Hutzinger *et al.*, 1985a; McConnell, 1985, as quoted in IPCS, 1994). However, prolonged exposure of laboratory animals to doses in the range of < 1 mg/kg bw/day to 100 mg/kg bw/day results in liver, kidney and thyroid changes, accompanied by effects in the nervous and immune systems, porphyria and skin disorders (IPCS, 1994).

A summary of outcomes of a number of the key toxicological studies on hexabromobiphenyl, including the NOAEL/LOAEL derived in each study is provided in Annex A, Table A.3 to this document. The studies included in Annex A, Table A.3 have been selected from the very large database on toxicological studies on hexabromobiphenyl, on the basis of the importance of the endpoint investigated (*e. g.* reproductive toxicity, carcinogenicity, other key target organ toxicity), robustness of the reported studies and the dose level (NOAEL/LOAEL) at which effects were reported. Table 2.2 below provides information on pivotal toxicological studies (also included in Annex A Table A.3) that provide information on the toxicity of hexabromobiphenyl at low levels of exposure, considered to be particularly relevant for characterisation of the toxicological risks of these compounds. Some of these studies have been used by US ATSDR to define Minimal Risk Levels (MRLs) for hexabromobiphenyl (US ATSDR, 2004).

Effects in toxicological studies included decreased circulating thyroid hormones in a 10-day gavage study in rats with a NOAEL of 1 mg/kg bw/day (Allen-Rowlands *et al.*, 1981, as quoted in US ATSDR, 2004), decreased lymphoproliferative responses in rats at a dose level of 3 mg/kg/day (LOAEL) (Luster *et al.*, 1980, as quoted in US ATSDR, 2004), and generalised toxicity in male Rhesus monkeys at 0.73 mg/kg bw/day (LOAEL) (Allen *et al.*, 1978; Lambrecht *et al.* 1978 (as quoted in US ATSDR, 2004)). PBBs produced porphyria in rats and male mice at doses as low as 0.3 mg/kg bw/day. The no-effect level was 0.1 mg/kg bw/day.

These results show that hexabromobiphenyl produced long-term toxicity in experimental animals at very low doses, a critical effect for the purposes of risk characterization being the effects seen in the thyroid in rats at doses as low as 0.05 mg/kg bw/day, comprising increased number and decreased size of follicles, accompanied by changes in levels of circulating T_3 and T_4 hormone (Akoso *et al.*, 1982, as quoted in US ATSDR, 2004).

Hepatocarcinogenicity of hexachlorobiphenyl has been demonstrated in a number of studies including repeated dose studies in Fischer-344/N rats and B6C3F1 mice (males and females) administered FireMaster^(R) FF-1 at dosages of 0, 0.1, 0.3, 1, 3, or 10 mg/kg bw/day (NTP 1983, NTP, 1992, as quoted in US ATSDR, 2004). Tumors included hepatocellular adenoma and carcinoma and, in female rats, cholangiocarcinoma. The lowest dose of FireMaster^(R) that produced tumors (primarily adenomas rather than carcinomas) in rats was 3.0 mg/kg bw/day for 2 years, and in mice the dose was 10 mg/kg bw/day (NTP 1983, as quoted in US ATSDR, 2004). Mice receiving 0.15 mg/kg bw/day in a study involving pre- and perinatal exposure in addition to lifetime exposure

did not suffer any adverse effects (NTP, 1992, as quoted in US ATSDR, 2004). The International Agency for Research on Cancer (IARC) in 1987 concluded that there was sufficient evidence that hexabromobiphenyl is carcinogenic in mice and rats and possibly carcinogenic to humans (Group 2B). Hexabromobiphenyl is not genotoxic in *in vitro* microbial and mammalian cell gene mutation assays (see Table 88 in IPCS, 1994), although it has been reported to interfere with cell-to-cell communication (Sleight, 1985 as quoted in IPCS, 1994). These results, coupled with the results of tumor promotion studies (*e. g.* Schwartz *et. al.*, 1980; Jensen *et. al.*, 1982, 1983, 1984; Jensen & Sleight, 1986; Rezabek *et. al.*, 1987; Dixon *et. al.*, 1988, as quoted in IPCS, 1994) indicate that these chemicals cause cancer by epigenetic mechanisms, involving both hepatic toxicity and hypertrophy, including cytochrome P-450 induction (IPCS, 1994).

Oral administration of hexabromobiphenyl was associated with adverse effects on reproductive parameters in a range of experimental animals (see Table 86 and 87 in IPCS, 1994). The most common adverse effects on reproduction were failure in implantation and decreases in pup viability of offspring. These effects were seen at a dose level of 28.6 mg/kg bw/day in a 15-day reproductive toxicity study in rats, with dosing between gestational day 0-14 (Beaudoin, 1979, as quoted in US ATSDR, 2004) and in mink at concentrations of 1 mg/kg diet (Aulerich and Ringer, 1979 as quoted in IPCS, 1994). Increased menstrual cycle duration and prolonged implantation bleeding were observed in female monkeys fed approximate daily dose levels of 0.012 mg/kg bw/day for 7 months before breeding and during pregnancy. Fetal deaths were also observed after approximately 1 year of exposure. Effects were attributed to decreases in serum progesterone (Lambrecht *et. al.*, 1978; Allen *et. al.*, 1978; 1979, (as quoted in US ATSDR, 2004).

Table 2.2 Pivotal toxicological studies on the toxicity of hexabromobiphenyl.

Species	Study type	Effect	LOAEL/ NOAEL
Rat	Short-term/acute toxicity 10 day repeat dose gavage study	decreased thyroid serum T4 hormones	3 mg/kg bw/day (LOAEL) 1 mg/kg bw/day (NOAEL)
Rat, Sprague Dawley	30-day dietary feeding study	increased number and decreased size of thyroid follicles	0.05 mg/kg bw/day (LOAEL)
Mice B6C3F1	In utero and post partum exposure from Gd 0-ppd 56	hepatocellular adenoma and carcinoma in offspring	1.5 mg/kg bw/day (LOAEL) 0.15 mg/kg bw/day (NOAEL)
Rhesus Monkey	25-50 wk dietary feeding study	34% weight loss in adult male, 0% weight gain in juvenile, proliferation of mucosal cells, chronic inflammation, severe ulcerative colitis, alopecia, keratinization of hair follicles and sebaceous glands, clinical chemical and hepatic changes	0.73 mg/kg bw/day (LOAEL, males)
Rat, Sprague Dawley	7 month dietary feeding study	decreased thyroid serum T3 and T4 hormones	0.45 mg/kg bw/day (LOAEL)
Monkey, Rhesus		increased menstrual cycle duration in 4/7; implantation bleeding in 2/7). 1/7 fetuses were aborted, 1/7 fetuses stillborn, 12% decreased birth weight and 22% decreased postnatal weight gain in 4/7 survivors	0.012 mg/kg bw/day (LOAEL)

Toxicity of hexabromobiphenyl in humans

Information on toxicological effects of PBBs (and by inference, hexabromobiphenyl) in humans has mainly been derived from the Michigan accident described in Section 2.1.4 of this draft Risk Profile (Carter (1976), Getty *et al.*, (1977), Kay (1977), Di Carlo *et al.*, (1978), Damstra *et al.*, (1982), Zabik (1982), and Fries (1985b), as quoted in EHC 152 (IPCS, 1994)). This accident resulted in widespread exposure of consumers for periods approaching 1 year, before the contamination of food by PBBs was identified and affected foodstuffs were removed from the food chain.

Adverse health effects reported included changes in liver enzymes, nausea, abdominal pain, loss of appetite, joint pain and fatigue (Anderson *et al.*, 1978b, 1979, as reported in IPCS, 1994), together with reports of skin disorders, including acne and hair loss, in the period following the contamination. (IPCS, 1994). Similar skin disorders have also been reported in workers with occupational exposure to PBBs (Anderson *et al.*, 1978a, as reported in IPCS, 1994), and also following exposure to the polychlorinated dioxins and furans.

Detailed epidemiological studies have been carried out on the health status of exposed individuals including immunological status, cancer incidence, reproductive effects and effects on development of young children. These studies have in the main failed to establish a definite link between any of these effects and exposure to PCBs, although some studies have reported decreased immune function in Michigan farm residents (Bekesi *et al.*, 1979, 1987) and effects have also been reported on pubertal development in young females (see endocrine-disrupting effects below).

There are no reports of acute hexabromobiphenyl intoxication in humans, and there is also no consistent epidemiological evidence for hepatocarcinogenicity in exposed humans. A relationship between increasing serum levels (>2 ppb) of PBBs and increasing risk of breast cancer was indicated in case-control studies of women exposed during the Michigan contamination episode (Henderson *et al.*, 1995; Hoque *et al.*, 1998), but according to US ATSDR, 2004 (and quoted from this source) the results are only suggestive due to factors such as the small number of cases, insufficient information on known breast cancer risk factors, and confounding exposures to other organochlorine chemicals.

Effects on endocrine systems

The PBBs (and by inference, hexabromobiphenyl) are considered to have effects on endocrine systems. They have been evaluated under the EU-Strategy for Endocrine Disrupters⁷ and have been placed in category 1 (evidence of endocrine-disrupting activity in at least one species using intact animals) in the priority list of chemicals established under the EU-Strategy. This categorisation is based on evidence of delayed vaginal opening in new-born rats, epidemiological evidence of hypothyroidism in workers exposed to polybrominated biphenyls and of increased incidence of breast cancer among women exposed to polybrominated biphenyls (as reported in BKH report, 2000). In an assessment (Blanck *et al.*, 2000) of pubertal development in girls and young women exposed in utero and via breast milk to high levels of PBBs (>7ppb), it was found that this population had an earlier age to menarche than a similar breastfed population exposed to lower levels of PBBs, or than a highly-exposed population who were not breastfed. Earlier pubic hair development was also seen in the more highly exposed population, suggesting an effect of PBBs on pubertal events (Blanck *et al.*, 2000).

⁷ http://europa.eu.int/comm/environment/endocrine/strategy/substances_en.htm

Conclusion on effects assessment and toxicity of hexabromobiphenyl

Hexabromobiphenyl is readily absorbed into the body and accumulates following prolonged exposure. Although the acute toxicity of hexabromobiphenyl is low, a number of chronic toxic effects including hepatotoxicity have been observed in experimental animals at doses around 1 mg/kg bw/day following long-term exposure, and effects are seen in the rat thyroid at doses as low as 0.05 mg/kg bw/day. Cancer was induced in animal studies at a dose of 0.5 mg/kg bw/day and the no-observed-effect level was 0.15 mg/kg bw/day. The International Agency for Research on Cancer has classified hexabromobiphenyl as a possible human carcinogen (IARC group 2B). The PBBs (and by inference, hexabromobiphenyl) are endocrine disrupting (ED) chemicals, and effects are seen on reproductive capacity in rats, mink and monkeys. Effects were seen in monkeys fed 0.012 mg/kg bw/day for 7 months before breeding and during pregnancy, the lowest effect level reported for hexabromobiphenyl in toxicology studies. There is epidemiological evidence of hypothyroidism in workers exposed to polybrominated biphenyls and of increased incidence of breast cancer in exposed women.

It can be concluded that hexabromobiphenyl is a bioaccumulative chemical with a range of potentially adverse effects on health, including carcinogenicity, reproductive toxicity, endocrine and other hormone-disrupting effects, at very low levels of exposure.

2.4.2 Ecotoxicity

Only few data are available on effects of PBBs on other organisms than mammals. Toxicity tests with technical decabromobiphenyl (Adine 0102) and bacteria (*Pseudomonas putida*) and the water flea *Daphnia magna* are quoted in EHS 152 (1994). The results were an EC10 of 53 mg/L for *Pseudomonas putida* (cell multiplication) and an EC50 > 66 mg/liter for *Daphnia magna* (immobilization, 24 hours). Because these concentrations exceed the solubility of HBB in water, the data may be of limited relevance to evaluating the environmental effects. However, the fact that the NOEC is reported to be < 2 mg/L indicates that the water fleas were affected at the lowest concentration tested.

MacPhee & Ruelle (1969) and Applegate *et al.*, (1957), report results from short term tests with hexabromobiphenyl (CAS No. 36355-01-8) and several species of fish in the range 5-10 mg/L (Quoted from the Ecotox data base (US EPA, 2006)). These concentrations are also above the water solubility and may also be of limited environmental relevance.

In a field study on water birds, correlations between behavioural effects and reproductive success were not unambiguously correlated to body burdens of PBBs. (EHS 152 (IPCS, 1994)).

In an untraditional fish early life stage test, Hornung *et al.*, (1996), injected halogenated organic contaminants into rainbow trout eggs. For 3,3',4,4',5,5'- hexabromobiphenyl they found an LD₅₀ of 3,910 µg/kg. This result is not comparable to those of traditional fish tests, where exposure is via the water but it is comparable to results of other test with similar exposure. Hornung *et al.* (1996), made such experiments to compare the toxicity of PBBs and PCBs and found that both 3,3',4,4'-tetrabromobiphenyl and 3,3',4,4',5,5'-hexabromobiphenyl were 10-fold more potent than identically substituted polychlorinated biphenyls.

Based on this, it seems to be relevant to expect the environmental toxicity of hexabromobiphenyl to be comparable to that of hexachlorobiphenyl.

3 SYNTHESIS OF THE INFORMATION

Hexabromobiphenyl belongs to a wider group of polybrominated biphenyls (PBBs). It has mainly been used as a fire retardant. Hexabromobiphenyl is already listed in Annex I of the UNECE Protocol on POPs.

According to available data, hexabromobiphenyl can be considered to be highly persistent in the environment. There is evidence of low or no degradation in water, soil and sediment, in the laboratory as well as in the field. Therefore, hexabromobiphenyl is considered to be highly persistent.

Hexabromobiphenyl is less volatile than many POP substances. However, extensive data on monitoring shows that it is found throughout the Arctic wildlife, demonstrating that it does have a high potential for long range environmental transport.

With measured weight-based BCF values in the range 4,700 - 18,100 and biomagnification factors in the aquatic food chain exceeding 100, hexabromobiphenyl is considered to be highly bioaccumulative and to have a high potential for biomagnification. These properties are demonstrated by several authors to be comparable to those of hexachlorobiphenyl (a PCB compound), for which the bioaccumulative properties are well documented.

Hexabromobiphenyl is readily absorbed into the body and accumulates following prolonged exposure. Although the acute toxicity of hexabromobiphenyl is low, a number of chronic toxic effects including hepatotoxicity have been observed in experimental animals at doses around 1 mg/kg bw/day following long-term exposure, and effects are seen in the rat thyroid at doses as low as 0.05 mg/kg bw/day. The International Agency for Research on Cancer has classified hexabromobiphenyl as a possible human carcinogen (IARC group 2B). The PBBs are endocrine disrupting chemicals, and effects are seen on reproductive capacity in rats, mink and monkeys. There is epidemiological evidence of hypothyroidism in workers exposed to polybrominated biphenyls and of increased incidence of breast cancer in exposed women. Data on toxicity to other species than laboratory mammals is scarce but suggests the environmental toxicity of hexabromobiphenyl is comparable to that of hexachlorobiphenyl.

Based on the available data, hexabromobiphenyl should be considered as a POP warranting global action.

Production and use of hexabromobiphenyl has ceased over the last decades but it cannot be excluded that it is still produced or used in some countries. In addition to emissions during manufacture or use, hexabromobiphenyl can enter the environment from the widespread use of flame-retarded products. A considerable part of the substance produced will probably reach the environment sooner or later because of the high stability of these compounds. Furthermore, some of these chemicals may form toxic polybrominated dibenzofurans during combustion processes.

4 CONCLUDING STATEMENT

It has been demonstrated that hexabromobiphenyl clearly meets all the criteria laid down in Annex D of the Stockholm Convention: It is very persistent in the environment. It has a great potential for bioaccumulation and in addition there is clear evidence of its biomagnification. Due to its physical and chemical properties and based on findings in environmental samples, it is verified that hexabromobiphenyl can be transported long distances in air, far from its sources. Hexabromobiphenyl is a possible human carcinogen and can also be regarded as a substance capable of disrupting the endocrine system.

As hexabromobiphenyl can travel in the atmosphere far from its sources, neither a single country nor group of countries alone can abate the pollution caused by this substance. Regional action has already been considered necessary and hexabromobiphenyl is totally banned under the Convention on Long-range Transboundary Air Pollution Protocol on Persistent Organic Pollutants. Although the production and use of hexabromobiphenyl seems to be ceased in most countries, its reintroduction remains possible. This could lead to increased releases and levels in the environment.

Based on the available data, hexabromobiphenyl is likely, as result of its long-range environmental transport, to lead to significant adverse human health and environmental effects, such that global action is warranted.

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ANNEX A

Table A.1 Concentrations of hexabromobiphenyl (PBB 153) in Arctic predators.

Year of sampling	Location	Species	Tissue	Concentration $\mu\text{g}/\text{kg}$ lipid
1999-2002	East Greenland	Polar bear (<i>Ursus maritimus</i>) ¹	Blubber	33-44
1998	Faroe Islands	Fulmar (<i>Fulmarus glacialis</i>) ¹	Fat	16-26
2001	Faroe Islands	Pilot whale (<i>Globicephala melas</i>) ¹	Blubber	8.7-17
< 1987	Arctic Ocean	Guillemot (<i>Uria aalge</i>) ²	Muscle	50 ⁶
2002	East Greenland	Ringed seal (<i>Phoca hispida</i>) ¹	Blubber	0.34-0.42
1998-2002	West Greenland	Ringed seal (<i>Phoca hispida</i>) ¹	Blubber	n.d.
< 1987	Svalbard	Ringed seal (<i>Phoca hispida</i>) ²	Blubber	4 ⁶
1981	Svalbard	Ringed seal (<i>Phoca hispida</i>) ³	Blubber	0.42
< 1988	Svalbard	Seal sp. ⁴	? (mean)	0.8
1998	East Greenland	Minke whale (<i>Balaenoptera acutorostrata</i>) ¹	Blubber	0.56-1.2
1999-2001	Barents Sea	Arctic char (<i>Salvelinus alpinus</i>) ⁵	Muscle	n.d.-52
1986	Lapland	Whitefish (<i>Coregonus sp.</i>) ²	Muscle	0.29
2002	East Greenland	Shorthorn sculpin (<i>Myoxocephalus scorpius</i>) ¹	Liver	n.d.
2002	West Greenland	Shorthorn sculpin (<i>Myoxocephalus scorpius</i>) ¹	Liver	n.d.

n.d. = Not detected. Limits of detection are not well described in the references.

1: Vorkamp *et al.*, 2004,

2: Jansson *et al.*, 1987,

3: Jansson *et al.*, 1993,

4: Krüger, 1988 (Quoted from EHC 152),

5: Evenset *et al.* 2005.

6: FireMaster^(R) BP-6

Table A.2 Concentrations of hexabromobiphenyl (PBB 153) in biota, collected in subarctic and temperate regions outside the vicinity of Michigan.

Year of sampling	Location	Species	Tissue	Concentration $\mu\text{g}/\text{kg}$ lipid
Aquatic species				
1979-85	Baltic Sea	Grey seal (<i>Halichoerus grypus</i>) ²	Blubber	26
< 1987	Baltic Sea	Harbour seal (<i>Phoca vitulina</i>) ¹	Blubber	20
< 1987	~North Sea	Harbour seal (<i>Phoca vitulina</i>) ¹	Blubber	3
< 1987	Baltic Sea	Guillemot (<i>Uria aalge</i>) ¹	Muscle	160
1987-88	US mid Atlantic	Bottlenose dolphin (<i>Tursiops truncatus</i>) ⁸	?	14-20
< 1999	North Sea	Whitebeaked dolphin (<i>Lagenorhynchus albirostris</i>) ¹⁰	?	13 (wwt)
1987	S. Sweden	Arctic char (<i>Salvelinus alpinus</i>) ²	Muscle	0.42
1986	Bothnian Bay	Herring (<i>Clupea harengus</i>) ²	Muscle	0.092
1987	Baltic Proper	Herring (<i>Clupea harengus</i>) ²	Muscle	0.16
1987	Skagerak	Herring (<i>Clupea harengus</i>) ²	Muscle	0.27
< 1988	Germany	River fish (average) ¹	?	0.60
< 1988	Baltic Sea	Fish ¹	?	2.39
< 1988	North Sea	Fish ¹	?	1.31
1997	USA, Great Lakes	Lake trout (<i>Salvelinus nanaycush</i>) (range of means) ⁶	Whole fish	0.19-2.08
Predatory birds				
< 1987	Baltic Sea	White tailed sea eagle (<i>Haliaeetus albicilla</i>) ⁷	Muscle	280
1977	USA, 29 states	Bald eagle (<i>Haliaeetus leucocephalus</i>) ⁹	Carcass	< 0.03 – 0.07 (wwt?)
1977	USA, 29 states	Bald eagle (<i>Haliaeetus leucocephalus</i>) ⁹	Brain	< 0.03 – 0.05 (wwt?)
1982-86	S. Sweden	Osprey (<i>Pandion haliaeetus</i>), corpses ²	Muscle	22
2003-2004	Belgium	7 species of predatory birds, corpses (range of medians) ³	Muscle	2-35
2003-2004	Belgium	7 species of predatory birds, corpses (range of medians) ³	Liver	2-43
1998-2000	Belgium	Little owl (<i>Athene noctua</i>) ⁵	Unhatched eggs	1-6
1991-2002	Norway	6 species of predatory birds (range of medians) ⁴	Unhatched eggs	0.2-9.4 $\mu\text{g}/\text{kg}$ wwt
Terrestrial herbivores				
1986	S. Sweden	Rabbit (<i>Oryctolagus cuniculus</i>) ²	Muscle	n.d.
1985-86	S. Sweden	Moose (<i>Alces alces</i>) ²	Muscle	n.d.
1986	N. Sweden	Reindeer (<i>Rangifer tarandus</i>) ²	Suet (fat)	0.037

n.d. = Not detected. Limits of detection are not well described in the references.

1: EHC 152 (IPCS, 1994), 2: Jansson *et al.* 1993, 3: Jaspers *et al.*, 2006, 4: Herzke *et al.*, 2005, 5: Jaspers *et al.*, 2006, 6: Luross *et al.*, 2002, 7: Jansson *et al.* 1987, 8: Kuehl *et al.* 1991 (quoted from US ATSDR, 2004), 9: Kaiser *et al.*, 1980 (quoted from US ATSDR, 2004), 10: de Boer *et al.*, 1999 (quoted from US ATSDR, 2004).

Table A.3. Summary of key toxicological studies on hexabromobiphenyl.

Species (test material)	Study type	Effect	LOAEL/NOAEL	Ref.
Rat Fischer 344/N (FF-1)	Short-term/acute toxicity, 14-day repeat dose, 5 single daily doses per week	Body weight loss, emaciation, hepatotoxicity, renal & adrenal changes, atrophy of thymus; necrosis of splenic lymphoblasts)	1000 mg/kg/day (LOAEL)	Gupta and Moore 1979 (as quoted in US ATSDR, 2004).
Rat	Short-term/acute toxicity 10 day repeat dose gavage study	decreased thyroid serum T4 hormones	3 mg/kg bw/day (LOAEL) 1 mg/kg bw/day (NOAEL)	Allen-Rowlands <i>et al.</i> 1981 (as quoted in US ATSDR, 2004).
Rat, Sprague Dawley (BP-6)	30-day dietary feeding study	increased number and decreased size of thyroid follicles	0.05 mg/kg/day (LOAEL)	Akoso <i>et al.</i> 1982 (as quoted in US ATSDR, 2004).
Mouse B6C3F1 (FF-1)	Short-term/acute toxicity, 14-day repeat dose, 5 single daily doses per week	Hepatocyte enlargement and single-cell necrosis	0.3 mg/kg bw/day (NOAEL)	Gupta <i>et al.</i> 1981 (as quoted in US ATSDR, 2004).
Guinea Pig (PBB not specified)	30-day dietary feeding study	vacuolation and fatty changes in liver	0.04 mg/kg bw/day	Sleight and Sanger 1976, (as quoted in US ATSDR, 2004).
Balb/c Mouse (BP-6)	Short-term/acute toxic, 10 day oral dietary study	suppressed antibody-mediated response to SRBC, thymic atrophy)	130 mg/kg bw/day (LOAEL)	Fraker and Aust 1978, (as quoted in US ATSDR, 2004).
Rat Fischer 344/N (FF-1)	6 month gavage study, 5 single daily doses per week	decreased lymphoproliferative responses and decreased delayed hypersensitivity responses)	3 mg/kg bw/day (LOAEL)	Luster <i>et al.</i> 1980 (as quoted in US ATSDR, 2004).
Rhesus Monkey (FF-1)	25-50 wk dietary feeding study	34% weight loss in adult male, 0% weight gain in juvenile, proliferation of mucosal cells, chronic inflammation, severe ulcerative colitis, alopecia, keratinization of hair follicles and sebaceous glands, clinical chemical and hepatic changes	0.73 mg/kg bw/day (LOAEL, males)	Allen <i>et al.</i> 1978; Lambrecht <i>et al.</i> 1978 (as quoted in US ATSDR, 2004).
Rat, Sprague Dawley (BP-6)	7 month dietary feeding study	decreased thyroid serum T3 and T4 hormones	0.45 mg/kg bw/day (LOAEL)	Byrne <i>et al.</i> 1987, (as quoted in US ATSDR, 2004).

Note: FF-1 and BP-6 in column 1 refer to FireMaster^(R) FF-1 and FireMaster^(R) BP-6, the PBBs used in the toxicity study described.

Table A.3 (continued) Summary of key toxicological studies on hexabromobiphenyl.

Species (test material)	Study type	Effect	LOAEL/NOAEL	Ref.
Rat Fischer 344/N (FF-1)	25 wk gavage study, 5 single daily doses per week	gastric ulcers, decreased serum thyroid T4 hormone) hepatic, haematological disorders, thymic atrophy, progressive nephropathy	0.3 mg/kg bw/day (LOAEL) 0.1 mg/kg bw/day (NOAEL)	NTP 1983, (as quoted in US ATSDR, 2004).
Rat Sprague-Dawley Holtzman (FF-1)	4 week gavage study, 5 single daily doses per week	decreased motor activity	6 mg/kg bw/day (LOAEL) 3 mg/kg bw/day (LOAEL)	Geller <i>et al.</i> 1979, (as quoted in US ATSDR, 2004).
Rat, Sprague Dawley (BP-6)	6 month gavage study, 5 single daily doses per week	delayed acquisition of locomotion and reduced open field activity in offspring).	2 mg/kg bw/day (LOAEL) 0.2 mg/kg bw/day (NOAEL)	Henck <i>et al.</i> 1994, (as quoted in US ATSDR, 2004).
Monkey, Rhesus (FF-1)		increased menstrual cycle duration in 4/7; implantation bleeding in 2/7). 1/7 fetuses were aborted, 1/7 fetuses still-born, 12% decreased birth weight and 22% decreased postnatal weight gain in 4/7 survivors	0.012 mg/kg bw/day (LOAEL)	Lambrecht <i>et al.</i> 1978; Allen <i>et al.</i> 1978; 1979, (as quoted in US ATSDR, 2004).
Rat, Wistar (BP-6)	15-day reproductive toxicity study, dosing between gestational day 0-14	no implantations in 2/5 rats	28.6 mg/kg bw/day (LOAEL) 14.3 mg/kg bw/day (NOAEL)	Beaudoin 1979, (as quoted in US ATSDR, 2004).
Rat, Sprague Dawley	Gavage study in pregnant rats, dosing between gestational day 7-15	Reproductive: Delayed vaginal opening in pups	0.04 mg/kg bw/day (NOAEL)	Harris <i>et al.</i> (1978) (as quoted in BKH Final Report 2000)
Rat, Sprague Dawley (BP-6)	40 day dietary feeding study	Reproductive deficits in learning behavior in offspring, 6 months after prenatal and lactational exposure)	0.2 mg/kg bw/day (LOAEL)	Henck and Rech 1986, (as quoted in US ATSDR, 2004).

Note: FF-1 and BP-6 in column 1 refer to FireMaster^(R) FF-1 and FireMaster^(R) BP-6, the PBBs used in the toxicity study described.

Table A.3 (continued) Summary of key toxicological studies on hexabromobiphenyl.

Species (test material)	Study type	Effect	LOAEL/NOAEL	Ref.
Rat, Fischer 344/N (FF-1)	6 month gavage study, 5 single daily doses per week dosages of 0, 0.1, 0.3, 1, 3, or 10 mg/kg/day	hepatocellular adenoma and carcinoma, cholangiocarcinoma (females only)	3 mg/kg bw/day (LOAEL)	NTP 1983, (as quoted in US ATSDR, 2004).
Mice B6C3F1 (FF-1)	6 month gavage study, 5 single daily doses per week dosages of 0, 0.1, 0.3, 1, 3, or 10 mg/kg/day	hepatocellular adenoma and carcinoma	10 mg/kg bw/day (LOAEL)	NTP 1983, (as quoted in US ATSDR, 2004)
Mice B6C3F1 (FF-1)	In utero and post partum exposure from Gd 0-ppd 56	hepatocellular adenoma and carcinoma in offspring	1.5 mg/kg bw/day (LOAEL) 0.15 mg/kg bw/day (NOAEL)	NTP 1992, (as quoted in US ATSDR, 2004).
Humans	Females accidentally exposed in the Michigan incident	relationship between serum PBBs and risk of breast cancer	relationship between serum PBBs of > 2 ppb and risk of breast cancer when compared with the reference group (<2 ppb),	Henderson <i>et al.</i> 1995, (as quoted in US ATSDR, 2004).
Humans	Michigan farm residents accidentally exposed in the Michigan incident	Significant reduction of in vitro immunological function		Bekesi <i>et al.</i> 1979, 1985 (as quoted in US ATSDR, 2004) Bekesi <i>et al.</i> , 1987
Humans	Females accidentally exposed in the Michigan incident	Possible disturbance in ovarian function as indicated by menstrual cycle length and bleed length		Davis <i>et al.</i> , 2005
Humans	Offspring of females accidentally exposed in the Michigan incident	breastfed girls exposed to high levels of PBB in utero had an earlier age at menarche	Effects at > or =7 ppb in breast milk	Blanck <i>et al.</i> , 2000, (as quoted in US ATSDR, 2004)

Note: FF-1 and BP-6 in column 1 refer to FireMaster^(R) FF-1 and FireMaster^(R) BP-6, the PBBs used in the toxicity study described.

ANNEX B

HEXABROMOBIPHENYL ISOMERS

IUPAC Number ⁸	Name	CAS Registry number ⁹
	Hexabromobiphenyl	36355-01-8
128	2,2',3,3',4,4' hexabromobiphenyl	82865-89-2
129	2,2',3,3',4,5 hexabromobiphenyl	
130	2,2',3,3',4,5' hexabromobiphenyl	82865-90-5
131	2,2',3,3',4,6 hexabromobiphenyl	
132	2,2',3,3',4,6' hexabromobiphenyl	119264-50-5
133	2,2',3,3',5,5' hexabromobiphenyl	55066-76-7
134	2,2',3,3',5,6 hexabromobiphenyl	
135	2,2',3,3',5,6' hexabromobiphenyl	119264-51-6
136	2,2',3,3',6,6' hexabromobiphenyl	
137	2,2',3,4,4',5 hexabromobiphenyl	81381-52-4
138	2,2',3,4,4',5' hexabromobiphenyl	67888-98-6
139	2,2',3,4,4',6 hexabromobiphenyl	
140	2,2',3,4,4',6' hexabromobiphenyl	
141	2,2',3,4,5,5' hexabromobiphenyl	120991-47-1
142	2,2',3,4,5,6 hexabromobiphenyl	
143	2,2',3,4,5,6' hexabromobiphenyl	
144	2,2',3,4,5',6 hexabromobiphenyl	119264-52-7
145	2,2',3,4,6,6' hexabromobiphenyl	
146	2,2',3,4',5,5' hexabromobiphenyl	
147	2,2',3,4',5,6 hexabromobiphenyl	
148	2,2',3,4',5,6' hexabromobiphenyl	
149	2,2',3,4',5',6 hexabromobiphenyl	69278-59-7
150	2,2',3,4',5,6' hexabromobiphenyl	93261-83-7
151	2,2',3,5,5',6 hexabromobiphenyl	119264-53-8
152	2,2',3,5,6,6' hexabromobiphenyl	
153	2,2',4,4',5,5' hexabromobiphenyl	59080-40-9
154	2,2',4,4',5,6' hexabromobiphenyl	36402-15-0
155	2,2',4,4',6,6' hexabromobiphenyl	59261-08-4
156	2,3,3',4,4',5 hexabromobiphenyl	77607-09-1
157	2,3,3',4,4',5' hexabromobiphenyl	84303-47-9
158	2,3,3',4,4',6 hexabromobiphenyl	
159	2,3,3',4,5,5' hexabromobiphenyl	120991-48-2
160	2,3,3',4,5,6 hexabromobiphenyl	
161	2,3,3',4,5',6 hexabromobiphenyl	
162	2,3,3',4',5,5' hexabromobiphenyl	
163	2,3,3',4',5,6 hexabromobiphenyl	
164	2,3,3',4',5',6 hexabromobiphenyl	82865-91-5
165	2,3,3',5,5',6 hexabromobiphenyl	
166	2,3,4,4',5,6 hexabromobiphenyl	
167	2,3',4,4',5,5' hexabromobiphenyl	67888-99-7
168	2,3',4,4',5',6 hexabromobiphenyl	84303-48-0
169	3,3',4,4',5,5' hexabromobiphenyl	60044-26-0

(US ATSDR (2004)¹⁰)

⁸ Ballschmiter and Zell 1980

⁹ From EHC 152 (IPCS, 1994).

¹⁰ Note: the US ATSDR List does not include the two CAS numbers included in EHC 192 1997