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Persistent Organic Pollutants Review Committee
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Geneva, 15–19 October 2012

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

Addendum

Risk profile on hexachlorobutadiene

At its eighth meeting, by its decision POPRC-8/2, the Persistent Organic Pollutants Review Committee adopted a risk profile on hexachlorobutadiene on the basis of the draft risk profile contained in document UNEP/POPS/POPRC.8/3. The text of the risk profile, as amended, is set out in the annex to the present addendum; it has not been formally edited.

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Annex

HEXACHLOROBUTADIENE

RISK PROFILE

Prepared by the ad hoc working group on hexachlorobutadiene
under the POPs Review Committee
of the Stockholm Convention

19 October 2012

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Executive summary

1. Hexachlorobutadiene (HCBD) is a halogenated aliphatic hydrocarbon mainly generated as a by-product in the manufacturing of chlorinated hydrocarbons. HCBD has experienced a variety of uses, spanning from an intermediate in chemical production to transformer, hydraulic or heat transfer liquid to a viticulture pesticide. Its use and production have ceased in the UN-ECE countries but information about ongoing application outside the UN-ECE is not currently available. The substance is still unintentionally released by industry, including during waste management.

2. HCBD is a lipophilic compound with a high vapour pressure and a Henry´s Law Constant that indicates volatilization from wet surfaces and water. Models show that a significant fraction of environmental HCBD will repartition into the atmosphere when released into water, and that almost all HCBD emissions into air will stay in the atmosphere.

3. Criteria for long-range transport of a chemical through the air are set to be greater than two days by the Stockholm Convention (Annex D criteria (d) iii). Predicted atmospheric half-lives for HCBD greater than one year consistently exceed the threshold of two-days set by the Stockholm Convention. With an atmospheric transport distance of more than 8 700 km, HCBD has a high potential to pollute remote areas. This assumption is supported by traces of HCBD in biotic and abiotic samples far from areas where the chemical has been used.

4. There are several lines of evidence for the persistence of HCBD in the environment. HCBD will not hydrolyse due to lack of hydrolysable functional groups. Data on photolysis are limited. Volatilisation is considered to be a major dissipation pathway from water and soil to the air compartment. Adsorption onto organic matter in soil and sediment will reduce bioavailability and therefore susceptibility to biodegradation. There is evidence that HCBD is not readily biodegradable and may not degrade under anaerobic conditions in soil. However, in one reactor study HCBD levels were reduced only under anaerobic conditions. It was shown, that if HCBD adsorbs to sediment it is not bio-available, which will lead to long term persistence in the environment. Findings on degradation pathways are somewhat contradictory.

5. Estimated half-lives in water range from 3 days to 12 months, exceeding the persistence threshold of two months, although there are indications that under favourable conditions faster degradation may be possible. Estimated half-lives in soil ranging from 4 to 26 weeks, reach the persistence threshold of six months. Half-life data for sediment are not available, although sediments are a sink for HCBD. Atmospheric half-life values consistently exceed by far two days, which gives evidence that HCBD persists in air. Monitoring data from remote regions add to the lines of evidence for the persistency of HCBD in the environment.

6. The bioconcentration potential of HCBD in aquatic organisms is confirmed by experimental data. In literature the bioconcentration factor (BCF) values range between 1 and 19,000 L/kg for fish, crustaceans, molluscs and algae. The wide range is explained with species differences in metabolism and differences in exposure concentrations. Evaluated BCF values for carp and fathead minnow in the range of 6,480 to 7,410 L/kg are available. Evaluated BAF values of 9,260 and 250,000 L/kg are available for crustaceans and a value of 17,360 L/kg for fish. There are limited and equivocal experimental and calculated data related to the biomagnification of HCBD. On the basis of measured BCF and BAF values of >5,000 L/kg it is concluded that HCBD has a potential for bioaccumulation.

7. HCBD is detected in abiotic and biotic media, even in remote areas such as the Arctic. HCBD was found in surface waters, drinking water, ambient air, aquatic and terrestrial organisms. HCBD levels in water and fish from European rivers (Rhine, Elbe) have decreased significantly over the last decades. Due to the scarcity of data it is difficult to identify a temporal trend for remote areas. Although recent (i.e. within the past 15 years) data on biota are very infrequent, HCBD contamination has been reported for Beluga blubber in 2003 (of up to 278 µg/kg lw) and for Polar bear fat (1–9 µg/kg ww) from 2002.

8. Experimental data on aquatic species revealed EC50 and NOEC values in the micro-gram per litre range which shows that HCBD is very toxic to aquatic organisms.

9. HCBD is toxic after repeated and chronic exposure at low exposure levels (i.e. 0.2 mg/kg). The target organ of toxicity is the kidney; biotransformation to reactive compounds leads to organ toxicity, genotoxicity and carcinogenicity after lifelong dietary exposure conditions. Exposure to HCBD and chemicals with similar mode of action has been shown to lead to additivity of toxic effects. Studies in laboratory rodents suggest gender differences i.e. higher female susceptibility with especially high susceptibility of female organisms at very young ages. No studies on effects on the immune system are available. It is known that HCBD is present in groundwater and drinking water at certain sites and relatively high degree of uncertainty inherent in the estimates of intake of HCBD in

food due to limited monitoring data is reported. Evidence of cancer in animals is sufficient to cause concern for populations that may be exposed to low levels of HCBD for long periods.

10. Based on the available evidence, HCBD is persistent, bioaccumulative and very toxic to aquatic organisms and toxic to birds. The comparison of effect data with monitoring data of marine sea water, freshwater as well as marine or freshwater sediments, indicates that the risk of significant adverse effects of HCBD to aquatic and sediment dwelling organisms is low but it cannot be excluded. Indeed, the level of uncertainty in identifying long-term risk according to the traditional risk assessment approach cannot be estimated with sufficient accuracy. In addition it should also to be taken into consideration that Arctic animals and top predators are exposed to a mixture of heavy metals and persistent organic substances.

11. HCBD is likely, as a result of its long-range transport, to lead to significant adverse human health and environmental effects such that global action is warranted.

1. Introduction

12. The European Union and its Member States submitted a proposal to list hexachlorobutadiene (HCBD) in Annex A, B or C of the Stockholm Convention on 10 May 2011 (UNEP/POPS/POPRC.7/3) together with a detailed dossier to support the proposal (UNEP/POPS/POPRC.7/INF/4).

13. HCBD is a halogenated aliphatic compound, mainly created as a by-product in the manufacture of chlorinated aliphatic compounds (most likely tri- and tetrachloroethene and tetrachloromethane). It has also been used as a pesticidal fumigant.

1.1 Chemical identity

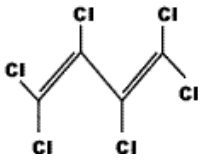
Name and registry number

Common name:	Hexachlorobutadiene
IUPAC Name:	1,1,2,3,4,4-hexachlorobuta-1,3-diene
Synonym:	HCBD; perchloro-1, 3-butadine; perchlorobutadiene; 1,3-hexachlorobutadine; 1,3-butadiene, 1,1,2,3,4,4-hexachloro-; 1,3-butadiene, hexachloro-; hexachlorobuta-1,3-diene;[1,2,3]
CAS registry numbers:	87-68-3
Common trade names:	C-46, Dolen-pur, GP40-66:120, UN2279.[4]

Structures

Molecular formula[1]:	C_4Cl_6, $Cl_2C{=}CClClC{=}CCl_2$
Molecular weight:	260.76 g/mol

Figure 1.1-1: Chemical structure



Physical-chemical properties

14. HCBD has a low water solubility and quite a high vapour pressure compared to other listed POPs (UNEP/POPS/POPRC.2/14/Add.2). The substance is lipophilic based on a log Kow close to 5 (cf. Table 1.1-1). The substance can volatilize due to its Henry's law constant from moist soil and water (HSDB, 2012). According IPCS (1994) it has a turpentine-like odour. Selected physical-chemical properties (majority of the values have been determined experimentally) are listed in Table 1.1-1.

1 Mackay et al. (2006)

2 UNEP/POPS/POPRC.7/INF/4

3 ACToR (2012)

4 IPCS (1994)

Table 1.1-1: Physical-chemical properties of HCBD

Melting Point (°C)	-21
Boiling Point (°C)	215[5]
Density (g/cm^3 at 20°C)	1.68[6]
Water solubility (mg/L at 25°C):	3.2 mg/L[7]
Vapour pressure (Pa at 20°C and 100°C)	20[8]and 2926[9]
Henry´s law constant (Pa m^3 /mol)	1044 (experimental), 2604 (calculated) [10]
Log Kow	4.78[11], 4.9[12]
Log Koa at 10°C	6.5[13]
Log Koc	Reported range: 3.7 to 5.4[14]
Physical state	Liquid

1.2 Conclusion of the Review Committee regarding Annex D information

15. The POPs Review Committee evaluated the proposal regarding HCBD (UNEP/POPS/POPRC.7/3) according to the requirements in Annex D of the Stockholm Convention at its seventh meeting in Geneva. In Decision POPRC-7/3 the Committee reached the conclusion that the proposal on HCBD fulfilled the screening criteria specified in Annex D. The Committee also decided to establish an ad-hoc working group to review the proposal further and prepare a draft risk profile in accordance with Annex E of the Convention.

1.3 Data sources

16. The draft risk profile is based on the following data sources:

(a) Proposal submitted by the European Community and its member States that are Parties to the Convention Proposal submitted (UNEP/POPS/POPRC.7/3, UNEP/POPS/POPRC.7/INF/4), 2011.

(b) Decision POPRC-7/3 of the POPs Review Committee, 2011.

(c) Information submitted by Parties and observers according to Annex E of the Convention: Azerbaijan, Bulgaria, Cameroon, Canada, China, Costa Rica, Estonia, Germany, Guatemala, Japan, Kiribati, Latvia, Mexico, Monaco, Myanmar, Netherlands, Norway, Poland, Romania, Sao Tome and Principe, Thailand, United States of America, International POPs Elimination Network (IPEN) & Alaska Community Action on Toxics, World Chlorine Council.

(d) This information is available on the Convention's website. (http://chm.pops.int/Convention/POPsReviewCommittee/POPRCMeetings/POPRC7/POPRC7Followup/HCBDAnnexEinformation/tabid/2465/Default.aspx).

(e) International Programme on Chemical Safety, Hexachlorobutadiene, Environmental Health Criteria 156, World Health Organization. Geneva, 1994. http://www.inchem.org/documents/ehc/ehc/ehc156.htm

(f) Toxicological profile for hexachlorobutadiene, United States of America Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, 1994. http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=865&tid=168

(g) International Agency for Research on Cancer, IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 73, World Health Organization. Geneva, 1999 http://monographs.iarc.fr/ENG/Monographs/vol73/volume73.pdf

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5 Horvath 1982, Lide 2003, all cited in Mackay et al. 2006

6 Horvath 1982 cited in Mackay et al. 2006

7 Shake flask-HPLC, Banerjee et al. (1980) cited in SRC PhysProp Database (2012)

8 Person and McConell (1975) cited in Mackay et al. (2006)

9 Environment Canada (1999)

10 Warner et al. (1987) cited in Mackay et al. (2006)

11 Shake flask-HPLC Banerjee et al. (1980), Sangster (1993), Hansch et al. (1995), cited (and recommended value) in Mackay et al. (2006)

12 Shake-flask-GC, both phases, Chiou (1985), cited in Mackay et al. (2006)

13 Vulykh et al. (2005)

14 HSDB (2012)

(h) Environment Canada (1999) Priority Substance List Assessment Report, Hexachlorobutadiene, ISBN 0-662-29297-9

(i) Euro Chlor Risk Assessment for the Marine Environment OSPARCOM Region - North Sea: Hexachlorobutadiene, 2002.

(j) NITE - Incorporated Administrative Agency, National Institute of Technology and Evaluation, Japan. Chemical Management Field. Information about the status of the implementation of GHS in Japan. Results of the GHS Classification. HCBD: ID 1012 http://www.safe.nite.go.jp/english/ghs_index.html

(k) US EPA, Health Effects Support Document for Hexachlorobutadiene, EPA 822-R-03-002, United States Environment Protection Agency. 2003. http://www.epa.gov/ogwdw/ccl/pdfs/reg_determine1/support_cc1_hexachlorobutadiene_healtheffects.pdf

(l) California EPA, Evidence on the carcinogenicity of 1,3-hexachlorobutadiene, December 2000. Reproductive and Cancer Hazard Assessment Section. Office of Environmental Health Hazard Assessment. California Environmental Protection Agency. http://ntp.niehs.nih.gov/ntp/htdocs/Chem_Background/ExSumPDF/Hexachlorobutadiene.pdf

17. In addition to these information sources, a literature search of public data bases was conducted that focused on recent scientific literature. The following databases were used: ACToR database (http://www.epa.gov/actor/), Pubmed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?DB=pubmed), SRC databases (http://www.srcinc.com/what-we-do/free-demos.aspx), OECD eChemPortal (http://www.echemportal.org/echemportal/ index?pageID=0&request_locale=en), TOXNET (http://toxnet.nlm.nih.gov/), The Carcinogenic Potency Database (http://potency.berkeley.edu/cpdb.html), NITE DataBase (http://www.safe.nite.go.jp/english/db.html), GESTIS (http://www.dguv.de/ifa/en/gestis/stoffdb/index.jsp), WHOLIS WHO (http://dosei.who.int), IPCS Inchem (http://www.inchem.org/), PAN pesticide database (http://www.pesticideinfo.org/), Google scientific search (http://scholar.google.com), Scirus publication search (http://www.scirus.com).

18. In general search terms include the chemical name or CAS number and/or a combination of technical terms because of the multiplicity of entries. For the same reason updated scientific articles were also preferentially selected. The reports listed above contained individual references which have not been listed specifically in this draft risk profile, unless otherwise stated.

1.4 Status of the chemical under international conventions

19. HCBD is subject to a number of international treaties and regulations:

(a) In December 2009 HCBD has been proposed according to Decision 2009/1 to amend Annex I (prohibition of production and use) of the UNECE Protocol on Persistent Organic Pollutants (POPs) under the Convention on Long-Range Transboundary Air Pollution. The amendment will come into force when 2/3rd of the Parties have adopted the amendment.

(b) The UN-ECE (United Nations Economic Commission for Europe) has included HCBD in Annex II of the Protocol on Pollutant Release and Transfer Registers (PRTR) to the AARHUS Convention on access to Information, Public Participation in Decision-making and Access to Justice in Environmental Matters.

(c) HCBD is currently under a review process by the Chemical Review Committee (CRC) for inclusion under the Rotterdam Convention. The review process was initiated by notifications of final regulatory action to ban or severely restrict HCBD by Canada and Japan (http://www.pic.int) (Thailand, 2011)

(d) Within the Great Lakes Bi-national Toxics Strategy, a U.S.-Canada agreement under the Great Lakes Water Quality Agreement, HCBD is identified as a Level II Substance (US EPA, 2012b)

(e) In the European Union, Decision No 2455/2001/EC on a first list of priority substances of the adopted EU Water Framework Directive 2000/60/EC listed HCBD in its Annex. In addition HCBD is regarded as priority hazardous substance thus it is subject to a step-wise cessation or phasing out of discharges, emissions and losses.

(f) HCBD is on the List of Substances of Possible Concern, Section B under the OSPAR Commission for the Protection of the Marine Environment of the Northeast Atlantic. Section B lists

substances which are of concern for OSPAR but which are adequately addressed by European Commission initiatives or other international forums.

(g) HCBD has been assessed by the European PBT working group under Council Regulation (ECC) No 793/93. It was concluded that HCBD fulfils the PBT and vPvB criteria as well as the POP screening criteria[15].

2. Summary information relevant to the risk profile

2.1 Sources

2.1.1 Production, trade, stockpiles

20. To date, HCBD is no longer intentionally produced in the UN-ECE region including the USA (terminated around 1970: Mumma & Lawless 1975) and Canada (Lecloux, 2004). Its intentional production in Europe ended in the late 1970s (Van Der Honing 2007) and it was never generated as a commercial good in the US or Canada (Lecloux, 2004), at least not in commercial quantities (ATSDR, 1994). Data about intentional production outside the UN-ECE region are not available (Lecloux, 2004). However, monitoring data from China (Li et al., 2008) and Taiwan (Juang et al., 2010) suggest that (by)production has continued at least until recently. Worldwide production of HCBD was estimated at 10,000 tons in 1982, but HCBD generated as waste by-product was much higher: 14,000 tons (1982) in the USA alone (IPCS, 1994 as cited in: Lecloux, 2004).

21. HCBD is still unintentionally generated during the production of chlorinated hydrocarbons, particularly of perchloroethylene, trichloroethylene and carbon tetrachloride (a.k.a tetrachloromethane, Halon 104, Freon 10 etc.): RIVM 2001, Lecloux 2004. It can also be formed during the production of vinyl chloride, allyl chloride and epichlorohydrin although a dossier prepared for the European chlor-alkali industry considers this extremely unlikely from a technological point of view (Lecloux, 2004). In the UN-ECE region, the combined production of perchloroethylene and tetrachloromethane was estimated to be the only remaining significant by-production of HCBD which is generally destroyed or recycled in the plant (Lecloux, 2004). However, European chlorine industry concede that a total cessation of industrial (HCB and) HCBD emissions is unrealistic as this could lead to plant closures and significant losses in jobs and business (BiPRO study, commissioned by Euro Chlor; Euro Chlor annual report 2006–2007). In the US, 9.95–10.31 Mio pounds (4 515–4 678 metric tons) of annual HCBD generation were reported for the toxics release inventory from 2005 to 2007. This represents an increase from the 8.4 million pounds reported in the 1997 Toxics Release Inventory (TRI) as total production-related waste in the U.S. (Rabovsky, 2000). In 2007, less than 0.1 % (ca. 4.5 metric tons), each, of the generated HCBD volume were disposed of or burned for energy recovery. Virtually all HCBD was treated, mostly on site. At the same time, 1.63 Mio pounds HCBD-containing hazardous waste was reported in the US, more than half of which was used for reclamation or (mostly energy) recovery. A further 41.5 % was destroyed or treated prior to disposal, and 5.3 % (86 773 pounds = 39.4 metric tons) were disposed of in landfills (US EPA 2010). Moreover, aluminium plasma etching in the semiconductor manufacture was recognised as an HCBD source (US EPA, 2000).

22. There are no natural sources of HCBD in the environment (Environment Canada 1999).

23. There are still considerable problems with waste dumps. One example for HCBD stockpiles in waste dumps is the Devil's swamp area in Louisiana (US). At the Orica dump in Australia large quantity of HCB contaminated with HCBD and other organochlorines are stored in drums (approximately 20,000 tonnes) (Rae, 2012). The examples document the potential of HCBD releases from former waste dumps. At Weston Quarries (UK), properties built on quarry spoil next to the waste dump had to be demolished for excessive indoor HCBD concentrations (Report of the Nicole workshop, 2004, Barnes et al., 2002, Crump et al., 2004). There is no insight in the total amount of waste sites worldwide, nor on their releases (Crump et al., 2004).

2.1.2 Uses

24. The large amounts of HCBD generated as a by-product were an incentive to find industrial applications (Lecloux, 2004). HCBD was used as intermediate in chemical industry or as a product. It was applied as a solvent (for rubber and other polymers); as a "scrubber" to recover chlorine-containing gas or to remove volatile organic components from gas; as hydraulic, heat transfer or transformer fluid; or in gyroscopes (Lecloux, 2004). HCBD was also used in the production of aluminium and graphite rods (WCC, 2002).

15 http://esis.jrc.ec.europa.eu/doc/PBT-evaluation/PBT_sum060_CAS_87-68-3.pdf

25. Apart from technical applications, HCBD was used as an insecticide in vineyards in the former Soviet Union, and to a lesser extent in Mediterranean European countries and in Argentina (Lecloux, 2004). It is unclear, whether the use as a fumigant for treating grapes has also stopped outside the EU (Van Der Honing, 2007). In the former Soviet Union, HCBD was also used as a fungicide (Bosma, 1994).

26. The ECHA C&L inventory[16] indicates that there are 31 notifiers for HCBD. This suggests that they produce or import or are interested to produce or import HCBD and put it on the market within Europe.

2.1.3 Releases to the environment

27. The information of the amounts released into the environment is scarce and old. According to National Science Foundation (1975) as cited in ATSDR (1994), 0.1 million pounds (=454 tons) of the HCBD produced in the US in 1975 were released into the environment. In 1987, 1,600 kg HCBD were released into the air, with another 86 kg discharged into the water and 32 kg injected into the ground as a way of waste disposal (EPA TRI as cited by IARC, 1999). Improved destruction or in-process recycling of HCBD during industrial production can have contributed to this large drop of releases from 1975 to 1987. By 1996, US releases were 1,100/120/430 kg (air/water/underground injection): National Library of Medicine (1998) as cited in IARC (1999). In 1990, US industries reported releases of 2.7 tons (EPA TRI, 1992, as cited in ATSDR, 1994). The 1997 Toxics Release Inventory (TRI) reported 8.4 million pounds of HCBD as total production-related waste in the U.S. (Rabovsky, 2000), but the actual emissions may be higher as the TRI only accounts for emissions above a certain threshold. On a local level, Chan & Kohli (1987) estimated an annual input to the St. Clair river in Canada of 240 kg for 1985.

28. The atmospheric burden of HCBD in the 1980s had been estimated to be 3.2 and 1.3 million kg/year for the northern and southern hemispheres, respectively (Class & Ballschmiter, 1987, as cited in ATSDR 1994).

29. In 2000, emission of HCBD in UN-ECE-Europe was estimated at 2.59 tons, 97% of which were attributed to magnesium production (Van Der Gon et al., 2007).

30. According to Euro Chlor (2007), a complete cessation of the unintentional by-products HCBD is economically unrealistic. In 1997, European chlorine industry emitted two kg HCBD into the air and 100 kg into water (WCC, 2002), and during 2001–2010 the average annual HCBD releases to air were 0.91 kg and to water 78.7 kg, estimated in the Euro Chlor COCEM project (WCC 2011). Estimated releases (to water only) from EU industry[17] including waste management for 2007–09 were in the range of 120–149 kg/y (cf. Figure 2.1.3-1). Actual industrial emissions are perhaps higher than recorded by the EU PRTR inventory mechanism, because the reporting threshold of 1 kg/y/facility is high compared to the cumulative emission reported. The PRTR data correspond to the annual industrial release of 140 kg/y estimated by Haskoning (2003). Questionnaires completed by several EU-countries indicate industrial emissions to surface water of 1.7 kg/y from chemical industry and 5.1 kg/y from plastics manufacturing. Pulp and paper industry contributes with 0.1 kg/y and releases from landfills with another 1.0 kg/y (ECOLAS 2005). Total industrial releases in this study were 10.6 kg/y, which is low compared to the EU-wide values mentioned above: the response rate (i.e., available inventory data) for the ECOLAS survey, however, was max. 48%, and only emissions to surface water were accounted for (ECOLAS 2005).

[16] http://echa.europa.eu/web/guest/regulations/clp/cl-inventory

[17] EU27 plus Switzerland, Iceland, Liechtenstein, Norway, Serbia; emissions above the threshold of 1 kg/a per facility reported by 15 facilities from Belgium, Czech Republic, France, Italy, Poland and United Kingdom.

Figure 2.1.3-1: European HCBD releases from industrial activities in 2009 (source: EEA, 2012a)

Pollutant releases / Activities

Pollutant: Hexachlorobutadiene (HCBD)
Year: 2009
Area: All Reporting States for E-PRTR
Facilities: 15

All values are yearly releases.

Contents:
Summary
Activities
Areas
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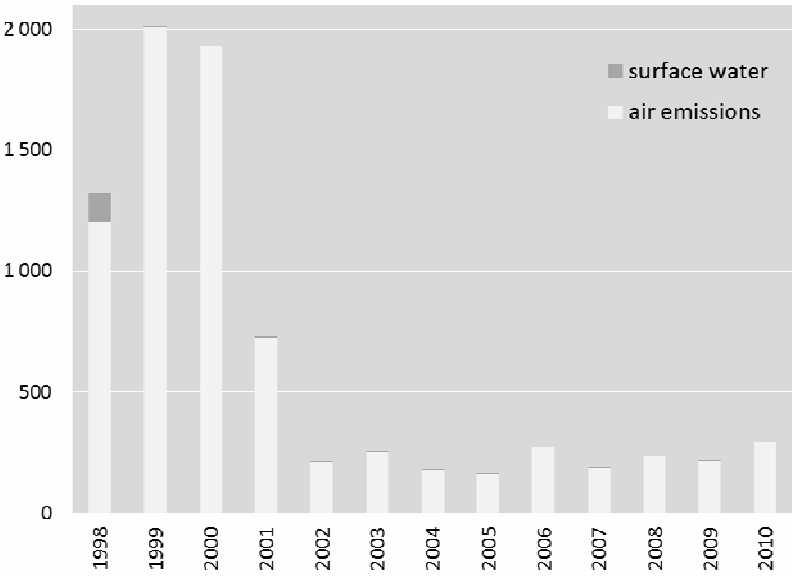
Facilities
Confidentiality

Releases per industrial activity		Facilities	Air	Water	Soil
1 Energy sector	Total	1	-	1.10 kg	-
	Accidental	0	-	0	-
1.(a) Mineral oil and gas refineries	Total	1	-	1.10 kg	-
	Accidental	0	-	0	-
4 Chemical industry	Total	2	-	41.1 kg	-
	Accidental	0	-	0	-
4.(a) Industrial scale production of basic organic chemicals	Total	2	-	41.1 kg	-
	Accidental	0	-	0	-
4.(a).(viii) Basic plastic materials (polymers, synthetic fibres and cellulose-based fibres)	Total	2	-	41.1 kg	-
	Accidental	0	-	0	-
5 Waste and waste water management	Total	12	-	78.0 kg	-
	Accidental	0	-	0	-
5.(a) Disposal or recovery of hazardous waste	Total	1	-	6.32 kg	-
	Accidental	0	-	0	-
5.(f) Urban waste-water treatment plants	Total	11	-	71.6 kg	-
	Accidental	0	-	0	-
Total	Total	15	-	120 kg	-
	Accidental	0	-	0	-

Of the same order of magnitude are the current HCBD releases to air and surface waters in the USA (cf. Figure 2.1.3-2; original data converted from pounds to kilograms: 1 lb = 0.4536 kg):

Figure 2.1.3-2: US HCBD releases (kg) to air and surface water (data source: US EPA, 2012)



31. There is still a potential of unintentional release of HCBD from production of chlorinated solvents in most parts of the world (Lecloux, 2004; Norway, 2011). Reports from Tamil Nadu province, South India (IPT 2005, Narayan 2011) suggest substantial[18] ongoing HCBD emissions from industry despite the lack of corresponding data for, e.g. Asia. Data of Juang et al. (2010) indicate that there are still considerable sources in SE Asia.

[18] "Substantial" in this context means "non-negligible", i.e. giving rise to environmental HCBD levels which are, spatially and technically, attributable to known industrial plants and are too high to safely exclude ecological or health risks; while at the same time it seems unlikely that such industrial releases are an exceptional phenomenon confined to said Indian province within the large Asian area for which no emission data are available.

32. While there are no intentional uses of HCBD in Canada, it was estimated in 2004 that HCBD may still be released from unintentional sources, including contaminants in chlorinated solvents (estimated maximum of 45g/year) and ferric/ferrous chloride (estimated maximum of 10 g/year) and byproducts generated by the magnesium industry (estimated maximum of 7 g/year). Other possible sources could include hazardous landfill leachates (Environment Canada 2004).

33. HCBD can also leach from waste landfills (Environment Canada, 1999). Recent measurements showed concentrations in the range of 0.008–0.08 µg HCBD per litre leachate from Polish municipal waste landfills (Matejczyk et al., 2011). Nevertheless, the overall shortage of data, particularly from non-UNECE countries and for HCBD emissions from waste, makes it difficult to rank current HCBD sources. For the EU, emissions from waste management are of the same order of magnitude and usually (yearly totals 2007–2009) larger than those from industry. Contrarily, for US industry, TRI data show that on site air emissions are almost six times the volume disposed (entirely in landfills).

34. In conclusion while in the UNECE-region, releases of by-produced HCBD have decreased by orders of magnitude over the last decades – but still continue – there is a crucial lack of information about by-production in non-UNECE countries. Reductions in the UNECE-region can be expected to be largely due to technical investments (recycling or destruction of the by-product on site, waste management), but the adoption of equally strict standards in other countries is not granted, and in fact is refuted by reports on current HCBD pollution in e.g. India.

35. HCBD waste was generated in large volumes in the past. Regardless of current waste management standards, notorious examples of HCBD waste dumps which now require remediation demonstrate the risk of inherited HCBD pollution. Again, little can be said about legacy HCBD stocks nor even about current HCBD releases from waste in non UNECE-countries. However, in some cases HCBD stored in contaminated environment was estimated at considerable volumes: Krantzberg et al. (1999) considered it likely to have around 400 kg of HCBD bound in contaminated sediment in the Great Lakes region.

2.2 Environmental fate

2.2.1 Persistence

Abiotic degradation

36. HCBD is not expected to undergo hydrolysis due to the lack of hydrolysable functional groups. According to IPCS (1994) HCBD absorbs light within the solar spectrum. Therefore degradation by direct photolysis may occur. IPCS (1994) mentions that mineralization >50% occurred in an experimental set-up using HCBD adsorbed to silica gel under the simulation of tropospheric UV light after 6 days. However the results (based on the study design) do not allow an estimation of the relevance or a degradation rate constant for environmental compartments.

37. As stated in Environment Canada (1999) HCBD persists in air until it is either degraded photochemically or deposited in water or soil when adsorbed on particulate matter. The main removal process from the atmosphere is by degradation at a rate solely defined by the rate of its gas-phase interaction with OH radicals according to the MSCE-POP (multicompartment POP) transport model (Vulyk et al., 2005).

38. Estimated half-lives based on degradation by reaction with hydroxyl radicals and ranging from 60 days to 3 years are reported, as well as half-lives of 840 days (2.3 years) in the northern hemisphere and 290 days (0.8 years) in the southern hemisphere, based on a hydroxyl radical rate constant of $2x10^{-14}$ cm^3/molecule/sec and a hydroxyl radical concentration of $7x10^5$ and $17x10^5$ molecules /cm^3, respectively (Environment Canada, 1999).

39. In UNEP/POPS/POPRC.7/INF/4 estimated half-lives in air of 365 days, based on a 12h day and $1.5x10^6$ OH/cm^3 and half-lives of 582 and 194 days, based on $7x10^5$ OH/cm^3 and $17x10^5$ OH/cm^3, respectively, are cited.

40. Mackey et al. (2006) report a half-life in air of 0.3 – 3.3 years based on an estimated rate constant for vapour phase reaction with OH radicals. HCBD can also be depleted by ozone, though this is of minor relevance based on a predicted ozone reaction half-life of 165,500 days (OECD, Canadian Categorization Results 2012).

41. HSDB (2012) states an estimation of tropospheric half-life on basis of monitoring data at remote sites of 1.6 years in the northern hemisphere and 0.6 years in the southern hemisphere.

42. According to Howard (1991), estimates for the rate of photochemical oxidation of HCBD by the hydroxyl radical could be based on the measured rate constant for the reaction of the hydroxyl

radical with tetrachloroethylene. The preferred measured rate constant for photochemical oxidation of this homologous perchlorinated olefin by the hydroxyl radical at 298 K is 1.6×10^{-13} cm^3/molecule/sec (Atkinson et al. 2008).

43. In conclusion HCBD is susceptible to photolysis and photooxidation by OH-radicals and ozone. However experimental data on direct photolysis are limited. Measured data (rate constant) on a homologous substance indicate for HCBD a half-life in air >2 days. The major removal process from HCBD in the atmosphere is predicted to occur via oxidation by OH-radicals. Predictions and mass-balance calculations based on monitoring data indicate a very long half-life in the atmosphere i.e. >1 year.

Biotic degradation including information on degradation pathways

44. According to UNEP/POPS/POPRC.7/INF/4, calculation with Syracuse Biowin model (linear and non-linear) results in the following prediction: HCBD does not biodegrade fast; ultimate biodegradation timeframe: recalcitrant; primary biodegradation timeframe: weeks. OECD, Canadian Categorization Results (2012) lists a predicted ultimate degradation half-life of 182 days and a probability of biodegradation based on MITI database of 0.0001 calculated with the Biowin model v 4.01. Japan (2011) submitted results from a test on ready biodegradability according to OECD TG 301C (adapted for volatile substances). Biological Oxygen Demand (BOD) values after 28 days were 6 – 33% (not readily biodegradable). High adsorption was detected in the experiment. According to HSDB (2012) high adsorption (based on the high Koc values) reduces bioavailability and therefore susceptibility to degradation.

45. In UNEP/POPS/POPRC.7/INF/4 it is stated that HCBD is recalcitrant under aerobic conditions while under anaerobic conditions reductive dechlorination is observed. On basis of the structure of HCBD it is expected that a dechlorination step is necessary before aerobic biodegradation can occur. However, Taylor *et al.* (2003) cites evidence that HCBD may not degrade under anaerobic conditions in soil. Bosma et al. (1994) found removal under anaerobic conditions (ascribed to anaerobic bacterial activity) after 4 months of acclimation, but no removal over three years under aerobic, not reductive conditions. The main degradation product in this study was 1,2,3,4-tetrachloro-1,3-butadiene (>90%), but no half-lives were calculated. This antifungal agent may then be degraded further aerobically. Extensive sequential reductive dechlorination of HCBD under anaerobic conditions was also reported by Booker et al. (2000). The main degradation products were isomers of tri- and dichloro-1,3-butadiene and traces of a monochloro-1,3-butadiene isomer. James (2009) showed that non-specific bacteria from activated sludge are able to anaerobically dechlorinate HCBD to chlorine-free C4 gases, namely 1,3-butadiene. According to IARC (2012) 1,3-butadiene is carcinogenic to humans (Group 1)

46. In HSDB (2012) it is stated that biodegradation takes place in aerobic and anaerobic aqueous batch tests. Tabak et al. (1981) found that static cultures of domestic wastewater inoculates were able to completely remove concentrations of 5 or 10 mg/L HCBD within seven days of incubation by bio-oxidation (cultivation flasks were sealed with glass stoppers to avoid volatilisation losses). Schröder (1987) found in an 8 days pilot low-loaded biological sewage treatment plant under aerobic conditions approximately 72% adsorption, 8% degradation, 15% volatilisation and 5% in the effluent wastewater.

47. In UNEP/POPS/POPRC.7/INF/4 a half-life in water of 30 days is cited without offering further data. According to Environment Canada (1999) degradation in water under anaerobic conditions is very slow and half-life in water is proportional to the amount of organic matter. Zoeteman et al. (1980) estimated disappearance half-lives (including volatilisation and adsorption) from monitoring data, obtaining 3–30 days and 30–300 days for rivers and lakes/groundwater, respectively. For the shorter half-life in river water, they assumed enhanced turbulence to be a major factor, increasing volatilisation, biodegradation and, possibly, photolysis. This is in line with HSDB, 2012 that suggest that volatilization will be a major pathway for dissipation from water according to the Henry´s Law constant. Mackey et al. (2006) cite an aqueous aerobic biodegradation half-life of 4 weeks – 6 months based on monitoring and acclimated aqueous screen test data. On the basis of this value the anaerobic half-life for surface water is given with 16 weeks – 2 years and for groundwater with 8 weeks - 12 months. Therefore, HCBD meets the threshold for persistence in water.

48. According to Environment Canada (1999) disposal to water has the potential for significant transport of HCBD to air or sediment. Prytula et al. (1996) found that most of the adsorbed HCBD was not bioavailable which will lead to long term persistence in natural sediments with desorption being the rate-determining step. Adsorption to sediment is indicated by the high reported Koc values. Sediments are a sink for HCBD in aquatic environments (Environment Canada, 1999).

49. There are only scarce data on persistence in soil. According to HSDB (2012) HCBD has low to no mobility in soil, expected from its estimated log Koc values (cf. Table 1.1-1), which will reduce its bioavailability. Volatilisation from soil is expected to be a major fate process. According to Environment Canada (1999) HCBD was found to be mobile in sandy soils -- in contrast to what has been stated before in this paragraph – in a dune infiltration study, with an average residence time of 100 days and little biodegradation. HCBD was also examined in soil-plant systems. After 2 years 4% of the applied radioactivity was bound in the non-extractable residues in the top 50 cm of the soil, which, according to Environment Canada (1999), suggest a potential of long-term accumulation. The remaining 96% were believed to have volatilized.

50. In UNEP/POPS/POPRC.7/INF/4 it is reported, that HCBD readily breaks down in soil (mainly under aerobic conditions). Environment Canada (1999) as well as Taylor *et al.* (2003) state that HCBD may not degrade in soil under anaerobic conditions. Mackey et al. (2006) cite an estimated half-life in soil of 4 weeks to 6 months based on estimated aqueous aerobic biodegradation half-life.

51. Vulykh et al. (2005) calculated with the MSCE-POP model the overall persistence expressed as half-life in the environment. It also showed that the value of the HCBD half-life in the atmosphere is most essential for the evaluation of its residence time in the environment. The half-life in the environment was 13 months, whereas for different compartments air, water and soil values of 14, 3 and 6 months were obtained.

52. There are several lines of evidence available to conclude on the persistence of HCBD. HCBD is not expected to hydrolyse based on its chemical structure. There are limited data on direct photolysis. There is empirical evidence that HCBD is not readily biodegradable and some estimated half-lives in water exceed the persistence threshold of two months, although there are indications that under favourable conditions faster degradation may be possible. Estimated half-lives for soil reach the persistence threshold of six months. Under anaerobic conditions HCBD may not be degraded and it is likely that HCBD exceeds the threshold in anaerobic soil. Thus persistency criteria may only be met partly for the soil compartment. However the available degradation data in soil are scarce. Half-life data for the sediment are not available.

2.2.2 Bioaccumulation

53. Two complementary sources of information have been analysed for assessing the bioaccumulation and biomagnification potential of HCBD: the screening assessment based on physical-chemical properties and the analysis of experimental data as well as estimations, including bioconcentration, bioaccumulation and biomagnification. The key elements of these assessments are presented below.

Screening assessment based on physical-chemical properties

54. The reported log K_{ow} for HCBD is 4.78. On basis of this log Kow a BCF of 2,307 L/kg for fish was calculated according to Veith et al. (1979) cited in the Technical Guidance Document on Risk Assessment (TGD, 2003), which is within the range of measured values.

Bioconcentration, biomagnification and bioaccumulation in aquatic species

55. In literature BCF values range from 71 -17,000 L/kg based on wet weight for flow through laboratory tests with algae, crustaceans, molluscs and fish in fresh and marine waters (IPCS, 1994). For fish BCF values from 1 – 19,000 L/kg on a whole body basis are reported in Environment Canada (1999). It also states that HCBD does not accumulate in plants (Environment Canada, 1999). The wide range of values was explained by species differences in metabolism and differences in exposure concentrations (ATSDR, 1994).

56. The NITE database (NITE, 2012) reported BCF values from a study with Carp *(Cyprinus carpio*) with a lipid content between 5.1% to 6.2 % of 6,280 and 7,720 L/kg, at exposure concentrations of 0.83 and 0.087 µg/l. For fathead minnow a BCF value of 6,918 L/kg is cited in (HSDB, 2012). For invertebrates a maximum BCF value of 2,000 L/kg in mussel *(Mytilus edulis)* is given in Environment Canada (1999). According to Gobas et al. (2009) this indicates that HCBD is possibly bioaccumulative.

57. IPCS (1994) states that mean BCF values in oligocheate worms in sediment in Lake Ontario were 29,000 L/kg based on dry weight of which about 8% is lipid (Oliver, 1987). Biomagnification was not observed in this study (HSDB, 2012).

58. As stated in IPCS (1994) observed bioaccumulation factors (BAF) based on wet weight in plankton, crustaceans, molluscs, insects and fish in surface waters are comparable to those observed in the laboratory and range from 33 to 11,700 L/kg. In a report (The Netherlands, 2012) three studies

were examined with BAF values between 6,760 L/kg lipid – 575,000 L/kg lipid. Within these studies one was identified as valid (Oliver et. al, 1988). In this study BAF values (normalised to 5% lipids) for the crustaceans *Mysis relicta* and *Pontoporeia affinis* of 9,260 L/kg and 250,000 L/kg were found. For the fish *Cottus cognatus* a BAF of 17,360 L/kg was found. Additionally, in the report (The Netherlands, 2012) a BAF value of 22,230 L/kg was calculated on basis of the higher BCF value of 7,410 L/kg for Carp (Japan, 2012) and on basis of a default BMF value of 3 (between the value of 2 for log Kow of 4.78 and the value of 10 for the BCF of 7,410 L/kg) according to Technical Guidance Document on Risk Assessment (TGD, 2003).

59. Environment Canada (1999) states, that HCBD does not biomagnify because of its fast depuration rate. The substance is eliminated from goldfish *(Carassius auratus)* with a half-life of 6.3 days. This is confirmed by IPCS (1994) where two fish studies are cited in which biomagnifications could not be observed. Kelly *et al.* (2007) calculated BMF-values for HCBD (based on log K_{ow}) in invertebrates, fish, reptiles, amphibians, birds, mammals and humans. These values are <1 for all of these organisms. In the Netherlands, 2012, a BMF of 3 was calculated on the basis of the BCF in accordance with the methodology of the TGD (2003)) which indicates a potential of biomagnification. However no trophic transfer is demonstrated since no food chain studies are available.

60. Measured data from aquatic species show BCF or BAF values >5,000 L/kg, clearly fulfilling the criteria in Annex D.

2.2.3 Potential for long-range environmental transport

61. Several information sources can be used for the assessment of the potential for long-range transport for HCBD: physical-chemical properties, modelling and the review of existing monitoring data in remote areas.

Screening of physical-chemical properties

62. The combination of volatility, sufficient atmospheric persistence (cf. section 2.2.2) and the occurrence of HCBD in biota from remote areas indicate a significant potential for long-range transport.

LRT model predictions

63. The MSCE-POP model (Vulykh et al., 2005), a multicompartment chemistry transport model, uses a benchmark approach to overcome model dependency of numerical values. Benzo(a)pyrene and hexachlorobenzene (HCB) were selected as benchmark substances. For their model, they assume HCBD half-lives of 14, 3, and 6 months in air, water and soil, respectively. The model predicts an atmospheric travel distance (TD; the distance after which the concentration has fallen beneath l/1000 of that at the source) of 8,784 km, and an atmospheric half-life of 118 days. The authors emphasize that a TD of this magnitude causes atmospheric HCBD pollution to spread over extremely long distance. Using HCB and BaP as benchmark substances in the same model, the authors estimate an environmental half life of HCBD which is less than half that predicted for HCB and about five times as long as that of B(a)P. MacLeod et al. (2007) identified a high LRT potential for HCBD with the OECD multimedia fate model assuming as input parameter predicted half lives (hours) of 9100, 1700 and 1700 for air, water and soil. Moreover the chemical partitions nearly completely to air in the model calculation, and thus fate processes in air determine its behaviour.

64. The long half-life and TD of atmospheric HCBD are of particular concern because modelling results from different authors show that a significant fraction of HCBD releases ends up in the atmosphere, unless released into soil. The steady state model EQC Level III used by Environment Canada and US EPA predicts more than 98% of atmospheric releases remain in the atmosphere, about 1% in soil and less than 1% in water and sediments. From releases into water, still 15 % will be found in the air, and another 15 % and 1 % in sediments and soil, respectively. Only when release into soil, about 99% of the contamination will be found in the soil and about 1% in air (DMER and AEL, 1996 modelling for and cited in Environment Canada, 1999). However this is not in line with the study reported in HSDB (2012) that suggested 96% loss from a soil-plant system.

65. Other sources report an air:water:solid partitioning of 78:2:20 or predict a theoretical distribution of > 99% in air (ECETOC 1988 and NORDIC 1988 as cited in SYKE 2012). According to IPCS (1994) intercompartmental transport occurs chiefly by volatilisation, adsorption on particulate matter and subsequent deposition or sedimentation.

66. HCBD was among the chemicals identified for inclusion in the Swedish long-term monitoring program based on empirical data of its overall frequency of detection in air and deposition, persistence in air, assessment of bioaccumulation, and whether the substance has been detected in remote air

and/or deposition samples. HCBD was included in the final ranking list of chemicals prioritized for long-term atmospheric monitoring because "these chemicals have properties which generate high potential for long-range transport and bioaccumulation and have also frequently been detected in atmospheric and/or deposition samples analyzed within the Swedish screening programs." (IPEN 2011, Palm-Cousins et al. 2011).

Confirmation based on measurements in remote areas

67. Belfroid et al. (2005) cite the work of Kaj & Palm (2004) and Kaj & Dusan (2004) who traced HCBD in air and atmospheric deposition in Sweden but not in sewage sludge, sediment, mussel or fish. They also refer to Vorkamp et al. (2004) who found HCBD in Greenlandic terrestrial mammals and birds, marine invertebrates, fish and mammals, and seabirds. Polar bear samples from Svalbard island also contained HCBD (Gabrielsen et al., 2004). Belfroid et al. (2005) emphasize that these positives came from regions where HCBD was never used, which is evidence of long-range transport of HCBD.

68. Earlier evidence of long-range transport was found by Murdoch et al. (1992) with sediment data from the Great Slave Lake in the Northwest Territories of Canada ranging in concentration from 0.01-0.23 ng/g.

69. In conclusion HCBD has a strong potential for long-range atmospheric transport as shown by models (half lives between 60 days and more than three years) and empirical evidence (occurrence of HCBD in biota and air from background sites).

2.3 Exposure

2.3.1 Environmental monitoring data

70. Recent (i.e. within the past 15 years) monitoring data are scarce. Table 2.3.1-1 gives examples of current HCBD levels in various media, observed in Estonia (Estonia, 2011). Table 2.3.1-2 lists values reported for biota in the EU region.

Table 2.3.1-1: HCBD concentrations in the Estonian environment (source: Estonia 2011)

Type of sample	Hexachlorobutadiene concentration	Number of samples	Year
Freshwater	<0.003 µg/l	14	2011
Freshwater	0.006 – 0.01 µg/l	7	2011
Marine waters	< 0.003 µg/l	6	2011
Marine waters	0.0002 – 0.01 µg/l	5	2011
Bottom sediments	< 1 µg/kg dw	36	2011
Biota (Perca fluviatilis) liver	< 0.05 µg/kg tissue ww	2 (composite sample)	2011
Biota (Perca fluviatilis) liver	0.07 – 0.38 µg/kg tissue ww	9 (composite sample)	2011
Biota (Perca fluviatilis) muscle	0.03 – 0.24 µg/kg tissue ww	11 (composite sample)	2011
Waste-water (effluent)	< 0.1 µg/l	10	2010
Freshwater	< 0.1 µg/l	16	2010
Stormwater	< 0.1 µg/l	29	2008
Stormwater	0.28 µg/l	1	2008

Table 2.3.1-2: HCBD concentrations in biota

country	year	species	sample size	concentration range [µg/kg]	base	source
Svalbard	2002	polar bear	15	1.2–8.9	wet weight (ww)	Gabrielsen et al. 2004
Greenland	1999–2001	terrestrial animals	17 (var. tissues/individual)	n.d. – 4.9	lipid weight (lw)	Vorkamp et al. 2004
		marine invertebrates	4	n.d.–0.57		
		marine fish	16 (var. tissues/individual)	n.d.–2.6		
		seabirds	8 (var. tissues/individual)	n.d.–3.4		
		marine mammals	25 (var. tissues/individual)	n.d.–0.8		
Spain	2005–06	*Crassostrea angulata*	3	< 0.07 LOD	wet weight	EEA 2012b
Denmark	2000	*Delphinapterus leucas*	45	< 8.22		
Denmark	2000	*Gadus morhua*	12	< 8.22		
Denmark	2000	*Mallotus villosus*	10	< 8.22		
Denmark	2000	*Monodon monoceros*	3	< 8.22		
Denmark	2000	*Myoxocephalus scorpius*	74	< 0.175 – < 8.22		
The Netherlands, UK, Spain	2002–09	*Mytilus edulis*	62	0.01 – < 0.4		
Denmark	2000	*Pandalus borealis*	21	< 8.22		
Denmark	1999	*Phoca hispida*	44	< 0.02 – < 2.2		
The Netherlands	2009	*Platichthys flesus*	71	0.1–0.6		
Denmark	2000	*Reinhardtius hippoglossoides*	11	< 8.22		
Denmark	2000	*Salmo salar*	7	< 8.22		
Denmark	2000	*Salvelinus alpinus*	20	< 8.22		
Denmark	2000	*Sebastes marinus*	5	< 8.22		

LOD…detection limit; all other "< " indicate values below the limit of quantification: such concentrations were detectable but remained below the level of the accepted measurement uncertainty

71. The WHO (2004) listed the following HCBD concentrations in water (cf. Table 2.3.1-3):

Table 2.3.1-3: HCBD concentrations in water (table modified from WHO, 2004)

Water body	HCBD [µg/l]	Source
in ambient water	0.05–5	IARC, 1979
Rhine	0.1–5	IARC, 1979
Ebre River water	0.2	Amaral et al., 1996
Mississippi	0.9–1.9	IARC, 1979
Louisiana	0.01–0.48	Almedia et al., 1997
Japan	< 0.02	Japan Environment Agency, 1982
effluent from a European chemical plant	6.4	IARC, 1979

72. During the 1990ies, two surveys in UK and Canada detected HCBD in drinking water at very low frequencies only: one out of 280 samples exceeded the detection limit of 0.4 ng/l in a survey of the Humber river (UK) catchments 1995–96, and five out of 2 994 samples from 143 Ontario (CAN) sites contained detectable traces of HCBD, with a maximum concentration of 6 ng/l (Meharg et al., 1998 and OMEE, 1996, as cited in Lecloux, 2004). Contrarily, the WHO (2004) noted that HCBD is frequently detected in ambient water (mean level usually < 0.1 µg/l), e.g. the Rhine (0.1–5 µg/l), and has been detected in drinking water at 2–3 ng/l. In 2006, HCBD levels in the wells of a drinking-water supply for Basel (Switzerland) were below the detection limit of 50 ng/l (Brüschweiler et al., 2010). HCBD releases from a disused waste dump contaminated groundwater (and indoor air) in the UK (COT, 2000).

73. A 1994–97 survey of rivers from six European countries yielded a 90% quantile of 12 ng/l (Govaerts et al., 2000 and 2004, as cited in Lecloux, 2004).

Air

In the Canadian High Arctic (Nunavut), HCBD was measured from 2002–2009 using continuous high volume sampling with ca. 52 samples per year. The method detection limit (MDL) ranged from 0.025 to 0.37 pg/m^3, with 0 to 20 % of all samples each year below MDL and 59 to 93 % of all samples each year above 3 times MDL (Hung, 2012). Kaj & Palm (2004) report atmospheric concentrations of 0.16 ng/m^3 (median) for two Swedish background stations.

Sediments

Some hotspots of local HCBD contamination were reported from the St. Clair River area at the US/Canadian border, with a maximum sediment concentration of 310 mg/kg dry weight (dw) in 1994 (Farara & Burt 1997, Kauss 1997 as cited in Environment Canada 2000). In an industrial zone, the topmost 5 cm of St. Clair River sediment contained 18.7 µg/kg dw (90% quantile) HCBD. This site is now completely remediated with regard to HCBD. European hotspots include sediment concentrations of up to 300 µg/kg dw which are related to industrial activity (Heinisch et al. 2007). Across Europe, the 90% quantile of 500 river and estuary sediment samples amounted to 4 µg/kg (1994–97; Govaerts et al. 2000, 2004 as cited in Lecloux 2004). Recent (2011) values for Northern Europe (Estonia) were below 1 µg/kg (Table 2.3.1-1) levels from other European countries are listed in Table 2.3.1-4..

Table 2.3.1-4: HCBD concentrations in sediment (EU region; source: EEA 2012b)

Country	Year	Sample size	Concentration range [µg/kg]
MT	2005-2006	38	<50 LOQ
DE	1990-2008	152	<0.003 - <1
DK	2007-2009	114	<0.005-0.8
NL	1985	2	0.1-0.2
ES	2006-2009	19	< 0.5 LOD - < 40

74. An example for sediment levels at polluted locations is 42.8 µg/kg (maximum value of ten four-plot transsects; transsect means between n.d. and 22.6) measured at Kaohsiung coast (Taiwan) in 1996 (Lee et al. 2000). The authors suggest the Tsoying outfall pipe and/or Hochin river as the major pollution source, indicating an (in 1996) ongoing substantial release.

Soil

75. Data on HCBD pollution of soil are scarce. On 30 Canadian agricultural sites, HCBD was below the detection limit (Webber and Wang, 1995 as cited in Lecloux, 2004), indicating very low if any pollution.

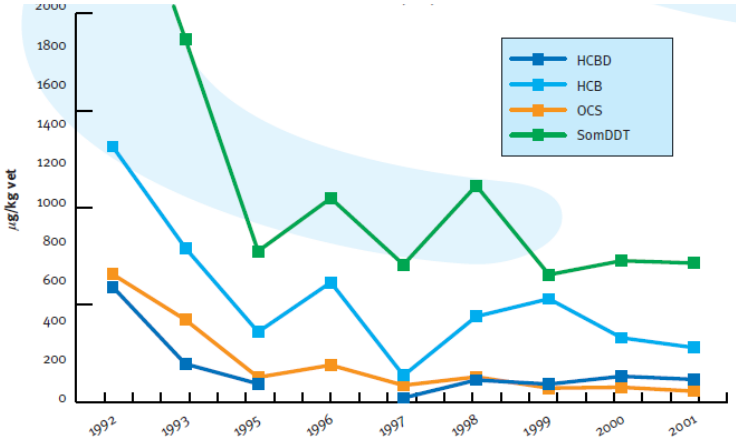
Biota

76. As noted earlier, recent monitoring data for HCBD are scarce, especially for HCBD levels in biota.

77. The level of 36 µg HCBD / kg ww in caged mussels exposed near three industrial areas of the St. Clair river for three weeks (Environment Canada, 1999) gives an example of concentrations close to sources.

78. HCBD levels in European eel (*Anguilla anguilla*) from Rhine river stretches (NL), attributed to industrial contamination, have decreased by least a factor of five during 1977–2002 according to RIWA (2004). However, the comparison of eel samples taken from numerous stretches along the Rhine in 1995 and 2000 suggests that the peak HCBD burden (median of most contaminated samples ca. 42 µg/kgww in both years), has moved upstream rather than declined (IKSR 2002 as cited in Hillenbrand et al., 2006). Plasma and fat samples of polar bears from Svalbard, Norway, contained between 1.2 and 8.9 ng HCBD / g ww with an arithmetic mean of 3.7 (Gabrielsen et al., 2004). According to Muir (2003) cited in Lecloux (2004) HCBD has been measured in beluga blubber with levels that vary from 278 µg/kg of lw in the St Lawrence River estuary to less than 0.1 µg/kg lw in Northern Quebec (East Hudson Bay).

Figure 2.3.1-1: Trends of HCBD and other organochlorines in European eel (*Anguilla anguilla*) from Rhine at Lobith (concentration in µg/kg fat) (Source: RIWA 2004).



Richman & Sommers (2010) found locally confined pronounced HCBD levels (up to 17 ng/kg d.w.) in Niagara river Quagga mussels and concluded on the influence of local sources. They report a marked decrease of HCBD concentrations from 1995 to 2003, suggesting the success of local remediation measures.

79. In 2004, annual HCBD loads in Elbe river (DE) were <0.6 kg/a, compared to 96 kg/a in 1989. It decreased strongly during 1995–2000 in the Elbe river. However, no such clear decrease (1987-2009), despite remediation measures, could be detected for mussels exposed at the mouth of Gill Creek river (Great Lakes region): Richman et al. (2011).

80. No clear trend in HCBD concentrations (mean +/− SE) could be detected in caged mussels deployed at the mouth of Gill Creek (1987–2009).

Human Exposure:

81. Exposure in many countries is expected to be relatively low due to current restrictions. Local sources of HCBD such as landfills, combustion and production sites of other chlorinated chemicals could lead to significant higher exposure conditions. For instance, in Weston Village, UK waste disposal of chemical industry has lead to high levels of HCBD contamination. HCBD exposure in 21 houses was identified to impose serious risks to human health; approximately half the people of the village of about 500 households left their homes due to health concerns (Barnes et al. 2002). Also in other regions exposure to HCBD from former hazardous waste sites is still of considerable concern, an example is the Devil's swamp area. According to a Health Impact Assessment of URS (Australia), living near a repackaging unit for HCBD-containing waste (n.b.: not a waste dump) caused an HCBD exposure which was estimated at 78% of the TDI for young children and 36% for adults for residential and recreational exposure (URS, 2006). Even though this is below the tolerable level, contribution to 78% of the TDI for young children seems not satisfying considering the potential genotoxicity of the compound, maybe lifelong exposure conditions and possible co-exposure to other hazardous substances. Levels reported in drinking water are given in the section 2.3.1. Recent data on levels in drinking water are scarce. Recently in Basel levels were below the limit of detection of 50 ng/l (Brüschweiler et al., 2010). In general a high degree of uncertainty inherent in the estimates of intake of HCBD in food due to limited monitoring data is reported. Tchounwou et al (1998) cited in US EPA (2003) demonstrated that aquatic organisms, particularly fish, may be a significant source of HCBD transmission from contaminated wetlands to humans. In some areas of the US (Bayou d'Inde, Devil's Swamp Lake, Bayou Baton Rouge, Calcasieu Estuary) concentrations of PCBs, HCB and HCBD have resulted in Fish Consumption Advisories. HCBD has been detected in human adipose tissue with concentrations ranging from 0.8 to 8 µg/kg wet weight. Also in human liver samples HCBD was found in concentrations ranging from 5.7 to 13.7 µg/kg wet weight (IPCS, 1994).

2.4 Hazard assessment for endpoints of concern

82. Several assessment reports addressing the toxicity of HCBD are available to date (ATDSR, 1994; IPCS, 1994; Environment Canada, 1999; IARC 1999; California EPA, 2000; US EPA, 2003).

83. HCBD is classified concerning health hazards according to Global Harmonized System (GHS) as follows: acute toxicity category 3 for oral administration, category 4 for dermal administration, category 1 for inhalation of HCBD vapour; not classifiable concerning irritation to skin or irritation of eyes due to insufficient data availability, sensitizing to the skin category 1, not classifiable for respiratory sensitization due to lack of data, germ cell mutagen category 2, carcinogen of the category

2 ("suspected human carcinogen"), as toxic to reproduction category 2 as Specific Target Organ Toxicity after single exposure (STOT-SE) of category 1 (kidney) and after repeated exposure (STOT-RE) of category 1 (kidney, liver, marrow). The classification is available via the e-chem portal of OECD and has been performed by NITE (2006). HCBD is classified as a chemical known to the State of California (USA) to cause cancer (California EPA, 2012). It should be noted that the classification notified to ECHA[19] by Industry identified additional classification for skin and eye irritation. However this is not the result of an industry harmonized classification.

84. It is classified concerning environmental hazards according to GHS as follows: hazardous to the aquatic environment due to acute and also chronic exposure in category 1 (NITE, 2006).

Ecotoxicity

85. According to UNEP/POPS/POPRC.7/INF/4 and IPCS, 1994, ecotoxicity data are available for a number of marine and freshwater species (fish, crustaceans, bacteria, algae, mollusk, protozoans, insects and snails). In most of the studies the concentration of HCBD is not reported, therefore the actual effect concentrations may be lower or higher than nominal concentrations. Acute LC_{50} values range from 0.032 mg/L for the marine crustacean *Palaemontes pugio* to 4.5 mg/L for the freshwater fish *Poecillia latiphinna*. There is only one outlier (LC50=470 mg/L after 48 h for *Leuciscus idus melonatus*). A valid chronic NOEC with 0.0065 mg/L is available for fish from a 28 days, Early Life Stage test with *Pimephales promelas* (flow through system and measurement of concentrations). Therefore it is concluded that HCBD is highly toxic to aquatic organisms. According to Environment Canada (1999) no chronic data were identified for aquatic invertebrates. It also states that bacteria and plants are less sensitive to HCBD than fish and invertebrates. For the calculation of a critical body burden in fish WCC (2002) used a BCF of 17,000 L/kg and a NOEC of 0.0065 mg/L resulting in a body burden of 111 mg/kg ww. However if a BCF of 7,720 L/kg (NITE, 2012) is used the critical body burden is 50.18 mg/kg ww. This is a simple prediction and it should be noted that facts like global distribution, the long duration of the HCBD pollution and its accumulation behavior makes prediction much more complicated. In addition sediment organisms are probably exposed to higher levels than aquatic species.

86. Environment Canada (1999) used the water sediment Equilibrium Partitioning approach to estimate a Critical Toxicity Value for sediment organisms with 20.8 µg/g dry weight. In a sediment dilution study and a spiked sediment acute toxicity test the lowest effect threshold values for the freshwater crustacean *Hyalella azteca* and the estuarine crustacean *Leptocheirus plumulosus* were identified with 0.63 $mg/kg_{1\%OC}$ and 1.4 $mg/kg_{1\%OC}$, respectively (Fuchsman et al., 2000). Arkoosh et al. (2001) exposed juvenile chinook salmon to HCBD concentrations which lead to liver concentrations comparable to those found in individuals living in contaminated sediments. The exposure resulted in an increased susceptibility of the salmon to disease (28% higher mortality after 7 days of exposure to *Vibrio anguillarum*). According to Environment Canada (1999) HCBD preferentially accumulates in livers of fish, where it can be biotransformed into polar metabolites that will reach the kidneys and could become nephrotoxic in fish.

87. According to IPCS (1994) there is only one reliable study available for birds (90 days with Japanese quail, *Coturnix coturnix japonica*) with a NOAEL of 3 mg/kg diet. Neuhauser et al. (1985) showed in a 2 days contact test on earthworms according to the OECD testguideline 207, that HCBD has an LC50 of 0.01 mg/cm^2. In this study 44 chemicals were tested, 10 chemicals were additionally tested in an artificial soil test. Comparing the LC50 values from the two different studies it may be expected, that the LC50 for HCBD in an artificial soil test would be in the range of 10 to 1000 mg/kg soil.

88. The water solubility is given with 3.2 mg/L. Therefore, based on the experimental data on aquatic species with LC50 and NOEC values in the micro-gram range it is concluded that HCBD is very toxic. These data provide sufficient evidence that HCBD may have severe adverse effects on some species in aquatic ecosystems at below the saturation concentration of this substance in water.

Toxicity in Humans

89. A limited number of studies concerning HCBD toxicity in humans are available. Two Russian Studies (Krasniuk et al. 1969 and Burkatskaya et al.,1982) reported adverse health effects in vineyard workers exposed to HCBD such as increased incidence of arterial hypotension, myocardial dystrophy, chest pains, upper respiratory tract changes, liver effects, sleep disorders, hand trembling, nausea and disordered smell functions (US EPA, 2003); but according to IPCS, 1994 co-exposure to other chemicals cannot be excluded and therefore these studies are of limited value for risk assessment.

[19] http://echa.europa.eu/web/guest/regulations/clp/cl-inventory

90. Increased frequency of chromosomal aberrations in the peripheral lymphocytes of exposed workers where reported by German (1986, cited in IPCS 1994); however the frequency of aberrations was not associated with the period of employment.

91. In vitro studies suggest that toxic metabolites of HCBD may be formed in humans, as it is documented for laboratory animals (IPCS, 1994).

92. In most occupational exposure studies with HCBD co-exposure to other chemicals cannot be excluded. Long term or epidemiological studies in the general population or sensitive populations are not available. Therefore hazard considerations are mainly based on data from laboratory animals.

Acute Toxicity

93. HCBD is in general moderately acutely toxic in laboratory animals (LD_{50} values ranging from 90 – 350 mg/kg bw) apart from being highly acutely toxic in female weanling rats following a single oral dose. The LD_{50} for weanling rats were 65mg/kg for male and 46 mg/kg for female rats (Kociba et al. 1977a in IPCS, 1994). Hook et al. (1983) observed severe renal damage at 50 mg/kg in females whereas similar effects were detected in males at concentrations of 200 mg/kg. The major target organ for HCBD induced toxicity is the kidney and to less extent, the liver.

Absorption and Metabolism

94. Animal studies with radiolabelled HCBD have shown that most of the compound is excreted within 72 hours via urine and feces. However in rats approximately 7% of the compound was detected in carcass and tissues, mainly in liver, brain and kidneys and in mice 6.7-13% was detected in carcass, especially in adipose tissue (IPCS, 1994). Most of the absorbed HCBD is transported to the liver and conjugated with glutathione. Glutathione conjugate is excreted with the bile into the intestinal tract, a cysteinyl derivative is formed and reabsorbed from the intestines and transported to the liver and subsequently to the body tissues (Coudhary et al. 1995).

Mode of action, target organ toxicity

95. In acute, short-term, subchronic and chronic studies via all routes of exposure (oral, dermal, inhalation, intraperitoneal) the renal proximal tubules are affected. The assumption that by preventing irritation the occurrence of other manifestations of systemic toxicity can be prevented is not correct for HCBD exposure via inhalation which leads to kidney injury below concentrations leading to irritating effects (Ceaurriz et al. 1988). Biotransformation to a reactive sulphur containing metabolite is expected to account for the observed nephrotoxicity as well as its genotoxicity and carcinogenicity. This hypothesis is supported by several studies and assessments. Studies with liver microsomes of human donors of both sexes indicate that cytochrome P450 from the 3A family may be involved, (Werner et al., 1995). Green et al. compared key metabolic steps in rats and humans, finding the key activation steps also in humans, but to less extent. (Green et al., 2003). Studies on mode of action were generally performed in laboratory animals. Renal toxicity is presumed to be due to bioactivation by glutathione conjugation to its corresponding cysteine s- conjugate and further cysteine conjugate β -lyase-dependent activation of 1-(cystein- S-yl)-1,2,3,4,4-pentachloro-1,3-butadiene (CPB) to a reactive thioketene in the proximal tubular cells resulting in covalent binding to cellular macromolecules (IARC, 1999). The kidney concentrates GSH- and cysteine S-conjugates and processes GSH conjugates to cysteine S-conjugates, which are conjugated to reactive intermediates to a substantial proportion (Dekant et al. 1989). It has been suggested that the unique sensitivity of the kidney to HCBD is related to the kidney´s ability to accumulate these organic ions (Rush et al.1984).

96. Kim and coworkers have shown a reduction of ATP in susceptible kidney cells leading to impaired cell function and proteins leakage and the presence of cysteine S-conjugate β –lyase in several regions of the nephron (Kim et al. 1996).

97. Biomarkers of renal effects were investigated by Trevisan and coworkers (Trevisan et al., 2005). Liver GSH depletion in male rats after 24 hours and a dose-dependent increase of kidney GSH-content in male rats were observed. A marked decrease of renal GS activity in both sexes according to the dose was reported. A loss of organic anion accumulation at the higher dose was earlier and greater in female rats.

98. Increases in mRNA, indicating metabolism of HCBD, oxidative stress and an inflammatory response within the kidney was detected in a 24 hour study at a dose level of 90 mg/kg HCBD intraperitoneally (Swain et al., 2010).

99. The metabolite N-acetyl-S-(1,1,2,3,4 pentachlorobutadienyl)-L-cysteine sulfoxide (N-AcPCBC-SO) has been detected in the urine of male, but not female, rats following oral administration of HCBD. Formation of this metabolite is mediated by cytochrome P450 3A

monooxygenases, which are expressed only in male rats (Birner et al., 1995; Werner et al., 1995a). This metabolite has been found to be cytotoxic to proximal tubular cells in vitro without activation by ß-lyase (Birner et al., 1995). An additional β –lyase independent metabolic activation reaction resulting in the formation of vinylsulfoxide has been described by Birner et al. (1997) and was detected more pronounced in male rats. A variety of chemicals have been identified to cause male rat-specific nephrotoxicity induced by accumulation of alpha2u-globulin in the kidney. Saito et al. (1996) have shown that no increase in urinary kidney type alpha2u-globulin were observed in adult rats treated with HCBD.

100. The toxicity of mixtures of nephrotoxicants with similar mode of action revealed that renal toxicity of the mixtures corresponded to the effect expected on the basis of additivity assumption. Combined exposure to four similar acting nephrotoxic compounds at their NONEL (no observed nephrotoxic effect level) showed similar effects than exposure to the individual compounds at their LONEL (lowest observed nephrotoxic effect level) (Jonker et al., 1996).

101. The lowest NOAEL (no observed adverse effect level) observed in studies for noncarcinogenic renal effects were 0.2 mg/kg bw/day (Schwetz et al. 1977, Yang et al. 1989). An overview on selected studies on renal toxicity effects is shown in Table 2.4-1.

Table 2.4-1: Renal toxicity studies on HCBD

Studies in experimental animals exposed to HCBD				
Oral administration				
Species	Exposure conditions	Effect levels	Effects reported	Reference
B 6C3F1 mice (10 males and 10 females per group)	Males: 0, 0.1,0.4, 1.5, 4.9, 16.8 Females: 0, 0.5, 1.8, 4.5, 19.2 mg/kg bw/d, oral for 13 weeks	LOEL: females: 0.2 mg/kg bw/d N OAEL: males: 1.5 mg/kg bw/d	histopathological effects in kidney	Yang et al., 1989; NTP, 1991
Wistar rats (5 males and 5 females per group)	0, 1.25, 5, 20mg/kg in the diet for 4 weeks	NOAEL: 1.25 mg/kg bw/d LOAEL: 5 mg/kg bw/d	Decreased body weight, Decreased relative weight of adrenals, effects on urinary and biochemical parameters, histopathological effects in kidney	Jonker et al., 1993
Wistar rats (10 males and 10 females per group)	0, 0.4 , 1.0, 2.5, 6.3, 15.6 mg/kg bw/day by gavage for 13 weeks	NOEL: females: 1.0 mg/kg bw/d males: 2.5 mg/kg bw/d L OAEL: females: 2.5 mg/kg bw/d males: 6.3 mg/kg bw/d	Effects on urinary parameters ; histopathological effects in kidney	Harlemann and Seinen, 1979
Sprague-Dawley rats (10–12 males and 20–24 females per group; 17 male and 34 female controls	0, 0.2, 2.0, 20 mg/kg bw/d in the diet for about 5 months	NOEL: 0.2 mg/kg bw/d LOEL: 2 mg/kg bw/d	Gross and histopathological changes in kidney	Schwetz et al., 1977

Studies in experimental animals exposed to HCBD				
Oral administration				
Species	Exposure conditions	Effect levels	Effects reported	Reference
Sprague-Dawley rats (39–49 males and 40 females per group; 90 male and 90 female controls)	0, 0.2, 2.0, 20 mg/kg bw/d for 2 years in the diet	NOEL: 0.2 mg/kg bw/d LO(A)EL: 2 mg/kg bw/d	Effects on urinary biochemical parameters; histopathological effects in kidney, effects on nervous system (20 mg/kg bw/d) Increased incidence of renal tubular adenoma/adenocarcinoma,	Kociba et al.1977
Wistar rats (male and female, 10 rats per group)	Intraperitoneal 50, 100, 200 mg/kg bw; Sacrifice: after 24 and 48 hours	No NOEL	Histopathological effects in pars recta of proximal tubule, Gender related differences in kidney biomarkers of HCBD- induced toxic effects: female rats show a significantly earlier and higher susceptibility of the kidney	Trevisan et al. 2005
Wistar rats, (male, six weeks of age) 21/group	0.1% N-nitrosoethyl-hydroxyethylamine (NEHEA) in the drinking-water for two weeks and then 0.1% HCBD in the diet for 30 weeks, One group NEHEA only, one group HCBD only One control group	LOAEL: 2 mg/kg bw/d	The incidence of renal tubular tumours in the group given NEHEA plus hexachlorobutadiene (15/21) was greater than that in rats given NEHEA alone (5/10), and the incidence of preneoplastic renal tubular hyperplasia was also increased (21/21 versus 4/10). No adenomatous hyperplastic foci and renal cell tumors were found in the HCBD group. It has been suggested by the authors that the exposure time might have been too short. DNA synthesis in tubular segments was estimated by immunostaining with bromodeoxyuridine	Nakagawa et al., 1998

Studies in experimental animals exposed to HCBD				
Oral administration				
Species	Exposure conditions	Effect levels	Effects reported	Reference
			(BrdU). In the HCBD +NEHEA group and in the HCBD group a significant increase in BrDU Labeling Indices was reported, whereas no such increase was seen in the NEHEA only group.	
Male and female Guernsey or Frisian calves of about 50 kg body weight	24 calves were dosed with haloalkene conjugates or HCBD (4 calves were treated with HCBD: 1: single dose of 50mg/kg; 2: 5 mg/kg bw/d for 7 days, 3: 2,5 mg/kg bw/d for 10 days, then 5mg/kg for 8 days and 4: 5 mg/kg bw/d for 8 days	NOEL/LOEL: 2.5 mg/kg	At 50 mg/kg: marked toxicity leading to death after 5 days 5 mg/kg: Increased plasma markers of liver injury, perirenal oedema in the kidneys, liver swelling, Histopathological examinations: extensive swelling of the tubular epithelium with degenerative changes	Lock et al., 1996

Table 2.4-1 gives an overview on studies demonstrating renal toxicity in laboratory animals and as well in domestic animals. In the NTP 13 weeks study a LOAEL of 0.2 mg/kg/bw/day for female mice has been derived (Yang et al., 1991), whereas in male mice a NOAEL of 1.5 mg/kg has been established, demonstrating higher susceptibility in females. In rats NOAELs were in the range of 0.2 mg/kg bw/day (Schwetz et al., 1977, Harlemann and Seinen, 1979) and 2.5 mg/kg bw/day. The key study referred to in several risk assessments is the two years carcinogenicity study by Kociba and Coworkers, 1977. This study demonstrated a clear cut dose-response relationship for HCBD–induced toxicity affecting primarily the kidney. According to the authors HCBD- induced renal neoplasms occurred only at a dose level higher than that causing discernible renal injury; however an additional treatment between 2 and 20 mg/kg group, would have been valuable in order to assess the carcinogenic potential. Also in calves HCBD induced nephrotoxicity has been observed; at a concentration of 5mg/kg bw/day for 8 days adverse effects in the liver and in the kidney have been documented (Lock et al.1996).

Genotoxicity:

102. Conflicting results concerning genotoxicity have been reported. HCBD was negative in several experiments using the standard *Salmonella typhimurium* mutagenicity test (Ames-test) (Yang et al., 1988, IARC, 1999), but positive results were obtained if an enhanced rat S9 activation system (protein enriched or addition of gluthathione) or rat-kidney microsomes were used (COT, 2000, Brüschweiler et al., 2010 IARC 1999). Also metabolites of HCBD have shown positive results in the Ames assay with *S. typhimurium* TA 100 strain (ICPS, 1994). Positive results were obtained in Sister chromatide exchange tests with Chinese hamster ovary CHO cells (Galloway et al. 1987) and in cell transformation assays with Syrian hamster embryo cells (Schiffmann et al. 1984). HCBD induced chromosome aberrations *in vitro* were detected in Chinese hamster lung fibroblast V79 cells with and without metabolic activation (Brüschweiler et al. 2010) whereas in Chinese hamster ovary CHO cells no chromosome aberrations could be detected (Galloway et al. 1987). Covalent binding to DNA has been observed *in vivo* in the kidney of rats as well as to mitochondrial DNA in female mouse liver and kidney (Schrenk and Dekant, 1989, IARC, 1999). Chromosomal aberrations *in vivo* were detected in mouse bone-marrow cells after inhalation and oral administration (German, 1988). Alkylation of

kidney DNA has been observed in rats *in vivo* and binding (covalent) to mitochondrial DNA, female NMRI mouse liver and kidney cells in vivo

103. According to the GHS classification by NITE (2006) which is based on positive results of chromosomal aberration tests *in vivo* after oral and inhalation exposure using the mouse marrow cells reported in IPCS (1994), it is classified as mutagenic category 2, as chemical which has the potential to induce heritable mutations in human germ cells. Overall it has been shown by various authors that HCBD has genotoxic potential.

Carcinogenicity:

104. After oral administration in rats, HCBD produced benign and malignant tumours in the kidneys of animals of each sex at a dose of 20 mg/kg bw/day (Kociba et al., 1977, study description see Table 2.4-1). It did not produce skin tumours after repeated application or show initiating activity in a two-stage initiation–promotion study in mice. Nakagawa et al. assumed that nephrotoxic agents are important factors for renal carcinogenesis and administered the carcinogen nitrosoethylhydroxyethylamine (0.1% in drinking water) for two weeks followed by a 30 weeks treatment period with HCBD (0,1% in the diet). HCBD enhanced the incidence of adenomatous hyperplasia and renal tubular tumours induced by N-nitrosoethylhydroxyethylamine approximately two-fold in this two-stage model of renal carcinogenesis (Nakagawa et al., 1998).

105. According to IARC there is inadequate evidence in humans and just limited evidence in experimental animals for the carcinogenicity of HCBD (IARC, 1999). Therefore IARC concluded HCBD as not classifiable to its carcinogenicity to humans (Group 3). According to the conclusion of the 2000 report by the Office of Environmental Health Hazard Assessment's Reproductive and Cancer Hazard Assessment Section of the California (USA) Environmental Protection Agency (Rabovsky, 2000), "there is evidence for the carcinogenicity of HCBD, based on the development of renal tubular neoplasms in female and male rats that received HCBD in the diet for approximately two years. Contributing to the weight of evidence are observations of mutagenicity in bacteria under conditions that favor the GSH/mercapturate/□-lyase pathway, genotoxicity in mammalian cells, and in vivo DNA binding in rats and mice. Chemical structural, functional, and metabolic analogies with recognized carcinogens, and evidence of tumor promoter activity further contribute to the weight of evidence." (California EPA, 2003). The US EPA determined HCBD as possible human carcinogen. Büschweiler and coworkers stated that based on their results and evidence for genotoxicity as well as tumour induction in a two year study, the carcinogenicity of HCBD should be re-evaluated (Büschweiler et al., 2010).

106. The latest assessment is based on the classification of the American Conference of Governmental Industrial Hygienists (ACGIH) as category A3 carcinogen (suspected to cause skin cancer at occupational exposure concentrations). Hence NITE classified HCBD as carcinogen of category 2 GHS "suspected human carcinogen" NITE (2006).

Effects on reproduction:

107. Fetal toxicity after intraperitoneal administration of HCBD from day 1 to 15 of gestation was observed by Hardin et al. 1981. The study protocol was reported to be a pilot study, using one dose (10 mg/kg bw/d) in 10 to 15 female Sprague –Dawley rats, which was selected in dose response studies as maximum tolerable dose. Changes in at least two maternal organ weights were seen as well as delayed fetal development. The development of the heart was delayed by 1-2 days and dilated renal pelvises and ureters were seen. The authors did not classify these effects as teratogenic but listed HCBD as a candidate for more extensive teratological screening by another route of administration.

108. Serious effects after one single intraperitoneally administered dose of HCBD were reported in a study which was conducted in 1966 by Poteryaeva. A dose of 20 mg/kg bw was administered to nonpregnant albino rats. The course of the subsequent pregnancy and its outcome were observed in 61 control animals and 86 newborns of treated mothers. The pregnancy rate was not influenced by the treatment, no other information on the health of the dams is given in the original paper, and therefore the relevance for risk assessment is limited. Lowered vitality, poor weight gain, changes in the peripheral blood and loss of coordination of movements were observed in the offspring beside from distinct pathological changes in the internal organs (hemorrhages in the lungs, degenerative and inflammatory changes in the liver and kidneys and destructive processes in the gastrointestinal tract).

109. Reproductive toxicity of HCBD via inhalation exposure has been investigated by Saillenfait et al. (1989). Pregnant Sprague- Dawley rats (19 – 25/group) were exposed to 2, 5, 10, 15 ppm corresponding to 21, 53, 107, 160 mg/m^3 for 6 hours/day from day 6 to 20 of gestation. Reduction of fetal body weight was reported at 15 ppm, a concentration affecting maternal weight gain. Non-significant incidence of hydroureter at 15 ppm and slight non-significant increase in the incidence

of extra 14th ribs at 10 ppm was observed. It was considered as category 2 according to GHS since in the perinatal period medication examination (feed-mix administration from pregnancy the 17th to after-delivery the 10th) of the rat, nephrotoxicity was acknowledged also in fetus by the dose nephrotoxicity etc. is observed in dam (NTP DB, 2006, in NITE, 2006).

110. Based on the available literature it is concluded that reproductive effects appear at maternal toxic concentrations, and therefore the risk of reproductive effects below levels revealing maternal toxicity are considered to be relatively low.

Neurological effects

111. In rats exposed to concentrations of 150 mg/kg /day for up to 10 weeks ataxia, demyelination and degeneration of femoral nerve fibers were observed (ATSDR, 1994).

Limit and guideline values

112. The World Health Organization developed a TDI value for HCBD of 0.2 µg/kg of body weight, based on the NOAEL of 0.2 mg/kg of body weight per day for renal toxicity in the 2-year feeding study in rats, using an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for limited evidence of carcinogenicity and genotoxicity of some metabolites (WHO, 2004). A provisional reference value of 0.6 µg/l has been derived as guideline value for drinking water (WHO, 2004). In Australia a drinking water guideline value of 0.7 µg/l has been established (NHRMC, 2004). According to US EPA (1980) exposure levels in drinking water for adults (life time exposure) should not exceed 1µg/l. The US EPA developed a preliminary health reference level (HRL) of 0.9 µg/L drinking water for HCBD (US EPA, 2001c), a concentration corresponding to 10^{-6} incremental cancer risk, calculated from the slope factor using the linear assessment method (US EPA, 2003). Regulatory standards for annual air concentrations according to NATICH, 1991 depending on the state have been set to 0.00 µg/m^3, 0.045 µg/m^3 0.8 µg/m^3 and 0.210 µg/m^3 respectively (ATSDR, 1994). The Committee on toxicity of chemicals in food, consumer products and the environment in the UK established a safe air concentration of 0.6 mg/m^3, or 60 ppb respectively, stating that the ALARP (as low as reasonably practicable) principle should be followed (COT, 2000).

Comparison of effect data with monitoring data

113. Risk assessments for POPs have been performed in the past. Recently improvements to address specific issues and to reduce uncertainties for risk assessments of POPs have been developed (Klecka and Muir, 2008). However, risks may be underestimated for persistent and bioaccumulative substances if they are assessed using traditional toxicity testing methods and approaches alone. van Wijk et al. (2009) considered that internal dose or critical tissue residue is a preferred approach for PBTs and POPs to reduce uncertainty in characterizing effects levels. According to ECHA (2008) the level of uncertainty in identifying long-term risk for possible persistent, bioaccumulative and toxic substances cannot be estimated with sufficient accuracy compared to other substances. In addition the consequences of an underestimation of adverse effects are not easily reversible by regulatory action.

114. A traditional risk assessment approach was followed in the risk characterisation for the marine environment of HCBD by WCC (2002) indicating no risk to marine aquatic, sediment dwelling organisms and risk to fish from bioconcentration. The risk assessment was conducted in the context of the OSPARCOM programme for the North Sea, and the assessment factor of 50 used was taken from EU risk assessment guidance applicable at the time. However, the used factor of 50 is not appropriate according to present guidance and a higher factor would be assigned for the listed data set. Concerning risk of secondary poisoning and biomagnification (based on $PNEC_{Oral/Food}$ without assessment factors and PECs calculated without considering BMF-factors), the results indicate little risk of toxicological effects for predatory species eating fish contaminated with HCBD. The estimated daily intakes of HCBD are several orders of magnitude below the no adverse effect levels. However, these conclusions are considered questionable, not only due to the derivation of the PNEC and PEC values but also due to the inappropriateness of the traditional approach for POP substances as indicated above. Environment Canada (1999) used measured concentrations from the St. Clair River, a locally contaminated site, for risk characterization and identified a risk to benthic organisms in the most contaminated portions of the river (but not for pelagic organisms).

3. Synthesis of information

115. HCBD, either as a by-product from organic synthesis or intentionally produced, had various uses, including its employment as an intermediary in chemical or metallurgical industry, ingredient of heat-dissipating, insulating or hydraulic fluids and the application as a pesticide. Production has decreased considerably over the last decades and it is no longer produced in the UN-ECE region;

information about intentional production and use outside the UN-ECE countries is incomplete. In 2000, an estimated 2.6 tons of HCBD were released to the environment in the UN-ECE area, more recent (2007–09) inventories give figures between 120–149 kg/a for EU industrial emissions (including waste management). Recent HCBD releases in the US are of the same order of magnitude (ca. 200–300 kg/a from 2007 to 2010).

116. HCBD is not expected to be hydrolysed based on its chemical structure. Limited data on photolysis, with unknown relevance under environmental conditions, are available. Volatilisation and adsorption will be major routes of dissipation from water and soil and thus increase persistence. Bioavailability will be a limiting factor for biodegradation, as well as for effects on biota. There is evidence that HCBD is not readily biodegradable and some estimated half-lives in water exceed the threshold of 2 months. However there are indications that under favourable conditions faster degradation may be possible. Estimated half-lives for soil reach the persistence threshold of six months. HCBD may not degrade under anaerobic conditions in soil. Half-life data for sediment are not available, although sediments are a sink for HCBD. Predicted half-lives in air are very long (>1 year) and concerning the distribution of HCBD in the environment air is a very important environmental compartment due to the physical-chemical properties of HCBD. Thus there is evidence that HCBD is otherwise sufficiently persistent to justify its consideration within the scope of the Stockholm Convention.

117. The assumption of a long-range transport potential for HCBD is supported by model results and by the occurrence of HCBD in environmental samples from regions far from HCBD sources. Models predict that HCBD released to air or water will partition to a significant extent into the atmosphere. Atmospheric HCBD has a very long half-life and a transport distance of 8,784 km, which enables HCBD pollution to spread over very long distances. HCBD has been found in mammals, birds and fish in remote places like Greenland or Svalbard Island.

118. The log Kow of HCBD is 4.78. The bioconcentration potential of HCBD in aquatic organisms is confirmed by experimental data. In literature the bioconcentration factor (BCF) values range between 1 and 19,000 L/kg for fish, crustaceans, molluscs and algae. The wide range is explained with species differences in metabolism and differences in exposure concentrations. Evaluated BCF values for carp and fathead minnow in the range of 6,480 to 7,410 L/kg are available. Evaluated BAF values of 9,260 and 250,000 L/kg are available for crustaceans and value of 17,360 L/kg for fish. Thus, reported BCFs and BAFs are above the criterion of 5,000. A calculated BMF based on the BCF of 3 indicate a potential of biomagnification, however this finding is not substantiated by field data. On the basis of these data it is concluded that HCBD has a potential for bioaccumulation, at least for some species.

119. The toxicity and ecotoxicity of HCBD is well documented. Experimental data on several environmental species (fish, crustaceans, bacteria, algae, mollusc, protozoan, insects, snails, birds and earthworms) provide sufficient evidence to conclude that HCBD is very toxic to the aquatic environment and toxic to birds.

120. Risk assessments for the marine environment was performed but the level of uncertainty in identifying risks to aquatic pelagic species according to the traditional risk assessment approach available at that time is higher. The risk assessment for the freshwater environment represents a locally contaminated site and identified a risk to benthic organisms.

121. Human data on toxicity of HCBD are scarce, therefore animal data have to be used for hazard considerations. In laboratory animals HCBD is not very acutely toxic but it is highly toxic on repeated or chronic exposure. The target organ of HCBD induced toxicity is the kidney, in laboratory animals as well as in calves. Biotransformation via cytochrome P450 3a via conjugation with glutathione leading finally to a reactive sulphur containing metabolite is expected to account for the observed nephrotoxicity as well as its genotoxicity and carcinogenicity. Genotoxicity was observed in vitro and in vivo. Chromosome aberrations were also detected in occupationally exposed humans. Carcinogenicity was observed in rats receiving HCBD via the diet in a two years study. Information on immunological function has not been identified.

122. Human in vitro data suggest that metabolic activation leading to toxic reaction products occurs also in humans, but to less extent.

123. There is considerable uncertainty in the estimates of intake of HCBD in food, the likely principal medium of exposure. Fish may be a significant source of HCBD transmission from contaminated wetlands to humans. Measured concentrations of PCBs, HCB and HCBD have resulted in Fish Consumption Advisories in the US. No data on HCBD exposure of the Arctic indigenous populations could be identified in order to compare exposure with effect data.

124. It is well documented that the Arctic indigenous population is suffering from health problems due to exposure to persistent organic pollutants (AMAP, 2009). Exposure to HCBD, a nephrotoxic agent, which leads to enhanced tumour formation if co-exposure with a carcinogen exists should therefore be minimised.

4. Concluding statement

125. Although production and use of HCBD has ceased in the UN-ECE countries, information about ongoing use or reintroduction outside the UN-ECE is insufficient. This increases the uncertainty of estimates of current HCBD releases, bearing the risk of unaccounted HCBD releases in global estimates. Industrial releases of HCBD from chemical industry in the UN-ECE are currently low, also because the by-product HCBD is selectively recycled or destroyed during production. However, for regions outside the UN-ECE, little is known about volumes and releases of HCBD generated as a by-product in chemical industry.

126. HCBD can undergo atmospheric long-range transport due to its high persistence in air and its occurrence in abiotic and biotic matrices in remote regions. Monitoring data are limited to identify a temporal trend in subarctic or Arctic environments.

127. HCBD meets the persistence criteria in Annex D based on experimental and modelled degradation data in water. Also its long half-life in air (measured and estimated information) provides evidence that HCBD is otherwise sufficiently persistent to justify its consideration within the scope of the Stockholm Convention.

128. HCBD fulfils the bioaccumulation criterion of Annex D based on a high BCF value in fish.

129. HCBD is very toxic to aquatic organisms. Very limited toxicological information on the effects of HCBD in humans is available, therefore animal data have to be used for hazard considerations. It is highly toxic after repeated and chronic exposure to laboratory animals (vertebrates). Its high toxicity to the kidneys, genotoxicity and carcinogenicity is of special concern especially for lifelong dietary low level exposure conditions.

130. Based on the inherent properties, and given the measured occurrence in environmental compartments and biota in remote areas, together with the high toxicity and the suspected carcinogenicity, it is concluded that HCBD is likely, as a result of its long-range transport, to lead to significant adverse human health and environmental effects such that global action is warranted.

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