	/	52 LOAEL 0.5mg/kg/day	*Poecilia reticulata* 4-12 NOEC=0.032 mg/L
	logKow=3.78		
	BCF		
56 ( )	BCF=1460	13 NOAEL 0.1mg/kg/day	- HCH
	FWMF	0.1mg/kg/day 2.5mg/kg/day	
	FWMFs 1		1
100 184	FWMF=7.2 PCB	12.5mg/kg/day	2
15	FWMF=2.9		
44%			
570	BMF	26 3.4mg/kg/day IARC possibly carcinogenic to human	
30%	BMF 1		
	betaHCH	NOAEL 0.1mg/kg/day	
		20mg/kg/day	

		HCH	
		30 60mg/kg/day NK	

United Nations
Environment
Programme

Stockholm Convention on Persistent Organic Pollutants
Persistent Organic Pollutants Review Committee
Third meeting
Geneva, 19–23 November 2007

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

Addendum

Risk profile on beta hexachlorocyclohexane

At its third meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on beta hexachlorocyclohexane, on the basis of the draft contained in document UNEP/POPS/POPRC.3/18. The text of the risk profile, as amended, is set out below. It has not been formally edited.

BETA HEXACHLOROCYCLOHEXANE

RISK PROFILE

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

November 2007

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Executive summary

Mexico, being Party to the Stockholm Convention, proposed lindane as well as alpha- and beta-hexachlorocyclohexane to be included in Annex A, B or C of the Stockholm Convention. After the risk profile on lindane had already agreed at the last meeting of the Review Committee in November 2006, the Committee concluded that beta-HCH also complied with the screening criteria laid down in Annex D of the Convention and further elaboration of the proposal and preparation of a draft risk profile should be done.

After almost forty years of extensive use worldwide, there has been a gradual replacement of technical hexachlorocyclohexane (HCH) by lindane (gamma-HCH). No significant uses of technical HCH have been reported after 2000. However releases into the environment may also occur from lindane production as well as from hazardous waste sites, landfills and contaminated sites. Because of its hazard profile and widespread abundance, technical HCH (including beta-HCH) is subject to national and international regulations and prohibitions.

Abiotic degradation processes do not play an important role in the fate of beta-HCH in the environment. Thus photolysis and hydrolysis are not significant. Under favourable conditions, beta-HCH is susceptible to biodegradation. However, compared to the gamma- and alpha-HCH, it is the most recalcitrant isomer. Laboratory and field data including a long-term soil study suggest that beta-HCH is persistent in soil, especially under low temperatures. It is mainly associated with particles and has a low leaching potential.

The physico-chemical properties of beta-HCH allow the dispersal of the substance from its sources to the Arctic mainly by long-range environmental transport via ocean currents. Beta-HCH has been detected in the Arctic Ocean and is present in marine, terrestrial species, and humans.

Beta-HCH exposure levels in local areas have declined after worldwide prohibitions and restrictions. However regions with recent exposure and/or high pollution can still show elevated levels. A special concern also arises from exposure of hazardous waste sites and dumping grounds from disposed beta-HCH residues from lindane production.

Due to its persistence, beta-HCH can still be detected at low background levels in all environmental media except in regions with recent usage and/or high pollution. Data from the abiotic environment in the Arctic are scarce, partly due to low levels compared with the other HCH isomers. In contrast to this fact, fairly high concentrations in Arctic biota including marine mammals and birds were detected with increasing levels.

Beta-HCH is present in terrestrial and aquatic food chains. Beta-HCH may bioaccumulate and biomagnify in biota and Arctic food webs, especially in upper trophic levels. In humans, accumulation in fat tissue and high concentrations in blood and breast milk may occur. Beta-HCH transfers from mothers to embryos and nursing infants.

Beta-HCH is acutely toxic to aquatic organisms and shows estrogenic effects in fish. Reduced fitness of offspring in birds as well as reduced retinol concentrations in polar bears is associated with beta-HCH and HCHs levels.

Toxicological studies with beta-HCH have demonstrated neurotoxicity and hepatotoxicity. Also, reproductive and immunosuppressive effects and effects on fertility were seen in laboratory animals. Beta-HCH has been classified in group 2B as possibly carcinogenic to humans by the International Agency on Research and Cancer (IARC). Several epidemiological studies indicate that beta-HCH might play a role in human breast cancer.

Human exposure to beta-HCH results mostly from ingestion of contaminated plants, animals and animal products. High exposure is expected in contaminated areas due to extensive use, former production, disposal sites and stockpiles.

Given the hazard profile and the exposure levels in the environment including the food chain, it can be concluded that beta-HCH may adversely affect wildlife and human health in contaminated and remote regions including the Arctic region. Arctic public health authorities believe the significant social, cultural and economic benefits of traditional foods outweigh the risks of contaminants such as HCH at present but give another reason for the quick control and elimination of all HCH isomers from traditional foods.

Based on the hazard profile, together with estimated daily intakes of beta-HCH of Arctic indigenous people that exceeds safe intake reference values, and given the widespread occurrence of beta-HCH in biota, including in remote areas far from likely sources, it is concluded that the substance is likely, as a result of its long-range environmental transport, to lead to significant adverse human health and environmental effects, such that global action is warranted.

1 Introduction

During the procedure for adding lindane to Annex A of the Stockholm Convention, the POPs Review Committee discussed the proposal of lindane and concluded that "other isomers of hexachlorocyclohexane should also be considered" (UNEP/POPS/POPRC.2/10). Thus Mexico submitted a proposal for listing beta hexachlorocyclohexane in Annexes A, B or C of the Stockholm Convention on 26th July 2006 (UNEP/POPS/POPRC2./INF/8). Austria on behalf of Germany prepared the first working draft on beta-HCH.

Beta-HCH is one of the five stable isomers of technical HCH, an organochlorine pesticide formerly used in agriculture. The modes of action of the HCH isomers differ quantitatively and qualitatively with regard to their biological activity in the central nervous system as the main target organ. Beta-HCH is mainly a depressant and the final effect of the mixed isomers depends on the composition (IPCS, 2001). In general HCHs are among the most studied pesticides with respect to environmental fate and effects (Breivik et al., 1999).

1.1 Chemical Identity

Chemical name: Beta-hexachlorocyclohexane (beta-HCH)

IUPAC name: (1-alpha, 2-beta, 3-alpha, 4-beta, 5-alpha, 6-beta)-Hexachlorocyclohexane

Common synonyms: beta-1,2,3,4,5,6-Hexachlorocyclohexane; beta-Benzenehexachloride; beta-BHC, benzene-cis-hexachloride; beta-HCH; beta-Hexachlorocyclohexane; beta-Hexachlorocyclohexane; beta-isomer; beta-lindane; Hexachlorocyclohexane-Beta; trans-alpha-benzenehexachloride; beta-benzenehexachloride (Chemfinder, 2007)

CAS number: 319-85-7

Chemical formula: $C_6H_6Cl_6$

Molecular weight: 290.83

Figure 1: Structure of beta-HCH (modified from Buser et al.,1995)
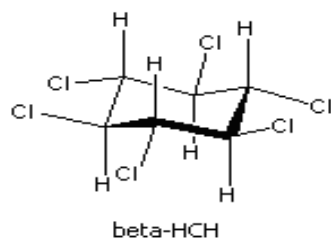
beta-HCH

1.1.1 Physico-chemical properties

Selected physico-chemical properties of beta-HCH are provided in Table 1. Beta-HCH is more soluble in water and octanol compared to other organochlorine pesticides. Its chemical structure seems to confer the greatest physical and metabolic stability (e.g. beta-HCH has a lower vapour pressure and a higher melting point than the alpha-isomer). The physico-chemical properties (a selection is given in Table 1) of beta-HCH allow for "cold condensation", an enrichment of the substance in cold climates compared to concentrations near sources, on altitudinal and latitudinal scales described by Wania and Mackay (1996).

The Henry's Law Constant is a factor of 20 lower than for alpha-HCH and decreases significantly with water temperature which favours partitioning from air to water. Also its relatively high log K_{oa} promotes partitioning from air to environmental organic phases. This is probably one reason why transportation pathways of alpha- and beta-HCH diverge in the environment (Li and Macdonald, 2005). Based on an extensive data analysis of the physico-chemical properties of alpha-, beta- and gamma-HCH Xiao et al. (2004) concluded that its different environmental behaviour is caused by a higher solubility in water and octanol rather than the lower volatility compared to the gamma- and alpha-isomer.

Table 1: Selected physico-chemical properties of beta-HCH

Melting Point (K)	314-315 [1]
Boiling Point (K)	333 at 67 Pa [1]
Water solubility (mol*m^{-3} at 25 °C)	1.44 [2]
Vapour pressure (Pa at 25 °C)	0.053 [2]
Henry´s Law Constant (Pa m^3 mol^{-1})	0.037 [2]
Log Kow (25°C)	3.9 [2]
Log Koa (25°C)	8.7 [2]
Physical state	crystalline solid [1]

[1] ATSDR (2005)

[2] Xiao et al. (2004)

1.2 Conclusion of the POP Review Committee of Annex D information

The POP Review Committee evaluated the proposal regarding beta-HCH submitted by Mexico (UNEP/POPS/POPRC.2/INF/8 as summarized by the Secretariat in document UNEP/POPS/POPRC.2/16) according to the requirements in Annex D of the Stockholm Convention at its second meeting in Geneva. In Decision POPRC-2/10 the Committee reached the conclusion that beta-HCH meets 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

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

- Proposal submitted by Mexico for listing alpha- and beta-HCH in Annexes A, B and/or C to the Convention (UNEP/POPS/POPRC2./INF/8), 2006.

- Decision POPRC-2/10 of the Review Committee, 2006.

- Information submitted by parties and observers according to Annex E of the Convention: specific and/or scientific information: Czech Republic, France, Germany, International POPs Elimination Network (IPEN), Japan, Norway, Switzerland, United States of America, general information: Algeria, Crop Life International, Kingdom of Bahrain, Mauritius, Mexico, Qatar, Republic of Lithuania and Turkey. This information is available on the Convention's website (http://www.pops.int/documents/meetings/poprc/prepdocs/annexEsubmissions/submissions.htm)

- Assessment of lindane and other hexachlorocyclohexane isomers, USEPA, 2006. http://www.epa.gov/oppsrrd1/REDs/factsheets/lindane_isomers_fs.htm

- International Programme on Chemical Safety, ALPHA- and BETA-HEXACHLOROCYCLOHEXANES, Environmental Health Criteria 123, World Health Organization. Geneva, 1992. http://www.inchem.org/documents/ehc/ehc/ehc123.htm

- Toxicological profile for hexachlorocyclohexanes, United States of America Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, 2005. http://www.atsdr.cdc.gov/toxprofiles/tp43.html

- The North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane (HCH) Isomers. 2006. North American Commission for Environmental Cooperation http://www.cec.org/pubs_docs/documents/index.cfm?varlan=english&ID=2053

In addition to these information sources a literature search of public data bases was conducted. The following databases were used: ECOTOXicology database (Ecotox, http://www.epa.gov/ecotox/) Hazardous Substances Data Bank (HSDB, http://toxnet.nlm. nih.gov/cgi-bin/sis/htmlgen?HSDB), Pubmed (http://www.ncbi.nlm.nih.gov /entrez/query.fcgi?DB=pubmed), Environmental Fate Data Base (EFDB http://www.syrres. com/esc/efdb_info.htm. In general search terms include the chemical name or CAS number and/or a combination of a technical term because of the multiplicity of entries. For the same reason, specific topical and updated articles were also considered.

The reports listed above contained individual references which were not listed again in this draft risk profile. References referred to in this document are provided in UNEP/POPS/POPRC.3/INF/28.

1.4   Status of the chemical under international conventions

Beta-HCH is a constituent of technical HCH, which is regulated at least by two international agreements. The first one is the 1998 Aarhus Protocol on Persistent Organic Pollutants (POPs) under the Convention on Long-Range Transboundary Air Pollution. Technical HCH is listed in Annex II of the protocol which restricted its use to an intermediate in chemical manufacturing only.

The second agreement is the Rotterdam Convention on the Prior Informed Consent (PIC) Procedure for Certain Hazardous Chemicals and Pesticides in International Trade. HCH (mixed isomers) is subject to the PIC Procedure and is listed in Annex III of the Convention.

Canada, Mexico, and the United States signed the North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane Isomers in 2006. The goal of the NARAP is for the three member countries to cooperatively take actions to reduce the risks associated with the exposure of humans and the environment to lindane and other HCH isomers.

In the European Union the production and use of technical HCH as an intermediate in chemical manufacturing will be phased out by the end of 2007 at the latest (Regulation (EC) No 850/2004). HCHs are also one of the priority substances (Decision No 2455/2001/EC) of the adopted EU Water Framework Directive 2000/60/EC.

Hexachlorocyclohexane isomers, including the beta-isomer, are on the List of Chemicals for Priority Action under the OSPAR Commission for the Protection of the Marine Environment of the Northeast Atlantic. The objective is the prevention of pollution of the maritime area by continuously reducing discharges, emissions and losses of hazardous substances.

2   Summary information relevant for the risk profile

2.1   Sources

2.1.1   Production

Beta-HCH by itself is neither intentionally produced nor placed on the market. It is produced as constituent of technical HCH used as organochlorine insecticide or chemical intermediate to manufacture enriched HCH (lindane). Currently no production data on technical HCH have been reported, whereas manufacture of lindane still takes place (IHPA, 2006).

Further details on the production and reuse of HCH residuals can be found in UNEP/POPS/POPRC.2/17/Add.4 (Risk Profile on Lindane) and IHPA (2006).

The following countries which submitted information according to Annex E stated that there was currently no production or use of beta-HCH: Czech Republic, Germany, Mauritius, Mexico, Norway, Qatar, Republic of Lithuania, Turkey, Switzerland and the United States of America.

2.1.2   Trade and stockpiles

Please see section 2.1.2 of the risk profile on alpha-HCH.

2.1.3   Uses

Please see section 2.1.3 of the risk profile on alpha-HCH.

2.1.4   Releases to the environment

There are several pathways for beta-HCH for entering the environment. Historically beta-HCH was released during the manufacture of technical HCH and its use as a pesticide. Li et al. (2003) estimated global emissions of beta-HCH from the usage of technical HCH between 1945 and 2000 at 850 000 tonnes, of which 230 000 tonnes were emitted into the atmosphere over the same period. In 1980, the usage of beta-HCH was around 36 000 tonnes, and the calculated primary emissions were 9 800 tonnes (83 % attributed to the application and 17 % to soil residues due to prior applications). In 1990, figures dropped to 7 400 (usage) and 2 400 tons (emissions). In 2000, emissions of beta-HCH from soil residues were 66 tonnes in the absence of direct usage of technical HCH. Also, as a result of the ban on technical HCH in northern countries, global emissions of beta-HCH have undergone a "southward tilt" (Li et al., 2003).

Releases of beta-HCH into the environment are also possible from hazardous waste sites (USEPA, 2006), stockpiles and residues of lindane production, which are not always controlled or maintained safely (IHPA, 2006). Also, contaminated sites (e.g. from former production plants) may contribute to the environmental burden of beta-HCH (Concha-Grana et al., 2006). Germany (submitted Annex E information, 2007) reported that there are still a few isolated local sources i.e. landfills and dumps in the former GDR (East Germany) from applications of technical HCH. As a result, higher concentrations of beta-HCH in fish of the river Elbe near the former production site were detected after heavy rainfalls and floods in 2003. However, quantitative estimates of releases from hazardous waste sites and landfills are not available.

2.2 Environmental fate

2.2.1 Persistence

Investigations of the hydrolysis and photolysis of beta-HCH are extremely limited. Only one literature study regarding photodegradation has to date been available. A photodegradation half-life for a thin film of beta-HCH equal to 152 hours has been reported (ATSDR, 2005). The relevance of this result is questionable with respect to the chosen test design which does not comply with internationally accepted test guidelines on photolysis and, as pointed out by ATSDR (2005) no absorption bands were observed in the studied spectral region. In general, photolysis is not expected to be an important environmental fate process for beta-HCH since no absorption of light > 290 nm takes place.

Based on the calculated atmospheric OH rate constant of 5.73×10^{-13} cm^3/molecule-sec (HSDB, 2006) the estimated half-life is 56 days (using an average hydroxyl radical concentration of 5×10^5 molecule/cm^3 according to the TGD (2003)).

USEPA (2006) concluded that HCH isomers are resistant to abiotic processes like photolysis and hydrolysis (except at basic pH).

Beta-HCH is in principle biodegradable under oxic and anoxic conditions. However several studies have suggested that significant degradation does mainly occur under anaerobic conditions (Middeldorp et al., 1996). Degradation was observed in pure cultures, soil slurry, soil microcosm, field studies and via bioremediation techniques in the soils of contaminated sites (Phillips et al., 2005). Effectiveness of removal varied depending on the test design and environmental factors.

In general the metabolic pathway of beta-HCH occurs anaerobically via dechlorination to tetrachlorocyclohexene and dichlorocyclohexadiene, an unstable metabolite. Chlorobenzene and benzene were formed as stable end products under methanogenic conditions. These metabolites can be further aerobically or anaerobically mineralised (Phillips et al., 2005). Compared to other HCH isomers laboratory data using radio-labelled beta-HCH have shown only minimal and incomplete mineralization (Sahu et al., 1995).

Beta-HCH is considered to be the most recalcitrant isomer due to its chemical structure (Decision POPRC-2/10, 2006). Under favourable laboratory conditions several strains of bacteria e.g. *Bacillus brevis*, *Bacillus circulans*, *Dehalobacter sp.* in conjuction with *Sedimentibacter sp.,* isolated from HCH polluted sites, have been identified as beta-HCH degraders (Gupta et al., 2000; van Doesburg et al., 2005). But only a few e.g. *Sphingobium sp.* were able to transform beta-HCH under aerobic conditions (Sharma et al., 2006).

Research on the intrinsic stimulation and additives for soil bioremediation of beta-HCH polluted sites is under way (e.g. Kumar et al., 2005; MacRae et al., 1984) but to remove the isomer remains a difficult challenge (Phillips et al., 2005). Regarding the effects on the intrinsic soil microbial population of an uncontaminated soil, Bhatt et al. (2006) showed that the application of technical HCH disturbed the microbial community irreversibly.

In general, climatic conditions as well as soil texture and organic matter altering substance sorption, water content, pH and bacterial growth influence degradation rates (IPCS, 1992). Phillips et al. (2005) stated that bacteria capable of degrading HCHs at extreme temperatures (< 5 °C or > 40°C) have not yet been reported.

Data on laboratory soil studies or field investigations are limited. Singh et al. (1991) reported half-lives of 100 and 184 days on cropped and uncropped plots respectively, in a sandy loam in India under subtropical conditions. The applied formulated HCH was immediately incorporated into the top layer of the soil. Soil samples were taken randomly from the plots in 0-15 cm depths. No quantitative information on losses of beta-HCH by volatilisation or leaching during the experiment is available in the citied study. In a temperate climate Doelman et al. (1990) observed in a semi-field study with contaminated soil no degradation of beta-HCH under anaerobic conditions. Stewart and Chisholm (1971) observed in a long-term field study after an application of technical HCH, 44 % of the beta-HCH isomer after 15 years in a sandy loam in Canada. Approximately 30 % of beta-HCH (from applied technical HCH) was observed after 570 days in a field test in Japan on agricultural field plots (Suzuki et al., 1975). Also, Chessells et al. (1988) showed that after a 20 year application history of technical HCH on sugar cane in Queensland, Australia, beta-HCH was found in concentrations which are more than one order of magnitude higher compared to the other isomers. Volatilisation from soil surfaces is considered not to be an important fate process (HSDB, 2006; Singh et al., 1991).

Beta-HCH was stable in a sediment/water study under laboratory conditions. In addition, isomerisation of alpha- to the beta-HCH isomer was observed (Wu et al., 1997). Detailed information regarding isomerisation can be found in the risk profile on lindane (UNEP/POPS/POPRC.2/17/Add.4). Levels of the beta-HCH isomer compared to alpha-, gamma- and delta-HCH were highest in porewater (1 423 ng/l) compared to concentrations in surface water (92.5 ng/l) and sediment (3.9 ng/g) of the Minjiang River Estuary, China (Zhang et al., 2003). No degradation half-lives in water or sediment are available, however, based on monitoring studies, it can be assumed that beta-HCH is persistent and does not undergo degradation easily.

2.2.2 Bioaccumulation

The octanol-water partition coefficient (log K_{ow} = 3.78) for beta-HCH indicates that it has a potential to bioaccumulate, especially in combination with its shown persistence in animal tissue (Walker et al., 1999),

The BCF according to the former OECD test guideline 305 E in zebra fish was equal to 1 460, which was the highest BCF (whole body) compared to determined values for alpha- (1 100) and gamma-HCH (850) (Butte et al., 1991). According to the ECOTOX database this was also the highest reported BCF. Nonetheless, the screening criteria were considered fulfilled by POPRC for beta-HCH as set out in the evaluation contained in the annex to its decision POPRC-2/10.

Several studies suggest that the relative proportions of HCH isomers vary dramatically across species in the Arctic marine food web (USEPA, 2006). Concentrations of beta-HCH increased with the trophic level especially in upper trophic levels (marine mammals) (USEPA, 2006; Hoekstra et al., 2003). Whereas it is assumed that organochlorine (OC) profiles in mammals are mainly influenced by their ability to biotransform and excrete OCs, high detected levels of beta-HCH in various mammalian species are another indication of its recalcitrant nature and slow elimination. Hop et al. (2002) showed that beta-HCH biomagnifies differently in poikilotherms and homeotherms. Beta-HCH increased more among homeotherms (birds and mammals) with the trophic level. Fisk et al. (2001) reported the highest BMF (biomagnification factor) in birds compared to the other trophic levels, but migration and prey items are also considered to influence the variability of the BMFs. These data are in line with findings from Moisy et al. (2001). In general, studies from Arctic marine food webs show that BMFs for nearly all examined species as well as obtained food web magnification factors (FWMFs), which represent the mean rate of increase per trophic level in the food chain, are greater than 1. For example Fisk et al. (2001) reported a FWMF of 7.2 which is comparable to higher chlorinated PCBs. A FWMF of 2.9 was calculated by Hoekstra et al. (2003) for the marine food web in the Beaufort-Chukchi Sea. However in sub-Arctic waters e.g. the White Sea, values for for beta-HCH were lower compared to the other food web studies. Differences in feeding habits and availability/levels of contaminants were suggested as being responsible by Muir et al. (2003).

Also, in the terrestrial food chain, beta-HCH may biomagnify. Data obtained from an investigation in south India showed that HCHs were the predominant OCs in biota. Elevated concentrations were measured in snails and subsequently their predators (e.g. little egret) showed BMFs above 1 (Senthilkumar et al., 2001). Also Wang et al. (2006) found beta-HCH as a major compound in mollusks (submitted Annex E information by IPEN, 2007).

Kelly at al. (2007) have recently shown that, for substances with a logKoa >6 and a logKow >2, the fish BCF is not a good predictor of biomagnification in air-breathing animals. This is well illustrated by beta-HCH, in the marine mammalian and terrestrial food webs, as such compounds biomagnify strongly up to 3000- and 400-fold respectively.

Fish, marine and terrestrial mammals as well as birds are the major nutrition sources of several human Arctic population groups and thus exposure through diet is much more likely than for most populations in the developed world. Levels of beta-HCH in breast milk among women from indigenous people on the Chukotka Peninsula, Russia (Chukotsky rayon, mean value 370 ng/g lipids) are highest compared to other northern towns of Russia and to levels in Canada (Nunavik, by 30 times; AMAP, 2004). Also, concentrations of maternal blood sampled between 1994 and 1997 were highest in Russian mothers (Arctic non-indigenous population, serum concentration 223 µg/kg lipid), but elevated levels were also found in Iceland (23 µg/kg) and in the Canadian Arctic (AMAP, 2003).

2.2.3 Long-range environmental transport

Many studies and monitoring data have detected beta-HCH regularly in the Arctic environment as well as in biota (e.g. AMAP, 2004; AMAP, 2003). Because technical HCH, including beta-HCH, was never extensively used in this remote area, this is evidence of its long range transport (UNEP/POPS/POPRC.2/17/Add.4).

Based on monitoring data from Arctic air, beta-HCH appears to be less subject to direct atmospheric loading into the high Arctic. This can possibly be explained by differences in the Henry's Law Constant and the air/octanol partition coefficient that show enhanced affinity to organic matter (Li et al., 2002). Thus rain scavenging is much more efficient for beta- than for alpha-HCH and besides, the frequency of precipitation is considerably higher in the North Pacific compared to the Arctic. This suggests that beta-HCH enters the Arctic probably by mechanisms involving wet deposition or partitioning into the North Pacific surface water and subsequently entering the Arctic in ocean currents passing through the Bering Strait (Li et al., 2003). The Bering and Chukchi Seas are the most vulnerable locations for beta-HCH loadings (Li et al., 2002). Concentrations of beta-HCH around the Bering Strait in the 1990s reached approximately 1.2 ng/l (Li and Macdonald, 2005). Thus "cold condensation" also occurred for beta-HCH, but mainly in the Pacific Ocean and Bering Sea upstream of the Arctic Ocean. Thus beta-HCH reached the Artic later compared to alpha-HCH and differed in its spatial distribution (Li et al., 2002). This spatial and temporal distribution is also reflected in residue levels in marine and terrestrial mammals as well as in local residents (Li and Macdonald, 2005).

Measurement of beta-HCH in high mountains in the Czech Republic is another proof for its long-range transport potential (submitted Annex E information by the Czech Republic, 2007).

According to model calculations with the OECD Pov and LRTP Screening Tool beta-HCH has similar persistence and long-range transport properties compared to already identified POPs such as PCBs and OCs (Wegmann et al., 2007). Model input properties of the chemicals include partition coefficients in air-water and octanol-water as well as half-lives in air, water and soil and the Henry's Law constant (based on figures contained in UNEP/POPS/POPRC2./INF/8). The model considers all environmental compartments quantitatively. The results of the model do not indicate absolute levels in the environment but help to compare possible POPs with identified POPs (reference chemicals: PCB congeners 28, 101, 180, HCB, carbon tetrachloride and alpha-HCH) according to their environmental persistence and potential for long range transport. Uncertainties in the chemical properties were investigated by Monte Carlo uncertainty analysis.

2.3   Exposure

Direct exposure to beta-HCH resulted from the production (including manufacture of lindane) and use of technical HCH. Because of the persistence, high exposure is also expected in contaminated areas due to extensive use, former production, disposal sites and stockpiles. Though usage of technical HCH has practically ceased worldwide monitoring data based on the ratio of the alpha/gamma-isomer still suggest possible releases of technical HCH in certain areas (Zhang et al. 2003; Qian et al., 2006; Zhulidov et al., 2000).

Exposure of the general public results mostly from the ingestion of contaminated plants, animals and animal products. Inhalation of ambient air and consumption of drinking water are further sources of exposure, although to a minor extent. Intake through indoor air may be considerable for people living in houses treated for pest-control purposes. Infants may be exposed during fetal development and breastfeeding.

2.3.1   Environmental monitoring data from local areas

Generally environmental levels in local areas have dropped after restrictions and prohibitions of the usage of technical HCH (IPCS, 1992). However, monitoring data show its ubiquitous distribution in all environmental media. For example, beta-HCH (up to 15 µg/kg dry substance) has been detected using passive monitoring in lichens in various locations (e.g. cities, industry, rural) in Switzerland (submitted Annex E information by Switzerland, 2007). Also, a recently (2004) performed monitoring programme in Japan revealed that beta-HCH had been detected in all specimens. The reported values (range) are as follows: water 0.031-3.4 ng/l, sediment 0.004-53 ng/g dry weight, shellfish 0.22-1.8 ng/g wet weight, fish trace-1.1 ng/g wet weight, bird 1.1-4.8 ng/g wet weight, air (warm and cold season) 0.53-110 pg/m^3 and 0.32-78 pg/m^3 (submitted Annex E information by Japan, 2007). The Czech Republic (Annex E information, 2007) reported that, with regard to HCHs, the most severe situation is in central and southern Moravia, where sediment particles are found in amounts of tens of ng/g and in some cases even in hundreds of ng/g (no information on which basis the concentrations are expressed was submitted).

However, heavily contaminated soils were found in the proximity of sources. HCH concentrations of 40 - 225 mg/kg were found in the topsoil around a chemical plant in Albania. Mean levels of 0.02 mg/kg were reported for soils from the Pearl River Delta in China, while Russian soils near the Lena River contained 0.001-0.017 mg/kg HCH (UNEP, 2003).

Compared to the other HCH isomers, concentrations of beta-HCH in the air are low. Elevated levels were detected in higher mountains (Mount Everest Region) of 11.2 pg/m^3 compared to up to 1 pg/m^3 in the Arctic (Li et al., 2006). Seasonal changes in beta-HCH concentrations in Japan (mean 23 pg/m^3) in 2000 were probably caused by re-emissions from a terrestrial source (Murayama et al., 2003). Unlike alpha- and gamma-HCH observed concentrations of beta-HCH in air at most locations near the Great Lakes in North America did not show significant trends between 1990 and 2003. The highest concentration was observed in Chicago with a maximum of 73 pg/m^3 (mean 12 pg/m^3, 1999-2003, gas phase, Sun et al., 2006a). Regarding the occurrence of beta-HCH in precipitation samples from the same region (mean concentrations 0.16 - 0.64 ng/l) a significant increase in concentrations at three Great Lakes stations over the last decade was observed (Sun et al., 2006b).

Levels in biota vary, depending on the location (recent usage and/or high pollution) and species. For example, concentrations of HCHs (mainly the beta-isomer) in one fish species (*Java tilapia*) from India amounted to up to 2 000 ng/g wet weight (Senthilkumar et al., 2001). Fish samples collected from the Nile River near Cairo in 1993 showed a concentration of beta-HCH of 1.5 ng/g wet weights (UNEP, 2003). Alpha-HCH is in most cases the dominant isomer in fish (Willett et al., 1998).

A global sampling study of free-range chicken eggs found that of 30 egg samples taken from 17 different geographic locations, beta-HCH was detected in all samples. Levels were particularly high in samples taken in Senegal and India. (Blake, 2005).

Birds and bats can accumulate higher concentrations of beta-HCH. According to submitted Annex E information by Norway (2007) Bustnes et al. (2006) concluded that beta-HCH levels in blood and eggs were higher in the endangered subspecies compared with the increasing subspecies of the black-backed gulls in Norway. One explanation might be the migration route through the Black Sea where HCH levels are considerable high.

In a study of resident and migratory birds collected from South India, the organochlorine contamination pattern varied depending on the migratory behaviour. Resident birds living in the same region for their entire life span contained relatively greater concentrations of HCHs (14-8800 ng/g wet weight). Long distance migratory birds which have their breeding grounds in Europe, Russia, the Middle East, Papua New Guinea and Australia contained HCHs at levels of 19-5500 ng/g. Among various HCH isomers, beta-HCH was the predominant contaminant in all the bird species (UNEP, 2003). Similar levels were reported in a later investigation (Senthilkumar et al., 2001) including residue levels of HCHs in egg yolks (range 350-49000 ng/g fat weight). Again beta-HCH was the predominant isomer in birds (no detailed values for beta-HCH were reported). In addition, HCHs concentrations (mainly the beta-isomer, up to 330 ng/g wet weight) in Indian bats were investigated, which were higher in 1998 than in 1995 and highest compared to other parts of the world.

A local source of beta-HCH was the usage of technical HCH in the Russian north against nuisance insects on domesticated reindeer by indigenous human populations (Li et al., 2004). However, no quantitative estimates of these exposure levels exist.

2.3.2 Exposure as a result of long-range environmental transport

The main transportation pathway of beta-HCH to the Arctic is assumed to be ocean currents (Li et al., 2002). Compared to levels of alpha-HCH in sea water, beta-HCH levels were lower - partly due to reduced emissions and different spatial and temporal distributions, e.g. beta-HCH reached its peak (approximately 0.3 ng/l) in the north American Arctic Ocean in 1994, around 10 years after the alpha-HCH levels had reached their peak. Enrichment of the upper waters of the North Pacific Ocean and Bering Sea (approximately 1.3 ng/l 1988-1999) caused higher concentrations in the Chukchi Sea and subsequent decreases towards the Arctic interior ocean (Li and Macdonald, 2005). Data on beta-HCH from surface water of the Canadian Archipelago in 1999 showed concentrations of 0.1 ng/l (Bidleman et al., 2007).

This spatial distribution is also reflected in the levels in biota. Hoekstra et al. (2002) found that bowhead whales exhibit a reversal in their blubber alpha-/beta-HCH ratios on their migration route between the Bering to the Beaufort Sea. Also elevated residues of HCH isomers in marine mammals of the Canadian Archipelago are likely due to the high concentrations of HCH isomers in the water because HCH isomers are the most abundant organochlorines in the Arctic Ocean (NARAP, 2006).

Beta-HCH is not so abundant in the Arctic abiotic environment and therefore it has not been studied as well as the other HCH isomers. Measured levels in the Arctic air (e.g. < 1 pg/m^3 from six Arctic circumpolar located sites between 2000-2003, Su et al. (2006)) and in terrestrial as well as freshwater ecosystems were low (AMAP, 2004). HCHs also show a high degree of spatial variability in the levels of contamination across the Russian north (AMAP, 2004).

Levels in the Arctic terrestrial environment (including carnivores) are much lower than in the marine compartment and its predators. However, beta-HCH has been detected in the fat of male Arctic foxes (up to 810 ng/g wet weight) in Alaska (AMAP, 2004). The highest levels of HCH in polar bears were detected in the Beaufort Sea population (approx. 770 ng/g wet weight in fat). Beta-HCH accounted for 93 % of HCH residues.

The metabolism of beta-HCH is very limited in Arctic seabirds, and therefore beta-HCH is detected more readily than alpha- and gamma-HCH. But concentrations vary notably between species, depending on the trophic position and migration. Higher levels of beta-HCH were observed in the North American Arctic in closer proximity to Asia where HCH was recently used. Levels were below 1 ng/g in bird tissue and 30 ng/g wet weight in eggs (AMAP, 2004).

Regarding temporal trends, it was shown that beta-HCH levels in seabirds, ringed seals and polar bears increased, whereas belugas showed no difference from 1982 to 1997 (AMAP, 2004).

2.3.3 Food

Daily intake values of beta HCH for the general population in adult human diets between 1986 and 1991 in the United States were reported to be below 0.001 µg/kg /day The average concentration of beta-HCH in 234 ready-to-eat foods was 0.0027 µg/kg (no information on which basis the concentrations are expressed, ATSDR, 2005). In the Total Diet Study conducted by USFDA in 2003 on 100 food items, beta-HCH was detected in 12 items (submitted Annex E information by IPEN, 2007). In the USA, the average daily intake of beta-HCH was <0.1-0.4 ng/kg body weight (bw) (depending on age) during the years 1982-1984 and was generally below 0.1 ng/kg bw during the years 1986-1991 (ATSDR, 2005). In a total diet study from Canada (1993-1996), an average daily dietary intake of 0.39 ng/kg bw beta-HCH was reported (EFSA, 2005). In fat-containing food products, levels ranged up to 0.03 mg/kg (fat) but in milk products levels up to 4 mg/kg (fat) were detected (WHO, 2003). In the United States and Canada levels in food are slowly decreasing. Within the European countries representative dietary intake studies are scarce. One was performed

in the Czech Republic. The median intake values for beta-HCH declined from 8.4 ng/kg bw in 1994 to 2.1 ng/kg bw in 2002 (EFSA, 2005). A local diet study from Spain showed elevated daily intakes of 0.1 µg beta-HCH (Urieta et al., 1996). Fish and clam samples from India contained 0.001 and 0.02 mg beta-HCH/kg wet weight respectively (Nair and Pillai, 1992). Because of the global trade of foodstuffs, feed ingredients and food products from regions with ongoing or recent use of HCHs, which are supposedly more contaminated, might be imported by countries where technical HCH has already been phased out.

High levels of beta-HCH levels in food are documented for the Arctic Region (AMAP, 2004). Subsistence foods in Alaskan communities from the years 1990 to 2001 were analysed for total HCH in order to estimate dietary intakes by indigenous people. Highest concentrations were found in marine mammals of whale (391 ng/g) and seal (215 ng/g). High concentrations were documented for walrus (20 ng/g), whitefish (20 ng/g) and salmon (26 ng/g). Berries contained 10 ng/g and ducks 7 ng/g (no specification if values referring to whole body or lipid basis reported) (USEPA, 2006).

2.3.4 Body burden

2.3.4.1 General population

Beta-HCH is the most prevalent HCH-isomer in human fatty tissue. The half-life of beta-HCH after inhalation exposure in the body is 7.2-7.6 years (ATSDR, 2005). Human biomonitoring studies in the United States showed that median levels of beta HCH in post-mortem human adipose tissue samples decreased over time (0.45 ppm in 1970 to 0.16 ppm since 1981) (ATSDR, 2005).

A comparison between body compartments showed median levels of 0.13 ng/g in whole blood and 18 ng/g in adipose tissue (ATSDR, 2005). According to the results of the National Reports on Human Exposure to Environmental Chemicals, beta-HCH serum concentrations in the US population have been declining since 1970. For all tested age groups (12 years and older), the 95th percentile of beta-HCH serum concentrations on a lipid-weight basis decreased from 68.9 in the years 1999-2000 to 43.3 ng/g in the years 2001-2002. Concentration levels (2001/2002) in females were higher (54.5 ng/g) than in males (29.2 ng/g). Highest concentration levels were found in the Mexican Americans (84.4 ng/g). Comparably low levels were found in the age group 12-19 years (8.44 ng/g) (CDC, 2005). Age-related increases in the levels of beta-HCH have been observed in several studies and documented by the German Commission on Biological Monitoring (Ewers et al., 1999).

Comparably high concentrations were detected in human blood serum samples from Romania. Beta-HCH was detected in all samples (n = 142) with a median concentration of 923 ng/g lipid (range 38-11690 ng/g) (Dirtu et al., 2006). High concentrations were reported for India due to agricultural use and Malaria control activities. Blood serum samples from India contained up to 0.02 mg beta-HCH/l, whereas adipose tissue contained up to 0.18 mg/kg (Nair and Pillai, 1992).

2.3.4.2 Indigenous population

Beta-HCH concentrations in blood plasma samples from different regions and ethnic groups of indigenous mothers of the Arctic were 0.04 - 0.11 µg/l (Canada), 0.07-0.56 µg/l (Greenland), 0.12 - 0.53 µg/l (Alaska), 0.31 - 3.1 µg/l Russian Arctic (maximum level: 11.6 µg/l), 0.16 - 0.21 µg/l (Iceland), 0.05 - 0.09 µg/l (Norway, Finland and Sweden) and 0.11 µg/l from the Faroe Islands (AMAP 2004, values given as geometric means, with the exception of Alaska which are given as arithmetic means). The highest concentrations in blood samples of the indigenous population were reported for the Russian Arctic.

Comparative investigations of the maternal blood and cord blood of indigenous mothers for beta-HCH in the Russian Arctic were highly dependent on the residential area. The mothers with the highest exposure (Chutkotsky District) had blood concentrations (µg/l plasma, geometric mean and range) of 2.0 (0.6 - 7.6) µg/l whereas the cord blood contained 0.8 (n.d.- 8.0) µg/l (AMAP, 2004:2). The variation in body burden for indigenous people may also be due to local sources in addition to variations in consumption of local marine foods (AMAP, 2004:2).

2.3.5 Exposure of children

Children are at specific developmental stages more vulnerable against chemical substances than adults. It is not known if children are more susceptible than adults to health effects from exposure to beta-HCH. Placental transfer of HCH in humans has been well documented (ATSDR, 2005; Falcon et al., 2004; Shen et al., 2006). Beta-HCH is lipophilic and accumulates in adipose tissue and breast milk. This is another relevant exposure source for children (USEPA, 2000). Several studies concerning beta-HCH in breast milk are listed in Table 2. It could be shown, that due to restrictions of use, concentrations are constantly declining.

It can be concluded that beta-HCH concentrations in breast milk are highly exposure-dependent. Whereas in some areas concentrations are very low, i.e. 13 ng/g in Poland, in other areas i.e. Russia, Ukraine, Romania they are very high (up to > 800 ng/g). In general it can be expected that in several East European and developing countries concentrations

are still very high. Especially high concentrations were reported for India and China (Wong et al., 2002). Extremely high levels were also reported for cotton pickers in Pakistan (UNEP, 2003).

Due to bioaccumulation in the Arctic marine food web, high concentrations were found in the breast milk of indigenous mothers of Arctic regions.

Table 2. Concentrations of beta HCH in breast milk

Country/region	Levels (lipid weight basis)	Comments	References	Year
Germany	0.12 mg/kg	Start of Monitoring program 1984	Fürst et al. in EFSA, 2005	1984
Germany	0.02 mg/kg	Continuous Monitoring since 1984	Fürst et al. in EFSA, 2005	2001
Spain	0.24 µg/g	51 samples	Hernandez et al. in Wong, 2002	1991
Canada	0.6-0.8ng/g	Lower concentration: population near Great lakes	Mes and Malcolm in ATDSR, 2005	1992
Canada	0,02 µg/g	497 samples	Newsome and Ryan in Wong, 2002	1992
Brazil	0.27 µg/g	40 samples	Paumgartten et al. in Wong, 2002	1992
Russia Murmansk	853 ng/g	15 samples	Polder et al. in Dirtu, 2006	1993
Russia Nonchegorsk	740 ng/g	15 samples	Polder et al. in Dirtu, 2006	1993
Ukraine	731 ng/g	200 samples	Gladen et a.l in Dirtu, 2006	1993-1994
Czech Republic	71 ng/g	17 samples	Schoula et al. in Dirtu, 2006	1993-1994
Kazakstan	2.21µg/g	33-76 samples	Hooper et al., in Won, 2002	1994
Siberian Russia	40 -142 µg/kg (geom.means)	Arctic Monitoring Assessment Programme	Klopov et al. 1998, 2000 in AMAP 2004	1994-1995
Northern Russia	120 -401 µg/kg (geom.means)	Arctic Monitoring Assessment Programme	Polder et al. in AMAP 2004	1994-1995
Australia	0.35µg/kg	60 samples	Quinsey et al in Wong, 2002	1995
Afrika, Uganda,	0.005-0.25 mg/kg	-	Ejobi et al. in ATDSR, 2005	1996
India	8.83 µg/kg	Delhi, Age group: 20-30 61 samples	Banerjee et al. in Wong, 2002	1997
India	0.022 – 0,078 mg/kg	Region under Malaria control	Dua et al. in ATDSR, 2005	1997
Pakistan	0 – 0.90 mg/kg	Cotton pickers	Masud and Parveen, 1998 in UNEP, 2003	1998
Nairobi, Kenya	0.0830-0.026 mg/kg	Urban population	Kinyamu et al.	1998
Japan, Osaka,	5.43 µg/g	Estimated use in Japan: 400 000 tons	Konishi et al. 2001	1972
Japan, Osaka,	0.21 µg/g	Ban of organochlorine compounds in 1970ies	Konishi et al. 2001	1998
Romania, Iassay	640 ng/g	19 samples	Covaci et al. in Dirtu, 2006	2000
Czech Republic	56 ng/g	43 samples	Cajka and Hajslova in Dirtu, 2006	2000
China, Hong Kong	15.96 µg/g	Uncontrolled agricultural use	Wong et al. 2002	1985
China, Hong Kong	0.95 µg/g	115 samples	Wong et al. 2002	1999
China, Guangzhou	1.11 µg/g	54 samples	Wong et al. 2002	2000
Turkey	149 ng/g	37 samples	Erdoorul et al. in Dirtu, 2006	2003
Poland	13 ng/g	22 samples	Jaraczewska et al. in Dirtu, 2006	2004
Sweden, Copenhagen	13.64/12.29 ng/g	Cases/Controls Cryptorchidism- study	Daamgard et al.	2006

2.3.6 Information on Bioavailability

Beta-HCH is moderately associated with organic matter in the environment. Uptake by plants and residues in vegetation as well as by food and feed is well documented (Willet et al. 1998; ATSDR, 2005; EFSA, 2005). Though beta-HCH is not assumed to be very mobile in soil there have been cases of groundwater contamination in the past (HSDB, 2006).

In biota, beta-HCH is selectively accumulated in certain tissues (e.g. liver, muscle, fat) and affects several organs (Willett et al., 1998). It can be concluded that beta-HCH is bioavailable in the environment and in biota.

2.4 Hazard assessment for endpoints of concern

2.4.1 Human Health

Information on the toxicity of beta-HCH is mostly derived from experimental studies in animals. Compared to lindane, the data available are limited, especially concerning human data because occupational exposure occurs mainly with technical-grade HCH and lindane.

Studies of acute/short-term toxicity via the oral route, subchronic and chronic oral toxicity studies and a limited number of studies of reproductive effects are available. No studies of the toxicity of beta HCH via inhalation and dermal application have been conducted. There is a lack of dose-response data after oral exposure in all relevant species. For the present risk profile, the most important findings concerning the hazard assessment have been reviewed. For further studies and details the more comprehensive toxicological profiles should be consulted (IPCS, 1992; ATDSR, 2005; USEPA, 2006).

Acute Toxicity/ Neurotoxicity: The concentration range for lethal acute toxic effects is - according to IPCS (1992) - 150 mg/kg to > 16000 mg/kg in mice and 600 mg/kg to > 8000 mg/kg in rats. Symptoms of acute toxicity affect mainly the nervous system: excitation, hunched posture, rough fur, dyspnoea, anorexia, tremors, convulsions and cramps.

Subchronic toxicity: In a 13-week study in rats, the effects of oral exposure to beta-HCH (0, 2, 10, 50, 250 mg/kg diet) were investigated. In all dose groups, liver effects were observed. At the highest dose tested (250 mg/kg diet) half of the animals died following ataxia, progressive inactivity, and coma. Observed effects included growth inhibition, decrease of red and white blood cells, increase of liver enzymes and liver effects (increase in organ weight, centrilobular hepatocytic hypertrophy). A decrease in thymus weight (50 and 250 mg/kg) and atrophy of the testes were observed. The females showed atrophy of the ovaries with impaired oogenesis and focal hyperplasiea as well as metaplastic changes of the endometrial epithelium, which was interpreted as a possible estrogenic action of beta-HCH (van Velsen et al., 1986). A NOAEL of 2 mg/kg diet (equivalent to 0.1 mg/kg bw/day) was established (IPCS, 1992; EFSA, 2005).

Chronic Toxicity: A long-term study (52 weeks) in rats with 0, 10, 100 and 800 mg/kg beta-HCH in their diet (i.e. 0.5, 5 and 40 mg/kg bw/day) led to liver enlargement and histological changes. Nearly all animals died. The LOAEL was 10 mg/kg diet (Fitzhugh et al., 1950).

A two-generation reproduction study of rats exposed to 10 mg/kg diet resulted in increased mortality and infertility. The NOAEL was 2 mg beta-HCH/kg diet (equivalent to 0.1 mg/kg bw/day) (van Velsen in IPCS, 1992).

Genotoxicity: Beta-HCH was not mutagenic to bacteria (_Salmonella typhimurium_ strains TA 98, TA 100, TA 1535 and TA 1537) with and without metabolic activation and did not induce DNA damage in bacteria. Positive results were seen in an in-vivo rat bone marrow chromosomal aberration study (EFSA, 2005).

Carcinogenicity: Studies of the carcinogenicity of beta-HCH are limited. Several studies in mice were performed, but their value is limited. On the one hand their duration, due to high mortality, was too short; on the other hand histopathological evaluations were missing. Studies in rats have been inadequate due to high mortality and small animal numbers. One study in mice is adequate for an evaluation of the carcinogenicity of beta-HCH. 200 mg/kg beta-HCH in the diet (equivalent to 40 mg/kg bw/day) for 110 weeks led to liver enlargement, hyperplastic changes and an increase in benign and malignant tumours in the exposed mice. In a 32 weeks study where 0, 100, 300, 600 mg/ per kg diet were given to mice, liver toxicity and atypical proliferation was observed in all dose groups (IPCS, 1992). In a 24-week study in mice - given 0, 50, 100, 200, 500 mg beta-HCH /kg diet - liver tumours and nodular hyperplasia in the highest dose group was observed (IPCS, 1992). In a 26-month study, liver cancer in mice was observed at a daily dose of 34 mg/kg (ATSDR, 2005). Based on these data beta-HCH has been classified as possible human carcinogen by IRIS (Integrated Risk Information System). Studies on the mode of action of carcinogenicity showed no clear initiating potential of beta-HCH. In one study the hepatocarcinogenic action of beta-HCH was shown with PCBs as promoting agent (ATSDR, 2005). It was suggested that the neo-plastic response observed with beta-HCH most likely occurs due to a non-genotoxic mechanism (IPCS, 1992). Beta-HCH has been shown to have tumour-promoting activity.

The International Agency for Research on Cancer (IARC) classified beta- HCH in group 2B: limited evidence for carcinogenicity. A positive association has been observed between exposure to beta-HCH and cancer, for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence. USEPA has classified technical HCH and alpha-HCH as probable human carcinogens and beta-HCH as a possible human carcinogen (ATSDR, 2005). The US Department of Health and Human Services (DHHS) has determined that HCH (all isomers) may reasonably be anticipated to cause cancer in humans (ATSDR, 2005).

Endocrine mediated toxicity: Degenerative changes in male reproductive tissues and sperm abnormalities in rats and mice were described (ATSDR, 2005). In a 13-week study, 0, 50, 150 mg beta-HCH/kg diet were given to Wistar rats. At 150 mg/kg diet, atrophy of the testes in males and increase in uterine weights in females and significantly reduced weight gains were reported (IPCS, 1992). Several other studies showed effects such as decrease in sperm counts and sperm abnormalities as well as histological effects on the testes and uterus at high doses of beta-HCH exposure (USEPA, 2006).

Animal studies and a study with MCF-7 cells showed weak estrogenic effects of beta-HCH.

Reproductive toxicity: Adverse reproductive effects after beta-HCH treatment have been observed in laboratory rodents and minks (ovarian atrophy, increased length of estrous cycle, disruption of ovarian cycling, decreased ovulation rate in female, and a decrease in the number of sperm and/or spermatids, degeneration of seminiferous tubules and testicular atrophy in male animals). Also embryotoxic effects were observed (ATSDR, 2005).

Beta-HCH has been shown to increase fetal deaths within 5 days of birth at a dose of 20 mg/kg/day given to rat dams (USEPA, 2006).

Immunotoxicity: Mice, treated with beta-HCH (60 mg/kg/day) orally for 30 days showed decreased lymphoproliferative responses to T-cell mitogens and decreased natural killer cytolytic activity. The NOAEL was 20 mg/kg/day (USEPA, 2006). Cortical atrophy of the thymus was observed at a dose of 22.5-25 mg/kg/day (van Velsen et al., 1986).

Effects in Humans: Adverse effects such as neurophysiological and neuropsychological disorders and gastrointestinal disturbances have been reported in workers exposed to technical HCH during pesticide or fertilizer formulation. Although beta-HCH is only a minor component of technical-grade HCH, it reached higher levels and persisted longer in the serum than either alpha- or gamma-HCH. 60-100 % of the total HCH measured in serum was beta-HCH (0.07-0.72 ppm). Workers suffered from paresthesia of the face and extremities, headache and giddiness, malaise, vomiting, tremors, apprehension, confusion, loss of sleep, impaired memory and loss of libido. Serum enzyme levels were enhanced as well as IgM (ATSDR, 2005). Inhalation of HCH (mixed isomers may lead to irritation of the nose and throat (IPCS, 2006). The observation of serious hepatic effects in animals (e.g., fatty degeneration and necrosis) suggests that the same results could potentially occur in workers following prolonged occupational exposure.

Beta-HCH levels were higher in the blood of women with miscarriages compared to a control group. Several other organochlorine pesticides were also higher in these women, and therefore it was not possible to establish a causal relationship (Gerhard, 1999).

A possible link between human exposure to HCH and breast cancer has been examined in several epidemiological studies. Most studies showed a weak - not statistically significant - correlation. A non-significant trend between beta-HCH in serum and cancer risk was observed during a 17-year follow-up of a Copenhagen cohort study (Hoyer et al., 1998). Blood levels of beta- HCH were higher in women with breast cancer (in the 31-50 age group) when compared to women without breast cancer (Mathur et al., 2002). In one Chinese study (article in chinese) a significant association between high beta-HCH concentrations in blood and breast cancer in premenopausal women was observed (Li et al., 2006).

In another study a possible association between breast milk concentrations of various organochlorine pesticides including beta-HCH and cryptorchidism was investigated. Beta-HCH was measurable, but not statistically significantly higher in case milk than in control milk. A combined statistical analysis of the eight most abundant persistent pesticides, including beta-HCH, showed that pesticide levels in breast milk were significantly higher in boys with cryptorchidism (Damgaard et al., 2006).

2.4.1.1 Risk characterisation

In 2006 the United States Environmental Protection Agency (USEPA) performed a risk assessment that indicated potential risks from dietary exposure to the alpha and beta HCH isomers to communities in Alaska and others in the circumpolar Arctic region who depend on subsistence foods, such as caribou, seal and whale. The dietary profile (intake rates) is based on the subsistence food harvest amounts of nearly 180 communities from the Community Profile Database Version 3.11 dated 3/27/01 from the Alaska Department of Fish and Game Division of Subsistence (data from 1990 to 2001, USEPA, 2006).

USEPA estimated beta-HCH exposures for Alaskan communities in the range of 0.00043-0.0032 mg/kg bw/day for female adults, 0.0014-0.010 mg/kg bw/day for children (age 1-6) and 0.00048-0.0036 mg/kg bw/day for children (age 7-12). The risk is expressed as a percentage of a maximum acceptable dose or reference dose (RfD). A level of concern is reached if the dietary risk exceeds 100 % RfD. The RfD for acute oral toxicity is 0.05 mg/kg/day. The RfD value for intermediate duration is based on a LOAEL of 0.18 mg/kg/day established in a subchronic study in rats and applying an uncertainty factor of 300 (ATSDR, 2005). On this basis USEPA established a chronic RfD of 0.00006 mg/kg/day by assessing another uncertainty factor of 10 for chronic exposure. RIVM calculated a chronic oral RfD of 0.00002 mg/kg/day for beta-HCH based on a NOAEL of 0.02mg/kg/day for observations of infertility in two semi-chronic oral studies on reproduction in rats and applying an uncertainty factor of 1000 (RIVM, 2001 in USEPA, 2006).

Levels of concern are reached if the dietary risk exceeds 100 % RfD. The acute dietary exposure estimates are not of concern according to USEPA (2006). USEPA's dietary risk assessment indicates that the chronic dietary exposure estimates for beta-HCH are above the levels of concern for both low and high end dietary intake estimates. The cancer dietary risk estimates for beta-HCH are also above the level of concern for both low and high-end dietary intake estimates. According to USEPA, the risk values (% cRfD) are 620-4700 for adult males, 720-5300 for adult females, 2 300-17 000 for children (1-6 years) and 800-6000 (7-12 years). The estimated cancer risk for adult males is 6.7×10^{-4} to 5.0×10^{-3} and 7.7×10^{-4} to 5.8×10^{-3} for adult females respectively. It should be noted that a general accepted cancer risk is 1×10^{-6}. Even though this risk estimation is very conservative due to the basic maximum detected levels it can be concluded that the dietary risks are of concern. Additionally, it has to be mentioned that the target organ of chronic toxicity is the liver and it can be expected that HCHs effects might be additive. It has to be considered that the RfD based on effects on fertility (RIVM, 2001 in USEPA, 2006) is remarkably lower and would be exceeded to an even greater extent.

As beta-HCH is present in cord blood and breast milk infants may be exposed to the damaging reproductive effects of HCH inside and outside the womb (USEPA, 2000).

Also, based on the study of Nair et al. (1996), levels of 0.198 mg beta-HCH/l in breast milk would lead to an intake of 0.1386 mg/l (700 ml intake) which is almost 100-fold higher than the safe intake of 0.0015 mg/child (5 kg) and only about three times lower than the LOAEL seen in animal studies (Pohl and Tylenda, 2000). Establishing the chronic RfD value of USEPA, a safe intake for a child with 5 kg would be even lower (0.0003 mg/kg) and would exceed the RfD 462-fold. Also in other regions intake levels with food and especially with breast milk are of high concern.

Anyway the unique social, cultural, spiritual and economic values of traditional foods have to be considered and strong efforts should be taken to minimize beta-HCH levels therein (CACAR, 2003).

2.4.2 Environment

Beta-HCH is acutely toxic to aquatic organisms. Compared to effect concentrations in algae and daphnia (IPCS, 1992), fish is the most sensitive taxon. An LC50 of approximately 1.7 mg/l was determined in an acute test (duration 24 hours) in zebra fish and neon (Oliveira-Filho and Paumgarten, 1997). IPCS (1992) reported an EC50 based on changes in fish behaviour of 47 µg/l (96 hours) and an LC50 in guppy of 0.9 mg/l (48 hours). In a prolonged toxicity study (duration 4 and 12 weeks) including histopathological changes, the NOEC in young guppy was 32 µg/l (Wester and Canton, 1991). Estrogenic activity of beta-HCH occurred in the form of alterations of vitellogenin production, testis atrophy, hermaphroditism in male and pituitary changes.

It seemed that beta-HCH is not very toxic to birds (IPCS, 1992) but that it may affect reproduction. In female birds with high concentrations of various organochlorines including beta-HCH, the body condition of the first and second chicken in the clutch was poorer (AMAP, 2004).

Monitoring data on effects in Svalbard polar bears revealed a significant negative correlation between retinol and HCHs (AMAP, 2004). Retinol is essential as it is required in reproduction, embryonic and foetal development, as well as in vision, growth, differentiation and tissue maintenance.

3 Synthesis of the information

Technical HCH, a mixture of five stable HCH-isomers, contains 5-14 % beta-HCH and was used extensively worldwide as organochlorine pesticide.

Though usage of technical HCH is currently negligible, releases into the environment may still occur. Local sources include hazardous waste sites, contaminated sites, stockpiles, landfills, or dumping grounds. Though no quantitative estimates of these releases exist, the amounts of HCH-residuals in the form of by-products from lindane production were estimated to range between 1.6-1.9 to 4.8 million tonnes. In addition many of local sources are expected to cause environmental pollution and are not maintained or controlled appropriately.

The physico-chemical properties of beta-HCH allow on a global scale for "cold condensation", but pathways of alpha- and beta-HCH diverge in the environment. Reasons are possibly greater physical and metabolic stability, higher water/octanol solubility, a lower Henry's Law Constant and a relatively high octanol-air partition coefficient, which favours partitioning to organic phases.

According to available data beta-HCH can be considered to be persistent in the environment. Though beta-HCH is biodegradable by various microbial strains under favourable conditions degradation rates in field experiments are low indicating very slow decrease under environmental conditions. Residues of beta-HCH remained for years in treated plots in several studies. The only determined DT50 values were 100 and 184 days on cropped and uncropped soil under subtropical conditions. In addition to degradation and plant up-take volatilisation and leaching may also have contributed to the disappearance of beta-HCH in this investigation.

Monitoring data from remote regions far from sources clearly indicate that beta-HCH has undergone long-range environmental transport. It is suggested that beta-HCH enters the Arctic by ocean currents passing through the Bering Strait after wet deposition and partitioning into the North Pacific Ocean.

Beta-HCH has a BCF (whole body) of 1 460 based on a laboratory study in fish. However, there are several field investigations in Arctic marine food webs available that suggest that beta-HCH may accumulate to high concentrations in upper trophic levels (i.e. marine mammals and birds). Thus BMFs as well as FWMFs were greater than 1. It has further been demonstrated that beta-HCH is found in breast milk of highly exposed indigenous mothers who consume a subsistence diet. Thus its high bioaccumulation potential is well documented.

Beta-HCH has been shown to be neurotoxic, hepatotoxic, to cause reproductive and immunosuppressive effects and effects on fertility and reproduction in laboratory animals.

Monitoring data on Arctic polar bears revealed a negative correlation with retinol concentrations and HCHs, which may impact a wide range of biological functions.

The International Agency for Research on Cancer (IARC) has classified beta-HCH in group 2B, possibly carcinogenic to humans. Several epidemiological studies indicate that beta-HCH might play a role in human breast cancer, at least beta-HCH is a known tumour promoting agent. Beta-HCH may adversely affect human health in contaminated areas and as well in Arctic regions. Based on the available toxicity data of beta-HCH it can be concluded that current concentrations of beta-HCH in food and human milk in these regions are of concern. The estimated cancer risk calculated by EPA, though very conservative, seems very high (5.0×10^{-3} to 7.7×10^{-4}).

It has to be taken into consideration that the Arctic population and wildlife are also exposed against a wide range of other persistent toxic substances, which may act in an additive way. Nevertheless it should be emphasized that traditional foods have unique social, cultural, spiritual and economic value and therefore it is strongly recommended to avoid foods in which beta-HCH levels are of concern.

4   Concluding statement

Though most countries have banned or restricted the use of technical HCH as a pesticide, replacing it in most cases by the use of lindane, the production process creates huge amounts of HCHs residuals. The continued production and existing stockpiles of these waste isomers have been a worldwide problem and contribute to the releases into the environment.

Beta-HCH is persistent and present in all environmental compartments; especially levels in the terrestrial as well as in the aquatic food chain give rise to concern to adversely affect human health. High exposure is expected in polluted areas, which are still present around the globe. High exposure ois also possibly expected as a result of long-range environmental transport.

Based on the inherent properties, together with estimated daily intakes of beta-HCH of Arctic indigenous people that exceeds safe intake reference values, and given the widespread occurrence of beta-HCH in biota, including in remote areas far from likely sources, it is concluded that the substance is likely, as a result of its long-range environmental transport, to lead to significant adverse human health and environmental effects, such that global action is warranted.

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