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 alpha hexachlorocyclohexane

At its third meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on alpha hexachlorocyclohexane, on the basis of the draft contained in document UNEP/POPS/POPRC.3/17. The text of the risk profile, as amended, is provided below. It has not been formally edited.

ALPHA 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 a 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 been agreed at the last meeting of the Review Committee in November 2006, the Committee concluded that alpha-HCH also complied with the screening criteria laid down in Annex D of the Convention and that 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 alpha-HCH as the main isomer) is subject to national and international regulations and prohibitions.

Alpha-HCH is susceptible to abiotic and biotic degradation at variable rates and degrees, depending on e.g. environmental media, site and climate. Alpha-HCH is expected to rapidly degrade in tropical conditions, whereas it accumulated in colder climates. Alpha-HCH is moderately persistent in soil. Based on values from aquatic compartments i.e. Arctic freshwater and sea water, it can be concluded that alpha-HCH shows high persistence in water in colder regions.

The physico-chemical properties of alpha-HCH allow the dispersal of the substance from its sources to the Arctic by a combination of long-range atmospheric transport and ocean currents. High levels of alpha-HCH have been detected in the Arctic Ocean, where it has built a large reservoir and is present in marine as well as in terrestrial species.

Alpha-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 alpha-HCH residues from lindane production. Due to its persistence, alpha-HCH can still be detected regularly at low background levels in the environment. Elevated levels have also been reported from the Arctic (levels in the Arctic Ocean are higher than in temperate oceans and lakes). Though alpha-HCH levels in air decreased more than twenty-fold from the 1980s onwards, there has been only a modest change in higher marine and terrestrial predators e.g. fur seals or polar bears.

Because alpha-HCH is present in the terrestrial and aquatic food chains, alpha-HCH may bioaccumulate and biomagnify in biota and Arctic food webs. The biomagnification factors (predator-prey comparison) for many of the examined species are greater than 1 (one). Some animals, especially birds, but also mammals, have the potential to metabolize alpha-HCH. As this is an enantioselective biotransformation, a distinctive accumulation of (+) or (-) alpha-HCH can occur in mammals (depending on the species).

Alpha-HCH is the isomer with the highest neurotoxic potential beside gamma-HCH. Alpha-HCH has been classified as possibly carcinogenic to humans (group 2B) by the International Agency for Research on Cancer (IARC), based on inadequate evidence of carcinogenicity in humans and sufficient evidence for carcinogenicity to animals. Alpha-HCH causes liver hyperplasia and liver tumours in (laboratory) rodents. From animal experiments it is known that alpha-HCH affects the immune system; immunosuppressive effects were observed in humans exposed to technical HCH as well. Epidemiological studies indicate an elevated incidence of breast cancer after exposure to alpha-HCH as well as hormonal disorders leading to infertility and abortions. A possible association with intrauterine growth retardation and aplastic anaemia has been postulated.

Based on the hazard profile and the exposure scenarios it can be concluded that alpha-HCH may adversely affect wildlife and human health in contaminated regions. The United States Environmental Protection Agency (USEPA) estimated, based on daily intake rates for the Arctic population, elevated cancer rates, though estimates are very conservative. It has to be considered that the liver is the target organ for all HCH-isomers, thereby leaving the risk of additive effects. Moreover the indigenous Arctic population as well as wildlife are exposed to a broad range of POPs including all HCH isomers and other pollutants leading to probably additive effects. Nevertheless 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.

For these reasons global action on alpha-HCH is warranted.

1   Introduction

In the proposal by Mexico to include lindane in Annex A, B or C of the Stockholm Convention and in the ensuing discussions, it was concluded that "other isomers of hexachlorocyclohexane should also be considered" (UNEP/POPS/POPRC.2/10). Thus Mexico submitted a proposal for listing alpha-hexachlorocyclohexane in Annexes A, B or C of the Stockholm Convention on 26th July 2006 (UNEP/POPS/POPRC2./INF/7). Austria (on behalf of Germany) prepared the first working draft on alpha-HCH.

Alpha-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. Alpha-HCH is mainly stimulating to the central nervous system, but 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 their environmental fate and effects (Breivik et al., 1999).

1.1   Chemical Identity

Chemical name: Alpha-hexachlorocyclohexane (alpha-HCH)
IUPAC name: (1a,2a,3b,4a,5b,6b)-Hexachlorocyclohexane
Common synonyms: 1,2,3,4,5,6-hexachlorocyclohexane, alpha isomer, (1alpha,2alpha,3beta,4alpha,5beta,6beta)-1,2,3,4,5,6-hexachlorocyclohexane, alpha-1,2,3,4,5,6-Hexachlorocyclohexane; alpha-benzene hexachloride, alpha-BHC, alpha-HCH, alpha-lindane; benzene-trans-hexachloride, Hexachlorocyclohexane-Alpha (Chemfinder, 2007)

Alpha-HCH is a chiral molecule; the enantiomers are shown in Figure 1.
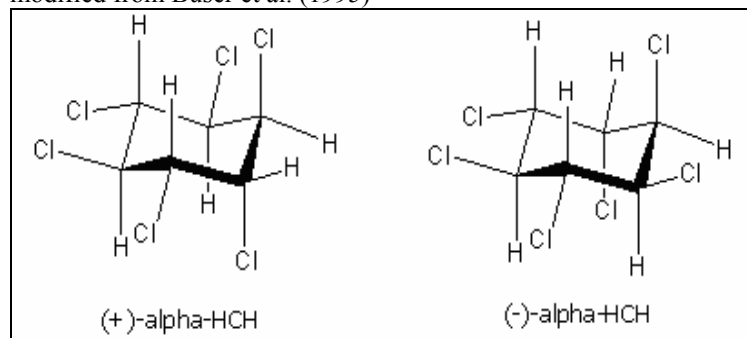CAS number:
Racemic: 319-84-6, (+) alpha-HCH: 11991169-2, (-) alpha-HCH: 119911-70-5
Chemical formula: $C_6H_6Cl_6$
Molecular weight: 290.83

Figure1: Structure of alpha-HCH, modified from Buser et al. (1995)

Stability and persistence of HCH isomers are attributed to the orientation of the chlorine atoms on the molecule. Axial chlorine atoms may probably provide available sites for enzymatic degradation. Alpha-HCH exhibits 4 axially and 2 equatorially orientated chlorine atoms. Thus it is thought that the molecule is more susceptible to degradation than the beta-isomer (Philips et al., 2005).

1.1.1   Physico-chemical properties

The physico-chemical properties (see Table 1 for selected properties) of alpha-HCH allow for long-range transport and "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). Alpha-HCH can volatilize due to its vapour pressure and low octanol-air partition coefficient from soil surfaces. The Henry's law constant is relatively low and decreases with temperature.

Table 1. Selected physico-chemical properties

Melting Point (K)	432 [1]
Boiling Point (K)	561 [1]
Water solubility (mol*m^{-3} at 25 °C)	0.33 [2]
Vapour pressure (Pa at 25 °C)	0.25 [2]
Henry´s Law Constant (Pa m^3 mol^{-1})	0.74 [2]
Log Kow (25°C)	3.9 [2]
Log Koa (25°C)	7.5 [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 alpha-HCH submitted by Mexico (UNEP/POPS/POPRC.2/INF/7 as summarized by the Secretariat in document UNEP/POPS/POPRC.2/15) according to the requirements in Annex D of the Stockholm Convention at its second meeting in Geneva. In Decision POPRC-2/9 the Committee reached the conclusion that alpha-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-hexachlorocyclohexane in Annexes A, B and/or C of the Convention (UNEP/POPS/POPRC2./INF/7), 2006.

- Decision POPRC-2/9 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, Germany, International POPs Elimination Network (IPEN), Japan, 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 technical terms 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 have not been listed specifically in this draft risk profile. Additional references are provided in UNEP/POPS/POPRC.3/INF/27.

1.4   Status of the chemical under international conventions

Alpha-HCH is a constituent of technical HCH, which is regulated by at least 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 to reduce the risks associated with the exposure of humans and the environment.

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 among the priority substances (Decision No 2455/2001/EC) of the adopted EU Water Framework Directive 2000/60/EC.

Hexachlorocyclohexane isomers, including the alpha-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

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

HCH is manufactured by photochemical chlorination of benzene which leads to the formation of mainly five stable HCH isomers. The yields of different isomers vary due to technical differences in the production process. The reported ranges are: alpha-HCH (55 - 80%), beta-HCH (5 - 14%), gamma-HCH (8 - 15%), delta-HCH (6 - 10%) and epsilon-HCH (1 - 5%) (Breivik et al., 1999). 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 alpha-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

Technical HCH was rapidly introduced in the 1940s on a large scale on the market, due to its universal insecticidal properties. The promising market opportunities worldwide arose in the search for an inexpensive alternative to DDT (IHPA, 2006). However, due to the decreasing effectiveness of the gamma> alpha> beta-isomer in controlling insects (Baumann et al., 1980) technical HCH was gradually replaced by lindane (> 99% gamma-HCH). However, the manufacture of lindane has resulted in a huge amount of HCH residuals, which must be disposed of or otherwise managed. IHPA (2006) calculated 1.9 to 4.8 million tons of HCH residuals based on global lindane production, in the absence of exact data. These estimates are far beyond the values reported by Walker et al. (1999) who reported stockpiles of approximately 2 785 tons of technical HCH and 45 tons of unspecified HCH material in Africa and the Near East.

2.1.3   Uses

Around 10 million tons of technical HCH were released into the environment between 1948 and 1997 (Li et al., 1999). Breivik et al. (1999) estimated technical HCH usage at approximately 400 000 tons in Europe alone between 1970 and 1996. The data illustrate the large uncertainties of these estimates. According to Li and Macdonald (2005) global usage of technical HCH was dominated by 10 countries headed by China, which consumed almost half of the total global quantity. The other countries were (in order of decreasing usage): Former Soviet Union, India, France, Egypt, Japan, United States, East Germany, Spain and Mexico. Usage of technical HCH was banned in most western countries and Japan in the 1970s but continued in China and Russia until 1983 and 1990. In 1990, India also banned technical HCH for agricultural use but

kept it for public health uses (AMAP, 2004a). Technical HCH usage steadily declined and now technical HCH is virtually no longer used worldwide. However, there are indications that the use of stockpiles, limited use for public health purposes and/or illegal use cannot be excluded (Zhulidov et al., 2000; Bakore et al., 2004; Qian et al., 2006).

2.1.4 Releases to the environment

There are several pathways of alpha-HCH for entering the environment. Historically, alpha-HCH was released during the manufacture of technical HCH and its use as a pesticide. Alpha- and beta-HCH have the same global emission patterns which, however, differ in scale. Li and Macdonald (2005) estimated the global usage of alpha-HCH (based on data on technical HCH) at 6 millions tonnes, with 4.3millions tonnes emitted into the atmosphere. After the 1940s emissions of alpha-HCH increased and peaked in the early 1970s. Due to the ban on the use of alpha-HCH in North America, in European countries and Japan, emissions decreased but reached again a peak in the 1980s because of frequent usage in Asian countries. After the 1980s, figures dropped due to further prohibitions and restrictions e.g. in China. Releases of alpha-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 alpha-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 alpha-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

Alpha-HCH is, in principle, degradable in environmental compartments by abiotic processes such as photodegradation or hydrolysis. Based on laboratory experiments from Ngabe et al. (1993), hydrolytic half-lives of alpha-HCH show strong temperature dependence. At 20°C, pH 8 the DT50 was 0.8 years whereas it increased at lower temperature (5°C, pH 7.8) to 26 years. Based on these degradation rates Harner et al. (1999) calculated a DT50 of alpha-HCH in the Arctic Ocean of 63 years.

In general, HCH-isomers do not absorb light > 290 nm. Thus it is expected that photolysis plays a minor role in the removal of alpha-HCH. Deo et al. (1994) reported half-lives of alpha-HCH in aqueous solution exposed to sunlight of 4 to 6 days. While the mechanism of this degradation is uncertain, it was shown that alpha- as well as gamma-HCH break-down by indirect photolysis with photosensitizing agents that may transfer the excitation energy to HCH (ATSDR, 2005; USEPA, 2006). Regarding photodegradation on hard surfaces, a half-life equal to 91 hours on a thin film has been reported (ATSDR, 2005). However, the relevance of this result is questionable when taking into consideration the arguments mentioned above.
The measured atmospheric OH rate constant of 1.4×10^{-13} cm^3/molecule-sec resulted in a corresponding half-life of 115 days (ATSDR, 2005) (using an average hydroxyl radical concentration of 5×10^5 molecule/cm^3 according to the TGD (2003)).

In conclusion, abiotic degradation is very slow especially at lower temperatures. Photolysis in aqueous media and air is considered to play an insignificant role in the degradation of alpha-HCH.

Biotic degradation of alpha-HCH has been found to take place in pure cultures, soil slurries, soil (semi-)field studies, sediment and water. Initially it was thought that HCH biodegradation in soil occurs under anaerobic conditions. However, several investigations show that alpha-HCH is aerobically degraded, in some cases even faster than anaerobically. Breakdown was also reported for methanogenic and sulfate reducing conditions (Phillips et al., 2005).

The anaerobic metabolic pathway of alpha-HCH leads via dechlorination to tetrachlorocyclohexene. Dichlorophenol and trichlorophenol as well as chlorobenzene and benzene were formed under methanogenic conditions, the last two as stable end products. These metabolites can be further mineralised aerobically or anaerobically (Bachmann et al., 1988; Phillips et al., 2005). In pure cultures as well as in flooded soil gamma-HCH is the most easily dechlorinated isomer followed by alpha-HCH under anaerobic conditions (Jagnow et al., 1977; MacRae et al., 1967).

Under aerobic conditions alpha-HCH was dehydrochlorinated to pentachlorocyclohexane in soil slurries. Further conversion to tetrachlorobenzene or trichlorobenzene may occur to yield dichlorobenzene (Deo et al., 1994). The aerobic degradation pathway of gamma-HCH was extensively studied with *Shingobium sp.* and results in several metabolites. It was suggested that alpha-HCH follows the same pathway than gamma-HCH. Complete mineralization of alpha-HCH was shown in laboratory studies under aerobic conditions (Phillips et al., 2005).

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). The moisture content of the soil enhances losses of alpha-HCH, which is attributed to higher volatility and/or microbial degradation (Chessells et al., 1988; Phillips et al., 2005). Bacteria capable of degrading HCHs at extreme temperatures (< 5 °C or > 40°C) have not yet been reported (Phillips et al., 2005).

Data on laboratory soil studies or field investigations are limited. Under various field conditions it is assumed that degradation rates are in the order of alpha > gamma > > beta (Suzuki et al., 1975, Stewart and Chisholm, 1971; cf. also section 1.1). Singh et al. (1991) reported field half-lives (i.e. dissipation, including losses by leaching and volatilisation) of around 55 days on cropped and uncropped plots in a sandy loam in India under subtropical conditions. This result is consistent with findings from Kaushik (1989) who reported an even shorter half-life for technical HCH under similar study conditions. Also, in temperate climate Doelman et al. (1990) observed in a semi-field study with contaminated soil > 50 % removal after 161 days, mainly attributed to a quick decline in the first few weeks, whereas degradation slowed down afterwards. Suzuki et al. (1975) also suggested that low residue levels (below 0.1 ppm) may resist microbial and physico-chemical action. Low concentrations of alpha-HCH may persist in the environment indefinitely because of low affinity of enzymes or transport system responsible of HCH degradation (Phillips et al., 2005). Stewart and Chisholm (1971) observed in a long-term field study after an application of technical HCH, 4 % of the alpha-isomer after 15 years in a sandy loam in Canada. In addition, Chessells et al. (1988) showed that after a 20 year application history of technical HCH on sugar cane in Queensland, Australia, alpha-HCH with the highest initial concentration is substantially less prevalent in the field and the detected levels were twice as much as the levels of the gamma-isomer.

Abiotic processes are not enantioselective, but biodegradation may be. If nonracemic alpha-HCH residues in the environment or biota are measured, enzymes are involved. However, racemic residues do not exclude the possibility of biotic degradation (cp. Suar et al., 2005). Also for monitoring purposes enantiomeric fractions (EFs, calculated by the formula EF = ER/(ER+1), ER = enantiomeric ratio: (+) /(-) alpha-HCH, Kallenborn et al., 2001) have been quantified for the characterisation of residues. Hegeman and Laane (2002) investigated the enantiomeric distribution of alpha-HCH in different environmental compartments obtained from 618 measurements. In general, the abiotic compartments showed average EFs close to 0.5. In soil, the preference tended to be the degradation of the (-) alpha-HCH (EF > 0.5), whereas in water an opposite tendency was found. Kurt-Karakus et al. (2005) reported a range of EFs for alpha-HCH of 0.4 - 0.89 (mean 0.5) in global background soils which covered a greater range than the EFs in ambient air of North America (0.47 - 0.52), suggesting that post-deposition degradation had taken place. However, since EFs vary considerably with site, caution is needed when using enantiomeric signatures in the air as a marker of reemissions from (soil) surfaces.

Based on the K_{oc} value and confirmed by field data, alpha-HCH is expected to have a low leaching potential (HSDB, 2006; Singh et al., 1991). However, groundwater pollution may occur in highly contaminated areas (Law et al., 2004). Detailed information regarding the relevance of isomerisation in the environment can be found in the risk profile on lindane (UNEP/POPS/POPRC.2/17/Add.4).

Alpha-HCH is able to biodegrade in sea water/sediment samples (HSDB, 2006) and freshwater (Padma and Dickhut, 2002). Helm et al. (2002) estimated the half-lives for alpha-HCH in a high Arctic lake at 0.6 to 1.4 years. For the Eastern Arctic Ocean enantioselective degradation for the (+) alpha- and (-) alpha-HCH with half-lives of 5.9 and 23.1 years was observed. If breakdown with hydrolysis was taken into consideration, the overall half-lives were 5.4 and 16.9 years for the (+) and (-) alpha-isomer respectively (Harner et al., 1999). Though sediment degradation rates are poorly known and thus the estimates are less certain, the half-life for alpha-HCH in sediments of a high Arctic lake was assumed to be approximately 2 years (Helm et al., 2002). Some data on α-HCH levels in sediment cores 30-40 years of age indicate long half-lives of α-HCH in sediments from different geographical areas (Barra et al., 2001; Rawn et al., 2001; Riching et al., 2005)

2.2.2 Bioaccumulation

The octanol-water partition coefficient (log Kow = 3.8) for alpha-HCH indicates a potential for bioaccumulation (ATSDR, 2005), though it is below the value of 5 stated in Annex D paragraph 1(c)(i) of the Stockholm Convention. A wide range of bioconcentration factors (BCFs) have been reported in several studies. For green algae, bioconcentration factors varied from about 200 in *Chlorella pyrenoidosacells* to 2700 (dry weight basis) and 13000 on a lipid basis, respectively in *Dunaliella*. Studies of invertebrates show BCFs in the range of 60 (8000 on a lipid basis) in *Artemia* to 2700 in polychaetes, depending on the lipid content of the animals (IPCS, 1992).

The BCF (whole body) for alpha-HCH according to the former OECD test guideline 305 E in zebra fish was equal to 1 100 under steady state conditions with uptake constants (k1) of 50 and clearance rate constants (k2) of 0.045. These values are similar to those of gamma-HCH (BCF 850, k1 = 50.8, k2 = 0.055) (Butte et al., 1991). Oliver et al. (1985) reported BCFs (whole body) ranging from 1 100 to 2 800 in rainbow trout.

In general, studies from Arctic marine food webs show food web magnification factors (FWMFs), which represent the mean rate of increase per trophic level in the food chain, greater than 1. The BMFs (biomagnification factor, predator-prey comparison) of alpha-HCH in zooplankton and Arctic cod are greater than 1, showing a potential for biomagnification. BMFs of alpha-HCH in seabirds were generally less than 1 with the exception of dovekie and black guillemot. Ringed seals showed a BMF of 2.5 (Moisey et al., 2001). It is suggested that alpha-HCH isomer has the potential to biomagnify in aquatic food webs and may increase at lower as well as in upper trophic levels, especially in marine mammals (USEPA, 2006; Hoekstra et. al., 2003a). The report of Hoekstra et al. (2003b) also confirms this presumption with a BMF of 9.85 in bowheads for alpha-HCH.

Fisk at al. (2001) reported on the influence of chemical and biological factors on the trophic transfer of POPs including alpha-HCH. In general, the highest BMF should be seen in homeothermes (birds and mammals) compared to poikilothermes (fish, invertebrates) attributed to their greater energy requirements. Within the homeothermes, seabirds usually have the highest BMFs, consistent with the greater energy demand in birds. But this is not applicable for alpha-HCH. Most seabirds appear to be able to induce the cytochrome P450 such as CYP2B, which are enzymes to metabolize alpha-HCH, so the ranking from highest to lowest biotransformation ability (usually for OCs: marine mammals > seabirds > fish > zooplankton) is not applicable for this compound. The BMF of alpha-HCH in poikilothermes is 1.3 and equal to that in homeothermes (Hop et al., 2002).

As alpha-HCH is a chiral compound, the determination of the ER or EF is important in order to understand species-specific metabolism and biotransformation. No enantioselective biotransformation in rainbow trout for alpha-HCH was observed by Konwick et al. (2006) in a dietary study showing consistent EFs in the fish. In an experiment of Wong et al. (2002) alpha-HCH was racemic throughout the course of the experiment with rainbow trout, fed with treated food. These results are in contrast with reports of enantioselective biotransformation in other species. The EF in benthic invertebrates, zooplankton and fish was 0.45 as a maximum. Ringed seals showed an EF of 0.51, while the EFs in seabirds range from 0.65 (dovekie) to 0.97 in glaucous gulls (Moisey et al., 2001). This suggests that seabirds preferentially metabolize the (-) enantiomer. Associated with a BMF of < 1 in seabirds, it has been found that both enantiomers of alpha-HCH are metabolized in birds (dovekie and black guillemot seem to have a lower capacity).

The EF of 0.51, considered together with the BMF of 2.5 in seals, indicates that mammals are not able to biotransform alpha-HCH in great amounts (Moisey et al., 2001). Nevertheless, Wiberg et al. (2000) found residues of alpha-HCH with nonracemic ERs in seals as well as in polar bears. According to Hoekstra et al. (2003b) accumulation of the (+) enantiomer occurs in bowhead whale and beluga, but (-) alpha-HCH enriches in bearded seal. Ringed seal show a slight accumulation of the (+) enantiomer (Hoekstra et al., 2003b) but sometimes the alpha-HCH residues are racemic (Fisk et al., 2002). This indicates an enantiospecific biotransformation and accumulation of alpha-HCH in the food chain. When investigating the EFs in krill, cod and penguin eggs, Corsolini et al. (2006) also found enantioselective biotransformation with an increase by 14 % of (+) alpha-HCH from the lower to the higher trophic level (from krill to penguin). There are interspecies differences in the enantiomeric profile of alpha-HCH in marine mammals, too. The BMF for calanus to bowhead for example is high (near 10 with a (+) alpha-HCH fraction of 16 and 4.5 of (-) alpha-HCH) (Hoekstra et al., 2003b).

Moisey et al. (2001) showed different BMFs in doveky, depending on the prey. Summed up, biomagnification is affected by many parameters such as contamination in biota, and consequently of food (prey), the trophic level and the ability to biotransform alpha-HCH.

Kelly at al. (2007) have recently shown that, for substances with a log Koa >6 and a log Kow >2, the fish BCF is not a good predictor of biomagnification in air-breathing animals. This is also 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. Alpha-HCH also meets these criteria.

Not only in the arctic food web, but also in organs of fur seals from the Pacific coast of Japan and double crested cormorants from the great lakes, alpha-HCH was detected (with an alpha-HCH ER from 1 in the muscle to 1.58 in fat). High alpha-HCH ERs were found in the brain of the cormorants (> 3.6) (Iwata et al., 1998). Willet et al. (1998) inferred from high alpha-HCH concentrations in marine mammal brain that this compound can cross the blood/brain barrier. Ulrich et al. (2001) also found in studies with rats that the alpha-HCH ER in brain, ranging from 2.8 to 13.5, is not caused by an enantioselective metabolism but that selective retention might be responsible.
Braune et al. (1999) detected alpha-HCH residues in the fat of caribou. Residues of alpha-HCH could also be found in livers and the adipose tissue of arctic foxes. The alpha-HCH ER of 2.2 in the liver, and 1.1 in the adipose tissue, indicates a stereoselective bioaccumulation also in terrestrial mammals (Klobes et al., 1997).

In conclusion high levels are found in Arctic biota because of the bioaccumulation potential of alpha-HCH (as a product of bioconcentration and biomagnification) and the historically particularly efficient deposition processes of this substance in the Arctic waters. The efficient accumulation is an effect of the combination of the physico-chemical properties of

alpha-HCH and the low temperature in the Arctic. In other words, alpha-HCH effectively accumulates in the Arctic ecosystem as a whole.

2.2.3   Long range environmental transport

Monitoring data on the environment including biota from remote regions such as the Arctic or Antarctica, where technical HCH has not been used, provide evidence of the long-range transport potential of alpha-HCH. Also the physico-chemical properties in combination with its stability allow alpha-HCH to undergo long range transport in the atmosphere. Primary emissions from the source regions (mainly in Asia) and Arctic air concentrations have synchronously decreased, suggesting a rapid dispersion of alpha-HCH from its sources to remote regions (Li and Bidleman, 2003). Especially high concentrations compared to the source regions were reported for the Arctic Ocean (see Table 2). It is assumed that after long range transport alpha-HCH accumulated in the cold water due to its low Henry's law constant and built a large reservoir (Li and Macdonald, 2005). HCHs including alpha-HCH are the most abundant pesticides in the Arctic air and water (Walker et al., 1999).

To understand pathways and the fate of alpha-HCH in the upper Arctic Ocean, Li et al. (2004) developed an Arctic Mass Balance Box Model. They concluded that the highest load of 6 670 tonnes was reached in 1982 mainly by gas exchange and ocean currents and decreased thenceforward by an average annual rate of approximately 270 tons/year. After 1990, ocean currents become the dominant input of alpha-HCH in the Arctic Ocean. However, the portion of alpha-HCH entering the Arctic atmosphere via long range transport from source regions played a prominent role (especially in the beginning). After the early 1990s alpha-HCH in the Arctic air came from both atmospheric transport and volatilization from the Arctic Ocean. It was suggested that a complete elimination of alpha-HCH mainly by degradation and ocean currents would require another two decades. In total 27 700 tons alpha-HCH were transported between 1945 and 2000 via long range transport to the Arctic Ocean.

According to model calculations with the OECD Pov and LRTP Screening Tool, alpha-HCH has similar persistence and long-range transport properties compared to already identified POPs such as PCBs and organochlorine pesticides (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/7). 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

Exposure to alpha-HCH resulted from the use of technical HCH, and from the production and manufacture of technical HCH and lindane. 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).

Human exposure to alpha-HCH results mostly from 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. As shown by a French pilot study alpha-HCH was detected in indoor air and on the hands of the general population in the Paris area in 42 and 35 % of the samples. Levels were low and ranged up to 1.8 ng/m^3 in air and up to 8.5 ng/hand (Bouvier et al., 2006).

Monitoring data from a wide range of biota including humans suggest that significant uptake from the environment occurs, which demonstrates the bioavailability of alpha-HCH. 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; see also Table 2). However, monitoring data show its ubiquitous distribution in all environmental media e.g. in monitoring activities in the Czech Republic (submitted Annex E information by the Czech Republic, 2007), in lichens of various locations in Switzerland (values given in table 2) or in a recently performed monitoring programme in Japan. Alpha-HCH had been detected in Japan in all but 7 fish specimens. The reported values are as follows: water 0.013 - 5.7 ng/l, sediment trace - 5.7 ng/g dw (dry weight), shellfish up to 1.8 ng/g ww (wet weight), fish up to 2.9 ng/g ww, bird 0.1 - 1.6 ng/g ww, air (warm and cold season) 0.02 - 3.2 ng/m^3 and 0.01 - 0.68 ng/m^3 (submitted Annex E information by Japan, 2007).

Table 2. Selected monitoring data of abiotic compartments and vegetation (values refer to alpha-HCH except otherwise stated)

Compartment	Country/region	Levels	Comments	References	Year
Air	Great Lakes, rural	< 1 - 84 pg/m^3	alpha-HCH, mean values, gas phase	Sun et al., 2006b	1992-2003
	Great Lakes, Chicago	52 pg/m^3	alpha-HCH, mean value, gas phase	Sun et al., 2006b	1996-2003
	Niigata, Japan	92 pg/m^3	Annual average, according to the authors a result of long-range trasport	Murayama et al., 2003	2000-2001
	Czech Republic (Kosetice)	**38**/21/17/22/**13** pg/m^3	Air and aerosol, annual mean concentrations	EMEP measurement, data online	1999-2003
	Finland (Pallas)	**24**/28/18/15/17/18/**9** pg/m^3	Air and aerosol, annual mean concentrations	EMEP measurement, data online	1996-2003
	Iceland (Storhofdi)	**17**/16/15/15/10/8/10/5/**7** pg/m^3	Air and aerosol, annual mean concentrations	EMEP measurement, data online	1995-2003
	Norway (Lista)	**94**/94/76/69/52/61/50/37 /25/19/17/17/**12** pg/m^3	Air and aerosol, annual mean concentrations	EMEP measurement, data online	1991-2003
	Sweden (Aspvreten)	**43**/57/61/50/-/67/**16** pg/m^3	Air and aerosol, annual mean concentrations	EMEP measurement, data online	1995-2002
	Ny-Aslund (Svalbard, Norway)	73 pg/m^3	∑HCHs, mostly alpha-HCH, highest annual average value reported in 1996	AMAP, 2004a	1996-1988
	Barents Sea and eastern Arctic Ocean	11 - 68 pg/m^3		Harner et al. (1999)	1999
	Arctic	23 +/- 10 pg/m^3	Uniform distribution, arithmetic mean, measurements from 4 Arctic sites	Su et al., 2006	2000-2003
Precipitation	Belgium (Knokke)	4.1 - 0.5 ng/l	annual mean concentrations	EMEP measurement data online	1996-2003
	Germany (Zingst)	1 - 0.3 ng/l	annual mean concentrations	EMEP measurement data online	1999-2003
	Finland (Pallas)	< 1 ng/l	precipitation + dry deposition annual mean concentrations	EMEP measurement data online	1996-2003
	Norway (Lista)	2.7 - 0.4 ng/l	annual mean concentrations	EMEP measurement data online	1991-2003
	Sweden (Aspvreten)	2.7 - 0.4 ng/l	annual mean concentrations	EMEP measurement data online	1995-2002
	Canada/Great Lakes	1 - 40 ng/L	81 samples	IPCS, 1992	1976-77
Soil	Russian Arctic	0.2 - 0.5 ng/g dw	∑HCHs, predominantly alpha-HCH, soil including peat and litter	AMAP, 2004a	200-2001
	Antarctica	< 0.01 – 0.026 ng/g dw		Borghini et al., 2005	1999
Seawater	Northern Barents Sea, Eastern Arctic Ocean	910 (350 - 1630) pg/l	Sample period: July-September	Harner et al., 1999	1996
	North American Arctic Ocean	~ 7.5 µg/m^3		Li and Macdonald, 2005	1983
	Canadian Archipelago and southern Beaufort Sea	3.5 (1.1 – 5.4) ng/L	Surface water, measurements in summer	Bidleman et al., 2007	1999
Freshwater, rivers	Russian north rivers	< 1 - 69 ng/l	Seven-year weighted mean concentrations	AMAP, 2004a	1190-1996
River and estuarine waters	Eastern and southern Asia and Oceania	up to max. 470 ng/l		Iwata et al., 1994	1989-1991
Sediment (Lake)	Southern Sweden	9.2 ± 6.3 ng/g dw	∑HCHs, data from the Swedish Monitoring Program, 2002	AMAP, 2004a	2002
Vegetation (lichen)	Taymir (Russia)	7 ng/g dw	Highest concentration in lichen compared to samples from Alaska, Urals and Kola	AMAP, 2004a	1991-1993

Compartment	Country/region	Levels	Comments	References	Year
	Switzerland	0.5 - 4 µg/kg dw	From various locations (e.g. cities, industry, rural)	Submitted Annex E information by Switzerland, 2007	2002
Moss	Antarctica	0.43 – 4 ng/g dw		Borghini et al., 2005	1999

Environmental levels can still be high in the proximity of sources. HCH concentrations in contaminated soil of 40 - 225mg/kg were found in the topsoil around a chemical plant in Albania (UNEP, 2003). Mean levels of 0.02 mg/kg were reported for soils from the Pearl River Delta in China, Russian soils near the Lena River contained 0.001 - 0.017 mg/kg HCH (UNEP, 2003). Levels of up to 12 000 mg/kg were detected in soil of a highly polluted area in Spain (Concha-Grana et al., 2006)

Levels in biota vary, depending on the location (recent usage and/or high pollution) and species. Alpha-HCH is in most cases the dominant isomer in fish (Willett et al., 1998). E. g. concentrations of HCHs (mainly the alpha-isomer) in several fish species from India ranged between 6 to 68 ng/g ww. Fish samples collected from the Nile River near Cairo in 1993 showed a concentration of alpha-HCH of 0.5 ng/g ww (UNEP, 2003).

Alpha-HCH was also determined in eggs of Dalmatian Pelican (*Pelecanus crispus*) as well as in eels (*Anguila anguila*), the main pelican prey species collected in the wetlands of Amvrakikos Gulf in Greece for a two year period, 1992 and 1993. The concentration in pelican eggs was 7.9 ± 3.2 ng/g and 6.5 ± 2.5 ng/g ww in eels (UNEP, 2003). Concentrations of alpha-HCH in perch from the Latvian coast were up to 21 ng/g lw (lipid weight) (range 50 - 60), which were considered as background load. Elevated levels of up to 126 ng/g lw were attributed to a recent discharge of technical HCH (Olsson et al., 1999).

A local source of alpha-HCH was the usage of technical HCH by indigenous human populations in the Russian north against nuisance insects parasitizing domesticated reindeer (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*

Highest measured levels of alpha-HCH have been reported for higher latitudes in air (e.g. Svalbard, Alert) as well as in seawater (Harner et al., 1999). As shown in table 2, alpha-HCH in air (e.g. from 94 pg/m^3 in 1992 to 12 pg/m^3 in 2003 in Norway) has decreased. AMAP (2004a) also summarized that concentrations of HCHs in Arctic air have been low since the mid 1990s due to worldwide prohibitions and restrictions. Before, in the 1980s, levels as high as approximately 900 pg/m^3 were measured in Arctic air (Li et al., 2002). Seawater levels in the eastern Arctic Ocean were generally lower than in the western part (Harner et al., 1999). Surface concentrations are highest in the Central Canadian Arctic Archipelago, intermediate in the Beaufort/Chukchi Seas and at the North Pole. In the 1990s levels in the Canadian Arctic Ocean were higher than anywhere else in the global marine environment (AMAP, 2004a).

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. Levels in beluga blubber decreased from approximately 190 to 140 ng/g lw between 1982 and 1997 in the southeast Baffin Bay (AMAP, 2004a). Levels of up to 196 ng /g ww were reported from Alaska (submitted Annex E information by IPEN, 2007) and of up to 344 ng/g ww from Arviat (Stern et al., 2005). Minke whales from Greenland had higher concentrations of the prevalent alpha-isomer in blubber (mean levels 40 - 55 ng/g ww), than individuals from the North Sea (below 30 ng/g) (AMAP, 2004a). No decline of ∑HCHs in blubber of narwhal from the Canadian Arctic was observed between 1982 and 1999.

Concentrations in ringed seal of the Canadian Arctic showed no significant change of ∑HCH concentration from the 1970s. The 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).

No temporal trend for Arctic cod and dab from the costal waters of Iceland was found for the period from 1991 to 2000, whereas results from Norway revealed a significant decrease (from 23 to 4 ng/g lw) of alpha-HCH residues in Arctic cod liver between 1987 to 1998 (Sinkkonen and Paasivirta, 2000).

Alpha-HCH has been detected in the muscle and liver of Arctic foxes (1.5 and 3 ng/g ww) in Canada (AMAP, 2004a). Levels in polar bear also reflect the spatial distribution of alpha-HCH being highest in Alaskan populations (in male polar bear up to 593 ng/g lw). No decline of alpha-HCH levels were reported for female polar bears in western Hudson Bay (concentrations up to 260 ng/g lw) from 1991 – 2002 (Verreault et al., 2005). Residues of alpha-HCH in East Greenland polar bears increased from 18 - 25 % during the 1990s (AMAP, 2004a).

2.3.3 Food

Daily intake values of alpha-HCH for the general population in adult human diets between 1986 and 1991 in the United States were reported to be 0.008 µg/kg. In the USA, the age dependent average daily intake of alpha-HCH declined from 3.3 – 16.1 ng/kg bodyweight (bw; 1982 – 84) to 0.5 – 2.7 ng/kg bw (1986 – 91) (ATSDR, 2005). In the Total Diet Study conducted by FDA in 2003 on 100 food items, alpha-HCH was detected in 35 items (submitted Annex E information by IPEN, 2007). In a Total Diet Study from Canada (1993 - 96), an average daily dietary intake of 0.37 ng/kg bw alpha-HCH was reported (Health Canada, 2003, in EFSA, 2006). Within the European countries, representative dietary intake studies are scarce. One was performed in the Czech Republic. The median daily intake values for alpha-HCH declined from 4.3 ng/kg bw in 1994 to 1.6 ng/kg bw in 2002 (EFSA, 2005). A local diet study carried out in Spain in the years 1990/91 estimated daily intakes below 0.1 µg alpha-HCH (Urieta et al., 1996).

Alpha-HCH has been found in cow's milk in countries where HCH had been used recently. Mean levels of alpha HCH in cow's milk of two different regions in India were 0.012 mg/kg lipid and 0.0045 mg/kg lipid, respectively (ATSDR, 2005). 140 bovine milk samples from 14 districts of Haryana, India (sampled within 1998 - 1999) were analysed for organochlorine pesticide residues. Four percent of the samples exceeded the maximum residue limit (MRL) of 0.05 mg/kg as recommended by WHO for alpha-HCH (Sharma et al., 2006). A monitoring study (192 samples) of cow's milk from Mexico revealed 0.001 - 0.201 mg/kg alpha-HCH (ATSDR, 2005).

Fish and clam samples from India contained 0.01 – 0.02 mg/kg ww and 0.26 mg/kg ww alpha-HCH respectively (Nair and Pillai, 1992). High levels of alpha-HCH in the food chain are documented for the arctic region (AMAP, 2004b; levels are reported under section 2.3.2.). Indigenous populations in the Arctic are particularly vulnerable from dietary exposure to alpha-HCH through subsidence food such as caribou, fish, seal and whale.

2.3.4 Body burden

Median levels of alpha-HCH in 25 American patients were 0.04 ng/g in the whole blood and 1.1 ng/g (maximum 9.6 ng/g) in biopsy fat (ATSDR, 2005). A Spanish study reported mean alpha-HCH levels of 1.43 µg/g (maximum 6.75 µg/g) in fat samples of children living in farm areas (Olea et al., 1999). Alpha-HCH has been detected in 1.7 % of the 4822 blood samples of German adults from 120 locations (detection limit: 0.1 µg/l) (Becker et al., 1998). Alpha-HCH was detected in blood serum from three of 186 (=1.6 %) Brazilian children (mean: 1.8 ppb) (ATSDR, 2005). Alpha-HCH has been detected in all samples (n = 142) of an eastern Romanian study in 2005 with a median concentration of 31 ng/g lipid (range 3 - 146 ng/g) (Dirtu et al., 2006). High concentrations were reported for India, due to agricultural use and malaria control. Blood serum contained up to 0.45 mg/l alpha-HCH, whereas adipose tissue contained up to 0.30 mg/kg. Breast milk contained 0.16 mg/l (mean) (Nair and Pillai, 1992). Scheele et al. (1998) investigated levels of several organochlorine compounds including alpha-HCH in bone marrow of 29 adults from Germany (collected between 1980 and 1991). Compared to adipose tissue, with generally highest levels of organochlorine compounds, alpha-HCH concentrations were 10-fold higher in bone marrow (mean: 0.050 mg/kg on dry lipid weight; max: 0.476 mg/kg). Alpha-HCH has also been detected in semen (ATSDR, 2005).

2.3.5 Exposure of children

Children are at specific developmental stages more vulnerable to risks from chemical substances than adults. It is unclear if children are more susceptible than adults to health effects from exposure to alpha-HCH although it is known that the developing brain is sensitive to the effects of different POPs. The specific enrichment of alpha-HCH in the mammalian brain might be a reason of concern. Placental transfer of alpha-HCH in humans is well documented (ATSDR, 2005; Falcon et al., 2004; Shen et al., 2006). Alpha-HCH accumulates to a higher extent in human placenta than in breast milk.

Mean alpha-HCH levels in breast milk of a Finnish cohort (43 mothers, 1997 – 2001) were 0.19 ng/g lipid, whereas placenta mean concentrations of alpha-HCH were 3.47 ng/g lipid. In a Danish cohort (43 mothers, 1997 – 2001), mean concentrations of 0.51 ng/g lipid in breast milk and 1.53 ng/g lipid in placenta were detected. A specific metabolic activity of the placental tissue is suspected (Shen et al., 2006). It could be shown that in case of restrictions of use, alpha-HCH concentrations in breast milk decline continuously. In Germany alpha-HCH was still found in 28 % of the breast milk samples analysed in 1984/85 whereas it could not be detected in 1990/91 and 1995 samples (Ott et al., 1999). More than 2 000 individual human milk samples from women living in Western Germany collected and analysed between 1984 and 2001 indicated that alpha HCH concentration declined from > 0.01 mg/kg fat to levels below detectability (detection limit of 0.001 mg/kg fat) (Fürst, 2004). In the framework of the 3rd WHO human milk field study, HCHs were analysed in 16 human milk pools from ten European countries. In Bulgaria, Russia and Ukraine, alpha-HCH was detected in

concentrations between 0.002 – 0.006 mg/kg lipid, whereas in the samples of Czech Republic, Germany, Ireland, Italy, Luxembourg, Norway and Spain alpha-HCH was not detectable (detection limit: 0.001 mg/kg lipid). In Nairobi, Kenya, 8.8% of 216 breast milk samples contained detectable alpha-HCH with a mean concentration of 0.013 mg/kg milk fat and a range of 0.002 – 0.038 mg/kg (Kinyamu et al., 1998). Breast milk samples from India contained 0.16 mg/l (mean) (Nair and Pillai, 1992). Another Indian study reports 0.045 mg/l alpha-HCH in breast milk (Nair et al., 1996). It can be concluded that alpha-HCH concentrations in breast milk strongly depend on exposure and that in several East European and developing countries concentrations are still very high.

2.4 Hazard assessment for endpoints of concern

Compared to technical HCH and lindane, limited data are available for alpha-HCH. A limited number of subchronic and chronic oral toxicity studies exist. No animal studies of the toxicity of alpha-HCH via inhalation and dermal application have been conducted. Studies on developmental, teratogenic and reproductive effects of alpha-HCH are missing. There is a lack of dose-response data after oral exposure for all relevant species. For the present risk profile, the most important findings concerning the hazard assessment have been reviewed. For more details please consider the reports listed under heading 1.2.

Acute Toxicity/ Neurotoxicity: Oral LD50 values range between 1000 and 4000 mg/kg bw for mice and between 500 and 4 674 mg/kg bw for rats. The signs of poisoning were central nervous stimulation: excitation, hunched posture, rough fur, dyspnoea, anorexia, tremors, convulsions, and cramps (IPCS, 1992).

Subchronic toxicity: In a 90-day study on rats carried out with dose levels of 0, 2, 10, 50, or 250 mg alpha-HCH/kg diet, growth was retarded and relative weight of organs (liver, heart, kidneys, and adrenals) increased at 250 mg/kg diet (equivalent to 12.5 mg/kg bw/day). At levels of 50 and 250 mg/kg, liver enzyme activities were modified and liver parenchyma cells enlarged. Liver weight increased at dose levels of 10 mg/kg diet (equivalent to 0.5 mg/kg bw/day) and reductions in white blood cell count were noted. Signs of immunosuppression (reduced serum levels of immunoglobulins G and M) were observed at 50 and 250 mg/kg diet. The NOAEL was 2 mg/kg alpha-HCH/kg diet (equivalent to 0.1 mg/kg bw/day; the LOAEL was 10 mg/kg diet) (IPCS, 1992).

Chronic Toxicity: When groups of 10 female and 10 male weanling Wistar rats were administered daily diets containing 0, 10, 50, 100, or 800 mg alpha-HCH /kg food (in corn oil) for 107 weeks, the highest dose level resulted in growth retardation, increased mortality, and slight kidney damage. With daily doses of 100 or 800 mg/kg, liver enlargement and histopathological changes in the liver were found. However, there were no liver changes at 50 mg/kg diet (NOAEL 50 mg/kg, LOAEL 100 mg/kg diet) (Fitzhugh et al., 1950).

Genotoxicity: Alpha-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. However, alpha-HCH induced DNA-fragmentation in human and rat hepatocytes. Oral exposure to alpha-HCH resulted in mitotic disturbances including an increased mitotic rate and increased frequency of polyploid hepatic cells in mice (ATSDR, 2005).

Carcinogenicity: Studies of the carcinogenicity of alpha-HCH are limited. Several studies in mice were performed, but their value is limited. Nevertheless, it is clear from the results that alpha-HCH, at high dose levels, produces nodular hyperplasia and hepatocellular carcinomas in mice (the incidence varying according on the strain) and also in rats (low incidence). Studies on initiation promotion and mode of action indicate that the neoplastic response observed with alpha-HCH is most likely due to a non-genotoxic mechanism. Alpha-HCH has been shown to promote tumors in the liver of mice and rats (IPCS, 1992). The International Agency for Research on Cancer (IARC) classified alpha- HCH in group 2B: possibly carcinogenic to humans. USEPA categorized alpha-HCH as probable human carcinogen. The department of Health and Human Services (DHHS) has determined that HCH (all isomers) may reasonably be anticipated to cause cancer in humans (ATSDR, 2005).

Immunotoxicity: Mice, treated with alpha-HCH (50 and 250 mg/kg/day- i.e. 0.5 and 2.5 mg/kg/bw/day) showed signs of immunosuppression (reduced serum levels of immunoglobulins G and M).

Effects in Humans: Adverse effects such as neurophysiological and neuropsychological disorders and gastrointestinal disturbances have been reported for workers exposed to technical HCH during pesticide or fertilizer formulation. Workers suffered from paraesthesia of the face and extremities, headache and giddiness, malaise, vomiting, tremors, apprehension, confusion, loss of sleep, impaired memory and loss of libido. Serum enzyme and IgM levels were enhanced (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 to HCH isomers.

A German study on organochlorine compounds in the peripheral blood of 486 women with hormonal disorders and/or infertility revealed that alpha-HCH concentrations were significantly higher in women with uterine fibroids, antithyroidal antibodies, luteal insuffiency and women highly susceptible to allergies. Obese women and women with a history of abortion had the highest HCH levels in blood (Gerhard, 1993).

In a pilot study with limited statistical power a possible association between exposure to organochlorines and the risk of childhood aplastic anaemia was shown. Alpha-HCH was significantly higher in children with aplastic anaemia than in those of controls ($p < 0.05$) (Ahamed et al., 2006).

The association between alpha-HCH exposure and intrauterine growth retardation (IUGR, < 10th percentile of birth weight for gestational age) was examined in India. Statistically significant associations ($p < 0.05$) between maternal blood levels of alpha-HCH and interauterine growth retardation were found (Siddiqui et al., 2003)

Effects in non-target organisms: Data on effects in non-target species are extremely limited. Alpha-HCH is acutely toxic to aquatic organisms. Effect concentrations in algae, zooplankton (brine shrimp and water flea) and fish of < 1 mg/l were reported (detailed values in IPCS, 1992; ECOTOX database, 2007). A LC50 of approximately 1.4 mg/l was determined in an acute test (duration 24 hours) in zebra fish (Oliveira-Filho and Paumgarten, 1997). In a long term study (70 days) with snails (_Lymnaea stagnalis_) a 50 % reduction of reproduction was found at a concentration of 65 µg/l. In fish no histopathological changes or influence on growth and behaviour could be detected in long-term experiments (test concentration 800 µg/L, duration 50 days, species guppies or pellets containing 10 - 1250 mg alpha-HCH/kg, duration 3 months, species rainbow trout) (IPCS, 1992). Monitoring data on Arctic polar bears revealed a negative correlation with retinol concentrations and HCHs, which may impact a wide range of biological functions (AMAP, 2004a).

Risk characterisation
USEPA performed a dietary risk assessment for Alaskan communities for alpha and beta-HCH in 2006. USEPA estimated alpha-HCH exposures for Alaskan communities in the range of 0.00057 - 0.0039 mg/kg bw/day for adults, 0.0021 - 0.051 mg/kg bw/day for children (age 1 - 6) and 0.00073 - 0.0050 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 (USEPA, 2006). The RfD value of 0.001 mg/kg/day for chronic exposure is based on a NOAEL of 0.1 mg/kg/day (the LOAEL is 0.5 mg/kg/day) established in a subchronic toxicity study in rats and applying an uncertainty factor of 100 (USEPA, 2006). For inhalation the reference concentration (RfC) of alpha-HCH is 0.00025 mg/m^3 based on a NOAEL of 0.025 mg/m^3 for observations of liver and kidney toxicity determined in an subchronic inhalation study in rats and applying an uncertainty factor of 100 (RIVM, 2001 in USEPA, 2006).

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 alpha-HCH are above the levels of concern for high-end dietary intake estimates. The cancer dietary risk estimates for alpha-HCH are also above the level of concern for both low and high-end dietary intake estimates. According to EPA, the risk values (% cRfD) are 57 - 390 for adult males, 67 – 460 for adult females, 210 – 5 100 for children (1 - 6 years) and 73 - 500 (7 - 12 years). The estimated cancer risk for adult males is 3.2×10^{-3} to 2.5×10^{-2} and 4.2×10^{-3} to 2.9×10^{-2} for adult females. It should be noted that these estimated incidences are at least four orders of magnitude higher than a general accepted cancer risk of 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.

3   Synthesis of the information

Technical HCH, a mixture of five stable HCH-isomers, contains 55 – 80 % alpha-HCH and was used extensively worldwide as an organochlorine pesticide. Though usage of technical HCH is negligible nowadays, releases into the environment may still occur. Local sources include hazardous waste sites, contaminated sites, stockpiles and 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 are assumed to range between 1.6 - 1.9 to 4.8 million tonnes. In addition, many sites are expected to cause environmental pollution and are not maintained or controlled appropriately.

The physico-chemical properties of alpha-HCH facilitate long-range atmospheric transport and allow for "cold condensation" on a global scale. In addition, the low Henry's Law Constant contributes to achieve high levels in the Arctic Ocean. Moreover, it was shown that Arctic air concentrations mimicked global usage data directly until the early 1990s. Also, monitoring data from remote regions e.g. the Arctic and Antarctica suggested that detected levels, which were sometimes higher than in source regions, originate from long range transport.

Hydrolysis contributes to the overall removal of alpha-HCH in aqueous solution under alkaline pH, but under environmental conditions has minor importance. Alpha-HCH may undergo enantioselective degradation which depends on the site and medium. Reported half-life and residue analyses in soil suggest moderate persistence. However, certain environmental conditions e.g. low concentrations or low temperatures resulted in longer half-lives. Half-lives for alpha-HCH in Arctic lakes were up to 1.4 years, whereas in the Eastern Arctic Ocean enantioselective degradation resulted in a range of approximately 5 to 17 years.

Alpha-HCH may bioaccumulate and biomagnify in biota and Arctic food webs. The BMFs as well as FWMFs in invertebrates, fish and terrestrial and marine mammals were greater than 1. Because of the individual potential to metabolize alpha-HCH, birds do not fit into this scheme. Most birds show BMFs < 1, independent of the trophic level. Especially in mammals, an enantiospecific accumulation of (+) or (-) alpha-HCH occurs (depending on the species). Combined with the lower potential for biotransformation alpha-HCH, - reaches high BMFs in mammals, with the highest concentrations in brain tissue (especially the (+) enantiomer). As all HCHs act on the central nervous system, this has to be seen with caution. To date, however, no enantiomer-specific toxicity studies for alpha-HCH are available and the reasons for the enrichment and differences are largely unclear.

Alpha-HCH has been shown to be neurotoxic, hepatotoxic, and to cause immunosuppressive effects and cancer in laboratory animals. The International Agency for Research on Cancer (IARC) has classified alpha-HCH in group 2B, possibly carcinogenic to humans. Several epidemiological studies indicate that alpha-HCH might play a role in human breast cancer. Alpha-HCH is a known tumour promoting agent.

Alpha-HCH may adversely affect human health in contaminated areas as well as in Arctic regions. Based on the available toxicity data of alpha-HCH, it can be concluded that current concentrations of alpha-HCH in food and human breast milk are a matter of concern. The estimated daily intake of alpha-HCH of Arctic indigenous people exceeds safe intake reference values, even though estimation is very conservative. The dietary risks of these populations are of concern. 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 alpha-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 lindane production process has produced 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.

Releases into the environment have dramatically decreased over the past 30 years, but levels in the environment suggest that alpha-HCH may persist in the environment (at lower concentrations). The cold Arctic Ocean, which is now eliminating alpha-HCH, was a sink which preserved the chemical from rapid degradation. Levels in Arctic biota do not thoroughly reflect the decreasing trend of the abiotic compartments.

Alpha-HCH is present in the terrestrial and the aquatic food chains and concentrations are a human health concern. 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 transport in the Arctic region. In addition, humans and wildlife are exposed to various contaminants that can influence the toxicological effects of alpha-HCH in an additive way. Based on the inherent properties, together with estimated daily intakes of alpha-HCH of Arctic indigenous people that exceeds safe intake reference values, and given the widespread occurrence of alpha-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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