別添3

α－ヘキサクロロシクロヘキサンの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 生分解は嫌気的条件で起こる。 【光分解性】 日光照射下での水溶液中の半減期は 4-6 日。固い表面上では半減期は 91 時間。 【加水分解性】 ・半減期は温度依存性を示し、pH 8 (20℃)で 0.8 年。pH 7.8(5℃)で 26 年。北極海で 63 年 【半減期】 ・水中:高緯度北極圏湖沼で 0.6 年-1.4 年と推定。東部北極海ではエナンチオ選択性の分解により、(+)異性体は 5.9 年、(-)異性体が 23.1 年。加水分解が考慮される場合は、(+)異性体は 5.4 年、(-)異性体が 16.9 年。 ・土壌中:亜熱帯地域のｲﾝﾄﾞの砂質ロームで 55 日。温帯地域では 161 日。ｶﾅﾀﾞの砂質ロームでの長期ﾌｨｰﾙﾄﾞｽﾀﾃﾞｨでは 15 年後に 4%が残留。高緯度北極圏湖沼堆積物で 2 年と推定。	【ｵｸﾀﾉｰﾙ/水分配係数】 logKOW=3.8 【BCF(経鰓的生物濃縮係数)】 ・単細胞緑藻類:BCF=200-2700(乾重量ﾍﾞｰｽ) ・鞭毛藻:BCF=13000(脂質ﾍﾞｰｽ) ・無脊椎動物:BCF=60(脂質ﾍﾞｰｽ 8000)-2750 ・ｾﾞﾌﾞﾗﾌｨｼｭ:BCF=1100(OECD TG 305E) ・ﾆｼﾞﾏｽ:BCF=1100-2800 【BMF(経口的生物濃縮係数)】 ・動物ﾌﾟﾗﾝｸﾄﾝ、ﾎｯｷｮｸｸﾀﾞﾗ:BMFs＞1 ・海鳥(ﾋﾒｳﾐｽｽﾞﾒとﾊｼﾞﾛｳﾐﾊﾟﾄを除く) BMFs＜1(alphaHCH は新陳代謝されるため) ・ﾜﾓﾝｱｻﾞﾗｼ:BMF= 2.5(脂肪組織) ・ﾎｯｷｮｸｸｼﾞﾗ:BMF=9.85 ・結論として、北極の生態系において、効果的な蓄積性が見られる。 【FWMF(食物連鎖による経口的生物濃縮係数)】 ・FWMFs＞1(北極海の食物連鎖の研究)	【反復投与毒性】 ラット(混餌 107 週):NOAEL 50mg/kg 主な毒性は、100mg/kg で肝肥大及び肝細胞の病理組織学的変化、800mg/kg で成長遅延、死亡率増加及び腎障害 ラット(混餌 90 日):NOAEL 0.1mg/kg/day 主な毒性は、0.5mg/kg/day で肝重量増加及び白血球数減少、2.5mg/kg/day で肝実質細胞肥大等、 12.5mg/kg/day で肝、心、腎及び副腎相対重量増加、成長遅延 【発がん性】 肝腫瘍 IARC グループ 2B (possibly carcinogenic to human) 【その他】 農薬、肥料の HCH 暴露により、感覚異常、頭痛、倦怠、嘔吐、振戦等 急性毒性試験において、背弯姿勢、呼吸困難、振戦、痙攣等神経症状 マウス:0.5mg/kg/day で血清中 IgG、IgM 減少	

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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.

K0820043 300108

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.

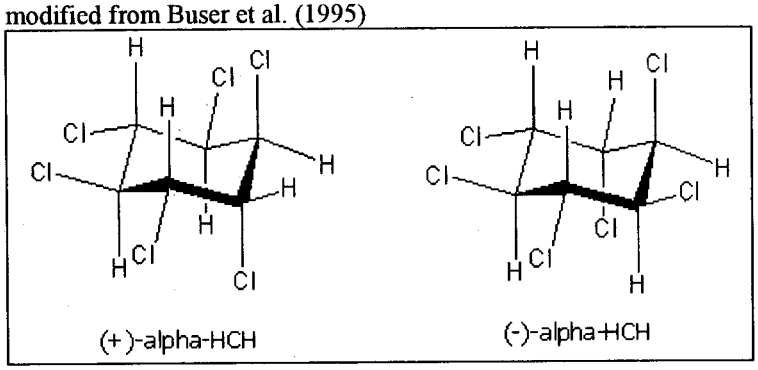
Alpha-HCH is one of the five stable isomers of technical HCH, an organochlorine pesticide formerly used in agriculture. The modes of action of the HCH isomers differ quantitatively and qualitatively with regard to their biological activity in the central nervous system as the main target organ. Alpha-HCH 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.

References

AMAP: Arctic Monitoring and Assessment Programme 2002: Persistent Organic Pollutants in the Arctic. Oslo, Norway, 2004a.

AMAP: Persistent Toxic Substances, Food Security and Indigenous Peoples of the Russian North Final Report. Arctic Monitoring and Assessment Programme, Oslo, 2004b.

Ahamed M., Anand M., Kumar A., Siddiqui M.K.: Childhood aplastic anaemia in Lucknow, India: incidence, organochlorines in the blood and review of case reports following exposure to pesticides. Clin Biochem. 39 (7), 2006, p. 762-6.

ATSDR: Toxicological profile for hexachlorocyclohexanes, United States of America Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, August, 2005. [http://www.atsdr.cdc.gov/toxprofiles/tp43.html; 2007-02-27].

Bachmann A., Walet P., Wijnen P., de Bruin W., Huntjens JL., Roelofsen W., Zehnder AJ.: Biodegradation of alpha- and beta-hexachlorocyclohexane in a soil slurry under different redox conditions. Appl Environ Microbiol. 54 (1), 1988, p. 143-9.

Bakore N., John PJ., Bhatnagar P.: Organochlorine pesticide residues in wheat and drinking water samples from Jaipur, Rajasthan, India. Environ Monit Assess. 98 (1-3), 2004, p. 381-9.

Barra, R; Cisternas, M., Urrutia, R., Pozo, K., Pacheo, P., Parra, O., Focardi, S. First report on chlorinated pesticide deposition in a sediment core from a small lake in central Chile (2001). Chemosphere, 45, 749-757

Baumann K., Angerer J., Heinrich R., Lehnert G: Occupational exposure to hexachlorocyclohexane. Body burden of HCH isomers. Int Arch Occup Environ Health. 47 (2), 1980, p. 119-27.

Becker KS., Kaus C., Krause P., Lepom C., Schulz M., Seifert B.: Umwelt-Survey 1998, Band III: Human-Biomonitoring. Stoffgehalte in Blut und Urin der Bevölkerung in Deutschland

Bidleman TF., Kylin H., Januntunen LM., Helm PA., Macdonald RW.: Hexachlorocyclohexanes in the Canadian Archipelago. 1. Spatial distribution and pathways of alpha-, beta- and gamma-HCHs in surface water. Environ. Sci Technol. 41 2007, p. 2688-2695.

Bouvier G., Blanchard O., Momas I., Seta N.: Pesticide exposure of non-occupationally exposed subjects compared to some occupational exposure: A French pilot study.

Borghini F, Grimalt JO, Sanchez-Hernandez JC, Bargagli R. Organochlorine pollutants in soils and mosses from Victoria Land (Antarctica). Chemosphere 58(3), 2005, p. 271-8.

Breivik, K., Pacyna, J. M., Münch, J.: Use of a-, b- and y-hexachlorocyclohexane in Europe, 1970-1996. Sci. Total Environ. 239 (1-3), 1999, p. 151-163.

Buser, H.F.; Müller M. Isomer and Enantioselective Degradation of Hexachlorocyclohexane Isomers in Sewage Sludge under Anaerobic Conditions. Environmental Science and Technology. 29, 1995, p. 664-672.

Braune B., Miur D., DeMarch B., Gamberg M., Poole K., Currie R., Dodd M., Duschenko W., Eamer J., Elkin B., Evans M., Grundy S., Hebert C., Johnstone R., Kidd K., Koenig B., Lockhart L., Marshall H., Reimer K., Sanderson J., Shutt L.: Spatial and temporal trends of contaminants in Canadian Arctic freshwater and terrestrial ecosystems: a review. The Science of the Total Environment 230, 1999, p. 145-207.

Buckmann AH., Norstrom RJ., Hobson KA., Karnovsky NJ., Duffe J., Fisk AT.: Organochlorine contaminants in seven species of Artic seabirds from northern Baffin Bay. Environmental pollution 128 2004, p. 327-338

Butte, W., Fox K., Zauke GP.: Kinetics of bioaccumulation and clearance of isomeric hexachlorocyclohexanes. Sci Total Environ. 109-110, 1991, p. 377-82.

CambridgeSoft Corporation: Chemfinder 2004, [http://chemfinder.cambridgesoft.com/result.asp; 2007-02-27]

CACAR: Canadian Arctic Contaminant Assessment Report II: Toxic Substances in the Arctic and Associated Effects – Human Health, Dept of Indian Affairs and Northern Development, Ottawa, Canada, 2003.

Chessells MJ., Hawker DW., Connell DW., Papajcsik IA.: Factors influencing the distribution of lindane and isomers in soil of an agricultural environment. Chemosphere 17 (9), 1988, p. 1741-1749.

Concha-Grana E., Turnes-Carou M., Muniategui-Lorenzo S., Lopez-Mahia P., Prada-Rodriguez D., Fernandez-Fernandez E.: Evaluation of HCH isomers and metabolites in soils, leachates, river water and sediments of a highly contaminated area. Chemosphere 64 (4), 2006, p. 588-95.

Corsolini S., Covaci A., Ademollo N., Focardi S., Schepens P.: Occurrence of organochlorine pesticides (OCPs) and their enantiomeric signatures, and concentrations of polybrominated diphenyl ethers (PBDEs) in the Adelie penguin food web, Antarctica. Environ Pollut. 140 (2) 2006 p. 371-82

Czech Republic: Format for submitting pursuant to Article 8 of the Stockholm Convention the information specified in Annex E of the Convention. February 2007.

Das AC., Chakravarty A., Sukul P., Mukherjee D.: Insecticides: their effect on microorganisms and persistence in rice soil. Microbiol Res. 150 (2), 1995, p. 187-94.

Deo P.G., Karanth, N.G. , Karanth, N.G.K. : Biodegradation of hexachlorocyclohexane isomers in soil and food environment. Critical Reviews in Microbiology, 20, 1994, p. 57-78.

Dirtu A.C., Cernat R., Dragan D., Mocanu R., Van Grieken R., Neels H., Covaci A.: Organohalogenated pollutants in human serum from Iassy, Romania and their relation with age and gender. Environ Int. 32 (6), 2006, p. 797-803.

Doelman P., Haanstra L., Loonen H. and Vos, A.: Decomposition of alpha - and beta -hexachlorocyclohexane in soil under field conditions in a temperate climate. Soil Biology and Biochemistry 22 (5), 1990, p. 629-634.

European Food Safety Authority (EFSA): Opinion of the Scientific Panel in Contaminants in the Food Chain on a Request from the Commission related to Gamma-HCH and other Hexachlorocyclohexanes as undesirable Substances in Animal Feed. The EFSA Journal 250, 2005, p. 1 – 39, [http://www.efsa.europa.eu/etc/medialib/efsa/science/contam/contam_opinions/1039.Par.0001.File.dat/contam_op_ej250_hexachlorocyclohexanes_en2.pdf, 2007-02-28]

EMEP POP data: Co-operative programme for monitoring and evaluation of the long range transmission of air pollutants in Europe. [http://www.nilu.no/projects/ccc/emepdata.html, 2007-04-2]

Falcon M., Oliva J.,Osuna E., Barba A. Luna A.: HCH and DDT residues in human placentas in Murcia (Spain).Falcon M, Oliva J,. Toxicology. 195 (2-3), 2004, p. 203-8.

Fisk AT., Hobson KA., Norstrom RJ.: Influence of Chemical and Biological Factors on Trophic Transfer of Persistent Organic Pollutants in the Northwater Polynya Marine Food Web. Environ. Sci. Technol. 35 (4), 2001, p. 732 -738.

Fitzhugh,O.G., Nelson, A.A., Frawley, J.P. The chronic toxicities of technical benzene hexachloride and its alpha, beta and gamma isomers. J Pharmacol Exp Ther. 100 (1) 1950, p 59-66.

Fürst P. 2004. Chemisches Landes- und Staatliches Vetrinäruntersuchungsamt Münster, Germany in EFSA, 2005.

Gerhard I.: Reproductive risks of heavy metals and pesticides in women. In Richardson, M.: Reproductive Toxicology, VCH, Weinheim, 1993, p. 167-183.

Germany: Format for submitting pursuant to Article 8 of the Stockholm Convention the information specified in Annex E of the Convention. February 2007.

Harner T., Kylin H., Bidleman TF. Strachan WMJ.: Removal of alpha- and gamma-Hexachlorocyclohexane and Enantiomers of alpha-Hexachlorocyclohexane in the Eastern Arctic Ocean. Environmental Science & Technology 33 (88), 1999, p. 1157-1164.

Hegeman WJ., Laane RW.: Enantiomeric enrichment of chiral pesticides in the environment. Rev Environ Contam Toxicol. 173, 2002; p. 85-116.

Helm PA., Diamond ML., Semkin R., Strachan WM., Teixeira C., Gregor D.: A mass balance model describing multiyear fate of organochlrorine compounds in a high Arctic lake. Environ. Sci Technol. 36 (5), 2002, p. 996-1003.

Hoekstra PF., O'Hara TM., Fisk AT., Borga K., Solomon KR., Muir DC.: Trophic transfer of persistent organochlorine contaminants (OCs) within an Arctic marine food web from the southern Beaufort-Chukchi Seas. Environ Pollut. 124 (3), 2003a, p. 509-22.

Hoekstra PF, O'Hara TM, Fisk AT, Karlsson H., Solomon KR, Muir DCG.: Enantiomer-specific Biomagnification of alpha-Hexachlorocyclohexane and Selected Chiral Chlordane-related Compounds within an Artic Marine Food Web. Environ.Toxicol.Chem. 22(10), 2003b, p.2482-2491.

Hoekstra PF., O'Hara TM., Pallant SJ., Solomon KR.: Bioaccumulation of Organochlorine Contaminants in Bowhead Whales. (Balaena mysticetus) from Barrow, Alaska. Archives of Environmental Contamination and Toxicology 42, 2002, p. 497-507.

Hop, H., Borga K., Gabrielsen GW., Kleivane L., Skaare JU.: Food web magnificaton of persistent organic pollutants in poikilotherms and homeotherms. Environ Sci Technol. 36 (12), 2002, p. 2589-97.

HSDB (U.S. National Library of Medicine: Hazardous Substance Database), 2006. [http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~MgLczu:4; 2007-02-27]

International HCH & Pesticides Association (IHPA): The Legacy of Lindane HCH Isomer Production, Vijgen J. 2006. [www.ihpa.info/library_access.php; 2007-02-27]

IPCS (International Programme on Chemical Safety). ENVIRONMENTAL HEALTH CRITERIA 123. Alpha- und Beta-Hexachlorocyclohexane. World Health Organization. Geneva, 1992.
[http://www.inchem.org/documents/ehc/ehc/ehc123.htm 2007-02-27]

IPCS (International Programme on Chemical Safety): Poisons Information Monograph 257, 2001.
[http://www.inchem.org/documents/pims/chemical/pim257.htm; 2007-02-27].

IPCS Intergovernmental Programme on Chemical Safety, Hexachlorocyclohexane (Mixed Isomers), 2006.
[http://www.inchem.org/documents/pims/chemical/pim257.htm#2.1%20Main%20risks% 20and%20target%20organs; 2007-07-12].

IPEN: Format for submitting pursuant to Article 8 of the Stockholm Convention the information specified in Annex E of the Convention. February 2007.

Iwata H, Tanabe S, Sakai N, Nishimura A, Tatsukawa R. Geographical distribution of persistent organochlorines in air, water and sediments from Asia and Oceania, and their implications for global redistribution from lower latitudesEnviron Pollut. 85 (1), 1994, p. 15-33.

Iwata H., Tanabe S., Iida T., Baba N., Ludwig JL., Tatsukawa R.:Enantioselektive Accumulation of alpha-Hexachlorocyclohexane in Northern Fur Seals and Double-Crested Cormorants: Effects on Biological and Ecological Factors in the Higher Trophic Levels. Environ. Sci. Technol. 32 (15), 1998, p. 2244-49.

Jagnow G,Haider K, Ellwardt PC.: Anaerobic dechlorination and degradation of hexachlorocyclohexane isomers by anaerobic and facultative anaerobic bacteria. Arch Microbiol. 115 (3), 1977, p. 285-92.

Japan: Format for submitting pursuant to Article 8 of the Stockholm Convention the information specified in Annex E of the Convention. February 2007.

Kaushik CP.: Loss of HCH from surface soil layers under subtropical conditions. Environ Pollut. 59 (3), 1989, p. 253-64.

Kallenborn R., Hühnerfuss H., Chiral Environmental Pollutants: Trace Analysis and Ecotoxicology. Springer Verlag 2001, Heidelberg, Germany.

Kelly B.C., Ikonomou M.G., Blair J.D., Mori, A.E., Gobas F.A.P.C.: Food Web-Specific Biomagnifaction or Persistent Organic Pollutants. Science 317, 2007, p. 236-238.

Klobes U., Vetter W., Glotz D., Luckas B., Skirnisson K., Hernsteinsson P.: Levels and enantiomeric ratios of chlorinated hydrocarbons in livers of Arctic fox (Alopex lagopus) and adipose tissue and liver of a polar bear (Ursus maritimus) sampled in Iceland. Intern. J. Environ. Anal. Chem. 69 (1) 1998, p. 67-81

Konwick BJ., Garrison AW., Black MC., Avants JK., Fisk AT.: Bioakkumulation, Biotransformation, and Metabolite Formation of Fipronil and Chiral Legacy Pesticides in Rainbow Trout. Environ. Sci. Technol. 40 (9), 2006, p. 2930-2936.

Kinyamu J.K., Kanja L.W., Skaare J.U., Maitho T.E.. Levels of organochlorine pesticides residues in milk of urban mothers in Kenya. Bull Environ Contam Toxicol. 60 (5),1998, p. 732-8.

Kurt-Karakus PB., Bidleman TF., Jones C.: Chiral Organochlorine Pesticide Signatures in Global Background Soils. Environ. Sci. Technol., 39 (22), 2005, p. 8671 -8677.

Law SA, Bidleman TF, Martin MJ, Ruby MV.: Evidence of enantioselective degradation of alpha-hexachlorocyclohexane in groundwater. Environ Sci Technol. 38 (6), 2004, p. 1633-8.

Li, Y.F.: Global technical hexachlorocyclohexane usage and its contamination consequences in the environment: from 1948 to 1997. The Science of the Total Environment, 232 (3), 1999, p. 121-158(38)

Li, YF., Macdonald, RW.: Sources and pathways of selected orpanochlorine pesticides to the Arctic and the effect to pathway divergence on HCH trends in biota: a review. The Science of the Total Environment 342, 2005, p. 87-106.

Li YF., Zhulidov AV., Robarts DR., Korotova LG.: Hexachlorocyclohexane Use in the Former Soviet Union. Arch. Environ. Contam. Toxicol. 48, 2004, p. 10-15.

Li YF., Bidleman TF.: Correlation between Global Emissions of alpha-hexachlorocyclohexane and its Concentrations in the Arctic Air. Journal of Environmental Informatics, 1, 2003, p. 52-7.

Li YF, Macdonald RW, Ma JM, Hung H, Venkatesh S.: Historical alpha-HCH budget in the Arctic Ocean: the Arctic Mass Balance Box Model (AMBBM). Sci Total Environ. 324 (1-3), 2004, p. 115-3.

Li YF., Macdonald, RW., Jantunen LMM., Harner T., Bidleman TF, Strachan WMJ.: The transport of ß-hexachlorocyclohexane to the western Artic Ocean: a contrast to α-HCH. The Science of the Total Environment 291, 2002, p. 229-246.

Moisey J., Fisk AT., Hobson KA., Norstrom RJ.: Hexachlorocyclohexane (HCH) isomers and chiral signatures of alpha-HCH in the Arctic marine food web of the Northwater Polynya. Environ Sci Technol. 35 (10), 2001, p. 1920-7.

MacRae IC., Raghq K., Castro TF.: Persistence and Biodegradation of Four Common Isomers of Benzene Hexachloride in Submerged Soils. J. Agr. Food Chem. 15, 1967, p. 911-914.

Murayama H., Takase Y., Mitobe H., Mukai H., Ohzeki T., Shimizu K., Kitayama Y.: Seasonal change of persistent organic pollutant concentrations in air at Niigata area, Japan. Chemosphere 52 (4), 2003, p. 683-94.

Ngabe B., Bidleman TF., Falconer RL.: Base Hydrolysis of alpha- and gamma-Hexachlorocyclohexanes. Environ. Sci. Technol. 27, 1993, p. 1930-1933

Nair A, Pillai MK. : Trends in ambient levels of DDT and HCH residues in humans and the environment of Delhi, India. Sci Total Environ. 30 (121), 1992, p.145-57.

Nair A., Mandpati R., Dureja P.: DDT and HCH load in mothers and their infants in Delhi, India Bull. Environ. Contam. Toxicol. 56 (1), 1996, p. 58 – 64.

NARAP: The North American Regional Action Plan 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, 2007-03-10]

Oliveira-Filho EC., Paumgartten FJ.: Comparative study on the acute toxicities of alpha, beta, gamma, and delta isomers of hexachlorocyclohexane to freshwater fishes. Bull Environ Contam Toxicol. 59 (6), 1997, p. 984-8.

Olsson A., Vitinsh M., Plikshs M., Bergman A. : Halogenated envrionmental contaminants in perch (Perca fluviatilis) from the Latvian coastal areas. The Science of the Total Environment, 239, 1999, p. 19-30.

Oliver BG., Niimi AJ.: Bioconcentration Factors of Some Halogenated Organics for Rainbow Trout: Limitations in Their Use for Prediction of Environmental Residues. Environ. Sci. Technol., 19(9), 1985, p. 842-849

Olea N., Olea-Serrano F., Lardelli-Claret P., Rivas A., Barba-Navarro A.: Inadvertent exposure to xenoestrogens in children. Toxicol Ind Health. 15 (1-2), 1999; p. 151-8.

Ott M., Failing K., Lang U., Schubring C. Gent H.J., Georgii S., Brunn H. Contamination of human milk in Middle Hesse, Germany--a cross-sectional study on the changing levels of chlorinated pesticides, PCB congeners and recent levels of nitro musks. Chemosphere 38 (1), 1999, p. 13-32.

Padma TV., Dickhut R.: Variations in α-HEXACHLOROCYCLOHEXANE enantiomer ratios in relation to microbial activity in a temperate estuary. Environmental Toxicology and Chemistry 22, 2002, p. 1421-1427.

Phillips TM., Seech AG., Lee H., and Trevors JT.: Biodegradation of hexachlo Environmental Toxicology and Chemistryro- cyclohexane (HCH) by microorganisms. Biodegradation 16, 2005, p. 363-392.

Pohl,H.R.; Tylenda,C.A.: Breast-feeding exposure of infants to selected pesticides: a public health viewpoint. Toxicol Ind.Health 16, 2000, p. 65-77.

Portig J., Stein K., Vohland HW.: Preferential distribution of alpha-hexachlorocyclohexane into cerebral white matter. Portig J, Xenobiotica, 1, 1989, p. 123-30.

Qian Y., Zheng M., Zhang B., Gao L., Liu W.: Determination and assessment of HCHs and DDTs residues in sediments from Lake Dongting, China. Environ Monit Assess. 116 (1-3), 2006, p. 157-67.

Rawn, F.K., Lockhart, W. L., Wilkinson, P., Savoie, D. A., Rosenberg, G. R., Muir, D. C. G. Historical contamination of Yukon Lake sediments by PCBs and organochlorine pesticides; influence of local sources and watershed characteristics (2001) Sci. Total Env. 280, 17-37

Riching, M., Koch, M., Rotard, W. Organic pollutants in sediment cores of NE- Germany: Comparison of the marine Arkona Basin with freshwater sediments. (2005) Marine Poll. Bull. 50, 1699-1705

Scheele J.S.: A comparison of the concentrations of certain pesticides and polychlorinated hydrocarbons in bone marrow and fat tissue. J. Environ. Pathol. Toxicol. Oncol. 17 (1), 1998, p. 65-8.

Sharma HR., Kaushik A., Kaushik CP.: Pesticide Residues in Bovine Milk from a Predominantly Agricultural State of Haryana, India. Environ Monit. Assess. 2006.

Shen H., Virtanen H.E., Main K.M., Kaleva M., Andersson A.M., Skakkebaek N.E., Toppari J., Schramm K.W. Enantiomeric ratios as an indicator of exposure processes for persistent pollutants in human placentas. Chemosphere. 62 (3), 2006, p. 390-5.

Singh G., Kathpal TS., Spencer WF., Dhankar JS.: Dissipation of some organochlorine insecticides in cropped and uncropped soil. Environ Pollut. 70 (3), 1991, p. 1219-39.

Sinkkonen S., Paasivirta, J.: Polychlorinated organic compounds in Arctic cod liver: trends and profiles. Chemosphere 40, 2000, p. 619-626.

Siddiqui MK., Srivastava S., Srivastava SP., Mehrotra PK., Mathur N., Tandon I.: Persistent chlorinated pesticides and intra-uterine foetal growth retardation: a possible association. Int Arch Occup Environ Health. 76 (1), 2003, p. 75-80.

Stewart DKR., Chrisholm D.: Long-term persistence of BHC, DDT and Chlordane in a sandy loam soil. Can.J.Soil Sci. 51, 1971, p. 379-383.

SRC PhysProp Database: The Physical Properties Database of the Syracuse Research Corporation [http://www.syrres.com/esc/physprop.htm; 2007-04-2]

Stern GA, Macdonald CR, Armstrong D, Dunn B, Fuchs C, Harwood L, Muir DC, Rosenberg B. Spatial trends and factors affecting variation of organochlorine contaminants levels in Canadian Arctic beluga (Delphinapterus leucas). Sci Total Environ. 351-352, 2005, p. 344-68.

Suar M., Hauser A., Poiger T., Buser R., Müller MD., Dogra C., Raina V., Holliger C., van der Meer R., Lal R., Kohler HPE.: Enantioselective Transformation of α-Hexachlorocyclohexane by the Dehydrochlorinases LinA1 and LinA2 from the Soil Bacterium Sphingomonas paucimobilis B90A. Applied and Environmental Microbiology, 71, 2005, p. 8514-8518.

Su Y., Hung H., Blanchard P., Patton GW., Kallenborn R., Konoplev R., Fellin P., Li H., Geen C., Stern G., Rosenberg B., Barrie LA. : Spatial and Seasonal Variations of Hexachlorocyclo-hexanes (HCHs) and Hexachlorobenzene (HCB) in the Arctic Atmosphere. Environmental Science and Technology 40, 2006, p. 6601-6607.

Sun P., Backus S., Blanchard P., Hites RA.: Temporal and spatial trends of Organochlorine pesticides in Great lake precipitation. Environmental Science and Technology 40, 2006a, p. 2135-2141.

Sun P., Blanchard P., Brice K., Hites RA.: Atmospheric organochlorine pesticide concentrations near the Great Lakes: temporal and spatial trends. Environmental Science and Technology 40, 2006b, p. 6587-6593.

Suzuki M., Yamato Y., Watanabe, T.: Persistence of BHC (1, 2, 3, 4, 5, 6-Hexachlorocyclohexane) and dieldrin residues in field soils. Bulletin of Environmental Contamination and Toxicology 14 (5), 1975, p. 520-529.

Switzerland: Format for submitting pursuant to Article 8 of the Stockholm Convention the information specified in Annex E of the Convention. February 2007.

TGD: Technical Guidance Document on Risk Assessment, European Communities, 2003. [http://europa.eu.int; 2007-29-05]

Ulrich EM., Willett KL., Caperell-Grant A., Bigsby RM., Hites RA.: Understanding Enantioselective Process: A Laboratory Rat Model for alpha-HCH Accumulation. Environ. Sci. Technol., 35(8), 2001, p. 1604-1609.

Urieta I., Jalon M., Eguilero. I.: Food surveillance in the Basque Country (Spain). II. Estimation of the dietary intake of organochlorine pesticides, heavy metals, arsenic, aflatoxin M1, iron and zinc through the Total Diet Study, 1990/91. Food Addit Contam. 13 (1), 1996, p. 29-52.

UNEP Chemicals, Regionally Based Assessment of Persistent Toxic Substances, 2003. [http://www.chem.unep.ch/Pts/gr/Global_Report.pdf; 2007-02-27].

USEPA, Assessment of lindane and other hexachlorocyclohexane isomers, 2006. [http://www.epa.gov/oppsrrd1/REDs/factsheets/lindane_isomers_fs.htm; 2007-02-27].

Verreault J, Muir DC, Norstrom RJ, Stirling I, Fisk AT, Gabrielsen GW, Derocher AE, Evans TJ, Dietz R, Sonne C, Sandala GM, Gebbink W, Riget FF, Born EW, Taylor MK, Nagy J, Letcher RJ. Chlorinated hydrocarbon contaminants and metabolites in polar bears (Ursus maritimus) from Alaska, Canada, East Greenland, and Svalbard: 1996-2002-Sci Total Environ. 2005 Dec 1;351-352:369-90.

Walker K., Vallero DA., Lewsi RG.: Factors influencing the distribution of Lindane and other hexachlorocyclohexanes in the environment. Environmental Science and Technology. 33 (24), 1999, p. 4373-78.

Wania, F., Mackay, D.: Tracking the distribution of persistent organic pollutants Environmental Science and Technology 30 (9), 1996, p. 390A-396A.

Wegmann, F., MacLeod, M., Scheringer, M. POP Candidates 2007: Model results on overall persistence and long-range transport potential using the OECD Pov & LRTP Screening Tool. Swiss Federal Institute of Technology, http://www.pops.int/documents/meetings/poprc/prepdocs/annexEsubmissions/All%20chemicals%20Switzerland.pdf (OECD Pov & LRTP Screening Tool available at http://www.sust-chem.ethz.ch/downloads)

WHO/Europe. 2003. Health risks of persistent organic pollutants from long-range transboundary air pollution. Joint WHO/convention task force on the health aspects of air pollution. Chapter 3. Hexachlorocyclohexanes [http://www.euro.who.int/Document/e78963.pdf, 2007-03-10]

Wiberg K., Letcher RJ., Sandau CD., Norstrom RJ., Tysklind M., Bidleman TF.: The Enanatioselective Bioaccumulation of Chiral Chlordane and alpha-HCH Contaminants in the Polar Bear Food Chain. Environ. Sci. Technol., 34(13), 2000, p. 2668-2674.

Willett KL., Ulrich EM., Hites RA.: Differential Toxicity and Environmental Fates of Hexachlorocyclohexane Isomers. Environmental Science and Technology 32, 1998, p. 2197-2207.

Wong CS., Lau F., Clarc M., Mabury SA., Miur DCG.: Rainbow Trout (Oncorhynchus mykiss) Can Eliminate Chiral Organochloride Compounds Enantioselectively. Environ. Sci. Technol., 36(6), 2002, p. 1257-1262.

Xiao H., Li N. and Wania F.: Compilation, Evaluation, and Selection of Physical-Chemical Property Data for α-, ß-, and γ-Hexachlorocyclohexane. J. Chem. Eng. Data 49 (2), 2004, p. 173 -185.

Zhang ZL., Hongb HS., Zhouc JL., Huanga J. and Yua G.: Fate and assessment of persistent organic pollutants in water and sediment from Minjiang River Estuary, Southeast China. Chemosphere 52 (9) 2003, p. 1423-1430.

Zhulidov, AV., Headley JV., Pavlov DF., Robarts, DR., Korotova GL., Vinnikov YY., Zhulidova OV.: Riverine fluxes of the persistent Organochlorine pesticides hexachlorocyclohexanes and DDT in the Russion Federation. Chemosphere 41, 2000, p. 829-841.

別添4

β－ヘキサクロロシクロヘキサンの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【光分解性・加水分解性】 非生物的な分解ﾌﾟﾛｾｽ（光分解や加水分解）では分解しない。 【半減期】 ・大気中：56 日(計算値) ・水中：水及び底質中の半減期のﾃﾞｰﾀはないものの、ﾓﾆﾀﾘﾝｸﾞに基づき残留性があり、容易に分解しないと推定される。 ・土壌中：亜熱帯地域のｲﾝﾄﾞの砂質ﾛｰﾑで 100 及び 184 日。温帯地域では嫌気性条件下で分解せず。ｶﾅﾀﾞの砂質ﾛｰﾑでの長期ﾌｨｰﾙﾄﾞｽﾀﾃﾞｨでは 15 年後に 44%が残留。日本の農地での長期ﾌｨｰﾙﾄﾞｽﾀﾃﾞｨでは 570 日後に 30%が残留。	【ｵｸﾀﾉｰﾙ/水分配係数】 logKow=3.78 【BCF（経鰓的生物濃縮係数）】 ｾﾞﾌﾞﾗﾌｨｼｭ：BCF=1460 【FWMF（食物連鎖による経口的生物濃縮係数）】 ・FWMFs＞1（北極海の食物連鎖の研究） ・FWMF=7.2（高塩素処理された PCB に相当） ・FWMF=2.9（ﾎﾞｰﾌｫｰﾄ・ﾁｭﾄｺ海の食物連鎖の研究による計算値） 【BMF（経口的生物濃縮係数）】 ・ｶﾀﾂﾑﾘに高い蓄積性が見られ、その捕食者（小さいｼﾗｻｷﾞなど）の BMF は 1 を超える。 ・ﾛｼｱのﾁｭｺﾄ半島の先住民の母乳含まれる betaHCH のﾚﾍﾞﾙが高い。	【反復投与毒性】 ラット（混餌　52 週）：LOAEL 0.5mg/kg/day 肝肥大、肝細胞の組織学的変化、ほぼ全動物死亡 ラット（混餌　13 週）：NOAEL 0.1mg/kg/day 主な毒性は、0.1mg/kg/day 以上で肝臓影響、2.5mg/kg/day 以上で胸腺重量減少、精巣萎縮、卵巣萎縮等、12.5mg/kg/day で死亡（運動失調、昏睡）、成長遅延、白血球・赤血球減少等 【発がん性】 マウス（26 週）：34mg/kg/day で肝腫瘍 IARC グループ2B（possibly carcinogenic to human） 【生殖毒性】 ラット（2世代繁殖試験）：NOAEL 0.1mg/kg/day 死亡率増加、不妊 ラット：20mg/kg/day を母胎投与で児死亡率増加 ミンク等で性周期かく乱、生殖器萎縮等の報告 【その他】	【慢性毒性】 グッピー *Poecilia reticulata* ：4-12週間試験 NOEC=0.032 mg/L（組織学的変化）。エストロゲン活性により、雄魚において、ビテロゲニン生成の変化、精巣の萎縮、雌雄同体現象、下垂体の変質が起こった。 ニワトリ：β-HCHを含む様々な有機塩素化合物に高濃度に曝露された雌が1回目及び2回目に産卵した雛鳥の身体状況が劣っていた。

		農薬、肥料の HCH 暴露により、感覚異常、頭痛、倦怠、嘔吐、振戦等 急性毒性試験において、背弯姿勢、呼吸困難、振戦、痙攣等神経症状 マウス（経口　30 日）：60mg/kg/day でリンパ球増殖、NK 活性減少	

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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.

K0763739 181207

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

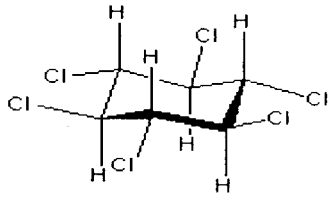
Common synonyms: beta-1,2,3,4,5,6-Hexachlorocyclohexane; beta-Benzenehexachloride; beta-BHC, benzene-cis-hexachloride; beta-HCH; beta-Hexachlorocyclohexane; beta-Hexachlorocyclohexane; beta-isomer; beta-lindane; Hexachlorocyclohexane-Beta; trans-alpha-benzenehexachloride; beta-benzenehexachloride (Chemfinder, 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 $6.7x10^{-4}$ to $5.0x10^{-3}$ and $7.7x10^{-4}$ to $5.8x10^{-3}$ for adult females respectively. It should be noted that a general accepted cancer risk is $1x10^{-6}$. 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.

References

AMAP: Arctic Monitoring and Assessment Programme 2002: Human Health in the Arctic. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway 2003.

AMAP: Persistent Toxic Substances, Food Security and Indigenous Peoples of the Russian North Final Report. Arctic Monitoring and Assessment Programme, Oslo, Norway, AMAP Report 2004:2 2004.

AMAP: Arctic Monitoring and Assessment Programme 2002: Persistent Organic Pollutants in the Arctic. Oslo, Norway, 2004.

ATSDR: Toxicological profile for hexachlorocyclohexanes, United States of America Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, August, 2005. [http://www.atsdr.cdc.gov/toxprofiles/tp43.html; 2007-02-27].

Bakore N., John PJ., Bhatnagar P.: Organochlorine pesticide residues in wheat and drinking water samples from Jaipur, Rajasthan, India. Environ Monit Assess. 98 (1-3), 2004, p. 381-9.

Baumann K., Angerer J., Heinrich R., Lehnert G: Occupational exposure to hexachlorocyclohexane. Body burden of HCH isomers. Int Arch Occup Environ Health. 47 (2), 1980, p. 119-27.

Blake A.: The Next Generation of POPs: PBDEs and Lindane, Working Group of the International POPs Elimination Network (IPEN). 2005. [http://www.oztoxics.org/ipepweb/egg/New%20POPs.html (pp:11) 2007-08-02]

Bidleman TF., Kylin H., Januntunen LM., Helm PA., Macdonald RW.: Hexachlorocyclohexanes in the Canadian Archipelago. 1. Spatial distribution and pathways of alpha-, beta- and gamma-HCHs in surface water. Environ. Sci Technol. 41 2007, p. 2688-2695.

Bhatt P., Kumar MS, Chakrabarti T.: Assessment of bioremediation possibilities of technical grade hexachlorocyclohexane (tech-HCH) contaminated soils. J Hazard Mater. 137, 2006.

Breivik K., Pacyna J. M., Münch J.: Use of a-, b- and y-hexachlorocyclohexane in Europe, 1970-1996. Sci. Total Environ. 239 (1-3), 1999, p. 151-163.

Buser H.F.; Müller M.. Isomer and Enantioselective Degradation of Hexachlorocyclohexane Isomers in Sewage Sludge under Anaerobic Conditions. Environmental Science and Technology. 29, 1995, p. 664-672.

Bustnes JO., Helberg M., Strann KB., Skaare JU.: Environmental pollutants in endangered vs. increasing subspecies of the lesser black-backed gull on the Norwegian coast. Environmental Pollution 144, 2006, p. 893-901.

Butte W., Fox K., Zauke GP.: Kinetics of bioaccumulation and clearance of isomeric hexachlorocyclohexanes. Sci Total Environ. 109-110, 1991, p. 377-82.

CambridgeSoft Corporation: Chemfinder 2004, [http://chemfinder.cambridgesoft.com/result.asp; 2007-02-27]

CACAR: Canadian Arctic Contaminant Assessment Report II: Toxic Substances in the Arctic and Associated Effects – Human Health, Dept of Indian Affairs and Northern Development, Ottawa, Canada, 2003.

CDC: National Report on Human Exposure to Environmental Chemicals. Third National Report. Department of Health and Human Services Centers for Disease Control and Prevention, 2005.

Chessells MJ., Hawker DW., Connell DW. and Papajcsik IA.: Factors influencing the distribution of lindane and isomers in soil of an agricultural environment. Chemosphere 17 (9), 1988, p. 1741-1749.

Concha-Grana E., Turnes-Carou M., Muniategui-Lorenzo S., Lopez-Mahia P., Prada-Rodriguez D., Fernandez-Fernandez E.: Evaluation of HCH isomers and metabolites in soils, leachates, river water and sediments of a highly contaminated area. Chemosphere 64 (4), 2006, p. 588-95.

Czech Republic: Format for submitting pursuant to Article 8 of the Stockholm Convention the information specified in Annex E of the Convention. February 2007.

Damgaard IN., Skakkebaek NE., Toppari J., Virtanen HE., Shen H., Schramm KW., Petersen JH., Jensen TK., Main KM.: Persistent pesticides in human breast milk and cryptorchidism. Environ Health Perspect. 114, 2006, p. 1133-1138.

Dirtu A.C., Cernat R., Dragan D., Mocanu R., Van Grieken R., Neels H., Covaci A.: Organohalogenated pollutants in human serum from Iassy, Romania and their relation with age and gender. Environ Int. 32 (6), 2006, p. 797-803.

Doelman P., Haanstra L., Loonen H. and Vos, A.: Decomposition of alpha - and beta -hexachlorocyclohexane in soil under field conditions in a temperate climate. Soil Biology and Biochemistry 22 (5), 1990, p. 629-634.

European Food Safety Authority (EFSA): Opinion of the Scientific Panel in Contaminants in the Food Chain on a Request from the Commission related to Gamma-HCH and other Hexachlorocyclohexanes as undesirable Substances in Animal Feed. The EFSA Journal 250, 2005, p. 1 – 39, [http://www.efsa.europa.eu/etc/medialib/efsa/science/contam/contam_opinions/1039.Par.0001.File.dat/contam_op_ej250_hexachlorocyclohexanes_en2.pdf, 2007-02-28]

Ewers U., Krause C., Schulz C., Wilhelm M.: Reference values and human biological monitoring values for environmental toxins. Report on the work and recommendations of the Commission on Human Biological Monitoring of the German Federal Environmental Agency. Int. Arch Occup Environ Health, 72 (4), 1999, p. 255-260.

Falcon M., Oliva J., Osuna E., Barba A. Luna A.: HCH and DDT residues in human placentas in Murcia (Spain).Falcon M, Oliva J,. Toxicology. 195 (2-3), 2004, p. 203-8.

Fisk AT., Hobson KA., Norstrom RJ.: Influence of Chemical and Biological Factors on Trophic Transfer of Persistent Organic Pollutants in the Northwater Polynya Marine Food Web. Environ. Sci. Technol. 35 (4), 2001, p. 732 -738.

Fitzhugh,O.G., Nelson, A.A., Frawley, J.P. The chronic toxicities of technical benzene hexachloride and its alpha, beta and gamma isomers. J Pharmacol Exp Ther. 100 (1) 1950, p 59-66.

Fürst P.: 2004. Chemisches Landes- und Staatliches Vetrinäruntersuchungsamt Münster, Germany in EFSA, 2005.

Gerhard I.: Reproductive risks of heavy metals and pesticides in women. Reproductive Toxicology 1993, p. 167-83.

Germany: Format for submitting pursuant to Article 8 of the Stockholm Convention the information specified in Annex E of the Convention. February 2007.

Gupta A., Kaushik C.P., Kaushik A.: Degradation of hexachlorocyclohexane (HCH; α, β, γand δ) by Bacillus circulans and Bacillus brevis isolated from soil contaminated with HCH. Soil Biology & Biochemistry 32 (11), 2000, pp. 1803-1805(3).

Hoekstra PF, O'Hara TM, Fisk AT, Borga K, Solomon KR, Muir DC.: Trophic transfer of persistent organochlorine contaminants (OCs) within an Arctic marine food web from the southern Beaufort-Chukchi Seas. Environ Pollut. 124 (3), 2003, 509-22.

Hoekstra PF., O'Hara TM., Pallant SJ. and Solomon KR.: Bioaccumulation of Organochlorine Contaminants in Bowhead Whales. (Balaena mysticetus) from Barrow, Alaska. Archives of Environmental Contamination and Toxicology 42, 2002, p. 497-507

Hop, H, Borga K, Gabrielsen GW, Kleivane, L., Skaare, JU.: Food web magnificaton of persistent organic pollutants in poikilotherms and homeotherms. Environ Sci Technol. 36 (12), 2002, p. 2589-97.

Hoyer AP., Grandjean P., Jorgensen T., Brock JW., Hartvig H.B.: Organochlorine exposure and risk of breast cancer. Lancet. 352 (9143), 1998, p.1816-20.

HSDB (U.S. National Library of Medicine: Hazardous Substance Database), 2006. [http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~MgLczu:1; 2007-02-27]

International HCH & Pesticides Association (IHPA): The Legacy of Lindane HCH Isomer Production, Vijgen, J. 2006. [www.ihpa.info/library_access.php, 2007-02-27]

IPCS (International Programme on Chemical Safety). ENVIRONMENTAL HEALTH CRITERIA 123. Alpha- und

Beta-Hexachlorocyclohexane. World Health Organization. Geneva, 1992. [http://www.inchem.org/documents/ehc/ehc/ehc123.htm 2007-02-27]

IPCS (International Programme on Chemical Safety): Poisons Information Monograph 257, 2001. [http://www.inchem.org/documents/pims/chemical/pim257.htm; 2007-02-27].

IPCS Intergovernmental Programme on Chemical Safety, Hexachlorocyclohexane (Mixed Isomers), 2006 [http://www.inchem.org/documents/pims/chemical/pim257.htm#2.1%20Main%20risks%20 and%20target%20organs; 2007-07-12]

IPEN: Format for submitting pursuant to Article 8 of the Stockholm Convention the information specified in Annex E of the Convention. February 2007.

Japan: Format for submitting pursuant to Article 8 of the Stockholm Convention the information specified in Annex E of the Convention. February 2007.

Kelly B.C., Ikonomou M.G., Blair J.D., Mori, A.E., Gobas F.A.P.C.: Food Web-Specific Biomagnifaction or Persistent Organic Pollutants. Science 317, 2007, p. 236-238.

Kinyamu JK., Kanja LW., Skaare JU., Maitho TE.. Levels of organochlorine pesticides residues in milk of urban mothers in Kenya. Bull Environ Contam Toxicol. 60(5):1998, 732-8.

Konishi Y., Kuwabara K., Hori S.: Continuous surveillance of organochlorine compounds in human breast milk from 1972 to 1998 in Osaka, Japan. Arch Environ Contam Toxicol. 40 (4), 2001, p. 571-8.

Kumar M., Chaudhary P., Dwivedi M., Kumar R., Paul D., Jain RK., Garg SK., Kumar A.: Enhanced Biodegradation of ß- and δ-Hexachlorocyclohexane in the Presence of α- and γ-Isomers in Contaminated Soils. Environ. Sci. Technol., 39 (11), 2005, p. 4005 -4011.

Li J., Zhu T., Wang F., Qiu XH.,Lin WL.: Observation of organochlorine pesticides in the air of the Mt. Everest region. Ecotoxicol Environ Saf. 63 (1), 2006, p. 33-41.

Li Y.F.: Global technical hexachlorocyclohexane usage and its contamination consequences in the environment: from 1948 to 1997. The Science of the Total Environment, 232 (3), 1999, p. 121-158(38)

Li YF., Macdonald, RW.: Sources and pathways of selected orpanochlorine pesticides to the Arctic and the effect to pathway divergence on HCH trends in biota: a review. The Science of the Total Environment 342, 2005, p. 87-106.

Li YF., Scholtz MT., and van Heyst BJ.: Global Gridded Emission Inventories of Beta-Hexachlorocyclohexane. Environmental Science & Technology 37 (16), 2003, p. 3493-3498.

Li YF., Macdonald, RW., Jantunen, LMM, Harner T., Bidleman TF, Strachan WMJ.: The transport of ß-hexachlorocyclohexane to the western Artic Ocean: a contrast to α-HCH. The Science of the Total Environment 291, 2002, p. 229-246.

Li YF., Zhulidov, AV., Robarts, DR., Korotova, LG.: Hexachlorocyclohexane Use in the Former Soviet Union. Arch. Environ. Contam. Toxicol. 48, 2004, p. 10-15.

Li, JY, Li H, Tao P, Lei FM.: Serum organochlorines pesticides level of non-occupational exposure women and risk of breast cancer: a case-control study. Wei Sheng Yan Jiu. 35 (4), 2006, p. 391-4.

Mathur V., Bhatnagar P., Sharma RG., Acharya V., Sexana R.: Breast cancer incidence and exposure to pesticides among women originating from Jaipur. Environ Int. 28(5), 2002, p. 331-6.

MacRae IC., Yamaya Y., Yoshida T.: Persistence of hexachlorocyclohexane isomers in soil suspensions. Soil Biology and Biochemistry, 16 (3), 1984, pp. 285-286.

Middeldorp PJM., Jaspers M., Zehnder AJB. and Schraa G.: Biotransformation of alpha-, beta-, gamma-, and delta - hexachlorocyclohexane under methanogenic conditions. Environmental Science and Technology 30 (7), 1996, pp.

2345-2349.

Moisey J., Fisk AT., Hobson KA., Norstrom RJ.: Hexachlorocyclohexane (HCH) isomers and chiral signatures of alpha-HCH in the Arctic marine food web of the Northwater Polynya. Environ Sci Technol. 35 (10), 2001, p. 1920-7.

Muir D., Savinova T., Savinov V., Alexeeva L., Potelov V., Svetochev V.: Bioaccumulation of PCBs and chlorinated pesticides in seals, fishes and invertebrates from the White Sea, Russia. Sci Total Environ. 306 (1-3), 2003, p. 111-31.

Murayama H., Takase Y., Mitobe H., Mukai H., Ohzeki T., Shimizu K., Kitayama Y.: Seasonal change of persistent organic pollutant concentrations in air at Niigata area, Japan. Chemosphere 52 (4), 2003, p. 683-94.

Nair A, Pillai MK. : Trends in ambient levels of DDT and HCH residues in humans and the environment of Delhi, India. Sci Total Environ. 30 (121), 1992, p.145-57.

Nair A., Mandpati R., Dureja P.: DDT and HCH load in mothers and their infants in Delhi, India Bull. Environ. Contam. Toxicol. 56 (1), 1996, p. 58 – 64.

Norway: Format for submitting pursuant to Article 8 of the Stockholm Convention the information specified in Annex E of the Convention. February 2007.

NARAP: 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, 2007-03-10]

Oliveira-Filho EC., Paumgarten FJ.: Comparative study on the acute toxicities of alpha, beta, gamma, and delta isomers of hexachlorocyclohexane to freshwater fishes. Bull Environ Contam Toxicol. 59 (6), 1997, p. 984-8.

Phillips TM., Seech AG., Lee H., and Trevors JT.:1Biodegradation of hexachlorocyclohexane (HCH) by microorganisms. Biodegradation 16, 2005, p. 363-392.

Pohl HR., Tylenda C.A.: Breast-feeding exposure of infants to selected pesticides: a public health viewpoint. Toxicol Ind.Health 16, 2000, p. 65-77.

Qian Y., Zheng M., Zhang B., Gao L., Liu W.: Determination and assessment of HCHs and DDTs residues in sediments from Lake Dongting, China. Environ Monit Assess. 116 (1-3), 2006, p. 157-67.
Senthilkumar K., Kannan K., Subramanian A. and Tanabe S: Accumulation of organochlorine pesticides and polychlorinated biphenyls in sediments, aquatic organisms, birds, bird eggs and bat collected from south India. Environ Sci Pollut Res Int.8 (1), : 2001, p. 35-47.

Sahu KS., Patnaik K K., Bhuyan S., Sreedharan B., Kurihara N., Adhya TK., Sethunathan N.: Mineralization of a-, y-, and beta-Isomers of Hexachlorocyclohexane by a Soil Bacterium under Aerobic Conditions, J. Agric. Food Chem. 43, 1995, p. 833-837.

Sharma P., RainaV., Kumari R., Malhotra S., Dogra C., Kumari H., Kohler HP., Buser HR., Holliger C., Lal, R.: Haloalkane Dehalogenase LinB Is Responsible for ß- and δ-Hexachlorocyclohexane Transformation in Sphingobium indicum B90A. Applied and Environmental Microbiology 72 (9), 2006, p. 5720-5727.

Shen H., Virtanen H.E., Main K.M., Kaleva M., Andersson A.M., Skakkebaek N.E., Toppari J., Schramm K.W. Enantiomeric ratios as an indicator of exposure processes for persistent pollutants in human placentas. Chemosphere. 62 (3), 2006, p. 390-5.

Singh G., Kathpal TS., Spencer WF. and Dhankar JS.: Dissipation of some organochlorine insecticides in cropped and uncropped soil. Environ Pollut. 70 (3), 1991, p. 1219-39.

Stewart DKR., Chisholm D.: Long-term persistence of BHC, DDT and Chlordane in a sandy loam soil. Can.J.Soil Sci. 51, 1971, p. 379-383.

Su Y., Hung H., Blanchard P., Patton GW., Kallenborn R., Konoplev R., Fellin P., Li H., Geen C., Stern G., Rosenberg B., Barrie LA. : Spatial and Seasonal Variations of Hexachlorocyclo-hexanes (HCHs) and Hexachlorobenzene (HCB) in the Arctic Atmosphere. Environmental Science and Technology 40, 2006, p. 6601-6607.

Sun P., Backus S., Blanchard P., Hites RA.: Temporal and spatial trends of Organochlorine pesticides in Great lake precipitation. Environmental Science and Technology 40, 2006a, p. 2135-2141.

Sun P., Blanchard P., Brice K., Hites RA.: Atmospheric organochlorine pesticide concentrations near the Great Lakes: temporal and spatial trends. Environmental Science and Technology 40, 2006b, p. 6587-6593.

Suzuki M., Yamato Y., Watanabe, T.: Persistence of BHC (1, 2, 3, 4, 5, 6-Hexachlorocyclohexane) and dieldrin residues in field soils. Bulletin of Environmental Contamination and Toxicology 14 (5), 1975, p. 520-529.

Switzerland: Format for submitting pursuant to Article 8 of the Stockholm Convention the information specified in Annex E of the Convention. February 2007.

TGD: Technical Guidance Document on Risk Assessment, European Communities, 2003. [http://europa.eu.int; 2007-29-05]

UNEP Chemicals, Regionally Based Assessment of Persistent Toxic Substances, 2003. [http://www.chem.unep.ch/Pts/gr/Global_Report.pdf; 2007-02-27].

Urieta I., Jalon M., Eguilero. I.: Food surveillance in the Basque Country (Spain). II. Estimation of the dietary intake of organochlorine pesticides, heavy metals, arsenic, aflatoxin M1, iron and zinc through the Total Diet Study, 1990/91. Food Addit Contam. 13 (1), 1996, p. 29-52.

USEPA, Assessment of lindane and other hexachlorocyclohexane isomers, 2006. [http://www.epa.gov/oppsrrd1/REDs/factsheets/lindane_isomers_fs.htm; 2007-02-27].

USEPA Memorandum: Lindane—Report of the FQPA Safety Factor Committee. August 2000: p 3.

van Velsen F.L., Danse L.H., Van Leeuwen F.X., Dormans J.A., Van Logten M.J. The subchronic oral toxicity of the beta-isomer of hexachlorocyclohexane in rats. Fundam Appl Toxicol. 6, 4, 1986, 697-712.

van Doesburg W., van Eekert MHA., Middeldorp PJM., Balk M., Schraa G, Stams AJM.: Reductive dechlorination of β-hexachlorocyclohexane (β-HCH) by a Dehalobacter species in coculture with a Sedimentibacter sp. FEMS Microbiology Ecology 54 (1), 2005, p. 87–95.

Walker K., Vallero DA. and Lewsi RG.: Factors influencing the distribution of Lindane and other hexachlorocyclohexanes in the environment. Environmental Science and Technology. 33 (24), 1999, pp. 4373-78.

Wang Y. et.al. 2006. Investigation of organochlorine pesticides (OCPs) in mollusks collected from coastal sites along the Chinese Bohaï Sea from 2002 to 2004. Environ Pollut. 146(1), 2007, p. 100-6.

Wania F., Mackay D.: Tracking the distribution of persistent organic pollutants Environmental Science and Technology 30 (9), 1996, p. 390A-396A.

Wester PW., Canton JH.: The usefulness of histopathology in aquatic toxicity studies. Comp Biochem Physiol C. 100 (1-2), 1991, p. 115-7.

Wegmann, F., MacLeod, M., Scheringer, M. POP Candidates 2007: Model results on overall persistence and long-range transport potential using the OECD Pov & LRTP Screening Tool. Swiss Federal Institute of Technology, [http://www.pops.int/documents/meetings/poprc/prepdocs/annexEsubmissions/All%20chemicals%20Switzerland.pdf] (OECD Pov & LRTP Screening Tool available at http://www.sust-chem.ethz.ch/downloads)

WHO/Europe. 2003. Health risks of persistent organic pollutants from long-range transboundary air pollution. Joint WHO/convention task force on the health aspects of air pollution. Chapter 3. Hexachlorocyclohexanes [http://www.euro.who.int/Document/e78963.pdf; 2007-03-10]

Willett KL., Ulrich EM., Hites RA.: Differential Toxicity and Environmental Fates of Hexachlorocyclohexane Isomers. Environmental Science and Technology 32, 1998, p. 2197-2207.

Wong C.K., Leung K.M., Poon B.H., Lan C.Y., Wong M.H. Organochlorine hydrocarbons in human breast milk collected in Hong Kong and Guangzhou. Arch Environ Contam Toxicol. 43 (3), 2002, p. 364-72.

Wu WZ., Xu Y., Schramm KW. and Kettrup A.: Study of sorption, biodegradation and isomerization of HCH in stimulated sediment/water system. Chemosphere 35 (9), 1997, p. 1887-1894.

Xiao H., Li N. and Wania F.: Compilation, Evaluation, and Selection of Physical-Chemical Property Data for α-, ß-, and γ-Hexachlorocyclohexane. J. Chem. Eng. Data 49 (2), 2004, p. 173 -185.

Zhang ZL., Hongb HS., Zhouc JL., Huanga J. and Yua G.: Fate and assessment of persistent organic pollutants in water and sediment from Minjiang River Estuary, Southeast China. Chemosphere 52 (9) 2003, p. 1423-1430.

Zhulidov, AV., Headley JV., Pavlov DF., Robarts, DR., Korotova GL., Vinnikov YY., Zhulidova OV.: Riverine fluxes of the persistent Organochlorine pesticides hexachlorocyclohexanes and DDT in the Russion Federation. Chemosphere 41, 2000, p. 829-841.

別添5

リンデンの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 非常に遅い。実験室の好気的条件下の土壌中で半減期は 980 日。嫌気的条件下ではより速く分解が進行。 【光分解性】 光に対しては安定。 【加水分解性】 ・半減期は 92-3090 時間。pH 5、pH 7 において安定であり半減期は 732 日。pH 9 における半減期は 43-182 日。海水中では pH 8(20℃)で 1.1 年。pH 7.6(5℃)のﾋｭｰﾛﾝ湖で 42 年。pH 8(0℃)の北極で 110 年など様々な推定値・算出値が報告されている。 【半減期】 ・大気中:OH ﾗｼﾞｶﾙとの気相反応の速度定数に基づく推定値は 2-3 日。対流圏での寿命は 7 日と推定。熱帯地域での対流圏寿命は 13 日と推定。Brubaker and Hites は大気中での寿命を 96 日と推定。 ・水中:河水では 30-300 日。湖水では 3-30 日。 ・土壌中:2-3 年。	【BCF(経鰓的生物濃縮係数)】 ・水生生物:BCF=10-6000(実験室)。BCF=10-2600(環境中)。BCF=3-36(Berny)。BCF=43-4220(湿重量ﾍﾞｰｽ)。BCF=11,000、1200-2100(脂質ﾍﾞｰｽ) ・ｴﾋﾞ:logBCF=2..26(脂質ﾍﾞｰｽ)。ﾆｼﾞﾏｽ:ogBCF=3.85(脂質ﾍﾞｰｽ)。動物ﾌﾟﾗﾝｸﾄﾝ:logBCF=4.3。無脊椎生物の平均 log BCF=2.28。脊椎生物の平均 log BCF=2.87 【BAF(経鰓及び経口による生物濃縮係数)】 ・ﾆｼﾞﾏｽ:logBAF=4.1 ・無脊椎生物の平均 log BAF=2.94。 ・脊椎生物の平均 log BAF=3.80。肉部分で 780、内臓部分で 2500、全魚体で 1400 という報告がある。 ・海洋哺乳類のﾘﾝﾃﾞﾝの濃度は、より疎水性の PCB や DDT と同等か又はより高ﾚﾍﾞﾙである。	【慢性毒性】 ラット(混餌):7mg/kg/day で肝臓壊死(38 週)、肝臓肥大(104 週) 【生殖毒性】 ウサギ(3 日/週で 12 週):0.8mg/kg/day で排卵率低下 ラット(5 日):6mg/kg/day(♂)で精子数減少 ラット(90 日):75mg/kg/day(♂)で性器萎縮、精子形成能かく乱 ラット(妊娠 15 日単回):30 mg/kg/day で雄児性行動変化、テストステロン濃度低下 マウス(妊娠 12 日単回):30 mg/kg/day で胎児の胸腺、胎盤重量低値 ラット(生殖試験:12 週暴露):1.7uM で成長速度低下、精子数減少、テストステロン濃度低下 【発がん性】 「発がん性を示す科学的根拠が示唆されるが、潜在的人発がん性を評価するには科学的根拠が不十分な物質」に分類(US EPA) 【その他】 リンデン含有殺虫剤摂取で人に発作痙	【慢性毒性】 淡水魚 :NOAEC=0.0029 mg/L(幼魚の生育低下) 水生無脊椎動物 :NOAEC=0.054mg/L(生殖能低下) カエル :0.0001 mg/Lで統計学的に有意な性比影響(71%雄)、エストロゲン活性の誘導、精子のプロゲステロン応答性変化。試験管内試験において、ビテロゲニン及びエストロゲン受容体の発現誘導。 無脊椎動物 :35日間試験 LOAEL=0.0135 mg/L(生殖能及び個体数への影響) ニワトリ及びニホンウズラ :それぞれ100及び25 ppmで孵化率低下。

		攣など神経毒性、実験動物で免疫抑制や抗体反応抑制など	

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Persistent Organic Pollutants Review Committee
Second meeting
Geneva, 6–10 November 2006

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

Addendum

Risk profile on lindane

At its second meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on lindane, on the basis of the draft contained in document UNEP/POPS/POPRC.2/10. The text of the risk profile, as amended, is provided below. It has not been formally edited.

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LINDANE

RISK PROFILE

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

November 2006

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Executive summary

Mexico proposed that gamma-hexachlorocyclohexane (lindane) be added to Annex A of the Stockholm Convention. The Review Committee evaluated Annex D information presented by Mexico at its first meeting and concluded that "Lindane meets the screening criteria specified in Annex D".

International initiatives on Lindane include the Protocol on Persistent Organic Pollutants of the Convention on Long Range Transboundary Air Pollution; the Rotterdam Convention; the OSPAR Commission for the Protection of the Marine Environment of the Northeast Atlantic, the Great Lakes Binational Toxics Strategy between the United States and Canada, and a North American Regional Action Plan on Lindane and Other Hexachlorocyclohexane Isomers under the Commission for Environmental Cooperation between Canada, United States and Mexico.

For each ton of lindane produced, around 6-10 tons of other isomers are also obtained. In the last years the production of lindane has rapidly decreased and it appears that only Romania and India are current producing countries. Lindane has been used as a broad-spectrum insecticide for seed and soil treatment, foliar applications, tree and wood treatment and against ectoparasites in both veterinary and human applications.

Once released into the environment, lindane can partition into all environmental media. Hydrolysis and photolysis are not considered important degradation pathways and reported half-lifes in air, water and soil are: 2.3 days, 3-300 days and up to 2 to 3 years, respectively. A half-life of 96 days in air has also been estimated.

Lindane can bio-accumulate easily in the food chain due to its high lipid solubility and can bio-concentrate rapidly in microorganisms, invertebrates, fish, birds and mammals. The bioconcentration factors in aquatic organisms under laboratory conditions ranged from approximately 10 up to 4220 under field conditions, the bioconcentration factors ranged from 10 up to 2600. Although lindane may bioconcentrate rapidly, bio-transformation, depuration and elimination are also relatively rapid, once exposure is eliminated.

Many studies have reported lindane residues throughout North America, the Arctic, Southern Asia, the Western Pacific, and Antarctica. HCH isomers, including lindane, are the most abundant and persistent organochlorine contaminants in the Arctic where they have not been used, pointing at evidence of their long-range transport.

The hypothesis that isomerization of gamma HCH to alpha HCH in air emerged as a possible explanation for higher than expected alpha HCH/gamma HCH ratios in the Arctic. However no conclusive experimental evidence of isomerization taking place in air has been produced to date. Also, although there is evidence that bioisomerization of lindane can take place through biological degradation, it seems that this process may play an insignificant role in the overall degradation of gamma-HCH.

Lindane can be found in all environmental compartments, and levels in air, water, soil sediment, aquatic and terrestrial organisms and food have been measured worldwide. Humans are therefore being exposed to lindane as demonstrated by detectable levels in human blood, human adipose tissue and human breast milk in different studies in diverse countries. Exposure of children and pregnant women to lindane are of particular concern.

Hepatotoxic, immunotoxic, reproductive and developmental effects have been reported for lindane in laboratory animals. The US EPA has classified lindane in the category of "Suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential". Lindane is highly toxic to aquatic organisms and moderately toxic to birds and mammals following acute exposures. Chronic effects to birds and mammals measured by reproduction studies show adverse effects at low levels such as reductions in egg production, growth and survival parameters in birds, and decreased body weight gain in mammals, with some effects indicative of endocrine disruption.

These findings and the evidence of its long range transport, as well as the fact that lindane is currently the object of local and global action initiatives, that also include thorough analysis and selection procedures, should be sufficient to warrant global action under the Stockholm Convention.

1. Introduction

1.1 Chemical identity

Mexico proposed that gamma-hexachlorocyclohexane (lindane) be added to Annex A of the Stockholm Convention on June 29, 2005. The proposal presented data on the gamma isomer, but mentioned as well that "other isomers of hexachlorocyclohexane should also be considered in this proposal".[1]

Lindane: gamma-hexachlorocyclohexane
Chemical formula: $C_6H_6Cl_6$
CAS number: 58-89-9
Molecular weight: 290.83

Physical and Chemical properties of gamma-HCH

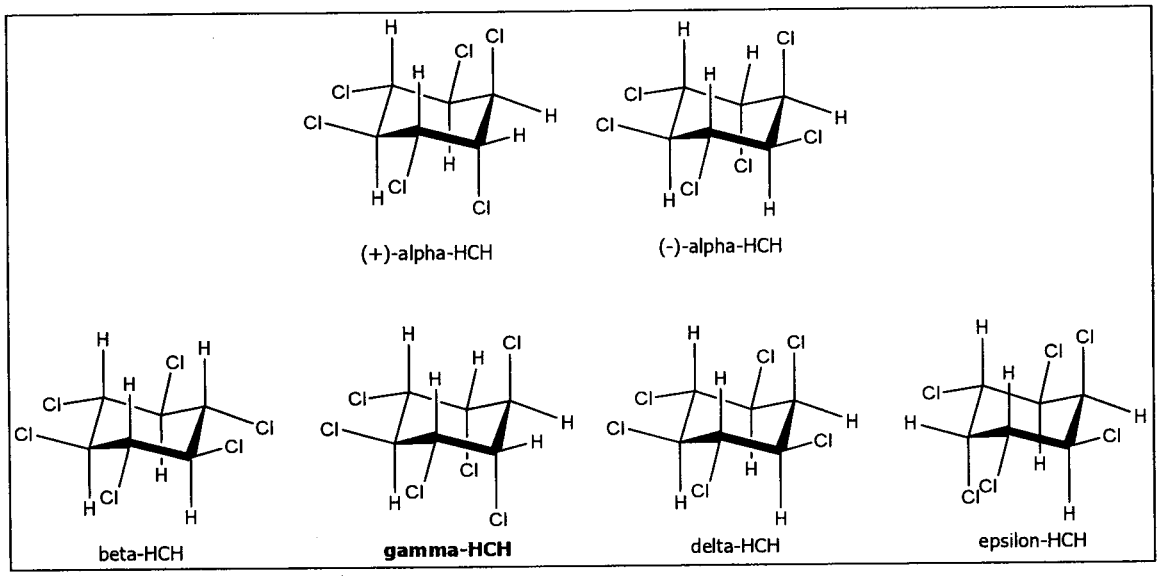
Physical state	Crystalline solid
Melting point	112.5 °C
Boiling point at 760 mmHg	323.4 °C
Vapor pressure at 20°C	4.2×10^{-5} mmHg
Henry's Law constant at 25°C	3.5×10^{-6} atm m^3/mol

ATSDR, 2005

Lindane is the common name for the gamma isomer of 1,2,3,4,5,6-hexachlorocyclohexane (HCH). Technical HCH is an isomeric mixture that contains mainly five forms differing only by the chlorine atoms orientation (axial or equatorial positions) around the cyclohexane ring. The five principal isomers are present in the mixture in the following proportions: alpha-hexachlorocyclohexane (53%–70%) in two enantiomeric forms ((+)alpha-HCH and (-)alpha-HCH), beta-hexachlorocyclohexane (3%–14%), gamma-hexachlorocyclohexane (11%–18%), delta-hexachlorocyclohexane (6%–10%) and epsilon-hexachlorocyclohexane (3%–5%). The gamma isomer is the only isomer showing strong insecticidal properties.

[1] UNEP/POPS/POPRC.1/8 and UNEP/POPS/POPRC.1/INF/8

Structure of alpha, beta, gamma, delta and epsilon HCH isomers



Modified from Buser et al., 1995.

The term "benzene hexachloride (BHC)" is also commonly used for HCH, but according to IUPAC rules this designation is incorrect. Nevertheless the term is used and therefore, gamma-BHC also designates lindane. In the present risk profile document, lindane refers to at least 99% pure gamma-HCH and the BHC term is not used.

1.2 Conclusion of the Review Committee regarding Annex D information

The Committee has evaluated Annex D information at its first meeting held in Geneva, from November 7th to 11th 2005, and has decided that "the screening criteria have been fulfilled for lindane" and concluded that "Lindane meets the screening criteria specified in Annex D." The Committee agreed that the alpha and beta isomers could be included in the discussions, although any decision to propose inclusion of the chemical in the Convention would apply only to lindane, the gamma isomer[2].

1.3 Data sources

Data sources provided by the proposing party, Mexico:

1. ATSDR Toxicological Profile Information Sheet 2001
2. AMAP. 1998. Persistent Organic Pollutants. Arctic Monitoring and Assessment Program (AMAP), 183-373. Oslo, Norway.
3. DeVoto, E., L. 1998. *Arch. Environ. Health* 53:147-55.
4. Extoxnet.1996. USDA/Extension Service/National Agricultural Pesticide Impact Assessment Program.
5. Gregor, 1989. Environ. Sci. technol. 23: 561-565.
6. IARC Monographs, http://monographs.iarc.fr
7. Mössner, S., 1994. Fres. J. Anal Chem. 349: 708-16.
8. Raum, E, A. 1998. *J. Epdiem. Commun. Health* 52 (suppl 1): 50S-5S.

[2] UNEP/POPS/POPRC.1/10

9. U.S Environmental Protection Agency. IRIS.
10. Walker, K., 1999. Environ. Sci. Technol. 33:4373-4378.
11. Wania,F., 1999. Environ. Toxicol. Chem. 18: 1400-1407.
12. WHO. 1991. Environmental Health Criteria 124 Lindane
13. Willett, K., 1998. Environ. Sci. Technol. 32: 2197-207.
14. Yi, F. L., Sci. and Technol. Vol 30, No 12, 1996.

Data sources used by the Committee:

1. UNEP/POPS/POPRC.1/8
2. Nagabe, et al., *Environmental Science and Technology.* 27: 1930–1933. 1993.
3. Harner, T. et al., *Environmental Science and Technology.* 33: 1157–1164. 1999.
4. Harner, T. et al., *Geophysical Research Letters.* 27: 1155–1158. 2000.
5. *Environmental Health Criteria No. 124: Lindane.* International Programme on Chemical Safety.
6. UNEP, ILO, WHO. Geneva. 1991. (http://www.inchem.org/documents/ehc/ehc/ehc124.htm).
7. Brock et al., *Alterra Report* 89, Netherlands. 2000.
8. *Guidance document on risk assessment for birds and mammals under Council Directive*
9. *91/414/EEC.* European Union. SANCO/4145/2000 – final, Brussels. 2002.
10. Arctic Monitoring and Assessment Programme. Norway. 2002.
11. Gregor, D., et al., *Environmental Science and Technology.* 23: 561–565, 1989.
12. Brubaker, W. W., and Hites, R.A. 1998. *Environmental Science and Technology* 32: 766–769.

The following parties and observers have answered the request for information specified in Annex E of the Convention: Republic of Macedonia, International HCH & Pesticides Association, Republic of Armenia, Haiti, World Wild Fund for Nature, CropLife International, International POPs Elimination Network, Morocco, Republic of Mauritius, European Community, Brazil, Republic of Lithuania, Canada, United States of America, Australia, Japan, Mexico, Lebanon and Poland. A more elaborated summary of the submissions is provided as separate **UNEP/POPS/POPRC.2/INF.18** document. *Summary of data submitted by Parties and observers for information specified in Annex E of the Convention.*

The following lindane assessment reports are publicly available through the internet:

- Assessment of Lindane and other Hexachlorocyclohexane Isomers. USEPA. February 2006 http://www.epa.gov/fedrgstr/EPA-PEST/2006/February/Day-08/p1103.htm

- Toxicological Profile for Hexachlorocyclohexane, Agency for Toxic Substances and Disease Registry, US Department of Health and Human Services, updated in 2005. http://www.atsdr.cdc.gov/toxprofiles/tp43.html

- USEPA Reregistration Eligibility Decision (RED) for Lindane. 2002. See RED and supporting health and eco assessments included in the docket. http://www.epa.gov/oppsrrd1/REDs/lindane_red.pdf

- The North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane (HCH) Isomers. Draft for Public Comment. October 2005. North

American Commission for Environmental Cooperation http://www.cec.org/files/PDF/POLLUTANTS/Lindane-NARAP-Public-Comment_en.pdf

- Health risks of persistent organic pollutants from long-range transboundary air pollution, Joint WHO/convention task force on the health aspects of air pollution. WHO/Europe. 2003. Chapter 3: Chapter 3/ Hexachlorocyclohexanes http://www.euro.who.int/Document/e78963.pdf

- Technical Review Report on Lindane. Reports on Substances Scheduled for Re-assessments Under the UNECE POPs Protocol. Prepared by Austria in 2004 (available: http://www.unece.org/env/popsxg/docs/2004/Dossier_Lindane.pdf)

- IPCS International Programme on Chemical Safety. Health and Safety Guide No. 54 LINDANE (Gamma-HCH) HEALTH AND SAFETY GUIDE. United Nations Environment Programme. International Labour Organisation. World Health Organization. Geneva, 1991. http://www.inchem.org/documents/hsg/hsg/hsg054.htm

1.4 Status of the chemical under international conventions

Lindane is listed as a "substance scheduled for restrictions on use" in Annex II of the 1998 **Protocol on Persistent Organic Pollutants of the Convention on Long-Range Transboundary Air Pollution**. This means that products in which at least 99% of the HCH isomer is in the gamma form (i.e. lindane, CAS: 58-89-9) are restricted to the following uses: 1. Seed treatment. 2. Soil applications directly followed by incorporation into the topsoil surface layer 3. Professional remedial and industrial treatment of lumber, timber and logs. 4. Public health and veterinary topical insecticide. 5. Non-aerial application to tree seedlings, small-scale lawn use, and indoor and outdoor use for nursery stock and ornamentals. 6. Indoor industrial and residential applications. All restricted uses of lindane shall be reassessed under the Protocol no later than two years after the date of entry into force. The Protocol entered into force on October 23th, 2003. [3]

Lindane, as well as the mixture of HCH isomers, is listed in Annex III of the **Rotterdam Convention** on the Prior Informed Consent Procedure as "chemicals subject to the prior informed consent procedure". The Rotterdam Convention entered into force 24 February 2004. [4]

Hexachlorocyclohexane isomers, including Lindane, the gamma isomer, are included in the List of Chemicals for Priority Action (Updated 2005) under the **OSPAR Commission for the Protection of the Marine Environment of the Northeast Atlantic**. Under this initiative, the Hazardous Substance Strategy sets the objective of preventing pollution of the maritime area by continuously reducing discharges, emissions and losses of hazardous substances, with the ultimate aim of achieving concentrations in the marine environment near background values for naturally occurring substances and close to zero for man-made synthetic substances. The OSPAR Convention entered into force on 25 March 1998. [5]

[3] Convention on Long-range Transboundary Air Pollution http://www.unece.org/env/lrtap/
[4] Rotterdam Convention http://www.pic.int.
[5] OSPAR Convention for the Protection of the Marine Environment of the Northeast Atlantic. http://www.ospar.org/

HCH (including lindane) is listed as a Level II substance in the **Great Lakes Binational Toxics Strategy** between the United States and Canada, which means that one of the two countries has grounds to indicate its persistence in the environment, potential for bioaccumulation and toxicity. [6]

A North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane Isomers is under development under the Sound Management of Chemicals project, which is an ongoing initiative to reduce the risks of toxic substances to human health and the environment in North America. This program is part of the Pollutants and Health Program of the **Commission for Environmental Cooperation** between the three NAFTA countries: Canada, United States and Mexico. (CEC, 2005)

Lindane is also listed under the **European Waterframework Directive**. This Directive is a piece of water legislation from the European Community. It requires all inland and coastal water bodies to reach at least "good status" by 2015. Lindane is one of the listed priority hazardous substances for which quality standards and emission controls will be set at EU level to end all emissions within 20 years. [7]

2. Summary information relevant to the risk profile

2.1 Sources

a) Production, trade, stockpiles

The manufacture of technical-HCH involves the photochlorination of benzene, which yields a mixture of five main isomers. This mixture of isomers is subject to fractional crystallization and concentration to produce 99% pure lindane, with only a 10-15 percent yield. The production of lindane is therefore inefficient as for each ton of lindane (gamma isomer) obtained, approximately 6-10 tons of other isomers are also obtained (IHPA, 2006). According to the *International HCH & Pesticide Association* (IHPA) (report and Annexes), there have been variations in the production methods for HCH and lindane, as well as for HCH isomers destruction or re-use. However, most of the methods to process or re-use the waste HCH isomers have been given up over the years and consequently, most of the waste products have been dumped over the last 50 years (IHPA, 2006). The lindane industry claims that modern production technology processes the waste isomers into TCB (trichlorobenzene) and HCl (hydrochloric acid) thereby reducing or eliminating environmental contamination from these byproducts (Crop Life, 2006).

Historical production of technical HCH and lindane occurred in many European countries, including the Czech Republic, Spain, France, Germany, United Kingdom, Italy, Romania, Bulgaria, Poland, and Turkey, and took place mainly from 1950 or earlier and stopped in 1970 to the 1990s . According to a research by IHPA, technical HCH and lindane have also been produced in other countries including Albania, Argentina, Austria, Azerbaijan, Brazil, China, Ghana, Hungary, India, Japan, Russia, Slovakia and the United States. Exact information is difficult to obtain, as many countries do not keep records of historical pesticides production, sales and usage or the industry considers this to be proprietary information (IHPA, 2006).

[6] Great Lakes Binational Toxics Strategy http://www.epa.gov/glnpo/gls/index.html

[7] European Union Water Framework Directive http://ec.europa.eu/environment/water/water-framework/index_en.html

It is estimated that global lindane usage from 1950 to 2000 for agricultural, livestock, forestry, human health and other purposes amounts to around 600 000 tons. The next table shows agricultural lindane usage in different continents in the period from 1950 to 2000 (IHPA, 2006).

Continent	Usage (tons)
Europe	287,160
Asia	73,200
America	63,570
Africa	28,540
Oceania	1,032
Total	**435,500**

It appears that in the last years the production of lindane has rapidly decreased leaving only a small number of producing countries. Romania, India, and possibly Russia are the only countries in the world still currently producing Lindane (IHPA, 2006 and USEPA, 2006, CEC, 2005 Annex A). Other sources indicate that Russia (Li et al., 2004) and China (USEPA, 2006) have stopped producing lindane. India produces and uses lindane for the control of mites in sugarcane at 200 tonnes per year.

Global lindane production between 1990 and 1995 was around 3 222 tons per year. In Europe, the top 10 countries with highest lindane usage between 1950 and 2000, representing 96% of the total usage in Europe, were: Czechoslovakia, Germany, Italy, France, Hungary, Spain, Russia, Ukraine, Yugoslavia and Greece (IHPA, 2006).

The 1998 Food and Agriculture Organization Inventory of Obsolete, Unwanted and/or Banned Pesticides found a total of 2785 tons of technical-grade HCH, 304 tons of lindane, and 45 tons of unspecified HCH material scattered in dumpsites in Africa and the Near East (Walker et al., 1999).

According to the information from the Arctic Council's Arctic Contaminants Action Program (ACAP) project on obsolete pesticides, possibly up to 1,000 tonnes of obsolete stockpiles of technical HCH and lindane still exist in the Russian Federation after the ban of production in the beginning of the 1990s.

b) Uses

Lindane has been used as a broad-spectrum insecticide, which acts by contact, for both agricultural and non-agricultural purposes. Lindane has been used for seed and soil treatment, foliar applications, tree and wood treatment and against ectoparasites in both veterinary and human applications (WHO, 1991).

As a consequence of its toxic, suspected carcinogenic, persistent, bioaccumulative and suspected endocrine disrupting properties, lindane became a substance of scrutiny for countries in the European Community. All uses of HCH including lindane have been banned, but Member States may allow technical HCH for use as an intermediate in chemical manufacturing and in products with at least 99% of the isomer content in the gamma form (lindane) for public health and veterinary topical use only, until December 31st 2007 (UNECE, 2004). Currently, the only registered agricultural use for lindane in the United States is for seed treatment and for lice and scabies treatment on humans (CEC, 2005). In Canada the major use of lindane has been on canola

and corn, but the only current allowable use of lindane is for public health purposes, as a lice and scabies treatment (CEC, 2005).

Information on current uses as informed by countries may be found on POPRC/LINDANE/INF.1

c) Releases to the environment

Considering every ton of lindane produced generates approximately 6 - 10 tons of other HCH isomers, a considerable amount of residues was generated during the manufacture of this insecticide. For decades, the waste isomers were generally disposed of in open landfills like fields and other disposal sites near the HCH manufacturing facilities. After disposal, degradation, volatilization, and run off of the waste isomers occurred (USEPA, 2006).

If the estimate of global usage of lindane of 600,000 tons between 1950 and 2000 is accurate, the total amount of possible residuals (if it is assumed that a mean value of 8 tons of waste isomers are obtained per ton of lindane produced) amounts to possibly 4.8 million tons of HCH residuals that could be present worldwide giving an idea of the extent of the environmental contamination problem (IHPA, 2006).

Air releases of lindane can occur during the agricultural use or aerial application of this insecticide, as well as during manufacture or disposal. Also, lindane can be released to air through volatilization after application (Shen et al., 2004). Evaporative loss to air from water is not considered significant due to lindane's relatively high water solubility (WHO/Europe, 2003).

2.2 Environmental fate

Persistence

A half-life for lindane in air of 2.3 days was estimated, based on the rate constant for the vapor-phase reaction with hydroxyl radicals in air; a tropospheric lifetime of 7 days due to gas-phase reaction with hydroxyl radicals was estimated, and a lifetime of 13 days was estimated for atmospheric reaction with OH radicals in the tropics (Mackay, 1997). Brubaker and Hites (1998) estimated a lifetime in air of 96 days for lindane. Lindane has half-lifes of 3-30 days in rivers and 30 to 300 days in lakes. Other studies report calculated or experimental hydrolysis half-lifes ranging from 92 to 3090 hours depending on the study; a persistence of about 2 to 3 years in soil is also reported (Mackay et al., 1997).

Once released into the environment, lindane can partition into all environmental media, but it is demonstrated that evaporation is the most important process in the distribution of lindane in the environment. Several studies focusing on the adsorption-desorption characteristics of lindane have shown that mobility of lindane is very low in soils with a high content of organic material, and higher in soils with little organic matter. The diffusion of lindane has also been investigated, showing it is strongly influenced by the water content of the soil and by temperature. The International Program on Chemical Safety states that when lindane suffers environmental degradation under field conditions, its half-life varies from a few days to three years depending on many factors including climate, type of soil, temperature and humidity (WHO, 1991).

Hydrolysis is not considered an important degradation process for lindane in aquatic environments under neutral pH conditions. Lindane is stable to hydrolysis at pH 5 and 7 with a half-life of 732 days and a half-life of 43 to 182 days at pH 9. Also, different estimated and calculated half-life values for lindane have been reported to be: 1.1 years at pH 8 and 20°C in seawater; 42 years at pH 7.6 and 5°C in Lake Huron, and 110 years in the Arctic Ocean at pH 8 and 0°C (USEPA, 2006).

Lindane is stable to light. Since lindane does not contain chromophores that absorb light, direct photolysis either in air, water or soil is not expected to occur. Even when indirect photolysis could occur with a photosensitizing agent, there is no clear evidence of lindane photodegradation. Lindane degrades very slowly by microbial action with a calculated half-life in soil of 980 days under laboratory aerobic conditions. Degradation takes place faster under anaerobic conditions than in the presence of oxygen. Possible degradation products are pentachlorocyclohexene, 1,2,4,-trichlorobenzene, and 1,2,3-trichlorobenzene (USEPA, 2006).

Bioaccumulation

The bioconcentration factors (BCF) in aquatic organisms under laboratory conditions ranged from approximately 10 up to 6000; under field conditions, the bioconcentration factors ranged from 10 up to 2600 (WHO, 1991). Other studies report bioconcentration factors (log BCF) ranging from 2.26 in shrimp to 3.85 in rainbow trout in early life stages on lipid basis and 4.3 in zooplankton and a bioaccumulation factor (log BAF) up to 4.1 in rainbow trout (Mackay et al., 1997). Also, uptake and elimination rate constants ranging from 180 – 939 h^{-1} and 0.031 – 0.13 h^{-1} respectively have been reported for rainbow trout in early life stages on lipid basis (Mackay et al., 1997).

Lindane can bio-accumulate easily in the food chain due to its high lipid solubility and can bio-concentrate rapidly in microorganisms, invertebrates, fish, birds and mammals. Bioconcentration factors (BCF) within aquatic species vary considerably, with experimental data revealing bioconcentration factors of 3-36 (Berny, 2002); 43-4220 on a wet weight basis, and a mean BCF of 11,000 on a lipid basis (Geyer et al., 1997); and also 1200-2100 (Oliver et al., 1985).

An average log BCF of 2.28 in invertebrate species and an average log BCF of 2.87 in vertebrate species can be calculated from different studies (Donkin et al., 1997, Renberg et al., 1985, Thybaud et al., 1988, Yamamoto et al., 1983, Butte et al., 1991, Carlberg et al., 1986, Kanazawa et al., 1981, Kosian et al., 1981 La Rocca et al., 1991, Oliver et al., 1985, Vigano et al., 1992). In the same way, an average log BAF of 2.94 in invertebrate species, and an average log BAF of 3.80 in vertebrate species can be calculated from other studies (Oliver et al., 1988, Chevreuil et al., 1991, Hartley et al., 1983, Caquet et al., 1992). Bioconcentration factors of 780 for fillet, 2500 for viscera and 1400 for whole fish tissues have also been reported (USEPA, 2002).

In an experiment carried out by Geyer et al. (1997), bioconcentration factors are shown to be dependent on the fish species and their lipid content; additionally, different modes of uptake, metabolism, sources of contamination and even experimental conditions, taken together could explain the significant variation observed for BCF values. Also, most data suggest that, although lindane may bioconcentrate rapidly, bio-transformation, depuration and elimination are relatively rapid once exposure is eliminated. (WHO, 1991).

The bioaccumulation of lindane has been observed for most taxonomic groups, from plants and algae to vertebrates. The environmental consequences of the combination of this bioaccumulation potential with a high toxicity – no-observed-adverse-effect levels (NOAELs) as low as 0.3 mg/kg body weight/day – and ecotoxicity – aquatic ecosystem no-observable-effect concentration (NOEC) below 1 µg/l (*Environmental Health Criteria No. 124, 1991;* and Brock et al., 2000) – should be

considered. For example, when measured field levels in earthworms (0.3 mg/kg for a soil containing 80 µg/kg) are weighed against mammalian toxicity data (*Environmental Health Criteria No. 124, 1991;*) using a realistic food intake ratio of 0.63 (*Guidance document on risk assessment for birds and mammals* 2002.) the comparison indicates an area of ecotoxicological concern which should be further explored.

Lindane has been reported in seabirds, fish and mammals in the Arctic (ATSDR, 2005). Lindane concentrations in marine mammals are found at equivalent or even higher levels than some of the more hydrophobic contaminants such as polychlorinated biphenyls (PCBs) and DDT (ATSDR, 2005). In addition, lindane has been reported in human breast milk among Inuit in the Arctic and in marine mammals (Arctic Monitoring and Assessment Programme, 2002).

Potential for long-range environmental transport

Many studies have reported HCH residues, particularly alpha and gamma isomers throughout North America, the Arctic, Southern Asia, the Western Pacific, and Antarctica. HCH isomers, including lindane, are the most abundant and persistent organochlorine insecticide contaminants in the Arctic, and their presence in the Arctic and Antarctic, where technical HCH and lindane have not been used, is evidence of their long-range transport. HCH isomers, including lindane, are subject to "global distillation" in which warm climates at lower latitudes favor evaporation into the atmosphere where the chemicals can be carried to higher latitudes. At midlatitudes, deposition and evaporation vary with season. At high latitudes, cold temperatures favor deposition (Walker et al., 1999).

Use of lindane in countries such as Canada, where usage was ~ 500 tons in 2000, and certain European countries, such as France, has contributed to gamma-HCH levels present in the Arctic air. Concentrations of lindane were detected at Alert in the Arctic and varied from 10-11 pg/m^3 in 1993 decreasing to 6.4 pg/m^3 in 1997 (CACAR, 2003).

In a study completed by Shen et al. in 2004, 40 passive air sampling stations were located along transects from the Canadian Arctic, down the east coasts of Canada and the U.S., along the Canada - U.S. border and in southern Mexico and Central America for one year. The elevated alpha-HCH levels (sampler volumetric air concentrations between 1.5 and 170 pg/m^3) in eastern Canada were explained by outgassing of alpha-HCH from cold arctic water flowing south, warming, and releasing the alpha-HCH back to the atmosphere. High concentrations of gamma-HCH (sampler volumetric air concentrations between 5 and 400 pg/m^3) were found in the Canadian prairies, north of Lake Ontario, southern Québec, the middle Atlantic states and southern Mexico, reflecting the influence of regional lindane usage (Shen et al., 2004). Transport over the Pacific Ocean of lindane was measured at a sampling site in Yukon and ranged 4-18 pg/m^3 (Bailey et al., 2000). HCH isomers, including lindane, were measured at a mountain site at Tenerife Island from June 1999 to July 2000. Air concentrations of gamma-HCH at this site ranged 18 - 31 (mean 26) pg/m^3 (Van Drooge et al., 2002).

Lindane is very prevalent in the marine environment and soils, and its atmospheric long range transport potential has been demonstrated for the European Union, (WHO/Europe, 2003) especially by the European Monitoring and Evaluation Program (EMEP). High concentrations of gamma-HCH in air occurred in France, Portugal, Spain, the Netherlands and Belgium. These can be explained by the high emission densities of lindane in these countries. Relatively high air concentrations were also found in Germany, Italy, Switzerland and Luxembourg, despite the lower

lindane emission densities in these countries. These elevated air concentrations were probably explained by atmospheric transport from the former high-density emission European countries (Shatalov and Malanichev, 2000; Shatalov et al., 2000).

a) Isomerization

The hypothesis that isomerization of gamma-HCH to alpha-HCH could be taking place in air emerged as a possible explanation for alpha-HCH/ gamma-HCH ratios that were found in the 80's as high as 18, when this ratio was expected to be around 5 according to the fraction of these two isomers found in the technical HCH mixture. (Oehme et al 1984a, Oehme et al., 1984b, Pacyna et al., 1988) However no conclusive experimental evidence of isomerization taking place in air has been produced to date.

In the same line, Walker et al. (1999) noted that if photochemical transformation of gamma-HCH to alpha-HCH in air takes place, one should see significant concentrations of alpha-HCH in the Southern Hemisphere air. However, recent measurements have found alpha-HCH levels are dropping over time in the Southern Hemisphere as well as in the Arctic Ocean, which is not consistent with the isomerization theory and a continued use of lindane. The ratio of alpha-HCH/gamma-HCH in air sampled in the Southern Hemisphere during the 1980s - 1990s was generally 1 to 2.3 (Ballschmiter et al., 1991, Bidleman et al., 1993, Iwata et al., 1993, Kallenborn et al., 1998, Lakaschus et al., 2002; Schreitmüller et al., 1995) and was 0.81 in the most recent study in Antarctica (Dickhut et al., 2005).

Other studies have suggested that differential air-sea gas exchange rates could lead to fractionation of the HCH isomers and preferential accumulation of alpha-HCH in air during long range transport over the oceans. This could account for some portion of the elevated alpha-HCH/gamma-HCH ratios observed during wintertime, but not for the very high ratios found in summer in the early studies. (Pacyna et al., 1988 and Oehme et al., 1991). Walker et al. (1999) concluded that even when the experiments show that photoisomerization is possible, evidence that this process is a substantial contributor to the high alpha/gamma ratios observed in the Arctic is indirect and subject to several interpretations.

Several studies have also reported photolytic isomerization of gamma-HCH to alpha-HCH. However, these studies have demonstrated isomerization in condensed media, but there is no evidence that isomerization takes place in the gas phase under ambient atmospheric conditions. Laboratory evidence shows that gamma-HCH can be transformed into other isomers in soil or sediments through biological degradation, but although the bioisomerization of lindane can take place, it seems that this process may play an insignificant role in the overall degradation of gamma-HCH (Walker et al., 1999 and Shen et al., 2004).

b) Environmental monitoring data

Poland reported concentrations of gamma-HCH in river sediments ranging from 2.4 to 9.4 µg/kg. Results from the National Veterinary Residue Control Programme in Poland indicate that food of animal origin contains levels of gamma-HCH below the level of action of 1000 µg/kg (Annex E information provided by Poland, 2006).

The Ministry of Environment in Japan has monitored Lindane in water finding a concentration of Lindane of 32 to 370 pg/l in 60 surveyed water specimens across the country in 2003. A total of 186 bottom sediment specimens were also surveyed in 2003 and Lindane was detected in all the

specimens, with a concentration of Lindane from traces (1.4) to 4000 pg/g dry, with a geometric mean of 45 pg/g dry. A recent survey in 2003 on shellfish, fish and birds shows that Lindane was detected in all the specimens with concentrations ranging from 5.2 to 130 pg/g-wet for shellfish, 130 pg/g-wet for fish, and 1,800 to 5,900 pg/g-wet for birds. Lindane was detected in all 35 specimens from 35 sites in Japan for ambient air in the warm season in 2003 with a concentration of Lindane ranging from 8.8 to 2,200 pg/m^3 with a geometric mean of 63pg/m^3. The survey on the same sites excluding one site during the cold season in year 2003 indicates a concentration of 3.1 to 330 pg/m^3 with a geometric mean of 14pg/m^3 (Annex E information provided by Japan, 2006).

Australia reported that none of the meat and crop samples monitored for residues in the country contained detectable levels of lindane (Annex E information provided by Australia, 2006).

The United States reported that gamma-HCH, was below the level of detection in all samples analyzed for the Third National Report on Human Exposure to Environmental Chemicals. Lindane was detected in fish tissue from lakes and reservoirs in the US EPA national Lake Fish Tissue Study, with levels ranging from 0.652 to 8.56 ppb. Lindane is being monitored in air and precipitation with the Integrated Atmospheric Deposition Network in the Great Lakes region with average concentration of 15-90 pg/m^3 in the early 90s, decreasing to 5-30 pg/m^3 since 2000. Average concentrations in precipitation (volume-weighted mean) at seven main sites during the years 1997- 2003 were 690-1400 pg/L for lindane. The most recent years of available analytical data in the U.S. EPA's Great Lakes Fish Monitoring Program indicate the concentration of Lindane in sport fish fillets (Chinook and Coho Salmon and Steelhead Trout) have ranged between trace detection and 0.005 ppm between 1982 and 2000. The National Oceanic and Atmospheric Administration's National Status and Trends (NS&T) Program has measured lindane in the tissues of bivalves throughout the coastal US and Great Lakes from 1986 to present. Over the Program's history, a total of 283 sites throughout the contiguous US, Alaska, Hawaii, and Puerto Rico have been sampled, with a total of 4,990 records for the gamma isomer. Median measured concentration for gamma-HCH was 0.56 (range 0-71.0) ng/g dry weight. A trends assessment using data pooled for the entire USA, indicates that there has been a statistically significant decline in lindane levels from 1986 through 2003. (Annex E information provided by the United States of America, 2006).

In Canada, a project was undertaken in 1999-2000 by Alberta Environment to characterize the pesticides found in a number of Alberta locations, and to determine their relative levels and seasonality. Lindane was detected in ambient air at Lethbridge in all samples starting from May to August. Lindane levels peaked on June 15 at 1.15 ng/m^3, while the low level of 0.23 ng/m^3 was present in ambient air on June 22, 1999. As lindane is used on treated seed that is planted in April and early May, lindane is then released into the atmosphere following seeding and hence the higher levels in May followed by a slow decline to low and/or undetectable levels in August and September (Kumar, 2001).

2.3 Exposure

Lindane can be found in all environmental compartments and levels in air, water, soil, sediment, aquatic and terrestrial organisms and food have been measured worldwide. Humans are therefore being exposed to lindane as demonstrated by detectable levels in human blood, human adipose tissue and human breast milk (WHO/Europe, 2003).

A special area of concern is the fact that HCH isomers, including lindane, accumulate in colder climates of the world. High concentrations of HCH isomers, including lindane, are found in the

Beaufort Sea and Canadian Archipelago (CEC, 2005). Through environmental exposure, gamma-HCH can enter the food chain and accumulate in fatty animal tissue constituting an important exposure pathway for Arctic or Antarctic animals as well as for humans who rely on these animals for their subsistence diets (USEPA, 2006)

General population exposure to gamma-HCH can result from food intake, particularly from animal origin products like milk and meat, as well as water containing the pesticide. Lindane was found to be 10 times higher in adipose tissue of cattle than in the feed (ATSDR, 2005) showing that animals may be exposed to the compound through food and even through ectoparasite treatment. Lindane has been detected in cow's milk in countries that still use the chemical as a pesticide. In a study performed in Uganda, Africa, the concentrations of gamma-HCH in cow's milk was 0.006–0.036 mg/kg milk fat, respectively. Mean levels of gamma-HCH analyzed in cow's milk samples from two separate areas in India were 0.002 and 0.015 mg/kg. A monitoring study of 192 samples of cow's milk from Mexico revealed 0.002–0.187 mg/kg of gamma-HCH (ATSDR, 2005).

Determinations of the lindane content in body tissues in the general population have been made in a number of countries. The content in blood in the Netherlands was in the order of < 0.1–0.2 µg/l. In the early 1980s, mean concentrations of gamma-HCH in human adipose tissue in Czechoslovakia, the Federal Republic of Germany and the Netherlands were 0.086, 0.024–0.061 and 0.01–0.02 mg/kg, respectively, on a fat basis. In total-diet and market-basket studies to estimate daily human intake of gamma-HCH, clear differences were observed with time: intake in the period around 1970 was up to 0.05 µg/kg body weight per day, whereas by 1980 intake had decreased to 0.003 µg/kg body weight per day or lower (WHO/Europe, 2003).

Individuals living in rural areas and on a non-vegetarian diet are more likely to be exposed to gamma-HCH as shown by a study performed in India, where women who consumed red meat, eggs and chicken had higher pesticide levels, including lindane, in blood than vegetarian women (ATSDR, 2005). Other sources of direct exposure include facilities at which lindane is still being produced, abandoned pesticide plants, and hazardous waste sites (USEPA, 2006).

Exposure of children to lindane is a particular concern. Gamma-HCH has been found in human maternal adipose tissue, maternal blood, umbilical cord blood and breast milk. Lindane has also been found to pass through the placental barrier. Mean breast milk concentration of lindane was 0.084 mg/l in a study in India. An average level of 6 ppb lindane in breast milk was obtained in a study in Alberta, Canada (ATSDR, 2005). In a study looking at organochlorine pesticides in human breast milk collected from 12 regions in Australia, lindane was detected in all samples with a mean of 0.23 ng/g lipid and a range of 0.08-0.47 ng/g lipid (Annex E information provided by Australia, 2006).

Lindane levels have also been found in human breast milk from different countries including Canada, Germany, the Netherlands and the United Kingdom. Lindane levels ranged from <0.001 to 0.1 mg/kg on a fat basis (WHO/Europe, 2003).

An additional exposure route for children exists in regions where lindane is applied directly to milk and meat producing livestock for pest control. On a body weight basis, children consume more milk per unit body weight than adults, and thus may be exposed to significant concentrations of lindane residues through drinking milk (CEC, 2005). Medical use of products to treat head lice and scabies is also of concern when applied to children, although most adverse effects have been observed after misuse. Another exposure to possibly significant amounts of lindane might occur through household dust in certain conditions, and are also of concern especially for children (ATSDR, 2005).

2.4 Hazard assessment for endpoints of concern

Lindane is the most acutely toxic HCH isomer affecting the central nervous and endocrine systems. In humans, effects from acute exposure at high concentrations to lindane may range from mild skin irritation to dizziness, headaches, diarrhea, nausea, vomiting, and even convulsions and death (CEC, 2005). Respiratory, cardiovascular, hematological, hepatic and endocrine effects have also been reported for humans, following acute or chronic lindane inhalation. Hematological alterations like leukopenia, leukocytosis, granulocytopenia, granulocytosis, eosinophilia, monocytosis, and thrombocytopenia, have been reported, following chronic human occupational exposure to gamma-HCH at production facilities (ATSDR, 2005).

Additionally, gamma-HCH has been detected in the blood serum, adipose tissue and semen of occupationally and environmentally exposed individuals (ATSDR, 2005). Serum luteinizing hormone levels were significantly increased in men occupationally exposed to gamma-HCH. Also, the mean serum concentration of follicle stimulating hormone was increased and testosterone was decreased in exposed individuals, but these trends were not statistically significant compared to unexposed controls (ATSDR, 2005).

The most commonly reported effects associated with oral exposure to gamma-HCH are neurological. Most of the information is from case reports of acute gamma-HCH poisoning. Seizures and convulsions have been observed in individuals who have accidentally or intentionally ingested lindane in insecticide pellets, liquid scabicide or contaminated food (WHO/Europe, 2003).

In India, blood levels of gamma-HCH were significantly higher in 135 breast cancer patients, 41-50 years of age, compared to a control group without the disease. However, in similar studies in other countries, a correlation between breast cancer incidence and elevated levels of gamma-HCH in blood was not observed (ATSDR, 2005).

Rats exposed to various concentrations of gamma-HCH through inhalation for 4 hours exhibited concentration-related neurological effects when observed for up to 22 days after exposure. Slight-to-moderate sedation was observed after exposure to 101 mg/m^3; slight-to severe sedation was noted after exposure to 378 mg/m^3; restlessness, excitation, and ataxia were seen after exposure to 642 and 2,104 mg/m^3; and spasms were also noted at the highest concentration of 2,104 mg/m^3 (ATSDR, 2005).

Hepatotoxic effects of lindane have been demonstrated in laboratory animals by numerous studies. Increases in cytochrome P-450 levels after inhalation of lindane aerosol at 5 mg/m^3 for 90 days and increases in cytochrome P-450 activity cytoplasmic superoxide dismutase, lipid peroxidation in rats after being fed 1.8 mg/kg body weight for 15 and 30 days, have been demonstrated. Chronic studies with a dose of 7-8 mg/kg body weight of lindane in the diet showed liver necrosis and fatty degeneration in rats exposed for 38 to 70 weeks, and hypertophy in Wistar rats exposed for 104 weeks (WHO/Europe, 2003). Rats exposed to 15 mg gamma-HCH/kg/day for 5 days and 2.5 mg gamma-HCH/kg/day for 21 days, showed significant increases in absolute liver weight, P-450 and EROD activity in a dose- and time-dependent manner (ATSDR, 2005).

Some evidence is available for immunotoxic effects, like immunosuppression and suppressed antibodies responses, caused by lindane in laboratory animals. Immunosuppression was observed in rats exposed to 6.25 and 25 mg/kg body weight for 5 weeks. Primary antibody response was

suppressed in albino mice being exposed to 9 mg/kg body weight per day in the diet for 12 weeks, and secondary antibody response suppression was observed after 3 weeks at the same dose (WHO/Europe, 2003).

Reproductive effects of lindane have been recorded in laboratory animals: female rats exposed orally to 10 mg/kg body weight per day for 15 weeks presented anti-estrogenic properties. Female rabbits exposed to gamma-HCH at 0.8 mg/kg body weight per day, 3 days per week for 12 weeks had a reduced ovulation rate (WHO/Europe, 2003). In male rats, reductions in the number of testicular spermatids and epididymal sperms were observed after an oral dose of 6 mg/kg body weight for 5 days, or a single dose of 30 mg/kg body weight of gamma-HCH. Testicular atrophy, seminiferous tubules degeneration and disruption of spermatogenesis were also reported in male rats fed 75 mg/kg body weight per day for 90 days (WHO/Europe, 2003). Lindane has therefore characteristics of an endocrine disrupting compound. Exposure to lindane during gestation with a single dose of 30 mg/kg of body weight at day 15 of pregnancy, induced altered libido and reduced testosterone concentration in male offspring rats (USEPA, 2006).

Developmental effects of lindane have also been reported. Decreased fetal weight, fetal thymic weight, and placental weight were observed in mice treated at 30 and 45 mg/kg by gastric intubation at day 12 of gestation. Fetotoxic effects of lindane were also observed and may be due to induced oxidative stress, enhanced lipid peroxidation and DNA single strand breaks in the fetal and placental tissues (WHO/Europe, 2003). Rats exposed to 1.7, 3.4 and 6.8 µM corresponding to exposure doses that might be encountered in contaminated vegetables (80-250 µg/kg) or contaminated drinking water (0.02 µg/l) for 12 weeks, showed an affected growth rate, decreased spermatozoid count, as well as decreased testosterone levels during gestation, lactation or weaning (WHO/Europe, 2003). Evidence of increased susceptibility of the young animal was noted in a rat multi-generation reproduction study and rat developmental neurotoxicity study (USEPA, 2002).

The available genotoxicity data indicate that gamma-HCH has some genotoxic potential. Gamma-HCH has been shown to increase chromosome clastogeny in bone marrow cells in mice exposed to 1.6 mg per kg body weight per day by gavage for 7 days (ATSDR, 2005). Nevertheless, lindane is not classified as genotoxic by the European Union (WHO/Europe, 2003). DNA damage was observed in cultures of rat nasal and gastric mucosa cells, and human nasal mucosa cells exposed to gamma-HCH and induced unscheduled DNA synthesis in certain types of cells, like human peripheral lymphocytes (ATSDR, 2005).

The International Agency for Research on Cancer (IARC) has classified lindane as possibly carcinogenic to humans; it has also classified technical HCH and alpha-HCH as possible human carcinogens (ATSDR, 2005). The US EPA has recently reclassified lindane in the category "Suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential". USEPA has classified technical-grade HCH and alpha-HCH as probable human carcinogens while beta-HCH is a possible human carcinogen (ATSDR, 2005).

Carcinogenicity of lindane has been tested by oral administration in different experiments. Some studies have shown no significant increases in endocrine, thyroid, pituitary, adrenal gland, liver, or ovary tumors in rats fed 10.8–33 mg/kg/day in the diet for 80 weeks, or 0.07–32 mg gamma-HCH/kg/day in the diet for 104 weeks, but poor survival rates limited the significance of such results (WHO/Europe, 2003). While other studies have reported hepatocellular carcinomas in mice exposed to 13.6–27.2 mg/kg/day in the diet for 80 or 104 weeks, and in mice exposed to 27.2 mg/kg/day in the diet for 96 weeks, these results were obtained in a strain of mouse that has a dominant mutation resulting in an increased susceptibility to formation of strain-specific neoplasms.

Lindane is highly toxic to aquatic organisms and moderately toxic to birds and mammals following acute exposures. Chronic effects to birds and mammals measured by reproduction studies show adverse effects at low levels such as reductions in egg production, growth and survival parameters in birds and decreased body weight gain in mammals, with some effects indicative of endocrine disruption. Acute aquatic toxicity data on lindane indicate that it is highly toxic to both freshwater fish (LC_{50} ranges of 1.7 to 131 ppb) and aquatic invertebrates (LC_{50} ranges of 10.0 to 520 ppb). Chronic aquatic toxicity data for freshwater organisms show reduction in larval growth in freshwater fish at a NOAEC of 2.9 µg/l, and decreased reproduction in aquatic invertebrates at a NOAEC of 54 µg/l (CEC, 2005 and USEPA, 2006).

Lindane produced statistically significant sex ratio effects (71% males) in frogs at a level of 0.1 ppb and estrogenic activity as well as altered sperm responsiveness to progesterone and induced expression of vitellogenin and estrogen receptors in *in vitro* tests (USEPA, 2006). Reproductive and population effects were found at a LOAEL of 13.5 µg/l lindane in invertebrate in a 35 day study. Lindane at 100 ppm and 25 ppm caused reduced hatchability in both laying hens and Japanese quails, respectively (USEPA, 2006).

In 2002, USEPA published a dietary risk assessment for indigenous people in the Arctic for lindane. This dietary risk assessment is based on a number of hazard and exposure assumptions, and estimates risk to communities in Alaska and others in the circumpolar Arctic region who depend on subsistence foods, such as caribou, seal and whale. The total dietary intakes for adults ranged from 0.000055 to 0.00071 mg/kg/day. For non-cancer effects, the Level of Concern was (LOC) =0.0016 mg/kg/day. The dietary risks for lindane did not exceed the LOC (USEPA, 2002).

Although the decision to include lindane in the Stockholm Convention would be based on the gamma isomer alone, the POPRC agreed that discussions could include the alpha and beta isomers. Therefore, information from a 2006 USEPA risk assessment on the alpha and beta isomers is included below.

In February 2006, USEPA published for public comment a risk assessment that discussed risks from lindane and the alpha- and beta-HCH isomers, by-products of the lindane manufacturing process (USEPA, 2006). Total dietary intakes were estimated for adults and children and ranged from 0.00057 to 0.051 mg/kg/day for alpha-HCH, and from 0.00037 to 0.01 mg/kg/day for beta-HCH. These dietary intakes were compared to USEPA's chronic level of concern (LOC). For non-cancer effects, the LOC is cRfD=0.00006 mg/kg/day for beta-HCH and a cRfD=0.001 mg/kg/day for alpha-HCH, based on the dose at which USEPA has concluded will result in no unreasonable adverse health effects. The cancer LOC is when the estimated upper bound cancer risk exceeds one in one million. The dietary risk assessment indicates that the chronic and cancer dietary risk estimates for alpha- and beta-HCH are above the USEPA levels of concern (LOC) for these Arctic populations based on high-end dietary intake estimates.

3. Synthesis of information

Lindane has been shown to be neurotoxic, hepatotoxic, immunotoxic and to have reproductive effects in laboratory animals. Human acute intoxication data show that lindane can cause severe neurological effects, and chronic data suggest possible haematological effects. The International Agency for Research on Cancer (IARC) has classified lindane as possibly carcinogenic to humans

(ATSDR, 2005). The US EPA classified lindane in the category "Suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential".

Human exposure to lindane, particularly in pregnant women and children, is a concern heightened by the ongoing presence of HCH isomers, including lindane, in human tissues and breast milk. Direct exposure from the use of pharmaceutical products for scabies and lice treatment should be of concern. Exposure from food sources is possibly of concern for high animal lipid content diets and subsistence diets of particular ethnic groups (USEPA, 2006 and CEC, 2005). Occupational exposure at manufacturing facilities should be of concern, because lindane production implies worker exposure to other HCH isomers as well, for example the alpha isomer is considered to be a probable human carcinogen (USEPA, 2006).

Lindane is very prevalent in the marine environment and soils, with higher concentrations often found in colder regions. The atmospheric long range transport potential of lindane has been demonstrated for the European Region (WHO/Europe, 2003).

Although current production of lindane seems to be declining with only a few producing countries remaining, the inefficient production process used to manufacture this insecticide over the years has been a world wide contamination problem which has left, and might still be leaving behind, an enormous legacy of contaminating waste products (IHPA, 2006).

The evaluation of laboratory experimental data of lindane would suggest a lower potential of bioaccumulation and biomagnification than that expected for other organochlorine pesticides. In fact, lindane should be considered a border case in terms of its potential for bioaccumulation. Fortunately, there is a large amount of monitoring data on biota allowing a real estimation of the risk profile of lindane in comparison with other organochlorine pesticides. The information provided by this huge amount of real field data is conclusive: lindane concentrations in biota samples collected far away from use areas is similar to that observed for other organochlorine pesticides, confirming the concern for persistence, bioaccumulation and long-range transport.

As the toxicity of lindane is also similar or even higher than that observed for other organochlorine pesticides, it should be considered that the concern related to the POP characteristics of lindane is equivalent to that observed for other chemicals already included in the Stockholm Convention. For example, Weisbrod et al., (2000) found lindane levels in pilot whales similar or just slightly lower than those found for aldrin, endrin, heptachlor or mirex. Also Sørmo et al. (2003) and Kannan et al. (2004) found equivalent levels for the sum of HCHs and for the sum of chlordanes in gray seal and sea otters respectively.

4. Concluding statement

Lindane has been the subject of numerous risk assessment reports by different agencies, diverse country regulations and international initiatives, indicating the general concern raised by this organochlorine compound and indicating global action has already been undertaken.

The information provided in the present document, as well as the information contained in the numerous risk assessment reports published on lindane, indicate that lindane is persistent, bioccumulative and toxic, and is found in environmental samples all over the world as well as in human blood, human breast milk and human adipose tissue in different studied populations, especially impacting Arctic communities that depend on subsistence foods. These findings indicate

that lindane 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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References

Arctic Monitoring and Assessment Programme. 2002. Norway.

ATSDR, 2005. Toxicological Profile for Hexachlorocyclohexanes, U.S. Department of Health & Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, August, 2005. http://www.atsdr.cdc.gov/toxprofiles/tp43.html

Australia, 2006. Format for submitting pursuant to Article 8 of the Stockholm Convention the information specified in Annex E of the Convention. January 2006.

Bailey, R., Barrie, L., Halsall, C., Fellin, P., Muir, D. 2000. Atmospheric organochlorine pesticides in the western Canadian Arctic: Evidence of transpacific transport. Journal of Geophysical Research. 105:11805-11811.

Ballschmiter, K., Wittlinger, R. 1991. Interhemispheric exchange of HCH, hexachlorobenzene, polychlorobiphenyls and 1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane in the lower troposphere. Environmental Science and Technology. 25:1103-1111.

Berny, Ph., Lachaux, O., Buronfosse, T., Mazallon, M., Gillet, C. 2002. Zebra Mussels (*Dreissena polymorpha*), as Indicators of Freshwater Contamination with Lindane. Environmental Research, Section A.90:142-151.

Bidleman, T., Walla, M., Roura, R., Carr, E., Schmidt, S. 1993. Organochlorine pesticides in the atmosphere of the Southern Ocean and Antarctica, January - March, 1990. Marine Pollution Bulletin. 26:258-262.

Buser, H.F.; Müller M. 1995. Isomer and Enantioselective Degradation of Hexachlorocyclohexane Isomers in Sewage Sludge under Anaerobic Conditions. Environmental Science and Technology.. 29:664-672.

Brock, T.C.M., R.P.A. van Wijngaarden & G.J. van Geest. 2000. Ecological risks of pesticides in freshwater ecosystems; Part 2: insecticides. 142 pp.

Brubaker, W.W., Hites, R.A. 1998. Environmental Science and Technology 32: 766–769.

Butte, W., K. Fox, G-P. Zauke. 1991. Kinetics of Bioaccumulation and Clearance of Isomeric Hexachlorocyclohexanes. Science of theTotal Environment. 109/110:377-382

CACAR. 2003. Canadian Arctic Contaminants Assessment Report II. Sources, occurrence, trends and pathways in the physical environment. Northern Contaminants Program. Indian and Northern Affairs Canada.

Caquet, T., E. Thybaud, S. Le Bras, O. Jonot, F. Ramade.1992. Fate and Biological Effects of Lindane and Deltamethrin in Freshwater Mesocosms. Aquatic.Toxicology. 23:261-278

Carlberg, G.E., K. Martinsen, A. Kringstad, E. Gjessing, M. Grande, T. KÄllqvist, J. U. Skåre, 1986. Influence of Aquatic Humus on the Bioavailability of Chlorinated Micropollutants in Atlantic Salmon. Archives of Environmental Contamination and.Toxicology. 15:543-548

CEC, 2005. Commission for Environmental Cooperation.The North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane (HCH) Isomers. Draft for public comment dated 5 October 2005.
http://www.cec.org/pubs_docs/documents/index.cfm?varlan=english&ID=1821

Chevreuil, M., P. Testard. 1991 Monitoring of Organochlorine Pollution (PCB, Pesticides) by a Filter Feeder Lamellibranch (*Dreissena polymorpha* Pallas) C.R. Acadadamy of. Science Ser.II 312:473-477

CropLife, 2006. Information submitted by CropLife International on behalf of Chemtura. Annex E information. Stockholm Convention.

Dickhut, R.M., Cincinelli, A., Cochran, M., Ducklow, H.W. 2005. Atmospheric concentrations and air-water flux of organochlorine pesticides along the western Antarctic Peninsula. Environmental Science and Technology. 39:465-470.

Donkin, P., J. Widdows, S.V. Evans, F.J. Staff, T. Yan. 1997. Effect of Neurotoxic Pesticides on the Feeding Rate of Marine Mussels (*Mytilus edulis*). Pesticide Science. 49:196-209

Environmental Health Criteria No. 124: 1991. Lindane. International Programme on Chemical Safety. UNEP, ILO, WHO. Geneva.. (http://www.inchem.org/documents/ehc/ehc/ehc124.htm).

Geyer, H.J. Scheunert, I. Brüggemann, R. Langer, D. Korte, F. Kettrup, A. Mansour, M. Steinberg, C.; Nyholm, N. Muir, D. 1997. Half-lifes and Bioconcentration of lindane (gamma-HCH) in different fish species and relationship with their lipid content. Chemosphere . 35:343-351.

Guidance document on risk assessment for birds and mammals under Council Directive 91/414/EEC. 2002. European Union. SANCO/4145/2000 – final, Brussels.

Hartley, D. M. J.B. Johnston. 1983 Use of the Freshwater Clam *Corbicula manilensis* as a Monitor for Organochlorine Pesticides. Bulletin of Environmental Contamination and Toxicology. 31:33-40

IHPA. 2006. The Legacy of Lindane HCH Isomer Production. A global Overview of residue Management, Formulation and Disposal. International HCH & Pesticides Association www.ihpa.info

Iwata, H., Tanabe, S., Sakai, N., Tatsukawa, R. 1993. Distribution of persistent organochlorines in the oceanic air and surface seawater and the role of ocean on their global transport and fate. Environmental Science and Technolology. 27:1080-1098.

Japan. 2006. Format for submitting pursuant to Article 8 of the Stockholm Convention the information specified in Annex E of the Convention. February 2006.

Kallenborn, R., Oehme, M., Wynn-Williams, D., Schlabach, M., Harris, J. 1998. Ambient air levels and atmospheric long-range transport of persistent organochlorines to Signey Island, Antarctica. Science of the Total Environment. 220:167-180.

Kanazawa, J. 1981 Measurement of the Bioconcentration Factors of Pesticides by Freshwater Fish and Their Correlation with Physicochemical Properties or Acute Toxicities. PesticideScience. 12:417-424

Kannan K., Kajiwara N., Watanabe M., Nakata H., Thomas N.J., Stephenson, M., Jessup D.A., Tanabe, S. 2004. Profiles of polychlorinated biphenyl congeners, organochlorine pesticides, and butyltins in Southern sea otters and their prey. Environmental Toxicology and Chemistry. 23:49–56.

Kosian, P., A. Lemke, K. Studders, G. Veith, 1981. The Precision of the ASTM Bioconcentration Test.EPA 600/3-81-022, U.S.EPA, Duluth, MN :20 p

Kumar, Y. 2001. Pesticides in Ambient Air in Alberta. ISBN 0-7785-1889-4. Report prepared for the Air Research Users Group, Alberta Environment, Edmonton, Alberta.

La Rocca, C., A. Di Domenico, and L. Vittozzi, 1991. Chemiobiokinetic Study in Freshwater Fish Exposed to Lindane: Uptake and Excretion Phase Rate Constants and Bioconcentration Factors. International Journal of Environmental Health Research. 1:103-116

Lakaschus, S., Weber, K., Wania, F., Bruhn, R., Schrems, O. 2002. The air-sea equilibrium and time trend of HCHs in the Atlantic Ocean between the Arctic and Antarctica. Environmental Science and Technology. 36:138-145.

Li Y. F., Zhulidov A. V., Robarts R. D., Korotova L. G. 2004. Hexachlorocyclohexane Use in the Former Soviet Union. Archives of Environmental Contamination and Toxicology. 48:10–15.

Li, Y.F., Macdonald, R.W., Jantunen, L.M., Harner, T., Bidleman, T. 2002. The Transport of beta-hexachlorocyclohexane to the western Arctic Ocean: a contrast to alpha-HCH. The Science of the Total Environment. 291:229-246.

Mackay, D., Shiu, W.Y., Ma, K-C. 1997. Illustrated Handbook of Physical-Chemical Properties of Environmental Fate for Organic Chemicals. CRC Press.

Oehme, M., Manø, S. 1984a. The long-range transport of organic pollutants to the Arctic. Fresenius Zeitschrift fur Analitishe Chemie. 319:141-146.

Oehme, M., Ottar, B. 1984b. The long range transport of polychlorinated hydrocarbons to the Arctic. Geophysical Research Letters. 11:1133-1136.

Oliver, B.G., and A.J. Niimi, 1985. Bioconcentration Factors of Some Halogenated Organics for Rainbow Trout: Limitations in Their Use for Prediction of Environmental Residues. Environmental Science and Technology. 19:842-849

Oliver, B.G. and A.J. Niimi. 1988. Trophodynamic Analysis of Polychlorinated Biphenyl Congeners and Other Chlorinated Hydrocarbons in the Lake Ontario Ecosystem. Environmental Science and Technology. 22:388-397

Pacyna, J., Oehme, M. 1988. Long-range transport of some organic compounds to the Norwegian Arctic. Atmos. Environ. 22:243-257.

Poland. 2006. Format for submitting pursuant to Article 8 of the Stockholm Convention the information specified in Annex E of the Convention.

Renberg, L., M. Tarkpea, E. Linden. 1985. The Use of the Bivalve *Mytilus edulis* as a Test Organism for Bioconcentration Studies. Ecotoxicology and Environmental Safety. 9:171-178

Schreitmüller, J., Ballschmiter, K. 1995. Air-water equilibrium of HCHs and chloromethoxybenzenes in the North and South Atlantic. Environtal Science and Technology. 30 :852-858.

Shatalov, V., Malanichev, A., Berg, T., Larsen, R. 2000. Investigation and assessment of POP transboundary transport and accumulation in different media. Part 1. EMEP report 4/2000, Meteorological Synthesizing Centre - East, Moscow.

Shatalov, V., Malanichev, A. 2000. Investigation and assessment of POP transboundary transport and accumulation in different media. Part 2. EMEP report 4/2000, Meteorological Synthesizing Centre - East, Moscow.

Shen, L., Wania, F., Lei, Y.D., Teixeira, C., Muir, D.C., Bidleman, T. 2004. Hexachlorocyclohexanes in the North American Atmosphere. Environnemental Science & Technology. 38 :965-975.

Sørmo. E., Skaare,J., Jüssi I., Jüssi M., Jenssen, B.M. 2003. Polychlorinated biphenyls and organochlorine pesticides in Baltic and Atlantic gray seal (*Halichoerus grypus*) pups. Environmental Toxicology and Chemistry.22:2789–2799.

Thybaud, E., S. Le Bras. 1988 Absorption and Elimination of Lindane by *Asellus aquaticus* (Crustacea, Isopoda). Bulletin of Environmental Contamination and Toxicology. 40:731-735.

UNECE, 2004. Technical Review Report on Lindane. Reports on Substances Scheduled for Re-assessments Under the UNECE POPs Protocol. Prepared by Austria in 2004 http://www.unece.org/env/popsxg/docs/2004/Dossier_Lindane.pdf

UNEP/POPS/POPRC.1/8

United States of America. 2006. Format for submitting pursuant to Article 8 of the Stockholm Convention the information specified in Annex E of the Convention. January, 2006.

USEPA, 2002. Revised EFED RED Chapter for Lindane, prepared by the Environmental Fate and Effects Division, Office of Pesticide Programs for the Lindane Reregistration Eligibility Decision (RED) for Lindane. U.S. Environmental Protection Agency.
http://www.epa.gov/oppsrrd1/reregistration/lindane/efed_ra_revised.pdf

USEPA, 2006. Assessment of Lindane and Other Hexachlorocyclohexane Isomers. U.S. Environmental Protection Agency. http://www.epa.gov/fedrgstr/EPA-PEST/2006/February/Day-08/p1103.htm

Van Drooge, B.L., Grimalt, J.O., Garcia, C.J.T., Cuevas, E. 2002. Semivolatile organochlorine compounds in the free troposphere of the North Eastern Atlantic. Environmental Science and Technology. 36:1155-1161.

Vigano, L., S. Galassi, and M. Gatto. 1992. Factors Affecting the Bioconcentration of Hexachlorocyclohexanes in Early Life Stages of *Oncorhynchus mykiss* Environmental Toxicology and Chemistry. 11:535-540

Walker, K., Vallero D.A., Lewis R.G. 1999. Factors influencing the distribution of lindane and other hexachlorohexanes. Environmental Science & Technology. 33:4373-4378.

Weisbrod A.V., Shea D., Moore, M.J., Stegeman J.J. 2000. Bioaccumulation patterns of polychlorinated biphenyls and chlorinated pesticides in Northwest Atlantic pilot whales. Environmental Toxicology and Chemistry.19:667–677.

WHO. 1991. IPCS International Programme on Chemical Safety. Health and Safety Guide No. 54 Lindane (gamma-HCH) health and safety guide. United Nations Environment Programme. International Labour Organisation. World Health Organization. Geneva, 1991. http://www.inchem.org/documents/hsg/hsg/hsg054.htm

WHO/Europe. 2003. Health risks of persistent organic pollutants from long-range transboundary air pollution. Joint WHO/convention task force on the health aspects of air pollution. Chapter 3. Hexachlorocyclohexanes
http://www.euro.who.int/Document/e78963.pdf

Yamamoto, Y., M. Kiyonaga, T. Watanabe. 1983. Comparative Bioaccumulation and Elimination of HCH Isomers in Short-necked Clam (*Venerupis japonica*) and Guppy (*Poecilia reticulata*). Bulletin of Environmental Contamination and Toxicology. 31:352-359