

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

Introductory information

Name of the submitting Party/observer

NGO Observer: Pesticide Action Network North America and Alaska Community Action on Toxics, on behalf of the International POPs Elimination Network (IPEN)

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Chemical name

Cyclohexane, 1,2,3,4,5,6-hexachloro-, alpha-isomer
Cyclohexane, 1,2,3,4,5,6-hexachloro-, beta-isomer

CAS=319-84-6 (alpha-HCH); 319-85-7 (beta-HCH)

Common trade names:

alpha-HCH:

- * Benzene hexachloride-alpha-isomer
- * alpha-Benzenhexachloride
- * alpha-BHC
- * Cyclohexane, 1,2,3,4,5,6-hexachloro-, alpha-
- * Cyclohexane, alpha-1,2,3,4,5,6-hexachloro-
- * ENT 9,232

- * alpha-HCH
- * alpha-Hexachloran
- * alpha-Hexachlorane
- * Hexachlorcyclohexan
- * alpha-Hexachlorcyclohexane
- * alpha-Hexachlorocyclohexane
- * alpha-1,2,3,4,5,6-Hexachlorocyclohexane
- * 1-alpha,2-alpha,3-beta,4-alpha,5-beta,6-beta-Hexachlorocyclohexane
- * alpha-Lindane

beta-HCH:

- * trans-alpha-Benzenehexachloride
- * beta-BHC
- * Cyclohexane, beta-1,2,3,4,5,6-hexachloro-
- * Cyclohexane, 1,2,3,4,5,6-hexachloro-, beta-
- * Cyclohexane, 1,2,3,4,5,6-hexachloro-, trans-
- * ENT 9,233
- * beta-HCH
- * beta-Hexachlorobenzene
- * 1-alpha,2-beta,3-alpha,4-beta,5-alpha,6-beta-Hexachlorocyclohexane
- * beta-Hexachlorocyclohexane
- * beta-1,2,3,4,5,6-Hexachlorocyclohexane
- * beta-Lindane

Date of submission : February 9, 2007

(a) Sources, including as appropriate (provide summary information and relevant references)

(i) Production data: Quantity and Location

¹HCH has been commercialized in two predominant products: technical HCH and purified gamma isomer, lindane. Technical HCH contains about 60-70% alpha-HCH, 5-12% beta-HCH and 10-15% gamma-HCH. These are the three most environmentally significant isomers.

²The manufacturing of technical-grade HCH involves the photochlorination of benzene, which yields an isomeric mixture consisting of alpha-HCH, beta-HCH, gamma-HCH, delta-HCH, epsilon-HCH, and inerts (IARC 1979); this reaction can be started by free-radical initiators such as visual or ultraviolet light, X-rays, or gamma-rays (Kirk-Othmer 1985). Treatment with methanol or acetic acid, followed by fractional crystallization, concentrates gamma-HCH to the 99.9% required in the technical-grade of gamma-HCH (IARC 1979); nitric acid is used to remove odor (SRI 1987). None of the isomers or technical-grade HCH are currently produced in the United States.

¹ Commission for Environmental Cooperation. North American Regional Action Plan on Lindane and Other Hexachlorocyclohexane (HCH) Isomers. November 2006.

² Agency for Toxic Substances and Disease Registry. USA Department of Health and Human Services. Toxicological Profile for Alpha-, Beta-, Gamma-, and Delta-Hexachlorocyclohexane. August 2005..

³ HCH isomers (including alpha- and beta-HCH) are a by-product of lindane manufacture. China, India, Romania and possibly Russia currently produce lindane for the world market... China is reported to have been the major world producer of technical HCH, accounting for more than 4.5 million tonnes between 1945 and 1983. In 1983, China banned both the production and usage of technical HCH. Recent information indicates that China has one company that currently produces lindane. There is no historical information on the amounts of HCH and/or lindane produced in India and usage information is limited. India used approximately 519,000 tonnes of HCH between 1979 and 1991. Historical technical-HCH production and usage information in the former Soviet Union is also limited. Li et.al. report usage in 1980 and 1985 to be 11,160 tonnes and 16,693 tonnes respectively. The use of technical-HCH was banned in the late 1980s for use on agriculture crops. However, use of existing stockpiles was allowed even after 1991.

⁴ Estimates of current production identify Romania, India, and China as the only known lindane-producing countries in the world. Production between 1990 and 1995 was approximately 3,222 tonnes per year. China has a continuous production of approximately 1,000 tonnes per year. In India, one production facility produces 300 kg/day, but has a capacity to produce 3 tonnes/day. Production estimates for Romania are uncertain.

⁵ According to a 2004 UNECE reassessment of lindane production and use, "With the scheduled accession of Romania to the EU in 2007 and subjection to the recently adopted EC Regulation on POPs, this [lindane] production site will have to be closed down in the near future.

(ii) Uses

⁶ Status of HCH in North America: As of January 1, 2005, there are no registered agricultural or veterinary uses of lindane in Canada. Canada has agreed to assess and manage risks from its sole remaining use of lindane as a pharmaceutical drug. Canada will address waste management issues, promote science and research, and strengthen outreach and education.

Mexico has agreed to eliminate all agricultural, veterinary, and pharmaceutical uses of lindane through a prioritized, phase-out approach. Reasonable timeframes for a voluntary phase out are currently being negotiated between the Federal Commission for Sanitary Risks Protection, Ministry of Health (COFEPRIS) and industry. Lindane is currently authorized for use in Mexico on livestock, as a seed treatment on six crops, as a flea treatment on domestic animals, and for public health campaigns. Lindane is also authorized for pharmaceutical use to control scabies and lice.

Technical-grade HCH was used as an insecticide in the United States and typically contained 10-15% gamma-HCH as well as the alpha, beta, delta and epsilon forms of HCH. Virtually all the insecticidal properties resided in gamma-HCH. Technical-grade HCH has not been produced or used in the United States in over 20 years.

³ Commission for Environmental Cooperation. Draft North American Regional Action Plan on Lindane and Other Hexachlorocyclohexane (HCH) Isomers. October 2005.

⁴ Vijgen, J. 2006. The Legacy of Lindane HCH Isomer Production. Main Report. A Global Overview of Residue Management, Formulation and Disposal. International HCH and Pesticides Association (ISBN 87-991210-1-8) www.ihpa.info/library_access.php

⁵ Hauzenberger, I. 2004. Reports on Substances Scheduled for Re-Assessments under the UNECE POPs Protocol, Technical Review Report on Lindane. Federal Environment Agency, Austria. http://www.unece.org/env/popsxg/docs/2004/Dossier_Lindane.pdf

⁷The United States has reviewed the six remaining lindane seed treatment uses and determined that the remaining uses are not eligible for reregistration. The United States will facilitate development of alternatives to lindane to treat lice and scabies, and to strengthen awareness raising initiatives regarding the remaining use of lindane as a pharmaceutical drug for applications involving children. There are no registered uses of lindane for veterinary purposes in the United States.

⁸ Total HCH usages for agricultural purposes in the former Soviet Union from 1950 to 1990 were estimated to be 1,960 kt for technical HCH and 40 kt for lindane. The total usage for the isomers was 270 kt for gamma-HCH, 1,270 kt for alpha-HCH, and 170 kt for beta-HCH. Use of HCH reached a peak in 1965: 130 kt for technical HCH, 2.7 kt for lindane, 18 kt for gamma-HCH, 86 kt for alpha-HCH, and 11 kt for beta-HCH.

⁹The total global usage of beta-HCH between 1945 and 2000 is estimated at 850 kt, 230 kt of which was emitted to the atmosphere over the same time period. Usage of beta-HCH was estimated to be around 36 kt in 1980 and 7.4 kt in 1990. Total beta-HCH emissions in 1980 were 9.8 kt with 83% attributed to the application in 1980 and 17% to soil residues due to prior applications. Total beta-HCH emissions in 1990 were 2.4 kt with 78% attributed to the application in 1990 and 22% to soil residues. While it assumed that no usage of technical HCH occurred in 2000, the global beta-HCH emissions in this year due to soil residues were estimated at 66 t. It has shown that the global beta-HCH emissions have undergone a "southward tilt" over the time period studied as more northern countries have banned the use of technical HCH.

¹⁰Data on current and historical usage of alpha-, beta-, and gamma-hexachlorocyclohexane (HCH) in Europe are presented in this 1999 paper. The data were collected and estimated as a part of a project studying the regional cycling of persistent organic pollutants (POPs) in the Baltic environment. The results suggest that 382,000 t of technical HCH and 81,000 t of lindane were used in Europe from 1970 to 1996. This is equivalent to an estimated cumulative usage of 259,000 t alpha-HCH, 235,000 t gamma-HCH and 20,000 t beta-HCH. The usage of technical HCH was the major source of gamma-HCH until the late 1970s, and thereafter lindane became the dominating source of this isomer. The pattern of decreasing concentrations in biota follows the pattern of reductions in usage for the studied period within the Baltic area.

(iii) Releases (Discharges, Losses, Emissions)

¹¹Information from lindane manufacturing facilities in India confirms that manufacture of 1 ton of lindane produces an average 9 tons of waste - a complex "muck" of alpha-, beta- and delta-HCH. One Indian lindane production facility produces an estimated 6000 metric tons (MT)/year of

^{6, 7} Commission for Environmental Cooperation. The North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane (HCH) Isomers. November 2006.

⁸ Li, YF et.al. 2005. Hexachlorocyclohexane use in the former Soviet Union. *Arch Environ Contam Toxicol*. 48(1):10-5.

⁹ Li YF et.al. 2003. Global gridded emission inventories of beta-hexachlorocyclohexane. *Environ Sci Technol*. 37(16):3493-8.

¹⁰ Brievik K et.al. 1999. Use of alpha-, beta- and gamma-hexachlorocyclohexane in Europe, 1970-1996. *Sci Total Environ*. 1;239(1-3):151-63

¹¹ Fact Sheet. *Lindane's Dirty Secret: Indian Facilities Dump Toxic Waste*. Compiled by Community Action for Pesticide Elimination as a project of the International POPs Elimination Network (IPEN) Pesticide Working Group. May 2005. (pp:6) <http://www.panna.org/campaigns/docsLindane/lindaneDirtySecret.pdf>.

muck. Industry representatives claim that the plants are now converting the HCH isomer waste into trichlorobenzene (TCB). However, experts say that only alpha- and gamma-HCH can be converted into TCB, and not the other two isomers beta- and delta-HCH. A team from Delhi University in India collected and analyzed 45 soil samples of surface and sub-surface soil from several agricultural sites in and around the HCH manufacturing plant of one of the prime producers of lindane in India, and nine samples of different commercial brands of drinking water from markets in Delhi for the presence of HCH residues. Thirty-nine of the 45 soil samples contained residues of beta-HCH (2.5 micro g/kg-463 mg/kg of soil) and the remaining showed the presence of gamma-HCH (0.08 micro g/kg – 43 mg/kg of soil). All nine samples of drinking water were found to contain residues of HCH, with three brands showing HCH residue levels up to 141 times higher than EEC norms.

Biodegradation of HCH isomers- a possible solution for HCH contaminated sites:

¹²A 2002 study was conducted to monitor the biodegradation of alpha-, beta-, gamma-, and delta-hexachlorocyclohexane (HCH) isomers in liquid culture by a bacteria of the *Pandoraea* species; and to determine the influence of pH and temperature on the biodegradation of alpha- and gamma-HCH in liquid as well as in soil slurry cultures. The results of this study suggest that this bacterial strain may effectively be used for remediating polluted sites and water contaminated with different HCH isomers over a range of environmental conditions. The *Pandoraea* species degraded 79.4% delta-HCH and 34.3% gamma-HCH in liquid culture at 4 weeks of incubation. alpha- and beta-HCH exhibited almost identical rates (41.6 and 42.4%, respectively) of degradation. The highest degradation of alpha- and gamma-HCH (67.1 and 60.2%, respectively) was observed at an initial pH of 8.0 in liquid; 58.4 and 51.7% rates of degradation of alpha- and gamma-HCH, respectively, at an initial pH of 9.0 were found in soil slurry cultures. An incubation temperature of 30 degrees C was optimum for effective degradation of alpha- and gamma-HCH isomers (62.5 and 57.7%, respectively) in liquid culture, and 54.3 and 51.9% rates of degradation of alpha- and gamma-HCH isomers, respectively, were found in a soil slurry. Increasing the soil/water ratio decreased the extent of degradation of both HCH isomers. Degradation of HCH isomers occurred concomitant with bacterial growth. Byproducts of growth from *Pandoraea* species significantly decreased the pH of the liquid and the soil slurry during the growth on HCH isomers.

¹³In another study examining biodegradation for HCH contaminated sites, researchers isolated a bacterium *Pseudomonas aeruginosa* ITRC-5 that mediates the degradation of all the four major isomers of HCH under aerobic conditions, both in liquid-culture and contaminated soils. In liquid-culture, the degradation of alpha- and gamma-HCH was found to be rapid and was accompanied with the release of 5.6 micro mole chloride ions and 4.1 micro mole CO₂ micro mole(-1) HCH-isomer. The degradation of beta- and delta-isomers was slow, accompanied with the release of 0.9 micro mole chloride ions micro mole(-1) HCH-isomer, and resulted in a transient metabolite 2,3,4,5,6-pentachlorocyclohexan-1-ol. The strain ITRC-5 also mediated the degradation of alpha-, beta-, gamma-, and delta-isomers in contaminated soils, where degradation of otherwise persistent beta- and delta-HCH was enhanced severalfold in the presence of alpha- or gamma-HCH. The degradation of soil-applied beta- and delta-HCH under aerobic conditions had not been reported earlier. The isolate ITRC-5 thus demonstrated potential for the

¹² Siddique T. et.al. 2002. Temperature and pH effects on biodegradation of hexachlorocyclohexane isomers in water and a soil slurry. *J Agric Food Chem.* 28;50(18):5070-6

¹³ Kumar, M. et.al. 2005 .Enhanced biodegradation of beta- and delta-hexachlorocyclohexane in the presence of alpha- and gamma-isomers in contaminated soils. *Environ Sci Technol.* 1;39(11):4005-11

bioremediation of HCH-wastes and contaminated soils.

(b) Hazard assessment for endpoints of concern, including consideration of toxicological interactions involving multiple chemicals (provide summary information and relevant references)

Hepatic effects:

alpha-HCH induced liver tumors in mice and rats, beta-HCH induced liver tumors in mice^{14,15}. In their study Schröter et. al checked the tumor initiating activity of HCH using the appearance of phenotypically altered foci in female rat liver as an end point. Foci were identified by means of the 7-glutamyltransferase (GGT) reaction and by morphological alterations. No evidence of initiating activity was found. Secondly, they determined quantitatively the ability of HCH isomers to promote tumor development. For this purpose growth and phenotypic changes of foci were used as an end point. Rats received a single dose of *N*-nitrosomorpholine. Then five different doses of each HCH isomer or phenobarbital (PB) (as a positive control) were administered continuously via the diet for 4, 15, and 20 weeks. Both number and size of altered foci were enhanced by doses of 2 to 3 mg/kg or more of the three isomers; in addition, foci phenotypes showed a pronounced shift towards strong expression of GGT and sharp demarcation from the surrounding liver. Based on daily doses the three HCH isomers were approximately equipotent; based on concentrations in liver or adipose tissue, gamma-HCH was severalfold more effective than alpha- and beta-HCH. Thirdly, size and DNA and monooxygenase activities of the liver were determined. At the highest doses tested PB was the most effective inducer of monooxygenases, alpha-HCH was the most potent inducer of liver growth, and all three HCHs were more potent than PB as inducers of focal expansion.¹⁶

¹⁷Most HCH isomers were shown to increase cytochrome P-450 content and the activities of associated enzymes in rodents and also produced liver necrosis and degeneration with higher doses.

¹⁸Animal studies have also reported that ingestion of alpha-, beta-, and gamma-HCH isomers, individually or as technical-grade HCH, has resulted in some degree of liver toxicity including increased microsomal activity, increased liver weight, mild-to-moderate liver necrosis and fatty degeneration, and liver cancer. Biochemical or gross hepatic changes often were not accompanied by histopathological changes... 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. Liver toxicity was used as the basis for an intermediate-duration oral MRL for beta-HCH and a chronic-duration oral MRL for alpha-HCH. The intermediate oral MRL for beta-HCH is based on a lowest-observed adverse-effect level (LOAEL) of 0.18 mg/kg/day for liver effects in rats (centrilobular hyalinization, with periportal fatty changes and focal necrosis at ≥ 4.5 mg/kg/day) exposed for 13 weeks. The chronic oral MRL for alpha-HCH is based on a hepatic no-observed-adverse-effect level (NOAEL) of 0.8

¹⁴ ATSDR Toxicological Profile. 2005, op cit.

¹⁵ European Food Safety Authority. Opinion of the scientific panel on 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*, 2005 (250). Available at: http://www.efsa.europa.eu/etc/medialib/efsa/science/contam/contam_opinions/1039.Par.0003.File.dat/contam_op_ej250_hexachlorocyclohexanes_summary_en2.pdf

¹⁶ Schroter, C. et.al. 1987. *Cancer Research*, 47, 80-88.

¹⁷ ATSDR Toxicological Profile, 2005, op.cit.

¹⁸ ATSDR Toxicological Profile, 2005, op.cit.

mg/kg/day in rats exposed for up to 107 weeks. Liver effects at higher doses of alpha-HCH progressed from slight histological changes at 3.5–4 mg/kg/day to hepatic cell atrophy, fatty degeneration, and focal necrosis at 56–64 mg/kg/day.

¹⁹The scientific literature regarding the cancer and non-cancer effects of HCH supports EPA's expressed concern that exposures to HCH isomers may be additive. HCH "mixed isomer" liver effects from chronic exposure include: increase in the enzymes lactate dehydrogenase, leucine aminopeptidase and gamma-glutamyl transpeptidase (Ryan & Terri, 1996), as well as liver cell changes (Philip et. al, 1989) and induction of oxidative enzymes (Gosselin et. al, 1984).

²⁰ IPCS-Inchem's Lindane comments concluded that technical grade alpha-and beta-HCH and gamma isomer (lindane) produced liver tumors in mice when administered orally; the technical grade also produced lymphoreticular neoplasms. Alpha-HCH enhanced the incidence of liver neoplasms induced in rats by N-nitrosodiethylamine (IARC, 1979; IARC, 1984).

²¹Studies on oral exposure to HCH isomers by mice concluded that a variety of morphological and biochemical lesions are produced in the liver during continued dietary intake of beta- and gamma-isomers of HCH by young rats (Srinivasan and Radhakrishnamurty 1988, 1989; Srinivasan et al 1988; Ravinder et al 1989). "The hepatotoxic effects produced by these HCH isomers in experimental animals include hepatomegaly, fatty metamorphosis of the liver, hyperlipemia, elevated levels of serum aminotransferases and alkaline phosphatase with associated lowerings of hepatic cytoplasmic enzymes. The hepatomegaly resulting from HCH isomers treatment has been shown to be predominantly due to hypertrophy." (Srinivasan et al, 1988)

Immunological Effects:

²²Gamma- and beta-HCH produced immunosuppression in intermediate-duration studies in rodents.

Neurological Effects:

²³The toxicity of the isomers varies, gamma-HCH being the most acutely neurotoxic followed by alpha-HCH. Beta-HCH penetrates less readily into the central nervous system, is more persistent and tends to accumulate in the body over time... Neurotoxicity and liver effects have been reported in fish and ruminants.

²⁴Acute- and intermediate duration exposure of animals to high oral or dermal doses of gamma- or beta-HCH affects the central nervous system as evidenced by behavior disorders, decreased nerve conduction velocity, neurochemical changes, convulsions, seizures, and coma.

²⁵Animals fed gamma- and alpha-HCH have had convulsions, and animals fed beta-HCH have become comatose.

¹⁹ WHO Intergovernmental Programme on Chemical Safety (IPCS), Inchem. Hexachlorocyclohexane (Mixed Isomers). Accessed at <http://www.inchem.org/documents/pims/chemical/pim257.htm#2.1%20Main%20risks%20and%20target%20organs>. March 2006.

²⁰ See full references at IPCS Inchem, op.cit.

²¹ See full references at IPCS Inchem, op.cit.

²² ATSDR Toxicological Profile, 2005.

²³ EFSA, 2005, op.cit.

²⁴ ATSDR Toxicological Profile. 2005, op.cit.

²⁵ Agency of Toxic Substances and Disease Registry, Tox FAQs, 2005. See <http://www.atsdr.cdc.gov/tfacts43.html>.

Reproductive Effects:

²⁶ HCH isomers have altered reproductive parameters in male and female animals including mink, rabbits, and rats. Effects included alterations in estrous cycle, embryotoxicity, and testicular and sperm alterations.

²⁷, ²⁸ Beta-HCH has been described as producing estrogen-like effects through nonclassical estrogen-dependent mechanisms of action.

²⁹ Information on the potential reproductive toxicity of HCH in humans is limited. An increase in serum luteinizing hormone levels was observed in male workers, but other reproductive hormone levels were not significantly altered. Additionally, increased blood levels of gamma-HCH and total HCH isomers were detected in women experiencing spontaneous abortion or premature delivery. Because the women were exposed to multiple organochlorine pesticides, it is difficult to establish a causal relationship between HCH exposure and adverse reproductive outcomes.

³⁰ Adverse reproductive effects have been observed in male and female laboratory animals orally exposed to gamma-, beta-, or technical-grade HCH. At higher doses of gamma-, beta-, or technical-grade HCH, degeneration of the seminiferous tubules or testicular atrophy were also observed in rats and mice.

³¹ Injury to the ovaries and testes was reported in animals given gamma-HCH or beta-HCH.

³² ³³ Reproductive effects of HCH isomers during fetal development is of particular concern given the recent findings of the U.S. Centers for Disease Control and Prevention that more than half the participants in a national survey of chemicals in blood and urine carried beta-HCH in their blood, with the highest levels found among women of childbearing age.

³⁴ EPA has also noted that lindane is "efficiently transmitted" from mother to child through breastmilk. When women carry HCH isomers in their bodies, infants may be exposed to their damaging reproductive effects both inside and outside the womb.

³⁵ A 2006 study investigated a possible human association between maternal exposure to 27 organochlorine compounds used as pesticides and cryptorchidism among male children. Within a

²⁶ ATSDR. Toxicological Profile. 2005, op.cit.

²⁷ Steinmetz, R., P. C. M Young, A.Caperell-Grant, E.A. Gize, B.V. Madhukar, N. Ben-Jonathan, R.M. Bigsby. 1996. Novel estrogenic action of the pesticide residue beta-hexachlorocyclohexane in human breast cancer cells *Cancer Res.* 56, 5403-5409 in NARAP

²⁸ EFSA. 2005, op.cit.

²⁹ ATSDR Toxicological Profile. 2005, op.cit.

³⁰ ATSDR Toxicological Profile. 2005, op.cit.

³¹ ATSDR Tox FAQs DATE, op.cit.

³² National Center for Environmental Health, U.S. Centers for Disease Control and Prevention, Second National Report on Human Exposures to Environmental Chemicals. January 2003; and Third National Report on Human Exposure to Environmental Chemicals. July 2005. Available at <http://www.cdc.gov/exposurereport>.

³³ Schafer, K.S. et.al. 2004. Chemical Trespass: Pesticides in Our Bodies and Corporate Accountability. Pesticide Action Network North America. Available at: www.panna.org

³⁴ EPA Memorandum: Lindane—Report of the FQPA Safety Factor Committee. August 2000: p 3.

³⁵ Damgaard IN. 2006. Persistent pesticides in human breast milk and cryptorchidism. *Environ Health Perspect.* 114(7):1133-8

prospective birth cohort, the researchers performed a case-control study; 62 milk samples from mothers of cryptorchid boys and 68 from mothers of healthy boys were selected. Milk was collected as individual pools between 1 and 3 months postpartum and analyzed for 27 organochlorine pesticides. Eight organochlorine pesticides were measurable in all samples (medians; nanograms per gram lipid) for cases/controls: of these beta-hexachlorocyclohexane (beta-HCH) was measured as: 13.6/12.3. Among the other organochlorine compounds tested, for gamma-HCH, and alpha-HCH both concentrations and detection rates were low (26.5-71.5%). HCH (alpha, beta, gamma), was measured in higher median concentrations in case milk than in control milk. Combined statistical analysis of the eight most abundant persistent pesticides showed that pesticide levels in breast milk were significantly higher in boys with cryptorchidism ($p = 0.032$). The study concluded that association between congenital cryptorchidism and some persistent pesticides in breast milk as a proxy for maternal exposure suggested that testicular descent in the fetus may be adversely affected.

³⁶A 2003 Indian study tested the association between DDT and HCH isomer exposure to Intra-Uterine Growth Retardation (IUGR- defined as <10th percentile of birth weight for gestational age). The researchers detected p,p'-DDT, o,p'-DDT, p,p'-DDD, p,p'-DDE and alpha-HCH, beta-HCH, gamma-HCH, delta-HCH in maternal blood, placenta and cord blood, collected at parturition, from mothers with babies suffering from IUGR (n=30) and from those with babies of normal weight (n=24), using gas-liquid chromatography equipped with electron capture detector (⁶³Ni). The adjusted odds ratios (ORs) for these pesticides in mothers and infants were determined by multiple logistic regression. There were statistically significant associations ($P < 0.05$) between maternal blood levels of alpha-HCH (OR=1.22; 95% CI: 1.02-1.46), gamma-HCH (OR=1.38; 95% CI: 1.05-1.80), delta-HCH (OR=1.61; 95% CI: 1.01-2.54), total HCH (OR=1.07; 95% CI: 1.01-1.13) and p,p'-DDE (OR=1.21; 95% CI: 1.03-1.42) and IUGR after adjustment for potential confounders. Also, significant association ($P < 0.05$) between cord blood levels of gamma-HCH (OR=1.14; 95% CI: 1.00-1.31), delta-HCH (OR=1.31; 95% CI: 1.00-1.75), total HCH (OR=1.07; 95% CI: 1.00-1.14) and IUGR were found after adjustment for potential confounders.

Carcinogenicity:

³⁷Long-term oral administration of alpha-HCH, beta-HCH, gamma-HCH, or technical-grade HCH to laboratory rodents produced liver cancer. The (U.S.) Department of Health and Human Services (DHHS) has determined that HCH (all isomers) may reasonably be anticipated to cause cancer in humans. The International Agency for Research on Cancer (IARC) has classified HCH (all isomers) as possibly carcinogenic to humans.

³⁸The U.S. EPA has additionally classified technical HCH and alpha-HCH as probable human carcinogens, beta-HCH as a possible human carcinogen.

³⁹HCHs were classified by IARC in group 2B (possibly carcinogenic) on the basis of inadequate evidence for carcinogenicity to humans, sufficient (for technical grade and the alpha-isomer) and limited evidence for carcinogenicity to animals (for beta- and gamma-HCHs).

³⁶ Siddiqui, MK et.al. 2003. Persistent chlorinated pesticides and intra-uterine foetal growth retardation: a possible association. *Int Arch Occup Environ Health*. 276(1):75-80.

³⁷ ATSDR Tox FAQs, 2005, op.cit.

³⁸ Ibid.

³⁹ EFSA. 2005, op.cit.

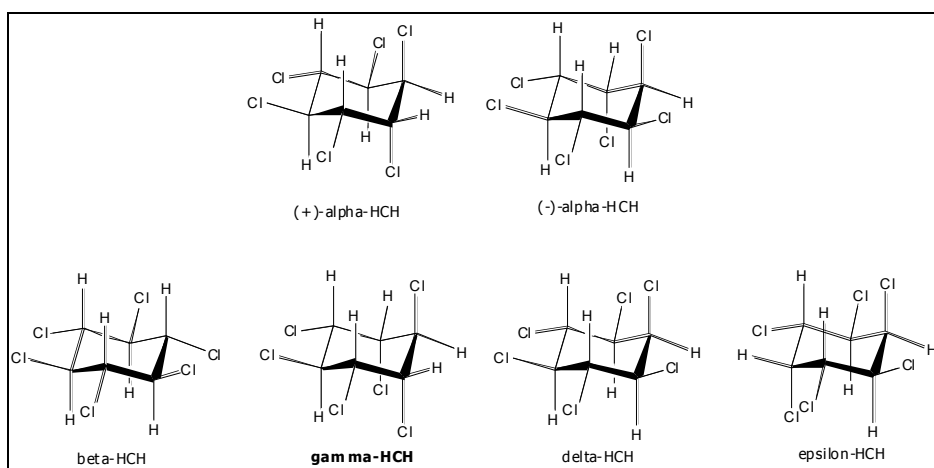
⁴⁰Lifetime feeding studies in mice revealed that technical grade HCH and some of its isomers, including lindane, increased the incidence of hepatocellular tumours. In such animal models lindane-induced damage may result from the generation of superoxide anion radicals and/or DNA single-strand breaks (SSBs) or via epigenetic mechanisms.

⁴¹In a Chinese study for describing the level of organochlorines pesticides residues in non-occupational exposure population in China and for testing the hypothesis that organochlorine pesticides exposure may be the risk factor to human breast cancer, a case-control study was designed. 90 newly diagnosed breast cancer patients from the Sichuan Province, and 136 healthy women from the same district as the cases were enrolled. The risk factors of breast cancer were investigated by a questionnaire. GC-ECD was used to measure the serum level of Organochlorines pesticide residues. The adjusted odds ratios (OR) of organochlorines pesticides residues to breast cancer were evaluated by logistic regression model. 8 organochlorines pesticide residues including DDTs and alpha-, beta-, gamma-, delta-HCHs (hexachlorocyclohexane) could be detected in serum of cases and controls. The detecting rate of beta-HCH, was 91.2%. There were no significant differences of serum level of organochlorines pesticides residues between cases and controls ($P > 0.05$). After adjusting confounding factors, delta-HCH level was positively related to the risk of breast cancer (adjusted OR > 2 , $P < 0.05$). High beta-HCH level was positively correlated to premenopausal women (adjusted OR was 3.06, $P < 0.05$). The study concluded that organochlorine pesticides residues, including DDTs and HCHs, may increase women's risk of breast cancer, particularly in premenopausal women in China.

(c) Environmental fate (provide summary information and relevant references)

Chemical/physical properties

⁴²Structure of alpha-, beta-, gamma-, delta- and epsilon -HCH isomers



⁴⁰ Kalantzi, O.I. et.al, 2004. Low dose induction of micronuclei by lindane. *Carcinogenesis* 25(4):613-22.

⁴¹ Li, JY. et.al. 2006 . Serum organochlorines pesticides level of non-occupational exposure women and risk of breast cancer:a case-control study. *Wei Sheng Yan Jiu.* 35(4):391-4

⁴² 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.

Persistence

⁴³ Although technical-grade HCH is no longer used as an insecticide in the United States, alpha-, beta-, gamma-, and delta-HCH have been found in the soil and surface water at hazardous waste sites because they persist in the environment. In general, HCH isomers and the products formed from them in the body can be temporarily stored in body fat.

⁴⁴ ⁴⁵ “Brubaker and Hites (1998) measured the reaction rate constants of alpha- and gamma-HCHs with OH radicals. Calculations based on these rate constants and a tropospheric average OH radical concentration gave estimated lifetimes in air of 120 d for alpha-HCH and 96 d for gamma-HCH.”

⁴⁶ ⁴⁷ “Several measurements have been made of gamma-HCH hydrolysis and fewer of alpha-HCH hydrolysis. These studies were reviewed by Ngabe et al. (1993), who also determined the basic hydrolysis rates of alpha- and gamma-HCH as functions of temperature and pH. Temperature has a very strong influence on the hydrolysis rates because the reaction of HCHs with OH⁻ ions and the dissociation of water (which produces OH⁻ ions) are both temperature dependent. Based on the rate constants of Ngabe et al. (1993), calculated half lives in seawater at pH 8 are 0.8 y for alpha-HCH and 1.2 y for gamma-HCH at 20°C. The reaction rates are much lower and the half lives correspondingly longer at 0°C: 80 y for alpha-HCH and 135 y for gamma-HCH. These calculations indicate that, while the HCHs will dissipate relatively quickly from the oceans at tropical latitudes, they will be far more persistent in the Arctic. Similar calculations indicated half lives of 26 y for alpha-HCH and 42 y for gamma-HCH in Lake Huron at pH 8 (the pH of the lake is 7.6-7.8) and 5°C (Ngabe et al., 1993).”

⁴⁸ ⁴⁹ “Microbial degradation proceeds faster than hydrolysis, especially in cold environments. Harner et al. (1999, 2000) estimated half lives in eastern Arctic Ocean water of 6 and 23 y for the (+) and (-) enantiomers of alpha-HCH and 19 y for gamma-HCH. The half lives of (+) and (-) alpha-HCH in a small arctic lake were estimated to be 0.6 and 1.4 y (Helm et al., 2002). These are much shorter than hydrolytic half lives. Harner et al. (2000) estimated that microbial degradation could account for about one-third of the annual loss of alpha- and gamma-HCHs from the Arctic Ocean.”

How are chemical/physical properties and persistence linked to environmental transport, transfer within and between environmental compartments, degradation and transformation to other chemicals?

⁴³ Agency for Toxic Substances and Disease Registry. USA Department of Health and Human Services. Public Health Statement on HCH. <http://www.atsdr.cdc.gov/toxprofiles/tp43-c1-b.pdf>. Aug 2005.

⁴⁴ Referenced in Bidleman, T. 2004. Letter and review to the North American Task Force on Lindane.

⁴⁵ Brubaker, W.W., Hites, R.A. 1998. OH reaction kinetics of gas-phase alpha- and gamma-hexachlorocyclohexane and hexachlorobenzene. *Environ. Sci. Technol.* 32, 766 - 769.

⁴⁶ Referenced in Bidleman, T. 2004. Letter and review to the North American Task Force on Lindane.

⁴⁷ Ngabe, B., Bidleman, T.F., Falconer, R.L. 1993. Base hydrolysis of alpha- and gamma-HCHs. *Environ. Sci. Technol.* 27, 1930-1933.

⁴⁸ Referenced in Bidleman, T. 2004. Letter and review to the North American Task Force on Lindane.

⁴⁹ Hamer, T., Jantunen, L., Bidleman, T., Barrie, L., Kylin, H., Strachan, W., Macdonald, R. 2000. Microbial degradation is a key elimination pathway of hexachlorocyclohexanes from the Arctic Ocean. *Geophys. Res. Lett.* 27, 1155-1158.

⁵⁰The accumulated information on environmental levels and trends of hexachlorocyclohexane (HCHs), among other chemicals, allows for the assessment of some spatial and temporal trends that can be attributed to deposition from long-range aerial transport (LRAT). Data suggest that environmental levels of alpha-HCH have generally decreased over the past 30 years, however, the evidence for decreasing trends in lindane (gamma-HCH) or beta-HCH is not as clear. Similar findings are also expressed in Arctic atmospheric monitoring data collected over the past 10-15 years. Tissue concentrations in the most highly exposed marine species (birds and mammals) generally do not exceed applicable thresholds of toxicity, however, some effects in highly exposed species have been associated with HCHs. Exposure among Arctic populations that consume marine mammals, can exceed some guidelines for dietary intake.

⁵¹ Alpha-HCH concentrations have been documented in the air and water in various geographic regions, including Canada, River Rhine, River Elbe, select rivers in the UK, and the North Frisian Wadden Sea sediments. “Even in Antarctica levels ranging from 0.2-1.15 ug/kg have been found.”

⁵² “Numerous studies of ambient air (Harner et al., 2001 and Waite et al., 1999), precipitation (Barrie et al., 1992 and Norstrom and Muir, 1994), and surface water (Harner, 1997 and Norstrom and Muir, 1994) have reported HCH residues, particularly alpha- and gamma isomers, throughout North America.”

⁵³ Annually integrated air concentrations of alpha- and gamma-hexachlorocyclohexane (HCH) were determined in 2000/2001 at 40 stations across North America using XAD-based passive air samplers to understand atmospheric distribution processes on a continental scale. Elevated levels of gamma-HCH in the atmosphere of the Canadian Prairies were consistent with the use of lindane as a seed treatment on canola. In contrast to gamma-HCH, the atmospheric concentrations of alpha-HCH showed a rather uniform distribution across Canada and the United States, which was expected for a chemical with no current use on the continent. Higher levels in the atmosphere over Atlantic Canada were explained by alpha-HCH evaporating from the waters of the Labrador Current, which is supported by the chiral composition of alpha-HCH and the temperature dependence of its atmospheric concentrations along the east coast of Canada. Alpha-HCH was found to be volatilizing from Lake Superior. Atmospheric HCH levels were seen to increase with elevation in the Canadian Rocky Mountains. The authors state “results suggest that evaporation, in particular from cold water bodies, is an important source of alpha-HCH to the North American atmosphere. Low levels of HCHs in Central America hint at efficient degradation under tropical conditions. Chiral analysis shows that (+)-alpha-HCH is often enriched in air over continental areas and at the Pacific Coast, which is opposite to the enantiomeric enrichment in the proximity to the Great Lakes and the Atlantic Ocean.”

⁵⁰ Economic Commission for Europe. Convention on Long-Range Transboundary Air Pollution. The 1998 Protocol on Persistent Organic Pollutants: an implementation guide. http://www.unece.org/env/wgs/POPs_draft_full_4.10.do

⁵¹ WHO working group; Alpha- hexachlorocyclohexane; *Environmental Health Criteria* Vol: 123, pp1-66. 1992.

⁵² U.S. EPA, Revised EFED RED Chapter for Lindane, Dec 2001. (pp 8). http://www.epa.gov/oppsrrd1/reregistration/lindane/efed_ra_revised.pdf

⁵³ Shen, L. et. al. 2004. Hexachlorocyclohexanes in the North American atmosphere. *Environ Sci Technol.* 15;38(4):965-75.

⁵⁴ Widespread distribution of 2,4-D, 2,4,5-T, Gamma- BHC and alpha-BHC were noted in Western Canadian surface waters between 1971-77. "Wide distribution of lindane and alpha-BHC was attributed to atmospheric transportation and deposition."

⁵⁵ In this 2006 study organochlorine and organophosphorous pesticide residues were measured in the Oueme River in Benin. More than 35 sediment samples were collected from nine locations along the river from upstream to downstream. Except for one location, all areas were contaminated by more than 20 pesticides. Organochlorine pesticides identified in significant quantities in the sediment samples included alpha-HCH, beta-HCH and lindane, along with pp'-DDE, op'-DDD, pp'-DDD, op'-DDT, pp'-DDT, alpha-endosulfan, beta-endosulfan, endosulfan sulphate, aldrin, dieldrin, endrin, telodrin, isodrin, cis- and trans-heptachlorepoxyde, hexachlorbutadiene, hexachlorobenzene and octachlorostyrene. In some areas, the concentrations of organochlorine pesticides in the sediment exceeded environmental quality standards.

⁵⁶ Concentrations of HCH (hexachlorocyclohexane) and DDT (Dichlorodiphenyltrichloroethane) were determined in shallow subsurface (5-30 cm depth) and deep soil layers (150-180 cm depth) from the outskirts of Beijing, China. Concentrations of total HCHs (including alpha, beta, gamma, delta-isomers) in shallow subsurface soils ranged from 1.36 to 56.61 ng/g dw (median 5.25 ng/g), and those in the deeper layers were approximately an order of magnitude less. The spatial distribution of HCHs and DDTs reflected the known historical usage of these pesticides.

⁵⁷ Air samples were collected for characterization of persistent organic pollutants (POPs) including alpha-HCH, beta-HCH, delta-HCH, gamma-HCH, among 18 POPs chemicals during the winter of 2000/2001 at the weather station of the Hong Kong Observatory (TMS) in Hong Kong, besides the routine monitoring of PCDD/Fs and 200 other toxic air pollutants (TAPs) at two urban TAPs stations. Concentrations of the pollutants detected at TMS station were evaluated and compared to those recorded at the urban stations. Though pesticides including alpha-HCH and other POPs were detected, these pesticides were found at relatively low concentrations of about 0.02-0.23 ng/m³. Concentrations of some of the monitored POPs were found to be higher whilst most of the monitored TAPs were at comparable levels to those measured at the urban stations during the same period. Given that there has not been any large-scale use of organochlorine pesticides recorded in Hong Kong since the decline of local farming activities in recent years, the results of the present study show that pesticides and POPs such as PCDDs/PCDFs are ubiquitous environmental contaminants present in the atmosphere of Hong Kong.

⁵⁸ In this study, multi-compartment monitoring of residue levels of organochlorine pesticides in the coastal marine environment of Mumbai, India, was examined. The concentration of total HCHs in seawater varied from 0.16 to 15.92 ng/L. The total HCH concentration in the sediment samples was in the range of 3.8 to 16.2 ng/g. Gamma-HCH contributed almost 55% to the total HCH. The concentration of total HCHs in different marine species varied from 0.87 to 33.73 ng/g. The variation in the beta-HCH in different compartments was not significant and this could

⁵⁴ Gummer WD, 1980. Pesticide monitoring in the prairies of Western Canada, *Environ. Sc. Res.* 16:345-72.

⁵⁵ Pazou, E.Y. et al. 2006. Organochlorine and organophosphorous pesticide residues in the Oueme River catchment in the Republic of Benin. *Environ Int.* ;32(5):616-23.

⁵⁶ Zhu, Y. et al. 2005. Organochlorine pesticides (DDTs and HCHs) in soils from the outskirts of Beijing, China. *Chemosphere.* 60(6):770-8

⁵⁷ Louie, PK and SIN, DW. 2003. A preliminary investigation of persistent organic pollutants in ambient air in Hong Kong. *Chemosphere.* 52(9):1397-403

⁵⁸ Pandit, G.G. et al. 2006. Distribution and fate of persistent organochlorine pesticides in coastal marine environment of Mumbai. *Environ Int.* 32(2):240-3.

be due to the high persistence and metabolically inactive nature of this isomer. Alpha-HCH was found to be more dominant in fish samples whereas the gamma-HCH was a major contributor in the sediment samples.

⁵⁹ “Like other persistent organic pollutants, lindane and other isomers of HCH can be transported over long distances by air currents. All HCH isomers vaporize and condense, touching down on oceans and freshwater bodies, where they may begin the cycle again. As a result of these characteristics, lindane and other HCH isomers tend to accumulate in colder climates, where they are trapped by low evaporation rates. Certain HCH isomers are some of the most abundant and pervasive organochlorine contaminants found in the environment, especially in the Arctic.”

⁶⁰In this paper, the researchers discussed the historical global usage and emissions for organochlorine pesticides (OCPs), including hexachlorocyclohexanes (HCHs). Relationships between the air concentrations of these OCPs and their global emissions are also discussed. Differences between the pathways of alpha- and beta-HCH to the Arctic Ocean were described in the context of environmental concentrating and diluting processes. These concentrating and diluting processes were shown to control the temporal and spatial loading of northern oceans and that the HCH burdens in marine biota from these oceans respond accordingly. The HCHs provide an elegant example of how hemispheric-scale solvent switching processes can alter the ocean into which an HCH congener partitions, how air-water partitioning controls the pathway for HCHs entering the Arctic, and how the various pathways impact spatial and temporal trends of HCH residues in Arctic animals feeding out of marine and terrestrial foodwebs.

⁶¹ A 2002 paper provides insight to pathways by which HCH isomers reach the Canada Basin of the Arctic Ocean. Alpha-HCH and beta-HCH, are compared with respect to their transport to and distribution within arctic waters. The two isomers differ in the ability of the airborne chemical to dissolve in seawater, with beta-HCH being about 20 times more soluble. This property is thought to account for the observed differences between alpha-HCH and beta-HCH distributions in air and ocean surface water. Being more soluble than alpha-HCH, beta-HCH is preferentially deposited into the North Pacific by rain and exchange with ocean surface water before reaching the high Arctic, and ocean currents then finish the job of delivering it to the Canada Basin. Evidence for removal of beta-HCH en route is also given by its depletion in high arctic air relative to alpha-HCH. Because of this difference, delivery of beta-HCH to the Canada Basin has lagged alpha-HCH by perhaps a decade or longer and the highest concentrations during the late 1980s and mid-1990s were observed in marginal seas rather than in the high Arctic. Beta-HCH is highly persistent in seawater and its deposition into the North Pacific does not ultimately protect the Arctic Ocean but only delays the input and alters its spatial distribution.

⁶²An Arctic Mass Balance Box Model (AMBBM) was developed to calculate a sequential historical alpha-hexachlorocyclohexane (alpha-HCH) budget in the Arctic Ocean from its introduction in the 1940s up to the present. The AMBBM is created in the context of the Arctic as

⁵⁹ Commission for Environmental Cooperation. Draft North American Regional Action Plan on Lindane and Other Hexachlorocyclohexane (HCH) Isomers. October 2005.

⁶⁰Li, Y.F. and D.W. McDonald. 2005. Sources and pathways of selected organochlorine pesticides to the Arctic and the effect of pathway divergence on HCH trends in biota: a review. *Sci Total Environ.* 15;342(1-3):87-106.

⁶¹ Li, Y.F. et al. 2002. The Transport of beta-hexachlorocyclohexane to the western Arctic Ocean: a contrast to alpha-HCH. *Sci. Total. Environ.*, 291/1-3. :229-246.

http://www.msc-smc.ec.gc.ca/data/gloperd/ArcticRes_e.cfm#TransBetaHCH

⁶²Li, Y.F. et al. 2004. Historical alpha-HCH budget in the Arctic Ocean: the Arctic Mass Balance Box Model (AMBBM). *Sci Total Environ.* 324(1-3):115-39.

a receptor, and has three major components: the air concentration module, the loading from Arctic river module and the transport/transformation module. The results of the model provide a more complete depiction of the behavior of alpha-HCH within the Arctic Ocean. Model output includes annual concentrations in Arctic air and water, annual alpha-HCH loading to, removal from the Arctic Ocean and annual cumulative burden of alpha-HCH in the Arctic waters from 1945 to 2000. The model results from the present study compare well with published data in the 1980s and 1990s and show that the alpha-HCH burden in the Arctic Ocean started to accumulate in the early 1940s and reached the highest value of 6670 t in 1982, 1 year before China banned the use of technical HCH. Since then the burden of alpha-HCH in Arctic waters has decreased quickly by an average annual rate of approximately 270 ty(-1) during the 1990s, decreasing from 4220 t in 1990 to 1550 t in 2000. The complete elimination of alpha-HCH from Arctic waters would require another two decades. The total loading between 1945 and 2000 was 27700 t accounting for approximately 0.6% of total global alpha-HCH emission from agricultural land to the atmosphere.

⁶³In the Arctic, the presence of HCH isomers in animals and humans indicates the long-range transport of these isomers, since none of the HCH isomers are produced or used in this region. Relative to numerous studies in Canada, there have been few analyses of persistent organic pollutants in people of the Alaskan Arctic and sub-Arctic. One study identified “widespread Alaska Native exposure to organochlorines that originated outside the Arctic, a finding also seen in other studies.” The mean level of HCH in blood serum of Alaska Native women by geographical area was reported as follows:

HCH mean (standard deviation) in ng/mL or ppb	
Southcentral (n=47)	0.28 (0.40)
Northwestern (n=28)	0.43 (0.54)
Southwestern (n=50)	0.32 (0.42)
Interior (n=6)	0.20 (0.43)

⁶⁴A later study evaluated maternal plasma concentrations of beta-HCH in women of the Aleutian and Pribilof Islands in Alaska compared with women in other areas of the circumpolar Arctic (1994-1996 geometric means, ppb lipid):

Aleutian/ Pribilof Is.	Canada	Greenland	Sweden	Norway	Iceland	Russia
N=40	N=67	N=117	N=40	N=60	N=40	N=51
24.7	9.3 18.5	9.2 8.1	32.1	222.5		

In addition to HCH, the study measured other organochlorine pesticides and PCBs. Levels of p,p'-DDE in Aleutian and Pribilof Island women were the highest in the circumpolar Arctic with a geometric mean of 503 ppb lipid (N=40).

Data concerning HCH isomers in the blood serum of Yupik people from St. Lawrence Island⁶⁵ revealed the following lipid-adjusted average and maximum concentrations in ppb:

⁶³ Rubin, C.H. et.al, 2001. Exposure to persistent organochlorines among Alaska Native women. *Int. J. Circumpolar Health*, 60 (2):157-69.

⁶⁴ Middaugh, J. et.al, 2001. Assessment of exposure to persistent organic pollutants in five Aleutian and Pribilof villages. *State of Alaska Epidemiological Bulletin*, 5(5):1-19.

⁶⁵ Carpenter, D, 2005. Presentation of unpublished data at the Alaska Conference on Health and Environment.

Alpha-HCH	4	24
Gamma-HCH (Lindane)	35	246
Delta-HCH	0	21

Beta-HCH was not detected in these analyses. The study also showed elevated levels of oxychlorane and trans-nonachlor compared with levels in people of the lower-48 states.

The presence of alpha- and beta-HCH in the traditional foods of the Alaskan native peoples is a cause of alarm. The Alaska Traditional Diet Project (March 2004) found “substantial reliance on many subsistence foods such as fish, terrestrial mammals, marine mammals, and wild plants.” Alaska Native people rely on traditional foods because of cultural importance, availability, preferences in taste and nutrition to store-bought foods.⁶⁶

The Alaska Traditional Diet Project also found that “the most common concerns expressed about subsistence foods were observations of fish and animals with parasites, diseases, or lesions; reduced numbers of fish and [other] animals; and the possible presence of contaminants in fish and [other] animals...there were many comments about unhealthy fish and animals, contamination, or generally reduced quality of subsistence foods. It appears that fears about safety have not yet caused these participants to avoid subsistence foods, but the anxiety they expressed is nevertheless real.”⁶⁷

While analyzing contamination of Alaska natives’ traditional foods by HCH isomers, these results stood out:

- In an analysis of persistent organic pollutants (POPs) in Alaskan murre eggs, researchers found beta-HCH among the major POPs in concentrations ranging from 59-282 ng/g lipid mass.

Researchers collected and analyzed contaminant levels in murre eggs from several colonies in Alaska. They measured concentrations of various PCB congeners and chlorinated pesticides, including alpha-, beta- and gamma-HCH. Statistical analyses showed variation among colony locations for all compounds except beta-HCH. Researchers found the following concentrations of HCH isomers (data are expressed in ng/g lipid weight),^{68 69}

	ALPHA-HCH	BETA-HCH	GAMMA-HCH
East Amatuli	16.1±7.3		4.66±7.1
St. Lazaria	9.51±4.0	143±50	1.97±1.7
Bogoslof Island	22.3±7.2		6.27±1.3
St. George Island	11.0±4.5	161±64	2.63±2.5
Little Diomedes	10.0±5.5	183±63	2.62±2.9

⁶⁶ Ibid.

⁶⁷ Ibid.

⁶⁸ Kucklick, J.R. et.al, op.cit.

⁶⁹ Vander Pol, S.S. et.al, 2004. Persistent organic pollutants in Alaskan murre (*Uria spp.*) eggs: geographical, species, and temporal comparisons. *Environ. Sci. Tech*, 38(5):1305-12.

While most “legacy” organochlorine contaminants have significantly declined in Canadian Arctic biota from the 1970s to the 1990s, HCH levels have “remained relatively constant in most species and proportions of the toxic beta-HCH isomer have actually increased in seabird eggs and in ringed seal blubber.”⁷⁰

- Seal oil is an important component of the Alaska Native diet, yet little information exists on the levels of contaminants in this rendered food source. People also consume muscle, liver, heart, kidney, and flipper of seal species, and contaminant levels may be more concentrated in certain tissues.

In one study of organochlorine pesticides in the blubber of ringed seals, “wet mass sum HCH (SUM-HCH, sum of alpha-, beta-, and gamma-HCH) values for samples that included beta-HCH measurements, ranged from 146 ng/g wet mass to 561 ng/g wet mass. Muir et.al. (1995) also measured variable SUM -HCH concentrations in ringed seal samples; 246 ± 231 ng/g in females and 274 ± 123 ng/g in males. Schanz et.al. (1996) reported gamma-HCH values in ringed seals from Barrow and Nome, Alaska from 2.1 ± 0.01 ng/g to 633 ± 4 ng/g. For the samples in which all three HCHs were measured, alpha-HCH contributed the most to the SUM-HCHs, ranging from 59% of SUM-HCH in RGSL-047 [sample number] to 68% in RGSL-053.”⁷¹

- Data published in the Alaska Traditional Knowledge and Native Foods Database (www.nativeknowledge.org) show a range of HCH levels in beluga whale blubber in ng/g wet wt.:

Sample site	HCH isomer	Sex	Range
Point Hope	alpha-	F (n=4)	162-180.3
	beta-	F (n=2)	99.1-188.2
	gamma-	F (n=4)	33.3-95.9
Point Lay	alpha-	F (n=6)	43.9-186.9
	alpha-	M (n=18)	70.8-196.3
	beta-	F (n=3)	22.3-144.1
	beta-	M (n=9)	120-180.8
	gamma-	F (n=6)	11.5-49.2
	gamma-	M (n=18)	39.6-64.9
	Sum-HCHs	F (n=3)	77.7-364.4
	Sum-HCHs	M (n=8)	265.3-478.3

⁷² A 1973 research paper documented the isomerization of gamma-HCH to alpha-HCH in the environment. The authors state that “the significance of this work is that we have demonstrated for the first time that micro organisms in pure culture can isomerizes gamma-HCH.” While subsequent studies of isomerization are inconclusive, the possibility remains that isomerization of the gamma-HCH isomer to alpha- and/or beta-HCH may be an important source of the more persistent HCH isomers in the environment, wildlife, and people.

⁷⁰ Muir, D.C., 2005. Contaminants in Canadian Arctic biota and implications for human health: conclusions and knowledge gaps. *Sci. Total Env.* 351-352:539-46.

⁷¹ Kucklick, J.R. et.al, 2002. Persistent organochlorine pollutants in ringed seals and polar bears collected from northern Alaska. *Sci. Total Environ.* 287:45-59.

⁷² Benezet, H. and F. Matsumura. 1973. Isomerization of gamma-HCH to alpha-HCH in the environment. *Nature* 243:480-48.

Bio-concentration or bio-accumulation factor, based on measured values (unless monitoring data are judged to meet this need)

⁷³ HCH isomers can be measured in blood, urine, body fat, breast milk, and semen of exposed persons. ⁷⁴HCH has been shown to cross the placenta in pregnant women. HCH has been detected in human breast milk, suggesting that it can be transferred to infants from women who nurse.

⁷⁵Lindane and other HCH isomers can bio-accumulate easily in the food chain due to their high lipid solubility and can bio-concentrate rapidly in micro organisms, invertebrates, fish, birds and mammals, however, bio-transformation and elimination are relatively rapid when exposure is discontinued.

⁷⁶The chronic effects of the beta-HCH isomer are of particular interest because of its predominance among all HCH isomers in mammals, including humans, and its apparent long biological half-life. A half-life of 7.2 years has been estimated for beta-HCH in humans. ⁷⁷A 2002 study shows that of the two HCH isomers, beta-HCH bioaccumulates more strongly and is more resistant to metabolism and micro bial degradation. Beta-HCH is the most prominent isomer in human fat.

⁷⁸The bioconcentration factor is higher and the elimination is slower for beta-HCH than for the other HCH isomers. Because the beta- isomer is the most persistent and bioaccumulative isomer of HCH and the alpha- and gamma- isomers can be converted into the beta- isomer within organisms, as much as 90% of HCH detected in human tissues and breastmilk is beta-HCH.

⁷⁹Chronic toxicities of HCH isomers, alpha-HCH, beta-HCH, gamma-HCH, and delta-HCH, increase in the following order: delta-, gamma-, alpha-, beta-. ⁸⁰ Because of the lipophilic properties and persistence in the environment, beta-HCH followed by alpha-HCH and to a less extent gamma-HCH may give rise to bioaccumulation and biomagnification through the food chain. ⁸¹Experts support the need for additional research to determine why the beta isomer is the most prevalent form of HCH detected in human samples when it only makes up a small percentage of the technical mixture and technical HCH is banned in many countries.

⁸² Alpha- and beta-HCH, by-products of gamma-HCH synthesis, are of major concern because due to their considerable persistence in biological systems they pollute the environment and certain nutrients; among the latter, human milk contains the highest levels of beta- HCH besides considerable amounts of alpha-HCH. HCHs are rapidly absorbed from the gastrointestinal tract,

⁷³ ATSDR Tox FAQs, op.cit.

⁷⁴ ibid. ATSDR Tox FAQs, op.cit.

⁷⁵ World Health Organization (WHO). 1991. Lindane (Environmental Health Criteria 124). 208 pp. referenced in NARAP.

⁷⁶ Steinmetz, R., P. C. M Young, A.Caperell-Grant, E.A. Gize, B.V. Madhukar, N. Ben-Jonathan, R.M. Bigsby. 1996. Novel estrogenic action of the pesticide residue beta-hexachlorocyclohexane in human breast cancer cells *Cancer Res.* 56, 5403-5409 in NARAP

⁷⁷ Li, Y.F. et.al. 2002. The Transport of beta-hexachlorocyclohexane to the western Arctic Ocean: a contrast to alpha-HCH. *Sci. Total. Environ.* 291/1-3. :229-246.

http://www.msc-smc.ec.gc.ca/data/gloperd/ArcticRes_e.cfm#TransBetaHCH

⁷⁸ Solomon, G. M. and P. M. Weiss, 2002. Chemical Contaminants in Breastmilk: Time Trends and Regional Variability. *Environmental Health Perspectives*, Vol 110, no. 6.

⁷⁹ Konishi, Y. et.al. 2001. Continuous Surveillance of Organochlorine Compounds in Human Breastmilk from 1972 to 1998 in Osaka, Japan. *Archives of Environmental Contamination Toxicology* 40, 571-578.

⁸⁰ EFSA. 2005, op.cit.

⁸¹ Solomon, G. M. and P. M. Weiss, 2002. Chemical Contaminants in Breastmilk: Time Trends and Regional Variability. *Environmental Health Perspectives*, Vol 110, no. 6.

⁸² EFSA, op.cit.

pass the placenta and are transferred into milk.⁸³ Among the HCH isomers, beta-HCH leaves the body the most slowly. alpha-HCH, delta-HCH, and gamma-HCH, and the products formed from them in the body, are more rapidly excreted in the urine; small amounts leave in the feces and expired air.

⁸⁴ Considering the available intake data from Czech Republic, Canada and USA and taking into account the decreasing concentration of HCHs in breast milk (about 80 % since the eighties in Germany), current exposure through food is likely to be very low. Beta-HCH is usually still present but alpha- and gamma-HCH are only occasionally found in human milk samples from European Countries, which banned the production and use of technical HCH in the late 1970s. Some East European and developing countries with a longer use of technical HCH show higher contamination levels in breast milk.

⁸⁵ Lindane and other HCH isomers occur in different compartments and trophic levels of the Arctic ecosystem and are accumulated by species at low trophic levels, while the biomagnification potential is low at the upper end of the food web.

⁸⁶ Noting that the partitioning of chlorinated hydrocarbons (OC) and polychlorinated biphenyls is in part dependent on the fat content of tissues, in their 1995 study Scheele. et. al compared the concentrations of CHC and PCB in bone marrow with that of depot fat and breast milk. They found that for Beta-HCH, HCB, Total-DDT, PCB-138, -153 and -180, the highest concentration (in mg/kg fat), (most cases significantly), were in the bone marrow, compared to breast milk and fat tissue. They postulate selective partitioning into bone marrow.

⁸⁷ “Alpha-HCH is regularly detected in fish and aquatic invertebrates, ducks, herons, barn-owls. Average of 70-80 ug/kg of Alpha- HCH was found in the subcutaneous fat of reindeer and Idaho mouse living in areas of negligible pesticide use.”

⁸⁸ Oral administration of alpha- and gamma-BHC to rats study: “After 8 wk of administration, tissue retention of alpha-BHC was 10-20 fold greater than that of gamma-BHC. Gamma-BHC was eliminated to a greater extent than alpha- BHC from tissues and in particular from fatty tissue. Alpha- BHC accumulated in fat and brain, while gamma- BHC showed low affinity for lipid.”

⁸⁹ To estimate levels of organochlorine residuals in the Japanese population and the contribution of dietary factors to these levels, the researchers determined serum levels of beta-

⁸³ ATSDR. Toxicological Profile. 2005, op cit.

⁸⁴ EFSA. 2005, op cit.

⁸⁵ Willett KL, Ulrich EM, Hites RA. 1998. Differential Toxicity and Environmental Fates of Hexachlorocyclohexane Isomers. *Environmental Science & Technology* 32: 2197-2207. Referenced in NARAP

⁸⁶ Scheele, J., Teufel, M., and Niessen, K.-H. 1995. A comparison of the concentrations of certain chlorinated hydrocarbons and polychlorinated biphenyls in bone marrow and fat tissue of children and their concentrations in breast milk. *J. Env. Path. Tox. Onc.* 14(1):11-14.; referenced in Great lakes Critical Pollutants. 1998. Health Effects Review, Vol 3 Issue 1 April- June 1998.

⁸⁷ WHO working group; Alpha- hexachlorocyclohexane; *Environmental Health Criteria* Vol: 123 pp 1-66. 1992.

⁸⁸ Eichler D, Heupt W, Paul W. 1983. Comparative study of the distribution of alpha-BHC and gamma-BHC in the rat with particular reference to the problem of isomerization, *Xenobiotica*; 13(11).

⁸⁹ Hanaoka, T. et.al. 2002. Residuals of beta-hexachlorocyclohexane, dichlorodiphenyltrichloroethane, and hexachlorobenzene in serum, and relations with consumption of dietary components in rural residents in Japan. *Sci Total Environ.* 286(1-3):119-27.

hexachlorocyclohexane (beta-HCH), hexachlorobenzene (HCB), p,p'-dichlorodiphenyldichloroethane (p,p'-DDD), 1,1-dichloro-2,2-bis(p-chlorophenyl) ethylene (p,p'-DDE) and p,p'-dichlorodiphenyltrichloroethane (p,p'-DDT) in 41 volunteers (14 men and 27 women) in a rural area of Northern Japan. These organochlorine levels were measured using gas-chromatography mass-spectrometry. By a self-administered dietary history questionnaire, the usual dietary intake was estimated. Their median levels (range) were as follows: beta-HCH, 0.50 (0.05-1.50); HCB, 0.20 (0.02-0.70); and total DDT (p,p'-DDE + p,p'-DDT), 5.0 (0.9-31.0) ng/ml serum. The beta-HCH levels were increased with rice and milk intakes, but the least squares means were not simply increased according to the quartile of the intakes. The study suggests that organochlorine compounds are transported into the human body via foods in the Japanese population.

⁹⁰ The residue levels of selected organochlorine pesticides (OCPs) dichloro-diphenyltrichloroethane (p,p'-DDT, o,p'-DDT, p,p'-DDE, p,p'-DDD), hexachlorocyclohexanes (alpha-, beta-, gamma- and delta-HCH) in gastropod and bivalve species of nine kinds of mollusks collected from ten coastal sites along the Chinese Bohai Sea were investigated from 2002 to 2004. The results showed that OCPs widely existed in the mollusks organisms. Along with p,p'-DDT, p,p'-DDE, beta-HCH was the major compound found in the mollusks.

(d) Monitoring data (provide summary information and relevant references)

The Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the U.S. These sites are then placed on the National Priorities List (NPL) and are targeted for long-term federal clean-up activities. alpha-, beta-, gamma-, and delta-HCH has been found in at least 146, 159, 189, and 126, respectively of the 1,662 current or former NPL sites.⁹¹

HCH in Human Blood:

⁹² The Center for Disease Control and Prevention (CDC) is engaged in an ongoing assessment of the U.S. population's exposure to environmental chemicals using bio-monitoring as a tool. Bio-monitoring involves assessment of human exposure to chemicals by measuring the chemicals or their metabolites in human specimens such as blood or urine. The results of these assessments have been published by the CDC in three National Reports on Human Exposure to Environmental Chemicals. The overall range of beta-HCH detected among US populations tested between 1999 and 2002 (across the CDC studies two and three) ranged from 49%-62%.

The third National Report on Human Exposure to Environmental Chemicals Report, 2005, presents exposure information for the U.S. population for 148 chemicals. The data for this report was collected between 2001 and 2002. The Report also includes the data from the Second Report, which contained data for 1999-2000. In the third CDC study 3097 individuals were tested for pesticides in their urine and 2517 individuals were tested for pesticides in their blood. The report shows that 46.2 ng/g lipid of beta- HCH was found in blood of adults over 20 tested in the US. Of these, women had 54.5 ng/g lipid of beta-HCH in their bodies. Mexican Americans had the highest levels of beta- HCH present in their blood at 84.4 ng/g lipid, as compared to 45.9 ng/g

⁹⁰ Wang, Y. et.al. 2006. Investigation of organochlorine pesticides (OCPs) in mollusks collected from coastal sites along the Chinese Bohai Sea from 2002 to 2004. *Environ Pollut.* March 8.

⁹¹ ATSDR. 2005, op cit.

⁹² National Center for Environmental Health, U.S. Centers for Disease Control and Prevention, Second National Report on Human Exposures to Environmental Chemicals. January 2003; and Third National Report on Human Exposure to Environmental Chemicals. July 2005. Available at <http://www.cdc.gov/exposurereport>.

lipid for Non-Hispanic Blacks and 33.5 ng/g lipid for Non-Hispanic Whites (pp. 10).

⁹³ Researchers from University of California, Berkeley, USA, measured para, para' (p,p')-DDE, p,p'-DDT, ortho, para' (o,p')-DDT, HCB, beta-HCH (the most persistent isomer of technical-grade HCH) and gamma-HCH in serum from 426 low-income pregnant Latina women living in an agricultural community in California, USA. Detection frequencies were 94% to 100%. Median levels (ng/g lipid) of p,p'-DDE (1,052), p,p'-DDT (13), beta-HCH (37) and HCB (65) were significantly higher than United States population levels. Multivariate analyses of p,p'-DDE, p,p'-DDT, o,p'-DDT, beta-HCH and HCB indicate that time spent living outside the United States and birthplace in an area of Mexico with recent use of OC pesticides were significant predictors of exposure. Time spent living in the United States was associated with increased serum levels of p,p'-DDE and beta-HCH, but the increase for each year lived in the United States was lower than for each year lived outside the United States. However, researchers observed no associations between serum levels of any OC compound and current intake of saturated fat or agricultural take-home exposure risk factors. Lactation history and recent weight gain were negatively associated with serum levels of some, but not all OC compounds studied.

HCH in breastmilk:

⁹⁴ "Studies looking at HCH contamination of breastmilk have been conducted around the world, including reported results in the following countries: Austria, Belgium, Brazil, Canada, China, Czech Republic, Denmark, Egypt, Finland, France, Germany, Greece, Hungary, India, Ireland, Israel, Italy, Japan, Kenya, Luxembourg, Mexico, Netherlands, Nigeria, Norway, Poland, Russia, Rwanda, Saudi Arabia, Spain, Sweden, Switzerland, Thailand, Turkey, Uganda, Ukraine, United Kingdom, United States, Vietnam, Yugoslavia and Zimbabwe."

⁹⁵ ⁹⁶ Several additional factors may affect the levels of HCH found in breastmilk. Like DDT, HCH breaks down more quickly in tropical climate zones than in temperate zones. Thus, levels of HCH in the environment, and perhaps in breastmilk, are likely to be relatively lower in warm climates if all other factors are equal. Also, as with other persistent organic compounds that bioaccumulate through the food chain, the concentration of HCH in breastmilk is strongly related to diet. A German study found that women who followed a low-fat diet had lower beta-HCH levels in their breastmilk than women whose diet included large quantities of meat.

⁹⁷ ⁹⁸ In general, countries that have monitored breastmilk for HCH residues over time have witnessed a steady decrease as lindane restrictions and bans take effect. For example breastmilk

⁹³ Bradman, A S. et.al. 2006. Factors predicting organochlorine pesticide levels in pregnant Latina women living in a United States agricultural area. *J Expo Sci Environ Epidemiol*. Oct 11.

⁹⁴ Natural Resources Defense Council on-line resource, *Healthy Milk, Healthy Baby. Chemicals: Hexachlorocyclohexane*. <http://www.nrdc.org/breastmilk/hch.asp#note2>

⁹⁵ Nair, A., et al 1996.. "DDT and HCH Load in Mothers and Their Infants in Delhi, India," *Bulletin of Environmental Contamination and Toxicology* 56: pp. 58-64 as cited in Natural Resources Defense Council on-line resource, *Healthy Milk, Healthy Baby. Chemicals: Hexachlorocyclohexane*. <http://www.nrdc.org/breastmilk/hch.asp#note2>

⁹⁶ Schade, G. and B. Heinzow. 1998. "Organochlorine Pesticides and Polychlorinated Biphenyls in Human Milk of Mothers Living in Northern Germany: Current Extent of Contamination, Time Trend from 1986 to 1997 and Factors that Influence the Levels of Contamination," *The Science of the Total Environment* 215: pp. 31-39 as cited in Natural Resources Defense Council on-line resource, *Healthy Milk, Healthy Baby. Chemicals: Hexachlorocyclohexane*. <http://www.nrdc.org/breastmilk/hch.asp#note2>

⁹⁷ Furst, P., C. Furst, and K. Wilmers. 1994. "Human Milk as a Bioindicator for Body Burden of PCDDs, PCDFs, Organochlorine Pesticides, and PCBs," *Environmental Health Perspectives* 102: pp. 187-93 as cited

monitoring data shows a clear downward trend over time in residues among women in the North Rhine Westphalia region of Germany, and a similar downward trend of average lindane and beta-HCH levels in Swedish breastmilk.

Table 1 shows data from a World Wildlife Fund (WWF) study, which shows the high values of HCH recorded in different geographic regions between 1971 and 1991. Table 2 illustrates the high levels of HCH isomers detected in different countries in studies from 1991 to 2002.

Table 1: Chemical contaminants found in human breastmilk and some concentrations recorded (data from Jensen and Slorach, 1991)⁹⁹

Compound	Typical values	High Values recorded	
	Milk fat mg/kg (ppm)	Whole milk micro g/kg (ppb)	Milk fat mg/kg (ppm)
alpha- HCH	0.2 Europe	160 Punjab, India 1979	2.25 Turkey 1984/5
beta- HCH		900 GDR 1971	19 Beijing, China 1982
gamma HCH		80 Spain 1973	3.79 FRG 1981/3
Total HCH		325 India 1979	7.83 Turkey 1984/5

Table 2: International comparison of HCH levels (micro g/g lipid weight) in human breastmilk¹⁰⁰

Country	Survey Year	HCHs
Developing and Former Socialist Countries		
Dalian, China	2002	1400 ^a
Shenyang, China	2002	550 ^a
Turkey	1995-96	480 ^a
Iran	1991	600 ^a
Brazil	1992	280 ^a
Mexico	1997-98	60 ^a
Kenya	1991	96 ^f
Kazakhstan	1994	2300 ^f
Russia	1996	560 ^g

in Natural Resources Defense Council on-line resource, *Healthy Milk, Healthy Baby. Chemicals: Hexachlorocyclohexane*. <http://www.nrdc.org/breastmilk/hch.asp#note2>

⁹⁸ Noren, K. and D. Meironyte. 2000. "Certain Organochlorine and Organobromine Contaminants in Swedish Human Milk in Perspective of Past 20-30 Years," *Chemosphere* ; 40: pp. 1111-1123 as cited in Natural Resources Defense Council on-line resource, *Healthy Milk, Healthy Baby. Chemicals: Hexachlorocyclohexane*. <http://www.nrdc.org/breastmilk/hch.asp#note2>.

⁹⁹ Lyons, G, 1999. Chemical Trespass: A toxic legacy: A WWF-UK Toxics Program report;. Accessed at http://www.oztoxics.org/cmwg/library/documents_1/chemical%20trespass.pdf (March 28 2006)

¹⁰⁰ Kunisue, T. et.al, 2004. Persistent organic pollutants in human breastmilk collected from Dalian and Shenyang, China. Accessed at <http://dioxin2004.abstract-management.de/pdf/p144.pdf> (March 27, 2006)

Developed Countries		
Japan	1998	210 ^g
Sweden	1997	-
Germany	1995-97	40 ^g
Canada	1996	23 ^a
Spain	1991	280 ^a
UK	1997-98	100 ^h

a=alpha-HCH+beta-HCH+gammaHCH; *f*=alpha-HCH+beta-HCH; *g*=beta-HCH only;
h=beta- HCH+gammaHCH

Breastmilk monitoring from around the world illustrates the widespread contamination of breastmilk with HCH isomers. The following summary bullets and tables include some key findings from country-specific scientific studies.

- Testing of 140 human milk samples in sub-Arctic locations of Russia revealed that beta-HCH levels in these samples were 10 times higher than corresponding levels in Norway.¹⁰¹
- A Brazilian breastmilk study¹⁰² of 40 lactating women living in Rio de Janeiro in 1992 revealed concentration of various HCH isomers (in micro g/g of milk fat) at: alpha-HCH: 0.001; beta- HCH: 0.27; gamma HCH: 0.005
- Human breastmilk collected from Inuit mothers in Arctic Quebec had concentrations of organochlorine (OC) pesticides (including HCH isomers) that were two to 10 times greater than those of samples from southern Quebec.¹⁰³ Inuit mothers exhibit the greatest body burden known from exposure to organochlorine residues present in the environment by virtue of their location at the highest trophic level of the arctic food web.¹⁰⁴
- From 1986 to 1997 more than 3,500 human milk samples were analyzed in northern Germany for OC compounds. Between summer 1995 and summer 1997 the median beta-HCH level was 0.036 mg/kg, value expressed on a fat basis.¹⁰⁵
- In New Zealand, a total of 53 milk samples were collected from October 1998 to May 1999 . beta-HCH was detected in all the samples and had a concentration of 16.3 ng/g fat. alpha-HCH was detected in 96% of samples at a mean concentration of 0.2 ng/g fat.¹⁰⁶

¹⁰¹ Polder, A. et.al, May 1 2003. Geographic variation of chlorinated pesticides, toxaphenes and PCBs in human milk from sub-Arctic and Arctic locations in Russia. *Science of the Total Environment*, 306(1-3):179-95

¹⁰² Paumgartena, F.J.R. et.al, 2000. PCDDs, PCDFs, PCBs and other organochlorine compounds in human milk from Rio de Janeiro. *Environmental Research*, 83 (3):293-7

¹⁰³ Craan, A. G. and D. A. Haines, 1998, op.cit.

¹⁰⁴ Dewailly, E. et.al, 1993. Inuit exposure to organochlorines through the aquatic food chain in arctic Quebec. *Environmental Health Perspectives*, 101(7):618-20.

¹⁰⁵ Schade, G. and B. Heinzow, 1998. Organochlorine pesticides and polychlorinated biphenyls in human milk of mothers living in Northern Germany: Current extent of contamination, time trend from 1986 to 1997 and factors that influence the levels of contamination. *Science of the Total Environment*, 215: 31-39.

¹⁰⁶ Bates, M. et.al, 2001. Investigation of organochlorine contaminants in the milk of New Zealand women.

Accessed at

[http://www.moh.govt.nz/moh.nsf/0/2143f4f9c3dffcb5cc256a5a007cbf36/\\$FILE/OrganochlorinesinMilkofNew](http://www.moh.govt.nz/moh.nsf/0/2143f4f9c3dffcb5cc256a5a007cbf36/$FILE/OrganochlorinesinMilkofNew)

- A Mexican study¹⁰⁷ of OC pesticides in maternal blood serum, umbilical cord serum and milk found levels of 0.10mg/kg on fat basis in colostrum for sum of all HCH isomers and 0.06 mg/kg in human mature milk. 100% of a sample of 60 breastmilk samples had detectable levels of beta-HCH isomer. 0.09 mg/kg on fat basis was the concentration of beta-HCH in colostrum and 0.06mg/kg on fat basis in human mature milk.
- The exposure levels of placenta and paired breast milk samples to selected organochlorine compounds and pesticides from Danish and Finnish samples have been investigated. p,p'-DDE is the dominant pollutant, beta-HCH, hexachlorobenzene, endosulfan-I, dieldrin, oxychlorane, cis-heptachlor epoxide and p,p'-DDT being the other major constituents. Their concentrations are linearly correlated between milk and placenta in similar patterns for Danish and Finnish samples. Milk samples have higher levels of these pollutants than placenta on lipid base. However, the apparently not correlated compounds, such as alpha-HCH, pentachlorobenzene, pentachloroanisole and methoxychlor, are generally accumulated more in placenta, which may suggest a tissue specific metabolic activity.¹⁰⁸

HCH in food:

¹⁰⁹ A sampling study of free-range chicken eggs conducted by the International POPs Elimination Network 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. "...many samples with intermediate lindane concentrations had high concentration of beta-HCH reflecting the relative half lives of the two chemicals."

¹¹⁰ The U.S. Food and Drug Administration found HCH isomers in food residues of 100 food items in the agency's most recent Total Diet Study. The Total Diet Study (TDS), is an ongoing program that determines levels of various contaminants and nutrients in foods. The foods collected in the TDS (TDS food list) represent the major components of the diet in the US population. The food list is based on results of national food consumption surveys and is updated from time to time to reflect changes in food consumption patterns. The food list was most recently updated in 2003, based on data from USDA's 1994-96, 1998 Continuing Survey of Food Intakes by Individuals (1994-96, 1998 CSFII) (USDA 2000), and will be reflected in the TDS analytical results beginning with MB 03-1. Alpha-HCH was identified in 35 items and beta-HCH in 12 items.

¹¹¹ One hundred forty seven samples of bovine milk were collected from 14 districts of Haryana,

ZealandWomen.pdf (March 30, 2006)

¹⁰⁷ Waliszewski, A. et. al, 2001. Organochlorine pesticide levels in maternal adipose tissue, maternal blood serum, umbilical blood serum, and milk from inhabitants of Veracruz, Mexico. *Archives of Environmental Contamination Toxicology*, 40:432-438.

¹⁰⁸ Shen, H et.al. 2007. From mother to child: Investigation of prenatal and postnatal exposure to persistent bioaccumulating toxicants using breast milk and placenta biomonitoring. *Chemosphere*. Jan 3.

¹⁰⁹ Blake A. 2005. *The Next Generation of POPs: PBDEs and Lindane*, Working Group of the International POPs Elimination Network (IPEN). <http://www.oztoxics.org/ipepweb/egg/New%20POPs.html> (pp:11)

¹¹⁰ Food and Drug Administration Total Diet Study: Summary of Residues Found Ordered by Pesticide, Market Baskets 91-3, 01-4. June 2003. <http://www.cfsan.fda.gov/~acrobat/tds1byyps.pdf>

¹¹¹ Sharma, HR. et.al. 2006. Pesticide Residues in Bovine Milk from a Predominantly Agricultural State of Haryana, India. *Environ Monit Assess*. Dec 16.

India during December 1998-February 1999 and analyzed for the presence of organochlorine pesticide (OCPs) residues. Sum-HCH, Sum-DDT, Sum-endosulfan and aldrin were detected in 100%, 97%, 43% and 12% samples and with mean values of 0.0292, 0.0367, 0.0022 and 0.0036 mg/kg, respectively. Eight percent samples exceeded the maximum residue limit (MRL) of 0.10 mg/kg as recommended by WHO for Sum-HCH, 4% samples of 0.05 mg/kg for alpha-HCH, 5% samples of 0.01 mg/kg for gamma-HCH, 26% samples of 0.02 mg/kg for beta-HCH as recommended by PFAA and 24% samples of 0.05 mg/kg as recommended by FAO for Sum-DDT. Concentrations of beta-HCH and p,p'-DDE were more as compared to other isomers and metabolites of HCH and DDT.

¹¹²Under a multi-centre study conducted by the Indian Council of Medical Research, 1712 samples of wheat grain/flour were collected from urban and rural areas in 11 states representing different geographical regions of India. These samples were analyzed for residues of DDT (2,2-bis (p-chlorophenyl)-1,1,1-trichloro ethane) and different isomers of HCH (1,2,3,4,5,6-hexachloro cyclohexane, a mixture of isomers) by gas-liquid chromatography. Different isomers of HCH were present in about 45-80% of the samples of wheat grain/flour. Medians of DDT and total HCH, respectively, for pooled samples of wheat grain were 0.013 and 0.035 mg kg⁻¹, while those for wheat flour were 0.01 and 0.02 mg kg⁻¹. Estimated daily intakes of DDT and different isomers of HCH through the consumption of wheat contaminated at their median and 90th percentiles constituted a small proportion of their acceptable daily intakes.

¹¹³Forty-nine samples of honey collected from markets of Portugal and Spain were evaluated for nine organochlorine pesticide residues including alpha-, beta-, and gamma-hexachlorocyclohexane (HCH) during 2001-02. The analytical procedure used was LLE extraction with ethyl acetate followed by gas chromatography-electron-capture detection (GC-ECD) for quantification, and mass spectrometry (GC-MS) for confirmation. Recoveries of spiked samples ranged from 68%, for beta-HCH for fortification levels between 10 and 100 micro g/kg, and 64%, for alpha-HCH, and 143% for gamma-HCH for fortification levels between 20 and 200 micro g/kg. Limits of quantification, using GC-ECD, were from 0.01 and 0.10mg/kg, and limits of detection between 0.001 and 0.02 mg/kg. Fourteen Valencian samples were contaminated, containing residues of HCB or/and HCH isomers. The frequency of detection was 56% for Spanish samples. In Portugal, 23 samples (95.8%) were contaminated. In Spanish samples, concentrations ranged from 0 to 2.24 mg/kg for HCH-total. The mean concentration and standard deviation was 0.579+/-0.747 mg/kg for HCH-total, with the gamma isomer contributing the highest values. The samples from Portugal showed higher levels. HCH-total ranged from 0 to 4.86 mg/kg. Mean concentration and standard deviation was 1.357+/-1.30 mg/kg for HCH-total.

¹¹⁴HCH isomers, along with DDT and other organochlorines, dioxin and PCBs, were found in butter samples taken in 23 countries in a 2000 study. Lindane and HCH isomers were also found in butter sampled by the U.S. Food and Drug Administration in 2003.

¹¹² Toteja GS. 2006. Residues of DDT and HCH in wheat samples collected from different states of India and their dietary exposure: A multicentre study. *Food Addit Contam.* 23(3):281-8.

¹¹³ Blasco, C. et.al. 2004. Determination of organochlorine pesticide residues in honey from the central zone of Portugal and the Valencian community of Spain. *J Chromatogr A.* 1049(1-2):155-60.

¹¹⁴ Santillo, D, Stringer, R.L. & Johnston, P.A. 2000. The Global Distribution of PCBs, Organochlorine Pesticides, Polychlorinated Dibenzo-p-dioxins and polychlorinated dibenzofurans Using Butter as an Integrative Matrix. *Greenpeace Research Laboratories Technical Note* 13/00, and Food and Drug Administration, op.cit.

(e) Exposure in local areas (provide summary information and relevant references)

- general

- as a result of long-range environmental transport

¹¹⁵Like other persistent organic pollutants, lindane and other isomers of HCH can be transported over long distances by air currents. Recent information suggests alpha-HCH to have a travel distance of 18,000 to 22,000 kms. ¹¹⁶All HCH isomers vaporize and condense, touching down on oceans and freshwater bodies, where they may begin the cycle again. As a result of these characteristics, lindane and other HCH isomers tend to accumulate in colder climates, where they are trapped by low evaporation rates. Certain HCH isomers are some of the most abundant and pervasive organochlorine contaminants found in the environment, especially in the Arctic.

¹¹⁷HCH isomers are the most abundant organochlorines in the Arctic Ocean. The highest concentrations of HCH isomers are in the Beaufort Sea and Canadian Archipelago. The elevated residues of HCH isomers in marine mammals of the Archipelago are likely from the high concentrations of HCH isomers in the water. There is an important relationship between meat and fish consumption and concentrations of HCH isomers in human milk and body fat. Various mammals, fish and birds that the indigenous people of the North depend on for subsistence have measurable quantities of the persistent, toxic and bioaccumulative HCH isomers. The indigenous people of the circumpolar Arctic region are concerned that their subsistence diets may increase their exposure to HCH isomers. One reason is that exposure through subsistence diets to HCH isomers that are found in the Arctic food chain result from production and use of HCH isomers in countries outside of North America.

¹¹⁸ Isomerization of lindane to alpha-BHC suggested to account for some of the occurrence of alpha- BHC in Canadian prairie pesticide monitoring. Beta-HCH may isomerise in aquatic environments and therefore may be a potential source of more biologically active isomers in the environment.

¹¹⁹ “The high relative concentration of alpha-HCH in the Arctic suggest that gamma-HCH may be transformed to other isomers in the environment. Laboratory studies show the significant photoisomerization of gamma-HCH to alpha-HCH is possible.”

¹²⁰ In this paper, the causes for persistence of alpha- BHC in atmospheric environment were explored. “Under identical conditions, photochemical studies carried out with alpha-, beta-, delta-BHC isomers unequivocally established that the alpha-isomer was the most stable conformer photochemically although the beta-isomer was the most prevalent metabolic product in mammalian species. Transformation of the BHC isomers to the stable alpha-form may have been

¹¹⁵ Shen, L. et. al. 2005., Atmospheric Distribution and Long-Range Transport Behavior of Organochlorine Pesticides in North America, *Environ. Sci. Technol.*; (Article) 39(2); 409-420 referenced in lindane NARAP

¹¹⁶ Commission for Environmental Cooperation. 2006, op.cit.

¹¹⁷ Ibid.

¹¹⁸ Deo PG, Hasan SB, Majumdar SK. 1980. Isomerization of Beta-HCH in aqueous solution, *J. Environ. Sci. Health B15(2)*:147-164.

¹¹⁹ Walker K, Vallerio DA, Lewsi RG. 1999. Factors influencing the distribution of Lindane and other hexachlorocyclohexanes in the environment; *Environmental Science and Technology*; 33 (24). 4373-78.

¹²⁰ Malaiyandi M, Shah SM. 1984. Evidence of photoisomerization of BHC isomers in the ecosphere, *J Environ Sci Health Part A Environ Sci Eng*; 19(8).

responsible for the presence of higher levels of the alpha-isomer than the gamma-form in the rain waters previously observed.”

- Information regarding bio-availability

^{121, 122} Especially high levels of HCH in breast milk have been associated with areas of high use. In China and Japan, HCH was commonly used as an insecticide in rice fields, and levels as high as 6,500 ppb of HCH in milk fat have been measured in these countries. Since Japan banned HCH in the 1970s, however, levels of the pesticide in breast milk have decreased. Average levels of HCH in breast milk in Osaka, Japan, dropped significantly between 1972 and 1998.

¹²³ Beta-HCH levels measured in India were nearly two orders of magnitude higher than that found in many other nations. The study reporting this data was conducted in Delhi, but similarly high beta-HCH levels have been detected elsewhere in India as well.

¹²⁴ EPA has noted that lindane is "efficiently transmitted" from mother to child through breastmilk. When women carry HCH isomers in their bodies, infants may be exposed to their damaging reproductive effects both inside and outside the womb.

(f) National and international risk evaluations, assessments or profiles and labelling information and hazard classifications, as available (provide summary information and relevant references)

¹²⁵ The International Chemical Safety Card issued by the National Institute for Occupational Safety and Health for beta-HCH identifies acute hazards/symptoms of exposure, first aid recommendations, and routes of exposure (inhalation, dermal exposure and ingestion). The Safety Card identifies effects of short-term exposure as “effects on the central nervous system,” including dizziness, nausea and tremors, and long-term exposure including “effects on the blood, liver, and kidney.” Beta-HCH is also identified as a possible human carcinogen with links to toxic reproductive effects.

¹²¹ Jensen, A.A. and S.A. Slorach. 1991. *Chemical Contaminants in Human Milk*, Boca Raton Ann Arbor Boston: CRC Press, Inc. as cited in Natural Resources Defense Council on-line resource, *Healthy Milk, Healthy Baby. Chemicals: Hexachlorocyclohexane*. <http://www.nrdc.org/breastmilk/hch.asp#note2>

¹²² Konishi, Y., K. Kuwabara, S. Hori. 2001. "Continuous Surveillance of Organochlorine Compounds in Human Breast Milk from 1972 to 1998 in Osaka, Japan," *Archives of Environmental Contamination and Toxicology* vol. 40: no. 4: pp. 571-578 as cited in Natural Resources Defense Council on-line resource, *Healthy Milk, Healthy Baby. Chemicals: Hexachlorocyclohexane*.

¹²³ Banerjee, B.D., S.S. Zaidi, S.T. Pasha, D.S. Rawat, B.C. Koner, Q.Z. Hussain. 1997. "Levels of HCH Residues in Human Milk Samples from Delhi, India," *Bulletin of Environmental Contamination and Toxicology* 59: no. 3: pp. 403-406; Sanghi, R., M.K. Pillai, T.R. Jayalekshmi, A. Nair, "Organochlorine and Organophosphorous Pesticide Residues in Breast Milk from Bhopal, Madhya Pradesh, India" *Human and Experimental Toxicology* 22: no. 2 (2003): pp. 73-76 as cited in Natural Resources Defense Council on-line resource, *Healthy Milk, Healthy Baby. Chemicals: Hexachlorocyclohexane*.

¹²⁴ EPA Memorandum: Lindane—Report of the FQPA Safety Factor Committee. August 2000: p 3.

¹²⁵ National Institute for Occupational Safety and Health/IPCSC/CEC, International Chemical Safety Card: Beta-Hexachlorocyclohexane (ICSC 0796). 1998. See <http://www.cdc.gov/niosh/ipcsneng/neng0796.html>

¹²⁶The International Chemical Safety Card issued by the National Institute for Occupational Safety and Health for alpha-HCH also provides information on acute hazards/symptoms of exposure, first aid recommendations, and routes of exposure (inhalation, dermal exposure and ingestion). The Safety Card identifies effects of short-term exposure as “effects on the central nervous system,” including dizziness, nausea and tremors, and long-term exposure including “effects on the blood and liver.” Alph-HCH is identified as a possible human carcinogen.

¹²⁷In February 2006 US EPA released for public comment a revised risk assessment for lindane that expanded the risk evaluation from lindane only to include other HCH isomers. The “Assessment of Lindane and Other Hexachlorocyclohexane Isomers” examines environmental fate and human health risk from exposure to alpha- and beta-HCH.

¹²⁸ In April 2000, the Sound Management of Chemicals Working Group of the North American Commission on Environmental Cooperation submitted their conclusions that lindane and other HCH isomers “pose risk to humans and wildlife” in North America (see http://www.cec.org/pubs_docs/documents/index.cfm?varlan=english&ID=1032). The Working Group “acknowledged that lindane is of regional concern and that there would be real benefits obtained from collective action in the development and implementation of a *North American Regional Action Plan on Lindane*.”

“Following these recommendations, in July 2002, the CEC Council of Ministers issued Resolution 02-07 directing the SMOG Working Group to develop a NARAP on lindane. Further information is available at: www.cec.org/programs_projects/pollutants_health/smoc/.” The final NARAP was released in November 2006 after a three year process of development and consultation through the Lindane Task Force.

(g) Status of the chemical under international conventions

The Convention on Long Range Transboundary Air Pollution (LRTAP)

¹²⁹ The UNECE Convention on Long-Range Transboundary Air Pollution focuses on a list of 16 substances that have been singled out according to agreed risk criteria. The Protocol severely restricts the use of DDT, HCH (including lindane) and PCBs. The Protocol includes provisions for dealing with the wastes of products that will be banned. As of Jan 26, 2007 there are 36 signatories to this protocol.

¹³⁰The 16 substances as POPs in this Convention include: aldrin, chlordane, chlordecone, DDT, dieldrin, endrin, heptachlor, hexachlorobenzene (HCB), **hexachlorocyclohexane (HCH)**, mirex, toxaphene, polychlorinated biphenyls (PCBs), hexabrominated biphenyls (HBBs),

¹²⁶ National Institute for Occupational Safety and Health/IPCS/CEC, International Chemical Safety Card: Alph-Hexachlorocyclohexane (ICSC 0795). 1998. <http://www.cdc.gov/niosh/ipcsneng/neng0795.html>.

¹²⁷ US Environmental Protection Agency, Office of Prevention, Pesticides and Toxic Substances, Assessment of Lindane and Other Hexachlorocyclohexane Isomers. Feb 2006.

¹²⁸ Ibid.

¹²⁹ United Nations Economic Commission for Europe. Convention on Long-Range Transboundary Air Pollution. Protocol on Persistent Organic Pollutants (POPs). http://www.unece.org/env/lrtap/pops_h1.htm

¹³⁰ European Environmental Agency. 2000. Kiev Report- Final draft Chapter- Chemicals. Accessed at <http://www.unece.org/env/europe/kyiv/chemicals.pdf>

polychlorinated dibenzodioxins and the related furans – known collectively as dioxins - and polyaromatic hydrocarbons (PAHs).

¹³¹In the case of technical HCH (containing a mixture of HCH isomers), parties of the LRTAP are required to restrict use to chemical manufacture. In the case of products where one of the isomers, the gamma form, is the major constituent (at least 99%), which includes Lindane, parties are required to restrict uses to a range of agricultural and public health applications detailed in Annex II of the Convention.

North American Regional Action Plan on Lindane

¹³²The 2006 North American Regional Action Plan for Lindane, developed under the Sound Management of Chemicals working group of the trinational Commission on Environmental Cooperation, identifies lindane as a priority chemical in the North American region and outlines a series of steps to be taken by the three governments in the region to minimize the public health and environmental risks posed by continued lindane use. Over the course of the Action Plan's development, the government of Mexico agreed to eliminate all uses of lindane, the Canadian government maintained its ban on agricultural uses, and the United States eliminated all remaining agricultural uses of lindane. Pharmaceutical use for lice and scabies control continues in both the United States and Canada.

¹³¹ UNECE, op.cit.

¹³² Commission for Environmental Cooperation. The North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane (HCH) Isomers. November 2006.