

## リンデンの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
<p><b>【生分解性】</b> 非常に遅い。実験室の好氣的条件下の土壤中では半減期は 980 日。嫌氣的条件下ではより速く分解が進行。</p> <p><b>【光分解性】</b> 光に対しては安定。</p> <p><b>【加水分解性】</b> ・半減期は 92-3090 時間。pH 5、pH 7 において安定であり半減期は 732 日。pH 9 における半減期は 43-182 日。海水中では pH 8 (20°C) で 1.1 年。pH 7.6 (5°C) のヒューロン湖で 42 年。pH 8 (0°C) の北極で 110 年など様々な推定値・算出値が報告されている。</p> <p><b>【半減期】</b> ・大気中: OH ラジカルとの気相反応の速度定数に基づく推定値は 2-3 日。対流圏での寿命は 7 日と推定。熱帯地域での対流圏寿命は 13 日と推定。Brubaker and Hites は大気中での寿命を 96 日と推定。 ・水中: 河水では 30-300 日。湖水では 3-30 日。 ・土壌中: 2-3 年。</p>	<p><b>【BCF(経鰓的生物濃縮係数)】</b> ・水生生物: BCF=10-6000 (実験室)。BCF=10-2600 (環境中)。BCF=3-36 (Berny)。BCF=43-4220 (湿重量ベース)。BCF=11,000、1200-2100 (脂質ベース) ・イビ: logBCF=2.26(脂質ベース)。ニジマス: logBCF=3.85(脂質ベース)。動物プランクトン: logBCF=4.3。無脊椎生物の平均 log BCF=2.28。脊椎生物の平均 log BCF=2.87</p> <p><b>【BAF(経鰓及び経口による生物濃縮係数)】</b> ・ニジマス: logBAF=4.1 ・無脊椎生物の平均 log BAF=2.94。 ・脊椎生物の平均 log BAF=3.80。肉部分で 780、内臓部分で 2500、全魚体で 1400 という報告がある。</p> <p>・海洋哺乳類のリンデンの濃度は、より疎水性の PCB や DDT と同等か又はより高レベルである。</p>	<p><b>【慢性毒性】</b> ラット(混餌): 7mg/kg/day で肝臓壊死(38 週)、肝臓肥大(104 週)</p> <p><b>【生殖毒性】</b> ウサギ(3 日/週で 12 週): 0.8mg/kg/day で排卵率低下 ラット(5 日): 6mg/kg/day(♂)で精子数減少 ラット(90 日): 75mg/kg/day(♂)で生殖器萎縮、精子形成能かく乱 ラット(妊娠 15 日単回): 30 mg/kg/day で雄児性行動変化、テストステロン濃度低下 マウス(妊娠 12 日単回): 30 mg/kg/day で胎児の胸腺、胎盤重量低値 ラット(生殖試験: 12 週暴露): 1.7uM で成長速度低下、精子数減少、テストステロン濃度低下</p> <p><b>【発がん性】</b> 「発がん性を示す科学的根拠が示唆されるが、潜在的な発がん性を評価するには科学的根拠が不十分な物質」に分類(US EPA)</p> <p><b>【その他】</b> リンデン含有殺虫剤摂取で人に発作瘡</p>	<p><b>【慢性毒性】</b> 淡水魚 : NOAEC=0.0029 mg/L(幼魚の生育低下) 水生無脊椎動物 : NOAEC=0.054mg/L(生殖能低下)</p> <p>カエル : 0.0001 mg/Lで統計学的に有意な性比影響(71%雄)、エストロゲン活性の誘導、精子のプロゲステロン応答性変化。試験管内試験において、ビテロゲニン及びエストロゲン受容体の発現誘導。</p> <p>無脊椎動物 : 35日間試験 LOAEL=0.0135 mg/L(生殖能及び個体数への影響)</p> <p>ニワトリ及びニホンウズラ : それぞれ 100及び25 ppmで孵化率低下。</p>

		攣など神経毒性、実験動物で免疫抑制 や抗体反応抑制など	
--	--	--------------------------------	--



Distr.: General  
21 November 2006

Original: English



**United Nations  
Environment  
Programme**

---

**Stockholm Convention on Persistent Organic Pollutants  
Persistent Organic Pollutants Review Committee  
Second meeting  
Geneva, 6–10 November 2006**

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

### **Addendum**

#### **Risk profile on lindane**

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

# **LINDANE**

## **RISK PROFILE**

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

**November 2006**

## CONTENTS

Executive summary.....	4
1. Introduction .....	5
1.1 Chemical identity .....	5
1.2 Conclusion of the Review Committee regarding Annex D information.....	6
1.3 Data sources .....	6
1.4 Status of the chemical under international conventions.....	8
2. Summary information relevant to the risk profile .....	9
2.1 Sources .....	9
a) Production, trade, stockpiles .....	9
b) Uses.....	10
c) Releases to the environment.....	11
2.2 Environmental fate .....	11
2.2.1 Persistence.....	11
2.2.2 Bioaccumulation .....	12
2.2.3 Potential for long-range environmental transport .....	13
a) Isomerization.....	14
b) Environmental monitoring data.....	14
2.3 Exposure.....	15
2.4 Hazard assessment for endpoints of concern .....	17
3. Synthesis of information.....	19
4. Concluding statement .....	20
Acknowledgements.....	21
References.....	21

## Executive summary

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

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

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

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

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

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

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

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

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

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

## 1. Introduction

### 1.1 Chemical identity

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

Lindane: gamma-hexachlorocyclohexane

Chemical formula: C<sub>6</sub>H<sub>6</sub>Cl<sub>6</sub>

CAS number: 58-89-9

Molecular weight: 290.83

#### Physical and Chemical properties of gamma-HCH

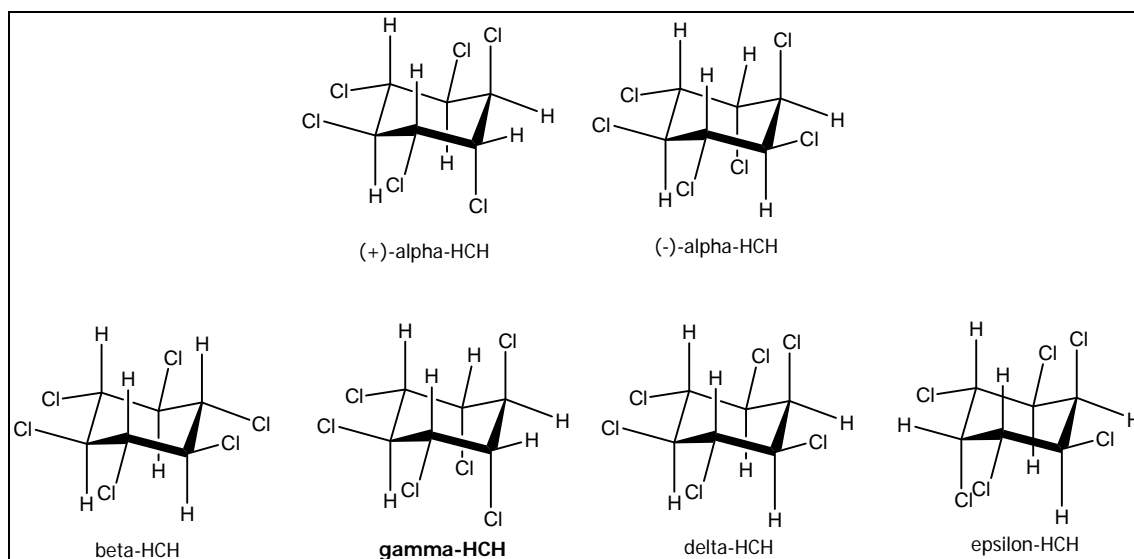
Physical state	Crystalline solid
Melting point	112.5 °C
Boiling point at 760 mmHg	323.4 °C
Vapor pressure at 20°C	4.2x10 <sup>-5</sup> mmHg
Henry's Law constant at 25°C	3.5x10 <sup>-6</sup> atm m <sup>3</sup> /mol

ATSDR, 2005

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

<sup>1</sup> UNEP/POPS/POPRC.1/8 and UNEP/POPS/POPRC.1/INF/8

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



Modified from Buser et al., 1995.

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

### 1.2 Conclusion of the Review Committee regarding Annex D information

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

### 1.3 Data sources

Data sources provided by the proposing party, Mexico:

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

<sup>2</sup> UNEP/POPS/POPRC.1/10



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

Data sources used by the Committee:

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

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

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

- Assessment of Lindane and other Hexachlorocyclohexane Isomers. USEPA. February 2006  
<http://www.epa.gov/fedrgstr/EPA-PEST/2006/February/Day-08/p1103.htm>
- Toxicological Profile for Hexachlorocyclohexane, Agency for Toxic Substances and Disease Registry, US Department of Health and Human Services, updated in 2005.  
<http://www.atsdr.cdc.gov/toxprofiles/tp43.html>
- USEPA Reregistration Eligibility Decision (RED) for Lindane. 2002. See RED and supporting health and eco assessments included in the docket.  
[http://www.epa.gov/oppsrrd1/REDS/lindane\\_red.pdf](http://www.epa.gov/oppsrrd1/REDS/lindane_red.pdf)
- The North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane (HCH) Isomers. Draft for Public Comment. October 2005. North

American Commission for Environmental Cooperation  
[http://www.cec.org/files/PDF/POLLUTANTS/Lindane-NARAP-Public-Comment\\_en.pdf](http://www.cec.org/files/PDF/POLLUTANTS/Lindane-NARAP-Public-Comment_en.pdf)

- Health risks of persistent organic pollutants from long-range transboundary air pollution, Joint WHO/convention task force on the health aspects of air pollution. WHO/Europe. 2003. Chapter 3: Chapter 3/ Hexachlorocyclohexanes  
<http://www.euro.who.int/Document/e78963.pdf>
- Technical Review Report on Lindane. Reports on Substances Scheduled for Re-assessments Under the UNECE POPs Protocol. Prepared by Austria in 2004 (available: [http://www.unece.org/env/popsxg/docs/2004/Dossier\\_Lindane.pdf](http://www.unece.org/env/popsxg/docs/2004/Dossier_Lindane.pdf))
- IPCS International Programme on Chemical Safety. Health and Safety Guide No. 54 LINDANE (Gamma-HCH) HEALTH AND SAFETY GUIDE. United Nations Environment Programme. International Labour Organisation. World Health Organization. Geneva, 1991. <http://www.inchem.org/documents/hsg/hsg/hsg054.htm>

#### 1.4 Status of the chemical under international conventions

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

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

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

<sup>3</sup>Convention on Long-range Transboundary Air Pollution <http://www.unece.org/env/lrtap/>

<sup>4</sup> Rotterdam Convention <http://www.pic.int>.

<sup>5</sup> OSPAR Convention for the Protection of the Marine Environment of the Northeast Atlantic. <http://www.ospar.org/>

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

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

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

## 2. Summary information relevant to the risk profile

### 2.1 Sources

#### a) Production, trade, stockpiles

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

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

<sup>6</sup> Great Lakes Binational Toxics Strategy <http://www.epa.gov/glnpo/gls/index.html>

<sup>7</sup> European Union Water Framework Directive [http://ec.europa.eu/environment/water/water-framework/index\\_en.html](http://ec.europa.eu/environment/water/water-framework/index_en.html)

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

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

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

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

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

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

## **b) Uses**

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

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

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

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

### **c) Releases to the environment**

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

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

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

## **2.2 Environmental fate**

### **Persistence**

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

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

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

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

### **Bioaccumulation**

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

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

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

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

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

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

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

### **Potential for long-range environmental transport**

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

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

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

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

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

#### **a) Isomerization**

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

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

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

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

#### **b) Environmental monitoring data**

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

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



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

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

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

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

### **2.3 Exposure**

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

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

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

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

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

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

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

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

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

## 2.4 Hazard assessment for endpoints of concern

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

### **3. Synthesis of information**

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

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

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

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

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

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

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

#### **4. Concluding statement**

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

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

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

### Acknowledgements

We are grateful to Jon Arnot and Don Mackay (Trent University), Frank Wania (University of Toronto), Janice Jensen (USEPA), John Vijgen (IHPA) for communications and helpful information provided to support the preparation of this document. We are particularly grateful to Terry Bidleman, Senior Research Scientist, Centre for Atmospheric Research Experiments, Environment Canada who provided the document presented as **UNEP/POPS/POPRC.2/INF.18** on “*Isomerization of lindane*”.

### References

- Arctic Monitoring and Assessment Programme. 2002. Norway.
- ATSDR, 2005. Toxicological Profile for Hexachlorocyclohexanes, U.S. Department of Health & Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, August, 2005. <http://www.atsdr.cdc.gov/toxprofiles/tp43.html>
- Australia, 2006. Format for submitting pursuant to Article 8 of the Stockholm Convention the information specified in Annex E of the Convention. January 2006.
- Bailey, R., Barrie, L., Halsall, C., Fellin, P., Muir, D. 2000. Atmospheric organochlorine pesticides in the western Canadian Arctic: Evidence of transpacific transport. *Journal of Geophysical Research*. 105:11805-11811.
- Ballschmiter, K., Wittlinger, R. 1991. Interhemispheric exchange of HCH, hexachlorobenzene, polychlorobiphenyls and 1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane in the lower troposphere. *Environmental Science and Technology*. 25:1103-1111.
- Berny, Ph., Lachaux, O., Buronfosse, T., Mazallon, M., Gillet, C. 2002. Zebra Mussels (*Dreissena polymorpha*), as Indicators of Freshwater Contamination with Lindane. *Environmental Research, Section A*.90:142-151.
- Bidleman, T., Walla, M., Roura, R., Carr, E., Schmidt, S. 1993. Organochlorine pesticides in the atmosphere of the Southern Ocean and Antarctica, January - March, 1990. *Marine Pollution Bulletin*. 26:258-262.
- Buser, H.F.; Müller M. 1995. Isomer and Enantioselective Degradation of Hexachlorocyclohexane Isomers in Sewage Sludge under Anaerobic Conditions. *Environmental Science and Technology*.. 29:664-672.
- Brock, T.C.M., R.P.A. van Wijngaarden & G.J. van Geest. 2000. Ecological risks of pesticides in freshwater ecosystems; Part 2: insecticides. 142 pp.
- Brubaker, W.W., Hites, R.A. 1998. *Environmental Science and Technology* 32: 766–769.

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

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

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

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

CEC, 2005. Commission for Environmental Cooperation. The North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane (HCH) Isomers. Draft for public comment dated 5 October 2005.

[http://www.cec.org/pubs\\_docs/documents/index.cfm?varlan=english&ID=1821](http://www.cec.org/pubs_docs/documents/index.cfm?varlan=english&ID=1821)

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

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

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

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

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

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

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

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

IHPA. 2006. The Legacy of Lindane HCH Isomer Production. A global Overview of residue Management, Formulation and Disposal. International HCH & Pesticides Association [www.ihpa.info](http://www.ihpa.info)



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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

UNEP/POPS/POPRC.1/8

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

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

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

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

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

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

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

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

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

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

---