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**Decision Document on *Lindane*
Under the Process for Identifying Candidate Substances
for Regional Action under
the Sound Management of Chemicals Initiative**

**Prepared by
The Substance Selection Task Force
for the Sound Management of Chemicals Working Group**

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Preface

This Decision Document is the main deliverable for the third stage in the *Process for Identifying Candidate Substances for Regional Action under the Sound Management of Chemicals Initiative* (Substance Selection Process). Its objectives are to:

1. provide a recommendation to the North American Working Group for the Sound Management of Chemicals (SMOC Working Group) regarding a possible North American Regional Action Plan (NARAP) for lindane;
2. review the results of the Substance Selection Process for lindane;
3. identify issues related to major NARAP implementation considerations; and
4. provide recommendations on the possible scope of a NARAP for lindane .

The Substance Selection Task Force (SSTF), a subsidiary body of the SMOC Working Group, administers the Substance Selection Process. Its mandate is to review substances as possible candidates for NARAPs to be developed by the three Governments of Canada, the United Mexican States, and the United States of America. The SSTF consists of two members from each of the Parties and one observer each from the ENGO, industry and academic sectors.

The SMOC Working Group is the principal body responsible for administering the Sound Management of Chemicals (SMOC) initiative. The SMOC initiative and the Working Group were established by the Commission for Environmental Cooperation (CEC), Council Resolution #95-5, Sound Management of Chemicals.

Council Resolution #95-5 was developed under the authority of the North American Agreement on Environmental Cooperation (NAAEC) and advances many of the commitments and obligations set out in the NAAEC. The Council (of Ministers) is the governing body of the Commission for Environmental Cooperation (CEC). The Commission was established as part of the North American Agreement on Environmental Cooperation. The Council of the Commission for Environmental Cooperation approved Council Resolution #95-5 on October 13, 1995, at its second regular meeting which was held in Oaxaca, Mexico.

A key focus of the SMOC initiative to-date has been the development of NARAPs for persistent and toxic substances that the Parties agree warrant collective regional action because they pose a significant risk to human health and the North American environment. The NARAPs reflect a shared commitment by the Parties to work cooperatively to build on domestic policies and laws, improve domestic capacities, and bring a regional perspective to the implementation of international environmental commitments that are in place or being negotiated to address persistent and toxic substances.

Each NARAP is necessarily unique resulting from the need to reflect differing circumstances for each Party, including production, use, and disposal practices for substances; natural endowments, climatic and geographical conditions; and economic, technological and infrastructure capabilities. The sharing and transfer of information and best practices to enhance national capacity for the

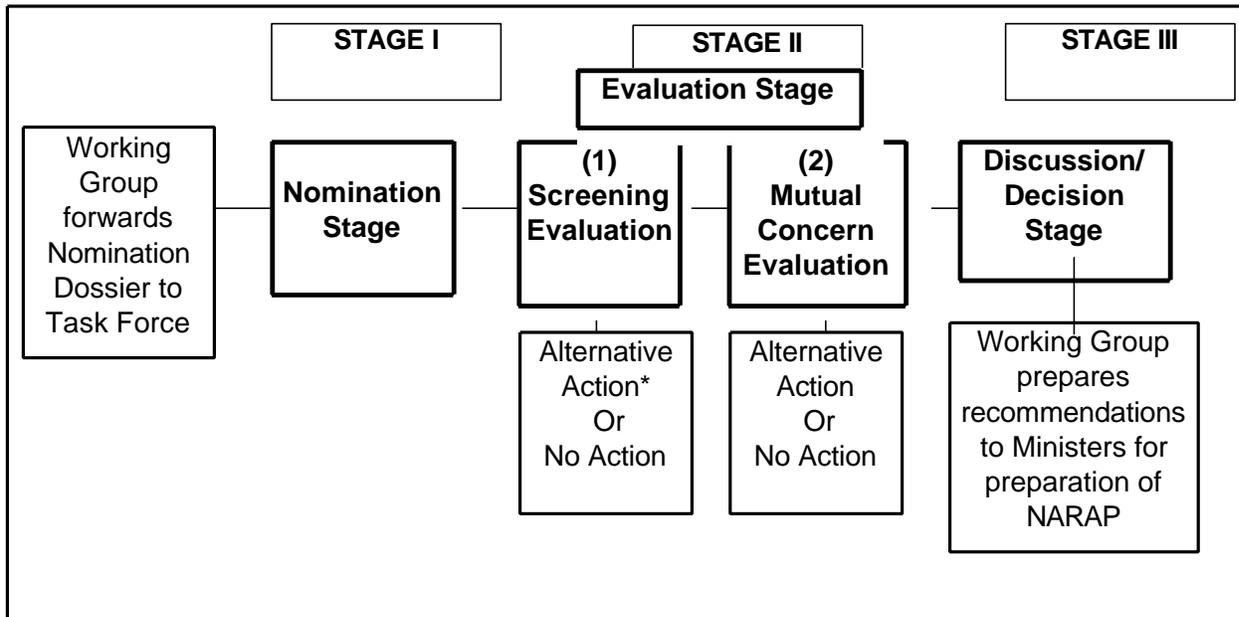
sound management of chemicals has been one common theme for NARAPs. To-date, NARAPs have been established for DDT, chlordane, mercury and PCBs.

The SMOC Working Group established the Substance Selection Process to facilitate systematic, rigorous and transparent consideration of substances to possibly be addressed by additional NARAPs. The process has three stages:

- (i) A *Nomination Stage* (Stage I) involving review of a Nomination Dossier prepared by one or more of the three Parties and referred to the SSTF by the SMOC Working Group. The Nomination Dossier contains standardized information for each nominated substance. The purpose of the review is to assess whether there is justification for the nominated substance to proceed to the next stage of the Substance Selection Process;
- (ii) An *Evaluation Stage* (Stage II) consisting of two parts. First, a *Screening Evaluation* to assess whether a substance deserves further attention on the basis of scientific considerations, including evidence of entrance to the environment, transboundary environmental movement, persistence, bioavailability and bioaccumulation, and that a credible risk assessment documents exists. Second, a *Mutual Concern Evaluation* to determine the degree to which all Parties agree there is a problem and that there would be real benefits from collective action;
- (iii) A *Decision Stage* (Stage III) in which a Draft Decision Document is prepared recommending a course of action to the Working Group for the nominated substance. The recommendation could be: 1) for the development of a NARAP, 2) for alternative action, or 3) for no action. The NARAP will also identify issues related to key implementation considerations.

The SMOC Working Group referred four Nomination Dossiers to the SSTF on 21 May, 1998: Dioxins and furans, hexachlorobenzene (HCB), lindane, and lead. This Decision Document is on lindane.

Figure 1: Flow Diagram of the Substance Selection Process



Executive Summary

The main conclusion of this Decision Document on Lindane is the recommendation for the development of a North American Regional Action Plan (NARAP) to be prepared under the Sound Management of Chemicals (SMOC) Program initiative. On January 15, 1999, the United States submitted a Nomination Dossier for Lindane. It provided the necessary rationale and background information to justify lindane be taken to the next stages of the Substance Selection Process, the Evaluation Stage. The outcome of the Evaluation Stage showed lindane deserves further consideration in the Substance Selection Process, and all Parties agree there is problem and real benefits would result from collective action. Based on this information, the Substance Task Force recommended that a draft Decision Document be prepared for the SMOC Working Group for further consideration in the development of a NARAP on Lindane. The major findings from this Decision Document are summarized below.

Lindane is a persistent organic pollutant (POP) with continued registered use as a pesticide and insecticide in the United States, Canada, and Mexico. It is used in the agricultural sector mainly for seed treatment for protection against insect pests, with minor uses by the veterinary and public health sectors. It is one of the most abundant and pervasive organochlorine insecticide contaminants in the environment. Lindane has been shown to be transported from temperate zones where it is used, to colder northern environments such as the Arctic. It can bioaccumulate to moderately- to highly-toxic levels in biota, wildlife, and humans. A wide variety of toxicological effects are recorded, such as, reproductive and endocrine impairments and can be neurotoxic, immunotoxic, mutagenic, genotoxic, and carcinogenic.

In this Decision Document, numerous benefits were identified in taking coordinated regional action, through the development of a NARAP, to reduce or eliminate the registered uses of lindane. The benefits from the NARAP are expected to be:

- promotes the development of a unified North American position on lindane.
- provides a mechanism for reducing or eliminating non-essential uses in each of the three countries
- encourages sound management practices and Integrated Pest Management approaches within each country by sharing information.
- reduces risk to environmental and human health on a trilateral scale.
- allows for further capacity building initiatives between regulatory agencies between the United States, Canada, and Mexico, and strengthen existing working relationships.
- builds on the experiences and lessons learned in the development of other NARAPs, specifically chlordane and DDT, as this would be the first NARAP developed for a POP actively used in all three countries.
- assists in the development of a Trilateral inventory of current uses and quantities imported and annually used in each country. This information will be pertinent to the development of other SMOC initiatives, in particular, the Environmental Monitoring and Assessment NARAP.

1.0 Principal Recommendation to the SMOC Working Group

We recommend the development of a North American Regional Action Plan (NARAP) on lindane under the *Process for Identifying Candidate Substances for Regional Action under the Sound Management of Chemicals Initiative* (Substance Selection Process). We believe a problem exists and real benefits would be derived from collective action in the development of a NARAP.

2.0 Review of the Results of the Substance Selection Process

2.1 Nomination

In January of 1999, the United States submitted a Nomination Dossier as a working document. It is not an official governmental or CEC document. The final conclusion of the Nomination Dossier was that lindane proceed to the next stage of the Substance Selection Process; The Evaluation Stage.

2.2 Summary Screening Evaluation - Stage II (1)

Considering the following arguments, the Substance Selection Task Force members agreed lindane met the criteria for Stage II(1):

Criterion (i) *'may enter', 'is entering' or 'has entered' the North American ecosystem (emissions, media, biota).* There was consensus that this criterion was met for all three countries.

Criterion (ii) *'available and acceptable risk assessment(s).'* There are Canadian, American, and other international documents that endorse lindane as a substance of trinational concern.

Criterion (iii) *'judgment on measured/predictive data based on the following: bioaccumulation, persistence, and bioavailable.'* There was consensus that adequate evidence exists for lindane being bioaccumulative and persistent.

Criterion (iv) *monitoring evidence of transboundary environmental transport for persistent organic pollutants (POPs) (e.g., appearance in biota, OR indirect evidence of transport potential, such as, air persistence > 2 days; and volatility ≥ 1000 Pa for POPs).* The Nomination Dossier (1999) sufficiently demonstrated long-range transport has occurs and this criterion has been met. Table 1 below provides a list of lindane's physicochemical properties that support the results of the Summary Screening Evaluation. On the basis of all information provided, all Parties agree that lindane poses significant environmental risks, and that real benefits would be obtained from the development of a Decision Document.

2.3 Physicochemical Properties of Lindane

Lindane is the common name of the γ -HCH, one of eight stereoisomers of 1,2,3,4,5,6-hexachlorocyclohexane ($C_6H_6Cl_6$) with a molecular weight of 290.83 grams. It is a white crystalline solid (CAS No. 58-89-9) which is stable in light, heat, air, carbon dioxide, and strong acids. HCH isomers are produced by photochemical chlorination of benzene, resulting in a product called Technical HCH (CAS No. 608-73-1). Technical HCH is mainly made-up of five HCH isomers; α -HCH (53-70%), β -HCH (3-14%), γ -HCH (11-18%), δ -HCH (6-10%), and ϵ -HCH (3-5%) [Howard 1989]. γ -HCH was first used in the 1940's as an efficient and effective insecticide. Pure lindane ($\geq 99\%$) is concentrated by treating HCH-isomer mixtures with methanol or acetic acid, and crystallizing. Even pure "lindane" contains small amounts of other HCH isomers. Lindane is not manufactured in Canada or the United States. It is however imported and used in formulation processes. Mexico produces and manufactures lindane, and imports Technical HCH [obtained from Dr. Victor Hugo Borja, Director, *Centro Nacional de Salud Ambiental*, January 2000].

The physicochemical properties of lindane (γ -HCH) and two other HCH isomers (α - and β -HCH) commonly found in the environment are summarized in Table 1. Lindane has a melting point of 112 °C, and a boiling point of 323.4 °C. A vapor pressure (VP) of 3.83×10^{-3} Pa and water solubility of 2.57×10^{-2} mol m⁻³ results in a Henry's Law Constant (H_c) of 0.149 Pa m³ mol⁻¹ at 20 °C. Lindane has a log octanol-water partition coefficient (Log K_{ow}) of 3.5, indicating its potential to bioaccumulate in the lipids of organisms. In field experiments, a bioaccumulation factor (BAF) of 4.1 and bioconcentration factor (BCFs) between 2.26 and 3.85 were recorded. It is persistent in water and resistant to biodegradation (water $t_{1/2}$ of 30 to 300 d). A soil half-life is estimated to be about 2 yr with a soil-sorption coefficient (K_{oc}) of 3.0. Lindane is also persistent in the air ($t_{1/2}$ of 2.3 to 13 d) with an estimated residence time of 17 weeks [Mackay *et al.* 1997]. Lindane and other HCH isomers in vapor form also appear to react with photochemically produced hydroxyl radicals, with a half-life of ≥ 2 days, at $5 \times 10^{+5}$ [OH]/cm³ [Atkinson 1987]. These properties enhance lindane's persistence, volatilization, long-range transport, wide-spread distribution, and its potential to bioaccumulate in the fatty tissues of living organisms to toxic levels.

2.4 Summary of the Mutual Concern Evaluation – Stage II(2)

2.4.1 Nature and Extent of Risk to Human Health or The Environment in North America

Lindane is a persistent organic pollutant (POP). Throughout North America there is a shared concern as a result of its ongoing use, potential for release and transformation, long-range transport, widespread distribution, potential to bioaccumulate, and impact on humans and the environment.

Table 1. Physicochemical Properties for Lindane (γ -HCH), and α - and β -HCH. Blank values represent no data; water solubility (C_s), vapor pressure (VP), octanol-water partition coefficient (K_{ow}), soil sorption coefficient (K_{oc}), Henry's Law Constant (H_c), half-life ($t_{1/2}$), bioaccumulation factor (BAF), bioconcentration factor (BCF).

	Levels of Concern ¹	Lindane (γ -HCH) ²	α -HCH ²	β -HCH ²
Melting Point (°C)		112.5 - 113.5	158	309
Boiling Point (°C)		323.4	288	
Density (g cm ⁻³ @ 20 °C)		1.87		
C_s (mg L ⁻¹ @ 20 °C)		7.3	10.1	0.7-5.0
VP (Pa @ 20 °C)	≤ 1000 Pa	0.00383	0.00333-0.084	3.73-4.90 x 10 ⁻⁵
H_c (Pa · m ³ mol ⁻¹ @ 20 °C)		0.149	0.87	0.116
log K_{ow}	≥ 5	3.5	3.8	3.8-4.2
log K_{oc}		2.38 - 3.52	3.25-4.10	3.36-3.98
air ($t_{1/2}$)	≥ 2 d	2.3 - 13 d	4 yr ³	
water ($t_{1/2}$)	≥ 6 months	30 - 300 d	11.5 yr ⁴	
sediment ($t_{1/2}$)	≥ 1 yr			
soil ($t_{1/2}$)	≥ 6 months	2 yr		
log BAF	≥ 3.7	4.1		
log BCF	≥ 3.7	2.26 - 3.85	1.93-3.38	2.66-3.08

1. Level of Concern values were selected by the Substance Selection Task Force on the basis of the results of a literature review.

2. Quoted by Mackay *et al.* (1997)

3. Model prediction for Arctic atmosphere [Wania and Mackay 1999]

4. Model prediction for Arctic Ocean [Wania and Mackay 1999]

Lindane is used as an insecticide and pesticide with contact, stomach, and respiratory effects on a broad spectrum of crop and crop seed insects, public health pests (i.e., flies, scabies, lice, scorpions, and bed bugs) and animal ectoparasites (i.e., fleas, ticks, horn flies, and ring worms) [Mackay et al. 1997].

Currently, lindane has registered uses as a pesticide and insecticide in the United States, Canada, and Mexico. In Canada, lindane is used predominantly in agriculture as a seed or soil treatment to protect crops against insect pests such as wireworms and flea beetles. These uses are summarized in Appendix A. At present, the only above ground uses of lindane permitted in Canada are limited to veterinary and public health uses as summarized in Table 2. All registered uses for seed treatment in the United States are listed in Table 2. Mexico also provided a list of current uses in the agriculture and public health sectors.

Table 2. Currently Registered Uses of Lindane in Canada, the United States, and Mexico.

<u>Seed Treatment:</u>	
Canada	barley, beans, broccoli, Brussels sprouts, cereal, cabbage, cauliflower, corn, flax, mustard, oats, peas, rutabaga, rye, soybeans, storage seed, and wheat
United States	barley, broccoli, Brussels sprouts, cabbage, cauliflower, celery, corn, collards, lettuce, kale, kohlrabi, mustard greens, oats, radishes, rye, sorghum, Swiss chard, spinach, and wheat
Mexico ¹	agricultural uses, such as, oats, barley, bean, sorghum and wheat
<u>Other Uses:</u>	
Canada	fruit and vegetable crops, tobacco, ornamentals, green house soil, flowering and herbaceous plants, lawn, veterinary uses (two products), forestry (spruce, pine, and tree), around industrial and residential buildings, and in shampoo to treat head lice and scabies
United States	public health uses
Mexico ¹	public health uses such as lice, scabies, and scorpions

1. Information from Dr. Victor Hugo Borja, Director, *Centro Nacional de Salud Ambiental*, personal communication, December 1999.

In the United States, estimates of annual usage of lindane between 1980 and 1990 show a decrease from 268 to 114 tonnes/yr (Table 3). During this same time period, Canada's usage increased from 200 to 284 tonnes/year, and Mexico's from 23 to 261 tonnes/year. The total global usage of lindane was estimated by Li *et al.* (1996) to be 11,900 tonnes in 1980, and 8,400 tonnes in 1990. From Table 3, it can be calculated for 1990 that the United States, Canada, and Mexico used 9% of the total global use of lindane.

Table 3. Estimated annual usage of lindane, on a tonnes/year basis, in 1980 and 1990 for the United States, Canada, Mexico, and Cumulative Global Use [Li *et al.* 1996].

	1980	1990
γ -HCH		
United States	268	114
Canada	200	284
Mexico	23	261
Global Usage	11,900	8,400

Estimates from Environment Canada data show the prairie provinces used 455 tonnes of lindane in 1997 and 510 tonnes in 1998 [World Wildlife Fund Canada Study 1999]. These values were

based on calculations of the number of canola seeds planted. The data in their report show that most of the use was in three prairie provinces (Manitoba, Saskatchewan, and Alberta) with minor amounts used in the other provinces (<1% of total Canadian usage). As lindane is no longer used as a seed treatment for canola in Canada (as of December 31, 1999), it is expected that the amounts used will be significantly lower than those reported for 1997 and 1998.

In 1992, the United States used 32 tonnes of lindane for agricultural uses, specifically on pecans (26 tonnes), squash (2.8 tonnes), safflower (1.5 tonnes), sugar beets for sugar (0.97 tonnes) and the rest on lettuce, sweet peppers, melons, cantaloupes, cauliflower, and hot peppers [United States Geological Survey 1992]. This value does not include other uses (i.e., home and public health uses).

2.4.2 Environmental Effects

There is a paucity of evidence on the potential environmental effects of lindane. However, the scientific documentation indicates that lindane bioaccumulates in food webs with a BAF of 4.1 and a BCF between 2.26 to 3.85. Lindane readily accumulates in microorganisms, invertebrates, fish, birds and humans [WHO 1991]. Biotransformation and elimination of lindane is relatively rapid [WHO 1991]. HCH isomers, including lindane, appear to penetrate the blood-brain barrier [Mössner *et al.* 1994]. Bioaccumulation of lindane in the brain tissue of marine mammals had concentrations equal to or exceeding those of more hydrophobic pollutants such as PCBs and DDT [Mössner *et al.* 1994]. The pathways that a contaminant may take on its way to the northern food chain are complex, depending on atmospheric and oceanic circulation, gas/particle partitioning, and food web structure [Barrie *et al.* 1992].

Lindane is not very toxic to bacteria, algae, or protozoa, with a “no-observable adverse effect level” (NOAEL) of 1,000 $\mu\text{g L}^{-1}$ [WHO 1991]. Toxicity for fungi is variable with a NOAEL ranging from 1,000 to 30,000 $\mu\text{g L}^{-1}$, depending on the species [WHO 1991]. A dose of 1000 $\mu\text{g L}^{-1}$ did not adversely affect the reproduction of molluscs [WHO 1991]. Lindane is highly toxic to some aquatic organisms (e.g., some fish and invertebrates). Chronic studies with *Daphnia magna* showed NOAELs in the range of 11 to 19 $\mu\text{g L}^{-1}$. In short-term and long-term studies with three species of fish, the NOAEL was 9 $\mu\text{g L}^{-1}$, and no effect on reproduction was observed at levels between 2.1 to 23.4 $\mu\text{g L}^{-1}$ [WHO 1990]. The concentration that causes death in 50% of a population (LC_{50}) of fish and invertebrates ranged from 20 to 90 $\mu\text{g L}^{-1}$ [WHO 1991]. The LC_{50} value for freshwater and marine crustacea varies from 1 to 1,100 $\mu\text{g L}^{-1}$ [WHO 1991].

The possibility for interconversion of one isomer of HCH to the other in the environment may be an important element to consider in assessing and managing the risks associated with lindane, as the isomers differ in human toxicity and potential for bioaccumulation. In air, γ -HCH is photochemically converted to α -HCH. Both γ -HCH and α -HCH can be biologically transformed to the more persistent β -HCH (CACAR 1997). β -HCH is very recalcitrant under environmental conditions and is much more resistant to biodegradation than the other HCH-isomers [Bachmann *et al.* 1988, Schwarzenbach, *et al.* 1993]. The interconversion is however, confusing and an issue that is still being debated. Transformation rates of lindane to other HCH isomers is largely determined by which environmental media lindane is released into (i.e., water, soil, sediment or air), pH, and by the type and abundance of transforming/biodegrading microbes. It is recommended

in a paper by Walker et al. (1999) that isomerization be considered in any dossier and Regional Action Plans addressing lindane under the Sound Management of Chemicals Program.

2.4.3 Human Health

2.4.3.1 Basic Toxicological Findings in Laboratory Animals

The acute toxicity of lindane has been studied in several animal species using various routes of administration. Lindane appears to have moderate to high acute toxicity in laboratory animals. This was based on the dose that has been calculated to cause death in 50% of several animal species including rats, mice, guinea pigs, dogs, and rabbits. These values range from 55 to 480 mg/kg when administered orally [WHO 1991]. The type of vehicle used in the acute oral toxicity studies (exposure to a chemical for a duration of 14 days or less) had an effect on the level of toxicity observed; oil appeared to be more toxic than aqueous solutions or suspensions. Young animals also appeared to be more sensitive than adults. Acute dermal (LD₅₀) of 900 mg/kg and 200 to 300 mg/kg were reported in rats and rabbits, respectively. An acute 4-hour inhalation (LD₅₀) of 1600 mg/kg was reported in rats [WHO 1991]. Lindane was not shown to be a skin irritant or sensitizer in animal studies, however, mild eye irritation has been observed in rabbits [WHO 1991].

Neurological effects in rats were reported following acute exposure to lindane. The most serious of these effects included seizures following a single gavage exposure of 30 to 60 mg/kg in the rats [ATSDR 1994]. Less serious effects such as increased spontaneous motor behavior at 10 mg/kg and increased rates of kindling acquisition at 3 to 20 mg/kg in rats have also been reported [ATSDR 1994].

Longer-term studies have also been conducted with lindane using several animal species and routes of administration. Rapid breathing, dermal infections, convulsions, and increases in liver and kidney weights have been observed in dermal studies of rabbits exposed to doses ranging from 60 to 400 mg/kg/d [US EPA 1998]. Death and increased liver weights were observed in inhalation studies in mice exposed to 1 to 10 mg/m³ lindane [US EPA 1998]. Signs of general systemic toxicity that included increased liver and kidney weights with associated histopathology, increased thyroid weights, and increased cytochrome P450 activity have been observed in oral studies in rats at doses as low as 10 mg/kg [WHO 1991]. Hematological effects such as, suppression of bone marrow cellularity, erythrocyte precursors, and granulocyte-macrophage progenitor cells were reported in male mice exposed to 20 mg/kg/d of lindane orally [ATSDR 1994]. No hematological effects were noted in beagle dogs exposed to 12.5 or 2.9 mg/kg/d lindane in the diet for 32 or 104 weeks, respectively [ATSDR 1994]. Immuno-suppression was observed in mice fed 0.012 to 1.2 mg/kg/d of lindane for 24 weeks [ATSDR 1994]. Lindane has also produced convulsions in rats given 12 mg/kg for 12 days and changes in several behavioral parameters have been noted in rats given 5 mg/kg lindane for 40 days [WHO 1991]. Other signs of neurotoxicity following exposure to lindane include alterations in operant conditioning in rats exposed to 2.5 mg/kg for 40 days and decreases in nerve conduction velocity in rats exposed to 25.4 mg/kg for 30 days [ATSDR 1994].

Overall, lindane does not appear to be mutagenic; negative results were consistently obtained and the studies that yielded positive results were either flawed or used lindane of unknown purity

[WHO 1991, ATSDR 1994, US EPA 1998].

Developmental toxicity studies on lindane have been conducted in rats, mice, and rabbits orally exposed. In rats, signs of maternal toxicity included decreases in food consumption and body weight gains, and deaths at doses ranging from 10 to 20 mg/kg/d; developmental toxic signs in the offspring included increased incidence of extra ribs at 20 mg/kg/d and increased fetal deaths at 10 mg/kg/d [ATSDR 1994, US EPA 1998]. Fetal deaths and decreased fetal weight were observed in mice exposed to 60 mg/kg [WHO 1991]. Rabbits showed signs of developmental toxicity that included increases in post-implantation loss and increased incidence of resorptions at doses as low as 5 mg/kg/d and increases in the incidence of extra ribs at 20 mg/kg/d [WHO 1991, ATSDR 1994]. Second and third-generation reproductive toxicity studies have been conducted in rats [WHO 1991, ATSDR 1994, US EPA 1998]. Appendix C summarizes the toxicological profiles of α -, β -, γ - and δ -HCH [U.S. Department of Health and Human Services 1997]. At 150 ppm (13 mg/kg/d), second-generation reproductive toxicity studies showed signs of reproductive and developmental toxicity that included; decreases in body weight gain, decreased viability in both generations of offspring, delayed onset and completion of tooth eruption and hair growth in the second generation offspring. No effects on fertility, mating, or gestation were observed. Increased liver weights and enlarged hepatocytes with vacuolization were observed in the third generation offspring fed 50 mg/kg of lindane in the diet over three generations. Doses as high as 100 mg/kg appeared to have no effect on fertility, litter size, breeding rate, offspring body weight, lactation, malformation rate, or maturation. A study in ewes exposed to 1 mg/kg lindane for 5 weeks prior to mating and throughout pregnancy and lactation did not show a marked effect on reproduction or any of the endocrine parameters assessed [Beard *et al.* 1999].

2.4.3.2 Principal Routes of Exposure

Like other organochlorines, the most wide-spread exposure to lindane by the general public is through food. There is an important relationship between meat and fish consumption and lindane concentrations in human milk and body fat [DeVoto 1998, Raum 1998].

The Canadian Arctic Contaminants Assessment Report [CACAR 1997] estimated daily dietary exposure levels for lindane to be 0.03 $\mu\text{g}/\text{kg}$ body weight in Canada and in several other countries. This is well below the acceptable daily intake of 1 $\mu\text{g}/\text{kg}$ body weight estimated by JMPR (1997) and adopted by Canada.

A number of potential lindane-sensitive subpopulations in North America have been identified. First, northern aboriginal populations are particularly at risk given the evidence of high levels of HCH isomers in their diet and that the Arctic is considered a 'sink' for persistent organic pollutants [Kuhnlein *et al.* 1995]. Another population in North America with a potential for chronic exposure is workers who formulate or use lindane. α -, β - and γ -HCHs have been detected in blood serum and adipose tissues of people occupationally exposed to HCH formulations. Another potential route of exposure to lindane by the public includes the use of lindane to treat external parasites such as lice and scabies. In the USA, approximately 2 % of families use lindane pesticides [Information from Keith Chanon, US EPA, personal communication, October 1999. Based on EPA data from 1987 to 1996, USDA/NASS 1990 to 1996, California 1993 to 1995, Technomic Consultants International 1990, USEPA National Home and Garden Pesticide Use Survey 1993, National Center for Food and Agricultural Policy 1992].

2.4.3.3 Human Health Effects

As with the environmental data, there is a lack of consistent human data available on lindane effects. Case studies have indicated that ingestion of very large amounts of lindane can result in convulsions and liver damage. Skin sensitization and allergic reactions can occur after dermal exposure (although patch tests in larger groups of subjects did not reveal any sensitization reactions) [WHO 1991]. Epidemiological studies have provided preliminary evidence of other health effects associated with lindane exposure. One study reported significantly higher luteinizing hormone (LH) levels and slightly lower testosterone levels in male workers than in controls in a lindane manufacturing plant [Tomczak *et al.* 1981]. In another study, women exposed to lindane during pregnancy had babies with significantly reduced birth weights and lengths [Karmaus and Wolf 1995]. An increased risk of non-Hodgkins lymphoma was reported in a case-control study of farmers in Iowa and Minnesota who reported using lindane on crops and animals [Cantor *et al.* 1992]. However, interpretation of these data is difficult. Causality cannot be established in any of these reports due to study limitations such as small sample sizes, concomitant exposures to other pesticides, lack of exposure data, and recall bias.

On the associated health effects, Parkinson's disease is negatively correlated with increased concentrations of lindane in the brain [Fleming *et al.* 1994]. However exposure to insecticides, including lindane, is positively associated (after adjusting for confounders) with low birth weights [Karmaus and Wolf 1995], an increased odds ratio of 1.2 for Non-Hodgkins lymphoma [Cantor *et al.* 1992], a 70% increased risk of Cardiovascular diseases [Flesch-Janys 1997], and reduced neutrophil function [Sliwinski *et al.* 1991]. In addition, lindane is significantly and highly correlated with reduced concentrations of thyroid and estrogen hormones, as well as increased total lymphocytes counts [Tomczak *et al.* 1981, Gehhard *et al.* 1998]. Body burdens of lindane were significantly and highly correlated (approximately 50%) to increased cancer mortality rates [Wang *et al.* 1988]. This is consistent with the decreased rate of breast cancer occurrences observed in Israel after banning lindane use [Westin 1993].

Many cohort studies have been published examining cancer rates in agricultural workers, a high risk activity for exposure to lindane. However, very few of these clearly identified either the differential effects of insecticides and herbicides, or, even less so, the influences of different insecticides [Doich *et al.* 1997]. This generality limits the usefulness of the conclusions in regards to the particular carcinogenic nature of lindane. A few studies indicate an increased risk of lung cancer [Barthel 1981], even when adjusting for smoking [Barthel 1981b], and a 2.7 times increased risk of chronic lymphatic leukemia cancer in males [Hansen *et al.* 1992].

There is some debate over the carcinogenic potential of lindane. In 1987, the International Agency for Research on Cancer (IARC) classified lindane as 'possibly' human carcinogen. The US EPA regulates lindane as group C, possible human carcinogen. Just recently, the EPA completed a final cancer re-assessment on lindane. The results from this second mouse oncogenicity study will be used to determine the re-registration eligibility decision of using lindane as a pesticide (see Appendix B). In addition, the EPA Cancer Science Advisory Review Committee will use this data to reevaluate the carcinogenic potential of lindane.

A recent Joint Meeting of the FAO Panel of Experts on Pesticide Residues (JMPR) in Food and the Environment and the World Health Organization (WHO) Core Assessment Group on Pesticide

Residues reevaluated the toxicity of lindane [FAO and WHO 1998]. The JMPR evaluation concluded that the toxicological effects that are relevant for estimating hazards for humans are those on the liver and central nervous system. Additional data are required to further investigate immunotoxicity effects.

The 1997 meeting established a temporary Acceptable Daily Intake (ADI) ≤ 0.001 mg/kg on the basis of a NOAEL of 0.5 mg/kg/d. This was based on a two-year cancer study on rats and using a safety factor of 500. Pending clarification of the immunotoxicity, this revised ADI provides a 10-fold margin of safety over the Lowest Observed Adverse Effect Level (LOAEL) of 0.012 mg/kg/d in a study of immunotoxicity in mice. A confirmatory study on immunotoxicity is to be provided to the JMPR by 2000. At that time, it has been recommended that the JMPR perform a full re-evaluation to consider all previously reviewed and new information regarding the toxicity of lindane.

US EPA's Office of Pesticide Programs has recently required three new neurotoxicity studies for lindane: an acute neurotoxicity study, a 90-day neurotoxicity study in mammals, and a developmental neurotoxicity study. These studies will be used during the re-registration process for lindane. US EPA established a chronic reference dose (RfD) for lindane using the same study selected for the ADI. Using an uncertainty factor of 100, the RfD was estimated to be 0.0047 mg/kg/d. It should be noted that this uncertainty factor will be re-evaluated during re-registration as required by the amendments to FIFRA (Federal Insecticide, Fungicide, and Rodenticide Act) and FFDCa (Federal Food, Drug and Cosmetic Act) required by the Food Quality Protection Act of 1996.

2.4.3.4 Information on Arctic Populations

Several sources have reported that the Arctic Indigenous Inuit peoples are at the highest risk of exposure and contamination from lindane and other HCH isomers [Kuhnlein *et al.* 1995]. The Arctic is a 'sink' for persistent organic pollutants. Once in the Arctic, lindane, as well as other organochlorines, bioaccumulate in the food web in due to their high lipid solubility. Because lindane concentrates in fatty tissues, people who consume a high fat diet are at a higher risk of lindane exposure. Indigenous Arctic peoples are more dependent on wildlife for food and this may increase their risk due dependence on a "traditional food" diet, such as Arctic seals, whales, fish, caribou, and polar bears [Kuhnlein *et al.* 1995]. Approximately 33% of the HCH contribution to the diet of a group of Sahtu'Dena/Metis women was from the consumption of whitefish, which was only 12% by weight of their diet [CACAR 1997].

2.4.4 Nature and Extent of the Evidence of Transboundary Environmental Transport in North America

There is substantial evidence in support of the long-range transboundary transport of lindane. Foremost, HCH isomers were detected in the Arctic and Antarctic, where lindane and Technical HCH have not been used. Moreover, lindane and other HCH isomers are considered to be the most abundant and persistent organochlorines found in the Arctic atmosphere, marine, terrestrial, and freshwater environments [Northern Contaminants Program 1997]. Levels of HCH isomers in surface sea water are an order of magnitude higher in the Arctic than in tropical and sub-tropical

regions. During winter months, long-range transport of lindane from Eurasia is clearly a dominant source of HCH isomers to Canada's Arctic [Northern Contaminants Program 1997].

Historically, the largest releases of lindane into the air come from agricultural applications. This was seen for the United States and Canada where most of the releases were related to the formulation products and its use as an insecticide and acaricide. Volatilization is rapid as seen with quick half-lives from soil ($t_{1/2}$ of 2-25 d) and plant foliage ($t_{1/2}$ of 0.29-0.73 d). In another study, 54% of the lindane applied to sunflowers and sugar beets volatilized within 24 hours (Neururer and Womastek 1991). Volatilization appears to be an important route of dissipation under the high-temperature conditions of tropical regions [WHO 1991]. Soil-bound lindane can get into the atmosphere by aerial spraying, wind erosion of the soil particulates, or volatilization. Lindane strongly adsorbs to soils with a large amount of organic matter. Water from rainfall or artificial irrigation causes lindane to leach from soils [WHO 1991].

Shindler [1999] identified several factors that enhance the movement of organochlorine pollutants from warmer areas to high altitudes and latitudes. These include climate warming, increased UV, temperature dependent volatility, and greater condensation in colder regions. "Cold-condensation" is a phenomena that occurs in high latitude regions of the world [Wania and Mackay 1996]. During summer months, semi-volatile compounds, like lindane, volatilize from warm locations (i.e., from temperate and tropical countries), travel north by long-range atmospheric transport, and condense in cooler environments [Blais *et al.* 1998]. Blais *et al.* (1998) also noted higher concentrations of lindane and α -HCH with elevation in the Canadian Rocky Mountain. This could explain the surprisingly high levels of chlorinated organic contaminants in fish from high altitudes [Campell 1997]. In addition, Blais *et al.* [1998] measured α/γ ratios between 1.2 and 3.1. These high ratios indicate other sources besides lindane contribute to this ratio. Technical-HCH has α/γ ratio between 4 and 15 and is a likely contributor [Metcalf 1997].

Levels of lindane and α - and β -HCH have been detected in tissues of arctic biota [CACAR 1997]. Since HCH is the predominant organochlorine contaminant in arctic air, this suggests a direct air-plant-animal pathway into the terrestrial food chain. Levels of HCH (mostly the α -isomer) in the fat of Arctic caribou ranged from 3.3 to 40 ng/g (on a lipid basis). A significant increase in HCH levels in biota was observed from west to east in the Canadian Arctic. Low levels of HCH residues (1.0 to 27.8 ng/g wet wt) were found in breast muscle of waterfowl and game birds harvested in northern Canada between 1988-94. HCH isomers were detected in mussels, sea urchins, and benthic amphipods (≤ 5.9 ng/g) sampled from Cambridge Bay in the North West Territories. HCH isomers have also been detected in marine mammals including ringed seal, harp seal, beluga whale, narwhal and walrus at concentrations ranging from 62 to 515 ng/g (wet wt). Marine mammals tend to be high in fat which allows for bioaccumulation of lindane. Marine mammals also comprise a large percentage of Arctic coastal peoples (i.e., Inuit) traditional food diet [CACAR 1997]. HCH levels between 4.8 to 69.5 ng/g (wet wt) were found in eggs of arctic sea birds. HCH residues in whitefish muscle sampled from Lake Laberge in the Yukon declined in the period between 1974 and 1992 as did HCH isomers in burbot liver from fish sampled at Fort Good Hope in the North West Territories from 1986 to 1994.

2.4.5 Degree to Which Human Health or Environmental Benefits in North America Can Be Demonstrated As A Result of Collective Action

Taking action to reduce lindane releases in North America is expected to have numerous health benefits. It is therefore expected that coordinated regional action to reduce or eliminate the registered uses of lindane would contribute to further reductions of lindane levels in the environment and human dietary exposure. As described in the Nomination Dossier for lindane (the gamma isomer of HCH), this persistent organic pollutant (POP) poses risks to humans and wildlife in North America. In the environment, lindane has been detected in air, surface water, groundwater, sediment, soil, and in fish and other organisms. In fact, HCH isomers are the most abundant and pervasive organochlorine insecticide in the Arctic.

Toxicological data indicate that chronic/long term/lifetime exposure to lindane can adversely affect the liver and nervous system of humans, and has the potential to cause cancer and immunosuppression. Workers who use imported lindane to formulate lindane products for sale in North America could have the greatest potential for chronic exposure. The next greatest potential would be those workers who are exposed on a routine basis during the use of these products. Although the general population is widely exposed to lindane through their diet, the levels of exposure may or may not be of concern. Aboriginal and northern populations are particularly at risk given the evidence of high levels of POPs, including lindane, in their diet.

Education and awareness raising programs are needed to target lindane users of the associated local- and long-range problems. There is a need for further information and concerted action on available alternative pest control measures.

3.0 Analysis of Major Implementation Considerations for Lindane

The purpose of this section is to explore a range of considerations that influence the priority and timing for developing and implementing a Regional Action Plan for lindane in North America.

3.1 *Public Health and Environmental Measures Available to Reduce Risk*

For each country, it is important to incorporate an Integrated Pest Management approach that encourages “responsible use” of lindane and other pesticides.

Exchanges of data, information, and monitoring and analytical technologies will be required to reduce remaining scientific uncertainties about the risks of lindane and to develop cost-effective alternatives, and strengthen capacity building efforts on a trinational basis.

As part of the ongoing re-registration efforts for lindane, the United States worked with the technical and end-use registrants to amend labels and registrations for supported uses only.

PMRA has worked with registrants and users to remove uses of lindane in Canada. In particular, PMRA has worked closely with the Canadian canola growers and registrants, and through this cooperation, a successful conclusion to the removal of lindane from canola seed treatments has been accomplished, as of December 31, 1999. With the canola uses gone, only 23 seed treatment products containing lindane remain. Due to work with registrants, the registration of lindane products for veterinary use and soil treatment will be discontinued as of December 31, 2000. All of this demonstrates that the number of allowed uses in Canada have been reduced substantially over the last few years.

More information and use of alternatives can also facilitate risk reduction.

3.2 *Benefits to Human Health and the Environment*

Efforts to reduce or eliminate uses of lindane in North America will reduce occupational exposure and contribute to lower levels in the ambient environment. Coordinated North America action will also provide a useful platform from which to lobby other countries/regions to take action on reducing/eliminating uses of lindane. It has been established that sources from outside North America contribute to levels of lindane in the North America environment.

A benefit of reducing exposure to lindane for all three parties would be a reduction of the risks posed to highly exposed sub-populations, including the chronic exposure of workers who formulate and use lindane, northern aboriginal population, and pregnant women and children. All three parties have sub-populations at higher risk due to contaminated traditional foods, multiple exposure pathways, and higher sensitivity.

Significant benefits can also be obtained through capacity building initiatives, reducing risks and releases, encouraging sound economic decisions and the development of a unified position on lindane. These are expanded below.

3.2.1 Capacity Building Initiatives

Trinational collaboration to develop and implement a NARAP on lindane will further strengthen existing partnerships between the three countries by encouraging:

1. exchange of information, technology transfer (i.e., disposal practices and production processes), and information on alternative practices. At the outset, Mexico may be the principal beneficiary of shared scientific knowledge, and, as a result, may avoid the problems encountered in recent decades by the United States and Canada;
2. the development, promotion, and implementation of Integrated Pest Management (IPM) principles and activities; and
3. a NARAP on lindane that reinforces/builds on experience/lessons learned with chlordane and on going work on DDT.

3.2.2 Reducing Risks

One of the ultimate goals of a NARAP on lindane would be to ultimately reduce the risks associated with lindane in North America. This can be achieved by

1. Controlling releases into the environment; and
2. Encouraging trinational collaboration to further identify and confirm risks to human health and the environment.

3.2.3 Sound Economic Decisions

A NARAP on lindane would promote sound management practices in North America by:

1. Unifying actions across North America;
2. Providing a level playing field for formulators, suppliers, and users of lindane and potential alternative products and approaches;
3. Focusing efforts on uses of lindane that contribute to atmospheric transport;
4. Improving the sharing of information on alternative pest control products and approaches, which help to minimize impacts on growers;
5. Helping to reduce costs associated with human health.

3.2.4 International Obligation (Commitments)

The development and implementation of a NARAP on lindane can further strengthen and build upon our international commitments by:

1. Helping Canada and the United States to meet the requirements of the UN-ECE on Long-Range Transboundary Air Pollution on Persistent Organic Pollutants protocol, including a reassessment of all existing uses of lindane within 2 years of ratification of the protocol, and any future action/commitments that may follow;
2. Helping to ensure that North America has a unified position on lindane.

3.3 *Sustainability of Food Production*

It is unknown if food production in Canada, the United States and Mexico will be affected by lindane reduction initiatives. Currently efficacy studies are being conducted on lindane alternatives. As these alternatives are applied in the same way as lindane, no substantial changes in agricultural practices are expected.

3.4 Feasibility and Availability of Alternatives

Lindane is a broad spectrum insecticide, and over the years a wide range of available and feasible alternative pest control products and practices have been developed to cover many of the original uses. Gaucho is currently registered for use in Canada and the United States as a seed treatment for canola. Helix is currently under review for use on canola in the United States. Canada and the United States are also evaluating for registration other lindane alternatives. Preliminary research is underway by the Canola Growers Association to determine the effectiveness of alternatives (such as Helix, Gaucho, Primer-Z) as seed treatments and to combat disease and insects [Canola Growers Association, personal communication, 1999]. A number of alternatives are currently being tested for their toxicity and effectiveness. The feasibility of using these alternatives remains undetermined.

3.5 Societal Capacity for Change

Lindane is used as an insecticide and pesticide, and as a public health chemical (i.e., head lice and scabies). In Canada, the United States and in Mexico, agricultural and public health uses are regulated under separate authorities. In the United States, the Food and Drug Administration regulates the public health uses, whereas insecticide and pesticide uses are regulated under US EPA. In Canada, under the authority of the *Pest Control Products Act* (PCPA), PMRA is responsible for the regulation of new and registered pesticides, whereas Health Canada is the regulatory agency of public uses.

3.5.1 Canada

In 1972, Canada's manufacturers voluntarily discontinued the production of Technical HCH (65-70% α -HCH) with the understanding that existing stocks would be sold or used [Special Review Announcement 1999]. Effective 7 October 1976, products containing Technical HCH were no longer acceptable for registration, sale or use. Use after this date represents a violation of the Pest Control Products Act.

On 15 March, 1999, PMRA announced a special review of pest control products containing lindane. The target date for the completion of this review is December 2000 [Special Review Announcement - SR99-01]. Lindane is under national and international scrutiny as a result of its persistence, potential for long range transport and widespread occurrence in the environment. Many unanswered questions remain regarding the potential impact on humans and wildlife of the various isomers of lindane found in the environment. The scope of issues surrounding lindane is potentially broad. Initial efforts will examine the chemistry of existing lindane products registered in Canada and the extent to which these products may contribute to levels of various isomers of HCH in the environment. Pending the completion of this special review, the PMRA will not consider use expansions for lindane. In addition, all product registrations will expire 31 December, 1999. All subsequent new products, registration renewals and amended registrations will be for a period not exceeding one year until this special review is complete.

The PMRA has worked with registrants and users to remove uses of lindane in Canada. Through voluntary agreements, lindane has been discontinued as a seed treatment use on canola as of December 31, 1999.

3.5.2 United States

Since 1978, the US EPA requested all products with Technical HCH be replaced with lindane (>99% γ -HCH). The US EPA no longer permits the manufacture, sale or distribution of products containing Technical HCH in the United States. The United States has limited the release of lindane by prohibiting aerial applications and fogger-type applications of the pesticide. More recently, as part of the ongoing re-registration efforts for lindane, the United States has worked with the technical and end-use registrants to amend labels and registrations for supported uses only. The United States registrants of lindane have agreed to voluntarily cancel all uses of except for seed treatments for 19 crops. A list of all canceled uses is summarized in Appendix C. The removal of the foliar and broadcast type applications and uses will limit the amount of lindane used in the United States and hence, the amount available for release into the environment. The formal removal of these 'old' uses should be finalized in 1999, with all affected labels being revised within two years. The EPA OPP Re-Registration Eligibility Decision (RED) for lindane is scheduled for completion in 2000.

3.5.3 Mexico

Between 1980 and 1990, lindane usage in Mexico increased from 23 to 261 tonnes. Imports of lindane into Mexico have decreased from 29.2 tonnes in 1997 to 20.5 tonnes in 1998 [obtained from Dr. Victor Hugo Borja, Director, *Centro Nacional de Salud Ambiental*, personal communication, December 1999].

3.5.4 Capacity for Change

Recent and planned reductions in uses of lindane in the United States demonstrates a capacity to change in order to reduce the risks posed by lindane. Canada's willingness to be the first country to ratify the UNECE's LRTAP also shows a commitment for societal change to reduce persistent organic pollutants (including lindane) from the global pool. Mexico's capacity to change is illustrated by their reduction in the use of certain POPs, such as its annual use of α -HCH from 1,218 tonnes in 1990 to zero-use since 1995 [Li, Yi-Fan, Sept 1999, personal communication].

3.6 Implications and Opportunities for Economy and Trade

Recent lindane imports of 100 to 150 tonnes/year are reported for Canada [Barrie *et. al.* 1992, Willett *et. al.* 1998]. Between 1994 and 1998, annual import of lindane to Mexico ranged from 8.24 to 29.2 tonnes. A summary of lindane imports into Mexico are listed in Table 4 below.

Table 4. Annual import of lindane in Mexico between 1994 and 1998 [Dr. Victor Hugo Borja, Director, *Centro Nacional de Salud Ambiental*, personal communication, December 1999].

Year	Lindane Imported (tonnes)
1994	8.24
1995	20.7
1996	21.1
1997	29.2
1998	20.5

Lindane is not manufactured in Canada or the United States, but continues to be manufactured/produced in Mexico. Since lindane is used in each country, further reduction or elimination or identification of alternatives should stimulate opportunities for economic development and trade.

3.7 National Capacity to Take Action, Available Expertise and Technology

3.7.1 Rationale for trilateral action

The major reasons to take trilateral action to reduce lindane concentrations in the environment include:

1. all three countries use lindane;
2. lindane is subject to long-range atmospheric transport to remote regions of North America;
3. lindane is believed to cross national boundaries in North America;
4. lindane can be detected in foods and other agricultural products that are traded between the three countries;
5. countries would benefit from shared information exchange and experience;
6. countries are now proceeding on various lindane-reduction initiatives that can be pooled for joint consideration and action.

3.7.2 Uncertainties

Another reason to take trilateral action would be to address areas where uncertainties exist, such as identified below:

1. A complete listing of uses, and quantities of lindane imported and used in North America;
2. The relative importance of North American sources to the Arctic; it is believed environmental loadings of HCH isomers vary from east to west, with North American sources more likely to

end up in the eastern Arctic; however, no attempts have been made to quantify this phenomenon;

3. The ability to predict the potential release of lindane from the environment as a result of climate change (i.e., global warming);
4. The need to develop and improve tools and information that quantitatively link emissions to environmental levels and general population exposure;
5. The risks associated with the various uses of lindane, taking into consideration more recent scientific knowledge and toxicology tests currently underway;
6. Further research is warranted to better assess lindane exposure and health effects using a well designed experimental methodology involving multiple cohort studies;
7. A major weakness in the literature is the lack of an effective assessment of exposure in relation to chronic health effects. This is crucial in order to clearly identify historical exposure and its correlation with increased cancer risks;
8. Exposure levels for populations in Mexico;
9. The presence and management of stockpiles of lindane;
10. The impact of HCH isomers released from hazardous waste sites.;
11. The inter-convertibility of lindane to other forms of HCH;
12. Information on low-cost and effective alternatives for lindane uses in Canada, the United States, and Mexico.

3.8 Jurisdictional and Regulatory Opportunities for Change

Lindane is a Level II substance in the Canada-United States Strategy for the Virtual Elimination of Persistent Toxic Substances in the Great Lakes. The United States and Canada are committed to making their best efforts to reduce Level II substances. Growing public concern over Persistent Organic Pollutants creates an opportunity for government to adopt stricter regulatory controls of lindane production, use and disposal. In addition to adopting stricter controls, governments will encourage stakeholders to undertake pollution prevention activities to reduce levels in the environment of those substances nominated jointly by both countries. Governments also recognize the value of strict enforcement of laws and policies regarding lindane.

3.9 International Commitments and Obligations

In June 1998, Canada signed UNECE's Protocol on Long-Range Transboundary Air Pollution on Persistent Organic Pollutants, and was the first country to ratify in December 1998. As Canada is the only country to ratify to date, fifteen more countries need to ratify the Protocol before its' entry into force. In this Protocol, Technical HCH is restricted to use as an intermediate product in chemical manufacturing. Products with at least 99% of γ -HCH are restricted to 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.

US EPA and the PMRA of Health Canada are sharing information regarding the re-registration and reevaluation of lindane through the NAFTA Technical Working Group on Pesticides. There has been an ongoing effort between the two countries to participate in and share registration and re-registration activities and assessments. The ongoing efforts between Canada, the United States, and Mexico to participate and share in registration and re-registration activities have been the result of the work of the NAFTA Technical Working Group on Pesticides.

4.0 Recommendations to the Working Group on the Scope of the North American Regional Action Plan for Lindane

We recommend a North American Regional Action Plan (NARAP) on lindane be prepared under the Sound Management of Chemicals Program initiative. A NARAP on lindane would reinforce and build on the experiences and lessons learned amongst the three countries in the development of NARAP on chlordane and the NARAP underway on DDT.

Lindane is a persistent organic pollutant registered for use as a pesticide in the United States, Canada, and Mexico that poses risks to humans and wildlife. Lindane is one of the most abundant and pervasive organochlorine insecticide contaminants. It is found in environments where it has not been used supporting the belief of long-range atmospheric transport. In the North American environment, lindane has been detected in air, surface water, groundwater, sediment, soil, and biota.

Toxicological data indicate lindane can adversely affect reproduction, nervous, endocrine, and immune systems, and has the potential to cause cancer in humans. Workers who use imported lindane to formulate lindane products for sale in North America could have the greatest potential for chronic exposure. The next greatest potential would be those workers who are exposed on a routine basis during the use of these products. Although the general population is widely exposed to lindane through their diet, the levels of exposure may or may not be of concern. Aboriginal and northern populations are particularly at risk given the evidence of high levels of lindane in their diet.

The development of a NARAP on lindane would assist in taking stock of current uses, along with quantities imported and used annual in each country. This information will be pertinent to the development of other SMOC initiatives, in particular the Environmental Monitoring and Assessment NARAP. The development of a NARAP would provide a mechanism for reducing or eliminating uses in each of the three countries and provide benefits on a trinational scale.

In each country, the public health and insecticide and pesticide uses are regulated under separate authorities. Therefore, it is also recommended that if a NARAP on lindane is developed, that the Task Force include members from both the public health and pesticide and insecticide regulatory agencies from each country. In addition, it is recommended members from industry, non-government organization, science communities be included on the NARAP Task Force. A final recommendation is that country status reports be part of the scope of the NARAP in order to harmonize information gathered on lindane between the three countries, such as the volumes imported, annually usage, and a list of uses in the public health and insecticide and pesticide sectors.

4.1 Potential contribution of NARAP

It is believed a wide-range of potential contributions would result from the development of the NARAP. We have identified the following:

1. The development of an action plan to reduce/eliminate the use of lindane;
2. Building on the work achieved to date with chlordane and DDT;
3. The first NARAP to be developed with a persistent organic pollutant actively used in all three countries (unlike DDT and chlordane);
4. Identify current uses and find ways to reduce those uses or the risks posed by those uses;
5. Identify alternative practices and pest control products;
6. As appropriate, reduce, restrict, substitute, and life-cycle manage the various uses of lindane in North America;
7. Collaborative assessment of risks associated with various uses of lindane;
8. Pollution prevention action (i.e., investigate methods for reducing/eliminating lindane from remaining essential uses);
9. Develop Integrated Pest Management practices/methods that encourages the use of lindane-alternatives and for remaining essential uses of lindane;
10. Ensure a level playing-field in terms of access to alternatives;
11. Further development of partnerships/voluntary initiatives;
12. Capacity building; including information, scientific and technical exchange;
13. Opportunity for this regional approach to be used as a model for cooperative actions by other countries.

4.2 NARAP Elements

It is recommended that the following elements should be considered in a NARAP on lindane:

1. Build upon the format/structure of completed NARAPs on chlordane, dioxins and furans, hexachlorobenzene, and the types of information which were considered in the NARAPs on chlordane and DDT.
2. Append country status reports which include uses, control of imports, and regulatory jurisdictions.

3. Provide actions to improve national capacities to adopt measures to reduce risks to human health and the environment.
4. Include short, medium and long-term risk reduction actions consistent with regional needs and objectives.
5. A strategy to address the financial commitments required by actions proposed in the NARAP.
6. Actions designed to improve the assessment of risk in the three countries by:
 - Updating and completing the regulatory status and uses of lindane for Canada , the United States, and Mexico;
 - Developing a strategy to estimate human and environmental exposures and risks in Mexico; and
 - Sharing expertise and knowledge on analytical capacities among the three countries.
7. Actions designed to analyze and implement risk reduction measures by:
 - Identifying alternatives that have been used in various agricultural sectors to reduce releases of lindane, including a review of the cost potential health effects of alternatives;
 - Ensuring that information on analysis and implementation of risk reduction measures is shared among the three parties; and
 - Based on this review and analysis, developing and implementing measures to reduce risks to human health and the environment, including exploring the effectiveness of voluntary approaches relative to other policy instruments.
8. Actions designed to determine the success of the NARAP, such as:
 - whether or not lindane is still registered for use in the countries;
 - the number of products or uses permitted; and
 - the levels of imports into the three countries.

5.0 Final Recommendations to SMOC

We acknowledge that lindane is a trilateral problem and that there would be real benefits obtained from collective action in the development of a North American Action Plan on Lindane. The NARAP should identify issues related to key implementation considerations.

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7.0 Appendices

Appendix A:
Table 2. Registered End-use Products Containing Lindane in Canada
(as of January 11, 2000).

COMPANY	REG #	PRODUCT NAME	CLASS	USES
To control wireworm (seed treatment):				
AGSCO INC.	14887.00	AGSCO DB-GREEN SEED DISINFECTANT & INSECTICIDE DUST	C*	BARLEY, OATS , RYE, WHEAT
AGSCO INC.	23366.00	AGSCO DB-GREEN L (LIQUID) SEED FUNGICIDE AND INSECTICIDE SEED TREATMENT	C	BARLEY, OATS , RYE, WHEAT
INTERPROVINCIAL CO-OP LTD.	10662.00	IPCO NM DUAL PURPOSE DRILLBOX SEED TREATMENT POWDER	C	BARLEY, CEREALS, CEREAL CROPS (GRAIN,CEREAL CROPS), OATS, RYE , WHEAT
INTERPROVINCIAL CO-OP LTD.	11451.00	CO-OP D-L + C DRILL BOX SEED TREATMENT POWDER	C	BEAN, CORN, PEA, SOYBEAN
NORAC CONCEPTS INC.	9505.00	AGROX B - 3 DUAL PURPOSE INSECTICIDE FUNGICIDE SEED TREATMENT	C	BEAN, CORN, PEA, SOYBEAN
NORAC CONCEPTS INC.	10896.00	AGROX D - L PLUS SEED TREATMENT POWDER INSECTICIDE - FUNGICIDE	C	BEAN, CORN, PEA, SOYBEAN
RHONE POULENC CANADA INC.	19035.00	ROVRAL ST MUSTARD SEED TREATMENT	C	MUSTARD, RAPE (CANOLA)
RHONE POULENC CANADA INC.	25282.00	FOUNDATION MUSTARD SEED TREATMENT	C	MUSTARD, RAPE (CANOLA)
RHONE POULENC CANADA INC.	25283.00	FOUNDATION CST MUSTARD SEED TREATMENT	C	MUSTARD, RAPE (CANOLA)
UNIROYAL CHEMICAL LTD/LTEE	11422.00	VITAFLO DP SYSTEMIC FUNGICIDE & INSECTICIDE	C	BARLEY, WHEAT
UNIROYAL CHEMICAL LTD/LTEE	14115.00	VITAVAX DUAL SOLUTION SYSTEMIC FUNGICIDE & INSECTICIDE	C	BARLEY, OATS, RYE, WHEAT
UNIROYAL CHEMICAL LTD/LTEE	15537.00	VITAVAX DUAL POWDER SEED PROTECTANT	C	BARLEY, FLAX, OATS, RYE, WHEAT
UNITED AGRI PRODUCTS	13951.00	CLEAN CROP DIAZINON LINDANE CAPTAN DRILL BOX SEED TREATMENT	C	BEAN, CORN, PEA, SOYBEAN
ZENECA AGRO	10339.00	MERGAMMA N-M DRILL BOX DUAL PURPOSE SEED TREATMENT	C	BARLEY, CEREALS, OATS, RYE, WHEAT
ZENECA AGRO	12767.00	MERBAMMA FLOWABLE DUAL PURPOSE SEED TREATMENT	C	BARLEY, CEREALS, OATS, RYE, WHEAT
To control flea beetles (seed treatments): note there are submissions in to remove canola from each of these				
*INTERPROVINCIAL CO-		IPCO BENOLIN-R INSECTICIDE-		

COMPANY	REG #	PRODUCT NAME	CLASS	USES
OP LTD.	14893.00	FUNGICIDE DUST (SEED TREATMENT)	C	RAPE (CANOLA)
*RHONE POULENC CANADA INC.	19035.00	ROVRAL ST MUSTARD SEED TREATMENT	C	MUSTARD, RAPE (CANOLA)
*RHONE POULENC CANADA INC.	24972.00	ROVRAL CST CANOLA SEED TREATMENT	C	RAPE (CANOLA)
*RHONE POULENC CANADA INC.	25282.00	FOUNDATION MUSTARD SEED TREATMENT	C	MUSTARD, RAPE (CANOLA)
*RHONE POULENC CANADA INC.	25283.00	FOUNDATION CST MUSTARD SEED TREATMENT	C	MUSTARD, RAPE (CANOLA)
*Zeneca AGRO CORPORATION	25726.00	SAPPHIRE FLOWABLE SEED TREATMENT	C	MUSTARD, RAPE (CANOLA)
*UNIROYAL CHEMICAL LTD/LTEE	15533.00	VITAVAX RS FLOWABLE SYSTEMIC LIQUID SEED PROTECTANT	C	BROCCOLI, BRUSSELS SPROUT, CABBAGE, CAULIFLOWER, MUSTARD, RAPE (CANOLA), RUTABAGA
*UNIROYAL CHEMICAL LTD/LTEE	16451.00	VITAVAX RS POWDER SEED TREATMENT	C	MUSTARD, RAPE (CANOLA)
*UNIROYAL CHEMICAL LTD/LTEE	22121.00	CLOAK SEED TREATMENT	C	BROCCOLI, BRUSSELS SPROUT, CABBAGE, CAULIFLOWER, MUSTARD, RUTABAGA (SEED TREATMENTS)
*UNIROYAL CHEMICAL LTD/LTEE	24467.00	VITAVAX RS FLOWABLE (UNDYED) SEED PROTECTANT	C	MUSTARD, RAPE (CANOLA)
*UNIROYAL CHEMICAL LTD/LTEE	24482.00	VITAVAX RS DYNASEAL SEED PROTECTANT	C	MUSTARD, RAPE (CANOLA)
*ZENECA AGRO	21020.00	PREMIERE PLUS FLOWABLE SEED TREATMENT	C	MUSTARD, RAPE (CANOLA)
*ZENECA AGRO	21946.00	PREMIERE FLOWABLE SEED TREATMENT	C	MUSTARD, RAPE (CANOLA)
*ZENECA AGRO	24447.00	PREMIERE NO DYE FLOWABLE SEED TREATMENT	C	MUSTARD, RAPE (CANOLA)
Veterinary-type products				HOST (PEST)
HARTZ CANADA INC.	8478.00	ITCH-STOP DOG LOTION (Salve)	D	DOG (M)
VETOQUINOL N.-A. INC.	15353.00	STOCKPEST LOUSE SPRAY CONCENTRATE (Applied by pump sprayer, cloth or brush)	C	LIVESTOCK (L,T) SHEEP, HORSE (L,F) SWINE (L,F,M)
UNITED AGRI PRODUCTS	11522.00	CLEAN CROP LINDANE 25 WP (Apply by spray or pressure sprayer)	C	BEEF CATTLE (H, L, F); GOAT HORSE, SHEEP (L,T,F) SWINE (L,F,M)
Soil treatments				
UNITED AGRI PRODUCTS	11522.00	CLEAN CROP LINDANE 25 WP (apply as an aqueous solution)	C	UNSPECIFIED CROPS OR TOBACCO SEEDLINGS: FOR WIREWORM

* = effected product (amended label or use withdrawn for canola/rape)

C = commercial class

D = domestic class

Pests controlled by Vet. Uses: L=Lice, T=ticks, F=fleas, H=hornflies, M=mangemites

Appendix B: List of End-Uses for Lindane in the United States

In the U.S. the following uses are the only uses that the data-producing technical registrant currently intends to retain, and for which data will be generated and submitted.

Seed treatment only for: barley, broccoli, Brussels sprouts, cabbage, cauliflower, celery, corn, collards, lettuce, kale, kohlrabi, mustard greens, oats, radishes, rye, sorghum, Swiss chard, spinach, and wheat.

Two Notices of Receipt of Requests for Amendments to Delete Uses in Certain Pesticide Registrations, that pertained to lindane product registrations and uses, were published in the Federal Register on December 2, 1998 (Volume 63, Number 231) and August 26, 1998 (Volume 63, Number 165). The following is a list of those lindane uses that are no longer being supported by the data-producing technical registrant.

Unsupported Uses

almonds, alfalfa, apples, apricots, asparagus, avocados, beans (all types), beets, cantaloupe, carrots, cherries, clover, cotton, cucumbers, cucurbits (all types), eggplants, flax, grapes, guava, lentils, mangoes, melons, mint, mushrooms, nectarines, okra, onions, peaches, peas (all types), pecans, pears, peppers, pineapples, plums, prunes, pumpkins, quinces, rape, safflower, soybeans, squash (all types), strawberries, sudan grass, sugar beets, summer squash, sunflower, tobacco, tomatoes, watermelon; livestock treatment to cattle, goats, horses, sheep, mules, hogs; cats; ornamentals, trees and shrubs; turf, lawns, golf courses; uncultivated areas, fallow or idle agricultural areas, recreational areas, commercial transportation facilities, processing handling/storage areas/plants; grain/cereal/flour bins and storage areas; farm or agricultural structures, including barns; wood protection treatment of buildings; treatment of stored timber and lumber (in industrial wood processing facilities only - no open forestry use); treatment of dogs to control fleas, ticks, lice, earmites, sarcoptic mange mites and scabies (psoroptic) mange mites.

There were 25 end-use lindane registrants (total of 83 products) who had relied on the lindane data-producing technical registrant to produce and submit the data necessary to maintain their registrations. Under FIFRA (Federal Insecticide, Fungicide, and Rodenticide Act), US EPA was required to offer these end-use registrants the options of deleting all unsupported uses from their labels, or of producing and submitting their own data. Letters were sent notifying the end-use registrants on January 15, 1999. At this time:

- § 29 end-use registrations have been amended by deleting the unsupported uses
- § 34 end-use registrations were voluntarily cancelled; two of these registrations have extended phase-outs
- § 18 end-use registrations contained only supported uses, and no changes were necessary

At this time the Reregistration Eligibility Decision (RED) Document is scheduled for 2001. With the exception of the mouse cancer study, all data necessary for making this decision, including three neurotoxicity studies, have been submitted. US EPA will be able to issue a RED

that considers at least the acute dietary risk considering both food and water, chronic (non-carcinogenic) dietary risk considering both food and water, and occupational risk for both short-term and intermediate-term duration of exposure. In the absence of the mouse cancer study, carcinogenic dietary risk and carcinogenic occupational risk will be characterized as best possible, considering the available, reliable data. Thus, the risk management decision, including triggers and possible criteria for cancellation, would be conditioned on the eventual review and weight-of-the-evidence evaluation of the results obtained in the mouse cancer study.

As required by the Lindane Registration Standard, the data-producing registrant submitted a petition to establish tolerances for residues of lindane in corn, and will be submitting another petition to establish tolerances for residues of lindane in barley, oats, rye, sorghum, and wheat. These tolerance petitions, as a result of seed treatment uses only, will be evaluated during the tolerance reassessments that will occur at the time of the RED. The technical registrant has also submitted a petition for establishing tolerances on canola. Prior to making a decision on the new proposed use on canola, a safety finding under the Food Quality Protection Act (FQPA) would have to be made for all existing uses of lindane.

Appendix C: Toxicological Endpoints of Lindane

Toxicological Endpoints of Lindane; excerpt from *U.S. Department of Health and Human Services 1997 Toxicological Profile of alpha-, beta-, gamma-, and delta hexachlorocyclohexane.*

Note: These tables provide limited information on lindane toxicological studies. They cannot substitute for a detailed description of the studies. The following definitions should be considered in using these tables:

LD₅₀ - The dose of a chemical which has been calculated to cause death in 50% of a defined experimental animal population.

NOAEL - No Observed Adverse Effect Level - The dose of chemical at which there were no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

LOAEL - Lowest Observed Adverse Effect Level - The lowest dose of chemical in a study or group of studies, that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

LOAELs have been classified into less serious or serious effects. Serious effects are those that evoke failure in a biological system and can lead to morbidity or mortality. Less serious effects are those that are not expected to cause significant dysfunction or death, or those whose significance to the organism is not entirely clear. A considerable amount of judgment may be required in establishing whether an end point should be classified as a NOAEL, a less serious LOAEL, or serious LOAEL. There are established guidelines and policies that are used by ATSDR to classify these endpoints. For this document LOAELs are for serious effects, unless otherwise stated.

Acute Exposure - Exposure to a chemical for a duration of 14 days or less.

Intermediate Exposure - Exposure to a chemical for a duration of 15 to 364 days.

Chronic Exposure - Exposure to a chemical for 365 days or more.

Table 3. Toxicology Endpoints of Lindane Obtained from U.S. Department of Health and Human Services (1997).

Inhalation Studies		
Study	Species, Duration	Results
Acute	Wistar Rat, 4 hours	LD ₅₀ = 1560 mg/m ³
Acute	CD-1 Mouse, 1 week	LOAEL of 10 mg/m ³ (16% mortality)
Acute	Wistar Rat, 4 hours	NOAEL of 603 mg/m ³ for respiratory, hepatic and renal system effects
Acute	Wistar Rat, 4 hours	less serious LOAEL of 101 mg/m ³ for sedation, and serious LOAEL of 642 mg/m ³ for restlessness, excitation and ataxia
Intermediate	Wistar Rat, 90 days	NOAEL of 5 mg/m ³ for hematological, hepatic, renal, body weight and respiratory system effects
Intermediate	CD-1 Mouse, 14 weeks	LOAEL of 1.0 mg/m ³ (2% mortality)

Oral Studies (Includes Gavage and Feeding)		
Study	Species, Duration	Results
Acute	Sherman Rat, once	LD ₅₀ = 88 mg/kg/day for males; LD ₅₀ = 91 mg/kg/day for females
Acute	Wistar Rat, once	LOAEL of 60 mg/kg/day for males (1/7 deaths)
Acute	Wistar Rat, 14 days	LOAEL of 72 mg/kg/day in males for 10% increase in kidney weight, altered excretion patterns, distention of glomeruli, swelling of tubular epithelia
Acute	B6C3F1 Mouse, 10 days	NOAEL of 40 mg/kg/day for respiratory, cardiovascular, gastrointestinal, hematological, hepatic, renal, endocrine and body weight effects; 10 mg/kg/day LOAEL for decreased marrow progenitor cell numbers
Acute	B6C3F1 Mouse, 10 days	LOAEL of 10 mg/kg/day for residual bone marrow damage, suppressed erythrocyte precursors and granulocyte-macrophage progenitor cells

Oral Studies (Includes Gavage and Feeding)		
Study	Species, Duration	Results
Acute	B6C3F1 Mouse, 3 days	NOAEL of 10 mg/kg/day; less serious LOAEL of 20 mg/kg/day for decreased bone marrow granulocyte-macrophage progenitors; serious LOAEL of 40 mg/kg/day for bone marrow hypocellularity, residual bone marrow damage, decreased erythrocyte precursors and granulocyte-macrophage progenitor cells and thymus cortex atrophy
Acute	Long-Evans Rat, once	LOAEL of 10 mg/kg/day for myoclonic jerks and seizures
Acute	Sprague-Dawley Rat, 4 days	NOAEL of 1 mg/kg/day and LOAEL of 10 mg/kg/day for seizures
Acute	Sprague-Dawley Rat, once	LOAEL of 30 mg/kg/day for seizures
Acute	Wistar Rat, once	LOAEL of 30 mg/kg/day for convulsions and decreased calmodulin mRNA expression in brain
Acute	Wistar Rat, once	LOAEL of 60 mg/kg/day for convulsions
Acute	Wistar Rat, once	LOAEL of 60 mg/kg/day for tonic-clonic seizures
Acute	Wistar Rat, once	NOAEL of 15 mg/kg/day and LOAEL of 20 mg/kg/day for convulsions
Acute	NMRI Mouse, once	NOAEL of 20 mg/kg/day and LOAEL of 50 mg/kg/day (females) for significantly increased convulsive threshold
Acute, reproductive	Female Long-Evans Rat , 7 days	NOAEL of 40 mg/kg/day
Acute, developmental	Female CFY Rats, Gestation Days 6 – 15	NOAEL of 20 mg/kg/day
Acute, developmental	Wistar Rat, once	developmental less serious LOAEL of 20 mg/kg/day for regional changes in brain noradrenaline and serotonin levels in suckling rats
Acute, developmental	Female New Zealand Rabbit, Gestation Days 6 - 18	NOAEL of 20 mg/kg/day
Intermediate	Fischer 344 Rat, 15 weeks	LOAEL of 20 mg/kg/day (2/12 deaths)
Intermediate	Wistar Rat, 12 weeks	NOAEL of 0.3 mg/kg/day and LOAEL of 1 mg/kg/day for hepatic and renal effects; NOAEL of 5 mg/kg/day for hematological effects
Intermediate	Wistar Rat, 15 days	NOAEL of 1.8 mg/kg/day for hepatic effects
Intermediate	Wistar Rat, 30 days	NOAEL of 1.8 mg/kg/day for hepatic effects

Oral Studies (Includes Gavage and Feeding)		
Study	Species, Duration	Results
Intermediate	Wistar Rat (4 – 64 weeks)	Hepatic: NOAEL of 4.5 mg/kg/day for males, 5.0 mg/kg/day for females; LOAEL of 9 mg/kg/day for males and 10 mg/kg/day for females, both displaying focal necrosis, fatty degeneration, 35% increase in liver weight) Renal: NOAEL of 4.5 mg/kg/day for males, 5.0 mg/kg/day for females; less serious LOAEL of 9 mg/kg/day for males and 10 mg/kg/day for females displaying focal nephritis Decrease in Body weight gain: males NOAEL of 72 mg/kg/day and less serious LOAEL of 144 mg/kg/day; females NOAEL of 80 mg/kg/day and less serious LOAEL of 160 mg/kg/day
Intermediate	Swiss albino Mouse, 24 weeks	LOAEL of 0.012 mg/kg/day for biphasic changes in cell and humoral-mediated immune system, 1.2 mg/kg/day for necrosis of thymus
Intermediate	Long-Evans Rat, 30 days	LOAEL of 10 mg/kg/day for myoclonic jerks and clonic seizures
Intermediate	Wistar Rat, 90 days	LOAEL of 90 mg/kg/day for tonic convulsions
Intermediate	Wistar Rat, 30 days	Less serious LOAEL of 2 mg/kg/day for decreased dopamine levels
Intermediate, reproductive	Female Fischer 344 Rat, 15 weeks	NOAEL of 5 mg/kg/day, less serious LOAEL of 10 mg/kg/day for disrupted ovarian cycling, antiestrogenic effects
Intermediate, reproductive	Female Hybrid Rabbit, 12 weeks	less serious LOAEL of 0.8 mg/kg/day for reduced ovulation rate
Intermediate, reproductive	Female New Zealand Rabbit, 12 - 15 weeks	NOAEL of 0.8 mg/kg/day
Intermediate, developmental	Female New Zealand Rabbit, 12 - 15 weeks	NOAEL of 0.8 mg/kg/day
Chronic	Wistar Rat, 2 years	Hepatic: NOAEL for males of 0.7 mg/kg/day, for females of 0.8 mg/kg/day; less serious LOAEL of 7 mg/kg/day for males and 8.0 mg/kg/day for females, both for periacinar hepatocytic hypertrophy Renal: NOAEL for males of 0.7 mg/kg/day, for females of 0.8 mg/kg/day; LOAEL of 7 mg/kg/day for males and 8 mg/kg/day for females, both for increased kidney weight, urinary volume, urea, and creatinine excretions
Chronic	B6C3F1 Mouse, 80 weeks	LOAEL of 13.6 mg/kg/day for males from hepatocellular carcinomas

Oral Studies (Includes Gavage and Feeding)		
Study	Species, Duration	Results
Chronic	F-1 Hybrid Mouse, 2 years	LOAEL of 27.2 mg/kg/day for females from hepatocellular carcinomas and lung tumors

Dermal Studies		
Study	Species, Duration	Results
Acute	Sherman Rat, once	LD ₅₀ = 1000 mg/kg/day for males, LD ₅₀ = 900 mg/kg/day for females
Acute	Wistar Rat, 24 hours	NOAEL of 600 mg/kg/day and less serious LOAEL of 1000 for dyspnea
Acute	New Zealand Rabbit, 4 hours	NOAEL of 132 mg/kg/day for respiratory, hepatic, renal and dermal effects
Acute	Wistar Rat, 24 hours	NOAEL of 600 mg/kg/day; less serious LOAEL of 1000 mg/kg/day for slight sedation and serious LOAEL of 2000 mg/kg/day for severe spasms
Intermediate	CrI:(WI)BR Rat, 13 weeks	NOAEL of 60 mg/kg/day and a LOAEL of 400 mg/kg/day for females, (23/49 deaths)
Intermediate	CrI:(WI)BR Rat, 13 weeks	NOAEL of 10 mg/kg/day for hepatic and female renal effects; less serious LOAEL of 10 mg/kg/day for male renal hyaline droplet formation effects and for rapid respiration or wheezing; less serious LOAEL of 60 mg/kg/day for hepatic effects and for female basophilic tubule effects
Intermediate	CrI:(WI)BR Rat, 13 weeks	less serious LOAEL of 10 mg/kg/day for hyperactivity and serious LOAEL of 60 mg/kg/day for ataxia, tremors, and convulsions

Appendix D:

***Factors Influencing the Distribution of Lindane and Other
Hexachlorocyclohexanes in the Environment***

Submitted to

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by

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I. HCH and the North American Free Trade Agreement

Heavy use of organochlorine insecticides, especially in the past, has led to the dispersal of these pollutants throughout the global environment. One such compound of major concern is 1,2,3,4,5,6-hexachlorocyclohexane (HCH). HCH can persist in the environment and be transported long distances from the areas of application. While the bulk of HCH used today is in the form of lindane, which is composed almost entirely of the gamma (γ) isomer of the compound, there is concern that this isomer can be transformed into other isomers that exhibit greater persistence and have potentially more deleterious effects on humans and wildlife.

The isomers of HCH are the subject of proposed action by the three countries comprising the North American Free Trade Agreement (NAFTA)—Canada, Mexico and the United States. The North American Agreement on Environmental Cooperation, a side agreement to NAFTA, was negotiated and ratified in 1993 by the three governments. Subsequently, the North American Council of the Commission for Environmental Cooperation approved Resolution #95-5 regarding the sound management of chemicals. The resolution recognized that cooperative actions are needed to protect and improve the environment and to achieve sustainable development. Regional management of persistent, bioavailable and toxic compounds may warrant special attention due to the risks they pose to human health and the environment.

Through the resolution, Task Forces were formed to prepare North American Regional Action Plans (NARAPs) for particular chemicals (e.g., mercury) likely to create regional contamination problems. NARAPs identify how the three parties will cooperate to manage and control the chemicals. The objectives of each NARAP may differ depending on the risks associated with the substance in question, and could range from further research to a total phase-out of use.

To develop a process by which additional substances could be identified for future NARAPs, a Task Force on Criteria was established. At the initial evaluation phase, chemicals are selected based upon physicochemical features such as persistence, tendency to bioaccumulate and susceptibility to long-range transport. At the later discussion stage, other factors such as the costs of mitigation and the feasibility of alternatives are also included. Based on these criteria, the Substance Selection Task Force has determined that a NARAP should be prepared for lindane and the other HCH isomers.

An important issue of concern to the Substance Selection Task Force is whether the NARAP should focus on lindane alone or include other HCH isomers. While the only form of HCH presently used in North America is lindane, high concentrations of other isomers, particularly α -HCH, in the Arctic could suggest that lindane is transformed into other isomers in the environment. The following review examines the recent literature on the processes affecting the fate and distribution of lindane and other HCH isomers in the environment.

II. Introduction and Background

Lindane is one of eight stereoisomers of HCH. Known as γ -HCH, its chlorine substituents are half equatorial and half axial (aaae). This means that half of the C-Cl bonds are within the plane of the ring (e) and the other half are outside of the plane (a). The isomers differ in terms of the arrangement of the chlorine atoms. One of the isomers, α -HCH, exists in two enantiomeric (mirror-image) forms.

HCHs are commercially produced by photochemical chlorination of benzene. The product, technical-grade HCH, consists principally of four isomers, α -HCH (53-70%), β -HCH (3-14%), γ -HCH (11-18%), and δ -HCH (6-10%) (Gunther & Gunther 1971; Howard 1989). This mixture is marketed as an inexpensive insecticide, but since γ -HCH is the only isomer that exhibits strong insecticidal properties, it has been common to refine it from the technical HCH and market under the name "lindane." However, all commercially-produced lindane contains small amounts of other HCH isomers.

All the HCH isomers are acutely toxic to mammals. In addition, chronic exposure has been linked to a range of health effects in humans, including immuno-suppression and neurological problems, and has been shown to cause liver cancer in rats and mice (Willett et al. 1998; ATSDR 1997; Choudhary and Wedge 1996). Of the different isomers, α -HCH exhibits the most carcinogenic activity and has been classified along with technical grade HCH as a Group B2 probable human carcinogen by the U.S. EPA (ATSDR 1997). As the most metabolically stable isomer, β -HCH is the predominant isomer accumulating in human tissues (Willett et al. 1998).

All isomers of HCH exhibit relatively high water solubilities and moderately high vapor pressures when compared to other organochlorine pesticides. Therefore, HCH is usually present in the environment as a gas in the atmosphere or dissolved in water, with only a small percentage adsorbed onto particles (Bidleman 1988). Brubaker and Hites (1998) measured the gas-phase reaction kinetics of the hydroxyl radical with α -HCH and γ -HCH and showed that these compounds have fairly long lifetimes in air and therefore can be transported long distances.

The physicochemical properties of HCH vary between isomers (Willett et al. 1998). For example, the vapor pressure of α -HCH is somewhat less than that of γ -HCH. α -HCH has also been shown to be slightly more lipophilic than γ -HCH (Log K_{ow} 3.8 versus 3.6). The Henry's Law constant for α -HCH is several-fold greater than that of γ -HCH, so α -HCH is more likely to partition to the air. Another important difference between the isomers is the persistence of the β -isomer. β -HCH is "very recalcitrant" under environmental conditions (Schwarzenbach, *et al.*, 1993). It is also more lipophilic than the other isomers. These properties may result from its significantly smaller molecular volume. Since β -HCH's bonds between H, C, and Cl at all six positions are equatorial (that is, within the plane of the ring), the molecule is denser and small enough to be stored in the interstices of lipids in animal tissues.

II. Production and use of HCH worldwide

Both technical grade HCH and lindane have been used for insect control in fruit, grain and vegetable crops, for vector control, and for seed treatment (Ware 1989). A medical formulation of lindane is also used on the skin for the control of head lice and scabies (ATSDR 1997). Commercial production of technical-grade HCH began in 1943. Its extremely low cost led to its wide use, particularly in some developing countries. However, it has a strong unpleasant odor which sometimes imparts unpleasant flavors to crops grown in soil treated with it (Ware 1989). Therefore, lindane (which is odorless) has been more widely used in developed countries. Total global production and use of the different HCH isomers is difficult to determine and estimates vary considerably. Voldner and Li (1995) estimated total use of technical grade HCH and lindane to be 550,000 and 720,000 metric tons, respectively. However, later calculations by Li et al. (1998), which incorporated new information about high production and use in China, placed total cumulative world consumption of technical grade HCH as high as 6 million metric tons.

Environmental and human health concerns led to the banning of technical grade HCH in many countries during the 1970s. China, India and the former Soviet Union remained the largest producers and users of HCH in the early 1980s. China, whose total production was estimated at 4.5 million metric tons (Huang 1989, cited in Li et al. 1998) banned production in 1983, although residual stocks may have been used until 1985. In 1990, production of technical grade HCH was also prohibited in the former Soviet Union and restricted to public health and specific crop uses. Only 29,000 metric tonnes were applied in 1990, most of it in India (Li et al. 1996). Lindane, however, is still used worldwide, including in North America and Europe.

In addition to HCH isomers produced and applied, considerable unused stockpiles of both technical grade HCH and lindane exist. The 1998 Food and Agriculture Organization (FAO) Inventory of Obsolete, Unwanted and/or Banned Pesticides found a total 2,785 tons of technical grade HCH, 304 tons of lindane and 45 tons of unspecified HCH material scattered in dump sites in Africa and the Near East. Some of the containers have deteriorated and are leaking, creating a serious threat to humans and wildlife (Wodageneh 1998). Stockpiles associated with earlier manufacturing of technical grade HCH may also be causing problems in Eastern Europe (Pruszyński and Stobiecki 1997).

III. Presence of HCH isomers in the environment

When HCH (either lindane or technical grade) is applied to the soil, it can either persist there sorbed to soil particles or be removed through several processes. Microbial and chemical degradation as well as uptake by crop plants can occur, but the primary process for removing HCH from soil is volatilization into the air (Buser and Muller 1995; Singh et al. 1991). HCH can also enter the air adsorbed onto resuspended particulate matter, but this process does not appear to contribute as much as volatilization to the movement of HCH isomers. Predictions based on the Junge-Pankow adsorption model indicate that HCH isomers are predominantly gaseous at moderate temperatures (Bidleman

1988), and Lane et al. (1992) showed by denuder measurements that over 95% of the α - and γ -HCH in ambient air was in the gas phase. Leaching into groundwater is also possible but is uncommon (ATSDR 1997; Page 1981). Once HCH isomers enter the environment, they are distributed globally (Simonich and Hites 1995) and can be found in air, surface water, soil and living organisms (Montgomery 1993).

The most common isomers found in the environment are α , β and γ . α -HCH is typically predominant in ambient air as well as in ocean water. β -HCH is the predominant isomer in soils and animal tissues and fluids, including human, (Willett et al. 1998) because its all equatorial (e e e e e e) configuration favors storage in biological media and affords it greater resistance to hydrolysis and enzymatic degradation.

Numerous studies of tropospheric air, precipitation and surface water have reported HCH, particularly the α and γ isomers, throughout North America (e.g., air - Poissant and Koprivnak 1996, Hoff et al. 1992; precipitation - Blais et al. 1998, Brun et al. 1991; surface water - Ridal et al. 1997, Ridal et al. 1996, McConnell et al. 1998), the Arctic (e.g., Jantunen and Bidleman 1998; Li et al. 1998; Fellin et al. 1996; Oehme et al. 1996; Muir et al. 1992; Hinckley et al. 1992), Southern Asia, the Western Pacific, and Antarctica (e.g., Iwata et al. 1994; Iwata et al. 1993a; Tanabe et al. 1982). In fact, HCH isomers are the most abundant and pervasive organochlorine insecticide contaminants in the Arctic (Oehme et al. 1996; Fellin et al. 1996; Barrie et al. 1992, Patton et al. 1989; Oehme and Mano 1984). The detectable presence of HCH isomers in the Arctic and Antarctic, where lindane and technical HCH have not been used, is further evidence of long-range atmospheric transport.

One interesting fact is the discrepancy between air and surface water concentrations in different climate zones. Sampling conducted in 1989 and 1990 by Iwata et al. (1993a) found air concentrations of HCH isomers around the Indian subcontinent to be very high compared to moderate surface water concentrations. The situation was reversed in the Arctic, where air concentrations were moderate and water concentrations were high. These observations suggest that HCH isomers (considered among the most volatile persistent organic pollutants) are subject to "global distillation" or "global gas chromatography" (Wania and Mackay 1996; Risebrough 1990), in which warm climates at lower latitudes favor evaporation into the atmosphere where the chemicals can be carried to higher latitudes. At mid-latitudes, deposition and evaporation vary with season (corroborated by field work by Ridal et al. 1997, Ridal et al. 1996 and McConnell et al. 1993). At high latitudes, cold temperatures favor deposition. Such a latitudinal gradient was observed for both α and γ -HCH in a global study of contaminants in tree bark by Simonich and Hites (1995). The latitudinal gradient favoring deposition to the high latitudes was even more striking for α -HCH in sea water (Wania and MacKay 1996). This cycle of volatilization of HCH isomers, particularly α -HCH, in warmer areas followed by condensation in colder areas has also been observed with changes in altitude (Blais et al. 1998; McConnell et al. 1998).

IV. Evidence for isomerization of lindane

Concern about the potential for conversion of γ -HCH into other isomers, particularly α -HCH, comes in part from the observed high concentrations of the α isomer relative to the γ isomer in the northern hemisphere. The ratio of α to γ in technical grade HCH varies between 4 and 7 (Iwata et al. 1993b). Therefore, residues of this mixture found in the environment could be expected to reflect that ratio unless some process had changed it. The use of lindane would, in effect, lowers this ratio. However, air and water samples far from pesticide application sites have often contained ratios much higher than 7 (Iwata et al. 1993a; Patton et al. 1989; Pacyna and Oehme 1988). Several hypotheses have been suggested to explain why so much of the HCH residue found in the environment is in the form of the α isomer.

Photo-isomerization in air: One possible explanation for the higher than expected α to γ ratios is that γ -HCH may be transformed by sunlight into α -HCH (which is more photostable) during long-range atmospheric transport (Zepp 1998; Barrie et al. 1992; Oehme 1991; Pacyna and Oehme 1988). This idea is supported by the laboratory studies of Steinwandter (1976) carried out with high-energy UV light. Hamada et al. (1981) also found that α -HCH was the main decomposition product of crystalline γ -HCH exposed to UV irradiation, while the other isomers were quite stable under similar conditions. Malaiyandi and Shah (1984) also produced significant amounts of α -HCH from both γ -HCH and β -HCH through irreversible photolysis by direct sunlight in the presence of ferrous salts.

These experiments clearly show that photo-isomerization is possible. However, evidence that this process is a substantial contributor to the high α/γ ratios observed in the Arctic is indirect and subject to several interpretations. Oehme (1991) suggested the seasonal fluctuations of the α/γ ratio as evidence for temperature-dependent photoisomerization. In the Arctic, the α/γ ratio is lower in the winter and spring (when light and therefore photoisomerization rates would be lower), and higher in the summer and fall (when Arctic air masses are fairly isolated and photoisomerization rates would be higher) (Patton et al. 1989). However, other factors such as the different rates of atmospheric volatilization and deposition of the isomers as well as seasonal use of lindane or technical HCH could also explain the fluctuations in the α/γ ratio (Oehme 1996; Hoff et al. 1992a; Patton et al. 1989). Furthermore, a study of seasonal fluctuations of the α/γ ratio in Quebec (Poissant and Koprivnjak 1996) found no increase in α -HCH levels following applications of lindane in spring, suggesting either that photo-isomerization is not the main process acting upon γ -HCH or that the sample sites were too close to application sites to allow time for photoisomerization to occur (presumably during more long-range atmospheric transport.). Since the absorption of solar radiation by γ -HCH in the troposphere is very weak, the rate of photoisomerization would be very slow.

Bio-isomerization in soil and sediments: Laboratory evidence shows that γ -HCH can be transformed into other isomers in soil or sediments through biological degradation. The orientation of chlorine atoms on the γ isomer makes irreversible transformation into α -HCH or β -HCH the most likely form of isomerization (Buser and Muller 1995). Early

work by Newland et al. (1969) found that more than 80% of the γ -HCH in a simulated lake impoundment was converted to α -HCH within 3 months. Benezet and Matsumura (1973) showed that γ -HCH could be transformed into α -HCH and several other compounds by a strain of *Pseudomonas putida*. Vonk and Quirijns (1979) showed that small amounts of α -HCH could be produced by soil microorganisms and by *E. coli*, but only under anaerobic conditions. Huhnerfuss et al. (1992) found that marine microorganisms in North Sea sediments could transform γ -HCH into essentially racemic mixtures of both enantiomers of α -HCH, but did not specify the rate of transformation or the percentage of γ -HCH transformed.

Recent quantitative studies have indicated that bio-isomerization may play an insignificant role in the overall degradation of γ -HCH. Waliszewski (1993) found that field applications of lindane to soil produced only trace amounts of other HCH isomers. In their study of degradation of HCH isomers in anaerobic sewage sludge, Buser and Muller (1995) found that only a very small percentage of γ -HCH could be transformed into α or δ -HCH, and the rate of conversion was extremely slow. Another field study of HCH applications to cropped and uncropped soil (Singh et al. 1991) found no evidence of isomerization, but did observe preferential uptake of the α isomer into plants.

V. Long-term trends in α and γ HCH concentrations in the environment

Comparisons of residues in the northern hemisphere, where the bulk of both technical HCH and lindane applications have occurred, and the southern hemisphere, where less HCH has been applied, most of it in the form of lindane (Li et al. 1996; Pacyna and Oehme 1988), provide conflicting evidence for and against large-scale transformation of γ -HCH into α -HCH. Ballschmiter and Wittlinger (1991) showed that the exchange of persistent organic compounds such as HCH occurs very slowly between the northern and southern hemispheres. Therefore, it can be assumed that the HCH concentrations in the water and air of the northern and southern hemispheres largely reflect pesticide emissions and subsequent atmospheric transport and transformation within each hemisphere independently. If transformation of γ -HCH into α -HCH and other isomers occurred on a large scale, one would expect to see significant concentrations of α -HCH in the southern hemisphere. In their examination of air and water contaminants in the western Pacific, eastern Indian Ocean and Antarctica, Tanabe et al. (1982) found γ -HCH to be the dominant isomer ($\alpha/\gamma < 1$) in the southern hemisphere (Tables 1 and 2). However, in 1987, Kurtz and Atlas (1990) found α/γ ratios as high as 7 and 16 in South Pacific air and water respectively. More recent measurements in the Southern hemisphere found α/γ ratios no higher than 2.3 (Schreitmuller & Ballschmiter 1995; Bidleman et al. 1993). If significant transformation of γ -HCH to α -HCH were occurring, the α/γ ratio would not be expected to drop over time. Therefore, the earlier high α/γ ratios may have reflected some significant technical HCH use in the southern hemisphere (Weber & Montone 1990). A considerable reduction in α -HCH concentrations has also been observed recently in Arctic air (Li et al. 1998). Haugen et al. (1998) found that concentrations of α -HCH in ambient air dropped by 50% between 1991 and 1995 in southern Norway while no such pattern was evident for

γ -HCH residues.

VI. Other explanations for the abundance of α -HCH in the environment

A mechanism based on the physiochemical properties of the α and γ isomers has been suggested to explain the high α/γ ratio observed in some locations (Oehme et al. 1996; Iwata et al. 1993b; Welch et al. 1991, Patton et al. 1989). Differences in the Henry's law constants of the α and γ isomers could affect their global distribution. The Henry's law constant, or the air/water partition coefficient, is a measurement of the tendency of a compound to partition between the gas phase in air and solution in water. The lower the value of the coefficient, the more likely a compound will dissolve into the water. At 20 °C in fresh water, the constant is 0.524 Pa·m³/mol for α -HCH and 0.257 for γ -HCH (Kucklick et al. 1991). Therefore, during long-range transport in air over oceans, γ -HCH is more likely to be removed either through direct partitioning into water or through washout in rain, leaving proportionately more α -HCH in the air (Iwata et al. 1993b). As a result of the global distillation process, the North Atlantic and Arctic Oceans serve as sinks for the predominantly α -HCH contamination.

It is important to note that the partitioning of HCH between air and water is a two-way street (McConnell et al. 1993). Therefore, as declining use of the different HCH products reduces the HCH load in the air, contaminants in the oceans may be re-released into the atmosphere, where they can be transported to other regions (Schreitmüller and Ballschmiter 1995). α -HCH could also be recycled from residues in contaminated soil.

Differences in degradation rates may also contribute to disproportionate accumulation of α -HCH. Research by Brubaker and Hites (1998) and Kelly et al. (1994) has indicated that reaction with the OH radical is the primary mechanism influencing the lifetime of HCHs in air. Brubaker and Hites (1998) found an approximately 25% longer atmospheric lifetime for α -HCH than γ -HCH in air (120 days versus 96).

In short, the observed fluctuations in the α/γ ratios in the northern hemisphere may be caused by spikes of lindane superimposed on a background of technical HCH. Haugen *et al.* (1998) reported that lower α/γ ratios in air at Lista, Norway were associated with movement of air parcels from central Europe during the seasons of lindane usage. Similar results were obtained by Harner *et al.* (1998) for ambient air samples taken over Barents Sea. The trends of these ratios would be expected to change as usage of technical HCH continues to drop and be replaced by lindane. Such a trend has recently been documented by Li et al. (1998), who observed a connection between declining α -HCH concentrations in Arctic air and reductions in global usage of technical HCH in the northern hemisphere (most notably after China discontinued use in the 1980's).

VII. Conclusions

Laboratory research indicates that significant photo- and bio-isomerization of γ -

HCH to α -HCH can occur, but field studies to date have not found evidence that these processes are either the main pathway for the removal of γ -HCH or the main sources of accumulated α -HCH in the environment. However, some conversion of γ -HCH to α -HCH in soils and sediments may also add to emissions of α -HCH. The significance of these sources compared to the simple recycling of *in situ* α -HCH residues will be difficult to establish. More reliable, quantitative information on γ -to- α -HCH transformation in soils and sediments is needed for such estimates. Therefore, we recommend that isomerization be considered in any dossier and the Regional Action Plans addressing lindane prepared under the Sound Management of Chemicals Program of the North American Free Trade Agreement.

VIII. Future research recommendations

Although use of technical HCH, which is presumably the main source of α -HCH in the environment, is declining, recycling of both the α - and γ -isomers from contaminated soils and water will continue for years to come. In addition, the stability of β -HCH and its tendency to accumulate in animal tissues means that existing residues of the isomer may continue to create human and environmental health hazards. Therefore, we suggest that individual HCH isomers, specifically α , β and γ -HCH, be measured in North America, rather than merely reporting total HCH and/or lindane. This additional monitoring effort would not be burdensome since the sample collection method(s) would remain the same. All three isomers are easily separable by gas chromatography, so little or no additional analytical costs would be associated with the determination of α -, β -, and γ -HCH in collected air samples over the cost of determining lindane alone. Isomer ratios are needed to estimate sources, transformation and potential fate. This information is essential to conduct meaningful exposure assessments and to evaluate the effectiveness of international prevention programs.

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Table 1: Temporal trends in HCH isomer concentrations in air.

Year	Location	mean conc. of α -HCH (pg/m ³)	mean conc. of γ -HCH (pg/m ³)	α/γ -HCH ratio	Reference
1980	NW Pacific South Pacific and Antarctica	1021 31 (geom mean)	580 69	1.1 - 2.6 0.3 - 0.5	Tanabe et al. 1982
1986 1987	Beaufort Sea	546 340	31 45	17.6 7.6	Patton et al. 1989
1987	Central Ontario N. Lake Ontario	301 124	56 15	3 - 10 2 - 20	Lane et al. 1992
1987	South Pacific NE Pacific NW Pacific	13 240 131	<3 27 5	4 - 7 6.8 - 13.3 26 - 33	Kurtz and Atlas 1990
1988	Bering Sea	251	68	2.0 - 3.7	Hinckley et al. 1992
1988 1989	Green Bay Great Lakes	268 219	136 40	2.4 6.0	McConnell et al. 1993
1990	South Pacific and Antarctica	4.0 (geom. mean)	3.8	0.3 - 2.3	Bidleman 1993
1990	NE Atlantic SE Atlantic SW Atlantic	81 3.6 7.1	72 5.4 14.3	0.3 - 4.6 0.4 - 1.4 0.4 - 0.6	Schreitmuller and Ballschmiter 1995
1991 1992 1993 1994 1995	Lista (South Norway)	84 82 67 59 47	48 60 43 59 37	0.1 - 7.5 (across 5 year period)	Haugen et al. 1998

Table 2: Temporal trends in HCH isomer concentration in surface water.

Year	Location	mean conc. of α -HCH (ng/m ³)	mean conc. of γ -HCH (ng/m ³)	α/γ -HCH ratio	Reference
1980	NW Pacific Antarctica	1.7 0.09	2.8 0.4	0.2 - 1.3 0.1 - 0.4	Tanabe et al. 1982
1987	Coral Sea South Pacific NE Pacific (nr. Alaska) NW Pacific	2.2 0.2 2.4 1.4	0.2 0.04 0.5 0.2	6.5 - 15.3 0.6 - 16 4.6 - 6.7 3.9 - 11.9	Kurtz and Atlas 1990
1989 1990	Green Bay Great Lakes (avg.)	1.1 1.0 - 1.4	0.4 0.3 - 0.5	3.3 2.4 - 4.5	McConnell et al. 1993
1990	NE Atlantic SE Atlantic	49 12.2	61 31.5	0.6 - 0.9 0.2 - 0.7	Schreitmuller and Ballschmiter 1995
1993-4 1994 1994	Chukchi Sea W. Arctic Ocean nr. Greenland Sea	2.1 2.4 0.9	0.4 0.5 0.2	5.3 4.8 4.5	Jantunen and Bidleman 1998