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21 June 2000

By electronic mail – Original will follow by FedEx

Dr. Andrew Hamilton
Commission for Environmental Cooperation
393, rue St. Jacques Ouest, Bureau 200
Montreal (Quebec) Canada H2Y 1N9

Re : Comments on Draft Decision Document on Lindane under the Process for Identifying Candidate Substances for Regional Action under the Sound Management of Chemicals Initiative.

Dear Dr. Hamilton:

The Centre Internationale d'Etudes du Lindane (CIEL) is pleased to submit comments to CEC on the subject document. We appreciate the opportunity to submit the enclosed comments.

Our comments are rather extensive, but given the nature, importance and breadth of the topics covered, we would have been remiss to do less. The comments are organized as follows: After some introductory remarks, we provide an overview of lindane based upon the most current GLP studies submitted to the U.S. Environmental Protection Agency and the European Union. We then review the regulatory status of lindane in countries and international bodies. Third, we address the issue of transport of lindane to the Arctic. And, finally we provide comments directed specifically to the draft Decision Document.

CIEL notes that its support and therefore its comments relate to seed treatment uses of lindane. Seed treatment rates are very low, provide a cost-effective and proven insecticide for growers and pose little risk to humans or the environment. We also note that we are supporting lindane composed of the gamma-isomer at 99.5 per cent purity. This should not be confused with HCH, a multi-isomer mixture containing alpha-HCH isomer, which is an environmental contaminant.

Our comments note that the document is internally inconsistent, does not take a risk-benefit approach to regulatory considerations and does not reflect the new studies that were undertaken and which have been submitted to the U.S. EPA, as part of the reregistration of lindane. This latter point is particularly disturbing in that the U.S. is the reported nominator of lindane for NARAP consideration.

Lindane is not a Persistent Organic Pollutant (POP) based upon deliberations by both the Economic Commission for Europe and the UNEP Negotiating Group for POPs. Current GLP-compliant, EPA/OECD guideline studies show that lindane is not genotoxic nor a reproductive or development toxicant. Nor does lindane appear

to be an oncogen based upon current studies, the latest of which is to be completed by the end of this year. Lindane does not cause severe acute toxicity, and it does not pose significant dietary or occupational exposure based upon analyses/conclusions from both the U.S. EPA and the WHO/FAO Joint Meeting on Pesticide Residues.

We also believe that the contribution of lindane to the atmospheric transport of HCH isomers is very minor and the use of HCH is being confused with the current and limited use of lindane. We hope that our comments will shed some light on this unclear and uncertain situation.

CIEL is very concerned about the focus on hazards rather than risks in the CEC Decision Document and the erroneous conclusions reached based upon selective interpretation, old data and the omission of current GLP studies submitted to EPA for reregistration. We are concerned that the pressures on lindane stem more from a lack of understanding of the current database and outmoded concepts regarding the compound than on an objective review of the facts.

Again, we appreciate the opportunity to comment. If you have any questions regarding these comments, we will be pleased to amplify them further. Please do not hesitate to contact CIEL at the following address:

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Best regards.

Sincerely yours,

/signed/
Edwin L. Johnson
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Enclosure

cc: **U.S. EPA**: J. Aidala, M. Mulkey, L. Rossi, J. Jones, G. LaRocca, M. McDavit
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Lindane Group

COMMENTS ON

CEC DECISION DOCUMENT ON LINDANE

UNDER THE

PROCESS FOR IDENTIFYING CANDIDATE SUBSTANCES

FOR

REGIONAL ACTION UNDER THE SMOC INITIATIVE

SUBMITTED BY:
CENTRE INTERNATIONAL D'ETUDES DU LINDANE (CIEL)

PREPARED BY:
TECHNOLOGY SCIENCES GROUP INC.

21 JUNE 2000

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COMMENTS ON THE "DECISION DOCUMENT ON LINDANE UNDER THE PROCESS FOR IDENTIFYING CANDIDATE SUBSTANCES FOR REGIONAL ACTION UNDER THE SMOC INITIATIVE"

A. INTRODUCTION

These comments are being submitted on behalf of the Centre International d'Etudes du Lindane (CIEL). CIEL and its member have invested significant resources to develop state of the art, GLP-and guideline-compliant data for reregistration of lindane by the U.S. Environmental Protection Agency (EPA) and by the European Union. INQUINOSA, a member company of CIEL, has also developed data on the canola seed treatment use and submitted a tolerance petition to EPA. Lindane data are GLP, guideline studies, which often refute the stated concerns, which are primarily based upon old data, and which were often generated under older protocols and with compounds of unknown isomer composition and purity. However, this new database is held by EPA and other regulatory agencies and has not been published in the public press. Thus it may not be available to groups considering the status of lindane, such as the CEC. CIEL has been reluctant to make these data public because of the need to protect the major investment it has made in intellectual property. CIEL also emphasizes that its support and consequently its comments relate to the seed treatment uses of lindane only. Seed treatment rates are very low, and are not a concern to humans or the environment. To clarify understanding of the products under discussion: Lindane is composed of 99.5% minimum ã-hexachlorocyclohexane (HCH) and should not be confused with technical HCH, a multi-isomer mixture, containing the á-HCH isomer as the primary component, which is an environmental contaminant.

B. ORGANIZATION OF THE DOCUMENT

Since these comments are rather lengthy, it appears worthwhile to outline the structure of this document.

First, we provide an overview of lindane based upon the most current studies performed under GLP and EPA guidelines and performed using lindane of known purity. We believe that it is important to provide a clear picture of the current understanding of lindane's properties from the most current, most reliable data. This section demonstrates that lindane is not highly acutely toxic, is not genotoxic, is not a reproductive or developmental toxicant and does not appear to be oncogenic based upon the weight of the evidence. Dietary exposure and occupational exposure is not considered to be of public health concern.

Second, there is a summary of the current regulatory status in various countries and in international fora. This section indicates that lindane is registered in many countries and reviews in the EU and US appear to be proceeding in a normal fashion. Finally, it has not been classified as a "persistent organic pollutant" (POP) although it has been considered in both ECE and UNEP deliberations on the subject.

Third, there is a detailed discussion of one of the apparent major issues, transport of lindane and HCH into the Arctic. It is concluded that the use of HCH in the past has presented the most plausible explanation for these residues and that the contribution of seed treatment uses in North America is minimal.

Fourth, we present specific comments on the draft CEC Decision Document on a section-by-section basis.

Given this structure, there may be some duplication, for which we apologize, however, given the importance of the proposed decision, we want to be certain that the comments cover all points of concern.

C. LINDANE OVERVIEW BASED UPON MOST CURRENT, GLP DATA

CIEL believes that these data, from current GLP studies based upon EPA guidelines, indicate clearly that lindane does not cause the health problems recited in the CEC document.

Toxicological Profile

Acute Toxicity: Lindane demonstrates moderate oral, dermal, and inhalation toxicity. Reported acute oral LD_{50} values in the rat range from 90 to 250 mg/kg, i.e., Category II. The acute dermal LD_{50} values were 200 to 300 mg/kg in rabbits and 900 to 1000 mg/kg in rats, i.e., Category II. The acute inhalation LC_{50} value in the rat was 1600 mg/L/4hr, i.e. Category IV. Lindane is not irritating to rabbit skin and is only slightly irritating to rabbit eyes. Lindane is not a dermal sensitizer.

Genotoxicity: Lindane has been evaluated in a comprehensive battery of genotoxicity studies. Tests in microorganisms and *in vivo* and *in vitro* studies, including Ames, gene mutation, and sister chromatid exchanges in laboratory animals, show **no** mutagenic nor genotoxic potential.

Reproductive and Developmental Toxicity: Lindane is neither a reproductive nor a developmental toxin. In a two-generation reproduction study on rats, the NOEL for reproductive and developmental toxicity was 1.71 mg/kg-bw/day. In a developmental toxicity study, the rat maternal NOEL was 5 mg/kg, and the developmental NOEL was 10 mg/kg. In a developmental neurotoxicity study, the no-adverse-affect level for neurotoxicity in offspring of rats dosed from implantation until mid-lactation was 120 mg/kg in the diet. Based on reduced food consumption, reduced weight gain, slight tachypnea and lethargy, the developmental and parental NOEL for the rabbit was greater than 20 mg/kg-bw/day.

Subchronic Toxicity: Ninety-day feeding studies were conducted using mice and rats. The NOEL in the mouse was greater than 10 ppm (highest dose tested). In the rat, the NOEL was 10 ppm (0.75 mg/kg-bw/day). Renal effects were observed but were related to á-2ì-globulin, a species-specific effect seen only in rats, and therefore are not relevant to human safety. Hepatocellular hypertrophy and neurotoxicity were observed at the higher dose levels. A 14-week inhalation study in mice had a NOEL of 0.3 mg/cubic meter. In a 90-day inhalation study in rats, the NOEL was 0.6 mg/cubic meter. Ninety-day dermal toxicity studies have been conducted in rats and rabbits. In both species, the NOELs were 10 mg/kg-bw/day.

Neurotoxicity: Acute neurotoxicity studies in rats showed No Effect Levels (NOELs) for behavior changes of 20 and 6 mg/kg-bw/day for male and female rats, respectively. In a subchronic study, the NOEL for routine toxicity and behavioral changes was 100 ppm for both sexes. A developmental neurotoxicity dietary study, 120 ppm was a no-adverse effect level for morphological and functional developments of the nervous system. No developmental neurotoxicity was observed. Maternal toxicity was only evident at 120 ppm, and the overall no-effect level in the study was 10 ppm.

Chronic Toxicity: A two-year feeding study was conducted in dogs. The NOEL was for this study 50 ppm. A chronic study in rats found a NOEL of 10 ppm (0.47 mg/kg-bw/day) based upon liver toxicity at higher dose levels.

Oncogenicity: Lindane is not carcinogenic to rats. A 2-year combined chronic toxicity/oncogenicity study in the rat was negative for carcinogenicity. A long-term feeding study in mice is underway, and after 66 weeks of dosing, there have been no clear treatment-related findings, including mortality, clinical signs, overall bodyweight gain, food consumption, hematology or macroscopic findings at necropsy. EPA considered none of the prior eight mouse studies adequate for a cancer risk assessment.

Animal Metabolism: Tetrachlorophenols, trichlorophenols, dichlorophenols, and tetrachlorocyclohexenols were identified in urine and feces of Sprague-Dawley rats fed diets containing lindane at 400 mg/kg diet four to five weeks. Male Wistar rats dosed orally with 8 mg/kg-bw/day for 19 days produced trichlorophenol, tetrachlorophenols, tetrachlorocyclohexenol, pentachlorocyclohexenol, and pentachlorophenol, either in the free form

or as conjugates. *In vivo* and *in vitro* studies on rats and other animal species have shown lindane to metabolize to cycloalkenes, including hexa-, penta-, and tetrachlorocyclohexene, and penta- and tetrachloro-2-cyclohexen-1-ol; chlorobenzenes, including mono-, di-, tri-, tetra-, penta-, and hexachlorobenzenes; chlorophenols, including di-, tri-, tetra-, and pentachlorophenols, and conjugates of glutathione, glucuronic acid, sulfate, and mercapturic acids.

Metabolite Toxicology: Dietary residues are comprised of lindane and a variety of metabolites. The dietary residues are qualitatively the same as those formed in the rat and have thus been bioassayed in the available toxicity studies. These metabolites are not considered to present a significant toxicological risk.

Endocrine Disruption: A specific evaluation of the potential effects on the endocrine systems of mammals has not been done. However, reproductive effects of lindane are observed only at dose levels higher than those causing other forms of toxicity. There are as yet no guidelines for the conduct of these studies so the scientific information does not exist for most currently registered pesticides.

The following assessments were conducted to satisfy requirements of the Food Quality Protection Act in the U.S.

Dietary Exposure

Food: Acute dietary exposure. The available data do not indicate any evidence of significant toxicity from a one-day or single event exposure by the oral route. The only food crop use for lindane at this time is seed treatment, which results in extremely low dietary exposure. Thus an acute dietary risk assessment is not necessary. Chronic dietary exposure: The proposed use would account for less than 3% RfD of 0.0047 mg/kg-bw/day for the US population overall. Non-nursing infants less than one year old, the most affected population, would be exposed to less than 7% of the RfD.

Drinking Water: Studies have shown that lindane has little or no tendency to move into groundwater. For this reason water has not been included in the dietary risk assessment.

Non-Dietary Exposure

Lindane has only a few remaining registered uses and the potential for non-occupational, non-dietary exposure to the general population is negligible. As a seed treatment, lindane is limited to a small number of crops with an extremely limited market share. The treated seed is either planted immediately, or stored in areas with limited public access prior to sale and shipment to the user. Potential exposure is basically limited to occupational scenarios, i.e. application to seed and planting treated seed, and appropriate worker protection equipment can be utilized to minimize exposure.

Safety Determination

U.S. Population: Using conservative exposure assumptions, the aggregate exposure to lindane will utilize less than 3% of the RfD for the US population, and less than 2% if market shares are completely taken into account. EPA and other regulatory bodies generally have no concern for exposures below 100% of the RfD. Therefore, based on completeness and reliability of the toxicity data and conservative exposure assessment, there is a reasonable certainty that no harm will result from aggregate exposure to residues of lindane. This assessment includes all anticipated dietary exposure and all other non-occupational contributions.

Infants and Children: In assessing the potential for additional sensitivity of infants and children to residues of lindane, EPA considers data from developmental toxicity studies in the rat and rabbit and the two-generation reproduction study in the rat. Developmental toxicity and neurotoxicity studies evaluate adverse effects on the developing organism resulting from pesticide exposure during prenatal development. Reproduction studies provide information on potential effects on the reproductive capacity of males and females exposed to the pesticide.

Developmental toxicity was not observed in developmental toxicity studies using rats and rabbits. In these studies, the rat maternal NOEL was 5 mg/kg-bw/day and developmental NOEL was 10 mg/kg-bw/day. The parental and

developmental NOELs for the rabbit were greater than 20 mg/kg-bw/day. Neurotoxicity to developing rats was not observed at the highest dose tested, 120 ppm in the diet (8.0 to 19.1 mg/kg-bw/day). In a two-generation reproduction study in rats, the NOEL for reproductive and developmental toxicity was 2 mg/kg-bw/day. The results suggest no special sensitivity of the developing organism to neurotoxicity.

Assuming 100 % market share for all crops potentially treated with lindane, nursing infants less than one year old would be exposed to 1.2 % of the RfD and non-nursing infants less than one year old would be exposed to 6.7 % of RfD. Children 1 to 6 years old would be exposed to 6.1 % RfD and 7 to12 years old to 4.0 % RfD. The actual dietary exposure will be considerably less, because the percent of seed treated with lindane ranges from about 1 percent for vegetables to a maximum 15 percent for corn.

There is no particular concern for the acute toxicity of lindane based upon available data. Hence it is not necessary to assess the acute dietary risk of lindane to selected subpopulations within the United States.

Section 408 of the FFDCA provides that EPA may apply an additional safety factor for infants and children in the case of threshold effects to account for pre- and post-natal toxicity and the completeness of the database. Based on the current toxicological data requirements, the database relative to pre- and post-natal effects for children is complete and an additional uncertainty factor is not warranted. The RfD of 0.0047 mg/kg-bw/day that has been established by the EPA is appropriate for assessing aggregate risk to infants and children as well as all other subgroups.

International Tolerances

The Codex Alimentarius Acceptable Daily Intake for lindane is 0.008 mg/kg-bw/day. Codex Maximum Residue Levels (MRLs) have been set for lindane in several commodities for which new or revised tolerances are currently requested in the United States. The Codex MRLs for these commodities are tabulated below.

COMMODITY	MRL[a] (PPM)
Brussels sprouts Cabbage Cauliflower	0.5
Cereal grains	0.5
Kohlrabi	1.0
Lettuce (head) Spinach	2.0
Meat of cattle, pigs and sheep	2 (fat)
Milks	0.01
Radish	1.0
Rape seed	0.05
Poultry meat	0.7 (fat)

[a] *Codex Alimentarius Commission 1986*

The WHO, 1991, concluded that "The daily intake and total exposure of the general population are decreasing gradually; however, they are clearly below the advised acceptable daily intake and are of no concern to public health" and with respect to occupational exposure, "as long as precautions to minimize exposure are observed, lindane can be safely handled."

D. NATIONAL AND INTERNATIONAL REGULATORY STATUS

Lindane is registered for use in many countries throughout the world. Lindane is registered and used in:

- European Union (United Kingdom, Germany, Spain, Portugal, Ireland and Greece)
- East Europe (Russia and Romania)
- Asia (China, India and Malaysia)
- South America (Brazil)
- Africa (French speaking countries)
- North America (United States, Canada and Mexico)

It is also approved in many other countries, but they represent a minor consumption. Lindane is being or has been reviewed in several countries and international regulatory bodies. We would like to summarize the status of lindane in these situations.

United States – CIEL has submitted all the required data to maintain seed treatment uses, except for a mouse carcinogenicity study that is due in December 2000. Registrants of the technical product have requested voluntary cancellation of all other uses. A petition to establish tolerances for use as a canola seed treatment has been submitted by INQUINOSA. Reregistration and tolerance reviews are now underway with a projected Reregistration Eligibility Decision (R.E.D.) due in mid-2001.

Canada – Canada has issued a notice of Special Review. In communications with CIEL, PMRA authorities have noted that they will work closely with the EPA and share data reviews. PMRA has set a target date of December 2000 to complete the review.

United Kingdom – Seed treatment formulations were cancelled in 1999. The action was based upon the very conservative UK operator exposure model in which cleaning of the seed treatment machinery resulted in a predicted overexposure. A formulation avoiding this problem could be registered. Other uses, including spray uses, are still on the market.

European Union – Lindane is being reviewed under Directive 91/414/EC for reregistration. The dossier has been completed and reviews have been favorable. A final decision is expected later this year. The commission is reviewing the last studies submitted by CIEL.

Economic Commission for Europe – The Commission considered lindane in the discussions of persistent organic pollutants (POPs), but they decided to exclude the chemical from the list of POPs adopted by ECE. Lindane is to be rereviewed within two years after the ECE POPs protocol comes into effect.

United Nations Environment Programme POPs Negotiations – Lindane has been considered and is not included in the list of POPs moving forward in the negotiations.

U.S.-Canada BiNational Toxics Strategy for the Great Lakes – Lindane is included on List 2, which includes substances that should be regulated to prevent pollution. The Pesticide Working Group of BNTS, at its most recent meeting, decided to await completion of country reviews of List 2 substances and to not meet again until November 2001.

Joint Meeting on Pesticide Residues-Codex Alimentarius – Maximum residue levels have been established for several commodities and the Acceptable Daily Intake (ADL) for lindane is 0.008 mg/kg bw. Dietary exposure analyses indicate that they were clearly below the ADL and are of no concern to public health.

E. COMMENTS REGARDING THE ENVIRONMENTAL TRANSPORT ISSUE

The literature used in the CEC document and in the GLP studies submitted to the US EPA and European Union suggest that current environmental problems in the Arctic region resulted from past uses of technical HCH rather than ongoing uses of lindane in NAFTA countries. This is reviewed below.

Is lindane (ã-HCH) the problem? The dominant contaminant in the Arctic is á-HCH rather than γ-HCH. This is evidenced by 1994 data collected at 39 locations from the Chukchi Sea across the North Pole to the Greenland Sea that gave an average á-HCH/ã-HCH ratio of over 5 (Jantunen and Bidleman, 1998). Other studies done in 1986 - 1993 cited by Jantunen and Bidleman, 1998 had similar á-HCH/ã-HCH ratios (3 and 10). Clearly, á-HCH is the most pervasive HCH isomer in the Arctic. á-HCH also is the dominant isomer in technical HCH (53 - 70% á-HCH and 11 to 18% ã-HCH as cited in the Decision Document, 19 April 2000; Howard 1989 reference). This translates into essentially the same isomer ratio as found in the Arctic environmental contamination (á-HCH/ã-HCH ratio of 3 to 6+). Lindane products marketed in the NAFTA countries are 99.5% ã-HCH so it will not yield an á-HCH/ã-HCH ratio similar to technical HCH unless extensive isomerization occurs under normal environmental conditions (discussed later). "Of the different isomers, á-HCH exhibits the most carcinogenic activity and has been classified along with technical grade HCH as Group B2 probable human carcinogen by the U.S. EPA (ATSDR 1997). As the most metabolically stable isomer, â-HCH is the predominant isomer accumulating in human tissues" (CEC Decision Document).

What factors affect the environmental persistence of HCH isomers? Hydrolysis, gas phase reactions with hydroxyl radicals, photolysis, and microbial degradation are all involved in removing HCH isomers from the environment.

A GLP hydrolysis study, accepted by EPA, conducted at pH's of 3, 7, and 9, gave half-lives for γ-HCH of 115.5, 281.7 and 35.4 days, respectively (MRID 001616-30). Buser and Muller, 1995, using data of Ngabe et al. reported similar hydrolysis rates for α-HCH and γ-HCH ($1.6 \times 10^{-5} - 1.6 \times 10^{-4}$ for α-HCH and $1.2 \times 10^{-5} - 1.2 \times 10^{-4}$ for γ-HCH at pH 7 – 8).

The γ-HCH isomer is more reactive with gas phase hydroxyl radicals than α-HCH (Brubaker and Hites, 1998). This study reported atmospheric lifetimes of 96 days for γ-HCH and 120 days for α-HCH while Atkinson, 1987, as reported in the CEC decision document, reported lifetimes of ≥ 2 days.

A GLP photolysis study in water (MRID 447931-01) conducted at pH 7 with 15 days of continuous illumination with simulated sunlight (xenon lamp) showed 91.80 % γ-HCH remaining, less than1% unknowns, and essentially the same result as the dark control (90.75 % γ-HCH remaining). This suggests essentially no photolysis in water. A GLP soil photolysis study (MRID 444406-05) conducted with ã-HCH coated on soil and irradiated 12 h/day for 30 days using a Xenon arc lamp (UV wavelengths simulating natural sunlight), also showed little alteration of ã-HCH (thirty day recovery of 85.9% ã-HCH, 2.3% unidentified extractable, 4.4% unextractable, and 0.2% trapped volatiles versus the dark control that had 92.0% ã-HCH, 2.6% unidentified extractable, 2.4% unextractable, and volatiles were not trapped). Although there potentially were some volatiles that were not trapped (total recovery of 92.8% in irradiated samples versus 97.0% in dark controls), minimal photolysis occurred in soil. Hamada, et al., 1981, showed that γ-HCH is degraded more rapidly than α-HCH when evaluated in crystalline state and 2-propanol solution using a mercury lamp that emits shorter wavelength UV than typical for sunlight and gamma rays from ^{60}Co. The degradation products were pentachlorocyclohexanes and pentachlorocyclohexenes, and α-HCH was also produced from crystalline γ-HCH using ^{60}Co. This is discussed further below. Overall, γ-HCH appears less stable to photolysis than other HCH isomers, although under most conditions γ-HCH is photolytically stable. This photo-stability is consistent with a lack of UV absorbance above 300 nm (Lindane – Summary of Data and Petition for a Time-Limited Tolerance Supporting Use as a Seed Treatment on Canola; document submitted to EPA).

Microbial degradation of γ-HCH gives predominantly γ-pentachlorocyclohexene (Benezet and Matsumura, 1973) although metabolites are not always observed probably due to further degradation proceeding faster than formation

(Buser and Muller, 1995). Comparison of active to sterilized sludge showed that γ-HCH is more rapidly degraded than α-HCH with the γ-HCH half-life being just 20 h.

Overall it appears that γ-HCH is slightly less persistent in the environment than α-HCH.

Does ã-HCH isomerize in the environment? Two possible mechanisms for conversion of ã-HCH to á-HCH are photo-isomerization and microbial 'degradation'.

Steinwandter, 1976, showed ã-HCH to á-HCH conversion (2% in two hours) for crystalline ã-HCH coated on quartz using a mercury vapor lamp with UV wavelengths down to 230 nm. The soil photolysis and aqueous photolysis studies done under GLP and in accordance with EPA guidelines showed no detectable isomerization of γ-HCH. Hamada, et al., 1981, produced á-HCH, ä-HCH, and pentachlorocyclohexane from ã-HCH by irradiation with ^{60}Co gamma rays and Malaiyandi and Shah, 1984, produced á-HCH from ã-HCH by mixing ã-HCH crystals with ferrous chloride and exposing to sunlight. Neither of these experiments simulated natural environmental situations.

Benezet and Matsumura, 1973, showed that the bacterium *Pseudomonas putida* was able to convert 3% of applied ã-HCH to á-HCH along with the predominant metabolite of ã-pentachlorocyclohexene and that small amounts of á-HCH formed from ã-HCH in ocean sediment. Huhnerfuss, et al., 1992, found trace conversion of ã-HCH to á-HCH for a mixed culture of marine organisms, but the á-HCH/ã-HCH ratio was not changed from 1.00. Buser and Muller, 1995, found a similar result in anaerobic sewage sludge with ã-HCH degradation proceeding 240 times faster than conversion to á-HCH. Waliszewski, 1993, evaluated at ã-HCH degradation in soil of a treated field and found that the extent of conversion to other HCH isomers is very limited and does not contribute to environmental contamination with other isomers. In a similar experiment Singh, et al., 1991, did not observe isomerization. These studies give a very consistent message that although microbial transformation of ã-HCH to á-HCH is technically possible, it does not occur to a significant extent. Although ã-HCH can convert to the more stable á-HCH isomer by both photolysis and microbial degradation, significant conversion under typical environmental conditions has not been demonstrated

How do á-HCH and ã-HCH reach the Arctic? HCH contamination of the Arctic is due to transport via rivers as well as atmospheric and oceanic advection from more southerly latitudes (Wania and MacKay, 1999; Iwata, et al., 1993). Henry's Law Constant is used to predict the distribution of semi-volatile chemicals between air and water (Kucklick, et al., 1991). A higher Henry's Law constant makes α-HCH more transferable across the air water interface making distant cold water bodies like the Arctic Ocean a more significant sink for this molecule and perhaps explaining the greater amount of α-HCH present in the Arctic environment (Iwata, et al., 1993). HCH isomers are transported in the environment, but they are not evenly distributed across the globe. For example, worldwide use of HCH is dominated by northern hemisphere countries (Li, et al., 1996) and the southern hemisphere air and oceans have much less α-HCH and γ-HCH contamination (Bidleman, et al., 1993; Iwata, et al., 1994). Contamination of air and water by α-HCH is also shown in Figures 2.18 A and B of the Canadian Arctic Contaminants Assessment Report (CACAR, 1997). This report shows that more tropical oceans are contaminated with α-HCH only in the vicinity of heavy HCH use areas like China and India. Overall, only a small amount of HCH is transported to the Arctic, but degradation rates are slower than in other zones and massive use of HCH in the 1980's led to accumulation in the Arctic Ocean (Wania and MacKay, 1999). Within NAFTA countries, technical HCH use was eliminated in Canada, effective October 7, 1976, and in the United States in 1978 (CEC Decision Document, 19 April 2000). Use of technical HCH was also banned in the former Soviet Union in the early 1990's and in China in the early 1980's (Li, et al., 1996). As of 1995, use of technical HCH in the temperate zone had decreased by a factor of 200 relative to 1980 and the Arctic Ocean began a gradual cleansing because degradation exceeded net inflow (Wania and MacKay, 1999).

Will banning lindane in NAFTA countries solve the problem of Arctic contamination? Potential for environmental contamination is enhanced by use of technical HCH because it contains only 11 – 18% of insecticidally-active γ-HCH (CEC Decision Document). Use of technical HCH for insect control began in the 1940's and maximal annual usage reached over 400 kt in 1980 (Li, 1999). Annual usage dropped to about 150 kt in 1983 following the banning

of HCH use in China and to below 50 kt in 1991 following banning of HCH in the former Soviet Union (Li, 1999). Li, et al, 1998 show those levels of α-HCH in the arctic atmosphere also dropped following these major reductions in worldwide usage. Annual usage of technical HCH was around 25 kt in 1995 (Li, 1999) with some apparently coming from former Soviet states, Eastern European countries and possibly Russia as well (Breivik, et al., 1999). The potential impact on the arctic environment from Northern Asian applications is large because 78% of the total riverine input to the Arctic Ocean comes from nine rivers in Russia and one in Canada (CACAR, 1997). The report says that high levels of HCH have been found in the Russian river and Wania and MacKay, 1999, suggest that usage in the Soviet Union may have caused most of the current Arctic contamination with α-HCH.

A model based on α-HCH shows that most (often >95%) of the α-HCH in the temperate, subtropical and tropical zones was emitted in those zones while most α-HCH in the polar zone originated in the temperate and boreal zones (Wania and MacKay, 1999). They also reported that if there were no further emissions of α-HCH after 1997 or even with constant emissions at 1997 levels, the Arctic Ocean and atmosphere would recover with half-lives of 11.5 and 4 years, respectively. Thus, there are areas of Northern Asia, Europe and North America that drain to the Arctic Ocean that are sensitive to HCH pollution. **However, responsible use of g-HCH for seed treatments and limited other uses in most areas of the world (including NAFTA countries) will not result in the environmental problems created by technical HCH.**

Environmental problems arose when annual HCH usage exceeded 300 kt in the 1970's and early 1980's (Li, 1999). More recent lower usage of all HCH isomers (e.g. 5 kt lindane in 1984; Poissant and Koprivnjak, 1996; and approximately 25 kt of technical HCH in 1995; Li, 1999) has led to significant environmental recovery. Data from 1989 and 1990 showed that air concentrations of HCH isomers were high enough to cause air to water transfer and net deposition of HCH isomers in the Arctic Ocean water (Iwata, et al., 1993). More recent data shows a reversal of this trend with the Arctic Ocean water cleansing itself by several mechanisms including water to air transfer due to lower atmospheric HCH concentrations (Harner, et al., 1999). Additionally, residues of HCH in foodstuffs in China have decreased about 5X for rice, 127X for fish, and 32X for poultry, eggs and meat between 1978 and 1992 (Li, et al., 1998). Also α-HCH in muscle of pike in Sweden declined along with technical HCH usage (Breivik, et al., 1999) as did HCH isomers in Arctic Cod liver (Sinkkonen and Paasivirta 2000). Clearly, lower usage has been associated with environmental recovery

Consistent with the very large decreases in the use of HCH and lindane, it was reported in the *Toronto Star* on March 5,1999 that Barry Hargrave, a marine ecologist with the Bedford Institute of Oceanography, reported lindane was one of the most common pollutants found in the Arctic 10 years ago, but **lindane levels have since dropped by more than 80 per cent in the air. This finding further supports the theory that past use of HCH and lindane, not current uses of lindane, are the sources of Arctic concentrations that will not be significantly impacted by seed treatment and other limited uses of lindane.**

F. COMMENTS ON THE DRAFT DECISION DOCUMENT

General Comments

The CEC Decision Document recommends establishing a North American Regional Action Plan (NARAP) for lindane. The NARAP would include the following components as described in section 4.0, last paragraph (section 4.2 addresses this as well with some differences):

- Require status reports for each country to establish (a) quantities imported, (b) annual usage, and (c) specific uses in public health and pesticide sectors.

- Establish Sound Management of Chemicals (SMOC) initiatives, in particular on environmental monitoring and assessment.

- Establish a task force of members from the public health and pesticide sectors and regulatory agencies of each country. The mandate of this task force is not specified.

- Provide a mechanism for reducing or eliminating lindane use in NAFTA countries (additional ideas along this line are in section 4.1 of the Decision Document).

Lindane should be regulated using a balanced approach towards environmental protection, human health, and cost-effective needs of agriculture and public-health disease control. Clearly, the benefits of lindane should be taken into account in any assessment of the chemical but benefits have not been addressed in the Decision Document. Lindane is a highly cost-effective insecticide for seed treatment. The application rate for lindane used as a seed protectant is extremely low, but lindane's broad-spectrum insecticidal activity and its unique fumigant action make it an ideal seed protectant. The low use rate results in very low or non-detectable residues in food commodities, a reality not shared by other products.

In addition, the Decision Document focuses on potential hazards and does not consider the minimal risk associated with use of lindane taking into account its low rate of exposure. Estimates of dietary and worker exposure are presented elsewhere.

Lindane is referenced throughout the CEC document as a "Persistent Organic Pollutant" (POP). This is incorrect in the strict sense since lindane was considered in both the ECE and UNEP POPs negotiations and was **not** included in the final list of either body after deliberation. In the technical sense as well, lindane is not a POP since recent studies show its half-life in soil to be between 17 days and 107 days.

The CEC Decision Document discusses HCH (a multi-isomer mixture) and lindane (specifically, γ-HCH) and often confuses the two compounds. Among HCH isomers, only γ-HCH, used as lindane, is effective for agriculture and public health disease control. Current products marketed in the NAFTA region are 99.5 per cent ã-isomer, and therefore HCH data should not be used to characterize lindane. Technical HCH registrations, and HCH stockpiles and hazardous sites could be eliminated in all countries without detriment to agriculture. Studies have shown a direct correlation between the banning of technical HCH in China, followed by India (agricultural uses) and the Soviet Union and significant decreases in α-HCH in the Arctic Atmosphere (Li, 1999). The dietary exposure problems involving Arctic indigenous peoples described in the CEC document (section 2.4.3.4) and Arctic environmental contamination problems (section 2.4.4) resulted from these massive uses of technical HCH in the 1980's and early 90's in Asian countries and will not be significantly affected by current uses of lindane, which is 99.5% ã-HCH in NAFTA countries.

The SMOC initiative recommendations for status reports, an environmental monitoring program, and a task force are noteworthy steps towards understanding the world-wide distribution of HCH, but the NARAP goal of reducing or eliminating lindane in NAFTA countries unfairly prejudges results and should not be a NARAP goal.

The environmental and toxicology data cited for lindane is incomplete and in some cases inaccurate. And the body of the text and the results of testing are often inconsistent with the conclusions reached in the Executive Summary. For example, the Executive summary identifies lindane as being genotoxic, whereas the detailed discussion states that it is not genotoxic. Similarly, reproductive effects are noted in the Executive Summary, whereas data show that lindane is not considered to be a reproductive or developmental toxin. These inconsistencies and errors will be addressed in our specific comments below.

CIEL Has The Following Comments On Specific Points In The CEC Document

The following specific comments are identified as to section of the CEC document addressed. Information cited has either been misstated, misquoted, or only partially reported.

Executive Summary

The executive summary is not consistent with the body of the document and the available literature concerning the potential health effects of lindane. For example, the executive summary states: "A wide variety of toxicological effects are recorded, such as, reproductive and endocrine impairments and (*sic*) can be neurotoxic, immunotoxic, mutagenic, genotoxic, and carcinogenic." Section 2.4.3.1 "Basic Toxicological Findings in Laboratory Animals" states that "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."

Similarly, in contrast to the conclusion in the executive summary that lindane is carcinogenic, the discussion in the body of the document regarding carcinogenicity states that there is "some debate over the carcinogenic potential of lindane" and that a definitive study (referred to a second mouse oncogenicity study whereas, in fact, it is the 9th mouse oncogenicity) is in progress". The availability of a definitive rat oncogenicity study, conducted recently and accepted by US and other regulatory authorities, is not even mentioned, presumably because it is clearly negative for carcinogenicity. **Immunotoxicity has not been observed in GLP studies** submitted to and accepted by worldwide regulatory agencies; the only suggestion of an effect is found in studies conducted in India with lindane of unknown purity. **Neurotoxic and reproductive effects are only found at high dose levels that are not relevant to current human exposure** levels as found in the recently conducted GLP studies.

Section 2.4.1

Paragraph 1. As stated earlier, lindane is not defined as a persistent organic pollutant by either the UN (UNEP) or the Economic Commission for Europe. The á-isomer is the predominant, and its presence most likely resulted from the use of technical HCH.

Only a small amount of ã isomer is being used in North America. There are not thousands of tons of mixed isomer, technical HCH, being used, since the North American countries banned it over two decades years ago. Thus are we truly concerned about the migration of a very minor amount of lindane, especially when hydrolytic and photolytic conversion under prevailing environmental conditions to other HCH isomers has not been clearly shown?

In Table 3, the number quoted for Canada 1980, 200 tons should be 286 tons. The amount of lindane used in Mexico appears to be incorrect. Li et al. quote a use of lindane of 35 tons in 1980 and 15 tons in 1990 (Table 1) and ã-HCH as 57.5 tons and 54.2 tons in 1980 and 1990 (Table 2).

In the final paragraph of this section, it is stated that USA use in 1992 was only 32 tons, and pecans accounted for 26 tons of this amount. Since the product is no longer used for foliar application, thus eliminating pecan uses, the tonnage must be quite small, and it is certainly less than six tons per year. One private source, a formulator, estimates 225,000 to 275,000 lbs. of technical lindane is used currently in the U.S.

Section 2.4.2

Paragraph 3. Isomerization in soil, in plants and in mammals has not been observed in GLP studies performed under EPA/OECD guidelines. However, as noted earlier in this response, isomerization by microbes and photolysis can occur.

Section 2.4.3.

The paragraph begins by noting "...there is a lack of consistent human data on lindane effects." The paragraph concludes, "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, or recall bias." This, however, does not prevent the author(s) from presenting a selective discussion implicating lindane as a causal agent for a variety of human health effects ranging from endocrine modulation, systemic and developmental toxicity to cancer, in spite of the openly acknowledged flaws and limitations of the studies from which the case is drawn.

The most obvious example of this is the use in the first paragraph of the Karmaus and Wolf, 1995, study to select lindane as the sole mentioned potential causal factor for reduced neonatal weight and length. In the ensuing paragraph, the author notes that it was "... exposure to insecticides, including lindane..." that is associated with this effect, although the degree and extent of this effect is not discussed in the Decision Document.

The Cantor, et al., 1992, study is cited as establishing a positive association between non-Hodgkins (sic) lymphoma in Midwestern farmers "...using lindane...", conveniently neglecting to cite data by the same group of authors published elsewhere showing a positive correlation between the same disease and the use of herbicides by farmers in the same geographical region.

The cardiovascular effects reported by Flesch-Janys, 1997, and reduced neutrophil function (Sliwinski, et al., 1991) attributed to lindane were found in combination with numerous other potential causative agents including polychlorinated dibenzo-p-dioxins and other potent toxic materials. The endocrine and hematopoetic effects reported by Tomzak, et al., 1981, and attributed to lindane in the decision document are in fact observed in the presence of other chlorinated hydrocarbons as well.

"Body burdens of lindane '...alleged to be' significantly and highly correlated with cancer mortality rates..." (Wang et al. 1988) are in fact based on levels of HCH and DDT in human earwax. How these observations are "..consistent with the decreased rate of breast cancer occurrence in Israel after banning lindane use (Westin, 1993)" is left to the reader's imagination. This is particularly intriguing given that this ban occurred only recently. For such a cause and effect relationship to be observed so rapidly is extraordinary, given the long latency periods typically required for expression of chemically-induced carcinogenicity, and would be worthy of publication in the *New England Journal of Medicine* or other prestigious journal.

Paragraph 3. Dismissal of "many" cohort studies as unable to identify causal factors does not prevent the authors from implicating lindane exposure with increased risk of lung cancer (Barthel 1981 actually studied pesticide exposed agricultural workers) and with leukemia (Hansen, et al., 1992 actually studied Danish gardeners). This is flawed logic.

Section 2.4.3.2

The Decision Document cites lindane-sensitive subpopulations; however a more accurate statement is that these subpopulations are exposed to higher levels of lindane due to their diet than the general public, but these levels of exposure are well below the acceptable daily intake of 1 ìg/kg-bw as adopted by PMRA. There is no evidence that one subpopulation is more sensitive to lindane than another.

Kuhnlein did not state that the Arctic is a "sink" for persistent organic pollutants. Rather Kuhnlein surveys diets and contributions of food sources to northern aboriginal groups. The residue of total HCH (á-, â-, ã-) is approximately 15 ìg/100g in "traditional" Inuit foods. There is no comment made as to what portion of the Inuit's diet comprises "traditional" foods. Other groups have diets with lower residues. All diets appear to give residues below WHO ADI levels and also below the Canadian TDI.

Workers who formulate or use lindane are not an issue to be addressed in this document, since controls to reduce exposure have not been taken into consideration, and therefore the issue is moot at this time. However, we have provided some comments in Section 2.4.5 on the low level of exposure from seed treatment.

Section 2.4.3.4

Again, Kuhnlein does not quote the Arctic as being a "sink".

Section 2.4.4

Paragraph 1. Levels of HCH isomers are higher in Arctic surface waters but not always by an order of magnitude. Authors Iwata, et. al., 1993, show that levels colder waters such as the Bering Sea (190 pg/l) and Gulf of Alaska 260

(pg/l) are about 2-5 times the levels in temperate/tropical waters such as the Caribbean, (36 pg/l) Mediterranean (150 pg/l) and East China Sea (78 pg/l). Many other geographic sites are quoted in the reference.

Paragraph 2. This paragraph deals with a historical situation and yet it is written in the present tense. The key point is that over the last ten years, the number of labeled uses for lindane has decreased, the volume of lindane used has decreased, and technical HCH has been banned in most countries. Banning the use of technical HCH has led to the elimination of the non-active isomers, in particular á-HCH, which comprises the majority of technical HCH. There has been a direct correlation between the banning of technical HCH in several major use countries and the decrease in á-HCH in the arctic atmosphere (Li).

The document cites Neururer and Womaster but use of this reference is somewhat misleading since there are no products labeled for foliar application of lindane in the U.S. or Canada. In the cited study, 54% lindane did evaporate from leaves of plants but that result is irrelevant for seed treatment or soil uses, the only agricultural uses in Canada and the U.S.

Paragraph 3. Wania and Mackay further support the point that banning of materials containing á- HCH has led to a marked decrease in levels of the isomer observed in the environment. Banning the already limited uses of lindane in the U.S. and Canada will not significantly decrease the levels of the á-HCH.

Paragraph 4. This paragraph points out that HCH residues are mostly á-isomer. If so, banning the use of lindane will not significantly impact the residue levels in the environment. See the comments in the above paragraphs to further substantiate this position.

The end of paragraph points out that residues of HCH in animals have declined since 1974 (until 1992) and since 1986 (until 1994), which is good news. Thus with the current low usage, decreases of the overall levels of HCH in the arctic will continue. Further significant decreases in the levels of alpha- and beta-isomers can be achieved by elimination of the use of technical HCH in other countries outside the NAFTA region.

Section 2.4.5

The concept of risk is ignored in summary paragraphs such as those found in Section 2.4.5 of document, which states, "Toxicological data indicate 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." (This sentence and the remainder of that paragraph are repeated verbatim in Section 4 of this document). It is further misleading to imply that workers are being exposed to unsafe levels of lindane in the formulation of products and that the general population "may or may not" be exposed to levels of concern. There are no data presented to support these unfounded statements and they are in direct contradiction to other assessments that have been performed. For example, Codex Alimentarius has expressed no concern for current dietary exposure to lindane and the WHO, 1991, concluded that "The daily intake and total exposure of the general population are decreasing gradually; however, they are clearly below the advised acceptable daily intake and are of no concern to public health" and, with respect to occupational exposure, "As long as precautions to minimize exposure are observed, lindane can be handled safely."

The summary of human health information in the CEC document is also flawed in that it does not address the purity of the lindane that was the subject of the cited studies. This is an important issue because it is known that the *alpha*- and *beta*-isomers previously present in lindane formulations are highly toxic. These isomers have been virtually eliminated from lindane that is currently in use, and toxicity seen in early studies of lindane is therefore not relevant to the toxicity of the material that is currently in use. This is borne out by the favorable toxicity results observed a wide variety of well-conducted studies in recent years using lindane of high purity. The broad-brush indictment in this document of lindane, as being associated with a variety of serious toxicities is incorrect or wrong or not relevant to current human exposures to lindane.

Paragraph 1. If lindane only makes up a very small portion of the HCH observed in the environment, taking action to reduce lindane releases will not result in numerous health benefits, in contrast to what is stated in this section of the Decision Document. There are very limited uses of lindane in the U.S. and Canada, and thus this contribution

to minimizing lindane residues in the environment is very small. Since the levels of lindane in the environment and in dietary samples are well below the levels of concern set by the various countries, lindane does not pose a risk to humans and wildlife in North America. This paragraph discusses lindane, but in the last sentence shifts to HCH isomers, and one might conclude that lindane is one of the most abundant and pervasive organochlorine compounds in the Arctic. This is simply not true as cited above.

Paragraph 2. Worker exposure is again raised without discussing means of controlling exposure. Exposure to lindane can be minimized by using methods dictated under the Worker Exposure Standard (EPA) and, further, exposure can be estimated through the use of the Pesticide Handlers Exposure Database (PHED). Discussion of worker exposure in this document without addressing precautionary protective equipment is without merit.

Worker exposure to lindane during manual seed treatment was evaluated by Dr. Richard Fenske of Rutgers University. The study was conducted on a South Dakota wheat farm using manual seed treatment (one of two distinct forms of treatment, the second being an automated and closed auger method). In summary, the study showed a lifetime average daily dose (LADD) of 0.077 micrograms/kg/day. Compared to the EPA RfD of 4.7 micrograms/kg/day based upon a 2-year rat study showing histological changes in the liver, increased spleen and liver weights and increases in platelet count, this exposure constitutes approximately 1 per cent of the RfD under reasonable but conservative occupational conditions. A similar exposure study conducted by Uniroyal Chemical Company (R. Bird) showed exposures of a similar magnitude.

To restate again, all evidence shows the levels of HCHs in the diets of aboriginal and northern populations are well below the level of concern. Dropping further uses of lindane will have only a very minimal impact in this exposure. The most significant positive impact on inadvertent dietary exposure is the banning of technical HCH in other countries and clean-up of work sites.

Paragraph 3. Integrated pest management is an important part of any farming program as is the control of resistance build-up. Lindane is a cost-effective insecticide that can play a part in an integrated pest management program. Discarding a useful agricultural tool, based on contamination resulting not primarily from the use of lindane but from technical HCH, and based on inaccurate conclusions about lindane regulatory data, is unfortunate for the farmer.

Section 3.6

Page 16. The word "Recent" does not match the 1992 reference of 8 years ago. We cannot find the 100-150 tons per year, quoted in the Willett, et. al., reference. However it does quote that earlier tonnage was 550-720 thousand tons and up to 6 million tons. These amounts obviously led to the current situation and in comparison current amounts are very low. Table 4 shows trivial amounts for Mexico.

Section 4.0

Page 19, Paragraph 2. **Lindane is not defined as a "persistent organic pollutant"** by the UN and other august bodies, and this statement must be corrected. Further, **lindane is not one of the most abundant and pervasive organochlorine insecticide contaminants**. A non-insecticidal isomer of lindane, á-HCH, is present in the environment at significant levels, which can be lowered by the discontinuance of the global use of technical HCH. There is only minor conversion of ã-HCH to á-HCH in the environment. The *gamma* isomer of HCH is found in the North American environment, but usually at extremely low levels when found.

Page 19, Paragraph 3. **Toxicological data show that lindane does not adversely affect reproduction, nervous and immune system**. **Workers formulating lindane minimize their exposure by the use of protective equipment that is well-defined by regulatory agencies. Further, workers who handle lindane products also can use protective equipment to minimize their exposure.** The dietary exposure levels are again defined by regulatory agencies and the levels of exposure are within the acceptable limits. The levels in aboriginal and northern populations are also well below the limits set by PMRA.

Page 20, Paragraph 1. The biggest HCH problem is technical HCH. Spending vast amounts of money on forming interagency task forces will only serve to divert government and private sector money and resources from the real problem. These limited resources should be invested where they are most needed. None of the proposals in Sections 4.0-4.2 will reduce á-HCH levels to any significantly lower levels; only the reduction in the use of technical HCH, as has historically been demonstrated, will impact á-HCH.

Appendix D

Page 38, Paragraph 1. There is no evidence that ã-HCH is converted into á-HCH in plants, mammals, or soil. There is some evidence for photolytic isomerization in the laboratory under non-environmental conditions. Thus we do not know that decreasing the use of ã-HCH will lead to decreased levels of á-HCH in the atmosphere or in food sources. We do know, however, that banning of technical HCH, which consisted primarily of á-HCH, has led to a significant reduction in the levels of the HCH isomers in the environment and in food sources.

Page 38, Paragraph 5. The authors state that the high concentration of isomers other than ã-HCH in the environment suggests that lindane is transformed into other isomers in the environment. This statement is not supportable by current knowledge. We understand that technical HCH is still heavily used by India, at a minimum, and this technical is primarily á-HCH. Uses in India have not been reduced in comparison to North America. We also know that there are stockpiles of HCH-containing materials that were unintentional by-products of production, which are available for volatilization to the atmosphere. However, current production practices result in either a by-product being produced from the wastes or environmentally sound disposal practiced. Thus, it is highly unlikely that further reducing lindane uses in North America will have any significant contribution to the reduction of á-HCH in the environment.

Page 39, Paragraph 3. The Decision Document states that all the HCH isomers are acutely toxic to mammals. For clarification, all chemicals are acutely toxic at some level! However, as noted in the Toxicology Summary, lindane is only moderately toxic by oral, dermal and inhalation routes, being in EPA Toxicity Categories II, II and IV respectively. WHO classifies lindane in Class II – "Moderately Hazardous."

Page 39, Paragraph 4. Bidleman, 1988, is ambiguous and his main conclusion is that additional study is needed. He does not specifically discuss ã-HCH or any HCH isomer.

Brubaker and Hites used gas phase reaction kinetics and estimated constants for á- and ã- isomers. This enables them to estimate lifetimes. These rates are higher than those calculated by Atkinson, leaving one to wonder which of the sets of rates is correct.

Page 39, Paragraph 5. Willett, et. al., 1998, discusses different properties of isomers of HCH. *Gamma*-HCH is the most rapidly metabolized HCH isomer. The â-isomer is most stable of the isomers and shows up in human tissues.

Schwartzenbach is a textbook and therefore not a primary resource from which to base the stability of â-HCH.

Page 40, Paragraph 4. Buser and Muller, 1995, did not discuss what is quoted in the Decision Document. The journal authors studied degradation in sewage sludge, and they showed faster degradation in active sludge. The comparative rates of degradation were: ã>á>â. The rates of degradation in the sewage sludge were 450 times the hydrolysis rate. In the sludge, the isomerization of ã to á was 240 times slower than overall degradation.

Singh, et. al., 1991, are also misquoted. The authors found no evidence of isomerization in soil plots treated with HCH mixed isomers. There also appears to be a preferential uptake of á-isomer into crops.

Page 41, Paragraph 2. When citing the Willett, et al., 1998, reference the authors of the Decision Document misquoted the journal article. Alpha- and ã- isomers are most common in soil, air and water. The â-isomer is most prevalent in human tissues.

Page 41, Paragraph 3. Hoff, et al., 1992, make the point that **á-isomer appears to be decreasing in air**, and there is more á-isomer in air in summer than in winter. The **ã-isomer shows the same pattern but at levels 10-20% of those of á-isomer.**

Brun, et al., 1991, is correct but does not reflect the total findings. The authors showed levels of á- and ã- isomers at various sites across Canada between 1979 and 1988. **Levels of the isomers decreased after 1982 when some uses of ã-HCH were withdrawn. The levels then decreased to and plateaued at a lower level.**

McConnell, et al., 1998, **do not study** surface waters. This paper deals with levels of á- and ã- isomers in Sierra snow. The **levels found by the authors are very low, usually less than 1.0 ng/l.**

Li, et al., 1998, discusses the **significant decreases in the use of technical HCH and the resulting decrease of HCHs observed in the Arctic**.

Page 41, Paragraph 4. Wania and Mackay, 1999, deal only with the á- isomer. However, the authors state that of the large amounts emitted in early 1980s probably only 1% remained in mid 1990s.

Page 42, Paragraph 2. The Steinwandter and the Hamada references deal with more powerful light sources than are encountered in normal sunlight at the earth's surface. Conversions in the atmosphere normally are simulated with Xenon arc lamps. These experiments failed to simulate vapor phase photolysis that most appropriately reflects what is occurring in the atmosphere.

Page 42, Paragraph 3. This paragraph is highly speculative. The Hoff reference supports seasonal fluctuation of isomer ratios and also makes the point that **á-isomer appears to be decreasing in the atmosphere**.

Page 42, Paragraph 4. The Buser and Muller, 1995, are misquoted**.** It is true that the orientation of chlorine atoms is important and ã-isomer with axial chlorine atoms is degraded most rapidly of all of the isomers, but the ã-isomer is degraded rather than converted to á-isomer. In 10 days, greater than 99% of the ã-isomer and greater than 90% of the á-isomers were degraded. After 50 hrs of incubation of ã-HCH, the amount of á-HCH increased from 0.05 to approximately 0.5% and then decreased. The ã-isomer primarily degrades to 1,3,4,5,6-pentachlorocyclohe-1-enes (PCCHs) and 3,4,5,6-tetrachlorocyclohex-1-enes (TCCHs). The authors also state that PCCHs and TCCHs are degraded even faster to further metabolites. Conversion of the ã-isomer to á-isomer was approximately 240 times slower than overall degradation.

Page 43. In the Decision Document, Benezet and Matsumura, 1973, are cited correctly, but their conclusions should be stated differently. Transformation of ã-HCH to á-HCH was minor (3%) in a simulated lake and degraded primarily to ã-PCCH. Àlpha-HCH was formed only in the presence of NAD and only to a level of 3%. The principal product was tetrachlorocyclohex-1-ene. Therefore degradation was occurring.

The citation of Vonk and Quirijns, 1979, is partially correct. Some á-isomer is formed from ã-isomer but also ã-TCCH and ã-PCCH are also formed from *E. coli*. À-TCCH was the major metabolite under aerobic conditions, while ã-PCCH was the major degradate under anaerobic conditions.

Huhnerfuss, et al., 1992, are cited correctly, and in addition show that ã-PCCH is formed from ã-HCH by marine microorganisms. The enrichment culture of marine microorganisms was unable to convert ã-PCCH to á-HCH, and the conversion of ã-HCH to á-HCH only occurred to the extent of less than 0.1%.

Page 43, Paragraph 2. Waliszewski, 1993, showed that in soil isomerization was unimportant. This concurs with GLP-guideline soil studies.

Page 44, Paragraph 3. Kelly, et al., 1994, is a review article that cites data retrieved from computerized and manual searches. Lifetimes of less than one day are reported for the combined HCHs. Although the table indicates lindane, it is more correctly stated as "total HCHs." Six U.S. locations with 465 samples are cited that range from non-detects to 7 ng/m^3.

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