



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

July 24, 2006

MEMORANDUM

SUBJECT: Agency Response to Comments on the 2002 Lindane RED

FROM: Mark T. Howard
Chemical Review Manager
Reregistration Branch 3

TO: Public Docket for Lindane (FDMS Docket # OPP-2002-0202)

The Agency received a broad range of comments in response to EPA's Notice of Availability for Public Comment on the Lindane Reregistration Eligibility Decision (67 FR 59500, September 23, 2002). The *Federal Register* Notice 60-day public comment period ran from September 23 to November 22, 2002. A total of 229 comments were received from registrants, private citizens, state and local government agencies, non-profit environmental and consumer groups, industry interest groups, and commodity-based associations. The vast majority of comments came from private citizens through an e-mail campaign asking to discontinue the use of lindane, particularly pharmaceutical uses of lindane. The attachments to this memo address new issues raised by the public. Several comments received were redundant from previous comment periods and responses can be found in earlier response to comment documents.

There are four attachments to this document, as follows: Attachment A, a memorandum from the Health Effects Division (HED), addresses comments on the human health risk assessment; Attachment B, a memorandum from the Environmental Fate and Effects Division (EFED), addresses comments on the environmental risk assessment; Attachment C, a memorandum from the Office of General Counsel, addresses a data compensation issue; and Attachment D, a document that lists all the names of stakeholder groups who submitted comments.

While the attachments to this document respond to technical questions and comments on the Lindane RED, this memorandum also describes EPA policy on whether the Federal Food, Drug, and Cosmetic Act (FFDCA) requires the Agency to include in its safety assessment those exposures resulting from the use of lindane in pharmaceutical products in response to the public comments on this issue.

Public Comments. Crompton Corporation argued that pharmaceutical uses should not be considered in the risk assessment. The Consumer Specialty Products Association argued that that EPA does not have the authority under FFDCA & FQPA to regulate any non-pesticide, food use

(such as pharmaceutical uses). The Consumers Union argued that FQPA requires that EPA consider pharmaceutical uses. Beyond Pesticides argued that all pharmaceutical uses should be included in the aggregate risk assessment. The American Chemistry Council argued that FQPA does not intend for EPA to incorporate any pharmaceutical use or non-pesticidal uses in its aggregate assessments. The Natural Resources Defense Council argued that EPA needs to aggregate pharmaceutical use in its risk assessments.

After carefully considering the comments from the public, FDA, public interest groups, industry groups, and other interested parties, EPA has concluded the following:

In determining the risk to human health, the Agency examines more than just dietary exposures. Section 408 of FFDCFA requires EPA to consider potential sources of exposure to a pesticide and related substances in addition to the dietary sources expected to result from a pesticide use subject to the tolerance. In order to determine whether to maintain a pesticide tolerance, EPA must “determine that there is a reasonable certainty of no harm. . . .” Under FFDCFA section 505, the Federal Drug Administration reviews human drugs for safety and effectiveness and may approve a drug notwithstanding the possibility that some patients may experience adverse side effects. EPA does not believe that, for purposes of the section 408 dietary risk assessment, it is compelled to treat a pharmaceutical patient the same as a non-patient, or to assume that combined exposures to pesticide and pharmaceutical residues that lead to a physiological effect in the patient constitutes “harm” under the meaning of section 408 of the FFDCFA.

EPA believes the appropriate way to consider the pharmaceutical use of lindane in its risk assessment would be to examine the impact that the additional non-occupational pesticide exposures would have to a pharmaceutical patient exposed to the same compound. Where the additional pesticide exposure has no more than a minimal impact on the pharmaceutical patient, EPA could make a reasonable certainty of no harm finding for the pesticide tolerances of that compound under section 408 of the FFDCFA. If the potential impact on the pharmaceutical user as a result of co-exposure from pesticide use is more than minimal, then EPA would not be able to conclude that pesticide residues were safe.

However, in the case of lindane, the Agency will be publishing an Addendum to the RED that addresses the continued registration of lindane. Thus, the co-exposure approach discussed above is not being presented in this document.

Further information on FDA and how it regulates lindane can be obtained from its website: www.fda.gov; e.g., <http://www.fda.gov/bbs/topics/ANSWERS/ANS00725.html>.

Attatchments



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460
Office of Prevention, Pesticides and Toxic Substances

February 28, 2003

MEMORANDUM

SUBJECT: **Lindane;** Chemical No. 009001. HED's Response to Public Comment on HED's Revised Risk Assessment for Lindane Registration Eligibility Document (RED)

DP Barcode: D287964
Reregistration Case #: 0315

FROM: Becky Daiss
Environmental Health Scientist
Reregistration Branch 4/HED (7509C)

THROUGH: Susan Hummel
Branch Senior Scientist
Reregistration Branch 4/HED (7509C)

TO: Mark Howard
Reregistration Branch 3
Special Review & Reregistration Division (7508C)

This provides the Health Effects Division's (HED) response to comments from the public on EPA's July 31, 2002 Revised Human Health Risk Assessment for Lindane (gamma-hexachlorocyclohexane). The following organizations submitted comments on the human health risk assessment; National Resources Defence Council (NRDC), National Pediculosis Association, Inc. (NPA), Pesticide Action Network North America (PANNA), Alaska Community Action on Toxics (ACAT), Beyond Pesticides, Office of the Attorney General of the State of New York, Crompton Corporation, American Chemistry Council (ACC), and Consumer Specialties Products Association, Inc (CSPA). This memorandum addresses only those comments that have not been raised and responded to in previous public comment and response documents. (B. Daiss, D282320, 4/25/02, D280623, 1/30/2002)

Comments on the Assessment of Risks from Use of Lindane for Treatment of Lice and Scabies

Public Comment: In comments on the blood level analysis used to assess potential risks from lindane used as a scabies treatment, Crompton Corporation disagrees with HED's use of a 10 fold uncertainty factor to account for variability of responses in humans. Crompton states that an uncertainty factor of 10 is not necessary because the comparison of blood levels rather than administered dose takes into account the pharmacokinetics portion of the 10-fold intraspecies uncertainty factor and that, therefore, a 3 fold factor is sufficient.

HED Response: HED believes that use of an uncertainty factor of 10 to address intraspecies variation in exposure related effects is reasonable regardless of the route of administration and irrespective of whether potential differences in pharmacokinetic uptake and distribution are accounted for.

Public Comment: NRDC, Office of Attorney General of the State of New York, PANNA, ACAT, and NPA commented on HED's failure to perform a Margin of Exposure (MOE) analysis for use of lindane to treat head lice. Several of these organizations submitted MOE analyses for EPA's consideration.

HED Response: As should have been pointed out in HED's Revised Assessment of Risk from Use of Lindane for Treatment of Lice and Scabies, HED did not conduct an MOE analysis of potential risk from lindane treatment of head lice because we do not believe that there is sufficient data to conduct a reasonable, scientifically sound quantification of MOE's associated with lindane treatment of head lice. Critical data on the dermal absorption associated with the short application interval typical of lice treatment are unavailable. While HED has data on dermal absorption of lindane associated with 24 hour exposure periods (which were used to assess potential risk from treatment of scabies), we do not have absorption data for the 5 to 15 minute exposure duration associated with head lice treatment. HED does not believe that the 24 hour dermal absorption factors derived from both human and monkey studies is applicable to 5 to 15 minute exposures, nor do we believe is possible to extrapolate to a shorter duration factor with any degree of certainty. A linear extrapolation of dermal absorption from 24 hours to 15 minutes would result in dermal absorption factors well below any of those used in the analyses submitted by commenters. An assumption of positive linear correlation is highly uncertain, however, and has minimal scientific basis. Commenters submitting MOE assessments also tended to assume that the amount of lindane available for absorption from head lice treatment was the same as that for scabies treatment. This is not the case as lindane products used for lice treatment are applied to a much smaller area (i.e., the scalp) than scabies treatment products, which are applied to the entire body below the neck. There are clearly uncertainties associated with the blood level analysis HED used to assess potential risks from use of lindane to treat lice, as discussed in the analysis. However, HED believes that the significant difference in blood levels associated with acute accidental ingestion which resulted in short-term adverse effects versus blood levels associated with label prescribed head lice treatment (0.00613 ug/mL vs 0.32 ug/mL respectively)

Attachment A

indicates that label prescribed use of lindane head lice products does not pose human health risks of concern.

Public Comment: NPA argued that the Agency for Toxic Substances and Drug Registration's (ATSDR's) NOAEL of 1 mg/kg/day for acute oral exposure should have been used by HED in its assessment of risk from lindane treatment of lice and scabies. NPA submitted an MOE analysis of potential risks from lice treatment in which it compared MOEs derived using the ATSDR NOAEL and the NOAEL used by HED in its analysis of risk from scabies treatment.

HED Response: HED used a NOAEL of 6 mg/kg/day based on an acute oral toxicity study in rats. The ATSDR NOAEL of 1 mg/kg/day is similarly based on a short-term oral rat study (4 days, 1 dose per day). HED believes that the determination of similar NOAELs by EPA and ATSDR supports the endpoint used in HED's assessment of scabies treatment. Use of a NOAEL of 1 mg/kg/day would not significantly increase the very low MOE's derived in HED's assessment of scabies treatment nor would it alter HED's conclusion that our analysis indicates MOE's of concern from both high and low-end treatment scenarios for all ages assessed. Regarding NPA's MOE analysis of head lice treatment, as noted in the response to the previous comment, HED does not believe that there is sufficient data to conduct a reasonable, scientifically sound quantification of MOE's associated with lindane treatment of head lice.

Comments on Assessment of Occupational Risk

Public Comment: Crompton Corporation argued that EPA should note that the occupational risks associated with treatment of canola seed are acceptable if respiratory protection is required of the seed treaters.

HED Response: HED agrees that use of respirators during treatment of canola seed would result in MOEs that are above the target MOE of 100 for occupational exposure and would therefore not pose risks of concern.



Office of Prevention, Pesticides,
and Toxic Substances

PC Code: 009001
DP Code: D287966

MEMORANDUM

DATE: March 26, 2003

SUBJECT: Response to Final Comments the RED **Lindane**

TO: Betty Shackelford, Branch Chief
Mark T. Howard, Team Leader
Special Review and Reregistration Division (7508C)

FROM: Nicholas E. Federoff, Wildlife Biologist, Team Leader
Faruque Khan, Ph.D., Environmental Scientist
José L. Meléndez, Chemist
Environmental Risk Branch V
Environmental Fate and Effects Division (7507C)

THROUGH: Mah T. Shamim, Ph.D., Chief
Environmental Risk Branch V
Environmental Fate and Effects Division (7507C)

EFED has received a number of comments from the registrant as well as other interested groups and individuals regarding the RED chapter. EFED comments are as follows:

Comments #34 California Regional Water Quality Control Board (CRWQCB)

The USEPA underestimates discharge during environmentally relevant time frames. The risk assessment should be structured to include concentrations estimated on 1-hour and four-hour frames, as well as lifetime exposure risk estimates.

EPA selected results from a statistical distribution for the estimation of lindane drinking water concentrations. The 10th percentile stream dilution factor (SDF) was recommended to represent acute concentrations likely to be found in drinking waters, while 50th percentile SDF was recommended to represent chronic concentrations. EFED should again indicate that these recommendations are based on statistical distribution curves, for the estimation of acute and

chronic time frames. These values are used for the estimation of risk of exposure to humans, according to the Guidelines for Exposure Assessment (USEPA, 1992a).

The analysis relies on dilution in estimating surface water concentrations of pesticides. However, numerous wastewater treatment plants discharge into otherwise dry streams or into shallow, poorly mixed water bodies composed primarily of their effluent:

EFED's purpose was to estimate concentrations of lindane in possible sources of drinking water. It is doubtful that wastewaters coming directly from treatment facility or plant would be used as a source of drinking waters.

Comments #43 Crompton Corporation

Lindane does not break down into pentachlorohexane, but into pentachlorohexene:

This issue has been addressed previously under DP Barcode D274510.

EPA states that lindane is highly persistent, with a half-life of 2.6 years in soil, while studies in the field showed shorter half-lives of 25, 65, and 107 days:

This issue has been addressed previously under DP Barcode D274510.

**Comments #47 Pesticide Action Network North America (PANNA), and Alaska
Community Action on Toxics (ACAT)**

PANNA and ACAT suggest that The Agency does not have sufficient evidence and/or data to suggest that mammals will be averse to the consumption of treated seeds and analysis of endocrine disrupting effects of lindane to wildlife.

EFED fully agrees with PANNA and ACAT and has stated such in our DRAFT chapter. We do have data regarding possible aversion in some avian species but none for mammalian species. In addition, we have strongly suggested from available data that lindane may be an endocrine disrupting compound and should fully be tested as such when such policy, directives and procedures become available within The Agency.

Comments #49 Beyond Pesticides

Lindane is highly persistent in soils and is stable in both fresh and salt water.

The issue of the persistence of Lindane in soil and water has been addressed previously in the RED chapter and under DP Barcode D274510.

Lindane's use as a lice and scabies treatment and its endocrine disrupting properties must be considered in the assessment of ecological risk. Also, EPA can't assume that mammals will express the same aversion to eating lindane treated seed as birds do.

EFED fully agrees with BEYOND PESTICIDES and has stated such in our DRAFT chapter. We do have data regarding possible aversion in some avian species but none for mammalian species. In addition, we have strongly suggested from available data that lindane may be an endocrine disrupting compound and should be fully tested as such when policy, directives and procedures become available within The Agency. Regarding risks from Lindane's scabies and lice use, EFED did run a "down the drain" model and concluded that risk from any additional concentrations was very minor and would not increase the aquatic risk substantially more than already stated in the RED chapter .

Comments #54 County Sanitation Districts, of Los Angeles County (CSDs)

The CSDs indicate that the EFED memorandum relied upon sales rates of lindane pharmaceuticals and theoretical calculations to determine lindane loadings to surface waters, not actual effluent concentrations at a POTW. The EFED reported 0.03 ppb from the Publicly Owned Treatment Works (POTWs) of Sanitation Districts of Los Angeles County. However, CSDs indicates that theoretical calculations were used while actual POTW effluent values were available to EPA. Data were submitted to the EPA by the Districts, including 474 influent lindane samples, and 743 effluent lindane samples (from 1990 to 1999). The OPP model does not account for the significant variability in the actual data. While the average effluent lindane concentrations among the wastewater treatment plants varied from 10 to 40 ppt, maximum effluent lindane concentrations up to 340 ppt were recorded.

The application of the 10th stream dilution values to determine acute risks is inappropriate. Acute risk is generally defined as a risk based on short-term exposure, not a risk based on having drinking water coming from a lower flow stream.

OPP-EFED used sales data of pharmaceutical usages of lindane and actual POTW effluent values of lindane for the year of 2000 to estimate the loadings to surface waters. The estimated concentrations are comparable for both scenarios. EFED was not aware of 743 effluent lindane concentrations collected during 1990 to 1999. However, using the reported maximum effluent lindane concentration of 0.340 µg/L (340 ppt), the estimated acute concentration 4.5E-03µg/L) and chronic concentration (3.4 E-04µg/L) are many fold lower than the DWLOC (Drinking Water Level of Comparison) for acute (170µg/L) and chronic (14µg/L) concentrations as well as current MCL (0.2µg/L) for lindane.

The EPA OPP needs to prepare a parallel document that considers the concentrations of lindane in surface waters that are not sources of drinking waters.

Attachment B

In general, the estimated acute and chronic concentrations of drinking water are always more conservative than the surface waters that are not sources of drinking waters. Therefore, the estimates of acute and chronic exposures due to pharmaceutical usages of lindane in non-drinking surface water bodies will be lower than the surface water sources of drinking water. EFED believes that further assessment of pharmaceutical usages of lindane in non-drinking surface water is not warranted at this time.

REFERENCE: U.S. Environmental Protection Agency. 1992a. Guidelines for Exposure Assessment. Federal Register 57(104): 22888 – 22938

MEMORANDUM

SUBJECT: **Lindane;** Chemical No. 009001. OGC's Response to Public Comment on the Lindane Registration Eligibility Document (RED)

Reregistration Case #: 0315

FROM: Gautam Srinivasan
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THROUGH: Kevin Lee
Assistant General Counsel
Pesticides and Toxic Substances Law Office (2333A)

TO: Mark Howard
Reregistration Branch 3
Special Review & Reregistration Division (7508C)

This memorandum responds to a comment submitted by Syngenta Crop Protection, Inc. on the Lindane Registration Eligibility Document.

Comment: Syngenta Crop Protection, Inc. ("Syngenta") objected to the use of an occupational exposure study (the "Helix Study") conducted by Syngenta to support the registration of the active ingredient thiamethoxam. Syngenta stated that the Helix Study meets the statutory and regulatory criteria for exclusive use protection. Because the Helix Study is an exclusive use study, Syngenta argued it was unlawful for EPA to use the Helix Study to evaluate certain on-farm seed treatment uses of lindane. Syngenta asked that EPA remove all references to the Helix Study from the lindane RED and that EPA not reregister any remaining uses of lindane until acceptable occupational exposure data are provided to EPA.

Response: EPA disagrees with Syngenta with regard to use of the Helix Study. EPA is not limited in the data it may consider when making a risk-benefit determination in connection with the development of a reregistration eligibility determination for a particular pesticide. EPA has long drawn a distinction between data that must be submitted to satisfy the requirements of 40 CFR part 158, and data that may be reviewed to make a risk-benefit determination. EPA has stated that when reviewing the risk-benefit criteria, "EPA may consider any relevant data without regard to who submitted the data, for what purpose, or when the data were submitted." 49 FR 30884, 30888 (Aug. 1, 1984). This includes review of exclusive use data. When, however, EPA reviews individual products to determine whether they have complied with the data requirements of registration or reregistration, EPA will ensure that the registrants of such products submit or cite required studies.

Attachment C

The fact that EPA reviews an exclusive use study in making a risk-benefit determination in a RED document does not deny the data owner the protections afforded by FIFRA. The economic interests of the data submitter are protected through the registration and reregistration of individual products. It is in connection with those activities that EPA must determine whether an applicant or registrant has submitted or cited data required for the registration or continued registration of the pesticide product.

An applicant for registration or reregistration may not satisfy a 40 CFR part 158 requirement by citing an exclusive use study. EPA explained this in detail in the 1984 FR notice: "The prohibition against unauthorized citation of an exclusive use study applies only to an applicant's right to cite another's study in his application for registration, not to the Agency's review of data to determine whether or not the pesticide should be registered on risk/benefit grounds. The Agency's review of data for this purpose in no way negates or compromises the rights of the exclusive use data submitter or undermines the intent of Congress in providing such protection. A second applicant who wishes to cite the exclusive use study must obtain the written authorization of the exclusive use data submitter. If permission is denied, the second applicant is not precluded from entering the market, but must first replicate the necessary data or obtain it from another source. Thus, the exclusive use data submitter is assured that no competitor enters the market without either having his permission to cite data submitted to EPA (which he may condition upon the payment of royalties or compensation) or having generated (or otherwise acquired) at least the equivalent set of data required for registration." 49 FR at 30888.

Therefore, it was not unlawful for EPA to utilize the Helix Study in making the risk-benefit determination captured in the lindane RED. EPA will not remove references to the Helix Study from the lindane RED. Such references do not violate or compromise Syngenta's exclusive use protection. EPA will, however, ensure appropriate protection for any data required for specific product registration or reregistration in connection with product registration and reregistration activities.

Attachment D

List of organizations submitting comments on the 2002 Lindane RED (OPP-2002-0202):

Various Private Citizens

California Regional Water Quality Control Board

County Sanitation Districts of Los Angeles

Technology Sciences Group, Inc.

Consumer Specialty Products Assoc. (CSPA)

Pesticide Action Network North America (PANNA)

Consumers Union

Beyond Pesticides

Syngenta Crop Protection, Inc.

National Pediculosis Association

American Chemistry Council

Natural Resources Defense Council (NRDC)

State of New York; Office of the Attorney General