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

JAN 27 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No. 359-686. Lindane: Review of the protocol for a 14 week inhalation study with mice (Bushy Run Research Center, Project No. 86-85-80201).

TOX CHEM No. 527
TOX Project No. 7-0181
Record No. 185397

FROM: John Doherty 1/20/87
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TO: George LaRocca
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THRU: Edwin Budd
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Budd 1/20/87
1/22/87

Mr. Charles A. O'Connor of the law firm McKenna, Conner and Cuneo on behalf of their client Centre International d'Etudes du Lindane (CIEL) is requesting the Environmental Protection Agency to review a protocol for a 14 week inhalation study with mice to satisfy data requirements for the insecticide lindane.

Study Title: Lindane Technical 14-Week Dust Aerosol Inhalation Study on Mice

Laboratory and Authors: Bushy Run Research Center (Project No. 86-85-80201)
Dennis R. Klonne
Darol E. Dodd
Linda J. Calisti
Fred R. Frank

Glenn S. Simon, Sponsor Representative

The purpose of this study is (as quoted from the protocol):

"To determine and evaluate the toxic effects in mice that may result from 14 weeks of exposure to a dust aerosol of the test material. Because the blood and kidney are suggested target organs, additional evaluations [e.g. bone marrow myelograms, histology n marrow and other blood cell producing organs (i.e. spleen, liver), additional sections of kidney for histologic evaluation, additional urinalysis parameters, etc.] will be performed to detect subtle changes that may be related to lindane technical exposure."

A copy of the protocol is attached. The specific details of the study will not be repeated here. Toxicology Branch (TB) has the following comments.

[Only aspects of the study related to particular problems associated with lindane will be commented on. It is the registrants responsibility to submit studies consistent with current EPA Guidelines.]

1. It should be noted that TB has reviewed a protocol for a 5 day pilot inhalation study in mice with lindane. Refer to review by J. Doherty signed 12/19/86.

   The pilot study will help to determine what methodologies will be used to assess for blood lindane, urinalyses and bone marrow myelograms. TB requested that the results of the five day pilot study together with the plans for using the information generated from this study in the 14 week study be submitted to EPA.

2. The study consists of exposing four groups of 45 male and 45 female mice to atmospheres containing either 0, a low dose, a mid dose or a high dose test level of lindane for up to 14 weeks, five consecutive days per week, 6 hours per day. Sacrifices will be made at weeks 6, 14 and 20. The group sacrificed at week 20 will represent a recovery group which will not be exposed to lindane after the 14th week.

   This basic protocol is acceptable to TB.

3. Method of generation of the atmosphere.

   No rational for selection of this method was included in either the protocol for the 5 day pilot study or the 14 week study.

   Since this method is substantially different from the method used for the rat 90 day inhalation study (Frauenhofer Istitut fur Toxkology, 1983), it is essential that blood levels of

lindane be determined. The study will not be considered a valid test if no lindane is detected in the blood or if there is no dose related increase in lindane in the blood.

The atmospheric levels of lindane also need to be frequently monitored such that it will assured that the method of generation results in atmospheres that are uniform throughout the chamber (near the regions of inhalation for the mice) and from day to day for each concentration. In this case uniformity refers to both atmospheric generation and particle size.

4. The dose levels that will be tested were not provided in the protocol. The registrant is reminded that the highest dose level tested should result in definite pharmacological signs. The dose levels which resulted in signs of kidney pathological changes may be used as a guide, but since the method of generation for each study is different, the blood levels are a more important index of exposure.

5. TB declines from making further comments on the special aspects of this study to assess for kidney and blood and bone marrow effects. Additional comments on the 14-week study will be made by TB when the registrant presents the results of the 5-day pilot inhalation study.

DRAFT

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PROTOCOL

TITLE: Lindane Technical 14-Week Dust Aerosol Inhalation Study on Mice

BRRC PROJECT NUMBER: 86-85-80201

SPONSOR: Centre International D'Etude Du Lindane
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Reviewed and Approved by:

Bushy Run Research Center:

Dennis R. Klonne, Ph.D. Date
Study Director

Darol E. Dodd, Ph.D., DABT Date
Manager, Inhalation Toxicology

Linda J. Calisti, B.S. Date
Group Leader, Good Laboratory Practices/Quality Assurance

Fred R. Frank, Ph.D. Date
Director

Sponsor Representative:

Glenn S. Simon, Ph.D., DABT Date

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Lindane toxicology review

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