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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Data Submitter No. 52904-C
Lindane: Review of Acute Inhalation LC50,
Primary Eye Irritation, Primary Dermal Irritation,
and Dermal Sensitization Studies

TOX CHEM No. 527
TOX Project No. 7-0165
Record No. 184298

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TO: George T. LaRocca, PM 15
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THRU: Edwin R. Budd, Section Head
Toxicology Branch
Hazard Evaluation Division (TS-769C)

Budd
2/2/87
1/21/87
LS/EK

Background:

The Centre International d'Etudes du Lindane (CIEL) has submitted four studies (see list below) to partially fulfill the data gaps indicated in the Toxicology Branch (TB) chapter of the Registration Standard for lindane.

TB Comments:

The four studies were reviewed by TB and found to be acceptable to meet the data requirements to fulfill the data gaps indicated in the Registration Standard.

The following studies were reviewed and are listed by study type, principal finding and CORE Classification. The DER and "one liners" are attached.

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<u>Study Type</u>	<u>Principal Finding</u>	<u>CORE Classification</u>
85-3 Acute Inhalation LC50 - Rats	LC50 = 1.56 mg/L both sexes (symptoms persist to day 9 and longer) Toxicity Category III (4 hour exposure).	GUIDELINES
85-4 Primary Eye Irritation - Rabbits	Score 0.6, no corneal involvement Toxicity Category III.	GUIDELINES
85-5 Primary Dermal Irritation - Rabbits	Primary Irritation Score = 0 Toxicity Category IV (4 hour exposure).	GUIDELINES
85-6 Dermal Sensitization - Guinea Pigs	Negative in the maximization type test	GUIDELINES

Attachments

Reviewed by: J.D. Doherty *J.D. Doherty 2/2/87*
Section II, Toxicology Branch (TS-769C)
Secondary reviewer: E.R. Budd
Section II, Toxicology Branch (TS-769C)

DATA EVALUATION REPORT

Study Type: 81-3, Acute Inhalation LC₅₀ -
Rats

TOX. Chem. No.: 527

MRID NO.: Not provided

Accession Number: 263946

Test Material: Lindane

Synonyms:

Study Number(s): Project No. 061637

Sponsor: CIEL

Testing Facility: RCC, Itingen, Switzerland

Title Of Report: Four-hour Acute Aerosol Inhalation Toxicity
Study With Lindane

Author(s): L. Ullmann

Report Issued: April 16, 1986

Conclusions:

LC₅₀ = 1.56 mg/L, Toxicity Category III. Symptoms persist
in dosed rats to day 9-10 and in some cases later.

Classification: Core-GUIDELINES.

Special Review Criteria (40 CFR 154.7) N/A

Review:

Four groups of ten rats (five males and five females per
group) were dosed by inhalation exposure to aerosols containing
either 0.101, 0.378, 0.642, or 2.104 mg/L of lindane for 4 hours
and observed for deaths, behavioral reactions and necropsied.

The aerosol was generated by a "Grafix Exactomat Injector"
(Cerutti AG, 3000 Bern/Switzerland). This apparatus forces the
lindane through a nozzle into a "high velocity air stream"
which discharges into the test chamber. The atmospheric

concentrations of lindane were determined by gravimetric techniques which included trapping the test aerosol in selection filters and quantitating the trapped aerosol. Particle size was assessed with the aid of a four-stage Cascade impactor.

Results:

1. The gravimetric analysis of the aerosols showed that the chamber concentrations were as indicated above with standard deviations of up to 10.6%.
2. Particle size determinations were reported as being usually 50% or more < 7 micrometers.
3. An LC₅₀ of 1.56 mg/L was determined for both sexes. Females were more susceptible than males (eight females died, but only three males died).
4. The symptoms reported included sedation, rhinorrhea, curved body posture (during exposure) ruffed fur, emaciation, stiff movements, diarrhea, restlessness, and excitation (higher doses), ataxia, aggressiveness, chromodacryorrhea, paddling movements and spasms. In some of the females, some effects (sedation) were still evident in days 10-19. The other effects often persisted up until day 10.
5. Necropsy revealed no pathological changes in the survivors (sacrificed at day 22), but effects in the lung (dark and discolored (red)) and in the stomach and intestines showed apparent effects in the rats which died as a result of exposure.

Conclusions:

This study is CORE GUIDELINES. Data were generated to assign technical lindane to Toxicity Category III via the inhalation route.

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Reviewed by: J.D. Doherty *J.D. Doherty 2/2/87*
Section II, Toxicology Branch (TS-769C)
Secondary reviewer: E.R. Budd
Section II, Toxicology Branch (TS-769C)

DATA EVALUATION REPORT

Study Type: 81-4, Primary Eye
Irritation - Rabbits

TOX. Chem. No.: 527

MRID No.: Not provided

Accession Number: 263946

Test Material: Lindane

Synonyms:

Study Number(s): Project No. 061672

Sponsor: CIEL

Testing Facility: RCC, Itingen, Switzerland

Title Of Report: Primary Eye Irritation Study With Lindane

Author(s): L. Ullmann

Report Issued: March 20, 1986

Conclusions:

Primary Eye Irritation Score of 0.6. Transient irritation only. No corneal involvement.

Classification: Core-GUIDELINES.

Special Review Criteria (40 CFR 154.7) N/A

Review:

The left eye of each of six rabbits (three males and three females, New Zealand White) was instilled with 0.1 g of test substance (lindane, 99.6%), the lids were then "gently held together" for about 1 second to prevent loss of the test article. The eyes of each rabbit were then observed at 1, 24, 48, and 72 hours after administration. In particular, each eye was scored for opacity (corneal irritation), iridic and conjunctival irritation, chemosis, and discharge. Eye examinations were made with a slitlamp 30 SL and a Vorta Cliphic diagnostic lamp.

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Necropsy was also performed when the rabbits were sacrificed 72 hours after administration of the test material.

The responses in the rabbits were confined to "irritation" of the conjunctivae, described as redness. Chemosis and discharge were also present in a few rabbits. The Primary Irritation Score was calculated to be 0.6. Most reactions were gone by 24 hours except for one rabbit.

This study is CORE GUIDELINES. Lindane is Toxicity Category III for eye irritation.

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Reviewed by: J.D. Doherty *J.D. Doherty 1/21/87*
Section II, Toxicology Branch (TS-769C)
Secondary reviewer: E.R. Budd
Section II, Toxicology Branch (TS-769C)

DATA EVALUATION REPORT

Study Type: 81-5, Primary Dermal
Irritation - Rabbits

TOX. Chem. No.: 527

MRID No.: Not provided

Accession Number: 263946

Test Material: Lindane

Synonyms:

Study Number(s): Project No. 061661

Sponsor: CIEL

Testing Facility: RCC, Itingen, Switzerland

Title Of Report: Primary Skin Irritation Study With Lindane in
Rabbits

Author(s): L. Ullmann

Report Issued: March 19, 1986

Conclusions:

Primary Irritation Score = 0
Toxicity Category IV.

Classification: Core-GUIDELINES.

Special Review Criteria (40 CFR 154.7) N/A

Review:

Six rabbits (three males and three females, New Zealand White) were prepared by shaving the dorsal surface to clear an area of approximately 100 sq centimeters. The test material was applied to this area one day after clipping as a 0.5 g sample and was covered with a patch of gauze and kept in place for 4 hours with occlusive dressing. After 4 hours the test material was removed and the rabbit skin was evaluated at 1, 24, 48, and 72 hours after removal of the dressing. The skin

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was especially examined for erythema, eschar, and edema formation. After 72 hours the rabbits were sacrificed and necropsied.

There were no obvious dermal reactions to lindane and the Primary Irritation Score was calculated to be 0. Necropsy was unremarkable.

This study is CORE GUIDELINES. Lindane is Toxicity Category IV based on dermal irritation.

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Reviewed by: J.D. Doherty *J.D. Doherty 2/2/87*
Section II, Toxicology Branch (TS-769C)
Secondary reviewer: E.R. Budd
Section II, Toxicology Branch (TS-769C)

DATA EVALUATION REPORT

Study Type: 81-6, Dermal Sensitization -
Guinea Pigs

TOX. Chem. No.: 527

MRID No.: Not provided

Accession Number: 263946

Test Material: Lindane

Synonyms:

Study Number(s): Project No. 061650

Sponsor: CIEL

Testing Facility: RCC, Itingen, Switzerland

Title Of Report: Test for Delayed Contact Hypersensitivity in the
Albino Guinea Pig with Lindane. Maximization
Test.

Author(s): L. Ullmann

Report Issued: April 18, 1986

Conclusions:

Negative in the Maximization test with guinea pigs.

Classification: Core-GUIDELINES.

Special Review Criteria (40 CFR 154.7) N/A

Review:

Two groups of Dunkin-Hartley albino guinea pigs were grouped as 10 males and 10 females as the test article treatment groups and 5 males and 5 females as the vehicle control groups. The guinea pigs were prepared for the study by clipping an area of the dorsal skin (6 x 8 cm) to make induction applications (intradermal and topical) and later challenge applications. (Note: a preliminary experiment was conducted to determine the suitable dose levels to be used for the main study.)

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Induction Phase:

The intradermal injections were made as a series of three kinds (Freund's complete adjuvant 50:50 with ethanol; the test article diluted to 0.5% with ethanol; and the test article as a mixture of Freund's complete adjuvant). One week after the injections, the area was again clipped free of hair and a 4 x 4 patch of filter paper (apparently saturated with a 25% solution of lindane) was applied and kept in place with aluminum foil and an elastic plastic bandage system for 48 hours (approximately).

Challenge:

Two weeks after the topical induction application, the guinea pigs were challenged with application of a patch saturated with a 25% solution of lindane. This time the patch was kept in place for 24 hours. A second (rechallenge) was performed 2 weeks after the first challenge. After each challenge the skin was evaluated for erythema and eschar formation.

Results:

The study report concludes that no positive sensitization reactions were observed as a result of either of the challenge applications. The reactions to the lindane treated guinea pigs were stated as being the same as the control (vehicle) treated animals. Necropsy on the sacrificed guinea pigs was unremarkable.

Conclusions:

This study is CORE GUIDELINES. No positive control was included but the data demonstrate that under this set of test conditions lindane did not induce dermal contact sensitization in guinea pigs. Data on the response of this strain of guinea pigs to similarly tested dinitrochlorobenzene as a positive control was provided in an appendix.