8-26-85

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Acute Inhalation Toxicity and Dermal Sensitization Studies With Chlorpyrifos. EPA ID No. 464-404 CASWELL #219AA

TO: Jay Ellenberger (12)
Registration Division (TS-767)

FROM: D. Stephen Saunders Jr., Ph.D. DSS 8/26/85
Toxicologist, Section V
TOX/HED (TS-769)

THRU: Laurence D. Chitlik, DABT
Head, Section V
TOX/HED (TS-769)
and
Theodore M. Farber, Ph.D.
Chief, Toxicology Branch
Hazard Evaluation Division (TS-679)

W. Teeters for 8-26-85

Action Requested

Review the submitted acute inhalation and dermal sensitization studies conducted with Dursban (chlorpyrifos).

Recommendations

1) The acute inhalation study in rats (#DWC 411/84774) was classified as Core-Supplementary data because actual chamber concentrations were not reported. No animals died as a result of treatment, and therefore the LC_{50} is greater than 0.2 mg/L (nominal concentration), the only dose tested. Doses higher than 0.2 mg/L (0.2 g/m^3) apparently could not be attained because the physical state of the test material is a waxy solid, and it was not possible to generate a more concentrated vapor (see review).

2) The dermal sensitization study in guinea pigs (study # not provided) was classified as Core-Minimum data. Dursban F Insecticide did not induce a skin sensitization reaction. The only apparent deficiency in this study was that the positive control was not fully identified, although it was effective in causing a skin sensitization reaction thereby demonstrating the sensitivity of the test species.

Data Evaluation Record

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Study Type: Acute inhalation toxicity in rats.

Study Identification: "Dursban Technical- Acute Inhalation Toxicity in Rats."

Lab. performing study:	Huntingdon Research Centre Huntingdon, Cambridgeshire, England
Sponsor:	Dow Chemical Europe Switzerland
Study no.:	DWC 411/84774 (Huntingdon)
Accession no.:	257590
Report date:	12-10-84
Submitted to EPA:	4/10/85
Study authors:	Hardy, C.J. and Jackson, G.C.
Project officer:	N.G. Carmichael (Dow)
Reviewed By:	D. Stephen Saunders Jr., Ph.D. Toxicologist, Section V TOX/HED (TS-769)
Approved By:	Laurence D. Chitlik, DABT Head, Section V TOX/HED (TS-769)

Conclusions: LC_{50} > 0.2 mg/L (nominal).

Classification: Core-Supplementary No analytical chamber concentrations.

Materials and Methods

A. Methods: (1) Test chemical: Dursban Technical, "a light brown waxy crystalline solid", lot no. EK 830516110; chlorpyrifos (O,O-diethyl-O-[3,5,6-trichloro-2-pyridyl] phosphorthioate); % a.i. not stated.

Doses tested: 0 and 0.2 g/m^3 nominal concentration for 4 hours.

Test animal: Male and female albino rats, 5/sex/dose, obtained from Hacking and Churchill Ltd., Huntingdon, England.

B. Methods- A photocopy of the submitted methods is appended. The protocol was reviewed and the following point(s) were noted:

1) Actual chamber concentrations were not reported, only nominal values were provided.

2) Only a single dose of 0.2 mg/L (nominal) was tested. The Registrant stated that it was necessary to use "rather heroic efforts to generate a vapor. The test material was heated to 55°C to make a molten substance and air was passed through this liquid material to generate a vapor." Toxicology Branch accepts this explanation, as it is clear that neither a dust or aerosol could be generated with the TGAI, and therefore generation of a test atmosphere was limited by the physical properties (i.e. state and vapor pressure) of the test compound.

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Results

A. Clinical Signs and Mortality- Data were submitted as summary tabulations. The investigators reported that "during exposure the rats showed signs of closing or partial closing of the eyes, excessive salivation, abnormal body posture, abnormal respiration pattern and discharge from the snout. These signs were considered to be consistent with the response to a mildly irritant vapour." The submitted summary tabulation supports this statement, however this reviewer notes that excessive salivation may also be indicative of cholinesterase inhibition.

No treatment-related clinical signs were noted after the exposure period, and no mortalities were reported during the 14-day observation period.

B. Body Weights- No effect of treatment on body weight gain was apparent.

C. Food and Water Consumption- No effect of treatment on food or water consumption was noted.

D. Necropsy Data: (1) Lung/body weight ratio- No effect of treatment on the relative lung weights was apparent. After the 14-day observation period, the relative lung weights in control and treated males were 0.46 $\pm$ 0.024% and 0.44 $\pm$ 0.030%, respectively, and in females these values were 0.51 $\pm$ 0.057% and 0.49 $\pm$ 0.018% for control and treated rats, respectively.

(2) Gross pathology- The only finding reported for any animals was "pale raised areas" of the lung. Two of 5 treated females were reported to have "many pale raised areas", whereas 1/5 control females had "few pale raised areas". Microscopic examination of these lesions were apparently not conducted.

Discussion

No mortalities occurred as a result of treatment, and therefore an LC_{50} could not be determined. Clinical signs were noted during exposure only, and no signs were noted during the observation period after exposure. No effect on lung weights was apparent, however a possible treatment-related lesion of the lungs of females was noted in the form of "pale raised areas", which were observed with apparent greater severity and frequency in treated females. Histological examination of these lesions would have been desirable since the lung was the target organ in this study.

Only a single dose was tested in this study, 0.2 g/m^3 (0.2 mg/L) nominal. Actual (analytical) concentrations from the breathing zone of the test animal are required under current guidelines. The use of a single dose is acceptable in the present study because it was apparently the highest concentration practically attainable due to the physical properties of the test compound (see "methods").

Classification: Core-Supplementary No analytical chamber concentrations.

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Chorpyrifos toxicology review

Page _____ is not included in this copy.

Pages 4 through 6 are not included in this copy.

The material not included contains the following type of information:

___ Identity of product inert ingredients

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X FIFRA registration data

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Data Evaluation Record

Study Type: Dermal sensitization in guinea pigs. Guideline §81-6. -T 046533

Study Identification: "Skin Sensitization Potential of Dursban F Insecticide".

Lab. performing study:	Toxicology Research Laboratory Health and Environmental Research Dow Chemical, USA Midland, Michigan
Sponsor:	Dow Chemical, USA Midland, Michigan
Study no.:	Not provided
Accession no.:	257589
Report date:	10-2-78
Submitted to EPA:	4/10/85
Study authors:	Henck, J.W., Lockwood, D.D. and Olson, K.J.
Reviewed By:	D. Stephen Saunders Jr., Ph.D. Toxicologist, Section V TOX/HED (TS-769)
Approved By:	Laurence D. Chitlik, DABT Head, Section V TOX/HED (TS-769)

Conclusions: Not a skin sensitizer.

Classification: Core-Minimum Identity of positive control not fully described.

Materials and Methods

A. Materials: (1) Test chemical: Dursban F Insecticide; lot no. not provided; chlorpyrifos (0,0-diethyl-0-[3,5,6-trichloro-2-pyridyl] phosphorthioate); % a.i. not stated. Positive control: "An epoxy resin (a known sensitizer)".

Doses tested: 10% solution of Dursban [redacted] positive control- 10% solution in [redacted] Tween 80 9:1.

Test animal: Male albino guinea pigs, 10/group, obtained from Buckberg Laboratory Animials, Inc., Tomkins Cove, NY.

B. Methods- "This method is a modification of the Maguire method (H.C. Maguire, 1973, 'The Bioassay of Contact Allergens in the Guinea Pig' J. Soc. Cosmet. Chem., 24:151-162). Test materials in 0.1 ml aliquots are applied to the clipped and depilated backs of Hartley albino guinea pigs, 6-8 weeks old, four times in ten days. At the time of the third application, 0.2 ml of Freund's adjuvant is injected intradermally at several points adjacent to the insult site. After a 2-week rest period, the animals are challenged on other sites, such as the clipped flanks, with the test material and with the solvent. Test solutions are applied as received (if they are not corrosive or an irritant) or as a solution or suspension in a penetrating solvent."

This method is consistent with current guidelines.

Results/Discussion

Data were submitted as individual animal findings.

The positive control, "DER sample 3", induced a skin sensitization reaction in the form of hyperemia and/or edema in 10/10 test animals at 24 and 48 hours after challenge. The test animals were therefore sensitive to a positive control. This positive control was not identified other than as "an epoxy resin (a known sensitizer)". All test chemicals should be fully identified.

No animals treated with 10% Dursban F Insecticide were observed to have a skin sensitization reaction up to 48 hours after challenge.

Classification: Core-Minimum Identity of positive control not fully described.