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

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APR -5 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: EPTC - Tox. Data Submitted Under MRID No. 417092-01
(cf: Acc. No. 24549)

Chemical (Caswell) No.: 435
RD Record No.: S-387895
HED Project No.: 1-0399

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Toxicology Branch I - Insecticide, Rodenticide Support
Health Effects Division (H7509C)

Registrant: ICI Agricultural, Wilmington, DE

Request

Review and evaluate the following sensitization study, submitted to support continued registration of products containing EPTC:

EPTC: Skin Sensitization to the Guinea Pig, performed at ICI's Central Toxicology Laboratory (UK), Study No. GG4927/GG4763, Report No. CTL/P/3019, dated September 10, 1990 (EPA MRID No. 417092-01).

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TB Conclusions

This study has been graded Core-Guideline Data, in demonstrating EPTC was a weak skin sensitizer in guinea pigs.

Attachment (DER)

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Reviewed By: Irving Mauer, Ph.D., Geneticist, 03-27-91
Section I, Toxicology Branch I - IRS (H7509C)
Secondary Reviewer: Karl P. Baetcke, Ph.D., Chief 4/8/91
Section I, Toxicology Branch I - IRS (H7509C)

DATA EVALUATION REPORT 008323

I. SUMMARY

MRID No.: 417092-01
ID No.: 041401
RD Record No.: S-387985
Caswell No.: 435
Project No.: 1-0399

Study Type: (81-6) Skin sensitization - guinea pig

Chemical: EPTC (S-ethyl dipropylthiocarbamate)

Sponsor: ICI Agricultural, Wilmington, DE

Testing Facility: ICI Central Toxicology Laboratory (CTL), Alderley Park, Macclesfield, Cheshire (UK)

Title of Report: EPTC: Skin Sensitization to the Guinea Pig.

Authors: R.C. Swann and D. Lees

Study Number: GG4927, GG4763 (Report No. CTL/P/3019)

Date of Issue: September 10, 1990

TB Conclusions:

The test article is a weak sensitizer in guinea pigs treated by the maximization procedure of Magnusson and Kligman.

Classification (Core-Grade): Guideline

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II. DETAILED REVIEW

A. Test Material - EPTC (from ICI Agrochemicals, UK)

Description: Yellow liquid
Batch (Lot): SA-360068-EP-UK
Purity (%): (Not stated)
Solvent/Carrier/Diluent: Corn oil

B. Test Organism - Rodents

Species: Guinea pig
Strain: Porcellus Dunkin Hartley (albino)
Age: (Not Stated)
Weights: 363 to 655 g ((males/females collectively))
Source: Harlan Porcellus Farms, Sussex (UK)

C. Study Design (Protocol) - This study was designed to assess the sensitization potential of EPTC when administered topically to guinea pigs, using the maximization test of Magnusson and Kligman (1970), an acceptable procedure according to FIFRA Tox-Testing Guideline 81-6.

Statement of Quality Assurance measures (inspections/audits) as well as of adherence to Good Laboratory Practice (GLP) were provided.

D. Procedures/Methods of Analysis - Following acclimation (1 week), dose levels for each stage of the main study were determined by preliminary ("sighting") testing (2 or more animals per group dosed at 4 levels by intradermal injection as well as topically). For the induction phase of the main study, 20 test males received three rows of injections (each 0.05-0.10 mL) into the depilated scapular region, with: (i) Freund's Complete Adjuvant plus corn oil (1:1), as the top pair; (ii) 10% w/v test compound in corn oil for the middle; and, (iii) 10% (w/v) test compound in 1:1 Freund's: corn oil for the bottom. One week later, filter papers soaked with 0.2 to 0.3 mL undiluted ("neat") test material were applied to the same (re-depilated) areas of test animals, held in place for 48 hours under surgical tape covered by adhesive bandage and secured by PVC. A group of 10 control males were treated in the same fashion as for test animals except that the test compound was not included in any of the applications. Application sites were inspected 24 hours after removal of the occlusive dressings.

Two weeks after induction, depilated flank areas of both test and control animals were covered with filter papers soaked with either 0.05 to 0.10 mL undiluted (neat) test

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chemical (left flank), or a 30 percent (w/v) preparation in corn oil (right flank), under occlusive dressings consisting of adherent rubber sheeting; over this patch, an adhesive bandage was placed and secured by PVC tape. Dressings were removed 24 hours later, and application sites scored at 24 and 48 hours for erythematous reactions according to the following four-point scale:

0 - no reaction

1 - scattered, mild redness

2 - moderate, diffuse redness

3 - severe redness and/or swelling

Sensitization responses were classified by subtracting percent of controls which responded from percent positive test animals, with such net responses defined as follows:

% Net Response	Evaluation
0	Not a sensitizer
1-8	Weak Sensitizer
9-28	Mild Sensitizer
29-64	Moderate Sensitizer
65-80	Strong Sensitizer
81-100	"Extreme" Sensitizer

Seven days after the initial challenge, the 20 test animals were rechallenged in the same fashion, but using two concentrations of test chemical in corn oil, 30 and 10 percent (w/v), and applications to different flank sites. A fresh group of 10 females, injected with Freund's Adjuvant 2 to 6 weeks previously, served as negative control for this rechallenge phase.

As positive control, the same procedure was employed in 20 males treated with 0.3 percent (w/v) formaldehyde (HCHO) in dionized water intradermally with a 30 percent (w/v) preparation topically for induction, and the latter preparation used for the challenge phase.

E. Results - Body weight was not adversely affected by either EPTC (or HCHO) treatment. Weight gain among test animals averaged 138 g over the treatment period, vs. 123.4 g for controls (See Report Tables attached).

Following first challenge with EPTC (either neat or 30%), only one of the 20 test animals showed mild erythematous

responses (Grade-1), discounted as equivocal by the investigators and ". . . probably caused by the occlusive bandage"; a Grade-1 response was also observed in one of the 10 solvent controls. Net percentage response for this first challenge was therefore 5 percent.

Following rechallenge a week later, none of the animals treated with 30 percent EPTC showed erythema, but one exposed to the 10 percent preparation did (Grade-1).

In contrast, Grade-1 or -2 responses were observed in 17 of 18 formaldehyde-treated animals (2 test animals died prior to challenge, for causes considered ". . . unrelated to treatment"). Hence net response was 94 percent for HCHO.

The authors concluded that EPTC (whether neat or as a 30 percent preparation in corn oil) was only mildly irritating, and elicited only a equivocally weak sensitization response on first challenge, which was not confirmed on rechallenge.

F. TB Evaluation - Core-Guideline Data

Attachment (Report Tables)

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Eptam Science Reviews

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