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

MAY 15 1987

005884

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Imazalil/PP#5F3250
Fecundal 6.5L - EPA Registration No. 43813-5

TOX Chem No. 497AB

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Applicant: Janssen Pharmaceutica
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Present Action

Janssen Pharmaceutica submitted a sensitization study to comply with toxicity data requirements for the above product Fecundal 6.5L (EPA Registration No. 43813-5).

Conclusion

Imazalil as a 6.5% w/w formulation is a weak sensitizing agent in the guinea pig.

Core Classification

Minimum.

Review of Study Submitted

1. Dermal Sensitization Study in Guinea Pigs with Imazalil (R23979) 6.5% W/W (5.8% W/V), Department of Toxicology, Janssen Pharmaceutica, Study No. 1682, August 26, 1986.

Procedure (Magnusson Guinea Pig Maximization Test)

Forty adult male albino guinea pigs outbred Pirbright strain with initial age between 2 and 3 months and body weight between 310 and 405 grams were used in this study.

A. Induction (Intradermal)

The procedure consisted of an initial intradermal injection on the 1st day (day 0) to the closely clipped shoulder region of the animal. A row of three injections were made in each side of the shoulder region. These injections were given as follows to 1 group of 20 guinea pigs.

(1) 0.1 mL of Freund's Complete Adjuvant plus water 50 w/w (Site 1).

(2) 0.1 mL of the test article at a slightly irritant concentration (Site 2).

(3) 0.1 mL of the test article at a slightly irritant concentration (in saline or another appropriate vehicle) emulsified with Freund's Complete Adjuvant (Site 3).

Another group, a placebo-induced control group of 20 guinea pigs, were given the same injections without the test material.

Epicutaneous Induction

One week later (day 7 of the study), the test article was incorporated in petrolatum at a slightly irritant concentration (maximum up to 25%) and spread over a 2 x 4 cm filter paper in a thick even layer and applied topically to the injection sites on the animals' shoulder region and occluded for 48 hours (up to day 9).

Scoring of the skin reactions were made 24 hours later (on day 10 of the study).

The placebo-induced group received only vehicle during this phase.

B. Challenge

Two weeks after the second induction (day 21 of the study) the treated group and the control placebo group were challenged with the test material at the highest nonirritating concentration. This concentration was spread over a 1 x 1 cm filter paper patch and applied topically on the left, clipped and shaved flank area (5 x 5 cm). The patch was kept under occlusion for 24 hours and removed (day 22 of the study). After 24 hours (day 23 of the study), final scoring of the skin reactions was made.

Results

Body weights of the animals taken on pretest, after second induction, and after challenge were comparable between placebo group and R23979 test group as computed by Mann-Whitney U Test (Table 1 of the report attached).

The first, intradermal induction produced irritation at the injection site. Severe irritation was produced when the test article or the vehicle were mixed with Freund Complete Adjuvant prior to application.

The second, epicutaneous induction produced at day 10 a slight irritation in 9 out of 20 in the placebo group and 14 out of 20 in the test article group (Tables 2a and 2b of the report attached).

The challenge reaction (day 23 of the study) a minimal reaction of mild redness (score 1) in 1 out of 20 in the placebo group and 1 out of 20 in the test article group was observed (Tables 2a and 2b of the report attached).

Conclusion

Imazalil as a 6.5% w/w formulation produced a slight "weak" sensitization reaction in the guinea pigs in this type of test.

Classification

Core-Minimum.

The results of the same test method using 2,4-Dinitro-1-chlorobenze (DNCB) as a positive control and test article were also reported. DNCB proved to be a sensitizer under the same conditions of testing, therefore, validating this method.

Imazalil toxicology review

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