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

007258

JUN 19 1989

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No.: 109701-3. Permethrin: Review of domestic animal safety study (with dogs) and proposal to conduct a study with puppies with the product 2% Permethrin Lotion Spray.

TOX CHEM No.: 652BB
TOX PROJECT No.: 9-0554
Record No.: 236662

FROM: John Doherty *John Doherty 5/18/89*
Section I, Toxicology Branch I (IRS)
Health Effects Division (H7509C)

TO: George LaRocca
Product Manager #15
Registration Division (H7505C)

THROUGH: William Greear *William B. Greear 5/17/89*
Coordinator Domestic Animal Product Registrations
Toxicology Branch I
Health Effects Division (H7509C) *1/30/89*

THROUGH: Edwin Budd *Edwin Budd 5/12/89*
Section Head
Section I, Toxicology Branch I (IRS)
Health Effects Division (H7509C)

Mr. Richard Hamer a consultant for the Verbac Corporation has submitted a domestic animal safety study with dogs testing the product 2% Permethrin Lotion Spray. The study was conducted in England by the Virbac Corporation's worldwide product development and registration program. Mr. Hamer previously submitted a protocol for the Agency to review for this type of study and Toxicology Branch I (TB-I) made comments for its revision (refer to J. Doherty memo dated May 11, 1988).

Mr. Hamer has indicated that the study submitted differs from the protocol recommended by TB-I in that only 2

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dogs per sex per dose level and not three as recommended were used and that groups of weanling dogs were not included.

Mr. Hamer has requested that the study be reviewed and considered for acceptability in meeting the Agency's request for a domestic animal safety study in mature dogs and has proposed that a second study with puppies be conducted and submitted to satisfy the safety requirements so that use of this product on puppies may be included on the label instructions.

TB-I has reviewed the study and the following comments apply.

Toxicology Branch Comments

1. The study has been reviewed and determined to be ACCEPTABLE with regard to demonstrating the safety of the product (2% Permethrin Lotion) in mature dogs. Refer to DER attached.
2. Mr. Hamer's suggestion for conducting a study with puppies (3 dogs/sex) testing the product at 5 times the recommended usage rate is acceptable to TB-I. TB-I wishes to advise the registrant the age of the puppies tested should all be within a few days or a week if possible. The age of the puppies at which the product will be tested will be incorporated on the label so that instructions not to treat puppies of a lesser age will be made.
3. A copy of the proposed label should be sent to TB-I when the registrant completes and submits the domestic animal safety study with puppies.

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Reviewed by: John Doherty *John Doherty 5/8/89*
Section I, Toxicology Branch (IRS) (H5709C)
Secondary reviewer: Edwin Budd *Edwin Budd 5/30/89*
Section I, Toxicology Branch (IRS) (H5709C) *A. by*

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DATA EVALUATION REPORT

STUDY TYPE: 85. Domestic Animal (Dog) Safety Study.

ACC. No.: None provided. TOX. CHEM. NO.: 652BB

TEST MATERIAL: 2% Permethrin solution in glycoether/water.

SYNONYMS: None

STUDY NUMBER(S): 33/881030

SPONSOR:

TESTING FACILITY: Huntingdon Research Center, Ltd.

TITLE OF REPORT:

"2% Permethrin Solution Dermal Tolerance Study in Beagle Dogs"

AUTHOR(S): R.J. Harling, M.H. Barker, S. Pandit, D.P. Buist,
and D. Crook

REPORT ISSUED: October 13, 1988

CONCLUSIONS:

This study demonstrated that treatment with a single dose of 2% Permethrin Solution at 1X, 3X and 5X the intended usage rate did not result in any signs of reactions in the test dogs.

Classification: ACCEPTABLE

Special Review Criteria (40 CFR 154.7) N/A

Quality Assurance Statement:

None Provided.

REVIEW

In this study, four groups of 2 male and 2 female beagle dogs (the age of these dogs was not stated) were treated with the test amterial (2% permethrin described as a solution in glycoether/water) by means of a mechanical sprayer to all areas of the animals body. The dose levels were 0 (vehicle control), 25 ml/kg, 5, 15, and 25 ml/kg of the test material. The dogs were dosed at the rate of 5 ml/kg with a 10 minute interval between doses to attain the dose levels of 15 and 25 ml/kg. These dose levels were selected because they represent 1X, 3X, and 5X the intended dose usage level. Following application the dogs were observed for 28 days for behavioral and local dermal reactions and extensive hematology and clinical chemistry analyses were made.

Results

There were no effects noted at any time at any dose level regarding behavioral or local dermal reactions, body weight gain, or food consumption. Hematology and clinical chemistry analyses were evaluated once before treatment and on days 2, 8, and 28 but no effects of treatment were evident.

Following sacrifice on day 28, all dogs were necropsied but no effects of treatment were noted. No effects on organ weight were evident either. The tissues were preserved after removal at necropsy but were not further processed microscopically.

CONCLUSION. This study is ACCEPTABLE with regard to demonstrating the safety of the 2% permethrin solution to adult dogs when tested at 1X, 3X, and 5X the intended dose level.