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

000462

MEMORANDUM

Date: November 13, 1980

#499

Subject: EPA Registration Number: 8568-RR

From: Deloris F. Graham DFG 11/19/80
FHB/TSS
E 11/20/80

To: Robert Taylor
Product Manager(25)

Applicant: C-R Chemical Research Company
11040 S.E. Mill Court
Portland, Oregon 97216

Active Ingredients:
Indole-3-Butyric acid.....1.0%
1-Naphthalenacetic acid.....0.5%
Inert Ingredient.....98.5%

Background: Submitted an Acute Oral, Eye Irritation, Skin Irritation and Dermal Sensitization. All except the Dermal Sensitization study were conducted by Willamete Laboratories. The Sensitization study was conducted by Leberco Laboratories. Method of support not indicated.

Recommendation:

(1) The Acute Oral, Dermal Irritation, Eye Irritation, and Dermal Sensitization studies are acceptable to support the conditioned registration of this product. However, for future submission please note:

(a) In the Acute Oral Study individual symptomology and necropsy reports must be submitted.

(b) In the Dermal Irritation Study four skin sites (two abraded and two intact) per animal must be used.

(2) An Acute Dermal and Acute Inhalation study must be submitted or these data must be cited.

(3) FHB/TSS objects to the conditional registration of this product until the previously requested studies are submitted or cited.

Label:

(1) As indicated by the Eye Irritation Study the appropriate signal word is WARNING. However, further labeling revisions may be necessary when previously requested information is submitted.

Review:

(1) Acute Oral Toxicity Study: Willamete Laboratories.

Procedure: 5M and 5F rats received a 5g/kg dose of the test material. Observations were made at 15 minutes, 1 and 4 hours after dosing and daily thereafter for 14 days. Necropsies performed on all animals. ok

Results: No mortalities. At 15 minutes after dosing all animals somewhat stuporous. No other symptoms observed during 14 day observation period. No abnormalities observed at necropsy.

Study Classification: Core Minimum Data. Individual symptomology and necropsy reports must be submitted.

Toxicity Category: IV-CAUTION

(2) Eye Irritation Study: Williamete Laboratories.

Procedure: 9 white rabbits received 0.1 ml dose of the test substance in the right eye. Animals were divided into two groups. Group I, consisted of 6 rabbits with treated unwashed eyes and Group II consisted of 3 rabbits with treated eyes washed 20-30 seconds after instillation of test material. Observations were made at 24, 48 and 72 hours, 4, 7 and 10 days after treatment. ok

Results: In Group I, at day 1, 1/6 animals had corneal opacity (1/6=20) and 1/6 on day 2 (1/6=20) which had cleared by day 4. One animal could not be scored because lids were not open. 4/6 had iris irritation (3/6=5, 1/6=10), and 1/6 could not be scored because lids were closed. 5/6 conjunctive redness (2/6=2, 3/6=3), chemosis (2/6=1, 2/6=3, 1/6=4) and discharge (3/6=2, 1/6=2, 1/6=3). All irritation had cleared by day 10 except slight discharge in 1/6 animals (1/6=1).

In Group II, at day 1, 1/3 animals had corneal opacity (1/3=20) and 2/3 had iris irritation (2/3=5) that had cleared by day 2. 3/3 had conjunctival redness (2/3=1, 1/3=2), discharge (3/3=1) and 2/3 chemosis (2/3=1). All conjunctival irritation cleared by day 7.

Study Classification: Core Guideline Data

Toxicity Category: II-WARNING

(3) Dermal Irritation Study: Willamete Laboratories

Procedure: 5M and 5F rabbits received 2g/kg dose of test material at abraded skin site under occlusive wrap for 24 hours. Observations made several times during day of application and twice daily thereafter for fourteen days. Necropsy performed on all animals. Body weights recorded before dosing, day 7 and day 14.

Results: On the 9th day 3/10 animals developed abdominal infections that were determined to be due to bites from other rabbit. Affected animals treated with 3000 units of penicillin G on 11th thru 14th day. No toxic or pharmacologic signs observed. Two of the affected animals appeared to recover by end of test period. One became moribund and was sacrificed on the 11th day after dosing.

Pathology findings - 3/9 rabbits exhibited cutaneous ulcers and subcutaneous ulcers and subcutaneous abcesses, the remaining six animals had no evidence of inflammation. No abnormalities were noted in the necropsy of the internal organs.

Study Classification: Core Mimimum Data. 4 sites (2 abraded and 2 intact) per animal must be used.

Toxicity Category: IV-CAUTION

(4) Dermal Sensitization Study: Leberco Laboratories, Assay # 04772; June 3, 1980.

Procedure: Before the experiment was started samples of the test material as it was, were injected intradermally into three guinea pigs. This concentration was found to be highly irritating. A dilution of 1 ml of test material to 25 ml in saline was made and tested. This test showed a very moderate irritation and was chosen as the dilution to be used for the sensitization study.

An initial injection of 0.05 ml of the 1 to 25 dilution was made interdermally into the skin of ten shaven pigs. Following this injection, 9 injections were made. The animals were allowed to rest for two week after a total of 10 intradermal injections had been made at which time they received a final 0.05 ml injection. Reaction readings were made 24 and 48 hours after each injection..

Results: Very slight erythema and edema at 24 and 48 hours. The area of reaction ranged from 2 to 7mm. The average of the challenge injection was less than the average of the previous injection. Test material not acting as a sensitizing agent.

Study Classification: Core Guideline Data

Indole-3-butyric acid toxicology review

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Pages _____ through _____ are not included in this copy.

The material not included contains the following type of information:

___ Identity of product inert ingredients

___ Identity of product impurities

___ Description of the product manufacturing process

___ Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commercial/financial information

X A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

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The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.
