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

006390

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

AUG 27 1987

MEMORANDUM

SUBJECT: EPA File Symbol 100-AIR(1)
Pramitol 3.75%

EPA File Symbol 100-AIN(2)
Pramitol 2.5%

EPA File Symbol 100-ATO(3)
Pramitol 1.5%

FROM: Deloris F. Graham DFG 9/8/87 = 9/9/87
Technical Support Section
Fungicide-Herbicide Branch
Registration Division (TS-767C)

TO: Robert J. Taylor, PM 25
Fungicide-Herbicide Branch
Registration Division (TS-767C)

APPLICANT: CIBA-GEIGY Corporation
P.O. Box 18300
Greensboro, NC 27419

ACTIVE INGREDIENT:(1)
Prometon 3.75%
INERT INGREDIENT: 96.25%

ACTIVE INGREDIENT:(2)
Prometon 2.5%
INERT INGREDIENT: 97.5%

ACTIVE INGREDIENT:(3)
Prometon 1.5%
INERT INGREDIENT: 98.5%

BACKGROUND:

Submitted Acute Oral, Acute Dermal, Acute Inhalation, Eye Irritation, Skin Irritation, and Dermal Sensitization

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Studies on EPA File Symbol 100-AIR; Eye Irritation Study on EPA File Symbol 100-AIN; Eye Irritation Study on EPA File Symbol 100-ATO. Studies conducted by Stillmeadow, Inc. Data under EPA MRID Nos. 402205-05 thru -12. Method of support not indicated.

RECOMMENDATION:

1. FHB/TSS finds these data acceptable to support conditional registration of the products on which tested.

2. Based on the eye study submitted with the complete acute battery of data of the 3.75% formulation the appropriate signal word is WARNING.

3. Since only eye studies were submitted for the 1.5 and 2.5% formulations only the toxicity category can be determined, which is WARNING for the 2.5% and CAUTION for the 1.5%. In order to determine appropriate precautionary labeling remaining acute data must be submitted and/or cited.

LABEL:

The statement "Keep children and animals off treated areas until areas are dry" should be deleted from under the heading "Hazards to Human and Domestic Animals" and placed under the heading "Directions For Use."

REVIEW:

(1) Acute Oral Toxicity Study on 3.75%: Stillmeadow, Inc.; Study No. 4092-86; May 16, 1986; EPA MRID No. 402205-05.

PROCEDURE:

Four groups consisting of five female rats each received one of the following doses: 3250, 4040, 4500, or 5700 mg/kg. A group of five male and five female rats received a 5050 mg/kg dose of the test material. Observations made for 14 days postdosing. Necropsy performed on all animals.

RESULTS:

At 4500 mg/kg, 1/5 F died; at 5050 mg/kg, 3/5 F died; at 5700 mg/kg, 5/5 F died. Toxic signs reported included activity decrease, alopecia, ataxia, body tremors, bradypnea, constricted pupils, diarrhea, dilated pupils, emaciation, exophthalmos, gasping, lacrimation, lethargy, loss of righting reflex, melanuria, nasal discharge, necrotic tail, piloerection, polyuria, ptosis, respiratory gurgle and salivation. Necropsy report revealed emaciation, epistaxis, lacrimation, polyuria, nasal discharge, salivation, discoloration of the lungs,

lungs edematous, discoloration of the liver and contents of the gastrointestinal tract; gastrointestinal tract distended with gas, and almost empty. LD_{50} for females reported to be 4875 mg/kg with 95% confidence limits between 4432 and 5362 mg/kg. LD_{50} for males reported to be greater than 5050 mg/kg.

STUDY CLASSIFICATION: Core Guideline Data

TOXICITY CATEGORY: III - CAUTION

(2) Acute Dermal Toxicity Study on 3.75%: Stillmeadow Inc.; Study No. 4093-86; May 5, 1987; EPA MRID No. 402205-06.

PROCEDURE:

Five male and five female rabbits with intact skin sites each received a 2010 mg/kg dose of the test material. The treated skin sites were placed under occlusive wrap for 24 hour exposure period. Observations made for 14 days post-dosing. Necropsy performed on each animal.

RESULTS:

No mortalities reported. Toxic signs reported included diarrhea, and decreased urination. Necropsy report revealed diarrhea; gastrointestinal tract distended with gas; brown liquid in stomach; green slurry throughout small intestine in one female rabbit. LD_{50} reported to be greater than 2010 mg/kg.

STUDY CLASSIFICATION: Core Guideline Data

TOXICITY CATEGORY: III - CAUTION

(3) Acute Inhalation Toxicity Study on 3.75%: Stillmeadow, Inc.; Study No. 4097-86; June 30, 1986; EPA MRID No. 402205-07.

PROCEDURE:

Five male and five female rats were exposed for four hours to a 2.59 mg/L analytical concentration (nominal conc. = 5.41 mg/L). Mass median aerodynamic diameter reported to be 2.748 micrometers with a geometric standard deviation of 2.485. Mean chamber temperature and relative humidity reported to be 71.8°F and 62.2% respectively. Observations made for 14 days postdosing. Necropsy performed on all animals.

RESULTS:

No mortalities or abnormalities at necropsy reported. Toxic signs reported include activity decrease, constricted pupils, exophthalmos, lacrimation, nasal discharge, piloerection, polyuria, ptosis, and respiratory gurgle. LC_{50} reported to be greater than 2.59 mg/L.

STUDY CLASSIFICATION: Core Guideline Data

TOXICITY CATEGORY: III - CAUTION

(4) Eye Irritation Study on 3.75%: Stillmeadow, Inc.; Study No. 4094-86; May 7, 1987; EPA MRID No. 402205-10.

PROCEDURE:

Nine rabbits received 0.1 ml of the test material in one eye each. The treated eyes of three of the rabbits were washed with deionized water for one minute thirty seconds after treatment. Observations made for 13 days posttreatment.

RESULTS:

At 24 hours posttreatment, 4/6 rabbits of the unwashed group had corneal opacity (1/6 = 5, 2/6 = 10, 1/6 = 15); 1/6 iris irritation (1/6 = 5); 6/6 of the unwashed group had conjunctive redness (5/6 = 2, 1/6 = 3) (1/3 = 1, 2/3 = 2), chemosis (2/6 = 1, 1/6 = 2, 3/6 = 3) (3/3 = 1) and discharge (1/6 = 1, 3/6 = 2, 2/6 = 3) (3/3 = 1).

At day 7, 3/6 and 2/3 had conjunctive redness (3/6 = 1) (2/3 = 1); 3/6 chemosis (3/6 = 1) and 2/6 discharge (2/6 = 1). All irritation had cleared by day 10.

STUDY CLASSIFICATION: Core Guideline Data

TOXICITY CATEGORY: II - WARNING

(5) Skin Irritation Study on 3.75%: Stillmeadow, Inc., Study No. 4095-86; April 28, 1986; EPA MRID No. 402205-11.

PROCEDURE:

Six rabbits with intact skin sites each received 0.5 ml of the test material under occlusive wrap for four hour exposure. Observations made for 10 days.

RESULTS:

At 24 hours posttreatment, 3/6 rabbits had erythema (3/6 = 1); 2/6 edema (2/6 = 1). At 72 hours, 1/6 had erythema (1/6 = 1) and edema (1/6 = 1). At 7 days, 1/6 had erythema (1/6 = 1) and edema (1/6 = 1); shallow lateral fissuring; sloughing of the skin of various thicknesses. All irritation had cleared by day 10. Maximum irritation score reported to be 2.3.

STUDY CLASSIFICATION: Core Guideline Data

TOXICITY CATEGORY: IV - CAUTION

(6) Sensitization Study on 3.75%: Stillmeadow, Inc.; Study No. 4096-86; June 6, 1986; EPA MRID No. 402205-12.

PROCEDURE:

Using the patch method ten male guinea pigs received 0.5 ml applications of a 50% v/v solution of test material (highest non-irritating dose) in diethyl ether on alternate days for a total of ten applications. Fourteen days after tenth induction phase application a challenge dose at treated site and a virgin skin site. Observations were made at 24 and 48 hours after each application. Another group of ten male guinea pigs were treated in similar manner as previous group except a 0.05% w/v solution of 2,4-dinitrobenzene, DNCB, in ethanol (positive control group) was used.

RESULTS:

One guinea reported dead on day 3 of study. Slight to moderate irritation noted in most animals of the test group during induction phase with eshar and shallow lateral fissuring; slight irritation noted in two animals at challenge of treated site and at virgin site. DNCB, positive control produced skin reaction significance higher at challenge of treated (3.7) and virgin site (2.7) that at initial induction phase treatment (0.0) thereby confirming it as a positive skin sensitizer. Based on results in test group it is concluded that this product is not a skin sensitizer.

STUDY CLASSIFICATION: Core Guideline Data

TOXICITY CATEGORY: Non-sensitizing

(7) Eye Irritation Study on 1.5%: Stillmeadow, Inc.; Study No. 4249-86; July 29, 1986; EPA MRID No. 402205-08.

PROCEDURE:

Nine rabbits received 0.1 ml of the test material in one eye each. The treated eyes of three of the rabbits were washed with deionized water for one minute thirty seconds after treatment. Observations made for 7 days posttreatment.

RESULTS:

At 24 hours posttreatmemt, 6/6 rabbits of the unwashed group and 3/3 of the washed group had conjunctive redness (1/6 = 1, 5/6 =2) (3/3 = 1); 5/6 & 3/3 chemosis (4/6 = 1, 1/6 = 2) (3/3 = 1) and 3/6 & 1/3 discharge (3/6 = 1) (1/3 = 1). Irritation in washed group had cleared at 72 hours and in unwashed group at day 4.

STUDY CLASSIFICATION: Core Guideline Data

TOXICITY CATEGORY: III - CAUTION

(8) Eye Irritation Study on 2.5%: Stillmeadow, Inc.; Study No. 4251-86; August 13, 1986; EPA MRID No. 402205-09.

PROCEDURE:

Nine rabbits received 0.1 ml of the test material in one eye each. The treated eyes of three of the rabbits were washed with deionized water for one minute thirty seconds after treatment. Observations made for 13 days posttreatment.

RESULTS:

At 24 hours posttreatment, 4/6 rabbits of the unwashed group had corneal opacity (4/6 = 10); 3/6 iris irritation (3/6 = 5); 6/6 rabbits of the unwashed group and 3/3 of the washed group had conjunctive redness (2/6 = 2, 4/6 = 3) (2/3 = 2, 1/3 = 3) and chemosis (2/6 = 2, 3/6 = 3, 1/6 = 4) (2/3 = 1, 1/3 = 2); 6/6 & 2/3 discharge (5/6 = 2, 1/6 = 3) (2/3 = 1).

At day 7, 2/6 had redness (2/6 = 1) and 1/6 discharge (1/6 = 1); apparent invasion of cornea by blood vessels. Irritation in washed group had cleared at day 7. Irritation in unwashed had cleared at day 10.

STUDY CLASSIFICATION: Core Guideline Data

TOXICITY CATEGORY: II - WARNING

RIN-0334-94 PROMETON REVIEWS (080804)

Page_____ is not included in this copy.

Pages 1 through 10 are not included.

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 quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

✓ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

____ FIFRA registration data.

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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.