4-28-87

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

006208

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

APR 9 1987

SUBJECT: EPA File Symbol 100-ATE
Apron T69 Fungicide

FROM: Mary L. Waller
Technical Support Section
Fungicide-Herbicide Branch
Registration Division (TS-767C)

MW 4/28/87

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TO: Lois A. Rossi, Acting PM 21
Fungicide-Herbicide Branch
Registration Division (TS-767C)

APPLICANT: Agricultural Division
Ciba-Geigy Corporation
P.O. Box 18300
Greensboro, NC 27419

ACTIVE INGREDIENTS:

| | |
|---|---|
| Metalaxyl: N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine, methyl ester . . . . . | 45% |
| Thiabendazole: 2-(4-thiazolyl)benzimidazole . . . . | 24% |
| INERT INGREDIENTS: . . . . . | 31% |

BACKGROUND:

The applicant has submitted an acute oral, acute dermal, acute inhalation, primary eye irritation, primary skin irritation, and dermal sensitization studies. The studies were conducted by Stillmeadow, Inc. The data are not accessioned. The method of support was not indicated.

RECOMMENDATION:

FHB/TSS finds the data acceptable to support registration of 100-ATE and the signal word is "DANGER" based on the primary eye irritation study.

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LABELING:

1. Revise the Statement of Practical Treatment for oral exposure as follows:

   If Swallowed: Call a physician or Poison Control Center. Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with finger. Do not induce vomiting or give anything by mouth to an unconscious person.

2. Delete the "Note to Physician" under the Statements of Practical Treatment.

3. Place the subheading "STORAGE AND DISPOSAL" and pertinent information immediately under the misuse statement located under the heading "DIRECTIONS FOR USE."

REVIEW:

(1) Acute Oral Toxicity Study: Stillmeadow, Inc., Project No. 4121-86; June 26, 1986.

PROCEDURE:

Five male and five female Sprague-Dawley rats were administered a single oral dose by intubation consisting of 5050 mg/kg of 0.25% test material suspended in corn oil. An additional four groups of five females each were dosed with either 2500, 2800, 3200, or 4040 mg/kg or the 0.25% test material suspension. Animals were observed three times on day of treatment and once daily thereafter for 14 days. Body weights were recorded on day of dosing and at 7 and 14 days. Animals were necropsied upon discovery of death or at study conclusion.

RESULTS:

At 2500 mg/kg, 1/5 females died. At 2800 mg/kg, 3/5 females died. At 3200, 4040, and 5050 mg/kg, 5/5 females died. No males died at the 5050 mg/kg dose level. The $LD_{50}$ for females was reported to be 2700 (2520-2900) mg/kg. The $LD_{50}$ for males was reported to be > 5050 mg/kg.

Toxic symptoms observed were activity decrease, ataxia, body tremors, chromodacryorrhea, constricted pupils, convulsions, dilated pupils, epistaxis, gasping, lacrimation, muscle

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tremors, nasal discharge, piloerection, polyuria, ptosis, respiratory gurgle, rigidity, salivation, sensitive to touch, and swollen tongue. Gross necropsy revealed discoloration of lungs and liver, edematous lungs, gastrointestinal tract distended with gas and contents discolored, and pronounced serosal blood vessels on gastrointestinal tract.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: III - CAUTION.

(2) Acute Dermal Toxicity Study: Stillmeadow, Inc., Project No. 4122-86; May 30, 1986.

PROCEDURE:

Five male and five female New Zealand white rabbits were clipped free of hair on the dorsal surface and 24 hours later, each animal received a topical treatment of 2010 mg/kg of test material (moistened with 2.00 mL/kg of physiological saline) applied to the clipped test site. Test sites were kept under occlusive wrap for 24 hours. After exposure, the treated areas were washed with tap water. Animals were observed at 30 minutes after treatment, at 3 and 6 hours after treatment, and once daily thereafter for 14 days. Animals were weighed prior to dosing and at 7 and 14 days. Animals were necropsied at study conclusion.

RESULTS:

No deaths occurred. The $LD_{50}$ was reported to be > 2010 mg/kg. Toxic symptoms observed were decreased defecation and diarrhea. No abnormalities were noted at necropsy.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: III - CAUTION.

(3) Acute Inhalation Toxicity Study: Stillmeadow, Inc.; Project No. 4126-86; June 24, 1986.

PROCEDURE:

Five male and five female Sprague-Dawley rats were exposed to a gravimetrically-measured mean concentration of 2.71 mg/L of test material for 4 hours in a 200 L stainless steel dynamic flow inhalation chamber. Animals were observed frequently on day of exposure and once daily thereafter for 14 days. Animals were weighed prior to exposure and on days 7 and 14. Animals were necropsied at study conclusion.

RESULTS:

No deaths occurred. The $LC_{50}$ was reported to be > 2 /1 mg/L. Toxic symptoms observed were activity decrease, constricted pupils, exophthalmos, lacrimation, nasal discharge, piloerection, ptosis, and salivation. Gross necropsy revealed no abnormalities.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: III - CAUTION.

(4) Primary Eye Irritation Study: Stillmeadow, Inc.; Project No. 4123-86; June 4, 1986.

PROCEDURE:

Nine New Zealand white rabbits which were examined previously and found to be free of ocular injury or irritation were each administered 100 mg of test material that was placed into the conjunctival sac of the right eye. The animal's eyelid was held shut for 1 second. The untreated left eye served as a control. Thirty seconds after treatment, 3/9 treated eyes were washed with water. Eye irritation was scored at 1, 24, 48, and 72 hours and at 4, 7, 10, 14, 17, and 21 days.

RESULTS:

Eye irritation in the unwashed group was scored as follows: at 24 hours, corneal opacity (3/6 = 40, 3/6 = 10), iris irritation (3/6 = 10, 3/6 = 5), conjunctivae redness (5/6 = 3, 1/6 = 2), chemosis (5/6 = 3, 1/6 = 2), discharge (4/6 = 3, 1/6 = 2, 1/6 = 1), fluorescein staining (6/6 - positive) and stippling (6/6 - positive); at 7 days, corneal opacity (1/6 = 40, 1/6 = 30), iris irritation (1/6 = 10, 3/6 = 5), conjunctivae redness (3/6 = 1), chemosis (5/6 = 1), discharge (1/6 = 2, 2/6 = 1), and fluorescein staining (4/6 - positive); at 14 days, corneal opacity (2/6 = 10) and conjunctivae redness (2/6 = 1); and at 21 days, corneal opacity (1/6 = 10, 2/6 = 5).

Eye irritation in the washed group was scored as follows: at 24 hours, corneal opacity (1/3 = 15), conjunctivae redness (3/3 = 2), chemosis (1/3 = 3, 2/3 = 1), discharge (1/3 = 3, 2/3 = 1) and fluorescein staining (2/6 - positive); at 7 days, conjunctivae redness (2/3 = 1), and chemosis (1/3 = 2); at 14 days, discharge (1/3 = 1); and at 21 days, discharge (1/3 = 1).

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: I - DANGER.

(5) Primary Skin Irritation Study: Stillmeadow, Inc.; Project No. 4124-86; May 16, 1986.

PROCEDURE:

Six New Zealand white rabbits were clipped free of hair on the anterior quadrant of the back. Twenty-four hours later, each animal received a topical application of 500 mg of test material moistened with 0.7 ml of deionized water. The moistened test material was placed on the clipped test site and covered with occlusive wrap for 4 hours of exposure. After exposure the wrap and residual test material were removed. Skin irritation was scored at 1, 24, 48, and 72 hours.

RESULTS: No irritation was observed.

STUDY CLASSIFICATION: Core Guideline Data .

TOXICITY CATEGORY: IV - CAUTION.

(6) Dermal Sensitization Study: Stillmeadow, Inc.; Project No. 4125-86; June 24, 1986.

PROCEDURE:

Two groups of albino guinea pigs were clipped free of hair on the back approximately 24 hours before each induction treatment. Animals received induction treatments which consisted of 6 hours of exposure under occlusive wrap administered on days 1, 3, 6, 8, 10, 13, 15, 17, 20, and 22. The test group received 500 mg of test material moistened with 0.7 ml of deionized water per treatment and the positive control group received 0.5 ml of 2,4-dinitrochlorobenzene (DCNB) as a 0.05% solution in ethanol. Two weeks after the last induction treatment, each group was challenged at the previously treated site and at a virgin site on the opposite rear side of the back.

RESULTS:

Twenty-four hours after the fifth induction treatment, 2/10 animals exhibited very slight erythema. The number of test group animals exhibiting very slight erythema and very slight edema increased with each subsequent induction treatment. By the last induction treatment 8/10 animals exhibited very slight erythema and 4/10 animals exhibited very slight edema. After challenge, 5/10 animals exhibited very slight

erythema and 2/10 exhibited very slight edema at the previously treated test site. No irritation was observed at the virgin site.

Irritation in the positive control group began after the third induction treatment (very slight to well-defined erythema and very slight edema) and increased in number of animals and severity through to the last induction treatment (moderate to severe erythema and moderate to severe edema). After challenge 10/10 animals exhibited well-defined erythema and very slight to moderate to severe edema at the previously treated site. At the virgin site, 10/10 animals exhibited very slight to well-defined erythema and 9/10 animals exhibited very slight to well-defined edema.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Nonsensitizer.

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