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

1-12-87

006369

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

~~DEC 15 1986~~

MEMORANDUM

SUBJECT: EPA File Symbol 190 ATN
Apron Plus Captan Fungicide Seed Protectant

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

TO: Richard F. Mountfort, PM 23
Fungicide-Herbicide Branch
Registration Division (TS-767C)

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

ACTIVE INGREDIENTS:

<i>375AA</i> Metalaxyl: N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine methyl ester	12.5%
<i>159</i> Captan	29.5%
Related derivatives	1.7%
INERT INGREDIENTS:	56.0%

BACKGROUND:

The applicant has submitted an acute oral, acute dermal, acute inhalation, primary skin irritation, primary eye irritation, and dermal sensitization study. The studies were conducted by Stillmeadow, Inc. The data Accession Number is 265182. The method of support was not indicated.

006369

1/2/11

RECOMMENDATION:

FHB/TSS finds the studies acceptable to support registration of 100-ATN. The signal word is DANGER based on the primary eye irritation study.

LABELING:

The proposed label should be revised as follows:

1. The "KEEP OUT OF REACH OF CHILDREN" statement and signal word "DANGER" should be moved so that it appears on the center front panel.
2. Add the following referral statement below the Statement of Practical Treatment for eye exposure: "See additional precautionary statements on back of container."
3. Place Statement of Practical Treatment for eye exposure on front panel below signal word. This placement is required for all Category I studies.
4. Revise second sentence under precautionary statements to read "Harmful or fatal if swallowed."

REVIEW:

- (1) Acute Oral Toxicity Study: Stillmeadow, Inc.; Project No. 4047-86; May 12, 1986.

PROCEDURE:

Five male and five female Sprague-Dawley rats were administered by oral intubation 5050 mg/kg of 25% w/v suspension of test material in corn oil. Three groups of five females were also dosed at 2600, 4040, or 5700 mg/kg. Animals were observed at least three times on the day of treatment and at least once daily thereafter for 14 days. Body weights were recorded prior to treatment and on days 7 and 14 or at discovery of death. Gross necropsy was conducted on each animal at discovery of death or at study conclusion.

RESULTS:

At 2600 and 4040 mg/kg, 1/5 females died. At 5050 mg/kg, 1/5 males and 3/5 female died. At 5700 mg/kg, 3/5 females died. The LD₅₀ for females was reported to be 4995 mg/kg with 95 percent confidence limits of 3196 to 7807 mg/kg. The LD₅₀ for males was reported to be > 5050 mg/kg.

006369

2

Toxic symptoms observed were decreased activity, aggressiveness, ataxia, body tremors, corneal opacity, convulsions, constricted pupils, diarrhea, emaciation, epistaxis, exophthalmos, gasping, lacrimation, nasal discharge, piloerection, polyuria, ptosis, respiratory gurgle, rigidity, salivation, and swollen tongue. Gross necropsy revealed discolored contents of the gastrointestinal tract, gastrointestinal tract distended with gas or empty, pronounced serosal blood vessels along the intestinal tract, discolored liver and lungs, edematous lungs, testes drawn into abdominal cavity.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category IV - CAUTION.

(2) Acute Dermal Toxicity Study: Stillmeadow, Inc.; Project No. 4048-86; April 10, 1986.

PROCEDURE:

Five male and five female New Zealand White rabbits were clipped free of hair on the dorsal surface of the trunk. Approximately 24 hours later, each animal received 2010 mg/kg of test material moistened with 2.0 mg/kg of 0.9 percent saline. The moistened test material was applied to a test site on the shaven area and covered with occlusive wrap for 24 hours. After exposure, the wrap was removed and the test site washed with tap water to remove residual material. Animals were observed at 30 minutes, 3 and 6 hours after treatment and at least once daily thereafter for 14 days. Body weights were recorded on day 0, 7, and 14. Animals were necropsied at study conclusion.

RESULTS:

No mortalities occurred. The LD₅₀ was reported to be > 2010 mg/kg. All animals appeared normal for the duration of the study. No abnormalities were noted at necropsy.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category III - CAUTION.

(3) Acute Inhalation Toxicity Study: Stillmeadow, Inc.; Project No. 4052-86; May 15, 1986.

PROCEDURE:

Four groups each consisting of five male and five female Sprague-Dawley rats were exposed for 4 hours in a 200 L stainless steel dynamic flow inhalation chamber to an aerosol generated from the test material. The mean gravimetric concentration of the

006369

3

aerosol was 1.98, 2.75, 2.96, or 5.99 mg/L per group. Two additional groups consisting of five males/group were dosed at 1.02 or 1.31 mg/L (mean gravimetric concentration). Animals were observed frequently on the day of exposure and once daily thereafter for 14 days. Body weights were recorded prior to exposure and at 7 and 14 days. Animals were necropsied at study conclusion or at discovery of death.

RESULTS:

At 1.02 mg/L, 1/5 males died. At 1.31 mg/L, 2/5 males died. At 1.98 mg/L, 5/5 males and 2/5 females died. At 2.75 mg/L, 4/5 males and 2/5 females died. At 2.96 mg/L, 5/5 males and 4/5 females died. At 5.99 mg/L, 5/5 males and 5/5 females died. The LC₅₀ for males was reported to be 1.39 mg/L with 95 percent confidence limits of 1.02 to 1.89 mg/L. The LC₅₀ was reported to be 2.41 mg/L with 95 percent confidence limits of 1.79 to 3.26 mg/L.

Toxic symptoms included decreased activity, alopecia adjacent to the eyes, ataxia, constricted pupils, corneal opacity, dilated pupils, epistaxis, exophthalmos, gasping, lacrimation, nasal discharge, piloerection, polyuria, ptosis, respiratory chirp or gurgle, salivation, and swollen neck. Gross necropsy revealed discolored gastrointestinal tract mucosa, discolored contents of the gastrointestinal tract, serosal blood vessels pronounced on gastrointestinal tract, gastrointestinal tract distended with gas or empty, discolored lungs, lungs enlarged and edematous, discolored liver, and testes drawn into abdominal cavity and variations thereof considered related to test material administration.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category III - CAUTION.

(4) Primary Eye Irritation Study: Stillmeadow, Inc.; Project No. 4049-86; April 9, 1986.

PROCEDURE:

Nine New Zealand White rabbits which were found to be free of ocular irritation or injury each received 100 mg of test material in the right eye. The treated eyes of 3/9 animals were washed with room temperature deionized water for 1 minute beginning 30 seconds after treatment. The untreated left eye of each animal served as a control. Eye irritation was scored at 1, 24, 48, and 72 hours and at 4, 7, 10, 14, 17, and 21 days after treatment. Eyes were examined with 0.2 percent fluorescein sodium ophthalmic solution at the 24-hour observation and again at each subsequent observation until found to be negative.

RESULTS:

Eye irritation in the unwashed group was scored as follows: at 24 hours, fluorescein staining (1/6), conjunctivae redness (3/6 = 3, 3/6 = 2), chemosis (3/6 = 3, 3/6 = 2) and discharge (4/6 = 3, 4/6 = 2); at 7 days, one animal found dead, conjunctivae redness (1/5 = 2, 1/5 = 1), chemosis (1/5 = 3, 1/5 = 1) and discharge (1/5 = 2, 1/5 = 1); at day 14, corneal opacity (1/5 = 10), conjunctivae redness (1/5 = 3), chemosis (1/5 = 3) and discharge (1/5 = 2); and at 21 days, corneal opacity (1/5 = 15), conjunctivae redness (1/5 = 2), chemosis (1/5 = 2) and discharge (1/5 = 1).

Eye irritation in the washed group was scored as follows: At 24 hours, conjunctivae redness (2/3 = 3, 1/3 = 2), chemosis (1/3 = 3, 2/3 = 2) and discharge (3/3 = 2); at 7 days, conjunctivae redness (2/3 = 1), chemosis (2/3 = 1) and discharge (2/3 = 1); and at 14 days, all irritation had cleared.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category I - DANGER.

(5) Primary Skin Irritation Study: Stillmeadow, Inc.;
Project No. 4050-86; March 14, 1986.

PROCEDURE:

Six New Zealand White rabbits were clipped free of hair from the anterior right quadrant of the dorsal surface of the trunk. Approximately 24 hours later, each animal received 500 mg of test material moistened with 0.5 ml of deionized water. The moistened test material was applied to the clipped test site and covered with occlusive wrap for 4 hours. After exposure, the wrap was removed, and the test site was washed to remove any residual material. Skin irritation was scored at 1, 24, 48 and 72 hours.

RESULTS: No irritation was observed.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: Category IV - CAUTION.

006369

5

(6) Dermal Sensitization Study: Stillmeadow, Inc.; Project No. 4051-86; April 18, 1986.

PROCEDURE:

Two groups each consisting of 10 male Hartley-Albino guinea pigs were clipped free of hair from the back of the trunk. Approximately 24 hours later, animals in each group received the first and subsequent induction treatments which were applied to a test site on the clipped back of each animal. Treatments were administered on days 1, 4, 6, 8, 11, 13, 15, 18, 20, and 22, as follows: the positive control group received 0.5 ml of 0.05 percent w/v solution of 2,4-dinitrochlorobenzene (DNCB) and the test group received 500 mg of test material moistened with 0.5 ml of deionized water. Test sites were covered with occlusive wrap for 6 hours of exposure. Animals were placed in restrainers during exposure. At the end of each exposure, restrainers, wraps, and patches were removed. On day 36, animals were given an identical treatment which was applied to the original test site and also applied to a new test site. Skin irritation was scored approximately 24 hours after each treatment and at 48 hours after treatment on days 1, 22, and 36.

RESULTS:

Six out of ten animals in the test group exhibited very slight erythema during the induction phase. Irritation in the test group subsided by the next observation period in all animals except one animal where irritation lasted for two observation periods. No irritation was observed in the test group at challenge treatment.

After the second induction treatment, 5/10 animals in the positive control group exhibited very slight erythema and 1/10 animals exhibited very slight edema. Irritation in the positive control group increased in number of animals and severity of irritation with each subsequent treatment. At day 22, 9/10 animals exhibited moderate to severe erythema, 1/10 animals well-defined erythema, and 10/10 animals exhibited moderate edema with eschar formation.

STUDY CLASSIFICATION: Core Guideline Data.

TOXICITY CATEGORY: NONSENSITIZER.

006369

6

METALAXYL

Page ___ is not included in this copy.

Pages 7 through 11 are not included.

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