7-29-82

005431

Date: July 22, 1982

Subject: EPA File Symbol 100-AEO
Ridomil MZ58 Fungicide

From: Deloris F. Graham DFG 7/29/82
FHB/TSS E 7/29/82

To: Henry Jacoby
Product Manager (21)

Applicant: CIBA-GEIGY Corporation
Agricultural Division
Post Office Box 18300
Greensboro, NC 27419

Active Ingredients:

Metalaxyl: N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine methyl ester	10.0%
Mancozeb: a coordination product of zinc ion and manganese ethylene bisdithiocarbamate	48.0%
Inert Ingredients	12.0%

Background: Submitted Acute Oral, Acute Dermal, Acute Inhalation, Eye Irritation, Skin Irritation and Dermal Sensitization Studies. Studies conducted by Stillmeadow, Inc., and ToxiGenus, Inc. Data under accession number 247494. Method of support not submitted.

Recommendations:

(1) FHB/TSS finds these data acceptable to support conditional registration of this product.

(2) The appropriate signal word is CAUTION.

Label:

(1) The "If swallowed" statement must be revised to include "If swallowed, drink large quantities of water and induce vomiting by placing finger in back of throat and contact local poison control center. Avoid alcohol. Never give anything by mouth to an unconscious person."

(2) The statement "This product may cause allergic skin reaction" must be included in precautionary statements.

Review:

(1) Acute Oral Toxicity Study: Stillmeadow, Inc.; Project #2436-81, February 2, 1982.

Procedure: 4 groups consisting of 5F rats each received one of the following doses: 2500, 2980, 3560 and 4230 mg/kg. One group consisting of 5M and 5F received 5030 mg/kg of the test material and one group consisting of 5M received 5990 mg/kg of the test material. Observations made daily for 14 days posttreatment. Necropsy performed on all animals.

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Results: At 2980 mg/kg, 1/4F died; at 3560 mg/kg, 2/5F died; at 4230 mg/kg 4/5F died; at 5030 mg/kg, 1/5M and 5/5F died.

Toxic signs observed included lacrimation, constricted pupils, activity decrease, piloerection, ptosis, lethargy, rigid muscle tone, salivation polyuria, dilated pupils, epistaxis, ataxia, swollen tongue, convulsions, yellow diarrhea, respiratory gurgle, sensitive to touch.

Necropsy revealed polyuria, yellow slurry in stomach and small intestines, animal partially cannibalized, yellow mucoid material in stomach and small intestines, chromod acryorrhea, clear discharge from nose, blood vessels pronounced on stomach.

LD_{50} for males is greater than 5990 mg/kg. LD_{50} for females was 3608 mg/kg with 95% confidence limits betwen 3115 and 4180 mg/kg. Combined LD_{50} for males and females was 5735 mg/kg with 95% confidence limits betwen 3556 and 9248 mg/kg.

Study Classification: Core Guideline Data

Toxicity Category: III-CAUTION

(2) Acute Dermal Toxicity Study: Stillmeadow, Inc., Project No. 2437-81; January 21, 1982.

Procedure: 5M and 5F rabbits received 2010 mg/kg of the test material at abraded skin sites under occlusive wrap for 24-hour exposure. Observations made daily for 14 days. Necropsy performed on all animals.

Results: No mortalities. Toxic signs included constricted pupils, activity decrease, redness in eyes, lacrimation, diarrhea, no feces, no urine, small amount of urine. Erythema, edema, shallow lateral fissuring and yellow staining of test site hairs were observed. No observable abnormalities at necropsy. LD_{50} greater than 2010 mg/kg.

Study Classification: Core Guideline Data

Toxicity Category: III-CAUTION

(3) Acute Inhalation Toxicity Study: ToxiGenics, Inc.; Study #420-0844; February 10, 1982.

Procedure: 5M and 5F rats weighing between 210 and 258 grams were exposed for four hours to a gravimetric concentration of 2.36 mg/l of the test material (nominal concentration 21.7 mg/l). Mean chamber temperature was 75°F. Average mass median diameter was 2.33 micrometers and geometric standard deviation of 2.26 micrometers. Observations made daily for 14 days post-exposure. Necropsy performed on all animals.

Results: No mortalities. Toxic signs observed included irregular breathing, crusty nose, crusty muzzle, crusty eye, yellow/brown-stained fur and poor coat quality. No observable abnormalities at necropsy. LC_{50} greater than 2.36 mg/l gravimetric concentration.

Study Classification: Core Guideline Data

Toxicity Category: III-CAUTION

(4) Eye Irritation Study: Stillmeadow Inc.; Project #2438-81; January 28, 1982.

Procedure: Nine New Zealand rabbits received 100 mg of the test material in one eye each. The treated eyes of three of the rabbits were washed, thirty seconds posttreatment. Observations were made 1, 24, 48, and 72 hours, 4, 7, 10, 13, and 16 days posttreatment.

Results: At 24 hours, 5/6 of the unwashed group had iris irritation (5/6 = 5); 6/6 and 2/3 had conjunctive redness (2/6 = 1, 4/6 = 2) 2/3 = 1), chemosis (2/6 = 1, 2/6 = 2, 2/6 = 3 (1/3 = 1); 5/6 discharge (3/6 = 1, 1/6 = 2, 1/6 = 3).

At 4 days, 3/6 corneal opacity (1/6 = 5, 1/6 = 10, 1/6 = 15); 5/6 redness (4/6 = 1, 1/6 = 2); 1/6 chemosis (1/6 = 1).

At day 13, 1/6 corneal opacity (1/6 = 5); no other irritation present.

At day 16, no corneal opacity or other irritation present.

Study Classification: Core Guideline Data.

Toxicity Category: III-CAUTION

(5) Primary Skin Irritation Study: Stillmeadow, Inc.; Project #2439-81; January 20, 1982.

Procedure: Six New Zealand rabbits received 500 mg of the test material at two abraded and two intact skin sites per animal under occlusive wrap for 24-hour exposure. Observations made at 24 and 72 hours.

Results: At 24 hours, 6/6 animals had erythema (5/6 = 1, 1/6 = 2) and edema (4/6 = 1, 2/6 = 2). No irritation at 72 hours. Primary Irritation Score was 1.13.

Study Classification: Core Guideline Data.

Toxicity Category: IV-CAUTION

(6) Dermal Sensitization Study: Stillmeadow, Inc.; Project #2440-81; February 12, 1982.

Procedure: Two treatment groups consisting of ten male guinea pigs were used. Group I animals were treated intradermally with a 0.50% W/V solution of 2,4-dinitrochlorobenzene in 0.9% saline as a positive control group. Group II animals were treated intradermaily with a 0.0001% W/V solution of the test material in 0.9% saline as a test group. The animals were treated on days 0, 2, 5, 7, 9, 12, 14, 16, 19, 21, and 35. The animals were treated on the first

treatment day by introducting 0.05 ml of the appropriate material intradermally. On each succeeding treatment day, the animals were treated with 0.1 ml of the appropriate material intradermally. Observations for skin reaction were made approximately 24 and 48 hours after each treatment.

Results: The average skin irritation scores for Group I (positive control) were 1.0 for the initial treatment and 3.7 for final treatment. A sensitizing reaction was produced by positive control as expected.

The average skin irritation scores for Group II (test group) were 0.4 for the initial treatment and 2.7 for the final treatment. The final irritation score is significantly greater than the irritation score. The test material produced a sensitizing reaction in guinea pigs when administered intradermally.

Study Classification: Core Guideline Data

Toxicity Category: Sensitizing Agent

METALAXYL

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Pages 5 through 11 are not included.

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____ Description of quality control procedures.

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