12-17-82

Date: December 17, 1982

Subject: EPA File Symbol: 100-AUR
Banner Fungicide

From: Debris F. Graham
FHB/IBS E 12/17/82

To: Henry Jacoby
Product Manager (21)

Applicant: CIBA-GEIGY Corporation
Agricultural Division
P.O. Box 18300
Greensboro, N.C. 27419

Active Ingredients:
1-[2-(2,4-dichlorophenyl)-4-propyl
-1,3-dioxolan-2y[]-methyl]-1H-1,2,
4-triazole 14.7%
Inert Ingredients 85.3%

Background: Submitted Acute Dermal, Eye Irritation, Primary Dermal Irritation and Dermal Sensitization Studies. Studies conducted by Stillmeadow, Inc. and Pharmakon Research International, Inc. Data under accession number 248442. Cite all method of support.

Recommendations:

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

(2) The Acute Dermal Toxicity Study was conducted on the Technical product and would not be sufficient to support conditional registration of this formulation.

(3) The appropriate signal word is WARNING.

Label:

(1) In the precautionary statement must be revised to include "Causes substantial but temporary eye injury".

(2) The statement "Causes irreversible eye damage" must be deleted.

Review:

1) Acute Dermal Toxicity Study: Pharmakon Research International, Inc.; Study # PH 430-CG-001-82; Aug. 30, 1982.

Procedure: 4 groups consisting of twenty New Zealand rabbits each received one of the following doses: 0.0, 3.0, 30.0, 1000.0 mg/kg. Group one & two consisted of 11M and 9F rabbits each; group three consisted of 10M and 10F rabbits and group four consisted of 13M and 7F rabbits. Group one was dosed at 0.0 mg/kg; group two dosed at 3 mg/kg; group three at 30 mg/kg and group four 1000 mg/kg. Test animals had intact and abraded skin sites. Test material was applied daily for 5 days per week for three consecutive weeks. One-half the animals in each group were abraded and the other half intact skin sites. Observations made daily for

mortality and toxic effects. Necropsy performed on all animals.

Results: One male animal died in group II and one female died in group IV. Slight dermal irritation observed that persisted throughout the study. Toxic signs observed included diarrhea. Necropsy revealed liver, yellow, small, white nodule; yellow foci, narrow, linear; scar adhesion; kidney: small, pale area white, small, numerous foci; minute, numerous pets; white to yellow discoloration; lung: red hepatization (1.0cm, diaphragmatic lobe); intestines: small, fluid filled; large and small mucoid enteritis; lymph node: mesenteric (1.0cm red area, white center); external: hind quarters, liquid feces extreme dehydration; peri-anal area soiled

Study Classification: Core Minimum Data. An equal number of males and females per dose must be used. LD50 for males and females with 95% confidence limits must be submitted.

Toxicity Category: II - WARNING

2) Eye Irritation Study: Stillmeadow, Inc.; Propit # 2573-82; April 20, 1982.

Procedure: Nine New Zaland rabbits received 0.1 ml of the test material in one eye each. The treated eyes of three of the rabbits were washed thirty seconds post treatment. Observations made at 1, 24, 48 and 72 hours and at 4, 7, 10, 13, 16, 19 and 21 days after treatment.

Results: At 24 hours, 4/6 animals of the unwashed group and 3/3 of the washed group had corneal opacity (1/6=5, 1/6=10, 3/6=15, 1/6=20) (2/3=5, 1/3=20); 5/6+2/3

iris irritation (5/6=5)(3/3=5); 6/6+3/3 conjunctive redness (3/6=2, 3/6=3)(2/3=2, 1/3=3), chemosis (4/6=2, 2/6=3)(1/3=2, 2/3=3) and discharge (1/6=1, 3/6=2, 2/6=3).

At day 7, 1/3 animals found dead: 1/6 and 1/3 had corneal opacity (1/6=15)(1/3=10) and iris irritation (1/6=5)(1/3=5); 2/6 and 1/3 conjunctive redness (2/6=1)(1/3=2); 4/6+2/3 chemosis (1/6=1, 4/6=2, 1/6=4)(1/3=2, 1/3=3); 1/6 and 1/3 discharge (1/6=2)(1/3=2).

At day 13, 1/6 and 1/3 had corneal opacity (1/6=10)(1/3=5); no iris irritation; 1/6 redness (1/6=1); 1/3 chemosis (1/3=2); 1/6 chemosis (1/6=1).

At day 21, 1/6 and 1/3 had corneal opacity (1/6=5)(1/3=5).

Apparent invasion of the cornea by blood vessels observed in some animals and hair loss around the eyes observed by some animals.

Study Classification: Core Guideline Data.

Toxicity Category: II - WARNING

(3) Skin Irritation Study: Stillmeadow, Inc.; Project # 2574-82; April 14, 1982.

Procedure: Six New Zealand rabbits received 0.5ml of the test material at two abraded and two intact skin sites per animal under occlusive wrap for 24 hour exposure period. Observations made at 24 and 72 hours after treatment, ~~dead~~ then daily thereafter through 13 days.

Results: At 24 hours, 6/6 had well defined erythema (6/6=2) and 6/6 had slight to moderate edema (4/6=2, 2/6=3). At 72 hours, 6/6 well defined erythema (6/6=2) and 6/6 slight to moderate edema (1/6=1, 2/6=2, 3/6=3). Erythema and edema persisted through

day 12 lessening in degree. Irritation had cleared by day 13.

Study Classification: Core Guideline Data.

Toxicity Category: III - CAUTION

(4) Dermal Sensitization Study: Stillmeadow, Inc.; Project # 2575-82; May 13, 1982.

Procedure: Two groups consisting of 10 male guinea pigs were treated intradermally with one of the following compounds: a 0.5% w/v solution of 2,4-dinitrochlorobenzene in 0.9% saline as a positive control group and a 0.01% v/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 introducing 0.05 ml of the appropriate test material intradermally. On each succeeding treatment day the animals were treated with 0.1 ml of the appropriate material. Observations were made at 24 and 48 hours after each treatment.

Results: The average irritation scores for group I (Positive Control Group) were 0.0 for the initial treatment and 3.4 for the final treatment. The final irritation score was significantly greater than the initial score thereby indicating a sensitizing reaction.

The average skin irritation scores for Group II (Test Group) were 0.0 for the initial treatment and 0.4 for the final treatment. The final irritation score is significantly greater than the irritation score thereby ~~predicating~~ a sensitizing reaction.

Study Classification: Core Guideline Data.

Toxicity Category: Potential Sensitizer.