10-20-83

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

005032

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: October 20, 1983

SUBJECT: EPA Registration Numbe . 501-42
Gustafson

FROM: Deloris F. Graham
FHB/TSS

TO: Henry Jacoby
Product Manager (21)

Applicant: Gustafson, Inc.
P.O. Box 220065
Dallas, Texas 75222

Active Ingredient:
Metalaxyl: N-(2,6-dimethylphenyl)
-N-(methoxyacetyl)alanine methyl ester....28.35%
Inert Ingredients.....71.65%

Background: Submitted Acute Oral, Acute Dermal, Acute Inhalation, Eye Irritation and Skin Irritation Studies. Studies conducted by Product Safety Labs. Data under accession number 250989. Method of support not indicated. Another Acute Oral Study submitted and given the accession number 251408.

Recommendation:

1. FHB/TSS finds all studies except the Acute Inhalation and one Acute Oral Study acceptable to support conditional registration of this product.

   a. In the Acute Inhalation Study actual concentration, not nominal must be used.

   b. In the Acute Oral Study, LD_{50} and 95% confidence limits must be determined.

2. The appropriate signal word is DANGER.

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Label:

1. The precautionary statements must be revised to include "DANGER. Causes irreversible eye damage."

2. The statement of practical treatment must be revised to include "In case of contact, flush eyes with plenty of water and get medical attention immediately."

3. The statement "Do not store near feed or food" must be deleted from precautionary statements and placed under the heading "Directions for Use."

4. See enclosed copy for appropriate storage and disposal statements.

Review:

1. Acute Oral Toxicity Study: Product Safety Labs; Report No. T-3030; May 6, 1983.

   Procedure: Five male and five female rats weighing between 200 and 300 grams received a single dose of 5.0 g/kg. Observations were daily for 14 days after treatment. Necropsy performed on all animals.

   Results: 2/5 M and 5/5 F died. Lethargy was the only toxic sign noted in the 3/5 M survivors. Necropsy revealed discolored liver and spleen; intestinal hemorrhage; pulmonary hemorrhage. LD_{50} less than 5.0 g/kg.

   Study Classification: Core Supplementary Data.
   LD_{50} must be determined.

2. Acute Oral Toxicity Study: Product Safety Labs; Report No. T-3193; August 8, 1983; EPA Acc. #251408.

   Procedure: Five groups consisting of 5 M and 5 F rats weighing between 200 and 300 grams each received one of the following doses: 2.5, 3.5, 4.5, 5.5 or 6.5 g/kg. Observations made daily for 14 days after treatment. Necropsy performed on all animals.

   Results: At 2.5 g/kg, 2/5 M and 3/5 F died; at 3.5 g/kg, 1/5 M and 4/5 F died; at 4.5 g/kg, 1/5 M and 5/5 F died; at 5.5 g/kg, 2/5 M and 5/5 F died; at 6.5 g/kg, 3/5 M and 5/5 F died. No signs of toxicity on gross pathological changes reported. LD_{50} reported as 2.9 g/kg, with 95% confidence limits between 1.8 and 4.6 g/kg.

   Study Classification: Core Guideline Data.

   Toxicity Category: III-CAUTION.

3. Primary Skin Irritation Study: Product Safety Labs; Report No. T-3058; May 16, 1983.

   Procedure: Six rabbits received 0.5 ml of the test material at two abraded and two intact skin sites per rabbit under occlusive wrap for a

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24 hour exposure period. Observations were made at 24 and 72 hours and at 4, 7, 10, 14, 17 and 21 days after treatment.

Results: At 24 hours, 6/6 animals had erythema (scores of 1 and 2) and edema (scores of 1, 2 and 3). At 72 hours, 5/6 had erythema (scores of 1, 2, and 3) and edema (scores of 2 and 3). Primary Irritation Score was 3.52. Irritation continued in some animals through day 17, had

cleared by day 21.

Study Classification: Core Guideline Data.

Toxicity Category: III-CAUTION.

4. Acute Inhalation Toxicity Study: Product Safety Labs; Report No. T-3065; May 13, 1983.

Procedure: Five male and five female Wistar rats weighing between 200 and 300 grams were exposed for 4 hours to 7.9 g of the test material (nominal concentration = 21.94 mg/l). Unknown analytical method. Observations were made for 14 days after exposure. Necropsy performed on all animals.

Results: No mortalities. No toxic signs reported. No gross pathology reported either. LC_{50} indicated as greater than 21.94 mg/l, nominal concentration determined gravimetrically.

Study Classification: Core Supplementary Data. Actual concentrations, not nominal concentrations, must be used. Chamber conditions, temperature, relative humidity, etc., must be submitted.

5. Acute Dermal Toxicity Study: Product Safety Labs; Report No. T-3073; June 1, 1983.

Procedure: Five male and five female New Zealand rabbits, weighing between 2.3-3.0 kg received 2.0 g/kg of the test material at abraded skin sites under occlusive wrap for 24 hour exposure period. Observations were made for 14 days after treatment. Necropsy performed on all animals.

Results: No mortalities or toxic signs reported. Necropsy report indicated slight intestinal hemorrhage in one male animal. LC_{50} greater than 2.0 g/kg.

Study Classification: Core Guideline Data.

Toxicity Category: III-CAUTION.

6. Eye Irritation Study: Product Safety Labs; Report No. T-3104; June 14, 1983.

Procedure: Nine New Zealand rabbits received 0.1 ml of the test material in one eye each. The treated eyes of three of the rabbits were washed with lukewarm water 30 seconds after treatment. Observations were made at 24, 48 and 72 hours, and at 4, 7, 10, 14, 17 and 21 days after treatment.

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Results: At 24 hours, 6/6 animals of the unwashed group and 2/3 of the washed group had corneal opacity (6/6=20) (2/3=20); 3/6 & 1/3 iris irritation (3/6=5) (1/3=5); 6/6 & 3/3 conjunctive redness (5/6=2, 1/6=3) (3/3=2), chemosis (1/6=2, 1/6=3, 4/6=4) (1/3=1, 2/3=2) and 6/6 & 2/3 discharge (1/6=1, 1/6=2, 4/6=3) (1/3=1, 1/3=2).

At 7 days, 6/6 & 3/3 corneal opacity (1/6=10, 3/6=20, 2/6=40) (1/3=15, 2/3=20); 4/6 & 2/3 iris irritation (4/6=5) (2/3=5); 5/6 & 3/3 redness (3/6=1, 2/6=2) (2/3=1, 1/3=2); 6/6 & 3/3 chemosis (6/6=2) (2/3=2, 1/3=3) 3/6 & 2/3 discharge (2/6=1, 1/6=2) (2/3=2).

At 14 days, 4/6 & 1/3 corneal opacity (1/6=20, 1/6=30, 1/6=40, 1/6=60) (1/3=30); 3/6 & 1/3 iris irritation (3/6=5) (1/3=5); 3/6 & 3/3 redness (3/6=1, 3/3=1). 4/6 & 1/3 chemosis (2/6=1, 2/6=2) (1/3=3); 2/6 & 1/3 discharge (4/6=1, 1/6=2) (1/3=2).

At 21 days, 4/6 & 1/3 corneal opacity (1/6=15, 2/6=20, 1/6=40) (1/3=20); 2/6 iris irritation (2/6=5); 4/6 & 2/3 redness (4/6=1) (2/3=1); 3/6 & 1/3 chemosis (1/6=1, 2/6=2) (1/3=3); 2/6 & 1/3 discharge (2/6=1) (1/3=2).

Study Classification: Core Guideline Data.

Toxicity Category: I-DANGER.

METALAXYL

Page_____ is not included in this copy.

Pages 5 through 7 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.

X ____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

____ FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

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.