

US EPA ARCHIVE DOCUMENT

MEMORANDUM

DATE: May 24, 1982

TO: Henry Jacoby
Product Manager (21)

FROM: Deloris F. Graham
FHB/TSS

SUBJECT: EPA Registration Number 618-67
Thiabendazole Microfine MSD

002825

002825

Applicant: Merck & Company, Inc.
P.O. Box 2000
Rahway, NJ 07065
Attention: R. R. Buck

Active Ingredients:

2-(4-thiazolyl)benzimidazole (Thiabendazole).....98.5%
Inert Ingredients.....1.5%

Background: Submitted Acute Oral, Acute Inhalation, Eye Irritation, and Primary Dermal Irritation Study. Studies conducted by Hazleton Laboratories. Data under Accession Number 247279. Method of support not applicable. Miscellaneous data, not requested.

Recommendations:

- (1) FHB/TSS finds these studies acceptable to support conditional registration of this product. However, for future submissions please note:
 - (a) In the Acute Oral Study individual symptomology and necropsy reports must be submitted;
 - (b) In the Eye Irritation Study individual scoring for corneal opacity, iris irritation, conjunctival redness, swelling, and discharge for each animal must be submitted; and
 - (c) In the Primary Dermal Study, four test sites (2 abraded and 2 intact) per animal must be used.
- (2) An Acute Dermal Study was not submitted. To support a conditional registration an Acute Dermal would have to be submitted and/or cited.
- (3) The appropriate signal word as determined by data submitted is WARNING.

1065

Label:

002825

- (1) The precautionary statements must be revised similar to the following:

"May be fatal if inhaled. Do not breathe (dust, vapor, or spray mist). Wear a mask or pesticide respirator jointly approved by the Mining Enforcement and Safety Administration and the National Institute for Occupational Safety and Health. Harmful if swallowed."

- (2) A statement of practical treatment must appear on the label similar to the following:

"If inhaled, remove victim to fresh air. If not breathing, give artificial respiration, preferably mouth-to-mouth. Get medical attention. If swallowed give one or two glasses of water and induce vomiting by placing fingers in back of throat. Never give anything by mouth to an unconscious person. Call a physician."

- (3) The statement "Do not contaminate water by cleaning of equipment or disposal of wastes" must appear under the heading "Directions for Use" subheading "Storage and Disposal."

Review:

- (1) Acute Oral Toxicity Study: Merck Sharp and Dohme Research Lab.; #81-2691; April 13, 1981.

Procedure: 5 groups consisting of 10 M and 10 F each weighing between 117 to 190 g received one of the following doses: 2,222; 3,333; 5,000; 7,500; 11,250 mg/kg. Observations made frequently on day of dosing then daily thereafter for 14 days. Necropsy performed on all animals.

Results: At 2,222 mg/kg, 2/10 F died; at 3,333 mg/kg, 2/10 M and 3/10 F died; at 5,000 mg/kg, 6/10 M and 4/10 F died; at 7,500 mg/kg, 8/10 M and 8/10 F died; at 11,250 mg/kg, 9/10 M and 9/10 F died. Toxic signs included decreased activity, bradypnea, ptosis, loss of righting reflex and alopecia. LD₅₀ for males 5,070 mg/kg with confidence limits between 3,982 and 6,389 mg/kg. LD₅₀ for females 4,734 mg/kg with confidence limits between 3,371 and 6,541 mg/kg.

Study Classification: Core Minimum Data. Individual symptomology and necropsy reports for each animal.

Toxicity Category: III - CAUTION

- (2) Acute Inhalation Study: Hazleton Laboratories; Project #284-129; October 23, 1981.

2

002825

Procedure: Two groups consisting of 5 M and 5 F rats weighing between 208 and 239 grams. One group was used as the control. The other group was exposed to a nominal concentration of 6.84 mg/l with gravimetric concentration from 89.80 to 552.20 ug/l (0.0898 mg/l to 0.5522 mg/l) of the test material. Particle size 4-5 μ . Standard deviation 2.24 μ observations were made twice daily for 14 days. Necropsy performed on all animals.

Results: No mortalities. Symptomology in test animals during exposure included squinted eyes, polypnea, alopecia, but had cleared by day one postexposure. Control animals normal.

At necropsy in test and control group - lungs: failed to collapse, pale spots; stomach: pale areas on glandular region; cecum: red foci; kidneys: pelvis dilated; uterine horn: distended with clear fluid; cervical lymph nodes: unequal in size.

At histopathology in test and control groups - lungs: focal subpleural accumulations of lymphocytes; peribroncheal and perivascular lymphoid; hyperplasia; pneumonitis, pleocellular inflammatory infiltrate, aspirated blood; alveolar macrophages (foci); liver: mononuclear cells; kidneys: focal nephropathy; uterus: hyclometria. In test animals only - kidneys: focal mineralization/cortical medullary junction; cecum: focal sub mucresal hemorrhage (terminal). In control animals only - cervical lymph nodes: lymphoreticular cell proliferation.

Study Classification: Core Guideline Data.

Toxicity Category: II - WARNING

(3) Eye Irritation Study: Merck Sharp and Dohme Research Lab.; TT #81-2693; April 13, 1981.

Procedure: Each of 5 M and 5 F rabbits received 0.1 g of the test material in the left eye. The eyes of 4 of the treated rabbits were washed, thirty seconds posttreatment. Observations made at 15 minutes, 2 hours, and 24 hours posttreatment, then once daily for 14 days.

Results: At 15 minutes slight conjunctiva injection with a slight to moderate clear colorless discharge. The discharge decreased to very slight at 2 hours. All eyes appeared normal at 24 hours.

Study Classification: Core Minimum Data. Individual scoring for corneal opacity, iris irritation and conjunctive redness, chemosis, and discharge for each animal.

Toxicity Category: III - CAUTION

(4) Primary Dermal Study: Merck Sharp and Dohme Research Lab.; TT #81-2692; April 13, 1981.

3

002825

Procedure: Six New Zealand rabbits, received 0.5 g of the test material at one abraded and one intact skin site per rabbit under occlusive wrap for 24 hour exposure. Observations made daily for two weeks.

Results: At 24 hours, 1/6 had slight erythema, but had cleared by 48 hours. No other irritation.

Study Classification: Core Minimum Data. Four sites (2 abraded and 2 intact) per animal must be used.

Toxicity Category: IV - CAUTION

4

002825

ACCEPTED
JUL 5 1974
Under the Federal Food, Drug, and Cosmetic Act

MERCK SHARP & DOHME INTERNATIONAL



50 Kilograms

Product 65731

THIABENDAZOLE

MICROFINE

MSD

For Making Antimycotic Formulations

CAUTION!

HARMFUL IF SWALLOWED

Do not contaminate water by cleaning of equipment or disposal of wastes

Active Ingredient

2-(4-thiazolyl)benzimidazole (Thiabendazole) 98.5%

Inert Ingredients 1.5%

EPA Est. 34899-NJ-1

EPA REG. NO. 618-67

8491001

Made in U.S.A.

Division of MERCK & CO., Inc.
RAHWAY, N.J., U.S.A.

5