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

005269

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORAMDUM

DATE: January 5, 1984

SUBJECT: EPA File Symbol: 619-OE

FROM: Deloris F. Graham
FHB/TSS

TO: Henry Jacoby
Product Manager (21)

Applicant: Merck & Co., Inc.
126 E. Lincoln Avenue
P.O. Box 2000
Rahway, New Jersey 07065

Active Ingredient:
2-(4-thiazolyl) benzimidazole.....90%
Inert Ingredients:.....10%

Background: Submitted Acute Oral, Acute Dermal, Acute Inhalation, Eye Irritation and Primary Dermal Irritation Studies. Studies conducted by Bio/dyanamics, Inc. Data not accessioned.

Recommendation:

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

(2) Based on the Acute Inhalation Study, the appropriate signal word is WARNING.

Label:

(1) The signal word WARNING must appear on label.

(2) Precautionary statements must be revised to include "Harmful if inhaled. If inhaled remove victim to fresh air and get medical attention."

Review:

(1) Acute Oral Toxicity Study: Bio/dyanamics Inc.; Project No.: 4462-83; August 19, 1983.

Procedure: Four groups consisting of five male and five female Sprague Dawley rats each received one of the following doses orally: 1.7, 2.5, 3.5 and 7.1 g/kg. Observations were made at 1, 2, and 4 hours after dosing and daily thereafter for 14 days. Necropsy performed on all animals.

Results: At 3.5 g/kg, 2/5 M & 1/5 F died; at 5.0 g/kg 3/5 M and 4/5 F died. At 7.1 g/kg, 3/5 M and 3/5 F died. Toxic signs reported included tremors, convulsions, prostration, miosis, atonia, emaciation, alopecia and unthrifty coat. Observations reported during necropsy included ocular discharge, oral discharge, nasal discharge, alopecia, urinary staining, fecal staining; lungs: red foci, discoloration; adrenals: red; testes: found in body cavity; urinary bladder: red fluid; stomach: walls red, contained test material; intestine: walls red, contained test material and red fluid; uterus: reddened, swollen. LD_{50} for males was reported to be 4.5 g/kg with 95% confidence limits between 3.3 and 5.7 g/kg. LD_{50} for females was reported to be 4.7 g/kg with 95% confidence limits between 3.4 and 6.0 g/kg. LD_{50} for males and females combined was reported to be 4.6 g/kg with 95% confidence limits between 3.7 and 5.5 g/kg.

Study Classification: Core Guideline Data.

Toxicity Category: III - CAUTION

(2) Acute Dermal Toxicity Study: Bio/dynamics, Inc.; Project No.: 4463-83; August 11, 1983.

Procedure: Five male and five female New Zealand rabbits weighing between 2.2 and 2.8 kg received a 2 g/kg dose at intact skin sites under occlusive wrap for 24-hour exposure period. Observations made at 1, 2,and 4 hours after dosing and twice daily thereafter for 14 days. Necropsy performed on all animals.

Results: No mortalities. Toxic signs reported included nasal discharge, eyes red, discoloration around eye, food consumption decrease, and desquamation. At necropsy one animal reported to have discoloration of lungs. LD_{50} greater than 2 g/kg.

Study Classification: Core Guideline Data

Toxicity Category: III - CAUTION

(3) Acute Inhalation Toxicity Study: Bio/dynamics, Inc.; Project No.: 83-7649; August 23, 1983.

Procedure: Five male and five female Sprague-Dawley rats were exposed for four hours to a mean analytical concentration of 0.2 mg/l of the test material. The average mass median aerodynamic diameter was 2.6 microns with an average geometric standard derivation of 2.5. Chamber temperature was 74°F with relative humidity 63%. Observations made at fifteen minute intervals during first hour of exposure, hourly for the remainder of exposure, and hourly for two hours postexposure, then daily through 15 days postexposure. Necropsy performed on all animals.

Results: No mortalities. Toxic signs reported included lacrimation, mucoid nasal discharge, dried red nasal discharge, chromodacryorrhea, labored breathing, fur matted and reduced activity. Decrease in body weight in male and female animals noted. Discoloration of lungs and kidneys reported at necropsy. The report stated these findings at necropsy had not been established as treatment related. The renal pelves were reported as dilated in 3/5 males.

Study Classification: Core Guideline Data

Toxicity Category: II - WARNING

(4) Eye Irritation Study: Bio/dynamics, Inc.; Project No. 4465-83; August 2, 1983.

Procedure: Six New Zealand rabbits received 0.1 cc (59.1 mg) in one eye each. Observations were made at 1, 24, 48 and 72 hours and 7 and 10 days after treatment.

Results: At 1 hour, 3/6 had corneal opacity (1/6 = 5, 1/6 = 10, 1/6 = 20); 2/6 iris irritation (2/6 = 5); 6/6 conjunctive redness (5/6 = 1, 1/6 = 2), chemosis (6/6 = 1), and discharge (4/6 = 1, 2/6 = 2).

At 24 hours, 6/6 redness (2/6 = 1, 4/6 = 2); stippling and ulceration noted. Corneal opacity and iris irritation had cleared.

At 72 hours, 4/6 redness (4/6 = 1).

At 7 days, 3/6 redness (3/6 = 1).

At 10 days, irritation had cleared except for a trace of iris irritation in one animal.

Study Classification: Core Guideline Data.

Toxicity Category: III - CAUTION

(5) Primary Dermal Irritation Study: Bio/dynamics, Inc.; Project No. 4464-83; August 2, 1983.

Procedure: Six New Zealand rabbits 0.5 g of the test material at intact skin sites under occlusive wrap for 4 hours of exposure. Obvservations made 30 minutes after 4 hour exposure, 24, 48 and 72 hours after exposure.

Results: At 24 hours, 6/6 slight erythema (5/6 = 1, 1/6 = 2) and no edema. At 72 hours, 1/6 erythema (1/6 = 1).

Study Classification: Core Guideline Data

Toxicity Category: IV - CAUTION

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Page_____ is not included in this copy.

Pages 4 through 5 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) _____.

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