UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, DC 20460

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OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Thiabendazole - Submission of Two Acute Studies
Submitted June 17, 1988 by Merk Sharp and Dohme.
EPA Id No.: 060101
Record No.: 234,289
Tox. Br. Project No.: 9-0286
Tox. Chem. No.: 849A

TO: G. Werdig
Product Manager #50
Registration Division (TS-767C)

FROM: Judith W. Hauswirth, Ph.D., Acting Chief
Toxicology Branch I - IRS
Health Effects Division (TS-769C)

Judith W. Hauswirth 12/7/88

THRU: William Burnam, Acting Director
Health Effects Division (TS-769C)

Action Requested: Review two acute studies submitted on thiabendazole as a result of a DCI.

Conclusions: These studies have been reviewed and the data evaluation reports are attached.

1. Acute Oral Toxicity in Rats

LD_{50} = 5.07 mg/kg for male rats
= 4.73 mg/kg for female rats
Toxicity Category: III (based upon LD_{50} for females)
Core Classification: Minimum

2. Acute Dermal Toxicity

LD_{50} > 2000 mg/kg
Toxicity Category: III
Core Classification: Minimum

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Reviewed by: Judith W. Hauswirth, Ph.D., Acting Chief
Toxicology Branch I - HFS

Judith W Hauswirth
12/7/85

DATA EVALUATION REPORT

STUDY TYPE: Acute Oral Toxicity Study in Rats 81-1 TOX. CHEM. NO.: 849A

MRID NO.: 407698-03

TEST MATERIAL: Thiabendazole

SYNONYMS:

STUDY NUMBER: TT #81-2691

SPONSOR: Merck Sharp and Dohme

TESTING FACILITY: Merck Sharp and Dohme Research Laboratories
West Point, PA

TITLE REPORT: Thiabendazole Veterinary (Lot ERM-211): Acute Oral Toxicity Study in Rats

AUTHOR(S): George R. Lankas

REPORT ISSUED: April 6, 1981

CONCLUSION: The acute oral LD_{50} for female rats was calculated to be 4734 mg/kg (range 3371-6541) and for males 5070 mg/kg (range 3962-6389). Signs of toxicity included decreased activity, bradypnea and ptosis within 30 minutes of dosing. Deaths occurred mostly within the first 24 hours after dosing.

Toxicity Category: III (based upon the LD_{50} for females)
Core Classification: Minimum due to reporting errors (see results section).
LD_{50} = 5.07 g/kg for males rats
= 4.73 g/kg for female rats

MATERIALS:

1. Test compound: Thiabendazole Veterinary; Lot ERM-211; Purity 98.5% by HPLC analysis.

2. Test animals: Species: rat; Strain: Crl:CD(SD) BR; Age: 6 to 7 weeks; Weight: 117-190 g; Source: Charles River Laboratories, Wilmington, MA.

METHODS:

Rats were administered the compound on day 0 by oral intubation. They were observed frequently on the day the compound was administered and daily thereafter. They were weighed at pretest and days 7 and 12. They were fasted for 24 hours prior to necropsy unless they died prior to day 14. Necropsy was performed on

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all animals.

RESULTS:

Mortality was as shown in the following table.

Dose	Males	Females
mg/kg	deaths/dosed	deaths/dosed
2222	0/10	2/10
3333	2/10	3/10
5000	6/10	4/10
7500	8/10	8/10
11250	9/10	9/10

Body weight data appeared to be reported for males only. Apparently there was an error from page 14-16 in Table #2. From dose level 2222 mg/kg on page 14 to page 16, the data are probably for females not males. In addition, body weight data were not given for days 7 and 14 for the one male in the 11250 mg/kg group that survived to final necropsy. Body weight gain was affected at dosage levels at and above 5000 mg/kg for both males and females.

Clinical signs of toxicity consisted of decreased activity, bradypnea, ptosis, loss of righting reflex and alopecia (two 3333 mg/kg females, only).

Findings at gross necropsy consisted mostly of petechial hemorrages of the thymus and pinpoint tan foci of the lung.

A signed statement was included that stated that this study does not fall under the requirements for 40CFR Part 160.

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Reviewed by: Judith W. Hauswirth, Ph.D., Acting Chief
Toxicology Branch I - HED

Judith W. Hauswirth
12/7/88

DATA EVALUATION REPORT

STUDY TYPE: Acute Dermal Toxicity Study in Rabbits 81-2 TOX. CHEM. NO.: 849A

MRID NO.: 407896-04

TEST MATERIAL: Thiabendazole

SYNONYMS:

STUDY NUMBER: 4004-86

SPONSOR: Merk Sharp and Dohme

TESTING FACILITY: Bio/dynamics, Inc.
East Millstone, NJ

TITLE REPORT: Thiabendazole (Batch #DR M6 17): Acute Dermal Toxicity Study in Rabbits

AUTHOR(S): Donna L. Blaszcak

REPORT ISSUED: December 8, 1986

CONCLUSION: The acute dermal LD_{50} for thiabendazole in the rabbit is >2000 mg/kg.

Toxicity Category: III
Core Classification: Minimum, purity of test material not given.

MATERIALS:

1. Test compound: Thiabendazole; off-white powder; Product #47962; Batch #DR M6 17; purity not stated.

2. Test animals: Species: rabbit; Strain: New Zealand; Age: at least 8 weeks; Weight: 2.1 to 2.6 kg; Source: Hazleton-Dutchland, Inc. Denver, Pennsylvania.

METHODS:

Five male and five female rabbits were used. One day prior to dosing the trunk of each animal was shaved to expose approximately 10% of the body surface area. The test chemical (dry powder) was placed on gauze and moistened with saline. The only dose level used was 2000 mg/kg, the limit dose for this test. The treated gauze was held in place with a impervious plastic sleeve and Elizabethan collars were placed on the animals. The animals were exposed to the test chemical for 24 hours, at which time the material was removed and the skin

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was wiped free of the material.

Animals were checked twice daily for mortality, 1, 2 and 4 hours after dosing for clinical signs of toxicity and daily thereafter for 14 days. Animals were weighed pretest and on days 7 and 14. At termination gross necropsy was performed on all animals.

RESULTS:

There were no deaths. Most animals gained weight from day 7 to termination of the study. Three animals showed decreased food consumption on the second day after dosing. There were no clinical signs of toxicity nor lesions seen at necropsy that could be attributed to treatment.

A quality assurance statement which was signed and dated was included.

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