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

MEMORANDUM

MAY 17 1990

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Review of Two Acute Toxicity Studies of Thiabendazole.

EPA No. 060101 Project No. 0-0231
Record No. 255161 Tox. Chem. No. 849A

TO: Frank Rubis, PM Team #50
Registration Division (H7505C)

FROM: John E. Whalan, D.A.B.T., Toxicologist
Section I, Toxicology Branch I
Health Effects Division (H7509C)

John E. Whalan 5-4-90

THRU: Roger L. Gardner, Acting Section Head
Section I, Toxicology Branch I
Health Effects Division (H7509C)

Roger Gardner 5-7-90

In response to a Data-Call-In for thiabendazole, Merck & Co., Inc. has submitted an acute oral toxicity study and an acute dermal toxicity study. The Toxicity Category by both routes is III. The oral study is Acceptable, but the dermal study is Unacceptable since it lacked a signed Quality Assurance Statement.

15

Reviewed by: John E. Whalan JW 5-4-90
Section I, Tox. Branch I (H7509C)
Secondary reviewer: Edwin R. Budd R.B. 5-7-90
Section I, Tox. Branch I (H7509C)

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007934

DATA EVALUATION REPORT

STUDY TYPE: Acute Oral Toxicity in Rats

ACCESSION NUMBER: N/A

TOX. CHEM. NO.: 849A

TEST MATERIAL: Thiabendazole Veterinary for Preformed Suspensions (98.5% pure) Lot No. ERM-211

MRID NO.: 412582-01

SYNONYMS: 2-(4-Thiazolyl)benzimidazole
Mertect
TBZ

STUDY NUMBER(S): TT #81-2691

SUBMITTED BY: Merck & Co., Inc.

TESTING FACILITY: Merck Sharp & Dohme Research Laboratories

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

AUTHOR(S): George R. Lankas

REPORT ISSUED: April 6, 1981 (Revised September 21, 1989)

CONCLUSIONS: The calculated LD_{50} and confidence intervals were as follows:

Males	5070 (3982-6389) mg/kg
Females	4734 (3371-6541) mg/kg
Combined	Not calculated

Clnical signs included decreased activity, bradypnea, ptosis, loss of righting reflex, and decreased weight gain. Pinpoint dark foci on the gastric mucosa was found in some animals which died within the first 2 days.

STUDY CLASSIFICATION: This study is ACCEPTABLE. Toxicity Category III. This study was performed prior to the institution of the EPA GLP's, and thus did not receive Quality Assurance review. This study satisfies data requirement 81-1 for an acute oral toxicity study.

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PROTOCOL: Groups of 10 male and 10 female Crl:CD(SD) BR rats (6-7 weeks old; 117-190 g) were dosed with thiabendazole suspended in 1% aqueous methylcellulose (Methocel 50). The doses used were 2222, 3333, 5000, 7500, and 11250 mg/kg. The rats were dosed by gastric intubation with a metal catheter and syringe. Food and water were available ad libitum except during an 13-24 hour period (presumably prior to dosing). The rats were observed several times on the day of dosing, and daily for the remaining 14 day recovery period. Body weights were measured prior to dosing, and on days 7 and 12. They were weighed on day 12 rather than 14 because the rats were fasted on day 13 in preparation for necropsy on day 14.

2

RESULTS: The pattern of mortality and the results of probit analysis were as follows:

Dose (mg/kg)	Deaths Male	Deaths Female
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

LD_{50} (95% Confidence Limits)	
Males	5070 (3982-6389) mg/kg
Females	4734 (3371-6541) mg/kg
Combined	Not calculated

Most of the deaths occurred within the first 24 hours after dosing, and three deaths occurred on day 2. Clinical signs were similar in both sexes. Within 30 minutes of dosing, rats in all groups had decreased activity, bradypnea, and ptosis. Three hours after dosing, all groups had a loss of the righting reflex, which persisted for approximately 24 hours.

Body weight gain did not seem to be affected in the 2222 mg/kg group, but but the survivors in all other groups had dose-related depressed weight gain, especially during the first week. There were no compound-related gross pathologic lesions found other than pinpoint dark foci on the gastric mucosa in some of the animals which died within the first 2 days.

3

007934
81-2

Reviewed by: John E. Whalan JW 5-4-90
Section I, Tox. Branch I (H7509C)
Secondary reviewer: Edwin R. Budd R. B. 5-7-90
Section I, Tox. Branch I (H7509C)

DATA EVALUATION REPORT

STUDY TYPE: Acute Dermal Toxicity in Rabbits

ACCESSION NUMBER: N/A

TOX. CHEM. NO.: 849A

TEST MATERIAL: Thiabendazole (99.9% pure)
Off-white powder
Lot No. #DR M6 17

MRID NO.: 412582-02

SYNONYMS: 2-(4-Thiazolyl)benzimidazole
Mertect
TBZ

STUDY NUMBER(S): 4004-86

SUBMITTED BY: Merck & Co., Inc.

TESTING FACILITY: Bio/Dynamics, Inc.

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

AUTHOR(S): Donna L. Blaszcak

REPORT ISSUED: December 8, 1986 (Revised September 25 and 29, 1989)

CONCLUSIONS: There was no apparent indication of toxicity at the dose tested. The LD_{50} was >2000 mg/kg

STUDY CLASSIFICATION: This study is UNACCEPTABLE. Toxicity Category III. The study introduction states that the report was reviewed by the Quality Assurance Unit, but there was no signed Quality Assurance Statement. This study does not satisfy data requirement 81-2 for an acute dermal toxicity study.

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PROTOCOL: Five male (2.1-2.6 kg) and 5 female (2.2-2.5 kg) New Zealand White rabbits (>8 weeks old) were dosed with 2000 mg/kg of thiabendazole. The dosing sites were shaved and unabraded, and represented 10% of the body surface area. The dry test article was applied to 4" x 12" strips of 8-ply gauze, moistened with saline, then applied to the dosing sites. Impervious plastic sleeves, secured with tape, contained the gauze. All rabbits were fitted with Elizabethan collars to prevent test article ingestion. After 24 hours, the doses were removed and the dosing sites were wiped clean. Food and water were available ad libitum.

The rabbits were observed for clinical signs 1, 2, and 4 hours after dosing, and daily thereafter during the 14-day recovery period. Body weights were measured prior to dosing, and on days 7 and 14. All rabbits were sacrificed on day 14 and examined grossly.

4

RESULTS: No rabbits died, and there were no clinical signs observed. Body weight gain was suppressed slightly during the first week, but probably not to a significant degree. Gross lesions included lung discoloration in 2 males and 2 females, and reddened uterus in 1 female. These lesions were probably not compound-related.

5