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DATA EVALUATION REPORT

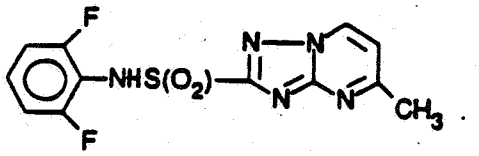
STUDY TYPE: Acute Oral Toxicity in Rats (Guideline 81-1)

EPA IDENTIFICATION NOS.:
MRID NO.: 419938-05
HED PROJECT NO.: 1-2384
CASWELL NO.: 889

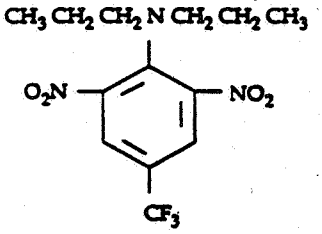
TEST MATERIAL: XRM-5313

SYNONYMS: Formulation containing: 2.6% XRD-498 [N-(2,6-difluorophenyl)-5-methyl(1,2,4)triazolo(1,5a) pyrimidine-2-sulfonamide] and 35.8% Trifluralin (Treflan; α,α,α-trifluoro-2,6-dinitro-N,N-dipropyl-p-toluidine)

XRD-498:



Trifluralin:



STUDY NUMBER: M-005313-002A

SPONSOR: DowElanco
9002 Purdue Road
Indianapolis, Indiana 44268-1189

TESTING FACILITY: The Toxicology Research Laboratory
Health and Environmental Sciences
The Dow Chemical Company
Midland, Michigan 48674

TITLE OF REPORT: XRM-5313: Acute Oral Toxicity Study in Fischer 344 Rats

AUTHORS: N.M. Berdasco
J.E. Battjes
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DATE REPORT ISSUED: May 31, 1991

CONCLUSION:

Toxicity Category: III (from 500 through 5000 mg/kg)

Median Lethal Dose:
LD_{50} (Males and Females) - Between 2000 and 5000 mg/kg of body weight

Core Classification: Guideline. The dose levels selected produced 100% mortality at 5000 mg/kg while no rats died at 500 or 2000 mg/kg. The LD_{50} value must therefore lie between 2000 and 5000 mg/kg, although extrapolation with acceptable limits of confidence is not feasible.

MATERIALS:

1. Test compound: Description: Orange liquid
   Sample reference: AGR 291670
   Source: DowElanco, Midland, Michigan
   Active ingredients: 2.6% XRD-498 and 35.8% Trifluralin

2. Test animals: Species: Rat
   Strain: Fischer 344
   Source: Charles River Breeding Laboratories, Inc. Kingston, New York
   Age: Approximately 11 weeks
   Weight: Males - 229-257 g; Females - 139-168 g

METHODS:

Rats were fasted the night before treatment. A single dose of the undiluted test material was administered by oral gavage to five males and five female rats each at the dose levels of 500, 2000, and 5000 mg/kg body weight. Animals were observed "frequently" on the day of treatment and at least once each workday for two weeks. Body weights were recorded on the day of treatment and on Days 2, 8, and 15 of study. A gross necropsy was performed on all animals.

RESULTS:

Mortality data and median lethal dose:

Numerical mortality data are presented in Table 1. All rats dosed at 5000 mg/kg died by Day 3 following treatment.

Table 1. Mortality (deaths/dosed)

Dose (mg/kg)	Males [number (%)]	Females [number (%)]
500	0 / 5 (0)	0 / 5 (0)
2000	0 / 5 (0)	0 / 5 (0)
5000	5 / 5 (100)	5 / 5 (100)

Note: Data were extracted from report No. M-005313-002A, page 13.

Based upon these mortality rates, the approximate LD_{50} value of 3162 mg/kg was established by the investigators for male and female rats by the

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Nonlinear Interpolation method (Stephan, 1977). The 95% confidence limits were not presented in the report.

Clinical signs of toxicity:

For male and female rats, decreased activity was noted at all dose levels. Facial and perineal (urine) soiling occurred at the 2000 mg/kg dose level. In all rats dosed at 5000 mg/kg, clinical observations in addition to decreased activity included palpebral closure, facial soiling, lacrimation, and/or shallow respiration.

Body weight data:

Mean body weight data are presented in Table 2. Body weights were depressed immediately after dosing (Day 1) for male and female rats at all dose levels. Rats that survived to study termination (500 and 200 mg/kg) began to regain body weight by Day 2 and demonstrated an overall body weight gain by Day 15. Continuing body weight depression was observed on Day 2 for all animals that were found dead prior to study termination (5000 mg/kg).

Table 2. Mean body weight data - grams

		Males					Females				
Dose (mg/kg)		Day -1	Day 1	Day 2	Day 8	Day 15	Day -1	Day 1	Day 2	Day 8	Day 14
500	Mean	243.9	224.0	234.8	258.2	272.5	159.3	145.0	152.6	163.5	167.8
	S.D.	7.5	10.2	8.1	6.9	10.3	7.3	6.7	7.4	8.7	8.6
	N	5	5	5	5	5	5	5	5	5	5
2000	Mean	240.8	219.9	208.0	239.9	265.5	157.7	144.4	137.8	155.8	166.9
	S.D.	7.8	7.1	15.7	5.6	3.4	8.6	7.6	6.1	8.6	8.5
	N	5	5	5	5	5	5	5	5	5	5
5000	Mean	247.7	223.3	212.3	c	c	159.8	145.4	134.6	c	c
	S.D.	10.6	13.5	10.8			11.8	10.3	10.0		
	N	4a	5	4b			5	5	4b		

a One body weight not recorded.
b Sample size decrease due to death of test animal.
c No data; all animals dead.
Note: Data were extracted from report No. M-005313-002A, pages 16-19.

Gross necropsy data:

In rats which died prior to study termination, congestion and edema of the lungs, slight lung hemorrhage, dark urine, and/or dark foci or hemolyzed blood in the stomach were noted. In addition, yellowish appearing fat and stomach contents were reported.

No internal macroscopic findings were reported in rats that survived to study termination.

STUDY DEVIATION:

The 95% confidence limits of the LD_{50} value were not presented in the report.

COMPLIANCE:

The following signed and dated statements were included:
- Statement of No Data Confidentiality
- GLP Compliance Statement
- Flagging Statement (negative)
- Quality Assurance Statement

DISCUSSION:

The dose levels selected did not produce a gradation of mortality incidence. At the 500 and 2000 mg/kg levels, there were no deaths, while at 5000 mg/kg all rats died within 3 days of treatment. Although the LD_{50} value clearly lies between 2000 and 5000 mg/kg, extrapolation (with a high degree of confidence) of a specific LD_{50} value would not be possible. The confidence limits of the LD_{50} value calculated by the investigators, 3162 mg/kg, were not presented, but would likely reflect the lack of accuracy in this reported value.

Based upon the criteria presented in 40 CFR Part 156.10, the Toxicity Category for acute effects following oral administration of the test material, XRM-5313, is III (from 500 through 5000 mg/kg), based upon mortality data indicating no deaths at 2000 mg/kg and 100% deaths at 5000 mg/kg.