

US EPA ARCHIVE DOCUMENT

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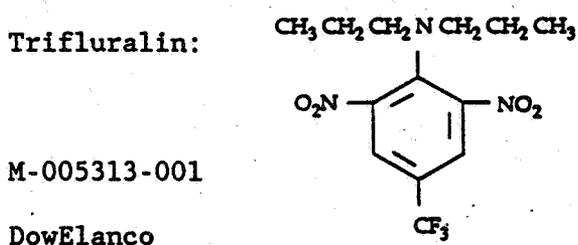
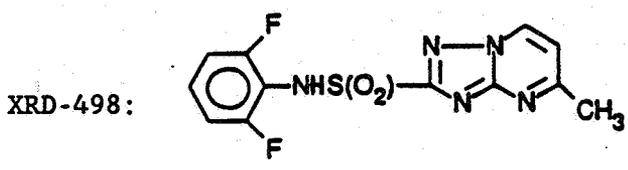
DATA EVALUATION REPORT

STUDY TYPE: Acute Inhalation Toxicity in Rats (Guideline 81-3)

EPA IDENTIFICATION NOS.: MRID NO.: 420033-02
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)



STUDY NUMBER: M-005313-001

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 Inhalation Toxicity Study with Fischer 344 Rats

AUTHORS: G.J. Bradley
J.E. Battjes
K.E. Stebbins

DATE REPORT ISSUED: May 22, 1991

CONCLUSION:

Toxicity Category: IV (greater than 5 mg/liter)

Median Lethal Concentration (4-hour):

LC₅₀ (Males and Females) - Greater than 5.92 mg/liter

Core Classification: Guideline

MATERIALS:

1. Test compound: Description: 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 10-12 weeks
Weight: Males - 206-234 g; Females - 150-158 g

METHODS:

The test material was aerosolized and administered by nose-only inhalation for a 4-hour interval to five male and five female rats at a time-weighted average concentration of 5.92 mg/liter.

A 42 liter chamber, measuring 30 cm diameter x 60 cm high, was used for the study. Compressed air was supplied to the chambers at an air flow of approximately 30 liters per minute, and the system temperature was maintained at 22°C. Measured amounts of test material were metered into a stainless steel spray nozzle, mixed with 30 liters/minute of dry compressed air while in the nozzle, and sprayed into the chamber. The test material was not recycled due to the fact that the mixture contained materials of varying vapor pressure.

During the exposure period, airflow through each chamber was determined with a calibrated manometer. Temperature, relative humidity, and air flow values were recorded every 30 minutes during the 4-hour exposure period.

Four times during the 4-hour exposure period, chamber air samples were drawn from a vertical stainless steel tube which projected into the animal breathing zone. Background samples were also taken before and 30-minutes after exposure with animals in the chamber. Aerosol particles were collected on teflon filters and vapors were collected on activated charcoal glass tubes. Exposure concentrations were calculated using a time-weighted average method. Nominal concentrations were also determined from the amount of test material used during the 4-hour exposure period.

Aerodynamic particle size distribution was determined twice during the exposure period by drawing samples from the animal breathing zone through a six-stage Cascade Impactor. The mass median aerodynamic diameter and geometric standard

deviation were determined for each sample as well as the average of the two samples.

The rats were examined prior to exposure, including "a penlight ophthalmic examination by a laboratory veterinarian." The animals were observed during the exposure period and daily until study termination. Body weights were recorded immediately prior to exposure and on Days 2, 4, 8, 11, and 15 of study. A gross necropsy, including examination of the eyes with a microscope slide using fluorescent illumination, was performed on all animals which were sacrificed on Day 15.

RESULTS:

Chamber analyses:

During the exposure, the chamber airflow remained constant at 30 liters/minute, the chamber temperature ranged from 20-21°C, and the relative humidity of the chamber averaged about 11%.

The time-weighted average concentration of the XRM-5313 aerosol was determined to be 5.92 mg/liter. The approximate nominal concentration was calculated to be 6.13 mg/liter, which was close to the analytical concentration; however the investigators reported that the nominal concentration value could not be accurately determined, "due to a small spill while measuring".

The mass median diameter was determined to be 4.17 μm with a geometric standard deviation of 2.62 μm . Since approximately 60% of the test material was collected in the charcoal tubes and was most likely an organic vapor, it was estimated by the study authors that the mass median diameter of approximately 64% of the total amount of test material was less than 1 μm . Pulmonary exposure to the test substance was probably adequate under these conditions.

Mortality data and median lethal concentration:

All animals survived the 4-hour exposure to the test substance as well as the 14-day postexposure period. Since the chamber concentration was determined experimentally, the LC₅₀ value is considered to be greater than 5.92 mg/liter.

Clinical signs of toxicity:

Following exposure to XRM-5313, many of the rats were noted to have soiled fur and reddish material around the nose. Some rats also had labored breathing or ptosis after exposure. These observations were no longer present by Day 9. Bilateral corneal opacity was also noted in one male rats, beginning with Days 7 and 8, and confirmed on Day 15.

Body weight data:

Mean body weight data are presented in Table 1. Although the rats showed an

initial postexposure weight loss, mean body weight values exceeded preexposure values by study termination.

Table 1. Mean body weight data - grams

Sex		Day 1	Day 2	Day 4	Day 8	Day 11	Day 15
Male	Mean	217.5	199.6	191.5	199.6	211.5	223.6
	S.D.	11.1	8.4	4.7	11.4	12.4	11.2
	N	5	5	5	5	5	5
Female	Mean	153.3	140.0	140.1	148.1	154.3	159.8
	S.D.	2.8	6.8	6.8	6.7	7.3	6.2
	N	5	5	5	5	5	5

Gross necropsy data:

With the exception of the bilateral corneal opacity noted in one male rat in-life and confirmed at necropsy, all rats appeared normal at gross pathological examination.

STUDY DEVIATIONS: None noted.

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 actual chamber concentration of the test substance, XRM-5313, was determined to be 5.92 mg/liter which exceeds the limit dose of 5 mg/liter recommended by EPA FIFRA Guideline 81-3. Further testing on additional animals is not considered to be necessary.

Based upon the criteria presented in 40 CFR Part 156.10, the Toxicity Category for acute effects following 4-hour inhalation exposure to the aerosolized test material, XRM-5313, is IV (greater than 5 mg/liter).