

TRADE SECRET

Study Title

H-22762: ORAL APPROXIMATE LETHAL DOSE (ALD) IN RATS

LABORATORY PROJECT ID: HL-1997-00867

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STUDY COMPLETED ON: December 5, 1997

PERFORMING LABORATORY: E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, P.O. Box 50
Newark, Delaware 19714-0050

WORK REQUEST NUMBER: [REDACTED]

Company Sanitized. Does not contain TSCA CBI

GENERAL INFORMATION

Substance Tested: [REDACTED]

Synonyms/Codes: • H-22762
[REDACTED]

Submitter's Notebook No [REDACTED]

Haskell Number: 22762

Purity: [REDACTED]

Known Impurities [REDACTED]

Physical Characteristics: Clear yellow liquid

Stability: The test substance appeared to be stable under the conditions of the study; no evidence of instability was observed.

Sponsor: E. I. du Pont de Nemours and Company
Wilmington, Delaware 19898
U.S.A.

Study Initiated/Completed: July 17, 1997 / (see report cover page)

In-Life Initiated/Completed: July 17, 1997 / August 20, 1997

All study records, raw data, and the final report are retained at Haskell Laboratory or at Iron Mountain, 200 Todds Lane, Wilmington, Delaware 19802 (formerly known as the E. I. du Pont de Nemours and Company Records Management Center).

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SUMMARY

H-22762 was administered as a single oral dose by intragastric intubation to male rats. Following dosing, the rats were weighed and observed for mortality and clinical signs of toxicity over a 14-day observation period.

Rats dosed at 5000, 7500, or 11,000 mg/kg were found dead 1 day after dosing. Clinical signs of toxicity and body weight losses were observed in lethally and non-lethally dosed animals.

Under the conditions of this study, the oral ALD for H-22762 was 5000 mg/kg of body weight. This substance is considered to be slightly toxic (ALD 500 - 5000 mg/kg) when administered as a single oral dose to male rats.

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SIGNATURE PAGE

Reviewed and Approved for Issue: Tracy A. Filliben 12/5/97
Tracy A. Filliben
Study Director

STUDY PERSONNEL

The following individuals were responsible for conduct of the study:

Manager: Nancy C. Chromey, Ph.D.
Study Director: Tracy A. Filliben,
Primary Technician: Tracy A. Filliben
Assisting Personnel: Carol Finlay, B.A.
M. Scott Karr, A.S.
Toxicology Report Preparation(s): John D. Oldham, Jr., B.S.

The following individual was responsible for assessing the health status of the animals on study:

Laboratory Veterinarian: Charles E. Cover, V.M.D.

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INTRODUCTION

The purpose of this test was to determine an approximate lethal dose (ALD) of H-22762 when administered as a single oral dose to male rats. The ALD was defined as the lowest dose administered which caused death either on the day of dosing or within 14 days post exposure.

MATERIALS AND METHODS

A. Animal Husbandry

Male Crl:CD[®](SD)BR rats, approximately 7-10 weeks old, were received from Charles River Laboratories. Rats were housed singly in suspended, stainless steel, wire-mesh cages. Each rat was assigned a unique identification number which was recorded on a card affixed to the cage. The rats were tail-marked, using a water-insoluble marker, with the last 3 digits of the animal number. Purina[®] Certified Rodent Chow[®] #5002 and water were available *ad libitum*.

Haskell Laboratory has an animal health monitoring program. This program is monitored and administered by the Laboratory Veterinarian. Water samples are periodically analyzed for total bacterial counts and for the presence of coliforms, lead, and other contaminants. Additionally, samples from freshly washed cages and cage racks are periodically analyzed to ensure adequate sanitation by the cagewashers. Data from this program are maintained separately from study records. Animal feed is certified by the manufacturer to meet specified nutritional requirements and to be free of a list of specified contaminants. On the basis of these analyses, there is no evidence suggesting that contaminants were present in the feed or water in amounts which may have interfered with the results of this study.

Rats were quarantined, weighed, and observed for general health for approximately one week. Animal rooms were maintained on a timer-controlled, 12-hour light/12-hour dark cycle. Environmental conditions of the rooms were targeted for a temperature of 23°C ± 1°C and relative humidity of 50% ± 10%. Excursions outside these ranges were of small magnitude and/or brief duration and did not adversely affect the validity of the study.

B. Protocol

The test substance administered neat to 1 rat per dose rate by intragastric intubation. The doses were calculated based on the test substance density of 1600 mg/mL and body weights collected on the day of dosing. Dose rates administered ranged from 2300 to 11,000 mg/kg of body weight in increments of approximately 50%. Additionally, 1 rat was dosed at 670 mg/kg. The dosing day was test day 1; postexposure day 14 was test day 15. Following administration of the test substance, rats were observed for clinical signs of toxicity.

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The rats were weighed and observed at least 3 times a week throughout the 14-day observation period. Observations for mortality and signs of illness, injury, or abnormal behavior were made daily throughout the study. Pathological examinations of test animals were not performed.

RESULTS

A. Dosage and Mortality Data

The dosage regimen and the mortality resulting over the 15-day test period are detailed below. The lowest dose of H-22762 which resulted in the death of a test animal was 5000 mg/kg. Rats dosed at 5000, 7500, or 11,000 mg/kg were found dead 1 day after dosing.

Dosage (mg/kg)	Dose Volume (mL)	Suspension Density (mg/mL)	Initial Body Weight (g)	Mortality
670	0.11	1600	257	No
2300	0.35	1600	246	No
3400	0.61	1600	285	No
5000	0.78	1600	249	Yes
7500	1.3	1600	279	Yes
11,000	2.0	1600	297	Yes

B. Clinical Signs and Body Weights

1. Nonlethal Doses

No clinical signs of toxicity were observed in the rat dosed at 670 mg/kg. Wet, yellow-stained perinium was observed in the rats dosed at 2300 and 3400 mg/kg within the first 2 days after treatment. The rat treated at 3400 mg/kg exhibited a weight loss of approximately 6% of initial body weight by 2 days after dosing.

2. Lethal Doses

The rat treated at 7500 mg/kg exhibited a weight loss of approximately 12% of initial body weight, tremors, spasms, wet underbody, and splayed hindlegs 1 day after dosing. This rat was found dead the same day. The rats treated at 5,000 and 11,000 mg/kg were found dead 1 day after dosing; no clinical signs of toxicity or weight losses were noted.

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CONCLUSION

Under the conditions of this study, the oral ALD for H-22762 was 5000 mg/kg of body weight. This substance is considered to be slightly toxic (ALD 500 - 5000 mg/kg) when administered as a single oral dose to male rats.

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