

TRADE SECRET

Study Title

H-24256: Oral Approximate Lethal Dose (ALD) in Rats

Laboratory Project ID: DuPont-3628

AUTHOR: Carol Finlay, B.A.

STUDY COMPLETED ON: December 14, 1999

PERFORMING LABORATORY: E. I. du Pont de Nemours and Company
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WORK REQUEST NUMBER: [REDACTED]

SERVICE CODE NUMBER: [REDACTED]

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CERTIFICATION

We, the undersigned, declare that this report provides an accurate evaluation of the data obtained from this study.

Reviewed by:

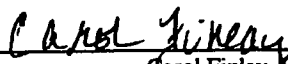


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14-Dec-1999

Date

Issued by Study Director:



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14-Dec-1999

Date

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STUDY INFORMATION

9th Collective Nomenclature: [REDACTED]Synonyms/Codes: [REDACTED]H-24256
[REDACTED]Haskell Number: 24256MSDS Reference Number: [REDACTED]CAS Registry Number: [REDACTED]Submitter's Notebook Number(s): [REDACTED]Composition: [REDACTED]Purity: [REDACTED]Known Impurities: [REDACTED]Physical Characteristics: [REDACTED]

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: October 19, 1999 / (see report cover page)

In-Life Initiated/Completed: October 20, 1999/ November 10, 1999

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SUMMARY

H-24256 was administered as a single oral dose by intragastric intubation to male rats at doses of 670, 2300, 3400, 5000, 7500, and 11,000 mg/kg. Following dosing, the rats were weighed and observed for mortality and clinical signs of toxicity over a 14- or 17-day period.

No deaths occurred. No clinical signs of toxicity or body weight losses were observed during the study.

Under the conditions of this study, the oral ALD for H-24256 was greater than 11,000 mg/kg of body weight. This substance is considered to be very low in toxicity (ALD greater than 5000 mg/kg) when administered as a single oral dose to male rats.

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INTRODUCTION

The purpose of this test was to determine an approximate lethal dose (ALD) of H-24256 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. Test Substance

The test substance, , was supplied by the sponsor as an [REDACTED] The test substance appeared to be stable under the conditions of the study. No evidence of instability, such as a change in color or physical state, was observed.

B. Animal Husbandry

Male CrI:CD[®](SD)IGS BR rats were received from Charles River Laboratories, Inc., Raleigh, North Carolina. 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. PMI Nutrition International, Inc. Certified Rodent LabDiet[®] 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 6 days. 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 $23 \pm 1^{\circ}\text{C}$ and relative humidity of $50 \pm 10\%$. Excursions outside these ranges were of small magnitude and/or brief duration and did not adversely affect the validity of the study.

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C. Protocol

The test substance was administered neat to 1 rat per dose rate by intragastric intubation. The volumes administered were calculated based on the test substance density of [REDACTED] mg/mL and body weights collected on the day of dosing. Doses 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.

The rats were weighed and observed 2 or 3 times a week throughout the 14-day (rats dosed at 3400, 5000, 7500, or 11,000 mg/kg) or 17-day (rats dosed at 670 or 2300 mg/kg) 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 AND DISCUSSION

A. Dosing and Mortality Data

The dose regimen and the mortality resulting over the 14- or 17-day observation period are detailed below. No deaths occurred during the study.

Dose (mg/kg)	Volume (mL)	Density (mg/mL)	Initial Body Weight (g)	Mortality
670	0.17	[REDACTED]	280	No
2300	0.59	[REDACTED]	279	No
3400	0.73	[REDACTED]	233	No
5000	1.3	[REDACTED]	279	No
7500	1.9	[REDACTED]	275	No
11,000	2.7	[REDACTED]	264	No

B. Clinical Signs and Body Weights

No clinical signs of toxicity or body weight losses were observed during the study.

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CONCLUSIONS

Under the conditions of this study, the oral ALD for was greater than 11,000 mg/kg of body weight. This substance is considered to be very low in toxicity (ALD greater than 5000 mg/kg) when administered as a single oral dose to male rats.

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