AR226_3255

TRADE SECRET

Study Title

H-25357: Oral Approximate Lethal Dose (ALD) in Rats

Laboratory Project ID: DuPont-11269

AUTHOR: Carol Finlay, B.A.

STUDY COMPLETED ON: August 9, 2002

PERFORMING LABORATORY: E.I. du Pont de Nemours and Company
Haskell Laboratory for Health and Environmental Sciences
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[redacted]

CERTIFICATION

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

Reviewed by: James C. Mackay II — 8-Aug-2002
James C. Mackay II
Associate Scientist
Date

Issued by Study Director: Carol Finlay — 9-Aug-2002
Carol Finlay, B.A.
Staff Toxicologist
Date

STUDY INFORMATION

Substance Tested: [redacted]

Synonyms/Codes: • H-25357
[redacted]

Submitter's Notebook Number(s): [redacted]

Haskell Number: 25357

CAS Registry Number: [redacted]

Composition: [redacted]

Purity: [redacted]

Known Impurities: [redacted]

Physical Characteristics: Amber liquid

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

Study Initiated/Completed: June 14, 2002 / (see report cover page)

In-Life Initiated/Completed: July 3, 2002 / July 22, 2002

STUDY PERSONNEL

Study Director:	Carol Finlay, B.A.
Management:	Scott E. Loveless, Ph.D.
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Toxicology Report Preparation:	Sean M. Callaghan, B.A.
Management:	Nancy S. Selzer, M.S.
Laboratory Veterinarian:	William Singleton, D.V.M., A.C.L.A.M.

SUMMARY

H-25357 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-day observation period.

No deaths occurred. No clinical signs were observed, and no biologically important body weight loss occurred during the study.

Under the conditions of this study, the oral ALD for H-25357 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.

INTRODUCTION

The purpose of this test was to determine an approximate lethal dose (ALD) of H-25357 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, H-25357, was supplied by the sponsor as an amber liquid. 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 Crl:CD®(SD)IGS BR rats were received from Charles River Laboratories, Inc., Raleigh, North Carolina. Rats were housed singly in stainless steel, wire-mesh cages suspended above cage boards. 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, LLC Certified Rodent LabDiet® 5002 and water were available *ad libitum*.

As specified in the Haskell Laboratory animal health and environmental monitoring program, the following procedures are performed periodically to ensure that contaminant levels are below those that would be expected to impact the scientific integrity of the study:

- Water samples are analyzed for total bacterial counts, and the presence of coliforms, lead, and other contaminants.
- Feed samples are analyzed for total bacterial, spore, and fungal counts.
- Samples from freshly washed cages and cage racks are analyzed to ensure adequate sanitation by the cagewashers.

Certified animal feed is used, guaranteed by the manufacturer to meet specified nutritional requirements and not to exceed stated maximum concentrations of key contaminants, including specified heavy metals, aflatoxin, chlorinated hydrocarbons, and organophosphates. The presence of these contaminants below the maximum concentration stated by the manufacturer would not be expected to impact the integrity of the study.

The animal health and environmental monitoring program is administered by the attending laboratory animal veterinarian. Evaluation of these data did not indicate any conditions that affected the validity of the study.

Rats were weighed and observed for general health during the 6-day quarantine period. 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 ± 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.

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 1090 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 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. Pathology examinations of test animals were not performed.

RESULTS AND DISCUSSION

A. Dosing and Mortality Data

No deaths occurred during the study. The dose regimen and the mortality resulting over the 15-day test period are detailed below.

Dose (mg/kg)	Volume (mL)	Density (mg/mL)	Initial Body Weight (g)	Mortality
670	0.14	1090	225.2	No
2300	0.46	1090	215.8	No
3400	0.90	1090	287.8	No
5000	1.2	1090	266.9	No
7500	1.8	1090	266.7	No
11,000	2.8	1090	281.7	No

B. Clinical Signs and Body Weights

No clinical signs were observed, and no biologically important body weight loss occurred during the study.

CONCLUSIONS

Under the conditions of this study, the oral ALD for H-25357 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.

RECORDS AND SAMPLE STORAGE

Specimens (if applicable), raw data, and the final report will be retained at Haskell Laboratory, Newark, Delaware, or at Iron Mountain Records Management, Wilmington, Delaware.