

TRADE SECRET

Study Title

H-23004: ORAL APPROXIMATE LETHAL DOSE (ALD) IN RATS

LABORATORY PROJECT ID: HL-1997-01291

AUTHOR: Tracy A. Filliben

STUDY COMPLETED ON: December 30, 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]

CERTIFICATION

Study Director:

Issued by: Tracy A. Filliben
Tracy A. Filliben
Toxicology Associate

12/30/97
Date

STUDY INFORMATION

Substance Tested: [REDACTED]

Synonyms/Codes: • H-23004

Haskell Number: 23004

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

Composition: [REDACTED]

Known Impurities: [REDACTED]

Physical Characteristics: Off-white 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: November 25, 1997 / (see report cover page)

In-Life Initiated/Completed: November 25, 1997 / December 19, 1997

STUDY PERSONNEL

Manager: Judith C. Stadler, Ph.D.

Study Director: Tracy A. Filliben

Primary Technician: Tracy A. Filliben

Toxicology Report Preparation(s): Maryanne M. Wilford, B.A.

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

SUMMARY

H-23004 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.

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

Under the conditions of this study, the ALD for H-23004 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-23004 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 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 was administered neat to 1 rat per dose rate by intragastric intubation. The doses were calculated based on the test substance density of 1000 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.

The rats were weighed and observed at least 2 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 AND DISCUSSION

A. Dosage and Mortality Data

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

Dosage (mg/kg)	Dose Volume (mL)	Density (mg/mL)	Initial Body Weight (g)	Mortality
670	0.17	1000	255	No
2300	0.60	1000	259	No
3400	0.92	1000	272	No
5000	1.3	1000	266	No
7500	1.9	1000	258	No
11,000	3.0	1000	275	No

B. Clinical Signs and Body Weights

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

CONCLUSIONS

Under the conditions of this study, the ALD for H-23004 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 RETENTION

All study records, raw data, and the final report are retained at Haskell Laboratory, Newark, Delaware, 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).