Study Title

Approximate Lethal Dose (ALD) of H-21951 in Rats

Laboratory Project ID

Haskell Laboratory Report No. 796-96

Author

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Study Completed On

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Performing Laboratory

E. I. du Pont de Nemours and Company
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[redacted]

GENERAL INFORMATION

Substance Tested: [redacted]

Synonyms/Codes:
- H-21951

[redacted]

Physical Form: [redacted]

Composition: [redacted]

Contaminants: [redacted]

Purity: [redacted]

Submitter's Notebook No.: [redacted]

CAS Registry No.: [redacted]

Sponsor: DuPont Specialty Chemicals
E. I. du Pont de Nemours and Company
Wilmington, Delaware

Study Initiated - Completed: 6/21/96 - 8/30/96

In Life Phase
Initiated - Completed: 6/22/96 - 7/8/96

Company Sanitized. Does not contain TSCA CBI

General Information (Continued)

All raw data and the final report will be stored in the archives of Haskell Laboratory for Toxicology and Industrial Medicine, E. I. du Pont de Nemours and Company, Newark, Delaware or at Iron Mountain (formerly DuPont Records Management Center, Wilmington, Delaware).

SUMMARY

H-21951 was administered as a single oral dose by intragastric intubation to male rats. No deaths occurred during the study. Clinical signs of toxicity were observed in non-lethally dosed animals. Under the conditions of this test, the ALD was greater than 11,000 mg/kg of body weight. This substance is considered to be very low in toxicity (ALD greater than 5000mg/kg) when administered as a single oral dose to male rats.

SIGNATURE PAGE

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INTRODUCTION

The purpose of this test was to determine an approximate lethal dose of H-21951 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 weeks old, were received from Charles River Laboratories, 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. 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 assure 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 density of the test substance was [redacted] In the absence of visible evidence to the contrary, the test substance was assumed to be stable under the conditions of administration. 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 daily until signs of toxicity subsided, and then 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. No deaths occurred during the study.

Dosage (mg/kg)	Dose Volume (mL)	Density (mg/mL)	Initial Body Weight (g)	Mortality
670	0.18	[redacted]	271	No
2300	0.63		284	No
3400	0.84		253	No
5000	1.2		244	No
7500	1.7		237	No
11,000	2.6		247	No

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B. Clinical Signs

Nonlethal Doses

Ruffled fur was observed in the rat treated at 5000 mg/kg 2 days after dosing. The rat treated at 11,000 mg/kg exhibited lethargy and low posture and carriage 1 day after dosing; no weight loss was observed. A weight loss of approximately 7% of initial body weight was observed in the rat treated at 7500 mg/kg 1 day after dosing. No clinical signs of toxicity or significant weight losses were observed in rats treated at 670, 2300, or 3400 mg/kg.

CONCLUSION

Under the conditions of this study, the ALD for H-21951 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.