

PDCN: 88950000112

DuPont Central Research and Development  
Haskell Laboratory for Toxicology and Industrial Medicine  
P.O. Box 50, Elkton Road  
Newark, DE 19714-0050  
Fax: (302) 366-5207



DuPont Central Research and Development

APR 21 AM 8:59

8EHQ-0595-13323

April 17, 1995

(B)

RECEIVED  
APR 17 1995

T. R. O'Bryan  
Risk Analysis Branch  
Office of Pollution Prevention and Toxics  
U.S. Environmental Protection Agency  
401 M Street SW  
Washington, DC 20460

Dear Mr. O'Bryan:

**Re: 8EHQ-95-13323**

As requested in your letter of April 10, 1995, enclosed are copies (one CBI and one Public) of the report on the study which was the subject of our letter of February 8, 1995.

The copy labeled CBI has the synonyms/codes, contaminants and business unit (sponsor) deleted.

Please let us know if you have any further questions.

Sincerely,

*Charles F. Reinhardt*

Charles F. Reinhardt, M.D.  
Director

CFR:dj  
(302) 366-5285

8EHQ-95-13323

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5/22/95

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Study Title

Approximate Lethal Dose (ALD) of H-20924 in Rats

Laboratory Project ID

Haskell Laboratory Report No. 36-95

COMPANY SANITIZED

Author

Tracy A. Filliben

Study Completed On

January 30, 1995

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

GENERAL INFORMATION

Substance Tested: 2-Pyrimidinamine, 4,6-dimethyl-

Synonyms/Codes: ● H-20924

Physical State: White solid

Composition: Not supplied by the sponsor

Contaminants:

Purity: 98.15%

Submitter's Notebook No.: None submitted

CAS Registry No.: 767-15-7

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

Study Initiated - Completed: 12/12/94 - 1/30/95

In Life Phase  
Initiated - Completed: 12/15/94 - 1/3/95

Approximate Lethal Dose (ALD) of

H-20924 in Rats

SUMMARY

H-20924 was administered as a single oral dose by intragastric intubation to male rats. Rats were found dead on the day after dosing. Clinical signs of toxicity were observed in lethally and nonlethally dosed animals. Under the conditions of this test, the ALD was 2300 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.

Work by: Tracy A. Filliben  
Tracy A. Filliben  
Toxicology Technician

Reviewed by: Carol Finlay  
Carol Finlay  
Toxicology Associate

Reviewed and Approved for Issue: Tracy A. Filliben 11/30/95  
Tracy A. Filliben  
Study Director

TF/alw

## INTRODUCTION

The purpose of this test was to determine an approximate lethal dose of H-20924 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®BR rats, approximately 7 weeks old, were received from Charles River Breeding 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 prior to testing. 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  $23^{\circ}\text{C} \pm 2^{\circ}\text{C}$  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.

### B. Protocol

The test substance was ground into a powder with a mortar and pestle, suspended in Mazola® corn oil, and administered to 1 rat per dose rate by intragastric intubation. 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 130 to 3400 mg/kg of body weight in increments of approximately 50%. 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. Surviving rats were weighed and observed daily until signs of toxicity subsided, and then at least 3 times per week throughout the 14- or 15-day observation period. Rats dosed at 130, 200, 300, and 450 mg/kg were inadvertently not weighed the day after dosing but were observed for mortality. This deviation did not affect the validity of the study. Observations for mortality were made daily throughout the study. Pathological examinations of test animals were not performed.

### C. Records Retention

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 in the DuPont Records Management Center, Wilmington, Delaware.

## RESULTS

### A. Dosage and Mortality Data

The dosage regimen and the mortality resulting over the 15- or 16-day test period are detailed below. The lowest dose of H-20924 which resulted in the death of a test animal was 2300 mg/kg. Rats were found dead on the day after dosing.

<u>Dosage</u> <u>(mg/kg)</u>	<u>Dose</u> <u>Volume</u> <u>(mL)</u>	<u>Suspension</u> <u>Concentration</u> <u>(mg/mL)</u>	<u>Initial Body</u> <u>Weight (g)</u>	<u>Mortality</u>
130	0.35	100	267	No
200	0.54	100	270	No
300	0.80	100	266	No
450	1.2	100	262	No
670	1.1	150	252	No
1000	1.2	200	232	No
1500	1.8	200	239	No
2300	3.9	150	253	Yes
3400	3.9	200	232	Yes

## B. Clinical Signs

### Nonlethal Doses

Incoordination, low posture, and low carriage were observed 1 hour after dosing in the rat dosed at 670 mg/kg. The rat treated at 1000 mg/kg exhibited lethargy, low posture, and low carriage, and the rat treated at 1500 mg/kg was prostrate by 1 hour after dosing. No other clinical signs of toxicity were observed in rats treated at 670, 1000, and 1500 mg/kg. No clinical signs of toxicity were observed in rats treated at 130, 200, 300, and 450 mg/kg.

### Lethal Doses

Rats treated at 2300 and 3400 mg/kg were prostrate by 1 hour after dosing and were found dead 1 day after dosing.

## CONCLUSION

Under the conditions of this study, the ALD for H-20924 was 2300 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.