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October 5, 2006

*MR # 299227*

**VIA FEDERAL EXPRESS**

TSCA Document Processing Center (7407M)  
EPA East – Room 6428  
Attn: FYI  
U.S. Environmental Protection Agency  
1201 Constitution Avenue, NW  
Washington, D.C. 20004-3302  
Phone: 202-564-8940

***PUBLIC COPY  
COMPANY SANITIZED  
NO CBI***

**Re: Submission No. 2-070  
Test substance [ ]**

**Company Sanitized**

Dear FYI Coordinator:

Please find enclosed a recently reviewed acute inhalation study report on the above-identified test substance. As based upon the EPA 1991 TSCA 8(e) Reporting Guide, results from this study fall within the moderate toxicity range (no deaths occurred; the LC50 would be greater than 6.2 mg/L). This report is being provided to EPA on an FYI basis.

Confidential Business Information (CBI) has been removed from this submission. The CBI version of this submission is being provided to EPA simultaneously with this public version.

For your convenience, also enclosed is a CD containing the public (no CBI) version of this submission (transmittal letter and report). Please contact me directly if you have any questions or require further clarification.

Very truly yours,

Andrea V. Malinowski



**Enclosures**

- Public copy of report for Submission No. 2-070 [HLR 226-92] (9 pages)
- CD labeled Submission No. 2-070 (FYI) – Public version



2-070

TRADE SECRET

Study Title

Inhalation Approximate Lethal Concentration (ALC)  
of \_\_\_\_\_ in Rats

*Company Sanitized. Does not contain TSCA CBI*

Author

Arthur J. O'Neill

Study Completed On

July 21, 1992

Performing Laboratory

B. I. du Pont de Nemours and Company  
Haskell Laboratory for Toxicology and Industrial Medicine  
Elkton Road, P. O. Box 50  
Newark, Delaware 19714

Medical Research No.

4581-910

*Company Sanitized. Does not contain TSCA CBI*

Laboratory Project ID:

Haskell Laboratory Report No. 226-92

Du Pont HLR 226-92

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted according to EPA TSCA Good Laboratory Practice Standards (40 CFR 792) and EPA FIFRA Good Laboratory Practice Standards (40 CFR 160). Any areas of noncompliance are documented in the study records. No deviations existed that affected the validity of the study.

Submitter: E. I. du Pont de Nemours and Company

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

Study Director:

 7/21/92  
Arthur J. O'Neill, B.A.  
Technician  
Acute and Inhalation Toxicology

GENERAL INFORMATION

Material Tested:

Synonyms/Codes:

Submitter's Notebook No.: N.B. AG0170-182

Purity: 98.8% by analysis

Composition: 98.8% by analysis

CAS Registry No.:

Sponsor: Du Pont Agricultural Products  
E. I. du Pont de Nemours and Co.  
Wilmington, Delaware 19898

Study Initiated - Completed: 02/17/92 - 07/21/92

In-Life Phase  
Initiated - Completed: 02/19/92 - 03/04/92

Inhalation Approximate Lethal Concentration (ALC)

of [ ] in Rats

SUMMARY

One group of 6 male Crl:CD®BR rats was exposed for a single 4-hour period to 6.2 mg/L [ ] in air. The test material was generated as a dust and the atmospheric concentration was determined by gravimetric analysis. After exposure, rats were weighed and observed for clinical signs of toxicity during a 14-day recovery period.

At a concentration of 6.2 mg/L no rats died. The mass median aerodynamic diameter (MMAD) of the dust generated during the exposure was 2.9 µm. Clinical signs observed during the study included stained facial fur, stained perinea, and ocular discharges. Immediately following the exposure, rats exhibited compound-coated fur, closed eyes, and lethargy. No adverse clinical signs were observed in any of the rats after the 2nd day of recovery. All rats had moderate to severe weight loss on the first day post exposure. For the remainder of the recovery period, rats exhibited normal weight-gain patterns.

Under the conditions of this study, the ALC for [ ] was greater than 6.2 mg/L. [ ] is considered to have a very low toxicity on an acute inhalation basis (ALC greater than 2.0 mg/L).

Reviewed by:

*Judith C. Stadler*  
Judith C. Stadler, Ph.D., D.A.B.T.  
Senior Research Toxicologist  
Acute and Inhalation Toxicology

Reviewed and  
Approved for Issue:

*A. J. O'Neill* 7/21/92  
Arthur J. O'Neill, B.A.  
Study Director

QUALITY ASSURANCE DOCUMENTATION

(H-19021)

Dates of Inspection:

Conduct - 2/19/92

Records, Report(s) - 6/25-26/92

Findings reported to:

Study Director - 6/26/92

Management - 7/10/92

Reported by: Donna R. Nott for DAVick 7/15/92  
Deborah A. Vick Date  
Quality Assurance Auditor

## INTRODUCTION

The purpose of this study was to determine an inhalation approximate lethal concentration (ALC) of \_\_\_\_\_ in male rats. The ALC is defined as the lowest atmospheric concentration tested which causes the death of 1 or more exposed rats either on the day of exposure or within at least 14 days post exposure.

## MATERIALS AND METHODS

### A. Test Substance

The test substance, \_\_\_\_\_ was supplied by the sponsor as a yellow powder with a purity of 98.8%. Prior to arrival, the test substance was air milled to a particle size of approximately 5 microns. The test substance was assumed to be stable under the conditions of this study.

### B. Animals

Young adult male Crl:CD®BR rats were obtained from Charles River Breeding Laboratories, Kingston, New York. The rats were approximately 46 days of age on arrival.

Rats have historically been used in safety evaluation studies for acute inhalation toxicity testing. The Crl:CD®BR rat has been chosen based on consistently acceptable health status and the extensive experience with the strain at this laboratory.

### C. Animal Husbandry

Quarantine and Animal Selection. Rats were quarantined after arrival for 6 days prior to testing. They were housed individually in 5" x 11" x 7" suspended, stainless steel, wire-mesh cages. Rats were weighed and observed 3 times during the quarantine period. Rats used on this study were obtained from the general population of stock rats released from quarantine.

Housing. Rats were housed in pairs during the test period in 8" x 14" x 8" suspended, stainless steel, wire-mesh cages.

Animal Room Environment. The animal rooms were maintained on a timer-controlled, 12-hour light/12-hour dark cycle. Environmental conditions of the rooms were within temperatures of  $23 \pm 2^{\circ}\text{C}$  and a relative humidity of  $50 \pm 10\%$ .

**Identification.** Each rat was assigned a unique 6-digit identification number which corresponded to a numbered card affixed to the cage. The rat assigned the lower number in each cage was identified by a slash in the right ear. Prior to exposure, tails of the rats and cage cards were color-coded with water-insoluble markers so that individual rats could be identified.

**Feed and Water.** Except during exposure, Purina Certified Rodent Chow® #5002 and tap water from the Wilmington Suburban Water Corporation were available ad libitum.

**D. Study Design**

One group of 6 male rats was exposed nose-only for a 4-hour period to an atmosphere of [ ] in air. Rats were approximately 54 days of age at the time of exposure and ranged in weight from 250 to 273 grams.

Rats could not be observed for mortality and clinical signs of toxicity during the exposure due to the dense chamber atmosphere and/or the test material covering the inside surfaces of the chamber, however, mortality and clinical signs of toxicity were observed immediately following exposure. During a 14-day, post-exposure period, rats were observed each day for mortality and were weighed and observed for clinical signs of toxicity daily, weekends excluded.

**E. Inhalation Exposure Conditions**

During the exposure, rats were individually restrained in perforated, stainless steel cylinders with conical nose pieces. The restrainers were inserted into the face plate of a 29-L, cylindrical, glass exposure chamber so that only the nose of each rat extended into the chamber.

Chamber airflow was set at the beginning of the exposure and adjusted as needed throughout the 4-hour period. Chamber temperature was targeted at  $23 \pm 2^\circ\text{C}$ . Temperature was measured continually with an Omega Model HH-51 Type K Thermocouple Thermometer and recorded 3 times during the exposure. Relative humidity was targeted at  $50 \pm 10\%$ . Humidity in the exposure chamber was measured twice during the exposure with a Reuter/Stokes Model RSS-230 Digital Psychrometer. Chamber oxygen concentration was targeted to at least 19% and was measured with a Biosystems Model 3100R Oxygen Analyzer twice during the exposure.

**F. Atmosphere Generation**

Test atmospheres of [ ] were generated by suspension of the test material in a stream of filtered air. The solid test material was metered into a Fluid Energy Model 00 Jet-O-Mizer jetmill using a K-Tron Model T-20 twin screw volumetric feeder controlled with a K-Tron Model K10S digital speed controller. A baffle positioned immediately inside the exposure chamber was

used to promote uniform chamber distribution of test material. Chamber concentrations were controlled by varying the feed rates at which the test material flowed into the jetmill.

Test atmospheres were exhausted through a high-capacity dust filter and an MSA charcoal/HEPA cartridge filter prior to discharge into the fume hood.

#### G. Characterization of Chamber Atmosphere

The atmospheric concentration of [ ] was determined at approximately 15-minute intervals by gravimetric analysis. Fifteen-minute intervals were chosen to ensure that any clogs in the generation system could be quickly detected and corrected. One-liter samples of chamber atmospheres were drawn from the breathing zone of the rats through a 25 mm filter cassette that contained preweighed Gelman glass fiber (Type A/E) filters. The filters were weighed on a Cahn Model 26 Microbalance. The atmospheric concentration of [ ] was calculated from the difference in the pre- and post-sampling filter weights.

A single sample to determine the particle size distribution (mass median aerodynamic diameter and percent particles less than 1, 3, and 10  $\mu\text{m}$  diameter) was taken with a Sierra® Series 210 cyclone preseperator/cascade impactor and Sierra® Series 110 Constant Flow Air Sampler<sup>1</sup>.

#### H. Records Retention

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

### RESULTS

#### A. Exposure Conditions

One 4-hour exposure was conducted with 6 male rats exposed to a chamber atmosphere of  $6.2 \pm 1.1$  mg/L [ ] in air. The chamber atmosphere ranged from 4.4 to 7.5 mg/L. A total of 16 samples were taken during the exposure.

A single particle size sample was taken during the exposure and resulted in a mass median aerodynamic diameter of  $2.9 \pm 1.8$   $\mu\text{m}$ . The percent of particles by mass less than 10, 3, and 1  $\mu\text{m}$  was determined to be 98%, 52%, and 3.8%, respectively.

During the exposure, the chamber airflow ranged from 24 to 30 L/min, chamber temperature ranged from 22 to 23°C, chamber relative humidity ranged from 57 to 67%, and chamber oxygen remained constant at 21%. Although chamber relative humidity was out of the targeted range during one of the readings, this is not considered to have affected the results of this study.

#### B. Mortality, Clinical Signs, and Body Weights

There were no deaths among the 6 rats exposed to 6.2 mg/L. Upon removal of the rats from restrainers, compound coated fur, closed eyes, and lethargy were observed. During the first 2 days of the recovery period the clinical observations in rats included stained facial fur, stained perinea, and ocular discharges. Rats had no abnormal clinical observations noted from the 3rd to 14th day post-exposure.

Moderate to severe body-weight losses (6.1-13%) occurred in all rats on the day following exposure. These initial weight losses were followed by a normal weight gain throughout the remainder of the post-exposure period.

#### CONCLUSION

Under the conditions of this test, the ALC for is greater than 6.2 mg/L. On an acute inhalation basis, is considered to have very low toxicity (ALC greater than 2.0 mg/L) by the inhalation route.

#### REFERENCES

1. Calculation described in Sierra Instruments, Inc., Bulletin 7-79-219IM, Instruction Manual: Series 210 Ambient Cascade Impactors and Cyclone Preseparators.