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Du Pont HLR 466-89

Study Title

Inhalation Approximate Lethal Concentration (ALC) of [redacted]

Author

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Study Completed On

September 6, 1989

Performing Laboratory

E. I. du Pont de Nemours and Company, Inc.
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, P. O. Box 50
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[redacted]

Laboratory Project ID

Haskell Laboratory Report No. 466-89

GENERAL INFORMATION

Material Tested:	[redacted]
Medical Research No.:	[redacted]
Haskell No.:	17,869
Physical Form:	White aqueous dispersion
Other Code:	[redacted]
Synonyms:	[redacted]
Purity:	[redacted]
Composition:	[redacted]
Stability:	The test material was assumed to be stable throughout the exposure phase of the study.
Sponsor:	Chemicals and Pigments Department E. I. du Pont de Nemours and Company, Inc. Wilmington, Delaware
Material Submitted By:	[redacted] Chemicals and Pigments Department E. I. du Pont de Nemours and Company, Inc. Jackson Laboratory Deepwater, New Jersey

GENERAL INFORMATION (Cont'd)

In-Life Phase
Initiated - Completed: 7/13/89 - 8/1/89

Notebook: [redacted]

There are 9 pages in this report.

Distribution: [redacted]

Inhalation Approximate Lethal Concentration (ALC) of [redacted]

SUMMARY

Groups of 6 male Crl:CD®BR rats were exposed for a single, 4-hour period to aerosols of [redacted] in air. Test atmospheres were generated by atomization of the liquid test material in a high pressure air stream. Atmospheric concentrations of [redacted] were determined by gravimetric analysis. After exposure, rats were observed for clinical signs of toxicity during a 14-day recovery period.

Deaths occurred following exposure to [redacted] at atmospheric concentrations of 590 mg/m^3 or greater; all deaths were post exposure and occurred within 24 hours of exposure. Clinical signs observed immediately after exposure included red nasal and ocular discharges, lethargy, and compound-covered faces. During the 14-day recovery period, rats exhibited lethargy, hunched posture, labored breathing, red nasal discharge and wet, yellow stained perineum; these clinical signs had resolved by day 3 post exposure. Although slight to severe weight losses were noted in surviving rats 1 day after exposure, these rats began to regain body weight by day 3 post exposure.

Under the conditions of this study, [redacted] is considered to be moderately toxic on an acute inhalation basis.

Work by: Clarence W. Hutt
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Reviewed and Approved for Issue: R Valentine 9/6/89
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RV:alr:HLR121.2

QUALITY ASSURANCE DOCUMENTATION

STUDY: [redacted] Inhalation Approximate Lethal Concentration (ALC) of [redacted]
H# 17,869

AUDITS:

Items Audited	Audit Dates
Protocol, conduct	7/13/89
Records, final report	8/24-25/89

SHORT-TERM AUDIT REPORT NUMBER: [redacted]
DATE FINDINGS REPORTED TO MANAGEMENT AND STUDY DIRECTOR: 8/25/89

Reported by: William J. Lynam 9/6/89

William J. Lynam
Quality Assurance Auditor

Date

INTRODUCTION

The purpose of this study was to determine a 4-hour inhalation ALC for [redacted] in male rats. The ALC was defined as the lowest atmospheric concentration tested that caused the death of 1 or more rats either on the day of exposure or within 14 days post exposure. Except as documented in the study records, this study was conducted according to the applicable Good Laboratory Practice Regulations.

MATERIALS AND METHODS

A. Animal Husbandry

Young adult male Crl:CD®BR rats were received from Charles River Breeding Laboratories, Raleigh, North Carolina. Each rat was assigned a unique 6-digit identification number which corresponded to a numbered card affixed to the cage. Rats were quarantined for approximately one week prior to testing, and were weighed and observed three times during the quarantine period. During the test, rats were housed in pairs in 8" x 14" x 8" suspended, stainless steel, wire-mesh cages. The rat assigned the lower number in each cage was identified by a slash in the right ear. Prior to exposure, rats' tails and cage cards were color-coded with water-insoluble markers so that individual rats could be identified after exposure. Except during exposure, Purina Certified Rodent Chow® #5002 and water were available ad libitum.

Animal rooms were maintained on a timer-controlled, 12 hour/12 hour light/dark cycle. Environmental conditions of the rooms were targeted for a temperature of 23 ± 2°C and relative humidity of 50 ± 10%. Excursions outside these ranges were judged to have been of insufficient magnitude and/or duration to have adversely affected the validity of the study.

B. Exposure Protocol

Groups of 6 rats, approximately 7-8 weeks old and weighing between 242 and 271 grams, were restrained in perforated, stainless steel cylinders with conical nose pieces. The restrainers were inserted into a face plate on the exposure chamber such that only the nose of each rat protruded into the chamber. The rats were exposed nose-only for a single, 4-hour period to aerosols of [redacted] in air. Rats were weighed prior to exposure, and were observed for clinical signs of toxicity during and immediately after exposure. Surviving rats were observed daily; rats were also weighed daily for 14 days post exposure, weekends excluded when warranted by the rats' condition.

C. Atmosphere Generation

Aerosol atmospheres of [redacted] were generated by atomization. The test material was metered into a Spraying Systems nebulizer with a Harvard® Model 22 Compact Infusion Pump. Conditioned, filtered houseline air introduced at the nebulizer (approximately 40 L/min) atomized the test material and discharged the resulting aerosol directly into a 38-L cylindrical glass exposure chamber. Test atmospheres were dispersed with a conical baffle within the chamber to promote uniform distribution. Chamber atmospheres were exhausted through a dry-ice cold trap and a MSA activated charcoal/HEPA cartridge filter prior to discharge into a fume hood.

D. Analytical

The atmospheric concentration of [redacted] aerosol was determined by gravimetric analysis during each exposure. Known volumes of chamber atmospheres were drawn through preweighed, Gelman glass fiber (Type A/E) filters at approximately 30-minute intervals. The filters were weighed on a Cahn Model 26 Automatic Electrobalance®. The atmospheric concentration of aerosol was calculated from the difference in the pre- and post-sampling filter weights. Since the test material was supplied as an aqueous dispersion, filters were placed in a desiccator after sampling to remove residual water; the aerosol concentrations reported herein are based on the dry filter weights.

Particle size (mass median aerodynamic diameter and percent less than 3 and 10 um) was determined with a Sierra Series 210 cascade impactor during each exposure[1]. Chamber temperature was measured twice per exposure with a mercury thermometer. Chamber oxygen concentration was determined with a Biosystems® Model 3100R oxygen monitor once per exposure. Exposure chamber relative humidity was measured once per exposure with a Belfort Model 566 psychrometer.

E. 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, Inc., Wilmington, Delaware.

RESULTS

A. Exposure Conditions and Associated Mortality

An aerosol of [redacted] was readily observed during the exposures; during trial runs, the aerosol coated the sides of the exposure chamber, preventing visual observation of the rats. Atmospheric concentrations of [redacted] and rat mortality data for each exposure are summarized in the following table.

Characterization of [redacted] Atmospheres and Rat Mortality

Concentration (mg/m^3)[a]				% Particles[b]		MMD[c]	Mortality
Mean	S.D.	Range	n	<3 um	<10 um	(um)	(# deaths/#exposed)
440	130	280 - 660	8	78	96	1.2	0/6
590	220	330 - 940	9	76	95	1.2	1/6
920	210	660 - 1300	7	79	97	1.2	3/6

[a] Values shown represent the mean, standard deviation (S.D.), range and number of observations (n) for each exposure. Particle concentrations were based on dry filter weights. Atmospheric concentrations based on wet filter weights obtained immediately after sampling were approximately 3-15% greater.

[b] Percent by weight of particles with aerodynamic diameter less than 3 and 10 um.

[c] Mass median aerodynamic diameter.

B. Clinical Observations

The coating of [redacted] on the chamber walls prevented visual observation of the rats during exposure. Upon release from the restrainers immediately after exposure, rats exhibited lethargy, compound-covered faces, and red nasal and ocular discharges. No rats died during exposure.

Deaths occurred among rats exposed to [redacted] at atmospheric concentrations of 590 mg/m^3 or greater; all deaths were post exposure and occurred within 24 hours of exposure. Clinical signs of toxicity observed in surviving rats during the recovery period included lethargy, hunched posture, labored breathing, red nasal discharge, and wet yellow-stained perineum; these clinical signs were transient and had resolved by day 3 post exposure. Surviving rats also had slight to severe weight losses (up to approximately 16% of initial body weight) 1 day after exposure; these rats began to regain weight by day 3 post exposure. Transient, sporadic weight losses were also noted in some rats from the 440 and 590 mg/m^3 groups during the second week of recovery.

DISCUSSION AND CONCLUSION

Under the conditions of this study, the approximate lethal concentration for [redacted] is 590 mg/m^3. Based on the measured atmospheric concentration of [redacted], the test material is considered to be moderately toxic on an acute inhalation basis (ALC between 200 and 800 mg/m^3).

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