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Du Pont HLR 624-87

Study Title

Inhalation Approximate Lethal Concentration of [redacted]

Author

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Study Completed On

November 10, 1987

Performing Laboratory

E. I. du Pont de Nemours and Company, Inc.
Haskell Laboratory for Toxicology and Industrial Medicine
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Medical Research No.

[redacted]

Laboratory Project ID

Haskell Laboratory Report No. 624-87

GENERAL INFORMATION

Material Tested: [redacted]

Medical Research No.: [redacted]

Haskell No.: 16,758

Physical Form: [redacted]

Synonyms: [redacted]

Purity: [redacted]

Composition: [redacted]

GENERAL INFORMATION (Cont'd)

Composition (Cont'd): [redacted]

Contaminants: [redacted]

Other Code: [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: J. R. Alender
Chemicals and Pigments Department
E. I. du Pont de Nemours and Company, Inc.
Jackson Laboratory
Deepwater, New Jersey

In-Life Phase Initiated - Completed: 10/15/87 - 11/3/87

Notebook: [redacted]

There are 10 pages in this report.

Distribution: [redacted]

Inhalation Approximate Lethal Concentration (ALC) of [redacted]

SUMMARY

Groups of 6 male Crl:CD®BR rats were exposed to aerosol/vapor atmospheres of [redacted] for a single, 4-hour period. Under the conditions of this study, the ALC for [redacted] was 21 mg/m^3. At an atmospheric concentration of 230 mg/m^3 of aerosol, the atmospheric concentrations of acetone and ethylene glycol [redacted] were 150 and 9.4 ppm, respectively. The concentrations of these vapors were well below those associated with animal mortality. All deaths occurred either during exposure or within 24 hours of exposure. No common clinical signs of toxicity were observed in surviving rats during the 14-day recovery period. Based on the atmospheric concentration of the aerosol, [redacted] is considered to be extremely toxic on an acute inhalation basis.

Work by: Robert T. Turner 11/9/87
Robert T. Turner
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RV:smk:HLR71.8

QUALITY ASSURANCE DOCUMENTATION

STUDY [redacted] Inhalation Approximate Lethal Concentration of [redacted]

Because short-term studies are numerous and routine in nature, representative studies from this test type are audited quarterly to ensure the studies are designed and conducted in compliance with the Good Laboratory Practice Standards.

Reported by: Kathleen L. Reed 11-10-87
Kathleen L. Reed Date
Quality Assurance Auditor

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, Kingston, New York. Each rat was assigned a unique 6-digit identification number which corresponded to a numbered card affixed to the cage. Rats were quarantined for one week prior to testing, and were weighed and observed twice 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, 8 weeks old and weighing between 230 and 277 grams, were restrained in perforated, stainless steel cylinders with conical nose pieces. Each group was exposed nose-only for a single, 4-hour period to an aerosol/vapor atmosphere of [redacted] in air. Rats were weighed prior to exposure, and were observed for clinical signs of toxicity during exposure. Surviving rats were weighed and observed daily for 14 days post exposure, weekends included when warranted by the rats' condition.

C. Atmosphere Generation

Mixed aerosol/vapor atmospheres of [redacted] were generated with a Spraying Systems air atomizing nozzle using a high pressure air stream. The test material was metered into the spray nozzle with a Harvard Model 975 compact infusion pump and atomized with high pressure air (approximately 24 L/min). The spray nozzle was connected directly to a cylindrical, glass 38-L exposure chamber that was fitted with a baffle to enhance aerosol dispersion. Atmospheric concentrations of [redacted] were controlled by varying the test material feed rate. Chamber atmospheres were exhausted through a dry ice cold trap and a MSA cartridge filter prior to discharge into a fume hood.

D. Analytical

Since the process of atmosphere generation produced aerosols of [redacted] and vapors of acetone and ethylene glcol, two different analytical procedures were used. The atmospheric concentration of aerosolized polymer was determined by gravimetric analysis. A gas chromatographic method was used to monitor the atmospheric concentration of acetone and ethylene glycol.

The atmospheric concentrations of aerosolized polymer were determined at approximately 30-minute intervals by gravimetric analysis during each exposure. Known volumes of chamber atmospheres were drawn through preweighed Gelman glass fiber filters. Filters were weighed on a Cahn Model 28 Automatic Electrobalance®. Atmospheric concentrations of [redacted] were calculated from the filter weight gain, determined from the pre- and post-sampling filter weights.

The atmospheric concentrations of acetone and ethylene glycol were determined at approximately 60-min intervals during some exposures. Samples were collected by bubbling known volumes of chamber atmospheres through tandem midget impingers containing water. Aliquots from both impingers were analyzed with a Hewlett Packard 5790A gas chromatograph equipped a with a flame ionization detector. Samples were chromatographed isothermally at 125°C on a 3' x 2 mm i.d. glass column packed with 80/100 mesh Porapak® Q. The atmospheric concentrations of acetone and ethylene glycol were determined by comparing the detector response of the samples with standard curves. Acetone and ethylene glycol standards were prepared as needed by the quantitative dilution of acetone and ethylene glycol in water.

Particle size (mass median aerodynamic diameter and percent particles less than 10 um) was determined with a Sierra Series 210 cascade impactor during each exposure.[1] During each exposure, chamber temperature was measured with a mercury thermometer, relative humidity was measured with a Bendix Model 566 psychrometer, and chamber oxygen concentration was measured with a Biosystems, Inc., Model 3100 oxygen analyzer.

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

Chamber temperatures ranged from 22-24°C, relative humidity varied from 34-46%, and chamber oxygen concentration was 21%. Atmospheric characterization and associated rat mortality data are summarized in Table 1. Atmospheric concentrations of acetone and ethylene glycol are presented in Tables 2 and 3, respectively.

Table 1

Characterization of [redacted] Atmospheres and Associated Rat Mortality

Concentration (mg/m^3)[a]				% Particles		Mortality
Mean	S.D.	Range	n	< 10 um AD[b]	MMD(um)[c]	(# deaths/# exposed)
11	10	0.34 - 24	5	95	2.3	0/6
21	17	0 - 42	6	94	2.8	1/6
63	39	1.4 - 96	5	99	1.6	4/6
230	17	210 - 260	5	97	1.8	6/6

[a] Values shown represent the mean, standard deviation (S.D.), range and number of observations (n) for each exposure.
[b] Percent by weight of particles with aerodynamic diameter less than 10 um.
[c] Mass median aerodynamic diameter.

Table 2

Atmospheric Concentrations of Acetone

Aerosol Concentration	Acetone Concentration (ppm)[a]			
	Mean	S.D.	Range	n
11 mg/m^3	NM	NM	NM	NM
21 mg/m^3	NM	NM	NM	NM
63 mg/m^3	66	31	27 - 100	4
230 mg/m^3	150	19	120 - 160	5

[a] Values shown represent the mean, standard deviation (S.D.), range and number of observations (n) for each exposure.

Table 3

Atmospheric Concentrations of Ethylene Glycol

Aerosol Concentration	Ethylene Glycol Concentration (ppm)[a]			
	Mean	S.D.	Range	n
11 mg/m^3	NM	NM	NM	NM
21 mg/m^3	NM	NM	NM	NM
63 mg/m^3	NM	NM	NM	NM
230 mg/m^3	9.4	5.0	5.0 - 18	5

[a] Values shown represent the mean, standard deviation (S.D.), range and number of observations (n) for each exposure.

B. Clinical Observations

Deaths occurred following exposure to [redacted] at concentrations of 21, 63 or 230 mg/m^3. Clinical signs of toxicity observed either during exposure or upon release from the animal restrainers among rats from these groups included diminished acoustic startle response, compound-covered faces, red nasal or ocular discharges, and labored or rapid breathing. All deaths occurred within 24 hours of exposure. Rats exposed to 11 mg/m^3 exhibited red nasal and ocular discharges during or immediately after

exposure. With the exception of slight to severe (up to 9% of initial body weight) weight losses within 24 hours of exposure in some rats, no clinical signs of toxicity were observed during the 14-day recovery period.

DISCUSSION AND CONCLUSION

Under the conditions of this study, the ALC for [redacted] was 21 mg/m^3. The amounts of acetone and ethylene glycol detected in the exposure chamber at an aerosol concentration of 230 mg/m^3 were 150 and 9.4 ppm, respectively. Although extensive inhalation toxicity data for acetone and ethylene glycol are not available in the literature for comparison, rat deaths have been reported after a 4-hour exposure to 16,000 ppm acetone[2]; no deaths were reported in rats after repeated exposure to ethylene glycol vapors at approximately 150 ppm for 8 hr/day for 16 weeks[3]. The concentrations of these solvents observed in this study were considerably less than those associated with lethality or adverse effects in rats. Based on the atmospheric concentration of the aerosol, [redacted] is considered to be extremely toxic on an acute inhalation basis (ALC less than 80 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.

[2] Smyth, H.F., Carpenter, C.P., Weil, C.S., Pozzani, U.C., and Striegel, B.S. Amer. Ind. Hyg. Assoc. J., 23, 95, 1962.

[3] Wiley, F.J., Heuper, W.C., and von Oettinger, W.F. J. Ind. Hyg. Tox., 18, 123, 1936.