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March 16, 2011

VIA CERTIFIED MAIL

Attn: TSCA Declassification Coordinator
U.S. Environmental Protection Agency
Office of Pollution Prevention and Toxics
Document Control Office (7407M)
1200 Pennsylvania Ave., NW
Washington, D.C. 20460

8EHQ-07-16807

Re: Declassification Activity - TSCA §8(e) Submission
Originally Assigned 8EHQ Number: 8EHQ-07-16807
Originally Assigned Bar Code: 88070000225

Supplemental Submission - Revised Public Copy of Submission

Dear TSCA Declassification Coordinator:

This submission is made in connection with the EPA 2010 CBI Declassification Challenge initiative.

Please find enclosed a revised public copy of the above-identified submission. Any information still claimed as confidential business information (CBI) in the attached report has been redacted and replaced by brackets. The originally assigned 8EHQ number has been added by the submitter to the first page of the enclosed revised public copy of the submission.

Very truly yours,

Andrea V. Malinowski

Enclosure

8911000018 8

Revised Public Copy - Submitted 03.16.11
Originally Assigned 8EHQ Number: 8EHQ-07-16807
Originally Assigned Bar Code: 88070000225

Study Title

Inhalation Approximate Lethal Concentration of Proventin 7

Author

Rudolph Valentine

Study Completed On

September 29, 1987

Performing Laboratory

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

Medical Research No.

8119-001

Laboratory Project ID

Haskell Laboratory Report No. 529-87

GENERAL INFORMATION

Material Tested:	Imidodicarbonimidic diamide, N-(2-methylphenyl)-
Medical Research No.:	8119-001
Haskell No.:	16,908
Physical Form:	White powder
Purity:	Approximately 100%
Synonyms:	• Proventin 7 • o-Tolylbiguanide
CAS Registry Number:	93-69-6
Other Codes:	NRD-317 Lot # 22-35.908 8627C N.R., Item 3862
Stability:	The test material was assumed to be stable throughout the exposure phase of the test.
Sponsor:	Textile Fibers Department E. I. du Pont de Nemours and Company, Inc. Wilmington, Delaware
Material Submitted By:	D. R. Kidder Textile Fibers Department E. I. du Pont de Nemours and Company, Inc. Seaford, Delaware
In-Life Phase Initiated - Completed:	8/24/87 - 9/23/87
Notebooks:	E-51312, pp. 71-145.

There are 8 pages in this report.

Inhalation Approximate Lethal Concentration (ALC) of Proventin 7

SUMMARY

Groups of 6 male Crl:CD®BR rats were exposed to particulate atmospheres of Proventin 7 for a single, 4-hour period. Under the conditions of this study, the ALC for Proventin 7 was 1400 mg/m^3. Based on the atmospheric concentration of Proventin 7, this material is considered to be slightly toxic on an acute inhalation basis.

Work by: Robert T. Turner 9/28/87
Robert T. Turner
Technician

Study Director: R. Valentine 9/29/87
Rudolph Valentine, Ph.D.
Research Toxicologist

Approved by: Nancy C. Chromey 9/29/87
Nancy C. Chromey, Ph.D.
Section Supervisor,
Acute and Developmental Toxicology Section

RV:smk:HLR69.12

QUALITY ASSURANCE DOCUMENTATION

STUDY: MR 8119-001 Inhalation Approximate Lethal
H# 16,908 Concentration of Proventin 7

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 9-29-87
Kathleen L. Reed Date
Quality Assurance Auditor

INTRODUCTION

The purpose of this study was to determine a 4-hour inhalation ALC for Proventin 7 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 229 and 288 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 a particulate atmosphere of Proventin 7 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 at least 14 days post exposure, weekends included when warranted by the rats' condition.

C. Atmosphere Generation

Particulate atmospheres of Proventin 7 were generated by suspension of the test material, either as supplied or after trituration with a jet mill, in an air stream. For two exposures, the test material was delivered to a mixing tube with a K-TRON Model T-20 Twin Screw Volumetric Feeder and suspended with a high pressure air jet. The air flow (approximately 30-70 L/min) swept the suspended dust into a 6000 mL cyclonic elutriator. The cyclone removed the larger particles by impaction and allowed the smaller particles to enter the 38-L glass exposure chamber. For other exposures, a jet mill was used in the generation system to increase the amount of inhalable test material. For these exposures, the test material was metered into a Fluid Energy Process & Equipment Company Model 00 Jet-O-Mizer with a K-TRON Model T-20 Twin Screw Volumetric Feeder. Test material entering the jet mill was entrained in an air stream (approximately 30 L/min) and pulverized by impaction with other particles within a reduction chamber. The test material exited the reduction chamber of the jet mill with a smaller particle size and was swept into the exposure chamber. Particles entering the exposure chamber were dispersed with a baffle to promote uniform distribution within the chamber. Atmospheric concentrations of Proventin 7 were controlled by varying the test material feed rate and/or the air flow rate. Chamber atmospheres were exhausted through a high capacity fiberpac dust filter and a MSA filter cartridge prior to discharge into a fume hood.

D. Analytical

Atmospheric concentrations of Proventin 7 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 Proventin 7 were calculated from the filter weight gain, determined from the pre- and post-sampling filter weights.

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 content 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 Hall of Records, E. I. du Pont de Nemours and Company, Inc., Wilmington, Delaware.

RESULTS

A. Exposure Conditions and Associated Mortality

During most exposures, dense dust atmospheres of Proventin 7 were generated. Chamber temperature was 20°C, relative humidity ranged from 52-72%, and chamber oxygen content was 21%. Atmospheric characterization and associated rat mortality data are summarized below.

Characterization of Proventin 7 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)
250[d]	96	130 - 460	9	74	7.0	0/6
1600[d]	840	130 - 3100	9	40	12	0/6
830[e]	87	660 - 940	9	93	2.3	0/6
1400[e]	160	1100 - 1600	9	91	3.0	1/6
2300[e]	260	1900 - 2900	9	84	3.6	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.
[d] Dust atmospheres were generated by suspension of the test material in an air stream and cyclonic elutriation.
[e] Dust atmospheres were generated by suspension of the test material after trituration in a jet mill.

B. Clinical Observations

Clinical signs of toxicity could not be determined during the exposures at atmospheric concentrations of 830 mg/m^3 or greater since the dense particulate atmosphere prevented visual observation of the rats. During exposure at 250 mg/m^3, rats did not exhibit an accoustic startle response and had compound-covered faces. Immediately following exposure, all rats from the 2300 mg/m^3 group were found dead. Surviving rats from the other exposure groups exhibited compound-covered faces, and red nasal and ocular discharges. In addition, rats from the 250 mg/m^3 group had red eyes and rats from the 830 and 1400 mg/m^3 groups exhibited gasping; labored breathing and dark eyes were also noted in the 1400 mg/m^3 group rats immediately after exposure.

One rat from the 1400 mg/m^3 group was found dead within 24 hours of exposure. Common clinical signs of toxicity observed in surviving rats during the postexposure period included compound-stained faces, brown- or compound-discolored fur, and blood- or urine-stained perineum. Rats from the 250, 830, 1400 and 1600 mg/m^3 groups also exhibited nasal and/or ocular discharges. Some rats from the 830 and 1400 mg/m^3 groups had lung noise and 1 rat from the 1400 mg/m^3 group exhibited hyperactivity and hunched posture. Most rats from all exposure groups exhibited severe (up to 23% of initial body weight) weight losses within 24 hours of exposure.

DISCUSSION AND CONCLUSION

Atmospheric concentrations of Proventin 7 exceeding 1600 mg/m^3 (MMD = 12 um) could not be generated with the test material as supplied and initially tested. To increase the atmospheric concentration of Proventin 7 and the percentage of inhalable particles (particles with an aerodynamic diameter less than 10 um were considered inhalable), test atmospheres were generated using a jet mill. Under the conditions of this study, the ALC for Proventin 7 was 1400 mg/m^3. Based on the atmospheric concentration of Proventin 7, this material is considered to be slightly toxic on an acute inhalation basis (ALC between 800 and 2000 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.

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