

DOW CORNING

CONTAINS NO CRI
8EHQ-0192-1047 SUPP.

January 8, 1992

21 - Pages

PDCN:

8890000217

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Room L-100
Office of Pesticides and Toxic Substances
U.S. Environmental Protection Agency
Attn: TSCA Section 8(e) Coordinator
401 M Street S.W.
Washington, D.C. 20460

RECEIVED RECEIPT OF S.
92 JAN 27 PM 1:41

Re: Followup Submission to 8EHQ-0890-1047
TSCA Section 8(e) Notification of Substantial Risk
Hexamethoxydisilylethane

Dear Sir:

In accordance with the provisions of Section 8(e) of the Toxic Substances Control Act (TSCA), as interpreted in the Statement of Interpretation and Enforcement Policy (40 FR 11110, March 16, 1978), Dow Corning Corporation is submitting the following final report as a followup to our Notification of Substantial Risk of August 10, 1990 (8EHQ-0890-1047).

Chemical Substance:

Hexamethoxydisilylethane
CASRN 18406-41-2

Manufacturer:

Dow Corning Corporation
2200 West Salzburg Road
Midland, Michigan 48686-0994

Submitted Study:

A 14-DAY REPEATED DOSE INHALATION TOXICITY STUDY WITH
DOW CORNING® X1-6145A ADDITIVE IN ALBINO RATS

Background:

On August 10, 1990, Dow Corning submitted a Notification of Substantial Risk under TSCA Section 8(e) concerning preliminary results obtained in an acute vapor phase inhalation toxicity study of DOW CORNING® X1-6145A Additive in rats, with the a copy of the final report being submitted to EPA August 21, 1990. In response to the Agency's request, Dow Corning provided additional followup to 8EHQ-0890-1047 in a letter of May 30, 1991, including notification of a planned 14-day vapor inhalation toxicity study with DOW CORNING® X1-6145A Additive in rats. This study now has been completed and Dow Corning is submitting the final report to EPA under this cover letter.

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EPA-OTS



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January 8, 1992

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Executive Summary:

A 14-day vapor inhalation toxicity study was initiated in rats to assess the inhalation toxicity of DOW CORNING® XI-6145A Additive, chemically described as hexamethoxydisilylothane, CASRN 18606-41-2. Three groups of five male and five female Sprague Dawley rats were to be exposed to target concentrations of 0, 3, and 10 ppm of the test material for six hours/day, five days a week, for two weeks. One male rat in the 10 ppm group died during the second exposure period. After the second exposure, all surviving test animals were clinically moribund in severe respiratory distress and the study was terminated. The actual overall mean exposure concentration of the test material for the test groups were 2.0 and 13.0 ppm.

Clinical signs observed in the two-day period included dyspnea, lethargy and nasal and/or oral discharges. Gross pathological examination revealed nasal passage occlusion and distension of the digestive tracts of all exposed animals. Histopathology of the respiratory tract revealed severe and extensive damage to the lining of the nasal cavity, trachea and bronchi in animals exposed to the test article. Lesions, consisting of necrosis and desquamation of respiratory tract epithelium and fibrinopurulent inflammatory exudate, were generally most severe in the most anterior level of the nasal cavity. Similar necrotizing lesions were present throughout the respiratory tree down to the level of the bronchi in most rats. Lung parenchyma was not involved with the test article-related lesions.

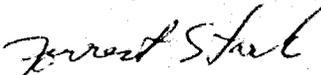
The occlusion of the nasal passages is possibly important in evaluating these data because rats are obligatory nasal breathers. Additional testing is necessary in non-obligatory nasal breathers to address this issue and to determine if rats are the appropriate model for evaluating the toxicity of DOW CORNING® XI-6145A Additive.

Actions:

Dow Corning will notify EPA of any further pertinent information that may be developed concerning this chemical substance.

If you require further information concerning this notification of substantial risk, please contact Dr. Rhyo G. Daniels, Regulatory Compliance Specialist, Dow Corning Product Safety and Regulatory Compliance Department, at the address provided below or by telephone at 517-496-4222.

Sincerely,



Dr. Forrest O. Stark
U.S. Area Vice-President
Director of Health and Environmental Sciences

TSCA SECTION 8(e) NOTIFICATION OF SUBSTANTIAL RISK

TOXICOLOGICAL STUDIES

TSCA CONFIDENTIAL BUSINESS INFORMATION CLAIMS

For purposes of Notification of Substantial Risk under Section 8(e) of the Toxic Substances Control Act (TSCA), the general PROPRIETARY designation on the attached toxicological study has been waived by Dow Corning Corporation.

Submitter: _____

Rhys G. Daniels

Date: _____

8 June 1992

Rhys G. Daniels, Ph.D.
Regulatory Compliance Specialist
Health and Environmental Sciences
DOW CORNING CORPORATION

A 14-DAY REPEATED DOSE INHALATION TOXICITY STUDY WITH
DOW CORNING® X1-6145A ADDITIVE IN ALBINO RATS

ABSTRACT

A 14-day vapor inhalation toxicity study was initiated in rats to assess the inhalation toxicity of DOW CORNING® X1-6145A Additive. Three groups of five male and five female Sprague-Dawley rats were to be exposed to target concentrations of 0, 3, and 10 ppm of DOW CORNING® X1-6145A Additive for six hours/day, five days a week, for two weeks. One male rat in the 10 ppm group died during the second exposure period. After the second exposure, all surviving test animals were clinically moribund in severe respiratory distress and the study was terminated. The actual overall mean exposure concentration of DOW CORNING® X1-6145A Additive for the test groups were 2.0 and 13.0 ppm. Clinical signs observed in the two-day period included dyspnea, lethargy and nasal and/or oral discharges. Gross pathological examination revealed nasal passage occlusion and distension of the digestive tracts of all exposed animals. Histopathology of the respiratory tract revealed severe and extensive damage to the lining of the nasal cavity, trachea and bronchi in animals exposed to the test article. Lesions, consisting of necrosis and desquamation of respiratory tract epithelium and fibrinopurulent inflammatory exudate, were generally most severe in the most anterior level of the nasal cavity. Similar necrotizing lesions were present throughout the respiratory tree down to the level of the bronchi in most rats. Lung parenchyma was not involved with the test article-related lesions.

The occlusion of the nasal passages is possibly important in evaluating these data because rats are obligatory nasal breathers. Additional testing is necessary in non-obligatory nasal breathers to address this issue and to determine if rats are the appropriate model for evaluating the toxicity of DOW CORNING® X1-6145A Additive.

PROPRIETARY

FORM 1000-10-73

REPORT NO.: 1191-1000-0413
FILE NO.: 7001
REFERENCE NO.: 11-91-1000-04
LOT NO.: 1000010
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CHECKED BY: W. H. Siddiqui
DEPARTMENT: Health and Environmental Sciences
SUPERVISOR: W. H. Siddiqui
LOCATION: Midland, Michigan
DATE: December 19, 1991
TITLE: A 14-Day Repeated Dose Inhalation Toxicity Study with
DOW CORNING® XI-6145A Additive in Albino Rats.

ABSTRACT

A 14-day repeated dose inhalation toxicity study was initiated in rats to assess the inhalation toxicity of DOW CORNING® XI-6145A Additive. Three groups of five male and five female Sprague-Dawley rats were to be exposed to target concentrations of 0, 3 and 10 ppm DOW CORNING® XI-6145A Additive for six hours/day, five days a week, for two weeks. One male rat in the 10 ppm group died during the second exposure period. After the second exposure all surviving test animals were clinically moribund in severe respiratory distress and the study was terminated. The actual overall mean exposure concentration of DOW CORNING® XI-6145A Additive for the test groups were 2.0 and 13.0 ppm. Clinical signs observed during the two-day period included dyspnea, lethargy and nasal and/or oral discharges. Gross pathological examination revealed nasal passage occlusion and distension of the digestive tracts of all exposed animals. Histopathology of the respiratory tract revealed severe and extensive damage to the lining of the nasal cavity, trachea and bronchi in animals exposed to the test article. Lesions, consisting of necrosis and desquamation of respiratory tract epithelium and fibrinopurulent inflammatory exudate, were generally most severe in the most anterior level of the nasal cavity. Similar necrotizing lesions were present throughout the respiratory tree down to the level of the bronchi in most rats. Lung parenchyma was not involved with test article-related lesions.

The occlusion of the nasal passages is possibly important in evaluating these data because rats are obligatory nasal breathers. Additional testing is necessary in non-obligatory nasal breathers to address this issue and to determine if rats are the appropriate model for evaluating toxicity of DOW CORNING® XI-6145A Additive.

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PROPRIETARY

I. INTRODUCTION

DOW CORNING® XI-6145A Additive is a ligand with relatively low vapor pressure which is used as an intermediate in the production of various elastomers and coatings. The objective of this screening study was to assess the inhalation toxicity of DOW CORNING® XI-6145A Additive in the rat following repeated inhalation exposures. The results of such a study are of value in assessing the human health hazard.

II. MATERIALS AND METHODS

A. Test Material

DOW CORNING® XI-6145A Additive, Lot Number BN089002 was used in this study. The purity of the material was ~99% as analyzed by gas chromatograph (area count).

B. Experimental Animals

Male and female CD® (Sprague-Dawley) rats (weighing between 100-160 g and 5-7 weeks of age) were obtained from Charles River Breeding Laboratories, Portage, Michigan. Upon arrival at the Toxicology Department, all rats were quarantined for one week. Approved animals were weighed and randomized into control and test groups using the Xybio ASLECT program. After randomization, test animals were ear tagged and color coded tags (listing the animal's sex, exposure level, animal, file and group numbers) were placed on the outside of each cage.

C. Animal Maintenance

The rats were housed individually in suspended stainless steel, wire mesh bottom cages. Before each exposure, animals were transferred into cages that were designed to be placed within the exposure chambers. After each exposure, the animals were returned to their original housing. The animals were fed certified Purina® rodent chow and water ad libitum except during exposures. The rats were housed during non-exposure periods in rooms designed to be maintained at 68-73°F and 30-70 percent relative humidity. A light cycle of alternating 12 hours light and 12 hours dark was maintained.

D. Experimental Design

Animal Groups

A structural outline of the experimental design is given below:

Group Number	Number of Animals		Test Material	Target Exposure Concentration (ppm)
	Male	Female		
I	5	5	Filtered Room Air	N.A.
II	5	5	DOW CORNING® X1-6145A Additive	3
III	5	5	DOW CORNING® X1-6145A Additive	10

The exposure levels (0, 3, and 10 ppm) were selected on the basis of available acute inhalation data (D.C. Report No. 1990-10000-35576), data from materials with similar structures, and chemical and physical properties of the test material.

E. Exposure Methods and Generating Equipment

Exposures were conducted in 450 liter stainless steel whole body exposure chambers. The chambers were operated under dynamic conditions where the chamber air was room air, which had been filtered (hepa and charcoal filters). The airflows through the chambers were kept at approximately 12 - 15 air changes per hour. Chamber temperature, humidity, and airflow were monitored continuously and were recorded every five minutes by the Camile® Data Acquisition System during the daily exposure period. The test material was introduced into the chambers through special designed glass J-tubes. The test material was metered into the J-tubes with FMI lab pumps. Instrument air which was filtered (Drierite) flowed through the J-tubes at a controlled rate. Glass beads and heating tape were used to help vaporize the test material. The air/vapor mixture passed into the inlet port at the top of the chambers. The exhaust air from the chambers was filtered with a hepa and charcoal filters and a water

cyclone. During the exposure periods, attempts were made to keep the actual concentrations of the test material in the chambers as constant as possible.

The duration of each exposure period was six hours after equilibration of the chamber concentration. The equilibration time, which is a function of chamber airflow, was approximately 20 minutes.

The amount of test material used during the exposure period was determined by pre- and post-measuring the weight of the test material in each graduated cylinder reservoir. The exposure duration (exposure period and equilibration time), test material used and airflow through the chambers were then used to calculate nominal concentrations.

Actual chamber concentrations were measured a minimum of once an hour by a Varian® 4600 Gas Chromatograph (G.C.), which was connected to a Varian® 402 Microprocessor. The G.C. was calibrated before the start of the study and one bag standard was prepared and analyzed during each exposure period.

F. Observations

All animals were observed daily during the post-exposure period for treatment-related signs of toxicity. In particular, any evidence of respiratory, dermal, behavioral, nasal and/or ocular changes.

G. Body Weight Measurements

Individual body weights were recorded on the initial day of the study and before necropsy (terminal weight).

H. Pathology

A gross pathological examination was conducted on all animals that died or were sacrificed at the termination of the study. The respiratory tract of the control and test-article exposed animals were collected, processed by standard techniques and examined microscopically.

II. RESULTS

Average chamber temperature and humidity calculated for the daily exposure periods are presented in Table I. The ranges of temperatures and humidity were 27-28°C and 30-32% R.H., respectively.

The mean daily nominal and actual atmospheric concentration data are summarized in Table II. Good agreement was observed between the actual and nominal concentrations. The overall mean concentrations of DOW CORNING® X1-6145A Additive to which the test groups were exposed were 2.0 and 13.0 ppm.

One male animal in the high dose group died during the second exposure period. After the second exposure all surviving exposed rats were clinically moribund in severe respiratory distress and the study was terminated. Clinical signs observed during the two-day period included dyspnea, lethargy and nasal and/or oral discharges.

Incidence of necropsy findings are presented in Table III. Gross tissue changes attributable to test article exposure were observed in all exposed rats of both sexes in both the 3 and 10 ppm exposure groups. Nasal passage occlusion was evident in all exposed rats and the digestive tract of these animals were distended with gas. The lungs of these animals were not grossly abnormal in any animal. Histopathology of the respiratory tract (Table IV) revealed severe and extensive damage to the lining of the nasal cavity, trachea and bronchi in rats of both sexes exposed to the test article. The lesions, consisting of necrosis and desquamation of respiratory tract epithelium and fibrinopurulent inflammatory exudate, were generally most severe in the most anterior level of the nasal cavity. Similar necrotizing lesions were present throughout the respiratory tree down to the level of the bronchi in most rats. There appeared to be a slight dose response with respect to severity between the 3 and 10 ppm levels with males tending to have more severe lesions than females within a given exposure level. Lung parenchyma was not involved with test article-related lesions.

There was no evidence in exposed or control animals of intercurrent disease which would influence the interpretation of these results. All other observed changes were judged to be incidental and typical of background findings in rats of this age and strain euthanatized in this manner.

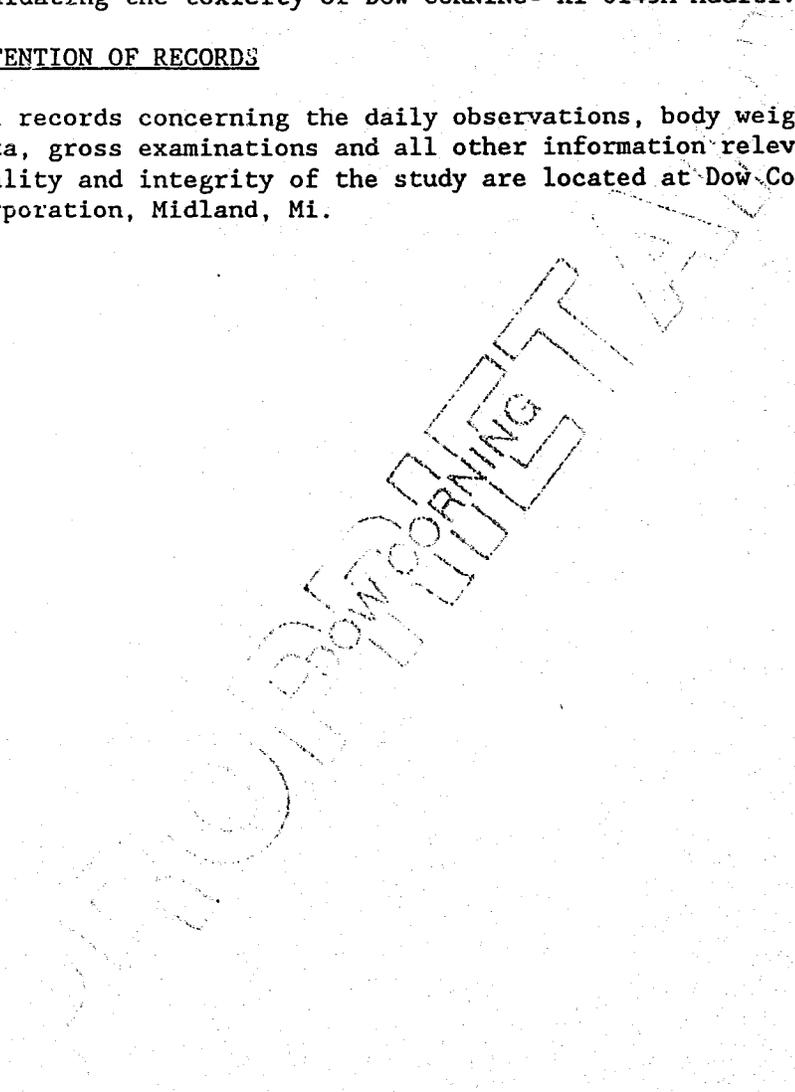
IV. DISCUSSION AND CONCLUSIONS

Exposure of rats to DOW CORNING® X1-6145A Additive at concentrations of 3 and 10 ppm for 6hr/day for two days resulted in morbidity and termination of the study. Microscopic examination of the respiratory tract of animals exposed to the test-article revealed necrosis and desquamation of epithelium lining the nasal cavity, nasopharynx, trachea and bronchi, with concomitant fibrinopurulent inflammation. The

occlusion of the nasal passages is possibly important in evaluating these data because rats are obligatory nasal breathers. Additional testing is necessary in non-obligatory nasal breathers to address this issue and to determine if the rat is the appropriate model for evaluating the toxicity of DOW CORNING® X1-6145A Additive.

V. RETENTION OF RECORDS

All records concerning the daily observations, body weights, exposure data, gross examinations and all other information relevant to the quality and integrity of the study are located at Dow Corning Corporation, Midland, Mi.



VI. SIGNATURE OF AUTHORS

This report constitutes pages 1-17, and Tables I-IV

Authors: *Gary B. Kolesar* Date: 11/26/91
Gary B. Kolesar, M.S., M.P.H.
Investigator

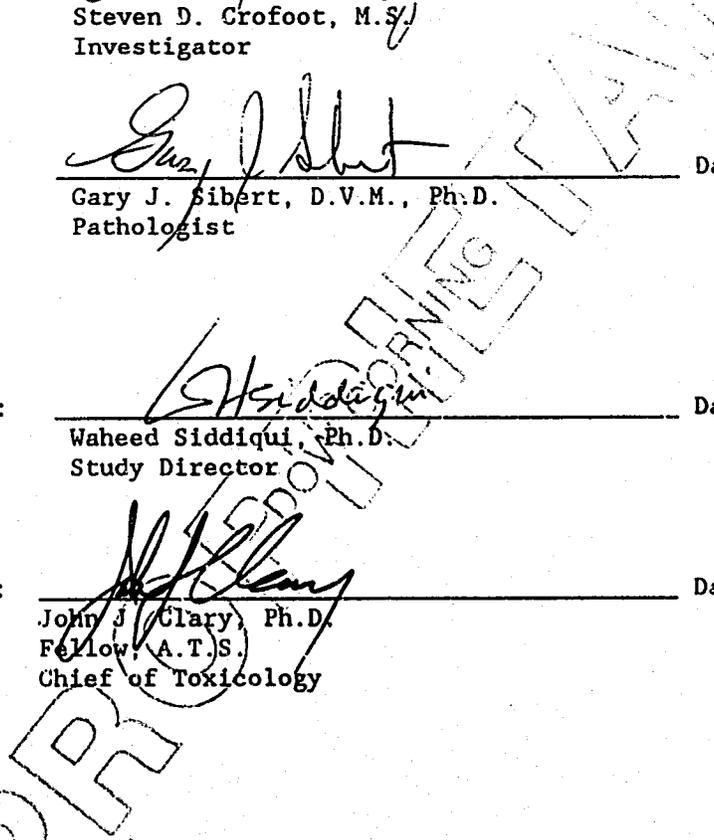
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Pathologist

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Waheed Siddiqui, Ph.D.
Study Director

Reviewed By: *John J. Clary* Date: Dec 6, 1991
John J. Clary, Ph.D.
Fellow, A.T.S.
Chief of Toxicology

Typed By: *Jean M. Bielby*
Jean M. Bielby



VII. QUALITY ASSURANCE STATEMENT

This report represents data generated by the Toxicology Department, Dow Corning Corporation, Midland, Michigan. This study was conducted according to the EPA Toxic Substances Control Act; Good Laboratory Practice Regulations 40 CFR Part 792 Thursday August 17, 1989. The results reported accurately reflect the data generated. All raw data is located at Dow Corning Corporation, Midland, MI.

Study Initiated: June 28, 1991

Study Completed: December 9, 1991

Experimental Start: July 8, 1991

Experimental Termination: July 9, 1991

Study Audited: June 20, 1991 and November 21, 1991

Audit Reports to Management: June 20, 1991 and November 25, 1991

Report Issued: December 10, 1991

Carolyn Hunter

Quality Assurance
Health & Environmental Sciences
Dow Corning Corporation
Midland, MI 48686-0994

December 9, 1991

Report Audit Date

Gary J. Sibert 26 Nov 91

Gary J. Sibert, Ph.D Date
Tox Liaison/Study Sponsor

Waheed H. Siddiqui 12/9/91

Waheed H. Siddiqui, Ph.D Date
Study Director

TABLE I

A 14-DAY REPEATED DOSE INHALATION TOXICITY STUDY OF
DOW CORNING® XI-6145A ADDITIVE IN RATS

DAILY MEAN TEMPERATURE (°C) AND RELATIVE HUMIDITY (%)
DURING TREATMENT PERIOD (MEAN ± S.D.)

Target Exposure Concentration (ppm)	Study Day													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
0 Temp.	28.0	27.0												
S.D.	0.9	1.1												
Humid.	32.0	31.0												
S.D.	3.1	3.2												
3 Temp.	27.0	27.0												
S.D.	0.7	0.8												
Humid.	32.0	31.0												
S.D.	2.4	2.1												
10 Temp.	27.0	27.0												
S.D.	0.8	0.5												
Humid.	32.0	30.0												
S.D.	3.3	2.5												

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TABLE II

A 14-DAY REPEATED DOSE INHALATION TOXICITY STUDY OF
DOW CORNING® XI-6145A ADDITIVE

DAILY NOMINAL ACTUAL CHAMBER CONCENTRATION (PPM)
DURING TREATMENT PERIOD (MEAN ± S.D.)

Target Exposure Concentration (ppm)	Study Day													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
3 Actual	3.0	1.5*												
S.D.	0.6	0.8												
Nominal	3.0	3.0												
10 Actual	10.0	15.0*												
S.D.	2.0	9.0												
Nominal	7.0	11.0												

* Target exposure concentrations were not maintained due to pump problems.

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TABLE III

Dow Corning Corporation
Health and Environmental Sciences
Midland, Michigan 48666-0994

Study Number: 7403
Study Title: A 14-Day Repeated Dose Inhalation Toxicity Study with DOW
CORNING (R) XI-6145A in Albino Rats.

NECROPSY FINDINGS

	CONTROL		3 ppm		10 ppm	
	Male	Female	Male	Female	Male	Female
Number on Study	5	5	5	5	5	5
Disposition						
Terminal Sacrifice	0	0	0	0	0	0
Elective Sacrifice	5	5	5	5	5	5
Moribund Sacrifice	0	0	0	0	5	0
Spontaneous Death	0	0	0	0	1	0
All Tissues						
Within Normal Limits	5	1	0	0	0	2
Nose						
Discharge	0	0	5	0	4	2
Plugged (obstruction)	0	0	5	0	4	2
Digestive Tract						
Gas Distention	0	0	5	0	3	2
Uterus						
Fluid-Filled (cycling)	—	—	—	—	—	2
Liver						
Congestion	0	0	0	0	1	0
Remaining Tissues						
Within Normal Limits	5	4	5	5	5	5

Handwritten signature
11 July 91

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TABLE IV
Incidence of Histopathologic Findings for All Study Animals
Robert G. Geil, D.V.M., Consulting Pathologist
14-Day Repeated Dose Inhalation Toxicity Study

PROPRIETARY

Project Number: DCC 7403 Species: Rat

Tissue/ Diagnosis/ Modifier(s)	0 ppm		3 ppm		10 ppm	
	M	F	M	F	M	F
	()	()	()	()	()	()
Lung	(5)	(5)	(5)	(5)	(5)	(5)
Within normal limits	4	1	0	2	0	1
Congestion	0	0	0	0	1	0
moderate	0	0	0	0	1	0
Desquamation, epithelium	0	0	5	1	5	4
bronchi, minimal	0	0	3	0	0	1
bronchi, mild	0	0	2	1	1	3
bronchi, moderate	0	0	0	0	2	0
bronchi, marked	0	0	0	0	2	0
Exudate, fibrinopurulent	0	0	1	0	2	0
bronchi, minimal	0	0	0	0	2	0
bronchi, mild	0	0	1	0	0	0
Hemorrhage	0	0	0	2	1	1
parenchyma, minimal	0	0	0	2	1	1
Necrosis, epithelium	0	0	5	0	4	3
bronchi, minimal	0	0	3	0	0	1
bronchi, mild	0	0	2	0	1	2
bronchi, moderate	0	0	0	0	1	0
bronchi, marked	0	0	0	0	2	0
Ossification	0	1	0	0	0	0
parenchyma, focal, mild	0	1	0	0	0	0
Perivascular inflammatory infiltrate	1	0	0	0	0	0
mild	1	0	0	0	0	0
Perivascular mononuclear infiltrate	0	0	0	1	0	0
minimal	0	0	0	1	0	0
Pneumonia, interstitial, acute	0	0	1	0	2	0
minimal	0	0	1	0	1	0
mild	0	0	0	0	1	0
Vascular mineralization	0	4	0	1	0	1
minimal	0	4	0	1	0	1
Nares	(5)	(5)	(5)	(5)	(5)	(5)
Within normal limits	5	5	0	0	0	0
Desquamation, epithelium	0	0	4	4	5	4
mild	0	0	1	2	2	3
moderate	0	0	2	2	3	1
marked	0	0	1	0	0	0
Exudate, fibrinopurulent	0	0	5	3	5	5
minimal	0	0	0	1	0	1
mild	0	0	0	2	1	4
moderate	0	0	4	0	2	0
marked	0	0	1	0	2	0

() = Total Examined

All modifiers are printed.

TABLE IV, Continued

Incidence of Histopathologic Findings for All Study Animals (continued)

Robert E. Geil, D.V.M., Consulting Pathologist

14-Day Repeated Dose Inhalation Toxicity Study

PROPRIETARY

Project Number: DCC 7403 Species: Rat

Tissue/ Diagnosis/ Modifier(s)	0 ppm		3 ppm		10 ppm	
	M	F	M	F	M	F
Nares (continued)						
Keratinosis, epithelium	0	0	4	4	5	4
mild	0	0	1	2	2	3
moderate	0	0	2	2	3	1
marked	0	0	1	0	0	0
Nasal Cavity I	(5)	(5)	(5)	(5)	(5)	(5)
Within normal limits	5	5	0	0	0	0
Desquamation, epithelium	0	0	5	5	5	4
moderate	0	0	0	1	0	0
marked	0	0	5	4	5	4
Exudate, fibrinopurulent	0	0	5	5	5	6
mild	0	0	0	2	0	0
moderate	0	0	0	2	1	2
marked	0	0	5	1	4	4
Necrosis, epithelium	0	0	5	5	5	5
moderate	0	0	0	0	1	0
marked	0	0	5	5	4	5
Nasal Cavity II	(5)	(5)	(5)	(5)	(5)	(5)
Within normal limits	5	5	0	0	0	0
Desquamation, epithelium	0	0	5	5	5	5
mild	0	0	0	1	0	0
moderate	0	0	1	3	1	2
marked	0	0	4	1	4	3
Exudate, fibrinopurulent	0	0	5	3	5	6
minimal	0	0	0	1	0	0
mild	0	0	3	2	1	2
moderate	0	0	2	0	4	3
marked	0	0	0	0	0	1
Necrosis, epithelium	0	0	5	4	5	4
moderate	0	0	1	3	1	2
marked	0	0	4	1	4	2
Nasal Cavity III	(5)	(5)	(5)	(5)	(5)	(5)
Within normal limits	5	5	0	0	0	0
Desquamation, epithelium	0	0	5	5	5	5
minimal	0	0	0	0	1	0
mild	0	0	4	2	2	2
moderate	0	0	1	3	2	3
Exudate, fibrinopurulent	0	0	0	0	1	0
mild	0	0	0	0	1	0
Exudate, serous	0	0	4	3	4	4
minimal	0	0	0	1	0	0
mild	0	0	2	2	3	4
moderate	0	0	2	0	1	0

() = Total Examined

All modifiers are printed.

TABLE IV, Continued

Incidence of Histopathologic Findings for All Study Animals (continued)
 Robert G. Geil, D.V.M., Consulting Pathologist
 14-Day Repeated Dose Inhalation Toxicity Study

PROPRIETARY

Project Number: DCC 7403 Species: Rat

Tissue/ Diagnosis/ Modifier(s)	0 ppm		3 ppm		10 ppm	
	M	F	M	F	M	F
Nasal Cavity III (continued)						
Necrosis, epithelium	0	0	5	2	5	5
minimal	0	0	0	0	1	1
mild	0	0	4	2	2	2
moderate	0	0	1	0	2	2
Nasal Cavity IV	(5)	(5)	(5)	(5)	(5)	(5)
Within normal limits	5	5	0	0	0	0
Desquamation, epithelium	0	0	5	5	5	5
minimal	0	0	0	1	0	1
mild	0	0	1	2	2	1
moderate	0	0	4	2	2	3
marked	0	0	0	0	1	0
Exudate, fibrinopurulent	0	0	1	0	0	1
mild	0	0	1	0	0	1
Exudate, serous	0	0	3	3	4	3
minimal	0	0	0	1	0	0
mild	0	0	0	2	4	2
moderate	0	0	3	0	0	1
Necrosis, epithelium	0	0	5	4	5	5
minimal	0	0	0	1	0	1
mild	0	0	1	2	1	1
moderate	0	0	4	1	4	3
Nasopharynx	(5)	(5)	(5)	(5)	(5)	(4)
Within normal limits	5	5	0	0	0	0
Desquamation, epithelium	0	0	5	5	5	4
minimal	0	0	0	0	0	1
mild	0	0	1	3	2	1
moderate	0	0	4	2	1	2
marked	0	0	0	0	2	0
Exudate, serous	0	0	1	0	0	0
mild	0	0	1	0	0	0
Necrosis, epithelium	0	0	5	3	5	3
minimal	0	0	0	1	1	0
mild	0	0	1	2	1	1
moderate	0	0	4	0	1	2
marked	0	0	0	0	2	0
Trachea (bifurcation)	(5)	(4)	(5)	(5)	(5)	(5)
Within normal limits	5	4	0	1	0	0
Desquamation, epithelium	0	0	5	4	5	5
minimal	0	0	0	0	0	1
mild	0	0	1	3	0	1
moderate	0	0	1	1	1	1
marked	0	0	0	0	4	2

() = Total Examined

All modifiers are printed.

TABLE IV, Continued
Incidence of Histopathologic Findings for All Study Animals (continued)
 Robert G. Gell, D.V.M., Consulting Pathologist
 14-Day Repeated Dose Inhalation Toxicity Study

PROPRIETARY

Project Number: DCC 7403 Species: Rat

Tissue/ Diagnosis/ Modifier(s)	0 ppm		3 ppm		10 ppm	
	-----		-----		-----	
	M	F	M	F	M	F
Trachea (bifurcation) (continued)						
Exudate, fibrinopurulent	0	0	1	2	2	0
minimal	0	0	0	2	0	0
mild	0	0	1	0	1	0
moderate	0	0	0	0	1	0
Necrosis, epithelium	0	0	5	3	5	5
minimal	0	0	0	0	0	1
mild	0	0	1	2	0	1
moderate	0	0	1	1	1	1
marked	0	0	3	0	4	2
Trachea (cervical)	(5)	(5)	(5)	(4)	(5)	(5)
Within normal limits	5	5	1	1	0	0
Desquamation, epithelium	0	0	4	3	5	5
mild	0	0	0	2	0	0
moderate	0	0	2	1	0	2
marked	0	0	2	0	5	3
Exudate, fibrinopurulent	0	0	0	1	2	0
minimal	0	0	0	1	0	0
mild	0	0	0	0	1	0
marked	0	0	0	0	1	0
Necrosis, epithelium	0	0	4	3	5	5
mild	0	0	0	2	0	0
moderate	0	0	2	1	0	2
marked	0	0	2	0	5	3

() = Total Examined

All modifiers are printed.

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