

ORIGINAL 8EHQ-94-12973

April 10, 1995

TSCA Document Processing Center (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
401 M Street S.W.
Washington, D.C. 20460

BC

ORIGINAL

95 APR 25 AM 8:14

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Re: Followup Submission to 8EHQ-94-12973
TSCA Section 8(e) Notification of Substantial Risk
1,1,1,3,5,5,5-Heptamethyl-6-hexyltrisiloxane

Contains No CBI

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 information as a followup to our Notification of Substantial Risk of August 22, 1994 (8EHQ-94-12973).

Chemical Substance:

1873-90-1 1,1,1,3,5,5,5-Heptamethyl-6-hexyltrisiloxane



8EHQ-94-12973
SP082 04/25/95

Manufacturer:

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



89950000183

Initial TSCA Section 8(e) Submission:

AN ACUTE INHALATION TOXICITY STUDY OF DOW CORNING® X2-1731 VOLATILE FLUID IN ALBINO RATS

EPA Document Control Number: 8EHQ-94-12973

Supplemental TSCA Section 8(e) Submission:

ACUTE INHALATION TOXICITY STUDY OF DOW CORNING® X2-1731 VOLATILE FLUID IN RATS

EPA Document Control Number: 8EHQ-94-12973 Suppl.

In the status report for 8EHQ-94-12973, dated March 15, 1995, EPA requested Dow Corning to provide:

- (3) a full copy of the final report (including the actual experimental protocol, applicable results of gross or histopathologic examinations, data, results of any statistical analyses, etc.) from each study mentioned in your submission.

RECEIVED
5/3/95

(4) a description of all voluntary actions taken by your company in response to the findings indicated in your submission.

In response to EPA's request, Dow Corning is submitting the following information at this time as a followup to 8EHQ-94-12973:

(A) Submission of Final Report

A copy of the final report on the Acute Inhalation Toxicity Study of DOW CORNING® X2-1731 Volatile Fluid previously has been submitted to EPA under a cover letter dated November 10, 1994, as a supplemental submission to our original TSCA §8(e) Notification of Substantial Risk. A copy of this supplemental submission is attached (Attachment 1).

(B) Voluntary Actions Taken in Response to Findings:

A copy of our original TSCA §8(e) Notification Substantial Risk of August 22, 1994, was provided to the Silicone Environmental, Health and Safety Council (SEHSC) for awareness of the member companies: a copy of the cover letter is attached (Attachment 2).

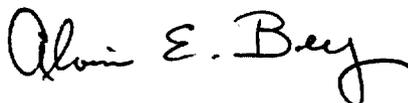
In response to the cited findings, Dow Corning has revised the Material Safety Data Sheet (MSDS) for DOW CORNING® 2-1731 Volatile Fluid, designating 3-hexyl=heptamethyltrisiloxane as a hazardous ingredient as defined at 29 CFR 1910.1200. A copy of the revised MSDS is attached (Attachment 3).

Dow Corning also has notified customers of the cited findings. Based on the acute lethality of aerosolized DOW CORNING® 2-1731 Volatile Fluid, we have recommended that applications in which this product could reasonably be expected to become aerosolized should be avoided. A copy of both the customer notification letter and the accompanying toxicological summary for DOW CORNING® 2-1731 Volatile Fluid are attached (Attachment 4).

Dow Corning will, of course 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. Rhys 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,



Alvin E. Bey
U.S. Area Vice-President
Corporate Director of HES

DOW CORNING

November 10, 1994

TSCA Document Processing Center (TS-790)
 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

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Re: Supplemental Submission to 8EHQ-94-12973
 TSCA Section 8(e) Notification of Substantial Risk
 1,1,1,3,5,5-Heptamethyl-3-hexyltrisiloxane

Contains No CBI

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 supplemental submission to our Notification of Substantial Risk of August 22, 1994 (8EHQ-94-12973).

Chemical Substance:

1873-90-1 1,1,1,3,5,5-heptamethyl-3-hexyltrisiloxane

Manufacturer:

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

Submitted Study:

ACUTE INHALATION TOXICITY STUDY OF DOW CORNING® X2-1731
 VOLATILE FLUID IN RATS

Dow Corning Corporation
 September 22, 1994

Background:

In a letter dated August 22, 1994, Dow Corning provided EPA with a Notification of Substantial Risk based on preliminary results obtained from an acute inhalation toxicity study of 1,1,1,3,5,5-heptamethyl-3-hexyltrisiloxane in albino rats. At this time, we wish to provide the Agency with a copy of the final report as a supplement to our original notification.

Executive Summary:

An acute inhalation toxicity study was conducted to determine the median lethal concentration (LC₅₀) in male and female rats via an aerosol inhalation exposure route to a research and development material identified as DOW CORNING® X2-1731 Volatile Fluid, chemically identified as 1,1,1,3,5,5,5-heptamethyl-3-hexyltrisiloxane (CASRN 1873-90-1).

The test material was aerosolized and administered for four hours by whole-body inhalation exposure to groups of five male and five female Fischer F344/N rats at target concentrations of 5.0, 2.0, and 1.0 mg/l, one concentration during each of three consecutive exposure periods. Actual gravimetrically determined exposure concentrations were 5.08, 2.01, and 0.95 mg/l, respectively. Aerosol particle sizes, determined as mass median aerodynamic diameter (MADD) were 0.27, 0.29, and 0.30 µm with geometric standard deviations (GSD) of 1.87, 2.22, and 3.58.

All animals died within 24 hours of the first exposure (5.08 mg/l). In a second exposure (2.0 mg/l), four of five male rats died within 2 hours of exposure with the remaining six animals surviving for the 14-day observation period. Due to the high mortality in male rats, a third exposure was conducted at a target concentration of 1.0 mg/l, with two of five male rats dying immediately following exposure while the remaining eight animals survived the 14-day observation period.

Common gross necropsy findings for all rats exposed at the 5.08 mg/l dose level and to those dying at the 2.01 and 0.95 mg/l dose levels included dark red or mottled lungs and/or fluid filled trachea. Adverse clinical observations for surviving animals at the two lower exposure levels included dyspnea and decreased activity or hypoactivity immediately after exposure.

In conclusion, male rats appeared to be more sensitive than female rats to inhalation of the aerosolized test material, with the calculated LC₅₀ for males being 1.12 mg/l; for females, 2.01 - 5.08 mg/l (estimated), and for the combined sexes, 1.8 mg/l.

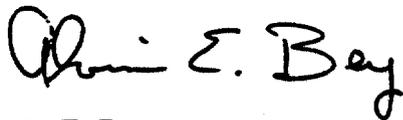
Actions:

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

U.S. Environmental Protection Agency
November 10, 1994
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If you require further information concerning this notification of substantial risk, please contact Dr. Rhys 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,

A handwritten signature in black ink that reads "Alvin E. Bey". The signature is written in a cursive style with a large initial "A" and a long, sweeping tail on the "y".

Alvin E. Bey
U.S. Area Vice-President
Corporate Director HES

**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: _____ Date: _____

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

DOW CORNING

ACUTE INHALATION TOXICITY STUDY OF DOW CORNING® X2-1731
VOLATILE FLUID IN RATS

Dow Corning Corporation
September 22, 1994

REPORT NO.: 1994-I0000-39581
FILE NO.: 8037
LOT NO.: PE062003
AUTHOR(S): IIT Research Institute
SUBMITTED BY: A. Hami
REVIEWED BY: Waheed H. Siddiqui
DEPARTMENT: Health and Environmental Sciences
STUDY MONITOR: Waheed H. Siddiqui
LOCATION: Midland, Michigan
DATE: September 22, 1994
TITLE: ACUTE INHALATION TOXICITY STUDY OF DOW CORNING® X2-1731
VOLATILE FLUID IN RATS

Contains No CBI

An acute aerosol inhalation toxicity study was conducted on Dow Corning® X2-1731 Volatile Fluid* in rats. The study was conducted using OECD testing guidelines, Part 403 and according to US EPA (TSCA) Good Laboratory Practice Standards, 40 CFR, Part 792, August 17, 1989.

The test material was aerosolized and administered for 4 hours by whole-body inhalation exposure to groups of five male and five female Fischer F344/N rats at target concentrations of 5.0, 2.0 or 1.0 mg/l, one concentration during each of three consecutive exposure periods. The actual exposure concentrations were 5.08, 2.01 and 0.95 mg/l, as determined gravimetrically by filter-collected aerosol samples. Aerosol particle sizes determined as mass median aerodynamic diameter (MMAD) were 0.27, 0.29, and 0.30 µm with geometric standard deviations (GSD) of 1.87, 2.22 and 3.58. All animals died within 24 hours of the first exposure. In a second exposure at a target concentration of 2.0 mg/l, four out of five male rats died within 2 hours of exposure with the remaining six animals surviving for the 14 day observation period. Due to the high mortality rate in male rats, a third exposure was conducted at a target concentration of 1.0 mg/l. Two out of five male rats died during or immediately following the third exposure, with the remaining eight animals surviving for the 14 day observation period.

Common gross necropsy findings for all rats exposed to 5.08 mg/l and to those dying at 2.01 and 0.95 mg/l included dark red or mottled lungs and/or fluid-filled trachea. Rats surviving the 2.01 and 0.95 mg/l exposures were normal upon scheduled necropsy. Adverse clinical observations for surviving animals at 2.01 and 0.95 mg/l included dyspnea and decreased activity or hypoactivity immediately after exposure. All surviving rats were virtually asymptomatic 24 hours after the exposures.

In conclusion, male rats appeared to be more sensitive than female rats to the inhalation of aerosolized Dow Corning® X2-1731 Volatile Fluid. The calculated LC₅₀ for male rats was 1.12 mg/l (95% CI: 0.26 to 4.84 mg/l), while the LC₅₀ for female rats could only be estimated to be greater than 2.01 and less than 5.08 mg/l. The LC₅₀ for male and female rats combined was 1.8 mg/l (95% CI: 0.81 to 4.01 mg/l).

* 3-Hexylheptamethyltrisiloxane

This report constitutes pages i-iii and pages 1-20, which include Tables 1-3, Appendix includes Protocol, Protocol Amendments, and Protocol Deviations.

Reviewed By: Waheed H. Siddiqui, Ph.D. Date: 9/16/94

Approved By: Robert G. Meeks, Ph.D., D.A.B.T. Date: 9/20/94
Toxicology Manager
Health and Environmental Sciences

Typed By:

Michelle L. Snook
Michelle L. Snook

PROPRIETARY

Contains No CBI

IITRI Project No.

L08500-1

Title

**ACUTE INHALATION TOXICITY STUDY OF DOW
CORNING® X2-1731 VOLATILE FLUID IN RATS**

Study Director

Richard D. Leonatti, B.S.

Aerosol Scientist

Narayanan Rajendran, Ph.D.

Report Date

September 1994

Type of Report

FINAL REPORT

Prepared By

**IIT Research Institute
Life Sciences Department
10 West 35th Street
Chicago, Illinois 60616-3799**

Prepared For

**Dow Corning Corporation
2200 West Salzburg Road
Midland, Michigan 48640**

Sponsor's Representative

Waheed H. Siddiqui, Ph.D.



COMMITMENT TO EXCELLENCE

INTRODUCTORY SUMMARY**PROPRIETARY****Major Study Milestones**

Study Initiation Date: January 11, 1994
Inhalation Exposures: January 24, February 17 and April 12, 1994
Completion of In-Life Phases: April 26, 1994

Study Participants

Richard D. Leonatti, B.S., Associate Biologist, Study Director
Narayanan Rajendran, Ph.D., Science Advisor, Aerosol Scientist
James M. Gerhart, Ph.D., D.A.B.T.; Senior Toxicologist
J. Brooks Harder, D.V.M., Veterinarian
Johnny Raymond, Senior Experimentalist
Ronald A. Boyne, Manager, Quality Assurance Unit

Summary

This report, entitled "Acute Inhalation Toxicity Study of Dow Corning® X2-1731 Volatile Fluid in Rats" (IITRI Project No. L08500-1), describes a study conducted for Dow Corning Corporation, 2200 West Salzburg Road, Midland, MI 48640. Dr. Waheed H. Siddiqui was the Sponsor's Representative. The study was conducted using OECD testing guidelines, Part 403 and according to US EPA (TSCA) Good Laboratory Practice Standards, 40 CFR Part 792, August 17, 1989.

The test substance, Dow Corning® X2-1731 Volatile Fluid, was aerosolized and administered for 4 hours by whole-body inhalation exposure to groups of five male and five female Fischer F344/N rats at target concentrations of 5.0, 2.0 or 1.0 mg/l, one concentration during each of three consecutive exposure periods. The actual exposure concentrations were 5.08, 2.01 and 0.95 mg/l, as determined gravimetrically by filter-collected aerosol samples. Aerosol particle sizes determined as mass median aerodynamic diameter (MMAD) were 0.27, 0.29 and 0.30 μm with geometric standard deviations (GSD) of 1.87, 2.22 and 3.58. After all animals died within 24 hours of the first exposure, the Sponsor requested a second exposure at a target concentration of 2.0 mg/l. Four out of five male rats died within 2 hours of this second exposure, with the remaining six animals surviving for the 14 day observation period. Due to the high mortality rate in male rats, a third exposure was requested by the Sponsor at a target concentration of 1.0 mg/l. Two out of five male rats died during or immediately following the third exposure, with the remaining eight animals surviving for the 14 day observation period.

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Common gross necropsy findings for all rats exposed to 5.08 mg/l and to those dying at 2.01 and 0.95 mg/l included dark red or mottled lungs and/or fluid-filled trachea. Rats surviving the 2.01 and 0.95 mg/l exposures were normal upon scheduled necropsy. Adverse clinical observations for surviving animals at 2.01 and 0.95 mg/l included dyspnea and decreased activity or hypoactivity immediately after exposure. All surviving rats were virtually asymptomatic 24 hours after the exposures.

In conclusion, male rats appeared to be more sensitive than female rats to the inhalation of aerosolized Dow Corning® X2-1731 Volatile Fluid. The calculated LC₅₀ for male rats was 1.12 mg/l (95% CI: 0.26 to 4.84 mg/l), while the LC₅₀ for female rats could only be estimated to be greater than 2.01 and less than 5.08 mg/l. The LC₅₀ for male and female rats combined was 1.8 mg/l (95% CI: 0.81 to 4.01 mg/l).

Submitted By:

Richard D. Leonatti 9-7-94

Richard D. Leonatti, B.S. Date
Associate Biologist
Study Director

Approved By:

Catherine Aranyi 9/7/94

Catherine Aranyi, M.S. Date
Manager of Research
Head, Inhalation Toxicology Program
Life Sciences Department

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GLP COMPLIANCE STATEMENT

PROPRIETARY

Study Title: Acute Inhalation Toxicity Study of Dow Corning®
X2-1731 Volatile Fluid in Rats

IITRI Project Number: L08500-1

Study Director: Richard D. Leonatti, B.S.

This study was conducted in accordance with U.S. Environmental Protection Agency (USEPA) Good Laboratory Practice (GLP) Standards as set forth in the Code of Federal Regulations (40 CFR Part 792). All analyses and attendant documentation pertaining to the characterization of the bulk test substance were the responsibility of the Sponsor. The raw data have been reviewed by the Study Director, who certifies that the information contained in this report represents an appropriate and accurate conclusion within the context of the study design and evaluation criteria.

All original raw data collected at IITRI are retained in the IITRI Archives, at 10 W. 35th Street, Chicago, IL 60616-3799, along with a copy of the final study report, for one year following the date of this report. Thereafter, the Sponsor will be consulted concerning their final disposition.

Study Director:

Richard D. Leonatti 9-7-94
Richard D. Leonatti, B.S. Date

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I. OBJECTIVE

The original objective of this study was to determine the acute toxicity (limit test) of Dow Corning® X2-1731 Volatile Fluid when administered as an aerosol by a single whole-body inhalation exposure at a concentration of 5 mg/l to male and female Fischer 344 rats. When the limit test resulted in 100% mortality, a second and third exposure at target concentrations of 2 mg/l and 1 mg/l, respectively, were conducted at the request of the Sponsor to estimate an LC₅₀ for this test substance.

II. MATERIALS AND METHODS

A. Test Substance

Identification:	Dow Corning® X2-1731 Volatile Fluid
Specific Gravity:	0.83 (@ 25°C)
Boiling Point:	Not Determined
Melting Point:	15°C
Flash Point:	79°C (Closed Cup)
Vapor Pressure:	< 5.0 mm Hg (@ 25°C)
Solubility in Water:	< 0.1%
Appearance:	Clear liquid

The test substance, Dow Corning® X2-1731 Volatile Fluid, Lot No. PEO 62003 (stripped), was received January 4, 1994. The test substance was stored in the original containers at room temperature (approximately 22°C). Determinations of stability, strength, purity and homogeneity of the bulk test substance and attendant documentation were the responsibility of the Sponsor. All remaining test substance will be returned to the Sponsor.

B. Test Atmosphere

Inhalation Exposure: Aerosols of Dow Corning® X2-1731 Volatile Fluid were introduced to a 500 liter stainless steel and glass Rochester-type inhalation exposure chamber for three separate single four-hour periods. The Rochester-type inhalation chambers are designed to produce spatially uniform test atmospheres. Conditioned room air, which was passed through coarse and HEPA filters before entering the exposure chamber, was used as supply air. Chamber exhaust was passed through a HEPA filter before being discharged to the outside environment. Chamber temperature and relative humidity were monitored with an electronic thermohygrometer (Cole-Parmer Co., Chicago, IL). The chamber airflow rate was monitored continuously with a calibrated Magnehelic differential pressure gauge (Dwyer Instruments, Michigan City, IN). Chamber

temperature, relative humidity and airflow rate were recorded at approximately 30-minute intervals during the exposures. The chamber oxygen concentration was measured three times during the exposures using a Lynn Model 6200 oxygen analyzer (Lynn Products Co., Lynn, MA).

Test Atmosphere Generation: The test atmosphere was generated by aerosolization of Dow Corning® X2-1731 Volatile Fluid using a Laskin nebulizer. The Laskin nebulizer was placed in a three-neck round bottom flask used as a reservoir for the test substance. Compressed air was passed through the nebulizer aspirating the test substance from the reservoir. The compressed air to the Laskin nebulizer was adjusted to generate aerosols at the required concentration levels in a consistent manner with particle sizes in the respirable range. The resulting aerosol was delivered to the exposure chamber via one-inch Tygon flexible tubing to establish consistent test atmospheres at the three target concentrations over the three four-hour exposure periods.

Test Atmosphere Monitoring: Aerosol mass concentration of Dow Corning® X2-1731 Volatile Fluid in the breathing zone of the rats was determined gravimetrically by filter samples collected once each hour during the exposures. The sampling train consisted of a pre-weighed filter in series with a dry-gas meter connected to a constant flow vacuum pump. The dry-gas meter measured the corresponding volume of chamber air sampled and the weight to volume ratio was determined. In addition, a real-time aerosol sensor was used to monitor exposure concentrations. This sensor was used only as a continuous indicator of short term changes in exposure concentration to guide laboratory personnel in correcting concentration excursions.

Aerosol Particle Size Distribution: Aerosol particle size was monitored in duplicate samples during each exposure with a Quartz Crystal Microbalance cascade impactor (California Measurements Inc., Sierra Madre, CA).

C. Animals and Animal Care

Animals: Male and female Fischer 344 (F344/N) rats approximately 6 weeks of age were purchased from Taconic Farms, Germantown, NY for use in this study. The first group of animals was received on January 13, 1994 and their body weight ranged from 110 g to 125 g (males) and 86 g to 93 g (females) the next day. An additional group of animals was received on February 10, 1994 and their body weight ranged from 118 g to 128 g (males) and 99 g to 104 g (females) the next day. A third group of animals was received on April 7, 1994, and their body weights ranged

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from 115 g to 129 g (males) and 115 g to 120 g (females) the next day. All three groups of animals were held in quarantine for approximately one week and were examined daily to ensure their health and suitability as test subjects. Rats selected for each of the exposures were identified by a uniquely numbered metal tag inserted through the pinna of the right ear and by a cage card.

Feed and Water: PMI Rodent Chow 5002 (Ralston Purina, St. Louis, MO) was provided *ad libitum*, except during the four-hour exposure period. City of Chicago municipal tap water was provided by means of an automatic watering system *ad libitum*, except during the four-hour exposure. No contaminants were known to be present in the food or water at levels which would interfere with the outcome of the study.

Environment: During the quarantine, exposure, and post-exposure observation periods, the rats were housed individually in suspended stainless steel cages. Neomycin-impregnated Deotized Animal Cage Boards® (Shepherd Specialty Papers, Kalamazoo, MI) were placed beneath the suspended cages to absorb liquids and retard the growth of ammonia-producing bacteria associated with animal feces and urine. The cage boards were removed during the exposure period. The animal room temperature and relative humidity ranged from 69 to 83°F and 26 to 56%, respectively, for the three groups of animals. Fluorescent lighting was provided automatically on a 12 hours light/12 hours dark schedule for all groups.

Assignment to Groups: The rats were randomly assigned to each exposure group by use of a computerized body weight stratification procedure.

Experimental Design: At each concentration level, a group of 5 rats/sex was exposed to an aerosol of Dow Corning® X2-1731 Volatile Fluid for a single four-hour period. Rats surviving the exposure period were observed for 14 days. The 5.08 mg/l, 2.01 mg/l and 0.95 mg/l exposures were conducted on January 24, February 17 and April 12, 1994, respectively.

D. Toxicology and Necropsy Endpoints

Mortality and Clinical Observations: The conditions of the exposure rendered observation of the animals for clinical signs impossible during the exposure period. All rats were observed for mortality and adverse clinical signs within 30 minutes after the termination of exposure. Surviving rats were then observed for 14 consecutive days.

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Body Weights: All rats were weighed upon arrival, at randomization, and immediately before exposure. All surviving rats were weighed seven and 14 days following the exposure.

Necropsy: All dead animals were subjected to gross necropsy immediately after death. At the end of the observation period, surviving animals were administered an intraperitoneal injection of sodium pentobarbital, euthanized by exsanguination and then subjected to gross necropsy. Gross necropsy included examination of all body surfaces and openings and of the external surface of the brain, heart, lungs and respiratory tract, liver, kidneys, gastrointestinal tract, and urinary bladder. The gastrointestinal tract and urinary bladder were opened and examined for lesions.

III. RESULTS

A. Test Atmosphere

Aerosol mass concentration and particle size distribution data determined from individual samples are provided in Table 1 of Section VI. The mean aerosol mass concentrations and particle size distributions for the three exposures are listed below:

Target Conc., mg/l	Actual Exposure Conc., mg/l		Particle Size Distribution	
	Mean \pm SD	N	MMAD, μ m	GSD
5.0	5.08 \pm 0.51	5	0.27	1.87
2.0	2.01 \pm 0.09	4	0.29	2.22
1.0	0.95 \pm 0.07	4	0.30	3.58

The aerosol mass concentrations at 5.08, 2.01 and 0.95 mg/l determined gravimetrically from filter samples collected at least once per hour during the exposure period were very close to the target concentrations. The nominal concentrations (ratio of total test substance to cumulative airflow volume used during the exposure) for the three exposures were 7.20, 2.55 and 1.77 mg/l, respectively. It must be noted that, because of the aerosol depositional losses in the generation system, the nominal concentration is an accurate indicator of test substance usage only and not of the actual exposure concentration.

Aerosol particle size distribution measured in duplicate samples during each exposure period with a Quartz Crystal Microbalance-based Cascade

Impactor resulted in mass median aerodynamic diameter (MMAD) values of 0.27, 0.29 and 0.30 μm with geometric standard deviations (GSD) of 1.87, 2.22 and 3.58 for the exposures conducted at 5.08, 2.01 and 0.95 mg/l, respectively.

The exposure chamber conditions for the three exposures shown below are presented as mean values (ranges are also presented for temperature and % relative humidity). The oxygen level in the chamber during the three exposures was 21%.

Target Conc., mg/l	Temp. °F	Rel. Hum. %	Airflow l/min
5.0	76 (76-77)	31 (30-35)	118
2.0	75 (74-75)	39 (35-42)	134
1.0	72 (N.V.) ^a	42 (38-44)	134

^a N.V.: No Variability

B. Toxicology Endpoints

Mortality: Exposure group mortality rates and LC₅₀ values with their 95% confidence intervals are summarized below. (Data for individual rats are shown in Table 2 of Section VI.)

Exposure Conc., mg/l	Mortality Incidences		
	Male Rats	Female Rats	Combined
5.08	5/5	5/5	10/10
2.01	4/5	0/5	4/10
0.95	2/5	0/5	2/10
Male Rat LC ₅₀ [*]	= 1.12 mg/l (0.26 to 4.84 mg/l)		
Female Rat LC ₅₀ ^{**}	= estimated to be greater than 2.01 and less than 5.08 mg/l		
Combined LC ₅₀	= 1.8 mg/l (0.81 to 4.01 mg/l)		

* Miller and Tainter. *Proc. Soc. Exp. Bio. Med.* 57:261-264, 1944.
 ** Probit values are undefined for mortality rates of 0 and 100%; therefore, the LC₅₀ for female rats can only be estimated from these data.

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Clinical Observations: Clinical observations summarized in Table 3 of Section VI were all obtained on the day of the exposures. The conditions of the exposure rendered observation of the animals for clinical signs impossible during the exposure period. No further adverse clinical signs were seen during the remaining 14-day periods. Clinical observations consisted of dyspnea, rough coat, and hypoactivity for the 5.08 mg/l exposure group; dyspnea, prostration, closed eyes, spasmodic twitching, decreased activity, and red material around the nose for the 2.01 mg/l exposure group; and dyspnea, closed eyes, decreased activity, and red material around the nose for the 0.95 mg/l exposure group.

Body Weights: Individual body weight data are also summarized in Table 2 of Section VI. All surviving rats gained weight during the study.

Gross Pathology: Gross necropsy findings are also summarized in Table 2 of Section VI. These consisted of mottled red lungs, dark red lungs and trachea filled with red fluid for the 5.08 mg/l exposure group; dark red lungs and trachea filled with red fluid for the 2.01 mg/l exposure group; and dark red lung and trachea filled with red fluid for the 0.95 mg/l exposure group .

IV. CONCLUSION

All rats died within 24 hours following a single four-hour inhalation exposure to the 5.08 mg/l of the aerosolized test substance. Four out of five male rats died within 2 hours of a single four-hour exposure to 2.01 mg/l of the test aerosol, all other animals in this group survived the 14 day observation period. Two out of five male rats died during or immediately after the four-hour inhalation exposure to 0.95 mg/l of the aerosol, all other rats survived. Using the method of Miller and Tainter (*Proc. Soc. Exp. Bio. Med.* 57:261-264, 1944), the calculated LC_{50} for male rats was 1.12 mg/l (95% CI: 0.26 to 4.84 mg/l), while the LC_{50} for female rats could not be made due to two exposure groups having a zero mortality incidence. The LC_{50} for female rats was estimated, however, to be greater than 2.01 and less than 5.08 mg/l. The LC_{50} for male and female rats combined was 1.8 mg/l (95% CI: 0.81 to 4.01 mg/l).

VI. TABLES

TABLE 1

PROPRIETARY

**INDIVIDUAL EXPOSURE CONCENTRATION AND
PARTICLE SIZE DISTRIBUTION DATA**

Target Conc., mg/l	Sample Number	Filter-Collected Aerosol Mass, mg	Sample Volume l	Aerosol Mass Concentration mg/l	Particle Size Distribution ^a	
					MMAD, μ m	GSD
5.0	1	55.40	11.724	4.73	0.26	1.78
	2	62.09	12.744	4.87	0.27	1.95
	3	75.85	12.999	5.84		
	4	71.67	13.452	5.33		
	5	62.07	13.452	4.61		
2.0	1	28.28	14.726	1.92	0.32	2.11
	2	31.44	15.519	2.03	0.26	2.32
	3	33.75	15.916	2.12		
	4	30.98	15.888	1.95		
1.0	1	22.05	26.338	0.84	0.35	2.69
	2	23.57	23.364	1.01	0.24	4.48
	3	22.53	23.562	0.96		
	4	22.70	23.392	0.97		

^a MMAD: Mass Median Aerodynamic Diameter; GSD: Geometric Standard Deviation

PROPRIETARY

TABLE 2

Body Weight, Disposition and Gross Necropsy Observation Summary for Male and Female Rats after Inhalation Exposure to a Test Atmosphere Generated from X2-1731 Volatile Fluid

Exposure Concentration (mg/l)	Animal Number	Sex	Body Weight, g				Disposition	Gross Necropsy Observations
			Day 0	Day 7	Day 14	Day 14		
5.08	121	M	179	--	--	--	Lungs mottled red Trachea filled with red fluid	
	122	M	192	-- ^a	--	--	Lungs mottled red Trachea filled with red fluid	
	123	M	172	-- ^a	--	--	Lungs mottled red Trachea filled with red fluid	
	124	M	179	-- ^a	--	--	Lungs mottled red Trachea contained red fluid	
	125	M	171	-- ^a	--	--	Lungs mottled red Trachea contained red fluid	
	126	F	115	-- ^a	--	--	Lungs mottled red	
	127	F	111	--	--	--	Lungs dark red	
	128	F	121	--	--	--	Lungs mottled red Trachea filled with red fluid	
	129	F	120	-- ^a	--	--	Lungs mottled red	
	130	F	121	--	--	--	Lungs mottled red Trachea filled with red fluid	

^a Died during or immediately after exposure period on day 0; therefore, no post exposure clinical observations.

PROPRIETARY

TABLE 2 (continued)

Body Weight, Disposition and Gross Necropsy Observation Summary for Male and Female Rats after Inhalation Exposure to a Test Atmosphere Generated from X2-1731 Volatile Fluid

Exposure Concentration (mg/l)	Animal Number	Sex	Body Weight, g				Disposition	Gross Necropsy Observations
			Day 0	Day 7	Day 14	Day 14		
2.01	141	M	161	-- ^a	--	--	Lungs dark red Trachea contained red fluid	
	142	M	163	--	--	--	Lungs dark red Trachea filled with red fluid	
	143	M	149	--	--	--	Lungs dark red Trachea filled with red fluid	
	144	M	159	179	211	SAC ^b	None	
	145	M	158	--	--	--	Lungs dark red Trachea filled with red fluid	
	146	F	121	130	140	SAC	None	
	147	F	110	120	132	SAC	None	
	148	F	119	127	138	SAC	None	
	149	F	121	126	137	SAC	None	
	150	F	126	132	144	SAC	None	

^a Died during or immediately after exposure period; therefore, no post exposure clinical observations.

^b SAC = Scheduled sacrifice after 14-day observation period.

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TABLE 2 (continued)

Body Weight, Disposition and Gross Necropsy Observation Summary for Male and Female Rats after Inhalation Exposure to a Test Atmosphere Generated from X2-1731 Volatile Fluid

Exposure Concentration (mg/l)	Animal Number	Sex	Body Weight, g				Disposition	Gross Necropsy Observations
			Day 0	Day 7	Day 14	Day 14		
0.95	181	M	145	174	193	SAC ^b	None	
	182	M	146	181	201	SAC	None	
	183	M	144	-- ^a	--	--	Lungs dark red Trachea filled with red fluid	
	184	M	146	175	199	SAC	None	
	185	M	147	-- ^a	--	--	Lungs dark red Trachea filled with red fluid	
	186	F	128	142	148	SAC	None	
	187	F	124	142	147	SAC	None	
	188	F	122	145	152	SAC	None	
	189	F	128	141	147	SAC	None	
	190	F	128	141	149	SAC	None	

^a Died during or immediately after exposure period on day 0; therefore, no post exposure clinical observations.

^b SAC = Scheduled sacrifice after 14-day observation period.

TABLE 3

PROPRIETARY

SUMMARY OF CLINICAL OBSERVATIONS
(5 rats/sex)

Exposure Concentration (mg/l)	Clinical Observation ^a	M	F
5.08	Rough coat	0	3
	Dyspnea	1	3
	Hypoactive	1	3
2.01	Dyspnea	4	5
	Prostrate	2	0
	Red material around nose	1	0
	Closed eyes	2	4
	Spasmodic twitching	2	0
	Decreased activity	4	5
0.95	Dyspnea	3	5
	Closed eyes	3	5
	Red material around the nose	3	0
	Decreased activity	3	5

^a All observations were made within 30 min. after completion of the inhalation exposure.

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APPENDIX

Protocol, Protocol Amendments, Protocol Deviation

PROTOCOL

PROPRIETARY

1. **Title:** Acute Inhalation Toxicity Study of Dow Corning[®]
X2-1731 Volatile Fluids in Rats (Limit Test)
2. **Sponsor:** Dow Corning Corporation
2200 West Salzburg Road
Midland, Michigan 48640
3. **Testing Facility:** IIT Research Institute
10 West 35th Street
Chicago, Illinois 60616
4. **Objective:** The objective of the study is to determine the acute inhalation toxicity of the test substance by exposing the animals to a concentration of 5 mg/l or the highest attainable concentration, if less than 5 mg/l, in a limit test.
5. **Duration:** The minimum duration of the study will be 15 days.
6. **Protocol Approval:** This protocol complies with specific requirements of the Sponsor.
 - a. **Study Director:** Richard D. Leonatti Date: 1-11-94
Richard Leonatti, B.S.
 - b. **Study Toxicologist:** James Gerhart Date: 1-11-94
James Gerhart, Ph.D., D.A.B.T.
 - c. **Aerosol Scientist:** Narayanan Rajendran Date: 1/11/94
Narayanan Rajendran, Ph.D.
 - d. **Manager of Research, Inhalation Toxicology:** Catherine Aranyi Date: 1/11/94
Catherine Aranyi, M.S.
 - e. **Sponsor's Representative:** Waheed H. Siddiqui Date: 1/14/94
Waheed H. Siddiqui, Ph.D.

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The information in this protocol shall not be disclosed outside the Client's organization and shall not be duplicated, used, or disclosed for any purpose other than to evaluate the protocol.

1 9 9 PROPRIETARY 8 1

7. Proposed Study Schedule:

- a. Animal Receipt: January 13, 1994
- b. Inhalation Exposure: January 24, 1994
- c. Completion of In-Life Phase: February 7, 1994
- d. Completion of Draft Final Report: March 25, 1994

8. Test Substance:

- a. Identification: The test substance, Dow Corning[®] X2-1731 Volatile Fluids, is a combustible liquid with a flash point of 79°C. The Lot No. is PEO 62003 (stripped). The expiration date of the test substance is January 1995. The composition, purity, stability, and method of synthesis, fabrication, and/or derivation of the test substance will be documented by the Sponsor before its use in the study. This documentation will be maintained by the Sponsor at the address indicated in Section 2 of this protocol.
- b. Handling and Personnel Hazards: Personnel will wear a laboratory smock and eye protection when working with the test substance. Appropriate protective measures will be implemented because of the flammable nature of the test substance.
- c. Assay: The Sponsor will be responsible for all necessary analyses on the bulk test substance and the attendant documentation.
- d. Storage: The test substance will be stored in a closed container at room temperature.
- e. Disposition: All quantities of test substance which are used will be documented. At the time of the acceptance of the final report by the Sponsor, arrangements will be made for the return of residual test substance to the Sponsor. If the Sponsor so requests, IITRI will make arrangements for the proper disposal of the residual test substance. The costs of return or disposal will be borne by the Sponsor. IITRI will not be required to retain any samples. Reserve samples will be retained by the Sponsor.

9. Test System:

- a. Model: Male and female Fischer 344 (F344/N, Taconic Farms, Germantown, NY) rats will be used in this study. The animals will be 34-45 days old at receipt. The body weight variation of the rats at the initiation of the study will not exceed $\pm 20\%$ of the mean weight for each sex.
- b. Selection Justification: The laboratory rat is a model widely used in toxicity testing. A significant body of experience with this animal exists against which its reaction to the test substance can be evaluated.
- c. Housing: Animals will be singly housed in stainless steel cages suspended over dectized cage boards. The cages will be equipped with water bottles or automatic watering.

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- d. **Cleaning and Sanitation:** Animal rooms and cages will be cleaned and sanitized before animals are introduced into them, and periodically thereafter in accordance with accepted animal care practice.
 - e. **Food:** PMI Rodent Diet No. 5002 (Purina Mills, Inc., St. Louis, MO) will be provided *ad libitum*, except during inhalation exposure. Neither the Study Director nor the Sponsor Representative is aware of any potential contaminants likely to be present in the certified diet at levels which would interfere with the results of this study.
 - f. **Water:** Tap water will be provided *ad libitum* except during inhalation exposure.
 - g. **Environmental Controls:** Animal rooms will be lighted with fluorescent lights and maintained on a 12-hour light/12-hour dark regimen. Room temperature and relative humidity will be recorded daily and, to the maximum extent possible, will be maintained between 66 and 77°F and 30 to 70% RH.
 - h. **Quarantine:** The rats will be held in quarantine for approximately one week prior to use. During the quarantine period the animals will be observed at least once daily. At the end of the quarantine period the animals will undergo a physical examination to ensure their suitability for use.
 - i. **Animal Identification and Group Assignments:** Animals selected for the study will be assigned a permanent identification number tag which will be inserted through the pinna of either ear. The identification numbers will be unique for this study. Animals will be randomly assigned to the exposure group by computer program.
10. **Inhalation Exposure Methods:**
- a. **Test Atmosphere Generation:** The generation system will consist of suitable spray and/or evaporation devices to generate the test atmosphere with filtered, compressed air. The output of the generator will be appropriately treated for removal of any coarse particles, if they are present. Details of test atmosphere generation methods will be documented in the study records and the final report.
 - b. **Test Atmosphere Monitoring:** Test atmosphere concentration in the breathing zone of the rats will be determined at least once per hour during the four-hour inhalation exposure period. For atmospheres containing aerosols, samples will be collected on a pre-weighed filter (placed in a plastic filter holder) using a constant flow rate provided by an appropriate vacuum pump. A dry gas meter connected to the pump will be used to measure the corresponding total volume of chamber air sampled. In accordance with instruction from the sponsor, the test atmosphere will not be analyzed for the potential presence of vapor-phase compounds. Details of all monitoring methods will be documented in the study records.

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- c. **Aerosol Particle Size:** Aerosol particle size distribution will be determined at least once during the four-hour exposure. A Quartz Crystal Microbalance (QCM) based cascade impactor (California Measurements, Sierra Madre, CA) will be used for these determinations.
- d. **Exposure Chambers:** The exposures will be conducted in a 0.25 m³ or 0.5 m³ stainless steel and glass inhalation chamber. During exposure the animals will be individually housed in stainless steel wire mesh cages. Temperature, relative humidity, airflow rate, and oxygen level within the chamber will be recorded at approximate one-hour intervals during the exposure. To the maximum extent possible, the chamber atmosphere temperature and relative humidity will be maintained between 68 and 75°F and 30 to 70% RH, respectively. Airflow rate may be adjusted as a means of controlling test atmosphere concentration, but enough air changes will be provided to maintain a safe oxygen level (at least 19%) for the animals.

11. Experimental Design:

- a. **Exposure Route Justification:** Inhalation of the test substance is a potential route of human exposure. This inhalation exposure study has been designed to simulate a worst-case exposure concentration.
- b. **Exposure Groups:** One group of 5 male and 5 female rats will be exposed for 4 hours to an atmosphere of the test substance at a target concentration of 5 mg/l or the highest attainable concentration, if less than 5 mg/l.
- c. **Mortality and Clinical Observations:** The animals will be observed during the exposure (to the extent possible), immediately after the exposure and at least once daily during a 14-day post-exposure observation period for signs of toxicity. All signs of altered behavior, changes in coat condition, unusual discharge of body fluid, lesions, or other relevant observations will be recorded. Animals found dead will be removed for gross necropsy.
- d. **Body Weight:** Body weights will be determined immediately before exposure, approximately seven days post-exposure, and just before necropsy.
- e. **Necropsy:** All exposed animals which die on test will be subjected to a gross necropsy, regardless of autolytic state. All exposed animals still alive at the termination of the observation period will be euthanized by intraperitoneal injection of sodium pentobarbital and subjected to a gross necropsy. The necropsy will include examination of all body surfaces and openings, the external appearance of brain, heart, liver, kidneys, lungs, gastrointestinal tract and the urinary bladder. The gastrointestinal tract and the urinary bladder will be opened and examined if lesions are present. A pathologist will be available for consultation during the necropsies.

12. Results:

Mortality, clinical observations, body weights, necropsy results, and other appropriate data will be tabulated and presented in a formal written report.

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1994-10000-39581

13. **Data Notebooks:**

a. **Contents:** All original data obtained at IITRI will be maintained in notebooks and will include but not necessarily be limited to the following:

- (1) Original signed protocol and all amendments.
- (2) Test substance information.
- (3) Animal receipt and identification records.
- (4) Inhalation exposure records.
- (5) Body weight and observation records.
- (6) Gross necropsy records.

b. **Storage:** All original data generated at IITRI and a copy of the final report will be retained in the IITRI Archives (located at 10 West 35th Street, Chicago, IL 60616) for one year after the submission of the signed final report. At that time, the Sponsor will be contacted in order to determine the final disposition of the raw data and will be responsible for all costs associated with continued storage of the raw data in the IITRI Archives or for the shipment of these materials to a new storage facility. IITRI's Quality Assurance Unit will maintain a complete record of the disposition of all raw data.

14. **Final Reports:**

One copy of a draft report will be submitted to the Sponsor for review. After receipt and review of the Sponsor's comments, appropriate changes will be made and two copies of a signed Final Report, including one bearing the original signature pages, will be provided to the Sponsor.

15. **Personnel:**

Curricula vitae for all personnel involved in the study are on file at IITRI.

16. **Regulatory References:**

- a. **Test Guidelines:** This study will be conducted in compliance with the requirements outlined in the O.E.C.D. Guidelines for Testing of Chemicals, "Acute Inhalation Toxicity", Section 4, No. 403, adopted May 12, 1981.
- b. **GLP Compliance:** The study will be conducted in compliance with EPA (TSCA) Good Laboratory Practice Standards (Title 40 CFR Part 792). The study will be performed according to the requirements of the protocol and the relevant IITRI Standard Operating Procedures in effect at that time. The IITRI Quality Assurance Unit will inspect critical phases of the study as required.

17. **Changes of the Protocol:**

No changes of the protocol will be made without the consent of the Sponsor. All changes to the protocol will be signed and dated by the Study Director and maintained with the protocol.

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In the event that the Sponsor authorizes a protocol change verbally, the change will be honored by IITRI and will be followed up with written verification.

18. Facilities Management/Animal Husbandry:

Currently acceptable practices of good animal husbandry will be followed, e.g., Guide for the Care and Use of Laboratory Animals; DHHS Publication No. (NIH) 85-23, Revised 1985.

19. Humane Treatment Statement:

I have reviewed the protocol for this study and have found that the study design will minimize pain or distress by the test animals within the objectives of the study. If anesthetic, analgesic, or tranquilizer drugs can be used, they are the proper type for the given species. If euthanasia is to be performed, the method is proper for the given species.

J. B. Harder
J. B. Harder, D.V.M.,
Clinical Veterinarian, IITRI

DATE: 1-25-94

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The information in this protocol shall not be disclosed outside the Client's organization and shall not be duplicated, used, or disclosed for any purpose other than to evaluate the protocol.

26.

PROTOCOL AMENDMENT *No.* PROPRIETARY

Study: Acute Inhalation Toxicity Study of Dow Corning X2-1731
Volatile Fluids in Rats (Limit Test)

Amendment No: 1
Date Effective: February 8, 1994

Reason for Amendment: Due to significant deaths in the initial limit study at 5.0 mg/l, the Sponsor requested the testing of an additional concentration, that of 2.0 mg/l. The following reflects the addition of this group to the main protocol.

<u>Section</u>	<u>Addition or Modification</u>
1. Title:	Acute Inhalation Toxicity Study of Dow Corning X2-1731 Volatile Fluids in Rats
4. Objective:	A second exposure concentration of 2.0 mg/l will also be evaluated.
7a. Animal Receipt:	February 10, 1994
7b. Inhalation Exposure:	February 17, 1994
7c. Completion of In-life Phase:	March 3, 1994
11b. Exposure Groups:	A second group of equal size will be exposed to a target concentration of 2.0 mg/l.

Reason for Amendment: Protocol clarification.

<u>Section</u>	<u>Addition or Modification</u>
9a. Model:	The weight range of animals upon receipt will be approximately 100 ± 25 g.

PROTOCOL AMENDMENT (cont'd)

Study: Acute Inhalation Toxicity Study of Dow Corning X2-1731
Volatile Fluids in Rats (Limit Test)

Amendment No: 1

Approval:

- a. Study Director: Richard D. Leonatti Date 2-15-94
Rick Leonatti, BS
- b. Study Toxicologist: James M. Gerhart Date: 2-15-94
James M. Gerhart, PhD, DABT
- c. Aerosol Scientist: Narayanan Rajendran Date 2/15/94
Narayanan Rajendran, PhD
- d. Manager of Research,
Inhalation Toxicology: Catherine Aranyi Date: 2/15/94
Catherine Aranyi, MS
- e. Sponsor's
Representative: Waheed H. Siddiqui Date 2/17/94
Waheed H. Siddiqui, PhD

PROTOCOL AMENDMENT

PROPRIETARY

IITRI Project No. L08500 Study No. 1

Study Title: Acute Inhalation Toxicity Study of Dow Corning X2-1731 Volatile Fluids in Rats

Amendment No.: 2

Date Effective: April 6, 1994

Reason for Amendment: Due to significant deaths of male rats at 2.01 mg/l, the Sponsor requested the testing of an additional concentration, that of 1.0 mg/l. The following reflects the addition of this group to the main protocol.

<u>Section</u>	<u>Addition or Modification</u>
4. Objective:	A third exposure concentration of 1.0 mg/l will also be evaluated.
7a. Animal Receipt:	April 7, 1994
7b. Inhalation Exposure:	April 15, 1994
7c. Completion of In-life Phase:	April 27, 1994 12 24 4-7-94 26
11b. Exposure Groups:	A third group of equal size will be exposed to a target concentration of 1.0 mg/l.

APPROVAL

a. Study Director: Richard D. Leonatti Date: 4/6/94
Richard Leonatti, BS

b. Study Toxicologist: James Gerhart Date: 4/13/94
James Gerhart, PhD, DABT

c. Aerosol Scientist: Narayanan Rajendran Date: 4/6/94
Narayanan Rajendran, PhD

d. Manager of Research Inhalation Toxicology: Catherine Aranyi Date: 4/6/94
Catherine Aranyi, MS

e. Sponsor's Representative: Waheed Siddiqui Date: 4/11/94
Waheed Siddiqui, PhD

PROPRIETARY

IITRI Project No. : L08500

Study No. : 1

Study Title : Acute Inhalation Toxicity Study of Dow Corning® X2-1731 Volatile Fluids in Rats

Date Effective : August 24, 1994

Reasons for Amendment: To calculate LC₅₀ values and modify the study title as requested by Sponsor

Section	Addition or Modification
1. Title	Acute Inhalation Toxicity Study of Dow Corning® X2-1731 Volatile Fluid in Rats
4. Objective	Data from the three exposures will be combined to calculate LC ₅₀ values.

Approval:

- a. Study Director: Richard D. Leonatti Date: 8-24-94
Richard Leonatti, B.S.
- b. Study Toxicologist: James Gerhart Date: 8.26.94
James Gerhart, Ph.D., D.A.B.T.
- c. Aerosol Scientist: N. Rajendran Date: 8-24-94
Narayanan Rajendran, Ph.D.
- d. Manager of Research, Inhalation Toxicology: Catherine Aranyi Date: 8/24/94
Catherine Aranyi, M.S.
- e. Sponsor's Representative: Waheed H. Siddiqui Date: 31 Aug. 1994.
Waheed H. Siddiqui, Ph.D. *Ph.D. D.A.B.T.*

PROPRIETARY
Page 1 of 1

Project No. L08500-1

PROTOCOL DEVIATION NO.1

STUDY TITLE: Acute Inhalation Toxicity Study of Dow Corning® X2-1731
Volatile Fluids in Rats

DATE(S): January 20, 22, 1994
February 25, 1994
April 16, 17, 25, 1994

PROTOCOL SECTIONS: 9.g. - Environmental Controls

s/s = should be

(1) (RE) RL 8-24-94 s/s afternoon

DESCRIPTION OF DEVIATION: The animal room temperature on the morning of 1/20/94 was 81 °F. Facility operations was notified and temperature returned within limits by that afternoon. The relative humidity (RH) was recorded at 29% on 1/22/94 in the morning. The next day, the RH was back within limit. The relative humidity was recorded at 29% on 2/25/94 in the afternoon. Facility operations was notified that day. The RH returned to normal in the ~~morning~~ ^{morning} of 2/26/94. Relative humidity was at 26% and 27% on 4/16 and 4/17/94, respectively. Facility operations was notified each day. The RH returned to normal in the morning of 4/18/94. The temperature was recorded at 83 °F, above the specified limit on 4/25/94. Facility operations was notified that morning and the temperature returned within limits that afternoon. These deviations were due to temperature and humidity fluctuations in the outside environment which could be corrected by facility operations by their adjusting of their environmental control equipment.

IMPACT ON STUDY: The deviations are not expected to have affected the results of the study.

Richard D. Leonatti

Richard D. Leonatti
Study Director

6-7-94

Date



DOW CORNING

Contains No CBI

August 22, 1994

To: Board of Directors
Silicone Environmental, Health and Safety Council
(SEHSC)

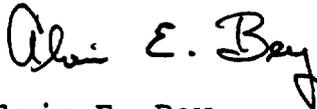
Re: TSCA Section 8(e) Notification of Substantial Risk
1,1,1,3,5,5,5-Heptamethyl-3-hexyltrisiloxane

Dear Sir/Madam:

Dow Corning Corporation is submitting the enclosed document to the United States Environmental Protection Agency under Section 8(e) of the Toxic Substances Control Act (TSCA). This courtesy copy is being provided to you and other members of the Silicone Environmental, Health and Safety Council for your awareness.

Dow Corning will continue its investigation of this situation. Naturally, we will inform you and other members of the Silicone Environmental, Health and Safety Council of any relevant significant new information which may be developed.

Sincerely,



Alvin E. Bey
U.S. Area Vice-President
Corporate Director HES

RGD94168.WP



DOW CORNING(R) 2-1731 VOLATILE FLUID

SECTION 1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Dow Corning Corporation	24 Hour Emergency Telephone:	(517) 496-5900
South Saginaw Road	Product Information:	(517) 496-6000
Midland, Michigan 48686	Product Disposal Information:	(517) 496-5813
	Transportation Information:	(517) 496-8577
	CHEMTREC:	(800) 424-9300

MSDS No: 2162661 Print Date: 03/28/95 Last Revised: 03/01/94

Generic Description: Organofunctional Siloxane
Physical Form: Liquid
Color: Colorless
Odor: Some odor
NFPA Profile: Health NA Flammability 2 Reactivity 0

Note: NFPA = National Fire Protection Association

SECTION 2. HAZARDOUS COMPONENTS

CAS Number	Wt%	Component	Exposure Limits
001873901	100	3-Hexylheptamethyltri-siloxane	None established.

Comments: The above ingredients are hazardous as defined in 29 CFR 1910.1200.

SECTION 3. EFFECTS OF OVEREXPOSURE

Acute Effects

Eye: Direct eye contact may cause temporary discomfort with mild redness and dryness similar to windburn.

Skin: A single prolonged exposure (24 to 48 hours) causes no known adverse effect.

Inhalation: No irritation to eyes and respiratory passages. No injury is likely from relatively short exposures of less than 8 hours.

Oral: Small amounts transferred to the mouth by fingers during use, etc., should not injure. Swallowing large amounts may cause digestive discomfort.

Repeated Exposure Effects

Skin: None Known.

DOW CORNING CORPORATION
MATERIAL SAFETY DATA SHEET

Page 2

DOW CORNING(R) 2-1731 VOLATILE FLUID

| Inhalation: None Known.

| Oral: None Known.

| Special Hazards

| This material contains the following components with the special hazards listed below.

| Carcinogens

| None Known

| Teratogens

| None Known

| Mutagens

| None Known

| Reproductive Toxins

| None Known

| Sensitizers

| None Known

| Comments: Please read the additional information below.

| The above listed potential effects of overexposure are based on actual data, results of studies performed upon similar compositions component data and/or expert review of the product.

+-----+
| SECTION 4. FIRST AID MEASURES
+-----+

| Eye: Immediately flush with water.

| Skin: No first aid should be needed.

| Inhalation: No first aid should be needed.

| Oral: No first aid should be needed.

| Comments: Treat symptomatically.

+-----+
| SECTION 5. FIRE FIGHTING MEASURES
+-----+

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Flash Point (Method): 174.99 DEGREE F / 79.44 DEGREE C
Autoignition Temperature: Not Determined
Flammability Limits in Air: Not Determined
Extinguishing Media: Carbon dioxide (CO2). Water. Water fog (or spray). Dry chemical. Foam.
Unsuitable Extinguishing Media: None
Fire Fighting Procedures: Self-contained breathing apparatus and protective clothing should be worn in fighting fires involving chemicals. Heat exposure pressurizes closed containers. Cool with water spray. If large amount is involved, evacuate area.
Unusual Fire Hazards: Vapors are heavier than air and can travel along ground to remote ignition sources. Static electricity may accumulate and ignite vapors. Prevent a possible fire hazard by suitable means, such as, bonding and grounding, inert gas purge, vapor dilution, and the like.
Hazardous Decomposition Products: Formaldehyde. Carbon oxides and traces of incompletely burned carbon compounds. Silicon dioxide.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Containment/Clean-up: Disposal of collected product, residues, and cleanup materials may be governmentally regulated. Observe all applicable local, state, and federal waste management regulations. Remove possible ignition sources and if needed, use nonsparking tools and equipment. To prevent possible spontaneous combustion, store rags, mops, absorbent, etc., used during cleanup only in appropriate containers or covered with water. Determine whether to evacuate or isolate the area depending on such specific factors as site location, population density, traffic flow, size of the release or spill, weather conditions, the material's hazards and risks to people, and whether a fire is underway or possible. Mop up, or wipe up, or soak up with absorbent and contain for salvage or disposal. For large spills, provide diking or other appropriate containment to keep material from spreading. Clean any remaining slippery surfaces by appropriate techniques, such as: several moppings or swabbings with appropriate solvents; washing with mild, caustic detergents or solutions; or high pressure steam for large areas. For nonsilicones, use typical industrial cleaning materials. Observe any safety precautions applicable to the cleaning material being used.

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Observe all personal protection equipment recommendations described in Sections 5 and 8. Local, state, and federal reporting requirements may apply to spills or releases of this material into the environment. See applicable regulatory compliance information in Section 15.

NOTE: See Section 8 for Personal Protective Equipment for Spills

SECTION 7. HANDLING AND STORAGE

Handling: No special precautions.

Storage: Keep container closed and away from heat, sparks, and open flame.

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Engineering Controls

Local exhaust: None should be needed

General Ventilation: Recommended

Personal Protective Equipment For Routine Handling

Eyes: Use proper protection - safety glasses as a minimum.

Skin: Washing at mealtime and end of shift is adequate.

Suitable Gloves: No special protection needed.

Inhalation: No respiratory protection should be needed.

Suitable Respirator: None should be needed.

Personal Protective Equipment For Spills

Eye: Use proper protection - safety glasses as a minimum.

Skin: Washing at mealtime and end of shift is adequate.

Inhalation/
Suitable Respirator: No respiratory protection should be needed.

Precautionary Measures: Avoid eye contact. Use reasonable care.

Comments: None

DOW CORNING(R) 2-1731 VOLATILE FLUID

|Note: These precautions are for room temperature handling. Use at elevated temperature, or aerosol/spray applications, may require added precautions.

|SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Physical form: Liquid
Color: Colorless
Odor: Some odor
Specific Gravity @ 25C: 0.83
Viscosity: 1.00 CST
Freezing/Melting Point: Not Applicable.
Boiling Point: Not Determined.
Vapor Pressure @ 25C: Not Determined.
Vapor Density: Not Determined.
Solubility in Water: None.
pH: Not Applicable.
Volatile content (Wt%): Not Determined.

|Note: The above information is not intended for use in preparing product specifications. Contact Dow Corning before writing specifications.

|SECTION 10. STABILITY AND REACTIVITY

|Chemical Stability: Stable.

|Hazardous Polymerization: Hazardous polymerization will not occur.

|Conditions to Avoid: None.

|Materials to Avoid: Oxidizing material can cause a reaction.

|Comments: None

|SECTION 11. TOXICOLOGICAL INFORMATION

|OPTIONAL SECTION - Complete information not yet available.

|SECTION 12. ECOLOGICAL INFORMATION

|OPTIONAL SECTION - Complete information not yet available.

|SECTION 13. DISPOSAL CONSIDERATIONS

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OPTIONAL SECTION - Complete information not yet available.

Call Dow Corning Environmental Mgmt. (517)496-6315, if more information is desired.

SECTION 14. TRANSPORT INFORMATION

DOT Information (49CFR 172.101)

Proper Shipping Name: COMBUSTIBLE LIQUID, N.O.S.

Hazard Technical Name: 3-HEXYLHEPTAMETHYLTRISILOX ANE

Hazard Class: COMBUSTIBLE LIQUID

UN/NA Number: NA1993

Packing Group: III

Call Dow Corning Transportation, (517)496-8577, if additional information is required.

SECTION 15. REGULATORY INFORMATION

Contents of this MSDS comply with the OSHA Hazard Communication Standard 29CFR 1910.1200

TSCA Status: For R&D purposes only. One or more of the components of this product may not be listed on the TSCA inventory of chemical substances. Product should be used solely for scientific experimentation, research or analysis under the supervision of technically qualified individuals.

EPA SARA Title III Chemical Listings:

Section 302 Extremely Hazardous Substances:
None

Section 304 CERCLA Hazardous Substances:
None

Section 312 Hazard Class:

Acute: N
Chronic: N
Fire: Y
Pressure: N
Reactive: N

Y = Yes N = No

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Section 313 Toxic Chemicals:

None present or none present in regulated quantities.

Supplemental State Compliance Information

<u>CAS Num- ber</u>	<u>Wt%</u>	<u>Component</u>
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California

Warning: This product contains the following chemical(s) listed by the State of California under the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65) as being known to cause cancer.

None Known.

Warning: This product contains the following chemical(s) listed by the State of California under the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65) as being known to cause birth defects or other reproductive harm.

None Known.

Massachusetts

No ingredient regulated by MA Right-to-Know Law present.

New Jersey

001873901	100	3-Hexylheptamethyltrisiloxane
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Pennsylvania

001873901	100	3-Hexylheptamethyltrisiloxane
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SECTION 16. OTHER INFORMATION

Prepared by: Dow Corning Corporation

This information is offered in good faith as typical values and not as a product specification. No warranty, expressed or implied, is hereby made. The recommended industrial hygiene and safe handling procedures are believed to be gener-

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|ally applicable. However, each user should review these recommendations in the |
|specific context of the intended use and determine whether they are appropriate. |
+-----+

(R) indicates Registered or Trademark of the Dow Corning Corporation.

* * * * * This is the last page. * * * * *

December 27, 1994

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RECEIVED

Contains No CBI

Dear

This letter is to inform you of recent laboratory findings in which aerosolized DOW CORNING® 2-1731 Volatile Fluid was evaluated for its potential to cause acute inhalation toxicity. When aerosolized, and under the conditions of testing, DOW CORNING® 2-1731 Volatile Fluid exhibited relatively high acute inhalation toxicity in laboratory rats. A Toxicological Summary for DOW CORNING® 2-1731 Volatile Fluid is provided for your evaluation and assessment.

Based on the acute lethality of aerosolized DOW CORNING® 2-1731 Volatile Fluid, we would recommend that applications in which this product could reasonably be expected to become aerosolized should be avoided.

Should you have questions about the information provided, please call me at the number listed below.

Sincerely,

Daniel W. Kelly, Ph.D., DABT
Product Toxicologist
Health and Environmental Sciences
(517) 496-5151

DOW CORNING® 2-1731 VOLATILE FLUID

55 APR 25 11 09:15

- I. Identification
- Product Name: DOW CORNING® 2-1731 VOLATILE FLUID
Class: Alkylmethylsiloxane Oligomer
- II. Toxicology Data

A. Acute ToxicologyOral

An acute oral toxicity study was conducted on DOW CORNING® 2-1731 Volatile Fluid. A dose level of 5,000 mg/kg was administered by oral gavage using a calibrated glass syringe fitted with a 14-gauge ball-tipped dosing needle. Following dosing, the animals were observed for signs of toxicity and behavioral abnormalities. No deaths or behavioral changes and no obvious effects on food consumption or body weight gains were noted during the 14-day observation period. On the basis of the data presented in this report, it is concluded that DOW CORNING® 2-1731 Volatile Fluid is practically non-toxic ($ALD_{50} > 5,000$ mg/kg body weight) when ingested on an acute basis by laboratory rats (1).

Eye

A primary eye irritation study was performed on the test material. A dose of 0.1 ml of undiluted DOW CORNING® 2-1731 Volatile Fluid was instilled into the left eye of an albino rabbit. The eye was flushed after 30 seconds for two minutes in a flowing stream of tepid water. The right eye was treated with 0.1 ml of test material as previously described, but the eye was left unwashed. Immediately after the unwashed eye was treated, each eye was observed for pain, conjunctiva and corneal response. Both eyes of the rabbit were also examined at one, 24, 48 hours and seven days post-instillation of the test material. Fluorescein stain was used at all readings except immediately following treatment. Direct contact of this material to the eyes of an albino rabbit produced no pain and very slight irritation to the conjunctiva which disappeared within an hour. The material is considered non-irritating although temporary discomfort is likely (1).

Skin

An acute skin irritation study was performed to determine the skin irritation potential of the test material in a male albino rabbit. A single 24 hour semi-occluded contact of the test material to the skin caused no irritation. Repeated prolonged contacts (ten applications over a 14 day period) caused no irritation. On the basis of the data presented in this report, it is concluded that the test material is not an irritant to the skin of rabbits (1).

Inhalation

An acute vapor inhalation toxicity study was conducted with DOW CORNING® 2-1731 Volatile Fluid in Sprague-Dawley rats. Male and female rats were exposed to 0.92 mg/l (74 PPM) of the test material for four hours. No mortality or overt signs of toxicity were observed in any of the test animals during the exposure or observation periods. No test article related gross pathologic changes were observed in tissues and/or organs at terminal sacrifice. These results suggest that the test material most likely will not present a significant acute inhalation hazard ($LC_{50} > 0.92$ mg/l in the rat) at the concentration and conditions of this study (2).

An acute aerosol inhalation toxicity study was conducted on DOW CORNING® 2-1731 Volatile Fluid in rats. The study was conducted using OECD testing guidelines, Part 403 and according to US EPA (TSCA) Good Laboratory Practice Standards, 40 CFR, Part 792, August 17, 1989.

The test material was aerosolized and administered for 4 hours by whole-body inhalation exposure to groups of five male and five female Fischer F344/N rats at target concentrations of 5.0, 2.0 or 1.0 mg/l, one concentration during each of three consecutive exposure periods. The actual exposure concentrations were 5.08, 2.01 and 0.95 mg/l, as determined gravimetrically by filter-collected aerosol samples. Aerosol particle sizes determined as mass median aerodynamic diameter (MMAD) were 0.27, 0.29, and 0.30 μ m with geometric standard deviations (GSD) of 1.87, 2.22 and 3.58. All animals died within 24 hours of the first exposure. In a second exposure at a target concentration of 2.0 mg/l, four out of five male rats died within 2 hours of exposure with the remaining six animals surviving for the 14 day observation period. Due to the high mortality rate in male rats, a third exposure was conducted at a target concentration of 1.0 mg/l. Two out

of five male rats died during or immediately following the third exposure, with the remaining eight animals surviving for the 14 day observation period.

Common gross necropsy findings for all rats exposed to 5.08 mg/l and to those dying at 2.01 and 0.95 mg/l included dark red or mottled lungs and/or fluid-filled trachea. Rats surviving the 2.01 and 0.95 mg/l exposures were normal upon scheduled necropsy. Adverse clinical observations for surviving animals at 2.01 and 0.95 mg/l included dyspnea and decreased activity or hypoactivity immediately after exposure. All surviving rats were virtually asymptomatic 24 hours after the exposures.

In conclusion, male rats appeared to be more sensitive than female rats to the inhalation of aerosolized DOW CORNING® 2-1731 Volatile Fluid. The calculated LC₅₀ for male rats was 1.12 mg/l (95% CI: 0.26 to 4.84 mg/l), while the LC₅₀ for female rats could only be estimated to be greater than 2.01 and less than 5.08 mg/l. The LC₅₀ for male and female rats combined was 1.8 mg/l (95% CI: 0.81 to 4.01 mg/l). (4)

B. Genetic Activity

Bacterial Reverse Mutation Assay

Dow Corning X2-1731 Volatile Fluid was tested in the Salmonella and E. Coli reverse mutation assay using tester strains TA98, TA100, TA1535, TA1537, TA1538 (Salmonella) and WP2 uvrA (E. Coli) in the presence and absence of Aroclor induced rat liver microsomal enzymes (S9 fraction). The assay was performed using dimethylsulfoxide as the vehicle at dose levels up to 5000 µg/plate in the plate incorporation method. No bacterial toxicity was observed; however, slight precipitate was observed at dose levels of 333 g/plate and above. No positive results were observed with or without metabolic activation. Under the conditions of this test, Dow Corning X2-1731 Volatile Fluid did not cause mutagenicity (3).

III. References

1. Acute Toxicological Properties and Industrial Handling Hazards of DOW CORNING® X2-1731 Volatile Fluid in Rats. July 10, 1991
2. An Acute Vapor Inhalation Toxicity Study of DOW CORNING® X2-1731 Volatile Fluid in Rats. August 4, 1992
3. Genetic Evaluation of DOW CORNING® 2-1731 Volatile Fluid in Bacterial Reverse Mutation Assays. June 17, 1994
4. Acute Inhalation Toxicity Study of DOW CORNING® 2-1731 Volatile Fluid in Rats. September 22, 1994

mak:1731
November 8, 1994