

DOW CORNING

8EHQ-0997-13585

PDN: 8896000045

~~154~~ (H)

August 15, 1997

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

OPPT SAC

1-16-98

Contains No CBi

Re: Supplemental Submission to 8EHQ-0296-13585
TSCA Section 8(e) Notification of Substantial Risk
Octamethylcyclotetrasiloxane

97 SEP -9 PM 8:00

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Dear Sir:

In accordance with the provisions of Section 8(e) of the Toxic Substances and Control Act (TSCA), as interpreted in the Statement of Interpretation and Enforcement Policy (40 FR 11110, March 16, 1978), Dow Corning is submitting the following information as a supplemental submission to our Notification of Substantial Risk of February 13, 1996 (8EHQ-9296-13585) and our supplemental submission of July 2, 1996. The information presented in this supplemental submission was generated in a preliminary range-finding inhalation reproductive toxicity study that we conducted as part of our Siloxane Research Program. While we do not believe that the results of this study represent a substantial risk to health or the environmental, we nevertheless are reporting them to EPA to ensure our compliance with the letter and spirit of TSCA Section 8(e). The high exposure levels at which statistical associations/significance are observed are much greater than human exposures.

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Chemical Substance:

556-67-2 Octamethylcyclotetrasiloxane



8EHQ-96-13585

Manufacturer:

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



Title of Recently Completed Study:

89970000289

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AN INHALATION RANGE-FINDING REPRODUCTIVE TOXICITY STUDY
OF OCTAMETHYLCYCLOTETRASILOXANE (D4) IN FEMALE RATS

Dow Corning Corporation
1997-I0000-42936
July 29, 1997

Background:

In letters dated February 13, 1996 and May 10, 1996, Dow Corning notified EPA of the results of two preliminary range finding reproductive toxicity studies on octamethylcyclotetrasiloxane (OMCTS, D₄) in Sprague-Dawley rats (8EHQ-0296-13585). We reported a statistically significant reduction in live litter size, the number of implantation sites, and pup viability on lactation days 1 and 4 as a result of whole body exposure of both male and female Sprague-Dawley rats to 700 ppm OMCTS prior to and during a two-week mating period and continuing through gestation day 21.

In an effort to ascertain whether these effects were due to male or female exposure, we initiated larger range-finding studies. In a letter dated July, 1996 and as a supplemental submission to our original notification, Dow Corning provided EPA with results obtained in an ongoing range finding reproductive toxicity study of OMCTS in female rats, reporting statistically significant decreases in the mean number of implantation sites and in mean viable litter size. We now are providing a copy of the recently completed final report as a further supplemental submission to our notification of February 13, 1996. A copy of this final report also is being provided to the Agency via a separate cover letter in compliance with TSCA Section 8(d).

Executive Summary:

Female Sprague-Dawley rats (22 rats/exposure concentration) were exposed by inhalation to OMCTS concentrations of 0 (filtered air control), 70, 300, 500 and 700 ppm six hours per day for at least 70 consecutive days prior to mating. Exposure continued through a mating interval in which the treated females were mated with males that had not been exposed to OMCTS. Exposure of the females was continued further until gestation day 20. Exposure then was discontinued until PND 4, at which time exposure of the dams continued until PND 21 when all surviving dams and offspring were euthanized.

Estrous cycle, time elapsed between pairing and coitus, fertility indices, mating indices, duration of gestation, and parturition were not adversely affected by OMCTS exposure at any concentration tested. Maternal toxicity was demonstrated in the F0 females at exposure levels of 300, 500, and 700 ppm by clinical signs, at exposure levels of 500 and 700 ppm by slight reductions in body weight gains during the first week of the pre-mating period, and at the 700 ppm exposure level by reductions in mean body weights and/or body weight gains

during the gestation and lactation periods. Mean liver weights (absolute and relative) were increased in the F0 females at exposure levels of 300, 500, and 700 ppm. A reduction in mean live litter size and in the number of implantation sites, and an increase in the number of dead pups on postnatal day 0 were noted in the 700 ppm group. Postnatal toxicity was not observed in F1 pups at exposure levels of 70, 300, or 500 ppm.

Actions:

Dow Corning will inform the Agency of any pertinent information that may be developed concerning this material. Further studies are being conducted to better understand this reproductive effect and relevance of these findings to humans.

If you have any questions concerning this study, please contact me at the address provided herein. If you require further general information regarding this submission, please contact Dr. Rhys G. Daniels, Regulatory Compliance Specialist, Regulatory Compliance Department, at 517-496-4222 or at the address provided herein.

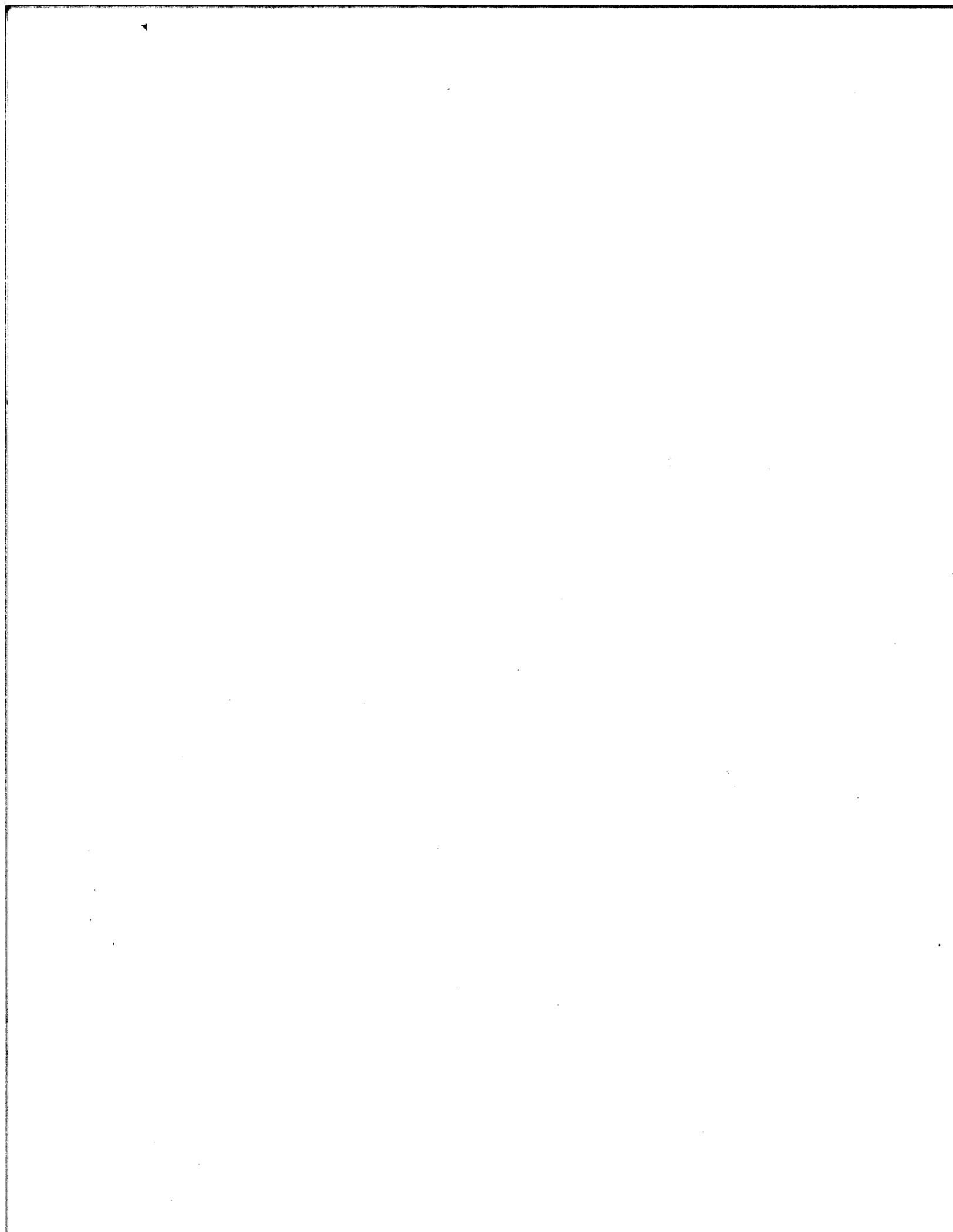
Sincerely,



Michael P. Hill
Americas Vice President and Corporate Director
Health and Environmental Sciences
(517) 496-4059

4057

RGD97136



8EHQ-099713585

DOW CORNING CORPORATION
HEALTH & ENVIRONMENTAL SCIENCES
TECHNICAL REPORT

WIL Research Laboratories, Inc.
1407 George Road
Ashland, Ohio 44805

Report No.: 1997-I0000-42936

Title: An Inhalation Range-Finding Reproductive Toxicity Study of Octamethylcyclotetrasiloxane (D4) in Female Rats

Study No.: 8463

External Testing Facility No.: WIL-51041

Test Article: Octamethylcyclotetrasiloxane (D4)

Study Director: Joseph F. Holson, Ph.D.
President, Director

Author: Ann S. Stump, Ph.D.
Senior Report Writer

Sponsor: Dow Corning Corporation

Sponsor Study Monitor: Vincent L. Reynolds, Ph.D., D.A.B.T.

Test Facility: WIL Research Laboratories, Inc.
1407 George Road
Ashland, Ohio 44805

Study Completion Date: July 29, 1997

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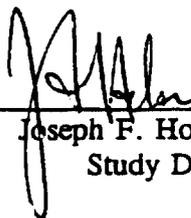
DC Study No. - 8463
External No. - WIL-51041

DC Report No. - 1997-I0000-42936
Security - INTERNAL

An Inhalation Range-Finding Reproductive Toxicity
Study of Octamethylcyclotetrasiloxane (D4) in Female Rats

COMPLIANCE STATEMENT

This study was conducted in compliance with the Good Laboratory Practice Regulations for Nonclinical Laboratory Studies of the United States Food and Drug Administration (21 CFR Part 58) and Environmental Protection Agency (40 CFR Parts 160 and 792) and the Standard Operating Procedures of WIL Research Laboratories, Inc. The study was conducted in accordance with the protocol as approved by the Sponsor, except as indicated in Appendix G.



Joseph F. Holson, Ph.D.
Study Director

7/29/97
Date



DC Study No. - 8463
 External No. - WIL-51041

DC Report No. - 1997-I0000-42936
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QUALITY ASSURANCE UNIT STATEMENT

<u>Date(s) of Inspection(s)</u>	<u>Phase Inspected</u>	<u>Date(s) Findings Reported to Study Director</u>	<u>Date(s) Findings Reported to Management</u>
9/19/95	Animal Care/Equipment	9/19/95	10/30/95
1/9/96	Necropsy	1/9/96	2/26/96
2/26/96	Histology-Microtoming	2/26/96	3/27/96
4/11, 12, 15, 16, 5/1, 2, 21-24/96	Study Records (Vol. I-6)	5/24/96	6/20/96
4/12, 15, 29, 30, 5/1, 28/96	Study Records (Vol. I-7)	2/28/96	3/27/96
4/12, 15-17, 5/24/96	Study Records (Vol. I-8)	5/24/96	6/20/96
4/15-16, 22-24, 5/6, 28/96	Study Records (Vol. I-9)	5/28/96	6/20/96
4/18-20, 5/3, 9, 20-21/96	Study Records (Vol. I-1)	5/21/96	6/20/96
4/22-25, 29-30, 5/1, 20/96	Study Records (Vol. A-1, A-2, A-3)	5/21/96	6/20/96
4/22-23, 5/2-3, 6, 10, 21-22/96	Study Records (Vol. I-4)	5/22/96	6/20/96
4/23-26, 29, 5/17/96	Study Records (Vol. A-6)	5/22/96	6/20/96
4/23, 25, 30, 5/1-3, 6-10, 13-16, 29/96	Study Records (Vol. A-17)	5/22/96	6/20/96
4/24-25, 5/17/96	Study Records (Vol. I-2)	5/17/96	6/20/96
4/24-25, 5/17/96	Study Records (Vol. I-3)	5/20/96	6/20/96
4/25-26, 29, 5/20/96	Study Records (Vol. I-5)	5/20/96	6/20/96
4/29-30, 5/1, 20/96	Study Records (Vol. A-7)	5/20/96	6/20/96
5/1-2/96	Study Records (Vol. A-8)	5/20/96	6/20/96
5/3, 6, 20/96	Study Records (Vol. A-9)	5/20/96	6/20/96
5/3, 6-10, 13, 20/96	Study Records (Vol. A-5)	5/20/96	6/20/96
5/6-7/96	Study Records (Vol. A-10)	5/20/96	6/20/96
5/6-8, 10, 28/96	Study Records (Vol. N-1)	5/20/96	6/20/96
5/7, 20/96	Study Records (Vol. A-11)	5/20/96	6/20/96
5/7-10, 28/96	Study Records (Vol. N-2)	5/20/96	6/20/96
5/8-9, 20/96	Study Records (Vol. A-13)	5/20/96	6/20/96
5/8, 20/96	Study Records (Vol. A-12)	5/20/96	6/20/96
5/9-10, 20/96	Study Records (Vol. A-14)	5/20/96	6/20/96
5/10, 20/96	Study Records (Vol. A-15)	5/20/96	6/20/96
5/10, 28/96	Study Records (Vol. H-1/P-1)	5/28/96	6/20/96
5/10, 13, 20/96	Study Records (Vol. A-16)	5/28/96	6/20/96
5/20/96	Study Records (Vol. A-4)	5/20/96	6/20/96



DC Study No. - 8463
External No. - WIL-51041

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Security - INTERNAL

<u>Date(s) of Inspection(s)</u>	<u>Phase Inspected</u>	<u>Date(s) Findings Reported to Study Director</u>	<u>Date(s) Findings Reported to Management</u>
5/21-26, 28, 31, 6/3, 4-7, 10-12/96	Draft Report (without Appendix B)	6/12/96	7/30/96
6/3-7, 10-11/96 6/12/96	Draft Report (Appendix B) Study Records (Vol. H-1/P-1 - Supplemental)	6/12/96 6/12/96	7/30/96 7/30/96
7/21-22/97	Study Records (A-4 Supplemental)	7/22/97	8/97
7/21-22/97	Draft Report (Appendix A)	7/22/97	8/97

This study was conducted and inspected in accordance with the current Good Laboratory Practice Regulations for Nonclinical Laboratory Studies of the United States Food and Drug Administration and Environmental Protection Agency, the Standard Operating Procedures of WIL Research Laboratories, Inc., and the Sponsor's protocol and protocol amendment(s). Quality Assurance findings, derived from the inspections during the conduct of the study and from the inspections of the raw data and draft report, are documented and have been reported to the Study Director. A status report is submitted to management monthly.

The raw data, the retention sample(s), the original protocol and amendments, and the final report are stored in the Archives at WIL Research Laboratories, Inc.

Deborah L Little

Deborah L. Little
Manager of Quality Assurance

7/29/97
Date



**An Inhalation Range-Finding Reproductive Toxicity
Study of Octamethylcyclotetrasiloxane (D4) in Female Rats**

TABLE OF CONTENTS

VOLUME 1	Page
Compliance Statement	2
Quality Assurance Unit Statement	3
I. Summary	15
II. Objective	19
III. Study Design	20
IV. Experimental Procedures	22
A. Study Schedule	22
B. Test and Control Articles	22
1. Test Article Synthesis	22
2. Test Article Identification	22
3. Test Atmosphere Monitoring	24
4. Exposure Methods	24
C. F ₀ Generation	26
1. Animal Receipt and Acclimation	26
2. Animal Housing	27
3. Diet, Drinking Water and Maintenance	28
4. Environmental Conditions	28
5. Assignment of Animals to Treatment Groups	29
6. Observations	30
a. Clinical Observations and Survival	30
b. Body Weights	31
c. Food Consumption	32

VOLUME 1 (continued)	<u>Page</u>
7. Reproductive Performance	32
a. Estrous Cycles	32
b. Breeding Procedures	32
8. Females Allowed to Deliver	34
D. F ₁ Litter Data	34
1. Litter Viability and Deaths	34
2. Litter Reduction	35
3. Clinical Observations	36
4. Body Weights	36
5. Food Consumption	36
6. Sex Determination	36
7. Selection of F ₁ Generation	36
8. Calculation of Litter Parameters	37
9. PND 21 and 28 Necropsies	37
a. Macroscopic Examinations	37
b. Organ Weights	38
E. Pathology	38
1. Macroscopic Examinations	38
2. Organ Weights	39
3. Microscopic Examination	39
F. Statistical Methods	41
G. Data Retention	42
V. Results	44
A. Chamber Concentrations	44



VOLUME 1 (continued)	<u>Page</u>
B. F₀ Generation	44
1. Clinical Observations and Survival	44
2. Reproductive Performance	45
3. Body Weights	46
a. Weekly	46
b. Gestation	47
c. Lactation	47
4. Food Consumption	48
a. Weekly	48
b. Gestation	48
c. Lactation	49
5. Gestation Length and Parturition	49
C. F₁ Litter Data	50
1. PND 0 Litter Data and Postnatal Survival	50
2. General Physical Condition and Mortalities	51
3. Pup Body Weights	52
4. PND 21 and 28 Necropsies	52
a. Macroscopic Examinations	52
b. Organ Weights - PND 28 Selected Pups	53
D. Pathology	54
1. Macroscopic Examinations	54
a. F ₀ Female - 25 Days Following the Breeding Period	54
b. F ₀ Females - Post-Mating Day 25	54
c. F ₀ Females - Lactation Day 21	54

DC Study No. - 8463
External No. - WIL-51041

DC Report No. - 1997-I0000-42936
Security - INTERNAL

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	<u>Page</u>	
VOLUME 1 (continued)	55	
2. Organ Weights	55	
a. F ₀ Females - Post-Mating Day 25	56	
b. F ₀ Females - Lactation Day 21	56	age
3. Microscopic Examinations	56	
a. F ₀ Females - Post-Mating Day 25	57	67
b. F ₀ Females - Lactation Day 21	58	69
VI. Discussion and Conclusions	61	
VII. Key Study Personnel and Report Submission	63	72
VIII. Approval Signatures	64	
IX. References		76

78
13
8
9
0
1



VOLUME 1 (continued)		<u>Page</u>
16.(F ₀)	Mean Food Consumption During Lactation (Grams/Kg/Day)	101
17.(F ₀)	Gestation Length Summary	102
18.(F ₁)	Summary of PND 0 Litter Data	103
18A.(F ₁)	Summary of Postnatal Survival - % Per Litter (PND 0-21)	104
18B.(F ₁)	Summary of Post-Weaning Survival (PND 21-28)	106
19.(F ₁)	Summary of Pup Observations During Lactation	107
20.(F ₁)	Summary of Pup Necropsy Findings - Found Dead Pups	108
21.(F ₁)	Summary of Pup Necropsy Findings - Euthanized Pups (Day 21 Surplus Pups)	109
22.(F ₁)	Summary of Pup Necropsy Findings - Euthanized Pups (Day 28 Surplus Pups)	110
23.(F ₁)	Gross Necropsy Observations Incidence Summary (Day 28 Selected Pups)	111
24.(F ₁)	Summary of Mean Pup Weights (Grams)	113
25.(F ₁)	Organ Weights (Grams) - Summary of Means (Day 28 Selected Pups)	114
26.(F ₁)	Organ Weights Relative to Final Body Weights (Grams/100 Grams) - Summary of Means (Day 28 Selected Pups)	116
27.(F ₀)	Gross Necropsy Observations Incidence Summary (Female - 25 Days After Breeding Period)	118
28.(F ₀)	Gross Necropsy Observations Incidence Summary (Females - Post-Mating Day 25)	119

VOLUME 1 (continued)		<u>Page</u>
29.(F ₀)	Gross Necropsy Observations Incidence Summary (Females - Lactation Day 21)	120
30.(F ₀)	Summary of Implantation Sites - Lactation Day 21	122
31.(F ₀)	Organ Weights (Grams) - Summary of Means (Females - Post-Mating Day 25)	123
32.(F ₀)	Organ Weights (Grams) - Summary of Means (Females- Lactation Day 21)	126
33.(F ₀)	Organ Weights Relative to Final Body Weights (Grams/100 Grams) - Summary of Means (Females - Post-Mating Day 25)	129
34.(F ₀)	Organ Weights Relative to Final Body Weights (Grams/100 Grams) - Summary of Means (Females - Lactation Day 21)	132
35.(F ₀)	Organ Weights Relative to Brain Weights (Grams/100 Grams) - Summary of Means (Females - Post-Mating Day 25)	135
36.(F ₀)	Organ Weights Relative to Brain Weights (Grams/100 Grams) - Summary of Means (Females - Lactation Day 21)	138
37.(F ₀)	Histomorphological Diagnosis - Summary Incidence (Females - (Post-Mating Day 25)	141
38.(F ₀)	Histomorphological Diagnosis - Summary Incidence (Females - Lactation Day 21)	144
39.(F ₀)	Ovarian Follicle Counts - Summary of Means (Post-Mating Day 25)	147
40.(F ₀)	Ovarian Follicle Counts - Summary of Means (Lactation Day 21)	148

INDIVIDUAL DATA - TABLES 41-77

VOLUME 2

	<u>Page</u>
41.(F ₀) Individual Reproductive Performance	150
42.(F ₀) Individual Body Weights (Grams)	155
43.(F ₀) Individual Body Weight Gains (Grams)	175
44.(F ₀) Individual Body Weights (Grams) During Gestation	195
45.(F ₀) Individual Body Weight Changes (Grams) During Gestation	200
46.(F ₀) Individual Body Weights (Grams) During Lactation	205
47.(F ₀) Individual Body Weight Changes (Grams) During Lactation	210
48.(F ₀) Individual Food Consumption (Grams/Animal/Day)	215
49.(F ₀) Individual Food Consumption (Grams/Kg/Day)	225
50.(F ₀) Individual Food Consumption During Gestation (Grams/Animal/Day)	235
51.(F ₀) Individual Food Consumption During Gestation (Grams/Kg/Day)	240
52.(F ₀) Individual Food Consumption During Lactation (Grams/Animal/Day)	245
53.(F ₀) Individual Food Consumption During Lactation (Grams/Kg/Day)	250
54.(F ₀) Individual Gestation Length (Days)	255
55.(F ₁) Individual Litter Viability	256
56.(F ₁) Individual Pup Viability	261
57.(F ₁) Individual Pup Observations During Lactation	276

VOLUME 3

58.(F ₁) Individual Pup Necropsies - Found Dead Pups	516
--	-----

VOLUME 3 (continued)		<u>Page</u>
59.(F ₁)	Individual Pup Necropsies - Euthanized Pups (Day 21 Surplus Pups)	521
60.(F ₁)	Individual Pup Necropsies - Euthanized Pups (Day 28 Surplus Pups)	550
61.(F ₁)	Individual Gross Description of Organs (Day 28 Selected Pups)	555
62.(F ₁)	Individual Pup Weights (Grams)	655
63.(F ₁)	Individual Litters - Mean Pup Weights by Sex (Grams)	685
64.(F ₁)	Individual Organ Weights and Final Body Weights (Grams) (Day 28 Selected Pups)	695
65.(F ₁)	Individual Organ Weights Relative to Final Body Weights (Grams/100 Grams) (Day 28 Selected Pups)	705
66.(F ₀)	Individual Gross Description of Organs (Female - 25 Days After Breeding Period)	715
67.(F ₀)	Individual Gross and Microscopic Description of Organs (Females - Post-Mating Day 25)	716
68.(F ₀)	Individual Gross and Microscopic Description of Organs (Females - Lactation Day 21)	723
69.(F ₀)	Individual Implantation Sites - Lactation Day 21	825
70.(F ₀)	Individual Ovarian Follicle Counts (Post-Mating Day 25)	830
71.(F ₀)	Individual Ovarian Follicle Counts (Lactation Day 21)	832
72.(F ₀)	Individual Organ Weights and Final Body Weights (Grams) (Females - Post-Mating Day 25)	834
73.(F ₀)	Individual Organ Weights and Final Body Weights (Grams) (Females - Lactation Day 21)	838

VOLUME 3 (continued)		<u>Page</u>
74.(F ₀)	Individual Organ Weights Relative to Final Body Weights (Grams/100 Grams) (Females - Post-Mating Day 25)	843
75.(F ₀)	Individual Organ Weights Relative to Final Body Weights (Grams/100 Grams) (Females - Lactation Day 21)	847
76.(F ₀)	Individual Organ Weights Relative to Brain Weights (Grams/100 Grams) (Females - Post-Mating Day 25)	852
77.(F ₀)	Individual Organ Weights Relative to Brain Weights (Grams/100 Grams) (Females - Lactation Day 21)	856

INDEX OF APPENDICES

VOLUME 4		
A.	Test Article Purity Analyses (WIL Research Laboratories, Inc.)	862
B.	Test Atmosphere Generation and Environmental Conditions During Exposure (WIL Research Laboratories, Inc.)	878
C.	Estrous Cycle Data and Evidence of Mating	954
D.	Individual Clinical Observations	960
E.	WIL Reproductive Historical Control Data (Charles River CD [®] Rats) - Summary	1109
F.	WIL Reproductive Historical Control Data (Charles River CD [®] Rats) - Individual	1114
G.	Deviations from the Protocol	1145

**An Inhalation Range-Finding Reproductive Toxicity
Study of Octamethylcyclotetrasiloxane (D4) in Female Rats**

I. SUMMARY

This study was conducted 1) to identify adverse reproductive effects that might occur following whole-body inhalation exposure of female rats to octamethylcyclotetrasiloxane (D4), and 2) to provide data useful for assisting in the selection of exposure concentrations for a two-generation reproductive toxicity study.

Groups of female Sprague-Dawley rats (N = 22) were exposed to test article six hours daily for at least 70 consecutive days prior to mating. Target test article concentrations were 70, 300, 500, and 700 ppm; the actual mean measured exposure concentrations were 72, 302, 498, and 700 ppm. The male rats used in this study served as cage control animals and were not exposed to the test article. A control group of identical design was exposed to clean, filtered air on a comparable regimen (females only); the control group males were not exposed to filtered air. Exposures of the females continued during the mating interval and throughout gestation and lactation until the day prior to necropsy, except that exposures were discontinued from gestation day 21 through lactation day 4. All animals were observed twice daily for appearance and behavior. Body weights were recorded weekly for both sexes prior to mating; maternal body weights were also recorded on gestation days 0, 7, 10, 14, and 20 as well as lactation days 1, 4, 7, 14, and 21. Female food consumption was measured for corresponding intervals prior to mating, during gestation, and during lactation. All F₀ females were allowed to deliver and rear their pups to weaning on lactation day 21. The offspring were potentially exposed *in utero* (placental transfer), through suckling and/or dermal contact during lactation, and via daily 6-hour exposures following weaning [postnatal day 21 (PND 21)] until the day prior to necropsy on PND 28.

The F₀ males were euthanized and discarded after the breeding period. The F₀ dams that delivered litters were necropsied on lactation day 21. F₀ females which failed to deliver were necropsied on post-mating day 25 (evidence of mating) or 25 days following the breeding period (no evidence of mating). Necropsies were also performed on 10 pups/sex/group on PND 28 and on all F₁ pups that died between PND 5 and 28. Selected organs were weighed from all F₀ females and F₁ weanlings at the scheduled necropsies. Selected tissues were examined microscopically, and ovarian follicle counts were obtained from F₀ females in the control and 700 ppm groups.

Estrous cyclicity, days between pairing and coitus, mating indices, fertility indices, duration of gestation, and the process of parturition were not adversely affected by test article exposure at any concentration tested.

All F₀ males and females survived to their scheduled euthanizations. Exposure-related clinical signs noted in the F₀ females one hour following exposure included dried red material around the nose and/or mouth (300, 500, and 700 ppm groups), and dried red material around the eyes and wet red material around the nose (700 ppm group).

Mean body weight gains were reduced in the 500 and 700 ppm group F₀ females during week 0-1 of the pre-mating period. Mean body weight gains in the 700 ppm group were reduced during gestation days 10-14 and 14-20. These reductions were accompanied by reductions in mean body weights in this group on gestation days 14 and 20. Mean body weights in the 700 ppm group remained reduced during lactation days 1, 4, 7, and 14. Food consumption was unaffected by exposure to the test article throughout the study in all treatment groups.

At the necropsies of nongravid F₀ females 25 days following the breeding period and on post-mating day 25, no gross findings related to test article exposure were observed at any exposure level. In the 700 ppm group females

that delivered litters, the mean number of implantation sites was reduced, and an increased numerical difference was noted between the number of implantation sites and the number of offspring. No effects of the test article were noted at the microscopic examination; ovarian follicle counts were similar between the control and 700 ppm groups. Mean liver weights (absolute and relative) were increased at exposure levels of 300, 500, and 700 ppm.

Mean live litter size and the mean number of pups born were reduced in the 700 ppm group relative to the control group values. Mean pup weights and pup survival were unaffected at all exposure levels throughout lactation. The percentage of males per litter at birth was unaffected by exposure to the test article. At the necropsies of surplus pups on PND 21 and PND 28 and at the necropsy of selected pups on PND 28, no exposure-related gross findings were noted. Organ weights (absolute and relative) in the F₁ selected pups were unaffected by exposure to the test article.

In conclusion, maternal toxicity was demonstrated in the F₀ females at exposure levels of 300, 500, and 700 ppm by clinical signs, at exposure levels of 500 and 700 ppm by slight reductions in mean body weight gains during the first week of the pre-mating period, and at an exposure level of 700 ppm by reductions in mean body weights and/or body weight gains during the gestation and lactation periods. Mean liver weights (absolute and relative) were increased in the F₀ females at exposure levels of 300, 500, and 700 ppm. Reductions in mean live litter size and in the number of pups born were noted in the 700 ppm group. Postnatal toxicity (F₁ pups) was not observed at exposure levels of 70, 300, or 500 ppm. Toxicity in the 700 ppm group was further demonstrated by a reduction in the number of implantation sites and an increased numerical difference between the number of implantation sites and the number of offspring.

DC Study No. - 8463
External No. - WIL-51041

DC Report No. - 1997-I0000-42936
Security - INTERNAL

This work was partially funded by the Silicones Environmental Health and Safety Council of North America.



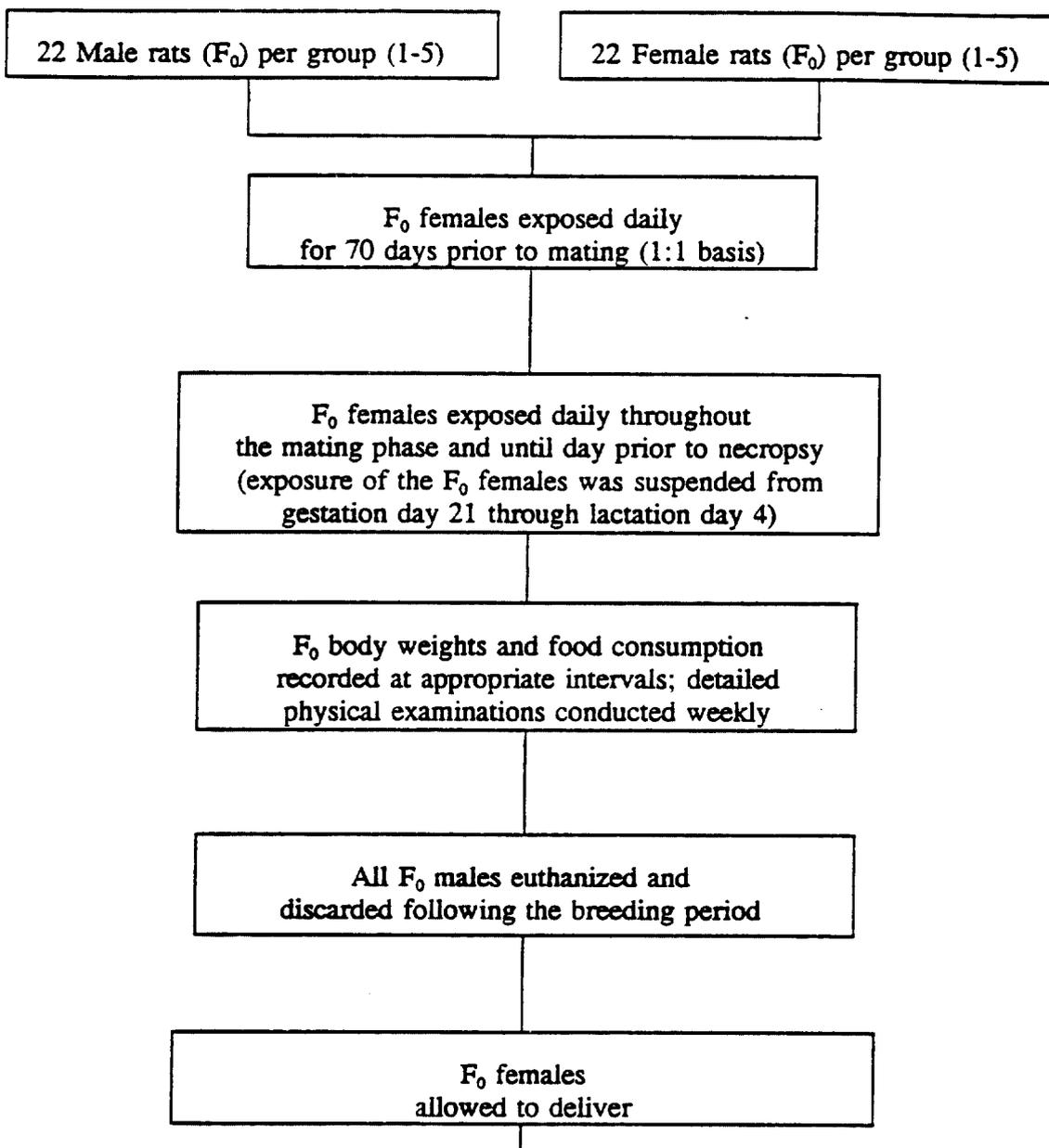
II. OBJECTIVE

The purposes of this study were:

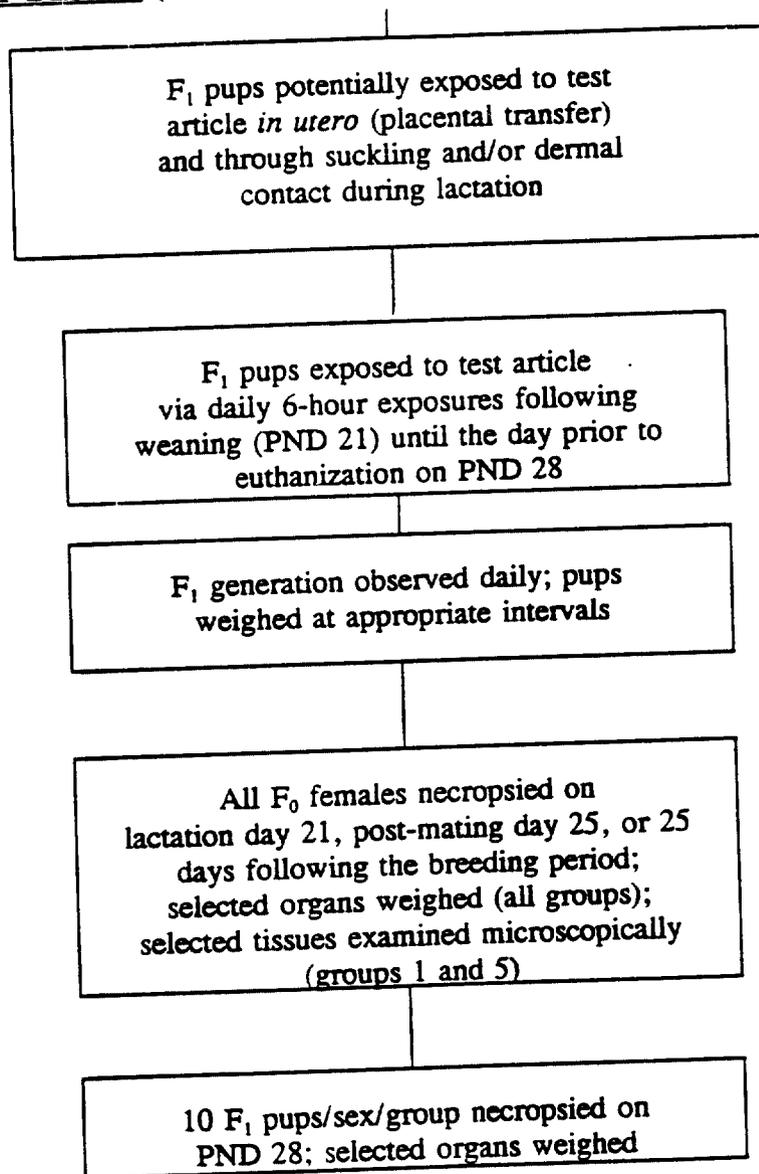
- 1) to identify adverse reproductive effects (if any) that might occur following whole-body vapor inhalation exposure of female rats to D4; and
- 2) to provide data useful for assisting in the selection of exposure concentrations for a two-generation reproductive toxicity study.

The route of administration was whole-body inhalation since this is a potential route of exposure for humans. A 70-day pre-mating exposure regimen was used in this study to be consistent with the regimen required by regulatory guidelines for a two-generation reproductive toxicity study¹. The animal model, the Sprague-Dawley CrI:CD®BR rat, is recognized as appropriate for reproduction studies¹ and was selected based on the availability of historical control data and because of its proven susceptibility to the effects of reproductive and developmental toxicants.

III. STUDY DESIGN



III. STUDY DESIGN (continued)



IV. EXPERIMENTAL PROCEDURES

A. STUDY SCHEDULE

Initiation of Exposure:	September 19, 1995 (Week 0)
F ₀ Breeding:	November 27, 1995 - December 12, 1995 (Weeks 9-12)
F ₀ Male Euthanizations:	December 13, 1995 (Week 12)
F ₀ Lactation Day 21 Necropsies:	January 9-17, 1996 (Weeks 16-17)
Experimental Termination (Last day of test article characterization):	June 16, 1997

At the request of the Sponsor, Dr. Joseph F. Holson served as Study Director due to his expertise in reproductive toxicology. Dr. Holson is the President, Director of WIL Research Laboratories, Inc.

Due to spacing constraints, the study title on the report tables was limited to "Inhalation RF Reproductive Toxicity Study of D4 in Female Rats."

B. TEST AND CONTROL ARTICLES

1. TEST ARTICLE SYNTHESIS

The test article was synthesized by Dow Corning Corporation (Carrollton, Kentucky) in August, 1994. The methods used in the synthesis of the test article are summarized in the Material Documentation Management System document for the test article. A copy of this document is included in the study records maintained by the Sponsor for this study.

2. TEST ARTICLE IDENTIFICATION

The test article, octamethylcyclotetrasiloxane (D4), was received from Dow Corning Corporation, Auburn, Michigan, on September 30, 1994, as follows:

<u>Label Identification</u>	<u>Quantity Received</u>	<u>Description</u>
Dow Corning 244 Fluid Lot LL084732 (Drum #1-008, #2-009, #3-010) Net. Wt. 430 lb. (195.0 Kg) Avoid freezing Caution - combustible	3 Drums Total gross weight: 649850.0 g Drum #1: 212850.0 g ^a Drum #2: 225100.0 g ^b Drum #3: 211900.0 g ^c	Clear colorless liquid

^a = This drum was used for method development.

^b = This drum was used for method development and animal exposures.

^c = This drum was used for animal exposures.

Retention and residual samples of the test article were analyzed for purity by the Analytical Chemistry Department at WIL Research Laboratories, Inc. Details of the sample collection and their analyses are presented in Appendix A. The test article purity was determined to be at least 99.59% D4. The test article was stable when stored at room temperature. Reserve 1.05, 22.7, and 50 g retention samples of the test article were taken from the first, second, and third drums, respectively, on October 5, 1994, September 15, 1995, and January 4, 1996, respectively. After completion of the exposure phase, residual samples of the test article were taken (9.26 g, 12.88 g, and 12.39 g for the first, second, and third drums, respectively). The retention and residual samples are stored in the Archives at WIL Research Laboratories, Inc., 1407 George Road, Ashland, Ohio 44805-9281. The test article has not been returned to the Sponsor, as it is being used on additional studies for this Sponsor.

3. TEST ATMOSPHERE MONITORING

Exposure concentrations within the chamber were measured seven to ten times during each daily exposure period by a validated gas chromatographic method. At least one standard was analyzed each day prior to exposure to confirm gas chromatographic calibration. Chamber ventilation rate, negative pressure, temperature, relative humidity, and oxygen content within the chamber were monitored continuously and were recorded approximately every 30 minutes. Nominal chamber concentrations were determined daily for each chamber by weighing the amount of test article used during atmosphere generation, converting this mass to volume using standard gas laws, and dividing this test article volume by the total volume of atmosphere displaced through the chamber during the exposure. Test atmosphere homogeneity data were generated during pre-study method development. The methodology and results of these analyses are presented in Appendix B.

4. EXPOSURE METHODS

Each group of animals was exposed in a 0.5, 1.0, or 2.0 cubic meter stainless steel and glass whole body inhalation chamber. The use of chambers of different sizes was a result of space constraints in the exposure room; however, all D4-treated animals were exposed in 1.0 cubic meter chambers. The chambers were operated under dynamic conditions at air flows of at least 12 to 15 air changes per hour, ensuring an adequate oxygen content of 19% or above and an evenly distributed exposure atmosphere. The F₀ females were exposed to the test atmosphere for daily 6-hour exposures (seven days a week) for 70 consecutive days prior to mating, and continuing through the day prior

to necropsy. However, exposure of these animals was suspended from gestation day 21 through lactation day 4 to avoid the possibility of the F₀ maternal animals delivering their offspring during the exposure period and to prevent confounding the interpretation of the survival data of the F₁ pups early in the postnatal period. Female no. 42218 (70 ppm group) was inadvertently not exposed to test article on lactation day 5. This protocol deviation was not expected to affect the study outcome, as it was a single occurrence in a single animal. The rats were removed from their home cages in the animal room and transported to the inhalation chambers for the 6-hour exposure period. The animals were exposed to test article at approximately the same time each day. The animals were returned to their home cages following exposure. The litters remained in the maternity cages with nesting material while the maternal animals were transported to the inhalation chambers for the daily exposure. The F₁ pups were potentially exposed to test article *in utero* (placental transfer), through suckling and/or dermal contact during lactation, and via 6-hour exposures following weaning (PND 21) until the day prior to euthanization on PND 28. Controls were set to maintain the temperature inside the exposure chamber between approximately 20°C and 26°C and relative humidity between approximately 30% and 70%. Exposure methods and conditions are detailed in Appendix B.

Each chamber was dedicated to one exposure group. In order to minimize any potential variation occurring due to positioning within the chamber, the cages were rotated around the available rack positions within the chamber on a daily basis throughout the study, in accordance with the standard operating procedures at WIL Research Laboratories.

Inc., with the following exception. The control group females were exposed in the same cage rack positions on study days 18 and 19. Because this deviation occurred only once during the study in one exposure group, it was not expected to affect the scientific validity of the study.

The following diagram presents the study group assignment:

<u>Group Number</u>	<u>Group Name</u>	<u>Test Article</u>	<u>Exposure Level (ppm)</u>	<u>Number of Animals</u>	
				<u>Male*</u>	<u>Female</u>
1	Control	Filtered Air	0	22	22
2	Low Dose	D4	70	22	22
3	Intermediate Dose-1	D4	300	22	22
4	Intermediate Dose-2	D4	500	22	22
5	High Dose	D4	700	22	22

* = The males in all exposure groups served as cage control animals and were not exposed to filtered air or test article.

C. F₀ GENERATION

1. ANIMAL RECEIPT AND ACCLIMATION

One hundred twenty-five female virgin Sprague-Dawley Crl:CD®BR rats were received from Charles River Breeding Laboratories, Inc., Portage, Michigan, on September 7, 1995, and 125 male Sprague-Dawley Crl:CD®BR rats were received from the same supplier on November 16, 1995. The females were 31 days old and the males were 79 days old upon receipt. Each animal was examined by a staff veterinarian upon receipt; the animals were initially weighed on the day following receipt. All animals were uniquely identified by a metal eartag displaying the animal number. The animals were housed for an acclimation period of 12 days prior to initiation of

exposure (females) or for 12 days prior to the initiation of breeding (males). During acclimation, individual body weights were recorded twice (following receipt and at randomization), and the animals were observed twice daily for mortality and moribundity.

2. ANIMAL HOUSING

Upon arrival, all F₀ animals were housed in clean wire-mesh cages suspended above cage-board. For a minimum of three days following receipt, the females were housed three per cage per sex. Thereafter, the females were housed individually until pairing. The animals were paired for mating in the home cage of the male. Following positive identification of mating (Section IV.C.7.), the males were housed in individual suspended wire-mesh cages until euthanization. Bred females were transferred to clean, individual plastic maternity cages with nesting material, ground corn cob bedding (Bed-O'Cobs®; The Andersons, Industrial Products Division, Maumee, OH 43537). The dams were housed in these cages through lactation day 21, the scheduled day of necropsy. Females which did not deliver were necropsied on post-mating day 25. The female (no. 42302; 500 ppm group) for which there was no evidence of mating was placed in a clean, plastic maternity cage with nesting material upon completion of a 15-day mating period. Twenty-five days following the conclusion of the mating period, this female had not delivered and was euthanized and necropsied. All animals were maintained in accordance with the National Institutes of Health "Guide for the Care and Use of Laboratory Animals²". The animal facilities at WIL Research Laboratories, Inc., are accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC).

3. DIET, DRINKING WATER, AND MAINTENANCE

The basal ration used in this study was Purina® Certified Rodent Chow® #5002, in meal form; the lot numbers used were recorded. The diet used at WIL Research Laboratories, Inc., is a certified feed with appropriate analyses performed and provided by the manufacturer. Municipal water supplying the facility is sampled for contaminants according to WIL Standard Operating Procedures. The results of these analyses are maintained at WIL Research Laboratories, Inc. Contaminants were not present in feed or water at levels which would interfere with the objectives of this study. Drinking water, delivered by an automatic watering system, and the basal diet were provided *ad libitum* throughout the acclimation period and during the study, with the following exception. Food and water were withheld during each daily exposure period.

4. ENVIRONMENTAL CONDITIONS

Except during exposure, all animals were housed throughout the acclimation period and during the study in an environmentally controlled room. Controls were set to maintain a temperature of 72° ± 4°F (22 ± 2°C) and a relative humidity between 30% and 70%. Room temperature and relative humidity were recorded twice daily (once in the morning and once in the afternoon) throughout the study period, with the following exceptions. On September 19 and 20, 1995 (study days 0 and 1), temperature and relative humidity were only recorded once daily. Temperature in the nonexposure animal room ranged from 67°F to 77°F (19°C to 25°C) and relative humidity ranged from 22% to 63% during the study period. On December 10, 1995 and January 4, 1996 (study days 82 and 107, respectively),

relative humidities of 7% and 16%, respectively, were recorded. The deviations from the target temperature and humidity levels were not expected to affect the outcome of the study. Light timers were calibrated to provide a 12-hour light/12-hour dark photoperiod (6:00 a.m. to 6:00 p.m. Eastern Standard Time), and air handling units were set to provide approximately 10 to 15 fresh air changes per hour. On December 21-22, 1995 (study days 93-94), the lights were inadvertently left on for a 36-hour period. In addition, as a result of a technical error, it was necessary to extend the light cycle by 44 minutes on December 2, 1995 (study day 74) to allow completion of the 6-hour exposure period and the in-life study procedures. These deviations from the 12-hour light/12-hour dark photoperiod were not expected to affect the outcome of the study.

5. ASSIGNMENT OF ANIMALS TO TREATMENT GROUPS

At the conclusion of the acclimation period, all available animals were weighed and examined in detail for physical abnormalities. At the discretion of the Study Director, animals judged to be in good health and meeting acceptable body weight requirements were selected for use in the computer randomization procedure. The individual body weights were entered into the WIL Toxicology Data Management System (WTDMS™). A printout containing the animal numbers, corresponding body weights, and individual group assignment was generated based on body weight stratification randomized in a block design. The animals were then arranged into groups according to the printout. The experimental design consisted of four exposure groups and a control group, with 22 males and 22 females per group. At exposure initiation, the females were 43 days old, and body weights

ranged from 126 g to 173 g. Sixty-four females were below the protocol-specified weight range (150-250 g). However, because the animals were within the protocol-specified age range (42-63 days), this protocol deviation was not expected to affect the outcome of the study. In addition, mean body weights were comparable across all exposure groups at the start of the study, and the low-body-weight females were approximately equally distributed across all exposure groups. At randomization, the males were 90 days old, and body weights ranged from 323 g to 492 g.

6. OBSERVATIONS

a. CLINICAL OBSERVATIONS AND SURVIVAL

The animals were observed twice daily for appearance, behavior, moribundity, and mortality. Detailed physical examinations were recorded weekly throughout the study period for the males and females. Females were also observed for pharmacotoxic signs during exposure and within approximately one hour after completion of exposure. On several occasions, observations were performed up to one hour and 43 minutes following exposure, as a result of time required for clearing residual test article from the chamber atmospheres at the end of the exposure period. No significant clinical signs were noted during the exposure periods; therefore, no table for these observations was included in this report. The configuration of the cages and the location of the chamber windows precluded observations during exposure for some females. However, the positions of the females in the inhalation chambers were rotated on a daily basis, allowing all animals to be observed periodically throughout the exposure period. All

significant clinical findings were recorded at the post-exposure observations. The observations included, but were not limited to, examinations for changes in the skin, fur, eyes, mucous membranes, respiratory, circulatory, autonomic and central nervous system function, somatomotor activity, and behavior patterns. Special attention was paid to the degree of salivation and lacrimation, presence or absence of urination and defecation (including polyuria and diarrhea), pupil size, degree of palpebral closure, presence of convulsions, tremors or abnormal movements, presence of posture and gait abnormalities, and the presence of any unusual or abnormal behaviors and any repetitive actions (stereotypies). Females which delivered were also observed twice daily during the period of expected parturition and at parturition for dystocia.

b. BODY WEIGHTS

Individual F₀ male body weights were recorded on a weekly basis until euthanization, beginning with the initiation of mating. Group mean body weights were calculated weekly. Corresponding body weight changes were also calculated for each weekly interval.

Individual F₀ female body weights were recorded on a weekly basis, beginning with the initiation of exposure and continuing until evidence of copulation was observed. Group mean body weights were calculated weekly. Individual and group mean body weight changes were calculated for each weekly interval. Once evidence of mating was observed, individual female body weights were measured on gestation days 0, 7, 10, 14, and 20, and on lactation days 1, 4, 7, 14, and 21. Group mean body weights were calculated for each of these days. Individual and group mean body weight changes were

calculated for each corresponding gestation or lactation interval and for gestation days 0-20 and lactation days 1-21.

c. FOOD CONSUMPTION

Individual F₀ female food consumption was measured weekly until the initiation of the mating period. Food intake was not recorded during the mating period. Once evidence of mating was observed, individual female food consumption was measured on gestation days 0, 7, 10, 14, and 20, and on lactation days 1, 4, 7, 14, and 21. Food intake was calculated as g/animal/day and g/kg/day for the corresponding body weight change intervals. When food consumption could not be measured for a given interval (due to spillage, weighing error, obvious erroneous value, etc.), the appropriate interval was footnoted as "NA" (Not Applicable) on the individual tables.

7. REPRODUCTIVE PERFORMANCE

a. ESTROUS CYCLES

Vaginal smears were prepared to assess the regularity and duration of the estrous cycle of each female for 10 consecutive days before pairing³. Estrous cycle data for the F₀ females are presented in Appendix C.

b. BREEDING PROCEDURES

Before pairing on November 27, 1995, male body weights ranged from 323 g to 492 g; female body weights ranged from 203 g to 331 g. The males were approximately 13 weeks old, and the females were approximately 16 weeks old. Animals were paired on a 1:1 basis within each exposure group after the females were exposed to the test article for 70 consecutive days. A breeding

record containing the male and female identification numbers and the date of cohabitation was prepared. The females were housed in the home cage of the male. Each mating pair was examined daily. Positive evidence of mating was confirmed by the presence of sperm in a vaginal smear or a copulatory plug. The day when evidence of mating was identified was termed gestation day 0. The animals were separated, and the female was housed in an individual plastic cage with nesting material. When evidence of copulation was not detected after 10 days of pairing, the female was placed with another male from the same exposure group for an additional five days. The second male always had positive evidence of mating detected with a previous female. When evidence of mating was not apparent after 15 days, the female was placed in a plastic cage with nesting material.

Pre-coital intervals were calculated according to the following method: Rats paired over a 12-hour dark cycle were considered to have been paired for "one" day.

Fertility indices were calculated as follows:

Female Mating Index (%) =	$\frac{\text{No. of Females with Evidence of Mating}}{\text{Total No. of Females Used for Mating}}$	X 100
Male Mating Index (%) =	$\frac{\text{No. of Males with Evidence of Mating}}{\text{Total No. of Males Used for Mating}}$	X 100
Female Fertility Index (%) =	$\frac{\text{No. of Females with Confirmed Pregnancy}}{\text{Total No. of Females Used for Mating}}$	X 100

$$\text{Male Fertility Index (\%)} = \frac{\text{No. of Males Siring at Least 1 Litter}}{\text{Total No. of Males Used for Mating}} \times 100$$

8. FEMALES ALLOWED TO DELIVER

All females were allowed to deliver naturally and rear their young to PND 21. During the period of expected parturition, the females were observed twice daily for initiation and completion of parturition and for signs of dystocia. The day on which delivery was judged complete was designated PND 0. When parturition was judged complete, litters were sexed and examined for gross malformations, and the numbers of stillborn and live pups were recorded. Individual gestation lengths were calculated using the date delivery initiated.

D. F₁ LITTER DATA

1. LITTER VIABILITY AND DEATHS

Each litter was examined daily for survival, and all deaths were recorded. All pups were individually identified by the application of tattoo markings on the digits (AIMS® Identification Systems, Piscataway, New Jersey 08854) on PND 0. A daily record of litter size was maintained. Intact offspring dying from PND 0 to 4 were necropsied using a modification of the Stuckhardt and Poppe⁴ fresh dissection technique (including the heart and the brain examined by a mid-coronal slice). The carcasses were examined if a skeletal anomaly was suspected. The carcasses were eviscerated and fixed in 100% ethyl alcohol. Following fixation, each fetus was macerated in potassium hydroxide and stained with Alizarin Red S by a method described by Dawson⁵. Gross lesions were preserved in 10% neutral buffered formalin for possible future microscopic examination. Pups dying

between PND 5 and 28 were necropsied, and the following tissues were collected and preserved in 10% neutral buffered formalin:

Adrenals (2)	Mammary gland
Aorta	Ovaries with oviducts (2)
Bone with marrow (sternum)	Pancreas
Brain (forebrain, midbrain, hindbrain)	Penis
Clitoral gland	Peripheral nerve (sciatic)
Eyes with optic nerve (2)	Pituitary
Gastrointestinal tract	Prepuce
Esophagus	Preputial gland
Stomach	Prostate
Duodenum	Salivary gland [submaxillary (2)]
Jejunum	Seminal Vesicles
Ileum	Skeletal muscle (vastus medialis)
Cecum	Skin
Colon	Spinal cord (cervical, midthoracic and lumbar)
Rectum	Spleen
Heart (atria, ventricles and septum)	Testes with epididymides (2)*
Kidneys (2)	Thymus (if present)
Liver (sections of two lobes)	Thyroid gland [both lobes with parathyroids if present (2)]
Lungs [including bronchi, fixed by inflation with fixative (2)]	Trachea
Lymph nodes (mesenteric and mandibular)	Urinary bladder
	Uterus with vagina
	All gross lesions and masses

* = Testes and epididymides were fixed in Bouin's solution

2. LITTER REDUCTION

To reduce variability among the litters, eight pups per litter, four per sex when possible, were selected using a computerized randomization program on PND 4. Culled pups were weighed, euthanized, and discarded.

3. CLINICAL OBSERVATIONS

Litters were examined daily for any adverse changes in appearance or behavior. Each surviving pup received a detailed physical examination on PND 1, 4, 7, 14, 21, and 28; only remarkable observations were reported. Pups were also observed for pharmacotoxic signs during exposure (from PND 21 through PND 27) and within approximately one hour after completion of exposure. Abnormalities in nesting and nursing behavior, if present, were recorded.

4. BODY WEIGHTS

Pups were individually weighed on PND 1, 4, 7, 14, 21, and 28.

5. FOOD CONSUMPTION

Food consumption was not recorded between PND 21 and 28 because the weaned pups were housed together during this period.

6. SEX DETERMINATION

Pups were individually sexed on PND 0, 4, and 21.

7. SELECTION OF F₁ GENERATION

When litters reached an age of 21 days, one male and one female per litter were selected to obtain 20 males and 20 females from each group for exposure between PND 21 and 27. (Note: The 70 and 500 ppm groups had 21 litters each. Therefore, two litters in each of these groups contained a male pup or a female pup that was not selected.) Selection was done randomly by computer generation. All other pups (designated "day 21 surplus pups") were necropsied with emphasis on developmental morphology, as described in section IV.9.a. From the 20 pups/sex/group selected for test article exposure, 10 pups/sex/group (designated "day 28 selected pups") were subjected to a complete necropsy examination and organ weight data collection as

described in section IV.9. The remaining 10 pups/sex/group (designated "day 28 surplus pups") were necropsied in the same manner as the day 21 surplus pups.

Selected female pup no. 42223-08 (500 ppm group) died on PND 25. Female pup no. 42225-09 (500 ppm group) was arbitrarily selected to replace this pup for exposure.

8. CALCULATION OF LITTER PARAMETERS

Litter parameters were defined as follows:

$$\begin{aligned} \text{Live Litter Size} &= \frac{\text{Total Viable Pups Day 0}}{\text{No. Litters With Viable Pups Day 0}} \\ \text{Postnatal Survival Between Birth and PND 0 or PND 4 (Pre-Selection) (\% Per Litter)} &= \frac{\Sigma (\text{Viable Pups Per Litter on PND 0 or PND 4/No. of Pups Born Per Litter})}{\text{No. of Litters Per Group}} \times 100 \\ \text{Postnatal Survival for All Other Intervals (\% Per Litter)} &= \frac{\Sigma (\text{Viable Pups Per Litter at End of Interval N/Viable Pups Per Litter at Start of Interval N})}{\text{No. of Litters Per Group}} \times 100 \end{aligned}$$

Where N = PND 0-1, 1-4 (Pre-Selection), 4 (Post-Selection)-7, 7-14, 14-21 or 4 (Post-Selection)-21

9. PND 21 AND 28 NECROPSIES

a. MACROSCOPIC EXAMINATIONS

The surplus F₁ pups were euthanized via carbon dioxide inhalation (day 21 surplus pups) or lateral tail vein injection of sodium pentobarbital (day 28 surplus pups) and necropsied on PND 21 or PND 28 with an emphasis on developmental morphology. Tissues were preserved in 10% neutral buffered formalin for possible future histopathological examination only as deemed necessary by the gross findings. The carcasses of the pups were then discarded. On PND 28, the day 28 selected pups were

euthanized via lateral tail vein injection of sodium pentobarbital and subjected to a complete necropsy examination, with the following exception. Pup no. 42281-07 was inadvertently euthanized via carbon dioxide inhalation. The necropsy included, but was not limited to, examination of the external surface, all orifices, and the cranial, thoracic, abdominal and pelvic cavities, including viscera. The tissues listed in Section IV.D.1. were collected and preserved in 10% neutral buffered formalin.

b. ORGAN WEIGHTS

The following organs from the day 28 selected pups were weighed: liver; ovaries; and testes.

E. PATHOLOGY

1. MACROSCOPIC EXAMINATIONS

When breeding was completed, all surviving F₀ males were euthanized and discarded on December 13, 1995. A complete necropsy examination was conducted on all F₀ females. All females which delivered were necropsied on lactation day 21, and the numbers of previous implantation sites were recorded. Bred females which did not deliver a litter were necropsied on post-mating day 25 (evidence of mating) or 25 days following the conclusion of the breeding period (no evidence of mating). A detailed gross necropsy was performed on each bred female that did not deliver to determine pregnancy status, with specific emphasis placed on anatomical or pathological findings which may have interfered with pregnancy. Uteri without macroscopic evidence of implantation were opened and placed in 10% ammonium sulfide solution for detection of implantation sites as described by Salewski⁶. All animals were euthanized with an injection of sodium

pentobarbital via the tail vein, with the following exception. Female no. 42302 (500 ppm group) was inadvertently euthanized via carbon dioxide inhalation. The necropsy included an examination of the external surface, all orifices, the cranial cavity, the external surfaces of the brain and spinal cord, and the thoracic, abdominal, and pelvic cavities including the viscera. The tissues listed in Section IV.D.1. were collected and preserved in 10% neutral buffered formalin. Tissues were inadvertently not collected from female no. 42302 (500 ppm group).

2. ORGAN WEIGHTS

The following organs from all F₀ females euthanized at scheduled termination were weighed:

Adrenals	Ovaries
Brain	Pituitary
Heart	Spleen
Kidneys	Thymus
Liver	Thyroid
Lungs	Uterus

Organ weights were inadvertently not collected for female no. 42302 (500 ppm group), which was euthanized 25 days following the breeding period.

3. MICROSCOPIC EXAMINATION

The following tissues from all F₀ females in the control and 700 ppm groups were examined microscopically:

Adrenals	Spleen
Brain-hypothalamus	Thymus
Kidneys ^a	Uterus ^d
Liver	Vagina
Lungs ^a	All gross (internal) lesions
Mammary gland ^b	
Ovaries ^c	
Pituitary	

- ^a = The kidneys from all females and the lungs from all females euthanized on lactation day 21 were examined microscopically even though not required by protocol.
- ^b = The mammary glands for control group females euthanized on post-mating day 25 were inadvertently not examined.
- ^c = The ovaries were serially sectioned to count follicles and assess follicular maturation.
- ^d = The uteri from females that failed to deliver were placed in ammonium sulfide solution for detection of implantation sites; these uteri were not examined microscopically.

The following procedure was used for the preparation of all tissues, with the exception of the ovaries. After fixation, the tissues were trimmed as described by Thompson⁷. Trimmed specimens were placed into properly labeled and numbered cassettes. The fixed tissue samples were processed into paraffin blocks. The labeled paraffin blocks were sectioned at 5-8 microns, and the paraffin ribbons of the sectioned tissues were placed on clean glass microscope slides labeled with the appropriate study, animal, group, and cassette numbers. Upon completion of staining with hematoxylin and eosin (AFIP Manual of Histologic Staining Methods⁸), coverslips were placed on the slides.

The ovaries were prepared as follows to obtain follicle counts and to assess follicular maturation^{9, 10}. The ovaries were fixed, trimmed, and embedded in paraffin blocks, as described previously. One ovary from each female was stored in the paraffin block. The remaining ovary from

each female was serially sectioned to obtain a minimum of 100 sections, and the sections were placed on clear glass microscope slides (five sections per slide) and stained with hematoxylin and eosin. A total of 10 random sections (selected by the computer from a base number of 100) were examined, and counts were obtained and classified as follows:

Corpora lutea

Mature

Degenerate

Oocytes with no follicular cells attached to the surface

Oocytes with multiple layers of follicular cells attached to the surface

Oocytes surrounded by a fluid-filled cavity

Oocytes with follicular fluid and a well-formed cumulus stalk

Microscopic examinations were performed by the late Dr. Robert R. Dahlgren, Director of Pathology and Veterinary Medicine, WIL Research Laboratories, Inc. The histopathological examination results were reviewed by Dr. Dahlgren, with the following exception. The results of the ovarian examinations were reviewed by Dr. Carney B. Jackson, Assistant Director of Pathology and Veterinary Medicine.

F. STATISTICAL METHODS

All analyses were conducted for a minimum significance level of 5% comparing each treated group to the control group; all means are presented with standard deviations (S.D.). All tests for significance at the 5% probability level were two-tailed for the group comparisons. The litter was used as the experimental unit. Data obtained from nonpregnant animals were excluded from statistical analysis following the mating period. Statistical analyses were not conducted on weekly female body weight and food consumption data after one or more animals had entered the gestational phase. The numbers of animals (N) used to calculate the means are provided on the individual data tables. All statistical tests are performed by a Digital®

MicroVAX® 3400 Computer (with appropriate programming) in this laboratory and are referenced on the report tables.

<u>STATISTICAL TEST</u>	<u>PARAMETER</u>
- Chi-square test ¹¹ with Yates' correction factor	Parental Mating and Fertility Indices
- ANOVA (two-tailed) with Dunnett's test ¹¹	F ₀ Body Weights and Weight Gains, Gestation and Lactation Body Weights and Weight Gains, Parental Food Consumption, Mean Litter Weights, Length of Gestation, Live Litter Sizes, Organ Weights, Implantation Sites, Number of Pups Born, Number of Unaccounted Sites
- Kruskal-Wallis test ¹¹	Pup Sexes at Birth, Postnatal Survival (PND 0-21)

The original protocol specified the use of pup-based statistics (Chi-square test with Yates' correction factor¹¹) for the evaluation of postnatal survival. Based on the recommendations of the Food and Drug Administration Guideline on Detection of Toxicity to Reproduction for Medicinal Products¹², Holson *et al*¹³, and Nelson and Holson¹⁴, the protocol was amended (Protocol Amendment VI) to replace these statistics with litter-based statistics (mean litter proportions), in which the litter is the experimental and statistical unit. For these analyses, the Kruskal-Wallis¹¹ test was used.

G. DATA RETENTION

The Sponsor has title to all documentation, records, raw data, specimens, or other work product generated from this study. All work product including raw paper data and specimens is retained in the Archives at WIL Research

DC Study No. - 8463
External No. - WIL-51041

DC Report No. - 1997-I0000-42936
Security - INTERNAL

Laboratories, Inc., until notification from the Sponsor regarding final disposition of the said work product.

Raw data in magnetic form, retention samples of the test article, the original protocol and amendments, and the original final report are retained at WIL Research Laboratories, Inc., 1407 George Road, Ashland, Ohio 44805-9281, in compliance with regulatory requirements.



V. RESULTS

A. CHAMBER CONCENTRATIONS

Summary Data: Appendix B

The F₀ females were exposed to target test article concentrations of 70, 300, 500, and 700 ppm. The actual measured mean exposure concentrations were 72, 302, 498, and 700 ppm, respectively.

B. F₀ GENERATION

1. CLINICAL OBSERVATIONS AND SURVIVAL

Summary Data: Tables 1, 3, 4

Individual Data: Appendix D

All F₀ females survived to the scheduled necropsies. Exposure-related clinical signs noted in the F₀ females one hour following exposure included dried red material around the nose and/or mouth, noted between weeks 1 and 15 at increased incidences in the 300, 500, and 700 ppm groups. Dried red material around the left and/or right eyes was noted between weeks 1 and 10, and wet red material around the nose was noted between weeks 1 and 12 at slightly increased incidences (relative to the control group) in the 700 ppm group. Other clinical signs noted in the treated groups occurred infrequently and/or at a similar frequency in the control group.

All F₀ males survived to the scheduled euthanization. Clinical signs noted in the untreated male animals were those commonly observed in healthy laboratory rats of this species and strain.

2. REPRODUCTIVE PERFORMANCE

Summary Data: Table 2

Individual Data: Table 41

Historical Control Data: Appendices C, E, F

Reproductive performance was not adversely affected by exposure to the test article. Male and female mating indices were 100%, 100%, 100%, 95.5%, and 100.0% in the control, 70, 300, 500, and 700 ppm groups, respectively. One female in the 500 ppm group had no evidence of mating, did not deliver, and was nongravid. Fertility indices for males and females were 90.9%, 95.5%, 90.9%, 95.5%, and 90.9% in the same respective dose groups. Males which did not sire a litter numbered 2, 1, 2, 1, and 2 in the control, 70, 300, 500, and 700 ppm groups, respectively. No males sired more than one litter. In the control, 70, 300, 500, and 700 ppm groups, 2, 1, 2, 0, and 2 females, respectively, had evidence of mating but did not deliver. All females that failed to deliver were found to be nongravid at the *post mortem* examination.

The mean numbers of days between pairing and coitus were 2.3, 3.2, 2.7, 3.0, and 2.6 in the control, 70, 300, 500, and 700 ppm groups, respectively, as compared to a mean value of 3.3 days and a range of 2.3 to 6.1 days in the WIL historical control data. The WIL reproductive historical control data base consists of data from 85 individual data sets generated between 1982 and 1994.

Individual variation in the estrous cycle occurred in all study groups. The regularity and duration of estrous were not affected by treatment.

3. BODY WEIGHTS

a. WEEKLY

Summary Data: Tables 5, 6

Individual Data: Tables 42, 43

During week 0-1, statistically significant ($p < 0.01$) reductions in mean body weight gain were noted in the 500 and 700 ppm group females; these effects were attributed to test article exposure. Mean body weight gains in these groups were unaffected by test article exposure throughout the remainder of the pre-mating period. Mean body weight gains in the 70 and 300 ppm groups were unaffected by exposure during the pre-mating period.

Statistically significant ($p < 0.05$) reductions in mean body weight gain were noted in the 500 and 700 ppm groups during week 3-4. However, because no exposure-response relationship was evident, the reductions were not considered to be exposure-related. Slight numerical decreases (statistically insignificant) in mean body weights were noted among treated female rats in the 300, 500, and 700 ppm groups relative to controls throughout the pre-mating period. Although the reductions in mean body weight at 300, 500, and 700 ppm were not statistically significant and did not appear to follow a clear exposure-response relationship, they were of the greatest magnitude in the 700 ppm group. The magnitude of the reductions in each group remained similar throughout the pre-mating period. The biological relevance, if any, of the body weight reductions remains uncertain.

Mean body weights and body weight gains in the untreated male animals were within normal ranges for this species and strain.

b. GESTATION

Summary Data: Tables 7, 8

Individual Data: Tables 44, 45

Mean body weight gains in the 700 ppm group were unaffected by test article exposure during gestation days 0-7 and 7-10. During gestation days 10-14 and 14-20 and when the entire gestation period (gestation days 0-20) was evaluated, slight reductions were observed in mean body weight gains in the 700 ppm group. Mean body weight gains in the 70, 300, and 500 ppm groups were unaffected by test article exposure throughout gestation. Slight numerical decreases (statistically insignificant) in mean body weights were noted among the treated rats relative to controls throughout the gestation period. These changes were statistically significant ($p < 0.05$) only in the 700 ppm group on gestation days 14 and 20. The reductions in mean body weights and body weight gains during late gestation in the 700 ppm group were likely due, at least in part, to the decreased viable litter size in this group (see section V.B.4).

c. LACTATION

Summary Data: Tables 9, 10

Individual Data: Tables 46, 47

Mean body weight gains in the 700 ppm group were similar to the control group values during lactation days 1-4, 4-7, and 7-14. During lactation days 14-21, the mean body weight loss observed in the 700 ppm group was milder than was observed in the control group; the difference was statistically significant ($p < 0.01$). When the entire lactation period (lactation days 1-21) was evaluated, a statistically significant ($p < 0.05$) increase in mean body weight gain was noted in

the 700 ppm group. Mean lactation body weight gains in the 70, 300, and 500 ppm groups were unaffected by test article exposure. Slight numerical decreases in mean body weights were noted among the treated rats relative to controls during lactation days 1, 4, 7, and 14. These decreases were often statistically significant ($p < 0.05$) in the 700 ppm group. Mean body weights in the treated rats were similar to the control group value on lactation day 21.

4. FOOD CONSUMPTION

a. WEEKLY

Summary Data: Tables 11, 12

Individual Data: Tables 48, 49

Weekly food consumption, evaluated as g/animal/day and g/kg/day, in F_0 females was unaffected by test article exposure at all exposure levels. Intermittent statistically significant ($p < 0.05$ or $p < 0.01$) increases and decreases in weekly food consumption were observed throughout the pre-breeding period. However, the differences were slight, were only observed using one method of evaluation (g/animal/day or g/kg/day), and/or were not observed to be dose-related.

b. GESTATION

Summary Data: Tables 13, 14

Individual Data: Tables 50, 51

Food consumption, evaluated as g/animal/day and g/kg/day, was not affected by exposure to the test article at any exposure level during gestation. A statistically significant ($p < 0.05$) reduction in food consumption, evaluated as g/animal/day, was noted in the 500 ppm group during gestation days 0-7. Because a similar reduction was not

observed in the 700 ppm group, the effect was not considered to be a result of test article exposure. Statistically significant ($p < 0.05$ or $p < 0.01$) increases in food consumption, evaluated as g/kg/day, were observed in the 500 and 700 ppm groups during gestation days 14-20. However, increases in food consumption are not considered to be toxicologically significant.

c. LACTATION

Summary Data: Tables 15, 16

Individual Data: Tables 52, 53

Food consumption, evaluated as g/animal/day and g/kg/day, was unaffected by exposure to the test article during lactation. The only statistically significant ($p < 0.05$) difference between the control and treated groups was a reduction in food consumption, evaluated as g/animal/day, in the 700 ppm group when the entire lactation period (lactation days 1-21) was evaluated. Because the reduction was slight (4 g/animal/day) and because the individual reductions for lactation days 1-4, 4-7, 7-14, and 14-21 and the reduction in the g/kg/day value for the entire interval (lactation days 1-21) were slight and not statistically significant, the effect was not believed to have been biologically relevant.

5. GESTATION LENGTH AND PARTURITION

Summary Data: Table 17

Individual Data: Table 54

Historical Control Data: Appendices E, F

The mean durations of gestation were comparable between the control and treated groups. No differences were statistically significant. The mean gestation durations in the 70, 300, 500, and 700 ppm groups were 21.9,

21.7, 21.8, and 22.0 days, respectively, compared to mean gestation durations of 21.8 days in the concurrent control group and 21.9 days (range = 21.5-22.8 days) in the WIL reproductive historical control data.

No signs of dystocia were observed at parturition in animals at any exposure level.

C. E, LITTER DATA

1. PND 0 LITTER DATA AND POSTNATAL SURVIVAL

Summary Data: Tables 18, 18A, 18B

Individual Data: Tables 55, 56

Historical Control Data: Appendices E, F

The mean live litter size (9.9 pups per litter) and the mean number of pups born (10.4 pups per litter) in the 700 ppm group were reduced relative to the control group values (a mean live litter size of 13.5 pups per litter and 13.6 pups born per litter); the differences were statistically significant ($p < 0.01$) and were attributed to treatment. The mean live litter size in the 700 ppm group was also below the range in the WIL historical control data (11.7-15.9 pups per litter). Mean live litter sizes and numbers of pups born in the 70, 300 and 500 ppm groups were similar to the control group values and were unaffected by exposure. The percentage of males per litter at birth was unaffected by exposure in all groups; differences between the control and exposed groups were slight and were not statistically significant.

The initial pup-based statistical analysis of pup data indicated a statistically significant increase in the number of pups dead on PND 0 at 700 ppm. This apparent finding was the result of pup-based statistics that were determined to be inappropriate^{12,13,14}. The findings from the pup-based statistical analysis are not presented in this report; however, they are

included in the raw data maintained at WIL Research Laboratories, Inc. for this study. Upon application of the appropriate litter-based statistics, it was found that pre-weaning pup survival (percent per litter) was not affected by test article exposure at any exposure level from birth to PND 0, PND 0 to 1, PND 1 to 4, PND 4 to 7, PND 7 to 14, PND 14 to 21, birth to PND 4 and PND 4 to 21. Differences between the control and exposed groups were slight and were not statistically significant.

Post-weaning pup survival was similar in all study groups. Between PND 21 and 28, 1, 0, 1, 1 and 0 pups in the control, 70, 300, 500 and 700 ppm groups, respectively, were found dead.

2. GENERAL PHYSICAL CONDITION AND MORTALITIES

Summary Data: Tables 19, 20

Individual Data: Tables 55, 56, 57, 58

Pups which were found dead from birth through PND 28 numbered 4, 12, 3, 13, and 10 in the control, 70, 300, 500, and 700 ppm groups, respectively. In these same groups, 3, 4, 3, 6, and 5 pups, respectively, were missing and presumed to be cannibalized; for purposes of statistical analyses, missing pups were treated as dead. The only malformations observed were cleft lip, maxillary micrognathia, and ablepharia in control group pup no. 42248-01. Clinical signs that were noted during the lactation period occurred infrequently and/or at a similar frequency in the control group.

In the necropsy of the pups that were found dead, one pup in the 700 ppm group had exencephaly (with fusion of the frontal and parietal bones and reduced ossification of the parietal bone). One pup in the 500 ppm group had renal papillae that were not fully developed. One pup in the 300 ppm group had dark red areas on the lungs. These findings

were considered to be sporadic and not related to test article exposure. One control group pup had red fluid contents in the bladder, dark red areas in the stomach, and dark red contents in the stomach and duodenum. Aside from the presence or absence of milk in the stomach, no other internal findings were noted at the necropsies of pups that were found dead.

3. PUP BODY WEIGHTS

Summary Data: Table 24

Individual Data: Tables 62, 63

Historical Control Data: Appendices E, F

No adverse effects of the test article were observed on mean pup weights on PND 1, 4 (before and after culling), 7, 14, 21, and 28 at any exposure level. Differences from the control group values were not statistically significant.

4. PND 21 AND 28 NECROPSIES

a. MACROSCOPIC EXAMINATIONS

Summary Data: Tables 21, 22, 23

Individual Data: Tables 59, 60, 61

At the necropsy of the day 21 surplus pups, no exposure-related findings were macroscopically evident. In the control, 70, and 300 ppm groups, 2, 1, and 4 pups, respectively, had dilation of one or both renal pelves. One pup in the 70 ppm group had distended ureters. No other remarkable findings were noted.

At the necropsy of surplus pups on PND 28, no macroscopic exposure-related findings were noted. In the 70, 300, and 500 ppm groups, 3, 1, and 1 pups, respectively, had dark red areas on the lungs. One pup in the 700 ppm group had dark red lungs (all lobes).

Two pups in the 70 ppm group each had a dilated right renal pelvis. No other remarkable findings were noted at any exposure level.

At the necropsy of selected pups on PND 28, no exposure-related macroscopic findings were noted. In the control, 70, 300, 500, and 700 ppm groups, 0, 1, 1, 0, and 1 males and 1, 1, 2, 2, and 1 females had dark red lungs (all lobes). In these same respective groups, 1, 1, 2, 1, and 1 males and 0, 0, 1, 0, and 0 females had mottled lungs (all lobes). One male in the 500 ppm group and one female in the 70 ppm group had multiple dark red areas on the lungs. One male in the 300 ppm group and one female each in the 70, 300, and 500 ppm groups had dilation of one or both renal pelvises. One female each in the 300, 500, and 700 ppm groups had one or more white areas on the liver. One male in the 500 ppm group and one female each in the control and 300 ppm groups had red fluid contents in the trachea. Other findings in the treated groups at the necropsies of the day 28 selected pups were observed infrequently (in single animals).

b. ORGAN WEIGHTS - PND 28 SELECTED PUPS

Summary Data: Tables 25, 26

Individual Data: Tables 64, 65

At the necropsy of the selected pups on day 28, no effects of exposure were observed on absolute or relative (to final body weights) organ weights. The only statistically significant ($p < 0.05$) differences between the control and treated groups were reductions in the absolute testicular weight in the 300 ppm group and in the relative ovarian weight in the 70 ppm group. As similar reductions were not observed at higher exposure levels, the differences were not considered to be treatment-related.

D. PATHOLOGY

1. MACROSCOPIC EXAMINATIONS

a. F₀ FEMALE - 25 DAYS FOLLOWING THE BREEDING PERIOD

Summary Data: Table 27

Individual Data: Table 66

One female in the 500 ppm group had no evidence of mating and was necropsied 25 days following the conclusion of the breeding period. This animal was nongravid, and no internal abnormalities were detected macroscopically.

b. F₀ FEMALES - POST-MATING DAY 25

Summary Data: Table 28

Individual Data: Table 67

In the control, 70, 300, and 700 ppm groups, 2, 1, 2, and 2 females, respectively, had evidence of mating but did not deliver and were necropsied on post-mating day 25. All of these females were nongravid. One female in the 700 ppm group had dark red lungs (all lobes). No other internal findings were noted at the necropsy of these animals.

c. F₀ FEMALES - LACTATION DAY 21

Summary Data: Tables 29, 30

Individual Data: Tables 68, 69

At the scheduled necropsy of F₀ females on lactation day 21, no exposure-related findings were noted at any exposure level. In the control, 70, 300, and 700 ppm groups, 2, 2, 1, and 1 females, respectively, had reddened mandibular lymph nodes. Two, one, and one animals in the 70, 300, and 500 ppm groups, respectively, had dilation of one or both renal pelves. Two females in the 70 ppm

group and one female in the 500 ppm group had dark red areas on the lungs. One or more cysts were noted on the spleen of one animal each in the control, 70, and 500 ppm groups. One animal each in the 70, 300, and 700 ppm groups had a reddened mediastinal lymph node, and one animal each in the 300 and 700 ppm groups had an enlarged mediastinal lymph node. One animal each in the 300 and 700 ppm groups had one or more white nodules in the mesentery. Other findings noted in females at the scheduled necropsy on lactation day 21 were observed infrequently, in single animals.

The mean number of implantation sites and the mean number of pups born were reduced, and the number of sites unaccounted for (the number of implantation sites not producing a pup) was increased in the 700 ppm group. The differences from the control group were statistically significant ($p < 0.05$ or $p < 0.01$) and were considered to be exposure-related. The mean number of implantation sites (12.3) and the mean number of sites unaccounted for (1.9) in the 700 ppm group were both within the ranges, but were below the mean and above the mean for these parameters, respectively, in the WIL historical control data. In the WIL historical control data, the mean number of implantation sites is 14.5 (range = 11.0 to 16.9), and the mean number of sites unaccounted for is 1.0 (range = 0.0 to 2.3).

2. ORGAN WEIGHTS

a. F₀ FEMALES - POST-MATING DAY 25

Summary Data: Tables 31, 33, 35

Individual Data: Tables 72, 74, 76

Mean liver weights (absolute and relative to final body weight and brain weight) were slightly increased (relative to the control group

values) in the 300 and 700 ppm group females euthanized on post-mating day 25. All other organ weight values (absolute and relative) in the exposed groups were similar to the control group values. None of the differences was statistically significant.

b. F₀ FEMALES - LACTATION DAY 21

Summary Data: Tables 32, 34, 36

Individual Data: Tables 73, 75, 77

Mean liver weights (absolute and relative to final body weight and brain weight) were increased in the 300, 500, and 700 ppm group females at the scheduled necropsy on lactation day 21. The differences between the control and treated groups were often statistically significant ($p < 0.05$ or $p < 0.01$) and were considered to be related to exposure to the test article. Other organ weights (absolute and relative) in these animals were similar to the control group values. The only other statistically significant ($p < 0.01$) differences between the control and treated groups were increases in mean uterine weights (absolute and relative to final body weight and brain weight) in the 70 ppm group. However, because similar increases were not observed at higher exposure levels, the increases were not considered to be exposure-related.

3. MICROSCOPIC EXAMINATIONS

a. F₀ FEMALES - POST-MATING DAY 25

Summary Data: Tables 37, 39

Individual Data: Tables 67, 70

At the microscopic examination of F₀ females on post-mating day 25, no exposure-related findings were noted. One female in the 700 ppm group had severe alveolar edema in the lungs (one lobe), and

two females in this group had immature development of the mammary gland. No other microscopic findings were noted in animals at any dose level.

No treatment-related effects were noted in the ovarian follicle counts for these females. Values in the 700 ppm group were generally similar to those in the control group.

b. F₀ FEMALES - LACTATION DAY 21

Summary Data: Tables 38, 40

Individual Data: Tables 68, 71

At the microscopic examination of F₀ females on lactation day 21, no exposure-related findings were noted. Four females in the 700 ppm group and one female in the control group had inactive mammary gland secretion. Two females in the 700 ppm group had alveolar histiocytosis, and two control group animals had acute alveolar hemorrhage. One female in the 700 ppm group and two females in the control group had hydrometra. Two control group females had renal tubular mineralization at the corticomedullary junction. No other microscopic findings were noted at the scheduled necropsy of F₀ females on lactation day 21.

No treatment-related effects were noted on the ovarian follicle counts for these females. Values in the 700 ppm group were generally similar to the control group values. The relative numbers of follicles at various stages of follicular development suggested that no striking depression of ovarian function was present. The analysis of randomly selected ovarian sections is expected to produce highly variable results, and this could have precluded the detection of a subtle effect on ovarian function.

VI. DISCUSSION AND CONCLUSIONS

Estrous cyclicity, days between pairing and coitus, mating indices, fertility indices, duration of gestation, and the process of parturition were not adversely affected by exposure of the F₀ females to the test article at exposure levels of 70, 300, 500, and 700 ppm. Fertility indices were 90.9% or higher, and mating indices were 95.5% or higher in all groups, including the control group.

All F₀ females and males survived to their respective euthanizations. Exposure-related clinical signs noted in the F₀ females during the observations made one hour following exposure included dried red material around the nose and/or mouth (noted at increased incidences in the 300, 500, and 700 ppm groups) and dried red material around the eyes and/or wet red material around the nose (observed at slightly increased incidences in the 700 ppm group).

Mean body weight gains in the 500 and 700 ppm group females were reduced (statistically significant) during week 0-1 of the pre-mating period. Mean body weight gains in these animals were unaffected by exposure throughout the remainder of the pre-mating phase. During gestation, mean body weight gains in the 700 ppm group were unaffected by test article exposure during days 0-7 and 7-10. During gestation days 10-14 and 14-20, mean body weight gains in the 700 ppm group were reduced relative to the control group values. These reductions were accompanied by statistically significant decreases in mean body weights in these animals on gestation days 14 and 20. The decreased body weight gains late in gestation among the 700 ppm group females were likely due, at least in part, to the decreased viable litter size seen with this treatment group. On lactation days 1, 4, 7, and 14, reductions (often statistically significant) in mean body weights were noted in the 700 ppm group. The mean body weight in these animals was similar to that in the control group on lactation day 21. Mean body

weight gains were unaffected by test article exposure throughout the study in the 70 and 300 ppm groups and during gestation and lactation in the 500 ppm group.

Food consumption, evaluated as g/animal/day and g/kg/day, was unaffected by exposure to the test article at exposure levels of 70, 300, 500, and 700 ppm during the pre-breeding, gestation, and lactation periods.

At the necropsies of the nongravid F₀ females 25 days following the breeding period and 25 days post-mating, no internal findings related to exposure to the test article were observed at any exposure level. In the 700 ppm group females that delivered litters, the mean number of implantation sites was reduced, and the number of sites unaccounted for was increased; the differences from the control group were statistically significant. These parameters were unaffected at exposure levels of 70, 300, and 500 ppm. Mean liver weights (absolute and relative to final body weight and brain weight) were elevated in the 300, 500, and 700 ppm groups; the differences were often statistically significant. Liver weights in the 70 ppm group were comparable to the control group values.

No exposure-related findings were noted at the microscopic examination of the F₀ females. No treatment-related effects were noted on the ovarian follicle counts for these females. The relative numbers of follicles at various stages of follicular development suggested that the ovaries were functional. However, the assessments were performed on lactation day 21; therefore, these results do not preclude the possibility that deficits in ovarian function occurred at the time of ovulation.

Mean live litter size and the mean number of pups born were reduced in the 700 ppm group relative to the control group values; the differences were statistically significant. These parameters were unaffected at exposure levels of 70, 300, and 500 ppm. Mean pup body weights and pup survival were unaffected at all exposure levels throughout lactation. The percentage of males per litter at birth was unaffected by exposure to the test article at all exposure levels. At the

necropsies of surplus pups on PND 21 and 28, the necropsies of pups found dead, and the necropsy of selected pups on PND 28, no exposure-related findings were noted. Organ weights (absolute and relative) for the PND 28 selected pups were unaffected by exposure to the test article.

In conclusion, maternal toxicity was demonstrated in the F₀ females at exposure levels of 300, 500, and 700 ppm by clinical signs, at exposure levels of 500 and 700 ppm by slight reductions in mean body weight gains during the first week of the pre-mating period, and at an exposure level of 700 ppm by reductions in mean body weights and/or body weight gains during the gestation and lactation periods. Mean liver weights (absolute and relative) were increased in the F₀ females at exposure levels of 300, 500, and 700 ppm. Reductions in mean live litter size and in the number of pups born were noted in the 700 ppm group. Postnatal toxicity (F₁ pups) was not observed at exposure levels of 70, 300, or 500 ppm. Toxicity in the 700 ppm group dams was further demonstrated by a reduction in the number of implantation sites and an increased numerical difference between the number of implantation sites and the number of offspring.



Joseph F. Holson, Ph.D.
Study Director

7/29/97
Date

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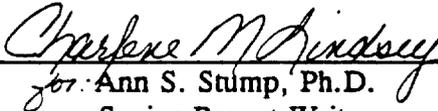
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VII. KEY STUDY PERSONNEL AND REPORT SUBMISSION

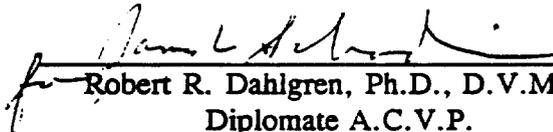
Study Supervisors:

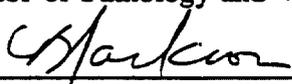
Sally A. Keets, A.S.	Manager of Vivarium
Daniel W. Sved, Ph.D.	Director of Metabolism and Analytical Chemistry
Kerin Clevidence, B.S.	Group Supervisor of Gross Pathology and Developmental Toxicology Laboratory

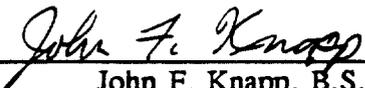
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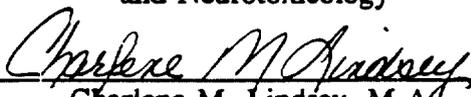
 Ann S. Stump, Ph.D. Senior Report Writer	<u>7/28/97</u> Date
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Reviewed By:

 Robert R. Dahlgren, Ph.D., D.V.M., * Diplomate A.C.V.P. Director of Pathology and Veterinary Medicine	<u>7/29/97</u> Date
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 Carney B. Jackson, D.V.M., D.A.C.V.P., D.A.C.V.P.M. Assistant Director of Pathology and Veterinary Medicine	<u>7/29/97</u> Date
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 John F. Knapp, B.S. Manager II, Developmental, Reproductive and Neurotoxicology	<u>7/29/97</u> Date
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 Charlene M. Lindsey, M.A. Manager of Technical Report Writing	<u>7/28/97</u> Date
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* = signed for the late Dr. Dahlgren

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VII. KEY STUDY PERSONNEL AND REPORT SUBMISSION (continued)

Reviewed By:

Mark D. Nemece
Mark D. Nemece, B.S., D.A.B.T.
Director of Developmental
and Reproductive Toxicology

7/29/97
Date

James L. Schardein
James L. Schardein, M.S., A.T.S.
Senior Vice President,
Director of Research

7/29/97
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Mark D. Stump
Donald G. Stump, Ph.D.
for: Staff Toxicologist, Developmental,
Reproductive and Neurotoxicology

7/29/97
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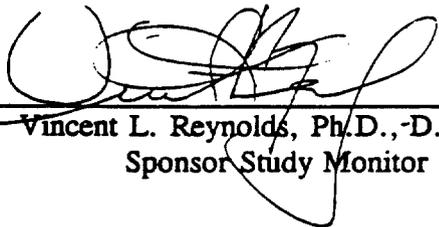
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An Inhalation Range-Finding Reproductive Toxicity
Study of Octamethylcyclotetrasiloxane (D4) in Female Rats

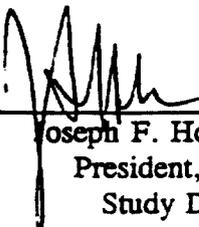
VIII. APPROVAL SIGNATURES

This report consists of pages 1 through 1147 including Tables 1 through 77 and Appendices A through G.



Vincent L. Reynolds, Ph.D., -D.A.B.T.
Sponsor Study Monitor

29 July 1997
Date



Joseph F. Holson, Ph.D.
President, Director
Study Director

7/29/97
Date

IX. REFERENCES

1. EPA OPPTS Health Effects Test Guidelines 870.3800 - Reproduction and Fertility Effects [Draft], July 1994.
2. NIH (1985) Guide for the Care and Use of Laboratory Animals. United States Department of Health and Human Services, Public Health Service, National Institutes of Health, NIH Publication No. 86-23, 83 pages.
3. Saunders, L.Z. (1969) In: Pathology & Toxicology Technique Manual, SK & F, Smith, Kline & French Laboratories, Philadelphia, PA, pp. 2-4.
4. Stuckhardt, J.L. and Poppe, S.M. (1984) Fresh visceral examination of rat and rabbit fetuses used in teratogenicity testing. *Teratogenesis, Carcinogenesis and Mutagenesis* 4:181-188.
5. Dawson, A.B. (1926) A note on the staining of the skeleton of cleared specimens with Alizarin Red S. *Stain Technol.* 1:123-124.
6. Salewski (Köln), V.E. (1964) Farbemethode zum makroskopischen Nachweis von Implantationstellen am Uterus der Ratte. *Naunyn - Schm. Archiv. für Exper. Pathologie und Pharm.* 247:367.
7. Thompson, S.W. (1966) Tissue processing and embedding. In: *Selected Histochemical and Histopathological Methods.* Charles C. Thomas, Springfield, IL, pp. 29-37.
8. American Registry of Pathology (1968) *Manual of Histologic Staining Methods of the Armed Forces Institute of Pathology*, 3rd ed., (Luna, L.G., ed.) McGraw-Hill Book Co., New York, NY, pp. 38-39.
9. Smith, B.J., Plowchalk, D.R., Sipes, I.G. and Mattison, D.R. (1991) Comparison of random and serial sections in assessment of ovarian toxicity. *Reprod. Tox.* 5(4): 379-383.
10. Pedersen, T. and Peters, H. (1968) Proposal for a classification of oocytes and follicles in the mouse ovary. *J. Reprod. Fert.* 17:555-557.

IX. REFERENCES (continued)

11. BMDP (1979) Biomedical Computer Programs. (Dixon, W.J. and Brown, M.B., eds.) University of California Press, Berkeley, CA, pp. 612, 780, 781.
12. Federal Register, Volume 59, No. 183, pp. 48746-48752, September 22, 1994.
13. Holson, J.F., Scott, W.J., Gaylor, D.W. and Wilson, J.G. (1976) Reduced interlitter variability in rats resulting from a restricted mating period, and reassessment of the "litter effect." *Teratology* 14(2):135-141.
14. Nelson, C.J. and Holson, J.F. (1978) Statistical analysis of teratologic data: problems and advancements. *Journal of Environmental Pathology and Toxicology* 2:187-199.

DC Study No. - 8463
External No. - WIL-51041

DC Report No. - 1997-I0000-42936
Security - INTERNAL

**An Inhalation Range-Finding Reproductive Toxicity
Study of Octamethylcyclotetrasiloxane (D4) in Female Rats**

SUMMARY TABLES 1-40



TABLE 1 (FO)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF SURVIVAL AND DISPOSITION

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP :	MALES															
	1			2			3			4			5			
WEEK	LIVE	FD	EE SE	LIVE	FD	EE SE	LIVE	FD	EE SE	LIVE	FD	EE SE	LIVE	FD	EE SE	
10	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0	
11	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0	
12	0	0	0 22	0	0	0 22	0	0	0 22	0	0	0 22	0	0	0 22	
WEEK = WEEK OF STUDY FD = FOUND DEAD EE = EUTHANIZED IN EXTREMIS SE = SCHEDULED EUTHANIZATION																
1-	0	0	0 PPM	2-	0	0 / 70 PPM	3-	0	0 / 300 PPM	4-	0	0 / 500 PPM	5-	0	0 / 700 PPM	



TABLE 1 (FO)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF SURVIVAL AND DISPOSITION

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP :	FEMALES														
	1			2			3			4			5		
WEEK	LIVE	FD	EE SE	LIVE	FD	EE SE	LIVE	FD	EE SE	LIVE	FD	EE SE	LIVE	FD	EE SE
0	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0
1	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0
2	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0
3	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0
4	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0
5	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0
6	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0
7	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0
8	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0
9	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0
10	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0
11	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0
12	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0
13	21	0	0 1	22	0	0 0	22	0	0 0	22	0	0 0	22	0	0 0
14	20	0	0 1	21	0	0 1	20	0	0 2	22	0	0 0	21	0	0 1
15	20	0	0 0	21	0	0 0	20	0	0 0	21	0	0 1	20	0	0 0
16	0	0	0 20	2	0	0 19	0	0	0 20	0	0	0 21	0	0	0 20
17	0	0	0 0	0	0	0 0	0	0	0 0	0	0	0 0	0	0	0 0

WEEK = WEEK OF STUDY FD = FOUND DEAD EE = EUTHANIZED IN EXTREMIS SE = SCHEDULED EUTHANIZATION

1- 0 / 0 PPM 2- 0 / 70 PPM 3- 0 / 300 PPM 4- 0 / 500 PPM 5- 0 / 700 PPM



TABLE 2 (FO)
INHALATION REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
SUMMARY OF REPRODUCTIVE PERFORMANCE

PROJECT NO.: WIL-51041
SPONSOR: DOW CORNING CORP.
SPONSOR NO.: 8463

PAGE 1

DOSE GROUP :	1		2		3		4		5	
	NO.	%								
FEMALES ON STUDY	22		22		22		22		22	
FEMALES THAT DIED DURING STUDY	0		0		0		0		0	
FEMALES EUTHANIZED 25 DAYS FOLLOWING BREEDING PERIOD	0	0.0	0	0.0	0	0.0	1	4.5	0	0.0
NONGRAVID	0	0.0	0	0.0	0	0.0	1	100.0	0	0.0
GRAVID	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
FEMALES EUTHANIZED ON POST-MATING DAY 25	2	9.1	1	4.5	2	9.1	0	0.0	2	9.1
NONGRAVID	2	100.0	1	100.0	2	100.0	0	0.0	2	100.0
GRAVID	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
FEMALES ALLOWED TO DELIVER	22		22		22		22		22	
NONGRAVID	2	9.1	1	4.5	2	9.1	1	4.5	2	9.1
GRAVID	20	90.9	21	95.5	20	90.9	21	95.5	20	90.9
DELIVERED	20	100.0	21	100.0	20	100.0	21	100.0	20	100.0
TOTAL LITTER LOSS	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
FEMALES WITH VIABLE PUPS	20	100.0	21	100.0	20	100.0	21	100.0	20	100.0
FEMALES WITH EVIDENCE OF MATING	22	100.0	22	100.0	22	100.0	22	100.0	22	100.0
NUMBER WHICH DELIVERED	20	90.9	21	95.5	20	90.9	21	100.0	20	90.9
NUMBER WHICH DID NOT DELIVER	2	9.1	1	4.5	2	9.1	0	0.0	2	9.1
FEMALES WITH NO EVIDENCE OF MATING	0	0.0	0	0.0	0	0.0	1	4.5	0	0.0
NUMBER WHICH DELIVERED	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
NUMBER WHICH DID NOT DELIVER	0	0.0	0	0.0	0	0.0	1	100.0	0	0.0
TOTAL FEMALES GRAVID	20	90.9	21	95.5	20	90.9	21	95.5	20	90.9
1- 0 / 0 PPM										
2- 0 / 70 PPM										
3- 0 / 300 PPM										
4- 0 / 500 PPM										
5- 0 / 700 PPM										



TABLE 2 (FO)
 INHALATION REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF REPRODUCTIVE PERFORMANCE

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

DOSE GROUP :	1		2		3		4		5	
	NO.	%								
MALES ON STUDY	22	100.0	22	100.0	22	100.0	22	100.0	22	100.0
MALES THAT DIED DURING STUDY	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
MALES WITH EVIDENCE OF MATING	22	100.0	22	100.0	22	100.0	21	95.5	22	100.0
NO. WHICH Sired AT LEAST 1 LITTER	20	90.9	21	95.5	20	90.9	21	100.0	20	90.9
NO. WHICH DID NOT SIRE 1 LITTER	2	9.1	1	4.5	2	9.1	0	0.0	2	9.1
MALES WITH NO EVIDENCE OF MATING	0	0.0	0	0.0	0	0.0	1	4.5	0	0.0
NO. WHICH Sired AT LEAST 1 LITTER	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
NO. WHICH DID NOT SIRE 1 LITTER	0	0.0	0	0.0	0	0.0	1	100.0	0	0.0
MALES Siring MORE THAN ONE LITTER	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
1- 0 / 0 PPM	22	100.0	22	100.0	22	100.0	21	95.5	22	100.0
2- 0 / 70 PPM	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
3- 0 / 300 PPM	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
4- 0 / 500 PPM	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
5- 0 / 700 PPM	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

NOTE: MALES WERE CONSIDERED TO HAVE Sired 1 LITTER IF THE PAIRED FEMALE WAS GRAVID, REGARDLESS OF DELIVERY STATUS



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 2 (FO)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF REPRODUCTIVE PERFORMANCE

PAGE 3

	1		2		3		4		5	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
MALE MATING INDEX	22/22	100.0	22/22	100.0	22/22	100.0	21/22	95.5	22/22	100.0
FEMALE MATING INDEX	22/22	100.0	22/22	100.0	22/22	100.0	21/22	95.5	22/22	100.0
MALE FERTILITY INDEX	20/22	90.9	21/22	95.5	20/22	90.9	21/22	95.5	20/22	90.9
FEMALE FERTILITY INDEX	20/22	90.9	21/22	95.5	20/22	90.9	21/22	95.5	20/22	90.9
MEAN PRE-COITAL INTERVALS (DAYS)	2.3	MA	3.2	MA	2.7	MA	3.0	MA	2.6	MA
S.D.	1.29	MA	1.95	MA	1.39	MA	1.28	MA	1.05	MA
N	22		22		22		21		22	

MALE (FEMALE) MATING INDEX (%) = NO. OF MALES (FEMALES) WITH EVIDENCE OF MATING / TOTAL NO. OF MALES (FEMALES) USED FOR MATING X 100

MALE FERTILITY INDEX (%) = NO. OF MALES SIRING AT LEAST 1 LITTER / TOTAL NO. OF MALES USED FOR MATING X 100

FEMALE FERTILITY INDEX (%) = NO. OF FEMALES WITH CONFIRMED PREGNANCY / TOTAL NO. OF FEMALES USED FOR MATING X 100

1- 0 / 0 PPM 2- 0 / 70 PPM 3- 0 / 300 PPM 4- 0 / 500 PPM 5- 0 / 700 PPM

NOTE: MALES WERE CONSIDERED TO HAVE Sired 1 LITTER IF THE PAIRED FEMALE WAS GRAVID, REGARDLESS OF DELIVERY STATUS
 MATING AND FERTILITY INDICES NOT SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 USING CHI-SQUARE TEST
 MA = NOT APPLICABLE



TABLE 3 (FO - DETAILED PHYSICAL EXAMINATIONS)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

PROJECT NO.: WIL-51041
 SPONSOR: DOM CORNING CORP.
 SPONSOR NO.: 8463

----- M A L E -----

TABLE RANGE: 09-19-95 TO 01-17-96

GROUP:	1	2	3	4	5
-NO SIGNIFICANT CLINICAL OBSERVATIONS	60/ 22	85/ 22	84/ 22	84/ 22	83/ 22
-SCHEDULED EUTHANIZATION	22/ 22	22/ 22	22/ 22	22/ 22	22/ 22
-HAIR LOSS RIGHT FORELIMB	0/ 0	0/ 0	0/ 0	0/ 0	3/ 1
-HAIR LOSS LEFT FORELIMB	2/ 1	0/ 0	0/ 0	0/ 0	3/ 1
-DRIED RED MATERIAL AROUND NOSE	1/ 1	2/ 2	1/ 1	2/ 2	0/ 0
-DRIED RED MATERIAL AROUND RIGHT EYE	2/ 1	0/ 0	0/ 0	0/ 0	0/ 0
-WET RED MATERIAL AROUND NOSE	0/ 0	0/ 0	0/ 0	2/ 2	0/ 0
-SOFT STOOL	3/ 3	1/ 1	0/ 0	0/ 0	2/ 2
-UPPER INCISORS MALALIGNED	0/ 0	0/ 0	3/ 1	0/ 0	0/ 0
1- 0 / 0 PPM	2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM	



TABLE 3 (FO - DETAILED PHYSICAL EXAMINATIONS)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

PROJECT NO.: WIL-51041
 SPONSOR: DOM CORNING CORP.
 SPONSOR NO.: 8463

----- F E M A L E -----

	TABLE RANGE: 09-19-95 TO 01-17-96				
	1	2	3	4	5
GROUP:	1	2	3	4	5
	295/ 22	284/ 22	320/ 22	301/ 22	356/ 22
-NO SIGNIFICANT CLINICAL OBSERVATIONS	2/ 2	1/ 1	2/ 2	0/ 0	2/ 2
-SENT TO LAB GESTATION DAY 25	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-POST-MATING PERIOD DAY 25 NECROPSY	20/ 20	21/ 21	20/ 20	21/ 21	20/ 20
-SENT TO LAB FOR SCHEDULED NECROPSY; LACTATION DAY 21					
-HAIR LOSS RIGHT FORELIMB	68/ 6	88/ 10	51/ 7	37/ 5	26/ 3
-HAIR LOSS LEFT FORELIMB	59/ 8	78/ 9	55/ 6	41/ 5	25/ 4
-WET YELLOW STAINING UROGENITAL AREA	0/ 0	0/ 0	1/ 1	1/ 1	0/ 0
-DRYED YELLOW STAINING UROGENITAL AREA	0/ 0	0/ 0	1/ 1	3/ 2	0/ 0
-DRYED TAN STAINING RIGHT FORELIMB	0/ 0	3/ 2	2/ 1	0/ 0	1/ 1
-DRYED TAN STAINING LEFT FORELIMB	0/ 0	2/ 2	3/ 2	0/ 0	0/ 0
-HAIR LOSS VENTRAL NECK	5/ 1	6/ 1	0/ 0	0/ 0	2/ 1
-SCABBING VENTRAL NECK	0/ 0	4/ 1	0/ 0	0/ 0	0/ 0
-MECHANICAL INJURY DISTAL END OF TAIL	0/ 0	0/ 0	1/ 1	6/ 1	0/ 0
-LACERATION DISTAL END OF TAIL	0/ 0	0/ 0	1/ 1	4/ 1	0/ 0
-WET RED MATERIAL DISTAL END OF TAIL	0/ 0	0/ 0	1/ 1	1/ 1	0/ 0
-%6 DIGIT ON RIGHT FORELIMB MISSING	0/ 0	0/ 0	12/ 1	0/ 0	0/ 0
-SCABBING RIGHT FORELIMB	2/ 1	3/ 2	0/ 0	0/ 0	5/ 1
-SCABBING LEFT FORELIMB	1/ 1	3/ 3	0/ 0	2/ 2	6/ 1
-HAIR LOSS LEFT HINDLIMB	3/ 1	6/ 2	9/ 3	3/ 1	10/ 1
-HAIR LOSS RIGHT HINDLIMB	7/ 3	7/ 2	9/ 3	7/ 1	10/ 1
-HAIR LOSS RIGHT LATERAL ABDOMINAL AREA	1/ 1	0/ 0	0/ 0	8/ 1	3/ 1
-HAIR LOSS VENTRAL THORACIC AREA	0/ 0	0/ 0	2/ 1	0/ 0	6/ 1
1- 0 / 0 PPM	2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM	



TABLE 3 (FO - DETAILED PHYSICAL EXAMINATIONS)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

----- F E M A L E -----

FINDING	TABLE RANGE: GROUP:				
	1	2	3	4	5
-HAIR LOSS VENTRAL ABDOMINAL AREA	1/ 1	0/ 0	7/ 2	0/ 0	9/ 1
-HAIR LOSS UROGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	4/ 1
-HAIR LOSS LEFT LATERAL ABDOMINAL AREA	1/ 1	0/ 0	0/ 0	0/ 0	3/ 1
-HAIR LOSS DORSAL POSTERIOR AREA	0/ 0	0/ 0	0/ 0	0/ 0	4/ 1
-HAIR LOSS BASE OF TAIL	3/ 3	0/ 0	0/ 0	0/ 0	4/ 1
-DRIED RED MATERIAL AROUND NOSE	0/ 0	0/ 0	0/ 0	2/ 2	0/ 0
-NET RED MATERIAL AROUND RIGHT EYE	1/ 1	1/ 1	0/ 0	1/ 1	0/ 0
-DRIED RED MATERIAL AROUND RIGHT EYE	6/ 2	9/ 1	0/ 0	10/ 3	0/ 0
-DRIED RED MATERIAL AROUND LEFT EYE	0/ 0	7/ 1	0/ 0	4/ 1	0/ 0
-LACRIMATION RIGHT EYE	0/ 0	3/ 1	0/ 0	2/ 1	0/ 0
-LACRIMATION LEFT EYE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0
-HAIR LOSS ON NOSE	1/ 1	0/ 0	0/ 0	1/ 1	0/ 0
-CHROMOACRYORRHEA LEFT EYE	2/ 1	0/ 0	0/ 0	0/ 0	0/ 0
-HAIR LOSS AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0
-RIGHT EAR APPEARS RED AND SWOLLEN	0/ 0	0/ 0	6/ 1	11/ 3	0/ 0
-SCABBING ON NOSE	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-DECREASED DEFECTION	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-NET RED MATERIAL FOUND ON CAGE BOTTOM	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0
-SOFT MOVABLE MASS RIGHT VENTRAL THORACIC AREA	0/ 0	3/ 1	0/ 0	0/ 0	1/ 1
12MM X 12MM X 5MM					0/ 0
-UPPER INCISORS MALALIGNED	12/ 2	21/ 3	0/ 0	8/ 2	0/ 0
-DRIED RED MATERIAL AROUND MOUTH	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0
-TEETH LONG, TRIMMED	12/ 2	18/ 3	2/ 2	13/ 2	0/ 0
1- 0 / 0 PPM	2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM	



DC Study No. - 8463
 External No. - WIL-51041

DC Report No. - 1997-I0000-42936
 Security - INTERNAL

PAGE 4

TABLE 3 (F0 - DETAILED PHYSICAL EXAMINATIONS)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

----- F E M A L E -----

FINDING	TABLE RANGE: 09-19-95 TO 01-17-96				
	GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5
-LEFT UPPER INCISOR BROKEN	4/ 1	0/ 0	1/ 1	6/ 1	0/ 0
-RIGHT UPPER INCISOR BROKEN	2/ 1	0/ 0	3/ 1	6/ 1	0/ 0
-SCABBING UPPER LIP	0/ 0	0/ 0	2/ 1	0/ 0	0/ 0
-FIRM IMMOVABLE MASS (1.0CM X 1.0CM X 1.0CM)	3/ 1	0/ 0	0/ 0	0/ 0	0/ 0
-RIGHT LATERAL ABDOMINAL AREA					
-SCABBING DISTAL END OF TAIL	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
1- 0 / 0 PPM	2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM	



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 4 (F0 - 1-HOUR POST-EXPOSURE)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

PAGE 1

----- F E M A L E -----

GROUP:	TABLE RANGE: 09-19-95 TO 01-16-96				
	1	2	3	4	5
-WET YELLOW STAINING UROGENITAL AREA	0/0	0/0	16/1	23/6	11/4
-DRIED RED STAINING DORSAL HEAD	15/9	15/8	23/9	15/6	40/9
-DRIED YELLOW STAINING UROGENITAL AREA	0/0	0/0	0/0	7/2	4/2
-DRIED TAN STAINING RIGHT FORELIMB	0/0	0/0	0/0	1/1	0/0
-DRIED TAN STAINING LEFT FORELIMB	0/0	0/0	0/0	1/1	0/0
-DRIED RED STAINING RIGHT FORELIMB	0/0	0/0	4/2	5/2	5/3
-DRIED RED STAINING LEFT FORELIMB	0/0	0/0	4/2	4/2	4/2
-DRIED YELLOW UROGENITAL STAINING	0/0	0/0	0/0	0/0	2/2
-DRIED RED MATERIAL AROUND NOSE	42/13	39/12	138/17	181/19	240/21
-WET RED MATERIAL AROUND RIGHT EYE	0/0	0/0	0/0	3/2	2/2
-DRIED RED MATERIAL AROUND RIGHT EYE	0/0	14/1	3/3	5/2	13/8
-DRIED RED MATERIAL AROUND LEFT EYE	0/0	9/1	2/2	2/2	7/5
-WET RED MATERIAL AROUND NOSE	0/0	3/3	3/3	1/1	6/4
-WET RED DISCHARGE AROUND MOUTH	0/0	1/1	0/0	0/0	0/0
-LACRIMATION RIGHT EYE	0/0	0/0	0/0	2/2	0/0
-LACRIMATION LEFT EYE	0/0	0/0	0/0	1/1	0/0
-DRIED TAN CRUSTY MATERIAL AROUND RIGHT EYE	0/0	0/0	0/0	1/1	0/0
-CHRONOACRYORRHEA RIGHT EYE	0/0	0/0	0/0	1/1	0/0
-CHRONOACRYORRHEA LEFT EYE	0/0	1/1	0/0	0/0	0/0
-SCABBING ON NOSE	0/0	1/1	1/1	0/0	0/0
-DRIED RED MATERIAL FOUND ON EXPOSURE CAGE	1/1	0/0	1/1	0/0	0/0
-SOFT STOOL	0/0	0/0	0/0	0/0	0/0
-UPPER INCISORS MALALIGNED	0/0	1/1	0/0	1/1	0/0
1- 0 / 0 PPM	2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM	



TABLE 4 (F0 - 1-HOUR POST-EXPOSURE)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

----- F E M A L E -----

	TABLE RANGE: GROUP:				
	1 09-19-95	2 TO 01-16-96	3	4	5
-DRIED RED MATERIAL AROUND MOUTH	0/ 5	3/ 3	15/ 6	17/ 11	30/ 11
-WET RED MATERIAL AROUND MOUTH	0/ 0	0/ 0	1/ 1	1/ 1	0/ 0
-WET RED VAGINAL DISCHARGE	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
1- 0 / 0 PPM	2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM	



PROJECT NO.: WIL-51041
 SPONSOR: DOM CORNING CORP.
 SPONSOR NO.: 8463

TABLE 5 (F0)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 BODY WEIGHTS (GRAMS) - SUMMARY OF MEANS

WEEK	GROUP:	M A L E				
		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
10	MEAN	411.	414.	409.	413.	412.
	S.D.	33.5	33.9	34.8	31.1	35.4
	N	22	22	22	22	22
11	MEAN	427.	429.	425.	431.	429.
	S.D.	33.3	34.8	35.2	33.8	38.0
	N	22	22	22	22	22
12	MEAN	459.	458.	453.	458.	456.
	S.D.	34.5	36.1	37.6	35.3	42.5
	N	22	22	22	22	22

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST



TABLE 5 (F0)
 INHALATION REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 BODY WEIGHTS (GRAMS) - SUMMARY OF MEANS

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

PAGE 2

GROUP:		FEMALE				
		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
WEEK	-2					
		MEAN	86.	86.	87.	86.
		S.D.	10.6	8.8	7.4	9.6
		N	22	22	22	22
	0	MEAN	148.	148.	148.	148.
		S.D.	11.1	10.8	10.3	10.3
		N	22	22	22	22
	1	MEAN	176.	176.	171.	169.
		S.D.	11.6	11.0	12.4	11.0
		N	22	22	22	22
	2	MEAN	196.	195.	189.	188.
		S.D.	14.0	16.0	13.7	12.2
		N	22	22	22	22
	3	MEAN	208.	210.	205.	204.
		S.D.	17.5	16.3	14.6	14.5
		N	22	22	22	22

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 5 (F0)
 INHALATION REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 BODY WEIGHTS (GRAMS) - SUMMARY OF MEANS

WEEK	GROUP:	FEMALE				
		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
4	MEAN	226.	226.	221.	218.	216.
	S.D.	18.5	17.7	11.3	15.0	15.5
	N	22	22	22	22	22
5	MEAN	237.	239.	233.	232.	229.
	S.D.	19.8	18.0	11.0	18.0	17.7
	N	22	22	22	22	22
6	MEAN	250.	251.	245.	243.	242.
	S.D.	21.8	19.4	14.1	21.1	18.9
	N	22	22	22	22	22
7	MEAN	257.	254.	253.	248.	247.
	S.D.	23.6	23.1	15.5	21.8	17.8
	N	22	22	22	22	22
8	MEAN	264.	262.	258.	256.	251.
	S.D.	25.0	22.2	12.9	24.4	17.4
	N	22	22	22	22	22

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 5 (FO)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 BODY WEIGHTS (GRAMS) - SUMMARY OF MEANS

PAGE 4

WEEK	GROUP:	F E M A L E					
		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM	
9	MEAN	271.	271.	264.	264.	258.	
	S.D.	23.9	21.9	14.8	25.8	19.5	
	N	22	22	22	22	22	
10	MEAN	280.	269.	271.	269.	266.	
	S.D.	24.6	18.8	14.8	26.0	19.3	
	N	13	18	16	19	19	
11	MEAN	A	A	A	299.	A	
	S.D.				0.0		
	N				1		
12	MEAN	A	A	A	295.	A	
	S.D.				0.0		
	N				1		
13	MEAN	A	A	A	301.	A	
	S.D.				0.0		
	N				1		

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST
 A = REFER TO GESTATION/LACTATION BODY WEIGHT TABLES



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 5 (F0)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 BODY WEIGHTS (GRAMS) - SUMMARY OF MEANS

PAGE 5

		F E M A L E				
GROUP:		0 / 0 PPH	0 / 70 PPH	0 / 300 PPH	0 / 500 PPH	0 / 700 PPH
WEEK	14	A	A	A	304. 0.0 1	A
	15	A	A	A	298. 0.0 1	A

A = REFER TO GESTATION/LACTATION BODY WEIGHT TABLES



TABLE 6 (F0)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 BODY WEIGHT GAINS (GRAMS) - SUMMARY OF MEANS

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP:	M A L E				
	0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
WEEK 10 TO 11					
MEAN	17.	14.	17.	17.	17.
S.D.	8.0	7.8	6.8	8.9	9.4
N	22	22	22	22	22
WEEK 11 TO 12					
MEAN	32.	29.	28.	27.	27.
S.D.	6.6	6.7	6.5	7.6	8.4
N	22	22	22	22	22

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST



TABLE 6 (FO)
 INHALATION REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 BODY WEIGHT GAINS (GRAMS) - SUMMARY OF MEANS

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP:		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
WEEK	-2 TO 0					
	MEAN	61.	62.	62.	61.	62.
	S.D.	4.5	6.3	5.6	7.1	6.8
	N	22	22	22	22	22
	0 TO 1					
	MEAN	29.	28.	28.	23.**	22.**
	S.D.	5.1	4.9	4.3	5.3	5.2
	N	22	22	22	22	22
	1 TO 2					
	MEAN	20.	19.	17.	18.	19.
	S.D.	5.8	7.1	7.5	4.3	4.4
	N	22	22	22	22	22
	2 TO 3					
	MEAN	12.	16.	14.	16.	16.
	S.D.	7.5	6.8	7.6	4.4	5.0
	N	22	22	22	22	22
	3 TO 4					
	MEAN	18.	16.	14.	13.*	13.*
	S.D.	6.3	6.9	6.4	4.7	4.3
	N	22	22	22	22	22

----- F E M A L E -----

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST
 ** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING DUNNETT'S TEST



TABLE 6 (FO)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 BODY WEIGHT GAINS (GRAMS) - SUMMARY OF MEANS

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP:		F E M A L E									
WEEK		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM					
4 TO 5	MEAN	11.	13.	12.	14.	13.					
	S.D.	6.9	5.7	5.8	6.2	7.6					
	N	22	22	22	22	22					
5 TO 6	MEAN	13.	12.	12.	12.	13.					
	S.D.	7.2	5.3	5.5	5.2	5.8					
	N	22	22	22	22	22					
6 TO 7	MEAN	6.	3.	7.	4.	5.					
	S.D.	8.2	6.1	5.2	5.4	5.9					
	N	22	22	22	22	22					
7 TO 8	MEAN	7.	8.	6.	9.	5.					
	S.D.	6.2	6.5	6.3	7.6	5.3					
	N	22	22	22	22	22					
8 TO 9	MEAN	7.	9.	6.	8.	7.					
	S.D.	6.9	5.0	5.2	5.9	5.6					
	N	22	22	22	22	22					

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST



TABLE 6 (FO)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 BODY WEIGHT GAINS (GRAMS) - SUMMARY OF MEANS

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP:		F E M A L E					
WEEK		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM	
9 TO 10							
	MEAN	6.	3.	6.	5.	5.	
	S.D.	5.9	6.7	4.7	6.5	5.7	
	N	13	18	16	19	19	
10 TO 11		A	A	A	5.	A	
	MEAN				0.0		
	S.D.				1		
11 TO 12		A	A	A	-4.	A	
	MEAN				0.0		
	S.D.				1		
12 TO 13		A	A	A	6.	A	
	MEAN				0.0		
	S.D.				1		
13 TO 14		A	A	A	3.	A	
	MEAN				0.0		
	S.D.				1		

A = REFER TO GESTATION/LACTATION BODY WEIGHT GAIN TABLES



TABLE 6 (F0)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 BODY WEIGHT GAINS (GRAMS) - SUMMARY OF MEANS

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

		----- F E M A L E -----				
GROUP:		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
WEEK 14 TO 15	MEAN	A	A	A	-6.	A
	S.D.				0.0	
	N				1	

A = REFER TO GESTATION/LACTATION BODY WEIGHT GAIN TABLES



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 7 (FO)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 MEAN BODY WEIGHTS (GRAMS) DURING GESTATION

DAY	GROUP :	MEAN BODY WEIGHTS (GRAMS) DURING GESTATION				
		1	2	3	4	5
DAY 0	MEAN	277.	274.	272.	267.	264.
	S.D./N	28.3/20	23.4/21	14.4/20	24.9/21	17.7/20
DAY 7	MEAN	308.	299.	298.	283.	292.
	S.D./N	27.0/20	28.8/21	20.1/20	40.2/21	20.4/20
DAY 10	MEAN	319.	309.	310.	306.	305.
	S.D./N	29.0/20	24.2/21	18.0/20	25.8/21	18.1/20
DAY 14	MEAN	338.	333.	331.	322.	317.*
	S.D./N	27.3/20	20.4/21	18.7/20	28.2/21	20.3/20
DAY 20	MEAN	408.	405.	401.	395.	380.*
	S.D./N	34.7/20	28.9/21	23.2/20	36.3/21	26.1/20

1- 0 / 0 PPM 2- 0 / 70 PPM 3- 0 / 300 PPM 4- 0 / 500 PPM 5- 0 / 700 PPM
 * = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING A TWO-TAILED DUNNETT'S TEST
 NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 8 (FO)
 INHALATION REPRODUCTIVE TOXICITY STUDY OF D₄ IN FEMALE RATS
 MEAN BODY WEIGHT CHANGES (GRAMS) DURING GESTATION

PAGE 1

GROUP :	1	2	3	4	5
DAY 0- 7 MEAN	31.	25.	26.	16.	28.
S.D./N	8.1/20	16.4/21	9.5/20	30.7/21	11.6/20
DAY 7- 10 MEAN	12.	10.	12.	23.*	13.
S.D./N	5.7/20	12.9/21	7.8/20	23.5/21	6.3/20
DAY 10- 14 MEAN	18.	24.	20.	16.	13.
S.D./N	9.1/20	12.3/21	4.7/20	9.4/21	13.3/20
DAY 14- 20 MEAN	71.	72.	70.	72.	63.
S.D./N	13.7/20	15.3/21	13.8/20	14.4/21	19.4/20
DAY 0- 20 MEAN	132.	130.	129.	128.	116.
S.D./N	17.2/20	17.1/21	18.3/20	20.9/21	25.5/20

1- 0 / 0 PPM 2- 0 / 70 PPM 3- 0 / 300 PPM 4- 0 / 500 PPM 5- 0 / 700 PPM
 * = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING A TWO-TAILED DUNNETT'S TEST
 MEAN DIFFERENCES CALCULATED FROM INDIVIDUAL DIFFERENCES
 NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN



TABLE 9 (FO)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 MEAN BODY WEIGHTS (GRAMS) DURING LACTATION

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

DAY	GROUP :	MEAN BODY WEIGHTS (GRAMS) DURING LACTATION				
		1	2	3	4	5
DAY 1	MEAN	311.	305.	300.	297.	292.*
	S.D./N	28.7/20	18.9/21	15.5/20	27.9/21	14.5/20
DAY 4	MEAN	324.	321.	316.	315.	308.
	S.D./N	30.5/20	19.4/21	16.3/20	31.0/21	16.2/20
DAY 7	MEAN	333.	328.	320.	321.	314.*
	S.D./N	28.1/20	20.9/21	13.9/20	27.1/21	15.3/20
DAY 14	MEAN	356.	350.	340.	341.	336.*
	S.D./N	29.1/20	21.4/21	12.3/20	25.5/21	16.1/20
DAY 21	MEAN	337.	337.	327.	334.	334.
	S.D./N	38.3/20	20.7/21	20.1/20	22.8/21	19.0/20

1- 0 / 0 PPM 2- 0 / 70 PPM 3- 0 / 300 PPM 4- 0 / 500 PPM 5- 0 / 700 PPM
 * = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP AT 0.05 LEVEL USING DUNNETT'S TEST



TABLE 10 (FO)
 INHALATION REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 MEAN BODY WEIGHT CHANGES (GRAMS) DURING LACTATION

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP :	1	2	3	4	5
DAY 1- 4 MEAN	13.	16.	16.	18.	16.
S.D./N	9.8/20	13.6/21	9.2/20	9.9/21	6.8/20
DAY 4- 7 MEAN	9.	6.	4.	6.	6.
S.D./N	8.1/20	7.9/21	8.1/20	9.1/21	7.1/20
DAY 7- 14 MEAN	23.	22.	20.	21.	22.
S.D./N	13.9/20	9.4/21	9.7/20	8.0/21	5.7/20
DAY 14- 21 MEAN	-19.	-13.	-13.	-7.	-3.**
S.D./N	24.2/20	10.8/21	18.7/20	11.7/21	10.5/20
DAY 1- 21 MEAN	26.	32.	27.	37.	42.*
S.D./N	26.9/20	13.5/21	20.3/20	17.1/21	15.3/20

1- 0 / 0 PPM 2- 0 / 70 PPM 3- 0 / 300 PPM 4- 0 / 500 PPM 5- 0 / 700 PPM
 * = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP AT 0.05 LEVEL USING DUNNETT'S TEST
 ** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP AT 0.01 LEVEL USING DUNNETT'S TEST
 MEAN DIFFERENCES CALCULATED FROM INDIVIDUAL DIFFERENCES



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 11 (FO)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 WEEKLY FOOD CONSUMPTION (GRAMS/ANIMAL/DAY) - SUMMARY OF MEANS

PAGE 1

GROUP:		F E M A L E				
WEEK	0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM	
0 TO 1	16. 1.2 22	16. 1.1 22	16. 1.0 22	15.** 1.1 22	15.* 1.0 22	
1 TO 2	17. 1.1 22	16. 1.7 21	17. 1.4 22	16.* 0.9 22	16.* 0.9 22	
2 TO 3	17. 1.2 22	17. 1.5 22	17. 1.4 22	17. 1.6 22	16. 1.3 22	
3 TO 4	18. 1.6 22	17. 1.4 22	18. 1.6 22	18. 1.3 22	18. 1.2 22	
4 TO 5	18. 1.6 22	17. 1.6 22	18. 1.6 22	19. 1.7 22	18. 1.3 22	

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST
 ** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING DUNNETT'S TEST



TABLE 11 (FO)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 WEEKLY FOOD CONSUMPTION (GRAMS/ANIMAL/DAY) - SUMMARY OF MEANS

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP:		F E M A L E				
WEEK		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
5 TO 6	MEAN	19.	18.	18.	19.	19.
	S.D.	1.9	1.6	1.5	1.8	1.7
	N	22	22	22	22	22
6 TO 7	MEAN	18.	17.	19.	19.	19.
	S.D.	1.7	3.1	1.9	1.9	1.2
	N	22	22	22	21	22
7 TO 8	MEAN	19.	18.	18.	19.	19.
	S.D.	1.9	1.7	1.4	1.9	1.7
	N	22	22	22	22	22
8 TO 9	MEAN	18.	18.	18.	19.	19.
	S.D.	1.6	1.9	1.6	1.8	1.4
	N	21	22	21	22	22
9 TO 10	MEAN	19.	18.	18.	18.	18.
	S.D.	2.0	2.6	1.5	1.4	1.3
	N	22	22	22	21	22

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST



TABLE 11 (FO)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 WEEKLY FOOD CONSUMPTION (GRAMS/ANIMAL/DAY) - SUMMARY OF MEANS

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP:	FEMALE				
	0 / 0 PPH	0 / 70 PPH	0 / 300 PPH	0 / 500 PPH	0 / 700 PPH
WEEK 10 TO 11					
MEAN	A	A	A	A	A
S.D.					
N					
11 TO 12					
MEAN	A	A	A	A	A
S.D.					
N					
12 TO 13					
MEAN	B	B	B	16.	B
S.D.				0.0	
N				1	
13 TO 14					
MEAN	B	B	B	18.	B
S.D.				0.0	
N				1	
14 TO 15					
MEAN	B	B	B	14.	B
S.D.				0.0	
N				1	

A = FOOD CONSUMPTION NOT RECORDED DURING BREEDING PERIOD
 B = REFER TO GESTATION/LACTATION FOOD CONSUMPTION TABLES



TABLE 12 (FO)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 WEEKLY FOOD CONSUMPTION (GRAMS/KG/DAY) - SUMMARY OF MEANS

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP:		F E M A L E				
WEEK	0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM	
0 TO 1	100.	96.	100.	94.**	97.	
MEAN	5.9	7.1	5.2	8.2	4.5	
S.D.	22	22	22	22	22	
N						
1 TO 2	91.	88.	91.	89.	90.	
MEAN	5.0	6.3	6.3	4.9	4.2	
S.D.	22	21	22	22	22	
N						
2 TO 3	84.	83.	85.	86.	84.	
MEAN	3.4	6.1	5.9	6.2	4.6	
S.D.	22	22	22	22	22	
N						
3 TO 4	84.	78.**	83.	83.	84.	
MEAN	4.3	4.4	5.5	4.0	4.7	
S.D.	22	22	22	22	22	
N						
4 TO 5	79.	75.*	80.	83.*	83.*	
MEAN	3.3	5.1	4.9	5.0	4.2	
S.D.	22	22	22	22	22	
N						

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST
 ** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING DUNNETT'S TEST



TABLE 12 (FO)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 WEEKLY FOOD CONSUMPTION (GRAMS/KG/DAY) - SUMMARY OF MEANS

PROJECT NO.: WIL-51041
 SPONSOR: DOM CORNING CORP.
 SPONSOR NO.: 8463

GROUP:		F E M A L E									
		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM					
WEEK	5 TO 6	77. 4.1 22	74. 3.9 22	77. 4.6 22	81.* 3.2 22	81.** 5.0 22					
	MEAN										
	S.D.										
	N										
	6 TO 7	73. 4.0 22	68. 11.4 22	75. 5.6 22	76.* 3.9 21	78.* 4.7 22					
	MEAN										
	S.D.										
	N										
	7 TO 8	71. 4.4 22	69. 5.7 22	72. 3.5 22	76.* 3.6 22	75. 5.1 22					
	MEAN										
	S.D.										
	N										
	8 TO 9	67. 3.3 21	66. 4.7 22	70. 3.9 21	74.** 4.5 22	74.** 5.4 22					
	MEAN										
	S.D.										
	N										
	9 TO 10	68. 4.3 13	66. 7.5 18	68. 4.2 16	70. 5.9 18	70. 3.8 19					
	MEAN										
	S.D.										
	N										

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST
 ** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING DUNNETT'S TEST



PROJECT NO.: WIL-51041
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 SPONSOR NO.: 8463

TABLE 12 (FO)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 WEEKLY FOOD CONSUMPTION (GRAMS/KG/DAY) - SUMMARY OF MEANS

PAGE 3

GROUP:		F E M A L E				
WEEK		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
10 TO 11	MEAN	A	A	A	A	A
	S.D.					
	N					
11 TO 12	MEAN	A	A	A	A	A
	S.D.					
	N					
12 TO 13	MEAN	B	B	B	54. 0.0	B
	S.D.				1	
	N					
13 TO 14	MEAN	B	B	B	59. 0.0	B
	S.D.				1	
	N					
14 TO 15	MEAN	B	B	B	47. 0.0	B
	S.D.				1	
	N					

A = FOOD CONSUMPTION NOT RECORDED DURING BREEDING PERIOD
 B = REFER TO GESTATION/LACTATION FOOD CONSUMPTION TABLES



TABLE 13 (FO)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 MEAN FOOD CONSUMPTION DURING GESTATION (GRAMS/ANIMAL/DAY)

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP :	1	2	3	4	5
DAY 0- 7 MEAN	20.	19.	19.	18.*	19.
S.D./N	2.0/20	2.6/21	2.4/20	4.6/20	1.8/20
DAY 7- 10 MEAN	23.	20.	22.	22.	21.
S.D./N	2.4/20	5.4/21	2.1/20	1.8/20	2.1/20
DAY 10- 14 MEAN	23.	23.	22.	23.	23.
S.D./N	2.8/20	4.8/21	1.7/20	2.6/21	2.1/20
DAY 14- 20 MEAN	23.	23.	23.	24.	24.
S.D./N	2.1/20	2.9/21	2.2/20	3.6/21	2.0/20
DAY 0- 20 MEAN	22.	21.	22.	21.	22.
S.D./N	2.0/20	2.0/21	1.7/20	2.7/21	1.5/20

1- 0 / 0 PPM 2- 0 / 70 PPM 3- 0 / 300 PPM 4- 0 / 500 PPM 5- 0 / 700 PPM
 * = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING A TWO-TAILED DUNNETT'S TEST
 NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN



TABLE 14 (FO)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 MEAN FOOD CONSUMPTION DURING GESTATION (GRAMS/KG/DAY)

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP :		1	2	3	4	5
DAY 0- 7	MEAN	70.	68.	67.	63.	67.
	S.D./N	7.0/20	7.7/21	5.9/20	14.7/20	6.8/20
DAY 7- 10	MEAN	72.	67.	71.	75.	70.
	S.D./N	6.2/20	16.0/21	4.0/20	10.8/20	6.4/20
DAY 10- 14	MEAN	69.	71.	70.	74.	74.
	S.D./N	6.7/20	15.0/21	4.8/20	8.3/21	6.2/20
DAY 14- 20	MEAN	61.	62.	63.	66.*	70.**
	S.D./N	4.5/20	6.3/21	5.1/20	6.6/21	4.5/20
DAY 0- 20	MEAN	66.	66.	67.	67.	69.
	S.D./N	4.7/20	5.6/21	3.2/20	6.1/21	3.9/20

1- 0 / 0 PPM 2- 0 / 70 PPM 3- 0 / 300 PPM 4- 0 / 500 PPM 5- 0 / 700 PPM
 * = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING A TWO-TAILED DUNNETT'S TEST
 ** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING A TWO-TAILED DUNNETT'S TEST
 NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN



TABLE 15 (FO)
 INHALATION REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 MEAN FOOD CONSUMPTION DURING LACTATION (GRAMS/ANIMAL/DAY)

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP :		1	2	3	4	5
DAY 1- 4	MEAN	35.	33.	33.	33.	31.
	S.D./N	9.5/20	8.8/21	6.0/20	9.0/21	4.7/20
DAY 4- 7	MEAN	37.	38.	36.	38.	35.
	S.D./N	7.5/20	4.5/21	3.8/20	7.8/21	4.8/20
DAY 7- 14	MEAN	48.	49.	46.	48.	44.
	S.D./N	6.3/20	4.7/21	3.7/20	6.7/21	6.8/20
DAY 14- 21	MEAN	56.	59.	53.	56.	51.
	S.D./N	9.0/20	5.3/21	4.2/20	7.3/21	8.4/20
DAY 1- 21	MEAN	47.	48.	45.	47.	43.*
	S.D./N	5.6/20	4.2/21	3.5/20	5.9/21	6.1/20

1- 0 / 0 PPM 2- 0 / 70 PPM 3- 0 / 300 PPM 4- 0 / 500 PPM 5- 0 / 700 PPM
 * = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP AT 0.05 LEVEL USING DUNNETT'S TEST



TABLE 16 (FO)
 INHALATION REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 MEAN FOOD CONSUMPTION DURING LACTATION (GRAMS/KG/DAY)

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP :		1	2	3	4	5
DAY 1- 4	MEAN	111.	106.	107.	109.	102.
	S.D./N	30.3/20	27.8/21	17.1/20	30.3/21	17.2/20
DAY 4- 7	MEAN	114.	117.	113.	120.	111.
	S.D./N	20.4/20	12.0/21	9.3/20	24.7/21	15.1/20
DAY 7- 14	MEAN	141.	145.	138.	143.	135.
	S.D./N	17.4/20	9.3/21	9.8/20	16.2/21	19.8/20
DAY 14- 21	MEAN	160.	173.	160.	166.	153.
	S.D./N	22.5/20	13.6/21	11.7/20	20.8/21	22.4/20
DAY 1- 21	MEAN	143.	148.	140.	146.	135.
	S.D./N	15.3/20	10.6/21	8.9/20	17.4/21	18.3/20
1- 0 / 0 PPM		2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM	

NONE SIGNIFICANTLY DIFFERENT FROM THE CONTROL GROUP USING DUNNETT'S TEST



PROJECT NO.: WIL-51041
 SPONSOR: DON CORNING CORP.
 SPONSOR NO.: 8463

TABLE 17 (F0)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 GESTATION LENGTH SUMMARY

PAGE 1

GROUP :		1	2	3	4	5
NO. OF ANIMALS		20	21	19	21	20
GESTATION LENGTH (DAYS)	MEAN	21.8	21.9	21.7	21.8	22.0
	S.D.	0.62	0.48	0.48	0.44	0.56
1- 0 / 0 PPM	2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM		

NONE SIGNIFICANTLY DIFFERENT FROM THE CONTROL GROUP USING DUNNETT'S TEST



PROJECT NO.: WIL-51041
 SPONSOR: DOM CORNING CORP.
 SPONSOR NO.: 8463

TABLE 18 (F1)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF PND 0 LITTER DATA

GROUP :	1	2	3	4	5
NUMBER BORN					
MEAN	13.6	13.9	13.5	12.7	10.4**
S.D.	2.14	1.74	2.74	2.15	3.57
N	20	21	20	21	20
SEX AT BIRTH (% MALES PER LITTER)					
MEAN	53.3	47.9	49.8	51.7	58.7
S.D.	11.97	16.14	11.51	15.32	13.48
N	20	21	20	21	20
LIVE LITTER SIZE (PND 0)					
MEAN	13.5	13.4	13.5	12.3	9.9**
S.D.	2.26	2.06	2.74	2.43	3.85
N	20	21	20	21	20

1- 0 / 0 PPM 2- 0 / 70 PPM 3- 0 / 300 PPM 4- 0 / 500 PPM 5- 0 / 700 PPM
 SEX COMPARED USING KRUSKAL-WALLIS, NUMBER BORN, AND LIVE LITTER SIZE COMPARED USING DUNNETT'S
 ** = SIGNIFICANTLY DIFFERENT FROM THE CONTROL GROUP AT THE 0.01 LEVEL



TABLE 18A (F1 - PND 0-21)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF POSTNATAL SURVIVAL - % PER LITTER

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP :	1	2	3	4	5
PND 0 (RELATIVE TO NUMBER BORN)					
MEAN	99.2	96.6	100.0	96.8	94.8
S.D.	3.73	8.64	0.00	8.19	9.92
N	20	21	20	21	20
PND 0 TO PND 1					
MEAN	99.0	99.0	98.7	97.4	99.6
S.D.	3.42	2.40	3.24	5.13	1.72
N	20	21	20	21	20
PND 1 TO PND 4 (PRE-SELECTION)					
MEAN	99.6	99.3	99.7	99.2	97.9
S.D.	1.86	2.23	1.32	3.64	4.50
N	20	21	20	21	20
PND 4 (POST-SELECTION) TO PND 7					
MEAN	100.0	100.0	100.0	100.0	100.0
S.D.	0.00	0.00	0.00	0.00	0.00
N	20	21	20	21	20
PND 7 TO PND 14					
MEAN	100.0	100.0	100.0	98.8	100.0
S.D.	0.00	0.00	0.00	5.46	0.00
N	20	21	20	21	20

1- 0 / 0 PPM 2- 0 / 70 PPM 3- 0 / 300 PPM 4- 0 / 500 PPM 5- 0 / 700 PPM
 STATISTICS PERFORMED USING KRUSKAL-WALLIS
 NONE SIGNIFICANTLY DIFFERENT FROM THE CONTROL GROUP



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 18A (F1 - PND 0-21)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF POSTNATAL SURVIVAL - % PER LITTER

PAGE 2

GROUP :	1	2	3	4	5

PND 14 TO PND 21					
MEAN	100.0	99.4	100.0	100.0	100.0
S.D.	0.00	2.73	0.00	0.00	0.00
N	20	21	20	21	20
BIRTH TO PND 4 (PRE-SELECTION)					
MEAN	97.6	95.0	98.4	93.6	92.4
S.D.	5.97	8.75	3.38	9.90	10.41
N	20	21	20	21	20
PND 4 (POST-SELECTION) TO PND 21					
MEAN	100.0	99.4	100.0	98.8	100.0
S.D.	0.00	2.73	0.00	5.46	0.00
N	20	21	20	21	20

1- 0 / 0 PPM	2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM	

STATISTICS PERFORMED USING KRUSKAL-WALLIS
 NONE SIGNIFICANTLY DIFFERENT FROM THE CONTROL GROUP



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 18B (F1 - PND 21-28)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF POST-WEANING SURVIVAL

PAGE 1

PND	GROUP : 1			2			3			4			5		
	LIVE	FD	SE	LIVE	FD	SE	LIVE	FD	SE	LIVE	FD	SE	LIVE	FD	SE
21	40	0	0	40	0	0	40	0	0	41A	0	0	40	0	0
22	40	0	0	40	0	0	40	0	0	41	0	0	40	0	0
23	40	0	0	40	0	0	40	0	0	41	0	0	40	0	0
24	39	1	0	40	0	0	40	0	0	41	0	0	40	0	0
25	39	0	0	40	0	0	40	0	0	40	1	0	40	0	0
26	39	0	0	40	0	0	39	1	0	40	0	0	40	0	0
27	39	0	0	40	0	0	39	0	0	40	0	0	40	0	0
28	0	0	39	0	0	40	0	0	39	0	0	40	0	0	0

PND = POSTNATAL DAY FD = FOUND DEAD SE = SCHEDULED EUTHANIZATION

1- 0 / 0 PPM 2- 0 / 70 PPM 3- 0 / 300 PPM 4- 0 / 500 PPM 5- 0 / 700 PPM

A = INCLUDES PUP NO. 42225-09, WHICH WAS SELECTED TO REPLACE PUP NO. 42223-08, WHICH DIED ON PND 25



TABLE 19 (F1)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF PUP OBSERVATIONS DURING LACTATION

PROJECT NO.: WIL-51041
 SPONSOR: DOM CORNING CORP.
 SPONSOR NO.: 8463

PAGE 1

FINDING	ALL OBSERVATION PERIODS				
	NUMBER OF PUPS WITH FINDING				
	1	2	3	4	5
NO REMARKABLE OBSERVATIONS	266	276	264	250	194
FOUND DEAD	4	12	3	13	10
CULLED ON SCHEDULED DAY	105	108	106	86	49
MISSING	3	4	3	6	5
SUBCUTANEOUS HEMORRHAGE(S)	1	5	1	3	3
SMALL IN SIZE	1	3	3	8	8
TAIL MISSING	0	0	1	0	0
APPEARS PALE IN COLOR	0	0	0	0	0
BODY COOL TO TOUCH	0	0	0	4	0
LACERATION	0	2	0	4	0
RED NASAL DISCHARGE	1	1	2	0	0
LEFT HINDLIMB SWOLLEN	0	0	0	0	1
SMELLING	1	1	0	0	1
HAIR LOSS	1	0	0	0	0
SCABBING	0	0	10	14	0
LEFT HINDLIMB MECHANICAL INJURY DUE TO ISCHEMIA	0	2	1	0	0
DISTAL END OF TAIL MISSING	0	1	0	0	0
SCHEDULED NECROPSY, LACTATION DAY 21	1	1	2	0	0
WET RED MATERIAL AROUND NOSE	120	127	119	121	103
APPARENT MECHANICAL INJURY	0	0	0	1	0
CLEFT LIP	1	1	0	0	0
MAXILLARY MICROGNATHIA	1	0	0	0	0
ABLEPHARIA	1	0	0	0	0
GASPING	1	0	0	0	0
SCHEDULED NECROPSY, LACTATION DAY 28	0	2	0	0	0
	39	40	39	40 A	40

1- 0 / 0 PPH 2- 0 / 70 PPH 3- 0 / 300 PPH 4- 0 / 500 PPH 5- 0 / 700 PPH
 A = INCLUDES PUP NO. 42225-09, WHICH WAS SELECTED TO REPLACE PUP NO. 42223-08, WHICH DIED ON LACTATION DAY 25



PROJECT NO.: WIL-51041
 SPONSOR: DOM CORNING CORP.
 SPONSOR NO.: 8463

TABLE 20 (F1 - FOUND DEAD PUPS)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF PUP NECROPSY FINDINGS
 FOUND DEAD PUPS

PAGE 1

	P U P S					L I T T E R S				
	1	2	3	4	5	1	2	3	4	5
GROUP:	4	12	3	13	10	3	6	3	8	6
NUMBER EXAMINED VISCERALLY	0	0	1	0	0	0	0	1	0	0
LUNGS	2	8	1	8	5	1	3	1	5	3
DARK RED AREA(S)	1	1	0	1	2	1	1	0	1	2
STOMACH	1	0	0	0	0	1	0	0	0	0
MILK NOT PRESENT	1	0	0	0	0	1	0	0	0	0
MILK PRESENT	1	0	0	0	0	1	0	0	0	0
DARK RED CONTENTS	1	0	0	0	0	1	0	0	0	0
DARK RED AREA(S)	1	0	0	0	0	1	0	0	0	0
INTESTINE	1	0	0	0	0	1	0	0	0	0
DUODENUM - DARK RED CONTENTS	1	0	0	0	0	1	0	0	0	0
BLADDER	1	0	0	0	0	1	0	0	0	0
RED FLUID CONTENTS	0	0	0	0	1	0	0	0	0	1
MALFORMATION	0	0	0	0	0	0	0	0	0	0
EXENCEPHALY	0	0	0	0	0	0	0	0	0	0
VARIATION	0	0	0	0	0	0	0	0	0	0
RENAL PAPILLAE) NOT FULLY DEVELOPED (MOO AND HOAR GRADE 1)	0	0	0	1	0	0	0	0	0	0
1- 0 / 0 PPM	2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM						



DC Study No. - 8463
 External No. - WIL-51041

DC Report No. - 1997-I0000-42936
 Security - INTERNAL

PROJECT NO.: WIL-51041
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 SPONSOR NO.: 8463

TABLE 21 (F1 - DAY 21 SURPLUS PUPS)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF PUP NECROPSY FINDINGS
 EUTHANIZED PUPS

PAGE 1

	P U P S					L I T T E R S				
	1	2	3	4	5	1	2	3	4	5
GROUP:	120	127	119	121	103	20	21	20	21	20
NUMBER EXAMINED VISCERALLY										
KIDNEY										
DILATED PELVIS	2	1	4	0	0	2	1	3	0	0
URETER										
DISTENDED	0	1	0	0	0	0	1	0	0	0
1- 0 / 0 PPM	2-	0 / 70 PPM	3-	0 / 300 PPM	4-	0 / 500 PPM	5-	0 / 700 PPM		



PROJECT NO.: WIL-51041
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 SPONSOR NO.: 8463

TABLE 22 (F1 - DAY 28 SURPLUS PUPS)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF PUP NECROPSY FINDINGS
 EUTHANIZED PUPS

PAGE 1

	P U P S					L I T T E R S				
	1	2	3	4	5	1	2	3	4	5
GROUP:	19	20	19	20	20	19	20	19	19	20
NUMBER EXAMINED VISCERALLY	19	20	19	20	20	19	20	19	19	20
LUNGS										
DARK RED AREA(S)	0	3	1	1	0	0	3	1	1	0
DARK RED	0	0	0	0	1	0	0	0	0	1
KIDNEY										
DILATED PELVIS	0	2	0	0	0	0	2	0	0	0
1- 0 / 0 PPM	2-	0 / 70 PPM	3-	0 / 300 PPM	4-	0 / 500 PPM	5-	0 / 700 PPM		



PROJECT NO.: WIL-51041A
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 SPONSOR NO.: 8463

TABLE 23 (F1 - DAY 28 SELECTED PUPS)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 GROSS NECROPSY OBSERVATIONS INCIDENCE SUMMARY

PAGE 1

	SCHEDULED NECROPSY									
	MALE					FEMALE				
	1	2	3	4	5	1	2	3	4	5
NUMBER OF ANIMALS IN GROUP	10	10	10	10	10	10	10	10	10	10
NUMBER OF ANIMALS EXAMINED	10	10	10	10	10	10	10	10	10	10
LYMPH NODE, MAND -REDDED	2	0	0	0	0	0	0	0	0	0
JEJUNUM -DIVERTICULUM	1	0	0	0	0	0	0	0	0	0
KIDNEYS -DILATED PELVIS -CYST(S) -ADHESIONS	0	0	1	0	0	0	1	1	1	0
LIVER -WHITE AREA(S)	0	0	0	0	0	0	0	0	1	1
LUNGS -DARK RED -MOTTLED -DARK RED AREA(S) -PALE	0	1	1	0	1	1	1	2	1	1
THYROID GLANDS -SMALL	0	0	0	0	0	0	0	0	0	0
TRACHEA -RED FLUID CONTENTS	0	0	0	1	0	1	0	1	0	1
1- 0 / 0 PPM	2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM						



TABLE 23 (F1 - DAY 28 SELECTED PUPS)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 GROSS NECROPSY OBSERVATIONS INCIDENCE SUMMARY

PROJECT NO.: WIL-51041A
 SPONSOR: DOM CORNING CORP.
 SPONSOR NO.: 8463

SCHEDULED NECROPSY

	GROUP:					MALE					FEMALE				
	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
NUMBER OF ANIMALS IN GROUP	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
NUMBER OF ANIMALS EXAMINED	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
URETER(S) -DISTENDED	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
LYMPH NODE -MEDIASTINAL - ENLARGED	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
NO SIGNIFICANT CHANGES OBSERVED - ALL EXAMINED TISSUES	6	8	6	8	7	9	8	5	7	8	0	0	0	0	0
1- 0 / 0 PPM	2-	0 / 70 PPM	3-	0 / 300 PPM	4-	0 / 500 PPM	5-	0 / 700 PPM							



TABLE 24 (F1)
 INHALATION REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF MEAN PUP WEIGHTS (GRAMS)

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463
 DOSE GROUP: 0 / 0 PPM

	0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
DAY 1 MEAN	6.8	6.7	6.6	7.0	7.1
S.D.	0.74	0.64	0.72	0.63	0.86
N	20	21	20	21	20
DAY 4 MEAN BEFORE SELECTION	9.6	9.7	9.4	10.1	10.5
S.D.	1.19	1.13	1.36	0.96	1.63
N	20	21	20	21	20
DAY 4 MEAN AFTER SELECTION	9.6	9.7	9.4	10.0	10.4
S.D.	1.20	1.07	1.42	0.98	1.67
N	20	21	20	21	20
DAY 7 MEAN	13.6	13.7	13.1	13.6	13.5
S.D.	1.62	1.58	1.74	1.30	1.67
N	20	21	20	21	20
DAY 14 MEAN	26.5	26.8	25.3	26.2	24.8
S.D.	2.83	2.33	2.78	2.45	3.09
N	20	21	20	21	20
DAY 21 MEAN	42.0	43.2	38.6	40.8	38.5
S.D.	6.40	4.59	4.56	4.43	5.97
N	20	21	20	21	20
DAY 28 MEAN	75.5	77.2	71.2	72.8	70.9
S.D.	9.56	7.39	7.62	6.75	8.58
N	20	21	20	21	20

NONE SIGNIFICANTLY DIFFERENT FROM THE CONTROL GROUP USING DUNNETT'S TEST



PROJECT NO.: WIL-51041A
 SPONSOR: DOM CORNING CORP.
 SPONSOR NO.: 8463

TABLE 25 (F1 - DAY 28 SELECTED PUPS)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS (GRAMS) - SUMMARY OF MEANS

PAGE 1
 WEEK 17

GROUP:	M A L E				
	0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
LIVER					
MEAN	4.5709	4.3072	4.0585	4.3250	4.1284
S.D.	0.76549	0.76810	0.59038	0.54784	0.50531
N	10	10	10	10	10
TESTES					
MEAN	0.5331	0.4949	0.4337*	0.5029	0.4729
S.D.	0.09852	0.08283	0.07347	0.07146	0.08285
N	10	10	10	10	10

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST



PROJECT NO.: WIL-51041A
 SPONSOR: DOM CORNING CORP.
 SPONSOR NO.: 8463

TABLE 25 (F1 - DAY 28 SELECTED PUPS)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF O4 IN FEMALE RATS
 ORGAN WEIGHTS (GRAMS) - SUMMARY OF MEANS

PAGE 2
 WEEK 17

GROUP:	F E M A L E				
	0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
LIVER					
MEAN	4.1109	4.1062	4.0362	4.0623	4.1730
S.D.	0.68210	0.62950	0.67727	0.63561	0.59962
N	10	10	10	10	10
OVARIES					
MEAN	0.0403	0.0356	0.0362	0.0349	0.0348
S.D.	0.00753	0.00285	0.00600	0.00472	0.00494
N	10	10	10	10	10

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST



TABLE 26 (F1 - DAY 28 SELECTED PUPS)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

PROJECT NO.: WIL-51041A
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP:	M A L E				
	0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
FINAL BODY WT					
MEAN	81.	77.	70.*	75.	73.
S.D.	10.3	9.9	8.4	8.3	8.7
N	10	10	10	10	10
LIVER					
MEAN	5.639	5.581	5.780	5.785	5.648
S.D.	0.5486	0.5458	0.4998	0.4957	0.5798
N	10	10	10	10	10
TESTES					
MEAN	0.656	0.644	0.617	0.671	0.642
S.D.	0.0539	0.0817	0.0595	0.0590	0.0615
N	10	10	10	10	10

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST



PROJECT NO.: WIL-51041A
 SPONSOR: DOM CORNING CORP.
 SPONSOR NO.: 8463

TABLE 26 (F1 - DAY 28 SELECTED PUPS)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

GROUP:		F E M A L E				
		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
FINAL BODY WT						
MEAN		70.	75.	69.	70.	67.
S.D.		10.9	7.7	7.5	8.0	9.7
N		10	10	10	10	10
LIVER						
MEAN		6.053	5.466	5.819	5.772	6.220
S.D.		1.8041	0.4471	0.6087	0.5603	0.7219
N		10	10	10	10	10
OVARIES						
MEAN		0.058	0.048*	0.053	0.050	0.052
S.D.		0.0073	0.0050	0.0102	0.0092	0.0072
N		10	10	10	10	10

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 27 (F0 FEMALE - 25 DAYS AFTER BREEDING PERIOD)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 GROSS NECROPSY OBSERVATIONS INCIDENCE SUMMARY

		SCHEDULED NECROPSY				
		FEMALE				
		1	2	3	4	5
GROUP:		22	22	22	22	22
NUMBER OF ANIMALS IN GROUP		0	0	0	1	0
NUMBER OF ANIMALS EXAMINED						
NO SIGNIFICANT CHANGES OBSERVED - ALL EXAMINED TISSUES						
1- 0 / 0 PPM	2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM		



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 28 (F0 FEMALES - POST-MATING DAY 25)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 GROSS NECROPSY OBSERVATIONS INCIDENCE SUMMARY

		SCHEDULED NECROPSY				
		FEMALE				
		1	2	3	4	5
NUMBER OF ANIMALS IN GROUP	GROUP:	22	22	22	22	22
NUMBER OF ANIMALS EXAMINED		2	1	2	0	2
LUNGS		0	0	0	0	1
-DARK RED						
INCISOR(S)		1	0	0	0	0
-MALALIGNED		1	0	0	0	0
-BROKEN						
NO SIGNIFICANT CHANGES OBSERVED - ALL EXAMINED TISSUES		0	1	2	0	1
1- 0 / 0 PPM	2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM		



TABLE 29 (F0 FEMALES - LACTATION DAY 21)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 GROSS NECROPSY OBSERVATIONS INCIDENCE SUMMARY

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

SCHEDULED NECROPSY

	FEMALE				
	1	2	3	4	5
NUMBER OF ANIMALS IN GROUP	22	22	22	22	22
NUMBER OF ANIMALS EXAMINED	20	21	20	21	20
LYMPH NODE, MAND					
-REDEEMED	2	2	1	0	1
-ENLARGED	0	0	1	0	0
JEJUNUM					
-DIVERTICULUM	0	0	0	0	1
KIDNEYS					
-DILATED PELVIS	0	2	1	1	0
LUNGS					
-DARK RED	0	1	0	0	0
-DARK RED AREA(S)	0	2	0	1	0
-MOTTLED	1	0	0	0	0
-WHITE AREA(S)	0	0	0	0	1
SPLEEN					
-CYST(S)	1	1	0	1	0
THYMUS GLAND					
-HEMORRHAGIC	0	1	0	0	0
THYROID GLANDS					
-ABSENT	0	0	0	0	1
-SMALL	0	1	0	0	0
1- 0 / 0 PPM	2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM	



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 29 (F0 FEMALES - LACTATION DAY 21)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 GROSS NECROPSY OBSERVATIONS INCIDENCE SUMMARY

	SCHEDULED NECROPSY							
	FEMALE							
	1	2	3	4	5			
NUMBER OF ANIMALS IN GROUP	22	22	22	22	22			
NUMBER OF ANIMALS EXAMINED	20	21	20	21	20			
URINARY BLADDER								
-THICKENED	0	0	1	0	0			
-CALCULI	0	0	1	0	0			
EXTERNAL SURFACE								
-SWOLLEN	0	1	1	0	0			
-HAIR LOSS	1	2	0	0	0			
INCISOR(S)								
-MALALIGNED	0	0	0	1	0			
-BROKEN	0	0	0	1	0			
URETER(S)								
-DISTENDED	0	0	0	1	0			
LYMPH NODE								
-MEDIASITINAL - REDDENED	0	1	1	0	1			
-MEDIASITINAL - ENLARGED	0	0	1	0	1			
MESENTERY								
-WHITE NODULE(S)	0	0	1	0	1			
NO SIGNIFICANT CHANGES OBSERVED - ALL EXAMINED TISSUES	16	12	14	16	14			
1- 0 / 0 PPM	2-	0 / 70 PPM	3-	0 / 300 PPM	4-	0 / 500 PPM	5-	0 / 700 PPM



TABLE 30 (FO)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 SUMMARY OF IMPLANTATION SITES - LACTATION DAY 21

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

PAGE 1

GROUP:		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
IMPLANTATION SITES						
MEAN		14.5	15.0	14.1	13.8	12.3*
S.D.		2.14	1.41	2.65	1.89	3.27
N		20	21	20	21	20
NUMBER BORN						
MEAN		13.6	13.9	13.5	12.7	10.4**
S.D.		2.14	1.74	2.74	2.15	3.57
N		20	21	20	21	20
UNACCOUNTED SITES						
MEAN		0.9	1.1	0.6	1.1	1.9**
S.D.		1.10	1.24	0.75	1.96	1.83
N		20	21	20	21	20

* = SIGNIFICANTLY DIFFERENTLY FROM THE CONTROL GROUP AT THE 0.05 LEVEL USING DUNNETT'S TEST
 ** = SIGNIFICANTLY DIFFERENTLY FROM THE CONTROL GROUP AT THE 0.01 LEVEL USING DUNNETT'S TEST



TABLE 31 (F0 FEMALES - POST-MATING DAY 25)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF O4 IN FEMALE RATS
 ORGAN WEIGHTS (GRAMS) - SUMMARY OF MEANS

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP:	F E M A L E				
	0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
BRAIN	MEAN S.D. N	2.05 0.064 2	1.85 0.000 1	2.01 0.085 2	MA 1.91 0.064 2
LIVER	MEAN S.D. N	10.46 2.432 2	9.86 0.000 1	11.16 1.442 2	MA 11.23 1.428 2
KIDNEYS	MEAN S.D. N	2.25 0.332 2	1.88 0.000 1	2.22 0.339 2	MA 2.11 0.537 2
HEART	MEAN S.D. N	1.04 0.134 2	1.00 0.000 1	1.05 0.205 2	MA 0.83 0.021 2
LUNGS	MEAN S.D. N	1.92 0.453 2	1.60 0.000 1	1.86 0.615 2	MA 2.29 1.549 2

MA = NOT APPLICABLE



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 31 (F0 FEMALES - POST-MATING DAY 25)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS (GRAMS) - SUMMARY OF MEANS

PAGE 2

GROUP:	F E M A L E									
	0 / 0 PPM		0 / 70 PPM		0 / 300 PPM		0 / 500 PPM		0 / 700 PPM	
SPLEEN	MEAN	0.64	0.48	0.56	0.56	0.56	MA	0.58	0.58	
	S.D.	0.057	0.000	0.000	0.000	0.000		0.148	0.148	
	N	2	1	2	2	2		2	2	
UTERUS	MEAN	0.86	0.56	0.71	0.71	0.71	MA	0.85	0.85	
	S.D.	0.523	0.000	0.141	0.141	0.141		0.311	0.311	
	N	2	1	2	2	2		2	2	
OVARIES	MEAN	0.1573	0.1680	0.1149	0.1149	0.1149	MA	0.1390	0.1390	
	S.D.	0.00318	0.00000	0.00071	0.00071	0.00071		0.03550	0.03550	
	N	2	1	2	2	2		2	2	
THYMSUS GLAND	MEAN	0.2454	0.3286	0.2651	0.2651	0.2651	MA	0.3147	0.3147	
	S.D.	0.03444	0.00000	0.03316	0.03316	0.03316		0.01725	0.01725	
	N	2	1	2	2	2		2	2	
THYROID GLANDS	MEAN	0.0190	0.0177	0.0224	0.0224	0.0224	MA	0.0208	0.0208	
	S.D.	0.00028	0.00000	0.00445	0.00445	0.00445		0.00509	0.00509	
	N	2	1	2	2	2		2	2	

MA = NOT APPLICABLE



TABLE 31 (F0 FEMALES - POST-MATING DAY 25)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS (GRAMS) - SUMMARY OF MEANS

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP:		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
----- F E M A L E -----						
ADRENAL GLANDS						
MEAN		0.0866	0.0607	0.0634	NA	0.0786
S.D.		0.02270	0.00000	0.01683	NA	0.00636
N		2	1	2		2
PITUITARY						
MEAN		0.0181	0.0109	0.0206	NA	0.0141
S.D.		0.00544	0.00000	0.01146	NA	0.00523
N		2	1	2		2

NA = NOT APPLICABLE



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 32 (F0 FEMALES - LACTATION DAY 21)
 INHALATION REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS (GRAMS) - SUMMARY OF MEANS

GROUP:	F E M A L E				
	0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
BRAIN					
MEAN	1.96	1.96	1.99	1.98	1.98
S.D.	0.097	0.084	0.079	0.078	0.118
N	20	21	20	21	20
LIVER					
MEAN	15.32	15.70	16.24	16.94*	17.77**
S.D.	2.499	1.296	1.646	1.878	1.660
N	20	21	20	21	20
KIDNEYS					
MEAN	2.51	2.58	2.58	2.58	2.55
S.D.	0.241	0.207	0.214	0.238	0.218
N	20	21	20	21	20
HEART					
MEAN	1.19	1.20	1.28	1.15	1.18
S.D.	0.174	0.134	0.217	0.110	0.139
N	20	21	20	21	20
LUNGS					
MEAN	1.77	1.70	1.70	1.69	1.67
S.D.	0.321	0.469	0.539	0.384	0.303
N	20	21	20	21	20

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST
 ** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING DUNNETT'S TEST



PROJECT NO.: WIL-51041
 SPONSOR: 3M CORNING CORP.
 SPONSOR NO.: 8463

TABLE 32 (F0 FEMALES - LACTATION DAY 21)
 INHALATION REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS (GRAMS) - SUMMARY OF MEANS

GROUP:		F E M A L E				
		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
SPLEEN	MEAN	0.59	0.67	0.65	0.66	0.66
	S.D.	0.096	0.114	0.105	0.138	0.099
	N	20	21	20	21	20
UTERUS	MEAN	0.48	0.61**	0.55	0.55	0.52
	S.D.	0.084	0.150	0.074	0.090	0.115
	N	20	21	20	21	20
OVARIES	MEAN	0.1381	0.1418	0.1337	0.1363	0.1282
	S.D.	0.02542	0.01619	0.01681	0.02029	0.01930
	N	20	21	20	21	20
THYMUS GLAND	MEAN	0.1587	0.1554	0.1683	0.1582	0.1701
	S.D.	0.04363	0.04842	0.03517	0.04426	0.05585
	N	20	21	20	21	20
THYROID GLANDS	MEAN	0.0226	0.0230	0.0235	0.0241	0.0265
	S.D.	0.00666	0.00662	0.00672	0.00719	0.00585
	N	20	21	20	21	19

** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING DUNNETT'S TEST



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 32 (F0 FEMALES - LACTATION DAY 21)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS (GRAMS) - SUMMARY OF MEANS

GROUP:	F E M A L E				
	0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
ADRENAL GLANDS					
MEAN	0.0818	0.0859	0.0836	0.0864	0.0880
S.D.	0.01043	0.01066	0.01157	0.01798	0.01084
N	20	21	20	21	20
PITUITARY					
MEAN	0.0180	0.0174	0.0158	0.0165	0.0172
S.D.	0.00489	0.00392	0.00393	0.00554	0.00533
N	20	21	20	21	20

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST



TABLE 33 (FO FEMALES - POST-MATING DAY 25)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP:		F E M A L E				
		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
FINAL BODY WT						
MEAN		297.	319.	277.	NA	264.
S.D.		15.6	0.0	17.0		26.2
N		2	1	2		2
BRAIN						
MEAN		0.689	0.580	0.726	NA	0.728
S.D.		0.0141	0.0000	0.0141		0.0962
N		2	1	2		2
LIVER						
MEAN		3.506	3.091	4.021	NA	4.256
S.D.		0.6357	0.0000	0.2751		0.1195
N		2	1	2		2
KIDNEYS						
MEAN		0.754	0.589	0.799	NA	0.795
S.D.		0.0721	0.0000	0.0735		0.1252
N		2	1	2		2
HEART						
MEAN		0.351	0.313	0.376	NA	0.315
S.D.		0.0269	0.0000	0.0509		0.0233
N		2	1	2		2

NA = NOT APPLICABLE



TABLE 33 (FO FEMALES - POST-MATING DAY 25)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP:	F E M A L E				
	0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
LUNGS					
MEAN	0.651	0.502	0.678	NA	0.843
S.D.	0.1867	0.0000	0.2638		0.5042
N	2	1	2		2
SPLEEN					
MEAN	0.216	0.150	0.203	NA	0.217
S.D.	0.0078	0.0000	0.0120		0.0346
N	2	1	2		2
UTERUS					
MEAN	0.285	0.176	0.259	NA	0.330
S.D.	0.1612	0.0000	0.0672		0.1513
N	2	1	2		2
OVARIES					
MEAN	0.053	0.053	0.042	NA	0.052
S.D.	0.0014	0.0000	0.0028		0.0085
N	2	1	2		2
THYMUS GLAND					
MEAN	0.083	0.103	0.097	NA	0.120
S.D.	0.0156	0.0000	0.0177		0.0049
N	2	1	2		2

NA = NOT APPLICABLE



TABLE 33 (FO FEMALES - POST-MATING DAY 25)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

PROJECT NO.: WIL-51041
 SPONSOR: DOM CORNING CORP.
 SPONSOR NO.: 8463

GROUP:		F E M A L E				
		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
THYROID GLANDS						
MEAN		0.007	0.006	0.008	MA	0.008
S.D.		0.0007	0.0000	0.0014		0.0014
N		2	1	2		2
ADRENAL GLANDS						
MEAN		0.029	0.019	0.023	MA	0.030
S.D.		0.0057	0.0000	0.0049		0.0007
N		2	1	2		2
PITUITARY						
MEAN		0.006	0.003	0.008	MA	0.005
S.D.		0.0014	0.0000	0.0035		0.0014
N		2	1	2		2

MA = NOT APPLICABLE



TABLE 34 (F0 FEMALES - LACTATION DAY 21)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP:		F E M A L E				
		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
FINAL BODY WT						
MEAN		337.	337.	327.	334.	334.
S.D.		38.3	20.7	20.1	22.8	19.0
N		20	21	20	21	20
BRAIN						
MEAN		0.587	0.583	0.612	0.593	0.592
S.D.		0.0647	0.0311	0.0539	0.0383	0.0333
N		20	21	20	21	20
LIVER						
MEAN		4.521	4.663	4.966**	5.063**	5.330**
S.D.		0.4605	0.2989	0.3531	0.3688	0.4921
N		20	21	20	21	20
KIDNEYS						
MEAN		0.755	0.768	0.791	0.772	0.765
S.D.		0.1153	0.0616	0.0849	0.0565	0.0698
N		20	21	20	21	20
HEART						
MEAN		0.357	0.358	0.391	0.344	0.353
S.D.		0.0540	0.0426	0.0614	0.0203	0.0388
N		20	21	20	21	20

** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING DUNNETT'S TEST



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 34 (F0 FEMALES - LACTATION DAY 21)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF O4 IN FEMALE RATS
 ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

GROUP:		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
----- F E M A L E -----						
LUNGS	MEAN	0.536	0.504	0.520	0.508	0.502
	S.D.	0.1542	0.1384	0.1552	0.1159	0.1023
	N	20	21	20	21	20
SPLEEN	MEAN	0.177	0.198	0.198	0.196	0.196
	S.D.	0.0301	0.0307	0.0269	0.0349	0.0236
	N	20	21	20	21	20
UTERUS	MEAN	0.146	0.181**	0.168	0.166	0.157
	S.D.	0.0301	0.0414	0.0246	0.0267	0.0365
	N	20	21	20	21	20
OVARIES	MEAN	0.042	0.042	0.041	0.041	0.038
	S.D.	0.0090	0.0055	0.0050	0.0054	0.0060
	N	20	21	20	21	20
THYMUS GLAND	MEAN	0.048	0.046	0.052	0.048	0.051
	S.D.	0.0136	0.0137	0.0117	0.0145	0.0168
	N	20	21	20	21	20

** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING DUNNETT'S TEST



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 34 (F0 FEMALES - LACTATION DAY 21)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

GROUP:	F E M A L E				
	0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
THYROID GLANDS					
MEAN	0.007	0.007	0.007	0.007	0.007
S.D.	0.0021	0.0019	0.0020	0.0021	0.0019
N	20	21	20	21	19
ADRENAL GLANDS					
MEAN	0.025	0.026	0.026	0.026	0.027
S.D.	0.0047	0.0037	0.0033	0.0047	0.0036
N	20	21	20	21	20
PITUITARY					
MEAN	0.006	0.005	0.005	0.005	0.005
S.D.	0.0017	0.0012	0.0013	0.0015	0.0016
N	20	21	20	21	20

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 35 (F0 FEMALES - POST-MATING DAY 25)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS RELATIVE TO BRAIN WEIGHTS (GRAMS/100 GRAMS)

PAGE 1

GROUP:	F E M A L E					
	0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM	
BRAIN WT (GRAMS)						
MEAN	2.05	1.85	2.01	MA	1.91	
S.D.	0.064	0.000	0.085		0.064	
N	2	1	2		2	
LIVER						
MEAN	509.880	532.973	554.203	MA	591.084	
S.D.	103.0785	0.0000	48.3703		94.7254	
N	2	1	2		2	
KIDNEYS						
MEAN	109.580	101.622	110.190	MA	111.295	
S.D.	12.8411	0.0000	12.2351		31.9280	
N	2	1	2		2	
HEART						
MEAN	51.023	54.054	51.821	MA	43.350	
S.D.	4.9816	0.0000	8.0144		2.5618	
N	2	1	2		2	
LUNGS						
MEAN	94.278	86.486	93.018	MA	121.373	
S.D.	25.0634	0.0000	34.5330		85.3436	
N	2	1	2		2	

MA = NOT APPLICABLE



TABLE 35 (F0 FEMALES - POST-MATING DAY 25)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS RELATIVE TO BRAIN WEIGHTS (GRAMS/100 GRAMS)

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP:	FEMALE				
	0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
SPLEEN					
MEAN	31.268	25.946	27.886	MA	30.331
S.D.	1.7932	0.0000	1.1774	MA	8.8077
N	2	1	2		2
UTERUS					
MEAN	41.676	30.270	35.504	MA	44.372
S.D.	24.2905	0.0000	8.5341		14.8499
N	2	1	2		2
OVARIES					
MEAN	7.691	9.081	5.723	MA	7.332
S.D.	0.0834	0.0000	0.2765		2.1086
N	2	1	2		2
THYRUS GLAND					
MEAN	12.030	17.762	13.233	MA	16.544
S.D.	2.0584	0.0000	2.2090		1.4581
N	2	1	2		2
THYROID GLANDS					
MEAN	0.930	0.957	1.109	MA	1.097
S.D.	0.0148	0.0000	0.1747		0.3041
N	2	1	2		2

MA = NOT APPLICABLE



TABLE 35 (F0 FEMALES - POST-MATING DAY 25)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS RELATIVE TO BRAIN WEIGHTS (GRAMS/100 GRAMS)

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP:		----- F E M A L E -----				
		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
ADRENAL GLANDS						
MEAN		4.217	3.281	3.160	NA	4.134
S.D.		0.9786	0.0000	0.7050		0.4723
N		2	1	2		2
PITUITARY						
MEAN		0.879	0.589	1.014	NA	0.745
S.D.		0.2390	0.0000	0.5260		0.2998
N		2	1	2		2

NA = NOT APPLICABLE



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 36 (F0 FEMALES - LACTATION DAY 21)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS RELATIVE TO BRAIN WEIGHTS (GRAMS/100 GRAMS)

PAGE 1

GROUP:		F E M A L E				
		0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
BRAIN WT (GRAMS)						
MEAN		1.96	1.96	1.99	1.98	1.98
S.D.		0.097	0.084	0.079	0.078	0.118
N		20	21	20	21	20
LIVER						
MEAN		780.445	802.238	816.495	857.270*	900.298**
S.D.		119.5629	71.7924	83.1506	89.2327	75.5059
N		20	21	20	21	20
KIDNEYS						
MEAN		128.320	131.992	129.423	130.510	129.078
S.D.		11.6543	10.8206	10.5342	11.5202	8.2494
N		20	21	20	21	20
HEART						
MEAN		61.010	61.316	64.118	58.303	59.663
S.D.		8.7507	6.4843	10.8626	5.8144	5.7099
N		20	21	20	21	20
LUNGS						
MEAN		90.358	86.611	85.459	85.840	84.925
S.D.		17.4401	23.8146	27.1149	19.8541	17.3905
N		20	21	20	21	20

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST
 ** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING DUNNETT'S TEST



TABLE 36 (F0 FEMALES - LACTATION DAY 21)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS RELATIVE TO BRAIN WEIGHTS (GRAMS/100 GRAMS)

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

GROUP:	F E M A L E				
	0 / 0 PPH	0 / 70 PPH	0 / 300 PPH	0 / 500 PPH	0 / 700 PPH
SPLEEN					
MEAN	30.381	34.049	32.592	33.311	33.209
S.D.	5.3539	5.5229	5.2053	6.6050	4.5190
N	20	21	20	21	20
UTERUS					
MEAN	24.748	31.199**	27.608	28.001	26.445
S.D.	4.4493	7.8167	4.1113	4.5502	5.5096
N	20	21	20	21	20
OVARIES					
MEAN	7.033	7.244	6.732	6.896	6.495
S.D.	1.1580	0.8884	0.9133	0.9976	0.9106
N	20	21	20	21	20
THYMUS GLAND					
MEAN	8.109	7.933	8.451	8.013	8.590
S.D.	2.2477	2.3896	1.7019	2.2515	2.7241
N	20	21	20	21	20
THYROID GLANDS					
MEAN	1.149	1.176	1.181	1.226	1.340
S.D.	0.3251	0.3473	0.3383	0.3783	0.2711
N	20	21	20	21	19

** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING DUNNETT'S TEST



PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

TABLE 36 (F0 FEMALES - LACTATION DAY 21)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 ORGAN WEIGHTS RELATIVE TO BRAIN WEIGHTS (GRAMS/100 GRAMS)

GROUP:	F E M A L E				
	0 / 0 PPM	0 / 70 PPM	0 / 300 PPM	0 / 500 PPM	0 / 700 PPM
ADRENAL GLANDS					
MEAN	4.184	4.392	4.207	4.474	4.461
S.D.	0.5614	0.5911	0.6050	0.8821	0.5475
N	20	21	20	21	20
PITUITARY					
MEAN	0.919	0.692	0.796	0.834	0.863
S.D.	0.2435	0.2102	0.2034	0.2812	0.2416
N	20	21	20	21	20

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST



TABLE 37 (F0 FEMALES - POST-MATING DAY 25)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 HISTOPATHOLOGICAL DIAGNOSIS -- SUMMARY INCIDENCE

PROJECT NO.: WIL-51041
 SPONSOR: 3M CORNING CORP.
 SPONSOR NO.: 8463

PAGE 1

	GROUP:					PAGE
	1	2	3	4	5	
----- FEMALE -----						
NUMBER OF ANIMALS IN DOSE GROUP	22	22	22	22	22	22
NUMBER OF ANIMALS EXAMINED	2	0	0	0	0	2
ADRENAL GLANDS						
TOTAL NUMBER EXAMINED	2	NA	NA	NA	NA	2
EXAMINED, UNREMARKABLE	2	NA	NA	NA	NA	2
BRAIN						
TOTAL NUMBER EXAMINED	2	NA	NA	NA	NA	2
EXAMINED, UNREMARKABLE	2	NA	NA	NA	NA	2
KIDNEYS						
TOTAL NUMBER EXAMINED	2	NA	NA	NA	NA	2
EXAMINED, UNREMARKABLE	2	NA	NA	NA	NA	2
LIVER						
TOTAL NUMBER EXAMINED	2	NA	NA	NA	NA	2
EXAMINED, UNREMARKABLE	2	NA	NA	NA	NA	2
LUNGS						
TOTAL NUMBER EXAMINED	NA	NA	NA	NA	NA	1
EXAMINED, UNREMARKABLE	NA	NA	NA	NA	NA	0
-EDEMA, ALVEOLAR	NA	NA	NA	NA	NA	1
SEVERE	NA	NA	NA	NA	NA	1
1- 0 / 0 PPM	2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM		
NA = NOT APPLICABLE						



TABLE 37 (F0 FEMALES - POST-MATING DAY 25)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 HISTOMORPHOLOGICAL DIAGNOSIS -- SUMMARY INCIDENCE

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

PAGE 2

	FEMALE				
	GROUP: 1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP	22	22	22	22	22
NUMBER OF ANIMALS EXAMINED	2	0	0	0	2
MAMMARY GLAND					
TOTAL NUMBER EXAMINED	0	MA	MA	MA	2
EXAMINED, UNREMARKABLE	0	MA	MA	MA	0
NOT EXAMINED	2	MA	MA	MA	0
-IMMATURE GLANDULAR DEVELOPMENT PRESENT	0	MA	MA	MA	2
	NONE	MA	MA	MA	2
OVARIES					
TOTAL NUMBER EXAMINED	2	MA	MA	MA	2
EXAMINED, UNREMARKABLE	2	MA	MA	MA	2
PITUITARY					
TOTAL NUMBER EXAMINED	2	MA	MA	MA	2
EXAMINED, UNREMARKABLE	2	MA	MA	MA	2
SPLEEN					
TOTAL NUMBER EXAMINED	2	MA	MA	MA	2
EXAMINED, UNREMARKABLE	2	MA	MA	MA	2
THYMUS GLAND					
TOTAL NUMBER EXAMINED	2	MA	MA	MA	2
EXAMINED, UNREMARKABLE	2	MA	MA	MA	2
1- 0 / 0 PPM	2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM	
MA = NOT APPLICABLE					



DC Study No. - 8463
 External No. - WIL-51041

DC Report No. - 1997-I0000-42936
 Security - INTERNAL

TABLE 37 (F0 FEMALES - POST-MATING DAY 25)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 HISTOMORPHOLOGICAL DIAGNOSIS -- SUMMARY INCIDENCE

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

PAGE 3

		----- FEMALE -----				
		GROUP:				
		1	2	3	4	5
NUMBER OF ANIMALS IN DOSE GROUP		22	22	22	22	22
NUMBER OF ANIMALS EXAMINED		2	0	0	0	2
UTERUS						
TOTAL NUMBER EXAMINED		0	NA	NA	NA	0
EXAMINED, UNREMARKABLE		0	NA	NA	NA	0
NOT EXAMINED		2	NA	NA	NA	2
VAGINA						
TOTAL NUMBER EXAMINED		2	NA	NA	NA	2
EXAMINED, UNREMARKABLE		2	NA	NA	NA	2
1- 0 / 0 PPM	2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM		
NA = NOT APPLICABLE						



TABLE 3B (F0 FEMALES - LACTATION DAY 21)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 HISTOPATHOLOGICAL DIAGNOSIS -- SUMMARY INCIDENCE

PROJECT NO.: WIL-51041
 SPONSOR: DOM CORNING CORP.
 SPONSOR NO.: 8463

	GROUP:							
	1	2	3	4	5			
NUMBER OF ANIMALS IN GROUP	22	22	22	22	22			
NUMBER OF ANIMALS EXAMINED	20	0	0	0	20			
ADRENAL GLANDS								
TOTAL NUMBER EXAMINED	20	NA	NA	NA	20			
EXAMINED, UNREMARKABLE	20	NA	NA	NA	20			
BRAIN								
TOTAL NUMBER EXAMINED	20	NA	NA	NA	20			
EXAMINED, UNREMARKABLE	20	NA	NA	NA	20			
KIDNEYS								
TOTAL NUMBER EXAMINED	20	NA	NA	NA	20			
EXAMINED, UNREMARKABLE	18	NA	NA	NA	20			
-MINERALIZATION, TUBULAR	2	NA	NA	NA	0			
MINIMAL	2	NA	NA	NA	NONE			
LIVER								
TOTAL NUMBER EXAMINED	20	NA	NA	NA	20			
EXAMINED, UNREMARKABLE	20	NA	NA	NA	20			
LUNGS								
TOTAL NUMBER EXAMINED	20	NA	NA	NA	20			
EXAMINED, UNREMARKABLE	18	NA	NA	NA	18			
-HEMORRHAGE, ACUTE, ALVEOLAR	2	NA	NA	NA	0			
MODERATE	2	NA	NA	NA	NONE			
-HISTIOCYTOSIS, ALVEOLAR	0	NA	NA	NA	2			
MINIMAL	NONE	NA	NA	NA	1			
MILD	NONE	NA	NA	NA	1			
1- 0 / 0 PPM	2-	0 / 70 PPM	3-	0 / 300 PPM	4-	0 / 500 PPM	5-	0 / 700 PPM
NA = NOT APPLICABLE								



TABLE 38 (F0 FEMALES - LACTATION DAY 21)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 HISTOMORPHOLOGICAL DIAGNOSIS -- SUMMARY INCIDENCE

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

	FEMALE				
	1	2	3	4	5
GROUP:	1	2	3	4	5
NUMBER OF ANIMALS IN GROUP	22	22	22	22	22
NUMBER OF ANIMALS EXAMINED	20	0	0	0	20
MAMMARY GLAND					
TOTAL NUMBER EXAMINED	20	NA	NA	NA	20
EXAMINED, UNREMARKABLE	19	NA	NA	NA	16
-INACTIVE GLANDULAR SECRETION PRESENT	1	NA	NA	NA	4
	1	NA	NA	NA	4
PITUITARY					
TOTAL NUMBER EXAMINED	20	NA	NA	NA	19
EXAMINED, UNREMARKABLE	20	NA	NA	NA	19
NOT EXAMINED	0	NA	NA	NA	1
SPLEEN					
TOTAL NUMBER EXAMINED	20	NA	NA	NA	20
EXAMINED, UNREMARKABLE	20	NA	NA	NA	20
NOT EXAMINED	0	NA	NA	NA	0
THYRUS GLAND					
TOTAL NUMBER EXAMINED	20	NA	NA	NA	20
EXAMINED, UNREMARKABLE	20	NA	NA	NA	20
UTERUS					
TOTAL NUMBER EXAMINED	20	NA	NA	NA	20
EXAMINED, UNREMARKABLE	18	NA	NA	NA	19
-HYDRONETRA	2	NA	NA	NA	1
MILD	1	NA	NA	NA	1
MODERATE	1	NA	NA	NA	1
1- 0 / 0 PPM					NONE
2- 0 / 300 PPM					
3- 0 / 70 PPM					
4- 0 / 500 PPM					
5- 0 / 700 PPM					
NA = NOT APPLICABLE					



DC Study No. - 8463
 External No. - WIL-51041

DC Report No. - 1997-I0000-42936
 Security - INTERNAL

TABLE 38 (F0 FEMALES - LACTATION DAY 21)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 HISTOMORPHOLOGICAL DIAGNOSIS -- SUMMARY INCIDENCE

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

PAGE 3

		----- FEMALE -----				
		GROUP:				
		1	2	3	4	5
NUMBER OF ANIMALS IN GROUP		22	22	22	22	22
NUMBER OF ANIMALS EXAMINED		20	0	0	0	20
VAGINA						
TOTAL NUMBER EXAMINED		20	NA	NA	NA	20
EXAMINED, UNREMARKABLE		20	NA	NA	NA	20
1- 0 / 0 PPM	2- 0 / 70 PPM	3- 0 / 300 PPM	4- 0 / 500 PPM	5- 0 / 700 PPM		
NA = NOT APPLICABLE						



TABLE 39 (F0 FEMALES - POST-MATING DAY 25)
 INHALATION RF REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 OVARIAN FOLLICLE COUNTS - SUMMARY OF MEANS

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

	0 / 0 PPM	0 / 700 PPM
CL M		
MEAN	92.5	66.0
S.D.	44.5	18.4
N	2	2
CL D		
MEAN	19.5	20.5
S.D.	6.4	14.8
N	2	2
NO FC		
MEAN	36.5	39.5
S.D.	26.2	14.8
N	2	2
MFC		
MEAN	25.5	55.0
S.D.	19.1	28.3
N	2	2
FFC		
MEAN	28.5	30.0
S.D.	21.9	25.5
N	2	2
FFCS		
MEAN	5.0	6.5
S.D.	7.1	7.8
N	2	2

CL M = NUMBER OF MATURE CORPORA LUTEA
 CL D = NUMBER OF DEGENERATE CORPORA LUTEA
 NO FC = NUMBER OF OOCYTES WITH NO FOLLICULAR CELLS ATTACHED TO THE SURFACE
 MFC = NUMBER OF OOCYTES WITH MULTIPLE LAYERS OF FOLLICULAR CELLS ATTACHED TO THE SURFACE
 FFC = NUMBER OF OOCYTES SURROUNDED BY A FLUID-FILLED CAVITY
 FFCS = NUMBER OF OOCYTES WITH FOLLICULAR FLUID AND A WELL-FORMED CUMULUS STALK



TABLE 40 (F0 FEMALES - LACTATION DAY 21)
 INHALATION REPRODUCTIVE TOXICITY STUDY OF D4 IN FEMALE RATS
 OVARIAN FOLLICLE COUNTS - SUMMARY OF MEANS

PROJECT NO.: WIL-51041
 SPONSOR: DOW CORNING CORP.
 SPONSOR NO.: 8463

	0 / 0 PPM	0 / 700 PPM
CL M		
MEAN	49.8	47.9
S.D.	18.3	17.5
N	20	20
CL O		
MEAN	20.8	18.9
S.D.	10.3	9.8
N	20	20
NO FC		
MEAN	56.3	55.9
S.D.	30.5	25.1
N	20	20
MFC		
MEAN	48.1	61.8
S.D.	18.3	17.1
N	20	20
FFC		
MEAN	41.4	47.9
S.D.	21.1	28.0
N	20	20
FFCS		
MEAN	2.4	4.5
S.D.	3.1	3.5
N	20	20

CL M = NUMBER OF MATURE CORPORA LUTEA
 CL O = NUMBER OF DEGENERATE CORPORA LUTEA
 NO FC = NUMBER OF OOCYTES WITH NO FOLLICULAR CELLS ATTACHED TO THE SURFACE
 MFC = NUMBER OF OOCYTES WITH MULTIPLE LAYERS OF FOLLICULAR CELLS ATTACHED TO THE SURFACE
 FFC = NUMBER OF OOCYTES SURROUNDED BY A FLUID-FILLED CAVITY
 FFCS = NUMBER OF OOCYTES WITH FOLLICULAR FLUID AND A WELL-FORMED CUMULUS STALK

