UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

008446

JUL 10 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: 3-(trimethoxysilyl)propyl dimethyl octadecyl ammonium chloride; 1. Range-Finding Developmental Toxicity Study in Rats, and 2. Developmental Toxicity Study in Rats.

Tox.Chem No.: 892B
MRID No.: 414380-02 and 03
HED Project No.: 0-1070
Submission No.: 262711

To: Jim Wilson/John Lee PM Team# 31
Antimicrobial Branch
Registration Division, (7505RD)

From: John C. Redden, Toxicologist 7/3/91
Section 3
Toxicology Branch 1
Health Effects Division (H7509C)

Thru: Henry Spencer, Ph.D. 7/3/91
Acting, Section Head Section 3
Toxicology Branch 1
Health Effects Division (H7509C) KB 7/3/91

ACTION:

The registrant has submitted for review of two 3-(trimethoxysilyl)propyl dimethyl octadecyl ammonium chloride studies; 1. Range-Finding Developmental Toxicity Study in Rats, and 2. Developmental Toxicity Study in Rats.

CONCLUSIONS:

In the Range-Finding Developmental Toxicity Study in Rats no maternal or developmental toxicity was reported. Early resorptions were consistent with historical control data supplied with the study. Abnormal findings were one dam with material around the nose and six animals with hair loss (1 in low dose, 2 in mid dose, and 3 in high dose). The hair loss is not significant, and there was no effect on body weights. The study classified as Core supplementary since a range finding study is not adequate for the

assessment of developmental toxicity (83-3).

In the Developmental Toxicity Study in Rats a slight increase in liver weights at the 1000 mg/kg/day dose level of the dams is not considered treatment toxicity. The maternal toxicity NOEL = 1000 mg/kg/day, HDT. Developmental NOEL ≥ 1000 mg/kg/day. However, a developmental LEL could not be established for fetal effects by the chemicals. The study's classification is core supplementary as the compound purity is not available. This study is upgradeable. Further testing above 1000 mg/kg/day is not considered appropriate for hazard identification in this chemical.

Reviewed by: John C. Redden 7/2/91
Section III, Tox. Branch I
Secondary reviewer: Hank Spencer 7/2/91
Section III, Tox. Branch

008446

DATA EVALUATION RECORD

GUIDELINES § 83-3

STUDY TYPE: Range-Finding Developmental Toxicity Study in rats.

MRID NUMBER: 414380-02.

TEST MATERIAL: 3-(trimethoxysilyl)propyl dimethyl octadecyl ammonium chloride.

SYNONYM: Dow Corning 5700 Hydrolysate.

SPONSOR: Dow Corning Corporation.

TESTING FACILITY: International Research and Development Corporation, Mattawan, Mi 49071.

TITLE OF REPORT: Range-Finding Developmental Toxicity Study in rats.

AUTHOR: York, R G.

REPORT ISSUED: March 5, 1990.

CONCLUSIONS:

Dow Corning 5700 Hydrolysate was administered by gavage as a single daily dose on days 6 through 15 of gestation. The volume each animal received was equivalent to 10 ml/kg. Dosage levels were 100, 300 and 1000 mg/kg/day. The control group received an equivalent dose of corn oil (vehicle). All animals were female. All animals were sacrificed on day 20 of gestation, and uterine examinations were performed. No maternal or developmental toxicity was reported. Early resorptions were consistent with historical control data supplied with the study. Abnormal findings were one dam with material around the nose and six animals with hair loss (1 in low dose, 2 in mid dose, and 3 in high dose). The hair loss is not significant, and there was no effect on body weights. A maximum tolerated dose was not reached.

CORE CLASSIFICATION: Core supplementary since a range finding study is not adequate for the assessment of developmental toxicity (83-3).

A. MATERIALS:

1. Test Compound: 3-(trimethoxysilyl)propyl dimethyl octadecyl ammonium chloride (Dow Corning 5700 Hydrolysate); description: white powder; lot# Bn029263; purity: not stated.

2. Test Animals: Species: rat; strain: Sprague-Dawley COBS CD; age: 84 day virgin female at initiation; weight 282 to 289 grams at initiation of dosing; source: Charles River Laboratories, Inc., Portage, Mi.

B. STUDY DESIGN:

1. Animal Assignment: Animals were acclimated to laboratory conditions for 10 days, their health and behavior were observed, and animals considered suitable were mated with stock male rats (same source but no age given). One female and one male rat were mated. After a copulatory plug was found this day was designated day 0, and the female was returned to an individual cage, assigned an animal number and identified by ear tag. Mated females were assigned consecutively in a block design to one control and three dose groups each consisting of five animals. Groups were gavaged with 0, 100, 300 and 1000 mg/kg/day. Female rats were individually caged and housed in an environmentally controlled room with a mean temperature ± standard deviation of 72 ± 0.5 F° and mean humidity ± standard deviation of 53 ± 4.2 %.

2. Preparation of Dosing Solutions: One shipment of DC 5700 Hydrolysate was obtained from the sponsor. It is not indicated if the compound was analyzed by the testing laboratory. The compound for each group was weighted and suspended with corn oil (the vehicle) using a tissue homogenizer. The suspension was transferred to a graduated cylinder and additional material was added to yield the target concentration. The cylinder was shaken by hand and the contents transferred to a capped container. The compound was prepared daily for the dosing levels. The compound was administered by intragastric intubation. The control group received the vehicle only.

3. Food and water consumption: Animals received Purina Certified Rodent Chow # 5002 and water ad libitum.

4. Statistics: Mean body weight gains and uterine parameters were compared to mean values for the control group.

5. Quality Assurance: A quality assurance statement was signed and date December 14, 1989.

C. METHODS AND RESULTS:

1. Observations: Females were observed twice daily for mortality and overt changes in appearance and behavior. The presence and duration of clinical signs of toxicity were recorded once daily on days 6 to 20 of gestation.

   Results: Table 1 summarizes data on survival, appearance and behavior. Survival was 100 % for control and dosed animals. Clinical signs for treated animals were hair loss and material around the nose. The clinical signs are not significant. There were no treatment related findings at the necropsy examination.

2. Body Weights: Maternal body weights were recorded on gestation days 0, 6, 9, 12, 16 and 20.

   Results: Mean body weights are summarized in Table 2. No compound- or dose-related effects on mean body weights was observed.

3. Uterine Examinations: On gestation day 20, the females were sacrificed by carbon dioxide inhalation. The uterus was excised and gravid uterine weight recorded. Location of viable and nonviable fetuses, early and late resorptions, and the total number of implantations were recorded. Thoracic and abdominal cavities and organs of the dams were examined for grossly evident morphological changes. Uteri from nongravid females were opened and placed in 10 % ammonium sulfide solution for detection of implantation sites.

   Results: Table 3 summarizes mean maternal observations at uterine examination. No developmental toxicity was evident at any dosage level.

D. STUDY AUTHOR'S CONCLUSIONS:

No evidence of maternal or developmental toxicity was observed at any level. Hair loss was observed in several animals, and material around the nose of one dam was seen. There were no abnormal necropsy findings. Group mean body weight and uterine parameters were comparable with control group mean values. On the basis of this study dosage levels of 100, 300, and 1000 mg/kg/day were selected for a developmental toxicity study.

E. REVIEWER'S DISCUSSION AND INTERPRETATION OF RESULTS:

The discussion and interpretation of results can be found in the body of the review, and are summarized as:

1. The purity of the compound is required.
2. Only a minimum number of animals were tested per group.
3. Hair loss was noted in a dose related fashion but was not considered to be significant.

7

Table 1: Summary of Antemortem and Necropsy Observations

	0 mg/kg/day		100 mg/kg/day		300 mg/kg/day		1000 mg/kg/day	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Number of Animals	5	-	5	-	5	-	5	-
Antemortem Observations.								
No visibleabnormalities[a]:	5	(100)	4	(80)	3	(60)	2	(40)
Material around Nose:							1	(20)
Hair loss:			1	(20)	2	(40)	3	(60)
Necropsy Observations.								
No gross lesions:	5	(100)	5	(100)	5	(100)	5	(100)

[a] Includes animals with no visible abnormalities throughout observation period

No.- Number

- Not applicable
Note: This table was extracted from the Final Report.

Table 2: Summary of group Mean Maternal Body Weights and Body Weight Changes

Day of Gestation	Group Mean Maternal Body Weights (grams) 0 mg/kg/day Mean	100 mg/kg/day Mean	300 mg/kg/day Mean	1000 mg/kg/day Mean
0	285	282	286	289
6	325	324	325	340
9	330	326	335	348
12	350	346	349	370
16	385	388	385	403
20	451	461	446	462
20[a]	369	365	362	380
Days of Gestation	Group Mean Maternal Body Weight Changes (grams)[b]			
0 - 6	40	42	40	52
6 - 9	5	2	10	8
9 - 12	20	20	15	22
12 - 16	36	43	35	33
16 - 20	66	72	61	59
6 - 16	61*	65*	60	63
0 - 20	167	179	160	174
0 - 20[a]	84	83	77	92

[a] Dam body weight minus the uterus and its contents

[b] Values represent the mean of the individual changes in maternal body weight for these intervals

* Each of these values (calculated by the reviewer) is one more than found in the Final Report (not significant).

Note: This table was extracted from the Final Report.

Table 3: Summary of Group Mean Maternal Observations at Uterine Examination

	0 mg/kg/day	100 mg/kg/day	300 mg/kg/day	1000 mg/kg/day
Animals examined	5	5	5	5
Nongravid:	1	0	1	0
Gravid:	4	5	4	5
Dams with resorptions only:	0	0	0	0
Dams with viable fetuses:	4	5	4	5
viable fetuses/dam	15.0	17.0	15.3	14.6
Postimplantation loss/dam:	1.0	0.8	0.8	1.4
Total implantation /dam:	16.0	17.8	16.0	16.0
Corpora lutea/dam	17.5	20.0	17.3	18.0
Group mean Preimplantation loss(%)[a]:	8.6	11.0	7.2	11.1
Group mean Postimplantation loss (%)[b]:	6.3	4.5	4.7	8.8
Group mean uterine weights (grams):	83	95	84	82

[a] $\frac{\text{Total No. Corpora lutea - Total No. Implantations}}{\text{Total No. Corpora lutea}}$

[b] $\frac{\text{Total No. Implantations - Total no. Viable Fetuses}}{\text{Total No. Implantations}}$

Note: This table was extracted from the Final Report.

01

Fox Chem No. 12b

Study/Lab/Study #/Date	Material	EPA MRID Accession No.	Results	TOX Category	CORE Grade
83-3 Range-finding developmental Toxicity study Species: rat IRDC 416-067; 3/5/1990	3-(trimethoxysilyl) propyl dimethyl octadecyl ammonium chloride No purity	414380-02	Levels tested 0, 100, 300 and 1000 mg/kg/day. No maternal or developmental toxicity at these levels. maximum tolerated dose was not reached purity not available. The study is not upgradeable	N/A.	Supplementary

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Reviewed by: John C. Redden, Toxicologist 7/2/91
Section III, Tox. Branch I
Secondary reviewer: Henry Spencer, Toxicologist 7/2/91
Section III, Tox. Branch

DATA EVALUATION RECORD

GUIDELINES § 83-3, 83-4

STUDY TYPE: Developmental Toxicity Study in rats.

MRID NUMBER: 414380-03.

TEST MATERIAL: 3-(trimethoxysilyl)propyl dimethyl octadecyl ammonium chloride.

SYNONYM: Dow Corning 5700 Hydrolysate.

STUDY NUMBER: 416-068

SPONSOR: Dow Corning Corporation.

TESTING FACILITY: International Research and Development Corporation, Mattawan, Mi 49071.

TITLE OF REPORT: Developmental Toxicity Study in rats.

AUTHOR: York, R G.

REPORT ISSUED: February 28, 1990.

CONCLUSIONS:

Dow Corning 5700 Hydrolysate was administered by gavage to pregnant Sprague Dawley rats as a single daily dose on days 6 through 15 of gestation. The volume each animal received was equivalent to 10 ml/kg. Dosage levels were 100, 300 and 1000 mg/kg/day. The control group received an equivalent dose of corn oil (vehicle). There were 25 animals per dose level. Dosage levels were established by a range finding study. All animals were sacrificed on day 20 of gestation, and cesarean section were performed on all the females followed by teratological examination of the fetuses. An increase in liver weights at the 1000 mg/kg/day dose level of the dams is considered to be treatment related. Body weight patterns and food consumption were not indicative of maternal toxicity. The fetal male to female ratio at the 1000 mg/kg/day dose level was significantly different from the control group, but was not considered to be biologically significant. The no-observable effect level (NOEL) for DC 5700 Hydrolysate when administered to gravid Charles River rats is considered to be 300 mg/kg/day for maternal and ≥ 1000 mg/kg/day for developmental toxicity. Lowest effect level (LEL) for 5700 Hydrolysate when administered to gravid Charles River rats for maternal toxicity is 1000 mg/kg/day. Neither the technical form nor the dosage form was tested for purity or stability in dosage form. The study fulfills the requirement for registration under 83-3A, when the purity of the test material is submitted.

CORE CLASSIFICATION:

The study is classified as supplementary, because the purity is not available. The study is upgradeable. NOEL for DC 5700 Hydrolysate maternally is 1000 mg/kg/day. The LEL for maternal toxicity can not be established for the study, and the NOEL developmentally is ≥ 1000 mg/kg/day. However, the dose of 1000 mg/kg is considered adequate for the evaluation of developmental toxicity hazard for this chemical and a repeat study is not required.

A. MATERIALS:

1. Test Compound: 3-(trimethoxysilyl)propyl dimethyl octadecyl ammonium chloride (Dow Corning 5700 Hydrolysate); description: white powder; lot# Bn029263; purity: not stated.

2. Test Animals: Species: rat; strain: Sprague-Dawley COBS CD; age: 84 day virgin female at initiation; weight 282 to 289 grams at initiation of dosing; source: Charles River Laboratories, Inc., Portage, Mi.

B. STUDY DESIGN:

1. Animal Assignment: Animals were acclimated to laboratory conditions for 12 days, their health and behavior were observed, and animals considered suitable were mated with stock male rats (same source but no age given). After a copulatory plug was found this day was designated day 0, and the female was returned to an individual cage, assigned an animal number and identified by ear tag. Mating began June 14, 1989. The last uterine examination was performed July 8, 1989. Mated females were assigned consecutively in a block design to one control and three dose groups consisting of 25 rats. Groups were dosed at 0, 100, 300 and 1000 mg/kg/day. Female rats were individually caged and housed in an environmentally controlled room with a mean temperature ± standard deviation of 67 ± 1.3 F° and mean humidity ± standard deviation of 63 ± 4.6 %.

2. Preparation of Dosing Solutions: One shipment of DC 5700 Hydrolysate was obtained from the sponsor. It is not indicated if the compound was analyzed by the testing laboratory. The compound for each group was weighed and suspended with corn oil (the vehicle) using a tissue homogenizer. The suspension was transferred to a graduated cylinder and additional material was added to yield the target concentration. The cylinder was shaken by hand and the contents transferred to a capped container. The compound was prepared daily for the dosing levels. The compound was administered by intragastric intubation. The control group received the vehicle only on a comparable basis.

3. Food and water consumption: Animals received Purina Certified Rodent Chow # 5002 and water ad libitum.

4. Statistics: The values of the treated groups were examined statistically with the control group the levels of significance at $p < 0.05$ and $p < 0.01$. Male to female

fetal sex ratios and proportions of litters with malformations and developmental variations were compared using the Chi-Square test with Yates' correction for 2 x 2 contingency tables and/or Fisher's exact probability test to determine the significance of the differences. Resorbed and dead fetuses, and postimplantation losses were compared by the Mann-Whitney U-test. Mean maternal body weights and liver weights, maternal food consumption, numbers of corpus lutea, total implantations, live fetuses, gravid uterine weight and mean fetal body weights were compared by analysis of variance, Bartlett's test for homogencity of variance and the appropriate t-test for equal and unequal variances using Dunnett's multiple comparison tables to determine the significance of differences.

5. Quality Assurance: A quality assurance statement was signed and date December 14, 1989.

C. METHODS AND RESULTS:

1. Observations: Females were observed twice daily for mortality and overt changes in appearance and behavior. The presence and duration of clinical signs of toxicity were recorded once daily on days 6 to 20 of gestation.

Results: Table 1 summarizes data on survival, appearance and behavior. Survival was 100 % for control and dose animals. Clinical signs for treated animals included a slight but significant ($p<0.05$) increase in liver weight compared to body weight for the 1000 mg/kg/day and was considered treatment related. All remaining clinical signs occurred in low incidence and were not considered to be the result of the test article.

2. Body Weights: Maternal body weights were recorded on gestation days 0, 6, 9, 12, 16 and 20.

Results: Mean body weights are summarized in Table 2. No compound or dose-related effects on mean body weights were observed.

3. Food Consumption: Individual food consumption was recorded on gestation days 6, 9, 16 and 20.

Results: Tables 2 and 3 summarize food consumption results. 100 mg/kg/day (g/animal/day) compared to the control group demonstrates a significant ($p<0.05$) decrease in consumption (gestation day 6-9).300 mg/kg/day (g/animal/day) compared to the control group demostrates a significant ($p<0.05$) increase in consumption (gestation day 9-12). 1000 mg/kg/day (g/kg/day) there was significantly ($p<0.05$) increased consumption for the overall treatment

and gestation period. Since similar increase for g/kg/day were not observed for the other groups this finding was considered to be inconsequential.

4. Cesarean Section Observation: On gestation day 20, the females were sacrificed by carbon dioxide inhalation. The uterus was excised and gravid uterine weight recorded. Location of viable and nonviable fetuses, early and late resorptions, and the total number of implantations were recorded. Thoracic and abdominal cavities and organs of the dams were examined for grossly evident morphological changes. Uteri from nongravid females were opened and placed in 10 % ammonium sulfide solution for detection of implantation sites. Maternal liver weights and postmortem body weights were recorded. Tissues were preserved in 10 % neutral buffered formalin if deemed necessary by the gross findings for possible histopathological examination and were subsequently discarded.

Results: Table 5 shows that liver weight increased at the 1000 mg/kg/day dose level was considered a result of treatment. The ratio of male and female offspring at the 1000 mg/kg/day dose level was significantly ($p<0.05$) different from the control group (Table 6). This was the only significant difference among cesarean section values of the treated groups and was not considered treatment related.

5. Fetal Morphological Observations: Individual fetuses were weighed, sexed, tagged and examined for external malformations and developmental variations. About one-half of the fetuses were placed in Bouin's solution for soft tissue examination using the Wilson razor blade technique. Crown rump length was measured after the fetuses had been placed in the fixative. They should have been measured before going into the fixative. The Study Director's opinion was that this deviation did not affect the results. The remaining fetuses were fixed in alcohol macerated in potassium hydroxide, stained with Alizarin Red S, cleared with glycerin (Dawson) for skeletal examination. Gross, visceral and skeletal alterations were classified as malformations or developmental variations.

Results: Table 7 summarizes the incidence of fetal malformation. None of the morphological effects for any of the treated groups are considered test article related by this reviewer. Table 8 summarizes the incidence of fetal developmental variations. The variety of developmental variations observed among the treated animals are not

considered to be treatment related. Since historical control data submitted with the study indicate that incidences of omphaloceles, microphthalmia do not exceed those of the laboratory historical data.

D. STUDY AUTHOR'S CONCLUSIONS:

Clinical signs in the dose groups were considered insignificant. The liver weight increase at 1000 mg/kg/day was considered treatment related. Body weight patterns of the dose groups were comparable with the control group. Food consumption was erratic among the groups but was not considered to be the result of treatment. At the 1000 mg/kg/day dose the ratio of male and female offspring was significantly different from the control group. This was the only difference and the author concluded it was not biologically significant. The no observable effect level of DC 5700 Hydrolysate was concluded to be 300 mg/kg/day for maternal and 1000 mg/kg/day for developmental toxicity when administered to gravid Charles Rivers COBS rats.

E. REVIEWER'S DISCUSSION AND INTERPRETATION OF RESULTS:

The discussion and interpretation of results can be found in the body of the review. The study is core supplementary as the compound's purity is not available. The study is upgradeable. A NOEL for maternal toxicity equals 1000 mg/kg/day (HDT), and an LEL can not be established at 1000 mg/kg/day (HDT) based on the slight increase in maternal liver weights. A developmental NOEL $\geq$ 1000 mg/kg/day (HDT) for this study in which an LEL could not be established for fetal effects by the chemical.

Table 1: Summary of Individual Maternal Antemortem and Necropsy Observations During Gestation

Females

	0 mg/kg/day		100 mg/kg/day		300 mg/kg/day		1000 mg/kg/day	
	No.	%	No.	%	No.	%	No.	%
Antemortem Observations								
No. of animals observed	25	-	25	-	25	-	25	-
No visable abnormalities	10	40	13	52	15	60	16	64
Labored breathing:							1	4
Material aroun eye/nose:	1	4	2	8	2	8	2	8
Anogenital staining	8	32	7	28	6	24	5	20
Body surface stained:							1	4
Scabbed area:	1	4						
Hair loss:	8	4	5	20	4	16	4	16
Necropsy Observations								
No of animals observed	25	-	24[b]	-	25	-	25	-
No gross lesions:	25	100	23	96	24	96	25	100
Lymph nodes-enlarged:			1	4				
Spleen-cysts:					1	4		
Kidney-hydronephrosis:			2	8				

No. = Number
- = Not applicable
b = One animal inadvertently not observed at necropsy.
Note: Table extracted from the Final Report.

Table 2: Females: Summary of Body Weight Values - Gestation

Parameters	DAY OF Study	0 mg/kg/day Mean	S.D.	N	100 mg/kg/day Mean	S.D.	N	300 mg/kg/day Mean	S.D.	N	1000 mg/kg/day Mean	S.D.	N
Body Weight grams	0	247	11.2	18	245	10.8	18	246	11.8	20	242	13.4	21
	6	273	11.9	18	270	11.1	18	273	12.9	20	271	14.4	21
	9	276	13.7	18	273	16.9	18	279	12.6	20	277	15.7	21
	12	292	15.5	18	292	15.0	18	294	13.3	20	292	16.9	21
	16	319	16.0	18	317	14.3	18	317	13.5	20	314	20.0	21
	20	378	24.5	18	378	25.8	18	378	19.3	20	374	28.0	21
Adjusted	20	308	18.7	18	307	17.3	18	308	14.6	20	308	18.8	21
Body Weight Change grams	0-6	26	7.0	18	25	6.6	18	27	7.3	20	29	8.1	21
	6-9	3	7.6	18	3	7.9	18	7	7.2	20	6	8.2	21
	9-12	16	10.4	18	19	6.4	18	15	4.1	20	15	9.2	21
	12-16	27	7.4	18	26	12.2	18	22	7.6	20	22	10.6	21
	6-16	46	11.6	18	47	9.8	18	44	10.5	20	43	12.9	21
	16-20	59	11.0	18	61	16.6	18	62	12.8	20	60	14.6	21
	0-20	131	19.1	18	133	24.8	18	132	18.6	20	132	25.3	21
Adjusted	0-20	61	13.4	18	62	14.4	18	62	12.8	20	66	12.5	21

S.D. = Standard Deviation
N = Number of Animals
Adjusted = Dam body weight minus the uterus and its contents.
Note1: Nongravid females not included in this table.
Note2: Table extracted from the Final Report.

Table 3: Females: Summary of Food Consumption Values - Gestation

Parameters	DAY OF STUDY	0 mg/kg/day Mean	S.D.	N	100 mg/kg/day Mean	S.D.	N	300 mg/kg/day Mean	S.D.	N	1000 mg/kg/day Mean	S.D.	N
Food Consumption g/animal/day	0-6	21.5	2.10	17	21.5	2.23	18	22.3	2.20	20	22.0	4.14	21
	6-9	17.8	3.77	18	15.2[1]	3.11	17	17.9	3.27	20	19.9	8.27	21
	9-12	17.9	2.17	17	17.9	1.74	18	19.9[1]	2.85	20	21.2	8.20	20
	12-16	19.8	2.06	18	21.1	5.45	18	20.4	2.67	20	20.2	3.70	21
	6-16	18.7	1.77	18	18.4	2.89	18	19.5	1.72	20	20.6	4.67	21
	16-20	27.3	2.47	18	27.4	3.12	18	26.2	5.98	20	28.0	2.39	21

1 = Significantly different from the control group ($p<0.05$).
S.D. = Standard Deviation
N = Number of animals

Table 4: Females: Summary of Food Consumption Values - Gestation

Parameters	DAY OF STUDY	0 mg/kg/day Mean	S.D.	N	100 mg/kd/day Mean	S.D.	N	300 mg/kg/day Mean	S.D.	N	1000 mg/kg/day Mean	S.D.	N
Food Consumption g/kg/day	0-6	78.6	5.85	17	79.6	6.28	18	81.7	6.35	20	81.3	15.0	21
	6-9	64.4	12.55	18	55.4	9.22	17	63.9	11.07	20	71.5	28.83	21
	9-12	61.2	5.81	17	61.3	4.61	18	67.4[1]	8.51	20	72.7	27.95	20
	12-16	61.9	5.17	18	66.5	18.32	18	64.2	7.07	20	64.3	10.65	21
	6-16	58.6	5.30	18	58.1	9.34	18	61.4	3.99	20	65.5[1]	13.45	21
	16-20	72.2	5.04	18	72.4	4.94	18	69.3	15.51	20	74.9	4.67	21
	0-20	56.3	3.26	18	56.3	6.36	18	57.3	4.79	20	60.1[1]	6.98	21

1 = Significantly different from the control group ($p<0.05$).
S.D. = Standard Deviation
N = Number of animals
Note: Table extracted from the Final Report.

Table 5: Females: Summary of Organ Weight Values - Terminal Sacrifice

Parameters	0 mg/kg/day Mean	S.D.	N	100 mg/kd/day Mean	S.D.	N	300 mg/kg/day Mean	S.D.	N	1000 mg/kg/day Mean	S.D.	N
Body Weight g	349	52.8	25	343	61.1	25	358	44.2	25	357	48.8	25
Liver g	15.44	2.927	25	15.29	2.913	24	16.10	2.612	25	16.47	2.471	25
Liver/Body Weight %	4.41	0.397	25	4.38	0.302	24	4.48	0.344	25	4.62[1]	0.221	25

1 = Significantly different from the control group; $p<0.05$.
S.D. = Standard Deviation
N = Number of animals
Note: Table extracted from the Final Report.

12

Table 6: Summary of Group Mean Maternal and fetal Observations at Cesarean Section

	0 mg/kg/day			100 mg/kg/day			300 mg/kg/day			1000 mg/kg/day		
	No.	%	S.D.	No.	%	S.D.	No.	%	S.D.	No.	%	S.D.
Animals examined:	25	-	-	25	-	-	25	-	-	25	-	-
Nongravid:	7	-	-	7	-	-	5	-	-	4	-	-
Gravid:	18	-	-	18	-	-	20	-	-	21	-	-
Dams with resorptions only:	0	-	-	0	-	-	0	-	-	0	-	-
Dams with viable fetuses:	18	-	-	18	-	-	20	-	-	21	-	-
Viable fetuses/dam:	13.3	-	2.74	13.3	-	3.32	13.2	-	4.24	12.4	-	4.04
Postimplantation loss/dam:	1.1	-	0.83	0.6	-	0.61	1.5	-	2.31	0.8	-	0.81
Total implantations/dam:	14.4	-	2.53	13.9	-	3.46	14.7	-	3.36	13.2	-	4.36
Corpora lutea/dam:	17.8	-	3.30	15.8	-	2.58	17.7	-	2.90	16.2	-	3.17
Mean Crown rump length cm:	3.5	-	0.12	3.5	-	0.16	3.5	-	0.14	3.5	-	0.11
Group mean uterine weights g:	70.1	-	14.12	71.3	-	17.69	70.3	-	21.24	66.5	-	21.06
Group mean preimplantation loss %[a]:	-	18.8	-	-	12.0	-	-	17.2	-	-	18.2	-
Group mean postimplantation loss %[b]:	-	7.7	-	-	4.4	-	-	9.9	-	-	6.1	-
Mean fetal body weight grams:	3.4	-	0.20	3.5	-	0.45	3.4	-	0.22	3.4	-	0.27
Fetal sex distribution:male	105	43.8	-	117	49.0	-	132	50.0	-	144[c]	55.2	-
female	135	56.3	-	122	51.0	-	132	50.0	-	117[c]	44.8	-

[a]Total No. Corpora Lutea - Total No. Implantations / Total No. Corpora Lutea X 100

[b]Total No. Implantations - Total No. Viable Fetuses / Total No. Implantations X 100

[c] Significantly different from the control group; $p<0.05$
- = Not applicable
No. = Number
S.D. = Standard Deviation
Note: Table extracted from the Final Report.

Table 7: Summary of the Incidence of Fetal Malformations

	0 mg/kg/day	100 mg/kg/day	300 mg/kg/day	1000 mg/kg/day
Number of litters examined:	18	18	20	21
Number of fetuses examined externally:	240	238[a]	263[a]	260[a]
Number of fetuses examined viscerally:	119	118	132	129
Number of fetuses examined skeletally:	121	121	132	132
Malformations Observed:	No. of fetuses (No. of litters)			
Anophthalmia:	1 (1)			
Microphthalmia:				2 (2)
Gastroschisis:			1 (1)	
Omphalocele:				2 (2)
Tail agenesis:			1 (1)	
Tarsal flexure:			1 (1)	
Edema:			1 (1)	
Malformed skull bones:			1 (1)	
Bent clavicle:			1 (1)	
Bent scapula:			1 (1)	
Amella:			1 (1)	
Bent limb bones:	1 (1)			1 (1)
Vetrebral agenesis:			1 (1)	
Pelvic malformations:			1 (1)	
Total fetuses(litters)with malformations:	2 (2)	0 (0)	1 (1)	5 (4)

[a]External observations were not recorded for one fetus
Note: Table extracted from the Final Report.

23

Table 8: Summary of the Incidence of Fetal Developmental Variations

	0 mg/kg/day	100 mg/kg/day	300 mg/kg/day	1000 mg/kg/day
Number of litters examined:	18	18	20	21
Number of fetuses examined externally:	240	238[a]	263[a]	260[a]
Number of fetuses examined viscerally:	119	118	132	129
Number of fetuses examined skeletally:	121	121	132	132
Developmental Variations Observed:		**No. of fetuses (No. of litters)**		
Renal papillae not developed:		1 (1)	1 (1)	
Distended ureter:		1 (1)	1 (1)	
Skull reduced in ossification:	2 (1)	3 (2)	2 (2)	
Hyoid unossified:	1 (1)		1 (1)	1 (1)
25 presacral vertebrae:			1 (1)	2 (2)
Greater than 13 pairs of full ribs:			2 (2)	
14th rudimentary rib(s):	6 (3)	7 (4)	12 (5)	6 (5)
Bent ribs:		1 (1)		2 (1)
7th cervical rib:	3 (3)		2 (2)	
Vertebrae reduced in ossification:	1 (1)		1 (1)	
Misaligned sternebra (e):	8 (6)	6 (5)	8 (6)	4 (3)
Sternebra #5 and/or #6 unossified:	3 (3)	7 (6)	4 (4)	8 (6)
Other sternebra (e) unossified:	1 (1)		1 (1)	1 (1)
Ischia reduced in ossification:	1 (1)			2 (1)
Total fetuses (litters) with developmental variations:	22 (12)	24 (11)	30 (14)	22 (12)

[a]External observations were not recorded for one fetus
Note: Table extracted from the Final Report.

Tox Chem No. 8926 | File Last Updated _____ | Current Date 11/6/29

Study/Lab/Study #/Date	Material	EPA Accession No.	Results	TOX Category	CORE Grade
83-3, 83-4 Developmental Toxicity Study ~~Range finding~~ IRDC 416-068; 2/28/1990	3-(trimethoxysilyl) propyl dimethyl octadecyl ammonium chloride	41438-03	Purity not available; Maternal NOEL = 1000 mg/kg/day; developmental NOEL ≥ 1000 mg/kg/day; study is upgradeable. 25/females/dose. Doses used 0, 100, 300, 1000 mg/kg. Notoxicity at 1000 mg/kg (HDT)	NA	Supplemental