

Study Title

Repeated Dose Oral Toxicity: 14-Day Feeding Study
with H-19683 and H-19704 in Male Rats

Author

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Study Completed On

May 15, 1995

Performing Laboratory

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine
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Laboratory Project ID

Haskell Laboratory Report No. 326-95

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GENERAL INFORMATION FOR H-19683

Substance Tested:

[REDACTED]

Synonyms/Codes:

• H-19683
[REDACTED]

Physical Form:

Pinkish vaseline-like solid

Contaminants:

[REDACTED]

Purity:

[REDACTED]

CAS Registry No.:

[REDACTED]

Substance Tested:

Octanoic acid, pentadecafluoro-. ammonium salt

Synonyms/Codes:

• H-19704
• C-8
• Ammonium perfluorooctanoate
[REDACTED]

Physical Form:

White solid

Purity:

[REDACTED]

CAS Registry No.:

[REDACTED]

Sponsor:

DuPont Fibers and
DuPont Speciality Chemicals
E. I. du Pont de Nemours and Company
Wilmington, Delaware

Study Initiated - Completed:

8/28/92 - 5/15/95

In Life Phase

Initiated - Completed:

9/16/92 - 11/25/92

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REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

SUMMARY

The purpose of this study was to evaluate the repeated oral dose toxicity and bioretentivity of H-19683 and H-19704 when incorporated into nutritionally adequate chow and fed to male rats for 14 consecutive days. Groups of 20 male rats each were fed diets containing either 30 or 300 ppm of H-19683 or 30 or 300 ppm of H-19704. Rats were sacrificed at the end of the 14-day feeding period and on recovery days 7, 28, and 56 and livers removed and weighed. Blood samples were taken for fluoride concentration analysis from rats sacrificed at the end of the feeding period and on recovery day 7.

No mortalities were observed during the study. No clinical signs of toxicity were observed in rats fed H-19683. Clinical signs of toxicity noted in rats from the 30 and 300 ppm dose groups of H-19704 during the feeding period included irregular respiration, rapid breathing, red nasal discharge and hunched posture. Significant decreases in mean body weights were observed in rats from the 300 ppm dose group of H-19704 on days 7 and 14 of the feeding period and on recovery day 7 compared to controls. Mean body weight gains of rats from this same group were significantly depressed during the first week of feeding.

Significant increases in mean relative liver weights were observed in rats from the 30 and 300 ppm dose groups of H-19683 sacrificed at the end of the feeding period. No other liver weight effects were observed in these rats during the study. Significant increases in mean absolute liver weights were observed in rats from the 30 and 300 ppm dose groups of H-19704 sacrificed at the end of the feeding period and on recovery days 7 and 28. Significantly increased mean relative liver weights were observed in rats from the 30 and 300 ppm dose groups of H-19704 sacrificed at the end of the feeding period and on recovery day 7, and in the 300 ppm dose group rats sacrificed on recovery day 28.

Mean blood fluoride concentrations of rats sacrificed on recovery day 0 were 0.30 ppm in control rats, 5.30 ppm in group III rats (30 ppm of H-19683), 8.19 ppm in group V rats (300 ppm of H-19683), 33.23 ppm in group VII rats (30 ppm of H-19704), and 71.52 ppm in group IX rats (300 ppm of H-19704). On recovery day 7, mean blood fluoride concentrations were 0.94 ppm for controls, 0.58 for group III, 0.56 ppm for group V, 19.26 ppm for group VII, and 22.20 ppm for group IX. No other blood was analyzed for fluoride concentration.

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REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

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REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

INTRODUCTION

The purpose of this study was to evaluate the repeated oral dose toxicity and bioretentivity of H-19683 or H-19704 when incorporated into nutritionally adequate chow and fed to male Crl:CD®BR rats for 14 consecutive days. The diet concentrations of H-19683 (30, or 300 ppm) and H-19704 (30, or 300 ppm) were specified by the sponsor. The dietary route of administration was selected because it is a potential route of human exposure.

MATERIALS AND METHODS

A. Test Substance

The test substances were supplied by DuPont Fibers and DuPont Speciality Chemicals, E. I. du Pont de Nemours and Company, Wilmington, Delaware. Available information about the identity, purity, composition, stability, and toxicity of H-19683 and H-19704 was provided by the sponsor.

B. Test Species

On 9/8/92, 109 male Crl:CD®BR rats, approximately 6 weeks old, were received from Charles River Laboratories, Inc., Kingston, New York. At study start, the body weights ranged from 196.0 to 240.1 grams. The Crl:CD®BR rat was selected on the bases of extensive experience with this strain and its suitability with respect to hardiness, longevity, sensitivity, and low incidence of spontaneous diseases.

C. Quarantine

Upon arrival at Haskell Laboratory, all rats were removed from shipping cartons and housed singly in stainless steel, wire-mesh cages suspended above cage Board (DACB) or R-2 Reemay-backed cage boards. The rats were fed Ground Purina® Certified Rodent Chow #5002 and water was available ad libitum. Each rat was assigned a temporary identification number which was recorded on a card affixed to the cage. The animals were weighed 3 times during the quarantine period and were observed daily for any gross signs of disease or injury.

On the basis of body weights and clinical observations, all rats were released from quarantine on 9/16/92 by the laboratory veterinarian.

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D. Assignment to Groups

After release from quarantine, 100 rats selected on the basis of body weight gain and freedom from any clinical signs of disease or injury, were distributed by computerized-stratified randomization into five experimental groups of 20 rats each. No statistically significant differences in group body weight means existed. Rats not assigned to a test group were killed by carbon dioxide asphyxiation and discarded without pathological evaluation.

E. Animal Husbandry

After assignment to treatment groups, each rat was individually identified by a 3-digit identification number marked on the tail with water insoluble ink. Additionally, each rat was assigned a unique 6-digit Haskell animal number. All rats were individually housed in stainless steel, wire-mesh cages suspended above Upjohn DACB cage boards.

<u>GROUP NO.</u>	<u>IDENTIFICATION NUMBER^a</u>	<u>TEST SUBSTANCE (ppm)</u>
I	101 - 120	0 (Control)
III	301 - 320	30 of H-19683
V	501 - 520	300 of H-19683
VII	701 - 720	30 of H-19704
IX	901 - 905	300 of H-19704

^a Each rat was also assigned a unique 6-digit Haskell Number

Animal rooms were maintained on a timer-controlled, 12-hour light/12-hour dark cycle. Environmental conditions of the room were targeted for a temperature of $23^{\circ} \pm 2^{\circ}\text{C}$ and relative humidity of $50\% \pm 10\%$. Excursions outside these ranges were of small magnitude and/or brief duration and did not adversely affect the validity of the study.

F. Diet Preparation and Sampling

During the test period, rats in each group were fed GPCRC (Ground Purina® Certified Rodent Chow® #5002) diet that contained 0, 30, or 300 ppm of F-19683 or 30 or 300 ppm of H-19704 (not adjusted for purity).

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The study design was as follows:

<u>Group Numbers</u>	<u>Dietary Concentrations (ppm)</u>
I	0 (Control)
III	30 ppm of H-19683
V	300 ppm of H-19683
VII	30 ppm of H-19704
IX	300 ppm of H-19704

For both diet concentrations prepared with H-19704, the appropriate amount of H-19704 was added to GPCRC and thoroughly mixed for 3 minutes in a Hobart high speed mixer. For each diet concentration prepared with H-19683, the appropriate amount of H-19683 was first added to a small amount of ground chow and mixed by hand until it appeared homogenous. The hand mixed portion was then added to the remainder of the ground chow weighed out for that diet in a Hobart high speed mixer and was mixed for approximately 3 minutes. After mixing, the diet was visually inspected to ensure it was free of clumps. The control diet was also mixed for the same period of time. Diets were prepared once for the two week feeding period and were stored refrigerated until used. Samples for concentration, homogeneity, and stability were taken for analysis at a later date if deemed necessary by the study director.

G. Body Weights

All rats were weighed and observed for clinical signs of toxicity on test days 0, 7, and 14 of the feeding period. Rats not sacrificed at the end of the feeding period were weighed and observed on recovery days 7, 14, 21, 28, 35, 42, 49, and 56. Cageside examinations to detect moribund or dead rats were conducted twice daily.

H. Food Consumption

Food consumption was not determined during this study.

I. Necropsy

On test day 14 of the feeding period and on recovery day 7, five rats from each group were anesthetized by chloroform anesthesia and blood was collected for fluoride concentration analysis. After blood collection, the rats were euthanatized by chloroform anesthesia and exanguination. The livers were collected and were weighed for liver weight/final body weight ratios. Additionally, 5 rats from each group were sacrificed on recovery days 28 and 56 and the livers were collected and weighed.

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J. Fluoride Concentration Analysis

Blood collected from rats sacrificed at the end of the 14-day feeding period and on day 7 of the recovery period were analyzed for flouried concentration by personnel from Jackson Laboratory, Chambers Works.

STATISTICAL ANALYSES

Body weights, body weight gains, and organ weights were analyzed by a one-way analysis of variance. When the test for differences among test group means (F test) was significant, pairwise comparisons between test and control groups were made with the Dunnett's test. Bartlett's test for homogeneity of variances was performed on the organ weight data. Significance was judged at $\alpha = 0.05$.

RECORDS AND SAMPLE RETENTION

All original records and the final report were retained at Haskell Laboratory or at the Records Management Center, E. I. du Pont de Nemours and Company, Wilmington, Delaware.

RESULTS AND DISCUSSION

A. Diet Sample Analysis

All diets prepared appeared to be thoroughly mixed. No clumps or other signs of non-uniform mixing were observed. Therefore, diet samples taken at the time of diet preparation were discarded without analysis.

B. Body Weights and Body Weight Gains (Tables 1-2; Appendix I)

Statistically significant decreases in mean body weights were observed in rats from the 300 ppm dose group of H-19704 on days 7 and 14 of the feeding period and on recovery day 7. Mean body weight gains of rats from this same group were significantly depressed during the interval 0-7 days on test compared to controls. The mean body weight gain of rats from the H-19683 30 ppm dose group was significantly increased during the interval 14-21 days on test compared to controls.

C. Clinical Observations (Appendix II)

No mortalities were observed during the study. Piloerection and brown nasal discharge were observed in all groups, including controls. These observations are not considered to be compound-related. The reason for the

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presence of the clinical signs is unknown. Clinical signs of toxicity noted in test rats exposed to 30 or 300 ppm H-19704 included irregular respiration, rapid breathing, red nasal discharge, and hunched posture. No clinical signs of toxicity were observed in rats treated with H-19683.

D. Mean Final Body and Organ Weights (Table 3, Appendix III)

Statistically significant increases in mean relative liver weights were observed in rats from the 30 and 300 ppm dose groups of H-19683 sacrificed at the end of the 14-day feeding period. No other liver weight effects were observed in these rats during the study.

Statistically significant increases in mean absolute liver weights were observed in rats from the 30 and 300 ppm dose groups of H-19704 sacrificed at the end of the feeding period and on recovery days 7 and 28. Significantly increased mean relative liver weights were observed in rats from the 30 and 300 ppm dose groups of H-19704 sacrificed at the end of the feeding period and on recovery day 7. Additionally, the 300 ppm dose group rats sacrificed on recovery day 28 had significantly increased mean relative liver weight.

**E. Mean Fluoride Concentrations Found in the Blood of Rats
(Table 4, Appendix IV)**

Mean blood fluoride concentrations observed on recovery day 0 were 0.30 ppm in control rats, 5.30 ppm in Group III rats (30 ppm of H-19683), 8.19 ppm in Group V rats (300 ppm of H-19683), 33.23 ppm in Group VII rats (30 ppm of H-19704), and 71.52 ppm in Group IX rats (300 ppm of H-19704). On recovery day 7, mean blood fluoride concentrations were 0.94 ppm for group I, 0.58 ppm for group III, 0.56 ppm for group V, 19.26 ppm for group VII, and 22.20 ppm for group IX. No other blood was analyzed for fluoride concentration.

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REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

TABLES

GROUP ARE DEFINED AS:

Group I - 0 ppm - Controls
Group II - 30 ppm of H-19683
Group V - 300 ppm of H-19683
Group VII - 30 ppm of H-19704
G IV - 300 ppm of H-19704

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REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
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TABLE 1

MEAN BODY WEIGHTS OF MALE RATS

DAYS ON TEST	GROUP: CONC. (PPM):	MEAN BODY WEIGHTS (g)				
		I 0	III 30	V 300	VII 30	IX 300
0	--	212.3(9.5) ^a	211.1(8.2)	214.2(10.0)	211.9(10.2)	213.3(9.0)
7	--	278.3(13.5)	278.7(14.5)	272.4(15.0)	285.2(14.4)	235.5(19.8)
14	--	329.7(20.7)	324.1(25.1)	320.1(21.5)	341.3(20.2)	287.4(16.5)
21	7	375.5(24.1)	373.8(26.4)	370.1(29.0)	385.0(22.5)	338.9(26.0)
28	14	408.9(30.2)	401.3(35.1)	413.8(32.5)	414.4(27.7)	380.1(28.5)
35	21	448.0(35.9)	432.4(39.5)	447.0(36.1)	455.7(30.2)	411.3(30.6)
42	28	489.6(41.2)	471.1(44.8)	484.7(39.0)	498.4(37.1)	447.7(33.1)
49	35	537.3(37.3)	496.8(43.4)	508.2(44.5)	507.1(40.1)	461.2(42.3)
56	42	562.6(40.7)	517.5(43.6)	528.4(47.1)	523.6(34.4)	481.9(48.4)
63	49	586.4(43.1)	536.0(46.5)	551.6(47.3)	544.7(38.1)	503.6(53.4)
70	56	621.6(42.9)	562.1(51.6)	577.6(44.5)	578.8(39.6)	527.1(54.1)

^a Standard deviation is reported in parentheses

Statistical methods: One-way AOV and Dunnett's tests were performed on weekly interval data. (See Statistical Analyses)

^{*} Statistically significant difference from control at alpha = 0.05.

REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
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TABLE 2

MEAN BODY WEIGHT GAINS OF MALE RATS

		MEAN BODY WEIGHT GAINS (g)				
DAYS ON TEST	GROUP: CONC. (PPM):	I 0	III 30	V 300	VII 30	IX 300
0-7	--	66.0(13.1) ^a	67.7(8.9)	58.3(12.2)	73.3(11.1)	22.1(19.8) ^a
7-14	--	51.4(11.8)	45.4(11.8)	47.6(9.3)	56.1(8.2)	52.0(13.7)
14-21	0-7	44.0(14.1)	54.6(7.7) ^a	51.7(8.9)	44.9(11.6)	52.5(12.7)
21-28	7-14	33.6(9.2)	24.9(7.0)	36.1(9.5)	32.5(9.7)	37.5(14.4)
28-35	14-21	39.1(9.6)	31.1(6.1)	33.2(6.7)	41.3(6.4)	31.2(6.5)
35-42	21-28	41.6(8.0)	38.7(7.4)	37.6(5.0)	42.7(10.3)	36.4(4.4)
42-49	28-35	22.3(1.6)	21.1(1.9)	15.9(7.9)	20.5(6.7)	16.8(6.4)
49-56	35-42	25.3(4.8)	20.7(3.3)	20.2(5.4)	16.5(19.9)	20.6(9.2)
56-63	42-49	23.8(5.4)	18.6(6.9)	23.2(1.3)	21.1(8.5)	21.8(7.1)
63-70	49-56	35.2(9.3)	26.1(6.7)	26.0(8.6)	34.1(5.3)	23.5(12.0)
0-70		406.8(49.7)	351.0(46.2)	363.7(54.0)	363.2(38.8)	313.4(47.6)

^a Standard deviation is reported in parentheses

Statistical methods: One-way ANOV and Dunnett's tests were performed on both weekly and summary interval data. (See Statistical Analyses)

^a Statistically significant difference from control at alpha = 0.05.

**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

TABLE 3

**H-19683 TEST DAY 14 RECOVERY DAY 0
MEAN FINAL BODY AND LIVER WEIGHTS FROM MALE RATS**

MEAN FINAL BODY WEIGHTS (grams)

GROUP	CONCENTRATION (PPM)	FINAL BODY	NUMBER OF ANIMALS
I	0	324.3 (31.0)	5
III	30	339.1 (34.3)	5
V	300	325.0 (23.4)	5

MEAN ABSOLUTE LIVER WEIGHTS (grams)

GROUP	CONCENTRATION (PPM)	LIVER
I	0	12.755 (2.044)
III	30	15.098 (1.768)
V	300	14.057 (1.358)

MEAN RELATIVE LIVER WEIGHTS (% of body weight)

GROUP	CONCENTRATION (PPM)	LIVER
I	0	3.916 (0.295)
III	30	4.448 (0.126)*
V	300	4.325 (0.275)*

STANDARD DEVIATION IN PARENTHESES

+ - SIGNIFICANTLY DIFFERENT ($P < 0.05$) FROM CONTROL GROUP BY LSD
- SIGNIFICANTLY DIFFERENT ($P < 0.05$) FROM CONTROL GROUP BY LSD AND
DUNNETT'S TEST.

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**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

TABLE 3 (CONTINUED)

H-19683 TEST DAY 21 RECOVERY DAY 7

MEAN FINAL BODY AND LIVER WEIGHTS FROM MALE RATS

MEAN FINAL BODY WEIGHTS (grams)

GROUP	CONCENTRATION (PPM)	FINAL BODY	NUMBER OF ANIMALS
I	0	376.0 (18.1)	5
III	30	368.5 (18.8)	5
V	300	355.1 (29.4)	5

MEAN ABSOLUTE LIVER WEIGHTS (grams)

GROUP	CONCENTRATION (PPM)	LIVER
I	0	16.261 (1.771)
III	30	15.212 (1.880)
V	300	15.545 (2.371)

MEAN RELATIVE LIVER WEIGHTS (% of body weight)

GROUP	CONCENTRATION (PPM)	LIVER
I	0	4.317 (0.281)
III	30	4.120 (0.342)
V	300	4.362 (0.316)

STANDARD DEVIATION IN PARENTHESES

- + - SIGNIFICANTLY DIFFERENT ($P < 0.05$) FROM CONTROL GROUP BY LSD
 # - SIGNIFICANTLY DIFFERENT ($P < 0.05$) FROM CONTROL GROUP BY LSD AND
 DUNNETT'S TEST.

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**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

TABLE 3 (CONTINUED)

**H-19683 TEST DAY 42 RECOVERY DAY 28
MEAN FINAL BODY AND LIVER WEIGHTS FROM MALE RATS**

MEAN FINAL BODY WEIGHTS (grams)

GROUP	CONCENTRATION (PPM)	FINAL BODY	NUMBER OF ANIMALS
I	0	464.2 (28.1)	5
III	30	466.5 (50.0)	5
V	300	476.9 (41.7)	5

MEAN ABSOLUTE LIVER WEIGHTS (grams)

GROUP	CONCENTRATION (PPM)	LIVER
I	0	17.737 (0.398)
III	30	18.787 (4.102)
V	300	18.555 (2.743)

MEAN RELATIVE LIVER WEIGHTS (% of body weight)

GROUP	CONCENTRATION (PPM)	LIVER
I	0	3.834 (0.290)
III	30	3.994 (0.457)
V	300	3.881 (0.355)

STANDARD DEVIATION IN PARENTHESES

+ - SIGNIFICANTLY DIFFERENT ($P < 0.05$) FROM CONTROL GROUP BY LSD
 # - SIGNIFICANTLY DIFFERENT ($P < 0.05$) FROM CONTROL GROUP BY LSD AND
 DUNNETT'S TEST.

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**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

TABLE 3 (CONTINUED)

**H-19683 TEST DAY 70 RECOVERY DAY 56
MEAN FINAL BODY AND LIVER WEIGHTS FROM MALE RATS**

MEAN FINAL BODY WEIGHTS (grams)

GROUP	CONCENTRATION (PPM)	FINAL BODY	NUMBER OF ANIMALS
I	0	621.6 (42.9)	5
III	30	562.1 (51.6)	5
V	300	577.6 (44.5)	5

MEAN ABSOLUTE LIVER WEIGHTS (grams)

GROUP	CONCENTRATION (PPM)	LIVER
I	0	22.466 (3.865)
III	30	20.322 (1.607)
V	300	22.858 (3.504)

MEAN RELATIVE LIVER WEIGHTS (% of body weight)

GROUP	CONCENTRATION (PPM)	LIVER
I	0	3.596 (0.405)
III	30	3.628 (0.296)
V	300	3.949 (0.400)

STANDARD DEVIATION IN PARENTHESES

+ - SIGNIFICANTLY DIFFERENT ($P < 0.05$) FROM CONTROL GROUP BY LSD
- SIGNIFICANTLY DIFFERENT ($P < 0.05$) FROM CONTROL GROUP BY LSD AND
DUNNETT'S TEST.

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**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

TABLE 3 (CONTINUED)

H-19704 TEST DAY 14 RECOVERY DAY 0

MEAN FINAL BODY AND LIVER WEIGHTS FROM MALE RATS

MEAN FINAL BODY WEIGHTS (grams)

GROUP	CONCENTRATION (PPM)	FINAL BODY	NUMBER OF ANIMALS
I	0	324.3 (31.0)	5
VII	30	345.0 (15.8)	5
IX	300	290.7 (10.9)†	5

MEAN ABSOLUTE LIVER WEIGHTS (grams)

GROUP	CONCENTRATION (PPM)	LIVER
I	0	12.755 (2.044)
VII	30	20.698 (0.972)†
IX	300	23.674 (1.752)†

MEAN RELATIVE LIVER WEIGHTS (% of body weight)

GROUP	CONCENTRATION (PPM)	LIVER
I	0	3.916 (0.295)
VII	30	6.003 (0.243)†
IX	300	8.139 (0.417)†

STANDARD DEVIATION IN PARENTHESES

- + - SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY LSD
 † - SIGNIFICANTLY DIFFERENT (P<0.05) FROM CONTROL GROUP BY LSD AND
 DUNNETT'S TEST.

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**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

TABLE 3 (CONTINUED)

H-19704 TEST DAY 21 RECOVERY DAY 7
MEAN FINAL BODY AND LIVER WEIGHTS FROM MALE RATS

MEAN FINAL BODY WEIGHTS (grams)

GROUP	CONCENTRATION (PPM)	FINAL BODY	NUMBER OF ANIMALS
I	0	376.0 (18.1)	5
VII	30	391.3 (25.8)	5
IX	300	331.5 (27.3)*	5

MEAN ABSOLUTE LIVER WEIGHTS (grams)

GROUP	CONCENTRATION (PPM)	LIVER
I	0	16.261 (1.771)
VII	30	22.711 (1.998)*
IX	300	22.034 (0.617)*

MEAN RELATIVE LIVER WEIGHTS (% of body weight)

GROUP	CONCENTRATION (PPM)	LIVER
I	0	4.317 (0.281)
VII	30	5.811 (0.490)*
IX	300	6.673 (0.396)*

STANDARD DEVIATION IN PARENTHESES

- + - SIGNIFICANTLY DIFFERENT ($P < 0.05$) FROM CONTROL GROUP BY LSD
* - SIGNIFICANTLY DIFFERENT ($P < 0.05$) FROM CONTROL GROUP BY LSD AND
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**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

TABLE 3 (CONTINUED)

**H-19704 TEST DAY 42 RECOVERY DAY 28
MEAN FINAL BODY AND LIVER WEIGHTS FROM MALE RATS**

MEAN FINAL BODY WEIGHTS (grams)

GROUP	CONCENTRATION (PPM)	FINAL BODY	NUMBER OF ANIMALS
I	0	464.2 (28.1)	5
VII	30	510.1 (40.4)	5
IX	300	450.9 (32.4)	5

MEAN ABSOLUTE LIVER WEIGHTS (grams)

GROUP	CONCENTRATION (PPM)	LIVER
I	0	17.737 (0.398)
VII	30	21.111 (1.844)*
IX	300	21.234 (1.852)*

MEAN RELATIVE LIVER WEIGHTS (% of body weight)

GROUP	CONCENTRATION (PPM)	LIVER
I	0	3.834 (0.290)
VII	30	4.148 (0.353)
IX	300	4.714 (0.310)*

STANDARD DEVIATION IN PARENTHESES

+ - SIGNIFICANTLY DIFFERENT ($P < 0.05$) FROM CONTROL GROUP BY LSD
* - SIGNIFICANTLY DIFFERENT ($P < 0.05$) FROM CONTROL GROUP BY LSD AND
DUNNETT'S TEST.

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**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

TABLE 3 (CONTINUED)

H-19704 TEST DAY 70 RECOVERY DAY 56

MEAN FINAL BODY AND LIVER WEIGHTS FROM MALE RATS

MEAN FINAL BODY WEIGHTS (grams)

GROUP	CONCENTRATION (PPM)	FINAL BODY	NUMBER OF ANIMALS
I	0	621.6 (42.9)	5
VII	30	578.8 (39.6)	5
IX	300	527.1 (54.1)#	5

MEAN ABSOLUTE LIVER WEIGHTS (grams)

GROUP	CONCENTRATION (PPM)	LIVER
I	0	22.466 (3.865)
VII	30	21.402 (2.558)
IX	300	19.835 (3.326)

MEAN RELATIVE LIVER WEIGHTS (% of body weight)

GROUP	CONCENTRATION (PPM)	LIVER
I	0	3.596 (0.405)
VII	30	3.696 (0.317)
IX	300	3.767 (0.508)

STANDARD DEVIATION IN PARENTHESES

- + - SIGNIFICANTLY DIFFERENT ($P < 0.05$) FROM CONTROL GROUP BY LSD
- SIGNIFICANTLY DIFFERENT ($P < 0.05$) FROM CONTROL GROUP BY LSD AND
DUNNETT'S TEST.

Company Sanitized. Does not contain TSCA CBI

REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

TABLE 4

MEAN FLUORIDE CONCENTRATIONS (PPM) FOUND IN THE BLOOD
OF MALE RATS TREATED WITH H-19683 OR H-19704

GROUP #	CONCENTRATION OF TEST SUBSTANCE	RECOVERY DAYS	MEAN FLUORIDE CONCENTRATION (PPM)
I	0 PPM (CONTROLS)	0	0.30
III	30 PPM OF H-19683	0	5.30
V	300 PPM OF H-19683	0	8.19
VII	30 PPM OF H-19704	0	33.23
IX	300 PPM OF H-19704	0	71.52
I	0 PPM (CONTROLS)	7	0.94
III	30 PPM OF H-19683	7	0.58
V	300 PPM OF H-19683	7	0.56
VII	30 PPM OF H-19704	7	19.26
IX	300 PPM OF H-19704	7	22.20

Company Sanitized. Does not contain TSCA CBI

REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

APPENDIX I

INDIVIDUAL BODY WEIGHTS

SD* = Sacrifice by Design

Company Sanitized. Does not contain TSCA CBI

REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

APPENDIX I

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP: I CONCENTRATION: 0 PPM

DAYS ON TEST:	0	7	14	21	28	35	42	49	56	63	70
RECOVERY DAYS	-	-	-	7	14	21	28	35	42	49	56
ANIMAL #											
524405	212.5	265.7	297.8	SD (DAY 14)							
524406	221.5	296.7	351.2	SD (DAY 14)							
524407	199.2	254.2	295.5	SD (DAY 14)							
524408	206.4	265.3	314.1	SD (DAY 14)							
524409	214.5	298.5	362.8	SD (DAY 14)							
524410	217.8	294.1	340.8	382.8	SD (DAY 21)						
524411	228.3	273.2	311.8	357.3	SD (DAY 21)						
524412	203.3	272.6	327.0	376.2	SD (DAY 21)						
524413	208.5	286.7	344.1	402.3	SD (DAY 21)						
524414	208.1	271.7	318.3	361.2	SD (DAY 21)						
524415	215.5	282.2	325.6	365.5	390.7	417.1	454.3	SD (DAY 42)			
524416	216.4	288.9	334.4	392.5	421.7	462.1	496.0	SD (DAY 42)			
524417	199.7	267.0	307.5	348.0	375.6	410.4	453.0	SD (DAY 42)			
524418	201.4	262.1	302.9	343.8	369.7	391.3	428.3	SD (DAY 42)			
524419	218.8	286.3	332.5	362.2	408.8	456.3	489.6	SD (DAY 42)			
524420	217.5	300.6	369.5	427.3	466.1	501.9	558.8	581.5	612.5	639.1	661.4 SD*
524421	233.1	264.5	342.2	344.6	390.6	434.9	480.0	501.4	528.6	558.5	599.4 SD*
524422	198.1	271.4	340.9	393.2	434.3	487.1	535.6	555.6	582.0	606.4	648.5 SD*
524423	209.3	287.7	345.1	399.3	434.6	480.6	529.2	552.6	576.3	599.0	641.6 SD*
524424	216.0	277.6	329.8	375.7	396.4	438.0	471.3	495.4	513.4	528.8	557.1 SD*

Company Sanitized. Does not contain TSCA CBI

REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

APPENDIX I (CONT.)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP: 111 CONCENTRATION: 10 PPM OF H-19683

DAYS ON TEST:	0	7	14	21	28	35	42	49	56	63	70
RECOVERY DAYS	-	-	-	7	14	21	28	35	42	49	56
ANIMAL #											
524425	211.5	287.0	346.3 SD (DAY 14)								
524426	222.3	310.9	384.3 SD (DAY 14)								
524427	198.6	267.1	304.6 SD (DAY 14)								
524428	203.9	270.8	305.1 SD (DAY 14)								
524429	212.3	290.9	355.2 SD (DAY 14)								
524430	210.8	273.7	307.2	354.9 SD (DAY 21)							
524431	228.7	296.6	339.3	396.6 SD (DAY 21)							
524432	204.4	260.6	293.4	349.5 SD (DAY 21)							
524433	208.9	268.9	309.7	365.0 SD (DAY 21)							
524434	205.5	276.3	319.6	376.6 SD (DAY 21)							
524435	223.7	294.8	355.6	418.7	491.1	535.8 SD (DAY 42)					
524436	216.9	279.3	329.1	378.1	426.1	459.0 SD (DAY 42)					
524437	202.4	259.5	289.1	333.6	374.9	409.8 SD (DAY 42)					
524438	205.4	263.8	307.8	348.8	394.4	433.1 SD (DAY 42)					
524439	210.4	283.5	329.0	389.0	448.0	494.8 SD (DAY 42)					
524440	214.6	272.7	310.9	358.8	419.4	450.7	469.6	488.0	509.0	527.6 SD*	
524441	222.3	298.5	354.3	421.9	494.4	543.6	563.4	581.8	601.1	637.1 SD*	
524442	202.6	257.3	295.7	346.2	362.3	395.2	424.9	448.7	478.0	502.1 SD*	
524443	206.1	280.3	317.6	374.7	400.6	435.0	481.4	502.3	538.1	567.1 SD*	
524444	209.9	282.3	329.0	394.0	409.2	445.0	477.8	499.8	554.0	576.8 SD*	

REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

APPENDIX I (CONT.)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP: V CONCENTRATION: 300 PPM OF H-19683

DAYS ON TEST:	0	7	14	21	28	35	42	49	56	63	70
RECOVERY DAYS	-	-	-	7	14	21	28	35	42	49	56
ANIMAL #											
524445	216.8	271.7	314.6	SD (DAY 14)							
524446	227.8	308.6	362.4	SD (DAY 14)							
524447	204.8	266.3	314.3	SD (DAY 14)							
524448	204.3	259.1	302.0	SD (DAY 14)							
524449	213.5	277.5	331.6	SD (DAY 14)							
524450	218.9	266.2	307.9	353.8	SD (DAY 21)						
524451	224.7	280.9	341.2	403.4	SD (DAY 21)						
524452	205.7	243.3	282.6	326.7	SD (DAY 21)						
524453	219.8	259.9	297.4	337.1	SD (DAY 21)						
524454	209.8	259.2	309.8	354.3	SD (DAY 21)						
524455	218.5	273.4	315.2	365.7	393.9	419.0	459.5	SD (DAY 42)			
524456	225.9	286.3	336.5	399.6	433.6	467.9	503.4	SD (DAY 42)			
524457	199.9	256.9	303.7	348.4	382.6	411.1	439.2	SD (DAY 42)			
524458	205.3	269.3	310.8	360.3	381.1	411.6	446.0	SD (DAY 42)			
524459	218.2	283.5	349.1	411.6	456.2	497.5	536.6	SD (DAY 42)			
524460	219.7	278.2	315.9	362.9	400.5	430.3	464.1	477.1	489.0	513.5	534.1
524461	236.0	288.9	329.4	373.5	400.1	430.7	473.9	480.9	501.5	525.1	565.5
524462	201.3	275.3	335.5	401.6	440.6	487.9	532.8	561.5	587.9	611.8	635.0
524463	203.0	289.0	352.4	414.5	467.0	495.6	536.5	551.8	570.7	593.7	612.6
524464	209.2	255.2	289.1	338.8	382.7	418.6	454.5	469.8	492.9	514.0	540.7

REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

APPENDIX I (CONT.)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

CONCENTRATION: 30 PPM OF H-19704

GROUP: VII

DAYS ON TEST:	0	7	14	21	28	35	42	49	56	63	70
RECOVERY DAYS	-	-	-	7	14	21	28	35	42	49	56
ANIMAL #											
524465	213.1	294.8	360.1	SD (DAY 14)							
524466	240.1	307.0	358.3	SD (DAY 14)							
524467	206.5	273.0	331.7	SD (DAY 14)							
524468	200.5	271.7	325.2	SD (DAY 14)							
524469	211.8	283.6	349.7	SD (DAY 14)							
524470	212.3	295.5	353.0	411.1	SD (DAY 21)						
524471	220.9	297.1	357.7	412.5	SD (DAY 21)						
524472	197.8	270.7	328.4	368.5	SD (DAY 21)						
524473	201.9	287.3	352.6	406.2	SD (DAY 21)						
524474	204.5	272.8	319.1	358.4	SD (DAY 21)						
524475	207.3	303.2	368.6	422.4	468.2	518.7	576.4	SD (DAY 42)			
524476	220.8	302.2	358.1	385.2	430.8	462.5	494.9	SD (DAY 42)			
524477	196.0	267.6	317.5	363.1	395.8	433.4	473.4	SD (DAY 42)			
524478	211.4	272.2	308.3	363.1	393.4	438.6	487.7	SD (DAY 42)			
524479	215.9	286.3	346.2	398.3	439.9	479.2	518.0	SD (DAY 42)			
524480	222.9	290.0	343.9	395.6	430.3	469.5	509.0	535.8	558.7	577.0	616.8 SD*
524481	218.6	312.5	381.3	397.2	416.1	465.0	523.9	549.6	531.2	565.9	593.5 SD*
524482	208.5	277.9	328.7	370.8	390.6	433.7	471.7	491.0	518.0	541.2	580.4 SD*
524483	216.6	267.6	313.5	353.5	379.1	411.4	437.9	447.8	468.2	480.7	512.1 SD*
524484	211.6	271.5	324.5	369.4	399.6	444.6	490.6	511.2	541.9	558.7	591.2 SD*

Does not contain TSCA CBI

REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

APPENDIX I (CONT.)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP: IX CONCENTRATION: 300 PPM OF H-19704

DAYS	0	7	14	21	28	35	42	49	56	63	70
ON TEST:											
RECOVERY DAYS	-	-	-	7	14	21	28	35	42	49	56
ANIMAL #											
524485	215.1	221.8	279.0	SD (DAY 14)							
524486	230.6	239.6	293.0	SD (DAY 14)							
524487	201.4	232.0	284.2	SD (DAY 14)							
524488	208.6	222.5	289.7	SD (DAY 14)							
524489	216.9	236.7	307.7	SD (DAY 14)							
524490	215.2	248.9	279.3	348.7	SD (DAY 21)						
524491	224.1	260.9	303.3	366.5	SD (DAY 21)						
524492	197.0	225.2	262.2	298.5	SD (DAY 21)						
524493	212.1	229.6	279.8	311.2	SD (DAY 21)						
524494	211.3	240.9	273.6	312.5	SD (DAY 21)						
524495	219.9	227.5	280.2	338.5	378.0	405.6	439.1	SD (DAY 42)			
524496	224.6	286.7	333.4	380.6	416.8	439.3	474.7	SD (DAY 42)			
524497	203.4	254.5	301.8	357.7	381.9	418.6	458.9	SD (DAY 42)			
524498	207.0	210.8	272.5	307.8	335.8	367.6	400.7	SD (DAY 42)			
524499	210.6	249.9	291.8	358.6	400.7	434.0	480.9	SD (DAY 42)			
524500	215.1	206.6	276.2	308.7	381.0	423.0	460.4	481.1	513.9	533.6	572.2 SD*
524501	229.3	220.6	298.7	366.8	412.1	448.1	484.1	500.9	524.8	548.0	575.1 SD*
524502	204.2	241.0	274.7	321.7	347.3	369.4	401.3	413.7	421.2	436.8	460.5 SD*
524503	209.5	248.8	297.4	362.1	399.8	433.4	468.1	493.1	511.5	544.8	549.9 SD*
524504	210.5	204.7	270.4	323.2	347.6	373.9	408.4	417.4	437.9	454.9	477.9 SD*

Company Sanitized. Does not contain TSCA CBI

REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

APPENDIX II

INDIVIDUAL CLINICAL OBSERVATIONS

NR = Not resolved

Company Sanitized. Does not contain TSCA CBI

REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

APPENDIX II

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP: I CONCENTRATION: 0 PPM

ANIMAL NUMBER	OBSERVATION	FIRST DAY OBSERVED	LAST DAY OBSERVED
524410	PILOERECTION	14	21 NR
524411	PILOERECTION	14	21 NR
524412	PILOERECTION	14	21 NR
524413	PILOERECTION	14	21 NR
524414	PILOERECTION	14	14
524415	PILOERECTION	14	14
524416	PILOERECTION	7	42 NR
524417	PILOERECTION	7	14
524418	PILOERECTION	7	14
524419	PILOERECTION	7	21
524420	PILOERECTION	7	21
524421	PILOERECTION	7	21
	COLORED DISCHARGE NOSE BROWN	28	35
	PILOERECTION	42	70 NR
524423	PILOERECTION	14	21
	PILOERECTION	42	70 NR

Company Sanitized. Does not contain TSCA CBI

**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

APPENDIX II (CONT.)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP: III CONCENTRATION: 30 PPM OF H-19683

ANIMAL NUMBER	OBSERVATION	FIRST DAY OBSERVED	LAST DAY OBSERVED
524425	PILOERECTION	14	14 NR
524426	PILOERECTION	14	14 NR
524427	PILOERECTION	7	14 NR
524428	PILOERECTION	7	14 NR
524429	PILOERECTION	14	14 NR
524430	PILOERECTION	7	21 NR
524431	PILOERECTION	7	21 NR
524432	PILOERECTION	7	21 NR
524433	PILOERECTION	7	21 NR
524435	PILOERECTION	7	21
	COLORED DISCHARGE NOSE BROWN	14	14
524436	PILOERECTION	14	21
524437	PILOERECTION	7	14
524438	PILOERECTION	7	14
524439	PILOERECTION	7	7
524440	PILOERECTION	42	70 NR
524441	PILOERECTION	7	21
524442	PILOERECTION	7	21
	PILOERECTION	42	70 NR
524443	PILOERECTION	7	21
	COLORED DISCHARGE NOSE BROWN	28	35
524444	PILOERECTION	7	21

Company Sanitized. Does not contain TSCA CB

REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

APPENDIX II (CONT.)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP: V CONCENTRATION: 300 PPM OF H-19683

ANIMAL NUMBER	OBSERVATION	FIRST DAY OBSERVED	LAST DAY OBSERVED
524445	PILOERECTION	7	14 NR
524447	PILOERECTION	7	14 NR
524448	PILOERECTION	7	7
	COLORED DISCHARGE NOSE BROWN	7	7
524449	PILOERECTION	7	21 NR
524450	PILOERECTION	7	14
524451	PILOERECTION	7	21 NR
524452	PILOERECTION	7	21 NR
524453	PILOERECTION	7	14
524454	PILOERECTION	7	7
524455	PILOERECTION	7	21
524456	PILOERECTION	14	21
524457	PILOERECTION	7	21
524458	PILOERECTION	14	14
524460	PILOERECTION	7	21
524461	PILOERECTION	14	21
524462	PILOERECTION	14	21
524463	PILOERECTION	42	70 NR

Company Sanitized. Does not contain TSCA CBI

REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

APPENDIX II (CONT.)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP: VII CONCENTRATION: 30 PPM OF H-19704

ANIMAL NUMBER	OBSERVATION	FIRST DAY OBSERVED	LAST DAY OBSERVED
524465	PILOERECTION	7	14 NR
	COLORRED DISCHARGE NOSE RED	14	14 NR
524466	PILOERECTION	7	14 NR
	COLORRED DISCHARGE NOSE BROWN	14	14 NR
524467	IRREGULAR RESPIRATION	14	14 NR
524468	PILOERECTION	14	14 NR
	RAPID BREATHING	14	14 NR
524469	PILOERECTION	7	14 NR
524470	PILOERECTION	7	21 NR
524471	PILOERECTION	7	21 NR
524472	PILOERECTION	7	21 NR
524473	PILOERECTION	7	7
524474	PILOERECTION	7	14
524475	PILOERECTION	7	21
524478	PILOERECTION	14	14
	PILOERECTION	42	42 NR
524479	PILOERECTION	7	14
524480	PILOERECTION	7	14
524481	PILOERECTION	14	14
	*COLORED DISCHARGE LEFT EYE(S) BROWN	21	21
	*COLORED DISCHARGE BOTH EYE(S) BROWN	28	70 NR
	*TOP TEETH CROOKED	28	70 NR
	*BOTTOM TEETH TOO LONG	28	28
	*COLORED DISCHARGE NOSE BROWN	28	28
524482	PILOERECTION	7	14
	PILOERECTION	28	28
524484	PILOERECTION	7	70 NR

* Attributed to malocclusion of the teeth

Company Sanitized. Does not contain TSCA CBI

REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

APPENDIX II (CONT.)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP: IX CONCENTRATION: 300 PPM OF H-19704

ANIMAL NUMBER	OBSERVATION	FIRST DAY OBSERVED	LAST DAY OBSERVED
524485	PILOERECTION	7	14 NR
524486	PILOERECTION	7	7
524487	PILOERECTION	7	7
524488	RAPID BREATHING	14	14 NR
524491	PILOERECTION	14	14
524492	PILOERECTION	7	7
524493	ALOPECIA LEFT HIND QUARTERS	7	21 NR
	PILOERECTION	7	7
524494	PILOERECTION	7	14
524495	PILOERECTION	14	21
524496	PILOERECTION	7	21
524498	PILOERECTION	7	42 NR
	HUNCHED OVER	7	7
524499	PILOERECTION	7	14
524500	PILOERECTION	7	21
	HUNCHED OVER	7	.
524501	PILOERECTION	7	14
524502	PILOERECTION	7	70 NR
524504	PILOERECTION	7	70 NR

Company Sanitized. Does not contain TSCA CBI

REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

APPENDIX III

INDIVIDUAL FINAL BODY WEIGHTS AND LIVER WEIGHTS

Company Sanitized. Does not contain TSCA CBI

**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS****INDIVIDUAL FINAL BODY AND ABSOLUTE LIVER WEIGHTS (grams) FROM MALE RATS
GROUP I - 0 PPM**

TEST DAY 14 ANIMAL NUMBER	RECOVERY DAY 0 FINAL BODY WT	LIVER WT
524405	297.8	11.295
524406	351.2	15.157
524407	295.5	10.371
524408	314.1	12.451
524409	362.8	14.499

GROUP MEAN	324.3	12.755
STD. DEV.	31.0	2.044

TEST DAY 21	RECOVERY DAY 7	
524410	382.8	16.752
524411	357.3	14.358
524412	376.2	15.408
524413	402.3	19.036
524414	361.2	15.753

GROUP MEAN	376.0	16.261
STD. DEV.	18.1	1.771

TEST DAY 42	RECOVERY DAY 28	
524415	454.3	17.501
524416	496.0	17.432
524417	453.0	18.374
524418	428.3	17.882
524419	489.6	17.495

GROUP MEAN	464.2	17.737
STD. DEV.	28.1	0.398

TEST DAY 70	RECOVERY DAY 56	
524420	661.4	26.406
524421	599.4	19.284
524422	648.5	26.333
524423	641.6	22.212
524424	557.1	18.097

GROUP MEAN	621.6	22.466
STD. DEV.	42.9	3.865

Company Sanitized. Does not contain TSCA CBI

**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

**INDIVIDUAL PIPAL BODY AND ABSOLUTE LIVER WEIGHTS (grams) FROM MALE RATS
GROUP III - 30 PPM**

TEST DAY 14	RECOVERY DAY 0	
ANIMAL NUMBER	FINAL BODY WT	LIVER WT
524425	346.3	15.729
524426	384.3	17.457
524427	304.6	12.963
524428	305.1	13.771
524429	355.2	15.572
GROUP MEAN	339.1	15.098
STD. DEV.	34.3	1.768
TEST DAY 21	RECOVERY DAY 7	
524430	354.9	14.495
524431	396.6	18.471
524432	349.5	13.976
524433	365.0	15.116
524434	376.6	14.003
GROUP MEAN	368.5	15.212
STD. DEV.	18.8	1.880
TEST DAY 42	RECOVERY DAY 28	
524435	535.8	24.960
524436	459.0	16.385
524437	409.8	15.757
524438	433.1	15.773
524439	494.8	21.060
GROUP MEAN	466.5	18.787
STD. DEV.	50.0	4.102
TEST DAY 70	RECOVERY DAY 56	
524440	527.6	20.851
524441	637.1	22.618
524442	502.1	19.299
524443	567.1	20.447
524444	576.8	18.393
GROUP MEAN	562.1	20.322
STD. DEV.	51.6	1.607

Company Sanitized. Does not contain TSCA CBI

**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

**INDIVIDUAL FINAL BODY AND ABSOLUTE LIVER WEIGHTS (grams) FROM MALE RATS
GROUP V - 300 PPM**

TEST DAY 14	RECOVERY DAY 0	
ANIMAL NUMBER	FINAL BODY WT	LIVER WT
524445	314.6	15.040
524446	362.4	15.836
524447	314.3	12.844
524448	302.0	12.747
524449	331.6	13.820
GROUP MEAN	325.0	14.057
STD. DEV.	23.4	1.358
TEST DAY 21	RECOVERY DAY 7	
524450	353.8	14.631
524451	403.4	19.682
524452	326.7	13.636
524453	337.1	15.003
524454	354.3	14.772
GROUP MEAN	355.1	15.545
STD. DEV.	29.4	2.371
TEST DAY 42	RECOVERY DAY 28	
524455	459.5	19.545
524456	503.4	19.180
524457	439.2	17.045
524458	446.0	14.867
524459	536.6	22.140
GROUP MEAN	476.9	18.555
STD. DEV.	41.7	2.743
TEST DAY 70	RECOVERY DAY 56	
524460	534.1	20.478
524461	565.5	23.355
524462	635.0	28.756
524463	612.6	21.269
524464	540.7	20.430
GROUP MEAN	577.6	22.858
STD. DEV.	44.5	3.504

Company Sanitized. Does not contain TSCA CBI

**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

**INDIVIDUAL FINAL BODY AND ABSOLUTE LIVER WEIGHTS (grams) FROM MALE RATS
GROUP VII - 30 PPM**

TEST DAY 14 RECOVERY DAY 0

ANIMAL NUMBER	FINAL BODY WT	LIVER WT
524465	360.1	21.718
524466	358.3	21.003
524467	331.7	19.086
524468	325.2	20.790
524469	349.7	20.892
GROUP MEAN	345.0	20.698
STD. DEV.	15.8	0.972

TEST DAY 21	RECOVERY DAY 7	
524470	411.1	23.372
524471	412.5	24.361
524472	368.5	24.350
524473	406.2	21.810
524474	358.4	19.661

GROUP MEAN	391.3	22.711
STD. DEV.	25.8	1.998

TEST DAY 42	RECOVERY DAY 28	
524475	576.4	23.014
524476	494.9	22.983
524477	473.4	20.776
524478	487.7	18.919
524479	518.0	19.864

GROUP MEAN	510.1	21.111
STD. DEV.	40.4	1.844

TEST DAY 70	RECOVERY DAY 56	
524480	616.8	25.762
524481	593.5	20.008
524482	580.4	20.143
524483	512.1	19.507
524484	591.2	21.592

GROUP MEAN	578.8	21.402
STD. DEV.	39.6	2.558

Company Sanitized. Does not contain TSCA CB1

**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

**INDIVIDUAL FINAL BODY AND ABSOLUTE LIVER WEIGHTS (grams) FROM MALE RATS
GROUP IX - 300 PPM**

TEST DAY 14	RECOVERY DAY 0	
ANIMAL NUMBER	FINAL BODY WT	LIVER WT
524485	279.0	23.269
524486	293.0	22.664
524487	284.2	21.723
524488	289.7	24.453
524489	307.7	26.260
GROUP MEAN	290.7	23.674
STD. DEV.	10.9	1.752

TEST DAY 21	RECOVERY DAY 7	
524490	348.7	22.845
524491	366.5	22.413
524492	298.5	21.230
524493	331.2	21.836
524494	312.5	21.845
GROUP MEAN	331.5	22.034
STD. DEV.	27.3	0.617

TEST DAY 42	RECOVERY DAY 28	
524495	439.1	21.474
524496	474.7	22.941
524497	458.9	19.103
524498	400.7	19.567
524499	480.9	23.084
GROUP MEAN	450.9	21.234
STD. DEV.	32.4	1.852

TEST DAY 70	RECOVERY DAY 56	
524500	572.2	20.888
524501	575.1	24.770
524502	460.5	16.900
524503	549.9	16.648
524504	477.9	19.969
GROUP MEAN	527.1	19.835
STD. DEV.	54.1	3.326

Company Sanitized. Does not contain TSCA CBI

**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

APPENDIX III (CONT.)

INDIVIDUAL ANIMAL FINAL BODY AND LIVER WEIGHTS

RELATIVE LIVER WEIGHTS (% of body weight) FROM MALE RATS

GROUP I - 0 PPM

<u>SACRIFICED (DAYS OF RECOVERY)</u>	<u>ANIMAL NUMBER</u>	<u>LIVER</u>
0	524405	3.7928
0	524406	4.3158
0	524407	3.5096
0	524408	3.9640
0	524409	3.9964
	GROUP MEAN	3.916
	STD. DEV.	0.295
7	524410	4.3762
7	524411	4.0185
7	524412	4.0957
7	524413	4.7318
7	524414	4.3613
	GROUP MEAN	4.317
	STD. DEV.	0.281
28	524415	3.8523
28	524416	3.5145
28	524417	4.0561
28	524418	4.1751
28	524419	3.5733
	GROUP MEAN	3.843
	STD. DEV.	0.290
56	524420	3.9924
56	524421	3.2172
56	524422	4.0606
56	524423	3.4620
56	524424	3.2484
	GROUP MEAN	3.596
	STD. DEV.	0.405

Company Sanitized. Does not contain TSCA CBI

**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

APPENDIX III (CONT.)

INDIVIDUAL ANIMAL FINAL BODY AND LIVER WEIGHTS

RELATIVE LIVER WEIGHTS (% of body weight) FROM MALE RATS

GROUP III - 30 PPM OF H-19683

<u>SACRIFICE (DAYS OF RECOVERY)</u>	<u>ANIMAL NUMBER</u>	<u>LIVER</u>
0	524425	4.5420
0	524426	4.5425
0	524427	4.2557
0	524428	4.5136
0	524429	4.3840
	GROUP MEAN	4.448
	STD. DEV.	0.126
7	524430	4.0842
7	524431	4.6573
7	524432	3.9989
7	524433	4.1414
7	524434	3.7183
	GROUP MEAN	4.120
	STD. DEV.	0.341
28	524435	4.6585
28	524436	3.5697
28	524437	3.8450
28	524438	3.6419
28	524439	4.2563
	GROUP MEAN	3.994
	STD. DEV.	0.457
56	524440	3.9520
56	524441	3.5501
56	524442	3.8437
56	524443	3.6055
56	524444	3.1888
	GROUP MEAN	3.928
	STD. DEV.	0.296

Company Sanitized. Does not contain TSCA CBI

**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

APPENDIX III (CONT.)

INDIVIDUAL ANIMAL FINAL BODY AND LIVER WEIGHTS

RELATIVE LIVER WEIGHTS (% of body weight) FROM MALE RATS

GROUP V - 300 PPM OF H-19683

<u>SACRIFICE (DAYS OF RECOVERY)</u>	<u>ANIMAL NUMBER</u>	<u>LIVER</u>
0	524445	4.7807
0	524446	4.3698
0	524447	4.0865
0	524448	4.2209
0	524449	4.1677
	GROUP MEAN	4.325
	STD. DEV.	0.275
7	524450	4.1354
7	524451	4.8790
7	524452	4.1739
7	524453	4.4506
7	524454	4.1693
	GROUP MEAN	4.362
	STD. DEV.	0.316
28	524455	4.2535
28	524456	3.8101
28	524457	3.8809
28	524458	3.3334
28	524459	4.1260
	GROUP MEAN	3.881
	STD. DEV.	0.355
56	524460	3.8341
56	524461	4.1300
56	524462	4.5285
56	524463	3.4719
56	524464	3.7784
	GROUP MEAN	3.949
	STD. DEV.	0.400

Company Sanitized. Does not contain TSCA CBI

**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH E-19683 AND E-19704 IN MALE RATS**

APPENDIX III (CONT.)

INDIVIDUAL ANIMAL FINAL BODY AND LIVER WEIGHTS

RELATIVE LIVER WEIGHTS (% of body weight) FROM MALE RATS

GROUP VII - 30 PPM OF E-19704

<u>SACRIFICED (DAYS OF RECOVERY)</u>	<u>ANIMAL NUMBER</u>	<u>LIVER</u>
0	524465	6.0311
0	524466	5.8618
0	524467	5.7540
0	524468	6.3930
0	524469	5.9743
	GROUP MEAN	6.003
	STD. DEV.	0.243
7	524470	5.6852
7	524471	5.9057
7	524472	6.6079
7	524473	5.3693
7	524474	5.4858
	GROUP MEAN	5.811
	STD. DEV.	0.490
28	524475	3.9927
28	524476	4.6440
28	524477	4.3887
28	524478	3.8792
28	524479	3.8347
	GROUP MEAN	4.148
	STD. DEV.	0.353
56	524480	4.1767
56	524481	3.3712
56	524482	3.4705
56	524483	3.8092
56	524484	3.6522
	GROUP MEAN	3.696
	STD. DEV.	0.317

Company Sanitized. Does not contain TSCA CB

REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

APPENDIX III (CONT.)

INDIVIDUAL ANIMAL FINAL BODY AND LIVER WEIGHTS

RELATIVE LIVER WEIGHTS (% of body weight) FROM MALE RATS

GROUP IX - 300 PPM OF H-19704

<u>SACRIFICED (DAYS OF RECOVERY)</u>	<u>ANIMAL NUMBER</u>	<u>LIVER</u>
0	524485	8.3401
0	524486	7.7352
0	524487	7.6436
0	524488	8.4408
0	524489	8.5343
	GROUP MEAN	8.139
	STD. DEV.	0.417
7	524490	6.5515
7	524491	6.1154
7	524492	7.1122
7	524493	6.5930
7	524494	6.9904
	GROUP MEAN	6.673
	STD. DEV.	0.396
28	524495	4.8905
28	524496	4.8327
28	524497	4.1628
28	524498	4.8832
28	524499	4.8002
	GROUP MEAN	4.714
	STD. DEV.	0.310
56	524500	3.6505
56	524501	4.3071
56	524502	3.6699
56	524503	3.0275
56	524504	4.1735
	GROUP MEAN	3.767
	STD. DEV.	0.508

REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS

APPENDIX IV

INDIVIDUAL FLUORIDE CONCENTRATIONS

Company Sanitized. Does not contain TSCA CBI

**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

APPENDIX IV

**INDIVIDUAL FLUORIDE CONCENTRATIONS (PPM) FOUND IN THE BLOOD
OF MALE RATS TREATED WITH H-19683 OR H-19704**

<u>GROUP #</u>	<u>CONCENTRATION OF TEST SUBSTANCE</u>	<u>TEST DAYS</u>	<u>RECOVERY DAYS</u>	<u>RAT #</u>	<u>PPM IN BLOOD</u>
I	0 PPM (CONTROLS)	14	0	101	0 (BLANK)
		14	0	102	0.32
		14	0	103	0.14
		14	0	104	0.35
		14	0	105	0.39
		21	7	106	0.45
		21	7	107	0.37
		21	7	108	0 (BLANK)
		21	7	109	0 (BLANK)
		21	7	110	1.99
III	30 PPM OF H-19683	14	0	301	3.91
		14	0	302	4.85
		14	0	303	4.47
		14	0	304	5.21
		14	0	305	8.04
			7	306	1.30
			7	307	0.34
		21	7	308	0 (BLANK)
		21	7	309	0 (BLANK)
		21	7	310	0.09
V	300 PPM OF H-19683	14	0	501	6.87
		14	0	502	7.26
		14	0	503	4.76
		14	0	504	15.09
		14	0	505	6.99
		21	7	506	0 (BLANK)
		21	7	507	0.25
		21	7	508	0.63
		21	7	509	0.70
		21	7	510	0.68

Company Sanitized. Does not contain TSCA CBI

**REPEATED DOSE ORAL TOXICITY: 14-DAY FEEDING STUDY
WITH H-19683 AND H-19704 IN MALE RATS**

APPENDIX IV (Continued)

**INDIVIDUAL FLUORIDE CONCENTRATIONS (PPM) FOUND IN THE BLOOD
OF MALE RATS TREATED WITH H-19683 OR H-19704**

<u>GROUP #</u>	<u>CONCENTRATION OF TEST SUBSTANCE</u>	<u>TEST DAYS</u>	<u>RECOVERY DAYS</u>	<u>RAT #</u>	<u>PPM IN BLOOD</u>
VII	30 PPM OF H-19704	14	0	701	38.19
		14	0	702	27.83
		14	0	703	33.99
		14	0	704	33.52
		14	0	705	32.62
		21	7	706	14.09
		21	7	707	25.88
		21	7	708	27.10
		21	7	709	17.44
		21	7	710	11.81
IX	300 PPM OF H-19704	14	0	901	64.51
		14	0	902	67.41
		14	0	903	54.44
		14	0	904	101.58
		14	0	905	69.65
		21	7	906	25.52
		21	7	907	20.26
		21	7	908	22.66
		21	7	909	18.42
		21	7	910	23.16

Company Sanitized. Does not contain TSCA CBI