

TRADE SECRET

Study Title

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

Laboratory Project ID: DuPont-2926

AUTHOR: Carol Finlay, B.A.

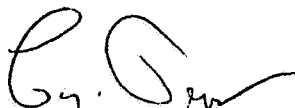
STUDY COMPLETED ON: September 5, 2000

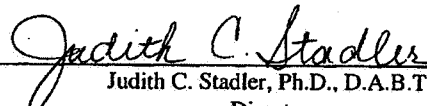
PERFORMING LABORATORY: E.I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, P.O. Box 50
Newark, Delaware 19714-0050

[REDACTED]
[REDACTED]

CERTIFICATION

We, the undersigned, declare that this report provides an accurate evaluation of data obtained from this study.

Reviewed by:  5 Sep 2000
Gary W. Jepson, Ph.D.
Senior Research Scientist
Date

Reviewed by:  05-SEP-2000
Judith C. Stadler, Ph.D., D.A.B.T.
Director
Date

Issued by Study Director:  05-Sept-2000
Carol Finlay, B.A.
Staff Scientist
Date

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STUDY INFORMATION

TEST SUBSTANCE:

Substance Tested: [REDACTED]

Synonyms/Codes: • H-24002
[REDACTED]

Haskell Number: 24002

Composition: [REDACTED]

Known Impurities: [REDACTED]

POSITIVE CONTROL:

Substance Tested: Potassium perfluoroalkyl sulfonate

Synonyms/Codes: • H-24019
[REDACTED]

• PFOS
[REDACTED]

Haskell Number: 24019

Composition: [REDACTED]

Known Impurities: [REDACTED]

STUDY INFORMATION (Continued)

POSITIVE CONTROL:

Substance Tested: [REDACTED]

Synonyms/Codes: • H-24020

- [REDACTED]
- C-8
 - Perfluorooctanoate, ammonium salt
 - PFOA
 - Ammonium perfluorooctanoate

Haskell Number: 24020

Composition [REDACTED]

Known Impurities: [REDACTED]

Sponsor: E. I. du Pont de Nemours and Company
Wilmington, Delaware 19898
U.S.A.

Study Initiated/Completed: April 30, 1999 / (see report cover page)

In-Life Initiated/Completed: July 11, 1999 / October 12, 1999

STUDY PERSONNEL

Study Director: Carol Finlay, B.A.
Management: Judith C. Stadler, Ph.D., D.A.B.T.
Primary Technician: Richard P. Mathena

Blood Fluorine Data Analysis: Gary W. Jepson, Ph.D.
Management: Matthew S. Bogdanffy, Ph.D., D.A.B.T.

Toxicology Report Preparation: Wanda F. Dinbokowitz

Laboratory Veterinarian: Wanda L. West, D.V.M., A.C.L.A.M.

SUMMARY

The objective of this study was to evaluate the potential for H-24002, when administered by gavage, to be absorbed and to accumulate in a mammalian system. Six groups of 5 male Crl:CD[®](SD)IGS BR rats each were given 75 mg/kg/day of H-24002. The test substance was administered to one group of 5 rats for 5 consecutive days and to 5 groups for 10 days. Approximately 2 hours after the first dose, blood was collected from the orbital sinus of each rat from the 5-dose group. On selected days (5, 10, 13, 24, 52, 94) 5 rats per group were euthanized and the blood and livers were collected. Body weights and clinical signs were recorded on each day of dosing and then approximately every other week during the recovery period. Additionally, 3 negative controls, deionized water, corn oil, and corn oil/acetone (80:20), and 2 positive controls, H-24019 (10 mg/kg/day) and H-24020 (20 mg/kg/day), were tested as described for H-24002.

No deaths occurred during the study. No clinical signs associated with the test substance were observed in rats given H-24002. Rats dosed with H-24019 exhibited diarrhea, salivation, alopecia, black ocular discharge, and staining of various parts of the body during the dosing period. Rats dosed with H-24020 exhibited wet perineum and diarrhea during the dosing period. The corn oil and corn oil/acetone negative control rats exhibited no clinical signs during the study.

The mean body weights and mean body weight gains of the rats dosed with the test substance, H-24002, were comparable to the deionized water and corn oil negative controls and greater than the H-24020 positive controls. Comparison of body weights between the rats dosed with the test substance and the corn oil/acetone negative control and H-24019 positive control rats was complicated by the fact that there was a difference in age on test day 1 between the rats. Accounting for the age difference at study start and the expected rate of body weight gain, it appears that the mean body weights and mean body weight gains of the rats dosed with the test substance, H-24002, are comparable to the corn oil/acetone negative controls and greater than the H-24019 positive controls.

A steady-state for fluorine levels in whole blood may not have been achieved during 10 consecutive days of dosing with 75 mg/kg H-24002. An area under the curve (estimated to infinity) was calculated and normalized for fluorine content for the test substance and each positive control. The AUCINF/D for the fluorine component of the test substance, H-24002, was 7031.0 compared to AUCINF/D values of 566,479.1 and 70,789.6 for the positive controls, H-24019 and H-24020, respectively.

Under the conditions of this study, administration of the test substance, H-24002, to male rats for 10 consecutive days resulted in low absorption and retention of fluorine in the blood. Dose-adjusted areas under the curve (AUCINF/D) for positive controls, H-24019 and H-24020, were approximately 81x and 10x the AUCINF/D for the test substance.

INTRODUCTION

The objective of this study was to define the potential of H-24002 to be absorbed and to bioaccumulate in a mammalian system, as indicated by analytical determination of total fluorine in blood and liver. The test substance was compared to 2 positive controls that were materials previously shown to bioaccumulate in mammals.

The dosage of 75 mg/kg/day was chosen based on available toxicity data and the results of a rangefinding study. In the initial rangefinding study, 5 rats were dosed with the test substance for 4 consecutive days at a dosage of 700 mg/kg. The study was terminated because the rats experienced an overall mean body weight loss of 21 grams. In a second rangefinding study, 5 rats were dosed with the test substance for 5 consecutive days at a dosage of 100 mg/kg. The rats experienced an overall mean body weight gain of 6 grams. Based on the results of this rangefinding study, the dosage of 75 mg/kg/day for the test substance was chosen for the study.

All blood samples were analyzed for total fluorine content. This report contains the results of those analyses. Results from analyses of selected liver samples will be presented in a supplemental report.

MATERIALS AND METHODS

A. Test Substance and Positive Control

The test substance, H-24002, was supplied by the sponsor as an amber brown liquid. The positive controls, H-24019 and H-24020, were supplied by the sponsor as white solids. The test substance and positive controls appeared to be stable under the conditions of the study. No evidence of instability, such as a change in color or physical state, was observed.

B. Test Species

Male CrI:CD[®](SD)IGS BR rats were received from Charles River Laboratories, Inc., Raleigh, North Carolina. The CrI:CD[®](SD)IGS BR rat was selected on the basis of extensive experience with this strain and its suitability with respect to longevity, hardiness, sensitivity, and low incidence of spontaneous diseases.

C. Animal Husbandry

1. Housing Environment

Rats were housed singly in stainless steel, wire-mesh cages suspended above cage boards. Animal rooms were maintained on an approximate 12-hour light/dark cycle (fluorescent light) and at a temperature of $23 \pm 1^\circ\text{C}$ and a relative humidity of $50 \pm 10\%$.

2. Feed and Water

Tap water was provided *ad libitum*. All rats were fed PMI Nutrition International, Inc. Certified Rodent LabDiet® 5002 chow. The feed is guaranteed by the manufacturer to meet specified nutritional requirements and to be free of specified contaminants.

3. Identification

Prior to assignment to groups, each rat was temporarily identified by cage identification. After assignment to groups, an individual identification number was marked or tattooed on the tail of each rat. The information on the cage labels included the unique 6-digit Haskell animal number assigned to each rat.

4. Animal Health Monitoring Program

As specified in the Haskell Laboratory animal health and environmental monitoring program, the following procedures are performed periodically to assure that contaminant levels are below those that would be expected to impact the scientific integrity of the study:

- Water samples are analyzed for total bacterial counts, and the presence of coliforms, lead, and other contaminants.
- Feed samples are analyzed for total bacterial, spore and fungal counts.
- Samples from freshly washed cages and cage racks are analyzed to ensure adequate sanitation by the cagewashers.

Certified animal feed is used, guaranteed by the manufacturer to meet specified nutritional requirements and not to exceed stated maximum concentrations of key contaminants, including specified heavy metals, aflatoxin, chlorinated hydrocarbons, and organophosphates. The presence of these contaminants below the maximum concentration stated by the manufacturer would not be expected to impact the integrity of the study.

The animal health and environmental monitoring program is administered by the attending laboratory animal veterinarian.

D. Quarantine and Pretest

Upon arrival at Haskell Laboratory, the rats were removed from shipping cartons and quarantined for 6 days. The rats were weighed 3 times during the pretest period and examined daily for any clinically apparent signs of disease or injury. The rats were observed daily for mortality and signs of illness, injury, or abnormal behavior.

On the bases of acceptable body weight gains and freedom from clinically apparent signs of disease or injury, the rats were released from quarantine by the laboratory animal veterinarian designee.

E. Study Design

Substance	Vehicle	Dosage (mg/kg)	Number of Animals
Negative Controls			
Deionized Water	Not applicable	0	30
Corn oil		0	30
Corn oil:acetone		0	30
Positive Controls			
H-24019	Corn oil: acetone	10	30
H-24020	Corn oil	20	30
Test Substance			
H-24002	Deionized Water	75	30

F. Assignment to Groups and Study Start

After the quarantine period, the rats were selected on the bases of adequate body weight gain, freedom from any clinical signs of disease or injury, and a body weight within $\pm 20\%$ of the mean. The selected rats were divided by computerized, stratified randomization into 6 groups of 5 rats, so that there were no statistically significant differences among group body weight means.

After assignment to groups, each rat was housed individually. The last 3 digits of the animal number was marked or tattooed on the tail of each rat. The rats were between 7 and 9 weeks of age at the time of dosing. Dosing began on test day 1.

Rats that were not assigned to the study were released for other laboratory purposes, or were sacrificed by carbon dioxide asphyxiation and discarded without pathological evaluation.

G. Dosing Material Preparation and Administration

1. Test Substance

H-24002 was administered as mg test substance received per kg weight of each animal. The liquid test substance received was diluted with deionized water so an accurate amount could be administered at the selected dose level. The amount of dosing mixture (mL) each rat received

was based on the body weight collected on each day of dosing and the dosing mixture concentration (7.5 mg liquid test substance/mL water). The rats were dosed at a volume of 1 mL/100 g of body weight. The dosing mixture was stirred on a magnetic stir plate throughout the dosing procedure to maintain homogeneity.

2. Positive Controls

The solid positive control compounds were suspended as emulsions in their respective vehicles. Corn oil was used as the vehicle for H-24019. It was necessary to dissolve H-24020 in acetone before suspending it in corn oil. The ratio of acetone to corn oil was 20:80. The amount each rat received was based on the body weight collected on each day of dosing and the suspension concentration. The dose volumes did not exceed 1 mL/100 g of body weight. The dosing suspensions were stirred on a magnetic stir plate throughout the dosing procedure to maintain homogeneity.

3. Negative Controls

Deionized water was chosen as a negative control because it was the vehicle for the test substance. Corn oil and corn oil:acetone (80:20) were chosen as negative controls because they were the vehicles for the positive controls. Each negative control rat received 1 mL of corn oil or corn oil:acetone. These rats were dosed in a separate room from the rats dosed with the test substance or positive controls.

H. Body Weights

All rats were weighed on each day of dosing and then weekly or every other week during the recovery period.

I. Mortality and Clinical Observations

Cage-site examinations to detect moribund or dead rats and abnormal behavior and appearance among rats were conducted at least once daily throughout the study. At every weighing, each rat were individually handled and examined for abnormal behavior and appearance.

J. Collection and Analysis of Blood and Livers

Approximately 2 hours after the first dose, 1-2 mL of blood was collected into EDTA tubes from the orbital sinus of each rat from Group I. At all other selected time points, 5 rats/group were euthanized by carbon dioxide anesthesia and exsanguination and blood and livers were collected according to the following schedules:

Group	Dosing Days	Tissue Collected	Sampling Time
I	1-5	Blood	Test day 1 (2 hours post dosing)
I	1-5	Blood and Liver	Test day 5 at sacrifice (2 hours post dosing)
II	1-10	Blood and Liver	Test day 10 (2 hours post dosing)
III	1-10	Blood and Liver	Test day 13
IV	1-10	Blood and Liver	Test day 24
V	1-10	Blood and Liver	Test day 52
VI	1-10	Blood and Liver	Test day 94

Five to 10 mL of blood was collected into EDTA tubes at sacrifice. The livers were weighed. The blood from all rats was refrigerated and the livers were frozen. The blood was appropriately packaged and shipped refrigerated to Jackson Laboratory, Deepwater, New Jersey where it was analyzed for total fluorine.

The total fluorine content of the blood samples was determined using a Wickbold torch combustion method, followed by analysis with a fluoride ion selective electrode. The liquid blood was decomposed or volatilized in the presence of wet oxygen and swept through an oxy-hydrogen flame in a closed quartz apparatus. The combustion products were collected in an aqueous absorbing solution and analyzed using a fluoride ion selective electrode. The analytical data (ppm F in each sample) was supplied to Haskell Laboratory personnel for evaluation of fluorine biopersistence.

K. Treatment of Fluorine Data

Noncompartmental analysis was conducted on blood fluorine data derived from rats dosed with H-24002 using WinNonlin Version 3.0 software (Pharsight Corp, Mountain View, CA). WinNonlin software provided a means of computing derived pharmacokinetic parameters from data files including area under the curve (AUCINF), C_{max} and terminal half-life (T_{1/2}). The AUCINF (concentration x time) represents the area under the blood concentration curve from the time of dosing extrapolated to infinity. The maximum observed concentration was C_{max} (concentration). The points included in determination of the terminal half-life were selected manually and given in units of time. Since the dosages and fluorine content for each positive control and the test material varied, all doses were normalized to 0.1 mmole/kg for comparative purposes. The accumulation index (AI, $1/(1-e^{-kt})$) and bioaccumulation index (BI, C_{max} x AI) were calculated and reported but not further used.

H-24019 and H-24020 were used as positive controls. Dosing diluents were used as negative controls, but because of variability and limited sensitivity of the analytical method, the background was set at 0.2 ppm fluorine. Since 0.2 ppm was the fluoride concentration limit of detection, any values listed as less than 0.2 ppm were excluded from further treatment.

The percent of fluorine and molecular weight of the test substance and positive controls were used as provided by the sponsor. The measurements resulting from analysis of total blood

fluorine were used as received (ppm F) from Jackson Laboratory. Fluoride ion was converted to micromolar (μM) equivalents of active component for further comparisons. The data and descriptions of data manipulation and presentation are provided in Appendix C.

RESULTS AND DISCUSSION

A. In-Life Toxicology

(Tables 1-2, Figure 1, Appendices A-B)

No deaths occurred during the study. Alopecia, considered unrelated to test substance administration, was observed in 1 rat dosed with the test substance, H-24002. Rats dosed with H-24019 exhibited diarrhea, salivation, alopecia, black ocular discharge, and staining of various parts of the body during the dosing period. Rats dosed with H-24020 exhibited wet perineum and diarrhea during the dosing period. Alopecia was observed during the recovery period in rats dosed with deionized water and the positive controls, H-24019 and H-24020. The corn oil and corn oil/acetone negative control rats exhibited no clinical signs during the study.

The mean body weights and mean body weight gains of the rats dosed with the test substance, H-24002, were comparable to the deionized water and corn oil negative controls and greater than the H-24020 positive controls. Comparison of body weights between the rats dosed with the test substance and the corn oil/acetone negative control and H-24019 positive control rats was complicated by the fact that there was a difference in age on test day 1 between the rats. This difference resulted in differences in mean body weights on test day 1. The H-24002 rats were younger and lighter in weight than the corn oil/acetone negative control and H-24019 positive control rats. Younger animals experience a period of rapid body weight gain. Older animals are expected to gain weight at a slower rate than younger animals. Accounting for the age difference at study start and the expected rate of body weight gain, it appears that the mean body weights and mean body weight gains of the rats dosed with the test substance, H-24002, are comparable to the corn oil/acetone negative controls and greater than the H-24019 positive controls.

B. Fluorine Data

(Tables 3-4, Figures 2-3, Appendix C)

1. Factors Influencing Interpretation of Analysis

The data used in the kinetic analysis were derived from a limited screen, and therefore several caveats and considerations are important. A couple of considerations of particular importance are (1) a single dose was used and kinetics may or may not be linear, (2) the kinetics apply only to blood, (3) steady-state may not have been achieved, and (4) the sample size is low and may impact calculation of the terminal half-life. A more complete list of considerations is shown in Appendix C.

2. Positive Controls

The positive controls were H-24019 and H-24020. The H-24019 normalized μM equivalents in rat blood continued to rise throughout the dosing period and may not have reached steady-state (Figure 2A). The C_{max} for H-24019 was 989.85 ± 116.90 ppm (Mean $\pm$ SD) with a terminal half-life of 40.5 days. The H-24019 AI was 59.0 and the BI was 58382.2. The H-24020 normalized μM equivalents in rat blood peaked after 5 days of dosing and then decreased throughout the dosing period (Figure 2B). The C_{max} for H-24020 was 518.12 ± 44.89 ppm (Mean $\pm$ SD) with a terminal half-life of 8.3 days. The H-24020 AI was 12.5 and the BI was 6497.5. For each of the positive controls, blood was sampled at seven time points throughout the study, with only four of them occurring post-dose. The small sample size and analytical variability should be taken into account when using the derived terminal half-life for comparative purposes. The total internal exposure resulting from a normalized dose was described by AUCINF/D and was the basis for comparison between positive controls and the test material. The AUCINF/D for the fluorine component was 566,479.1 and 70,789.6 for H-24019 and H-24020, respectively.

3. Test Substance

The H-24002 normalized μM equivalents in rat blood continued to rise throughout the dosing period and may not have reached steady-state (Figure 2C). The C_{max} for H-24002 was 39.60 ± 2.62 ppm (Mean $\pm$ SD) with a terminal half-life of 15.7 days. Blood was sampled at seven time points throughout the study, with only four of them occurring post-dose. The small sample size and analytical variability should be taken into account when using the derived terminal half-life for comparative purposes. The H-24002 AI was 23.1 and the BI was 916.0. The total internal exposure resulting from a normalized dose was described by AUCINF/D and was the basis for comparison between H-24002 and positive controls. The AUCINF/D for the fluorine component of H-24002 was 7031.0 as compared to AUCINF/D values of 566,479.1 and 70,789.6 for H-24019 and H-24020, respectively. The data, calculations and equations are shown in Appendix C.

CONCLUSIONS

Rats dosed for 10 consecutive days with 75 mg/kg H-24002 exhibited no mortality or test substance-related clinical signs of toxicity and had mean body weights and mean body weight gains that were comparable to the negative controls. A steady-state for fluorine in the blood may not have been achieved during the 10-day dosing period.

Under the conditions of this study, administration of H-24002 to male rats for 10 consecutive days resulted in low absorption and retention of fluorine in the blood. Dose-adjusted areas under the curve (AUCINF/D) for positive controls, H-24019 and H-24020, were approximately 81x and 10x the AUCINF/D for the test substance.

RECORDS AND SAMPLE STORAGE

Specimens (if applicable), raw data, and the final report will be retained at Haskell Laboratory, Newark, Delaware, or at Iron Mountain Records Management, Wilmington, Delaware.

TABLES

TABLE 1
MEAN BODY WEIGHTS (g)

Test Days	<u>Negative Controls</u>			<u>Positive Controls</u>		<u>Test Substance</u>
	Deionized Water	Corn Oil	Corn Oil: Acetone	H-24019	H-24020	H-24002
1	226.8	229.8	297.6	291.5	227.5	234.6
2	232.8	234.1	299.6	291.5	232.4	239.3
3	240.3	241.4	309.4	298.3	242.0	248.4
4	249.0	250.4	314.3	304.1	248.9	256.1
5	259.1	259.3	321.5	308.6	252.4	264.8
6	268.3	266.8	326.0	312.7	259.8	271.2
7	277.1	271.2	334.9	317.5	263.3	274.2
8	283.6	281.9	339.2	317.3	269.8	288.6
9	290.2	285.2	345.2	318.4	278.5	294.3
10	298.3	295.9	351.7	318.9	283.9	301.9
13	313.6	321.1	350.7	329.1	289.1	322.1
18	352.6	-	-	-	-	-
20	-	350.5	369.8	359.7	311.3	364.7
24	419.4	378.3	401.0	387.9	340.9	371.9
25	378.7	-	-	-	-	-
27	-	-	-	393.9	-	416.0
32	400.7	-	-	-	-	-
33	-	-	-	-	-	444.9
34	-	407.8	411.4	416.9	402.9	-
39	449.5	-	-	-	-	-
41	-	434.5	-	-	425.0	473.7
46	463.5	-	-	-	-	-
47	-	454.9	-	-	438.2	499.5
51	-	-	-	-	-	532.7
52	469.7	464.7	527.6	438.1	465.6	-
53	511.0	-	-	-	-	-
54	-	-	-	-	-	506.6
55	-	487.0	-	-	452.3	-
60	528.0	-	-	-	-	525.9
61	-	505.1	-	-	465.8	-
62	-	-	-	523.4	-	-
67	547.7	-	-	-	-	-
68	-	515.4	-	-	470.9	-
74	558.0	-	-	-	-	-

TABLE 1 (Continued)
MEAN BODY WEIGHTS (g)

Test Days	<u>Negative Controls</u>			<u>Positive Controls</u>		<u>Test Substance</u>
	Deionized Water	Corn Oil	Corn Oil: Acetone	H-24019	H-24020	H-24002
76	-	-	539.0	563.4	-	562.3
80	-	-	-	570.7	-	-
81	573.0	-	-	-	499.2	-
82	-	-	-	-	-	578.1
88	589.5	-	-	-	-	586.4
90	-	556.2	562.2	585.3	527.8	-
94	584.6	566.9	567.8	597.9	538.7	593.9

- Indicates the animal was not weighed.

TABLE 2

MEAN BODY WEIGHT GAINS (g)

Test Days	<u>Negative Controls</u>			<u>Positive Controls</u>		<u>Test Substance</u>
	Deionized Water	Corn Oil	Corn Oil:Acetone	H-24019	H-24020	H-24002
1-5	32.3	29.5	23.9	17.1	24.9	30.2
1-10	71.5	66.1	54.1	27.4	56.4	67.3
10-13	15.3	25.2	-1.0	10.2	5.2	20.2
10-24	121.1	82.4	49.3	69.0	57.0	70.0
10-51/52	171.4	168.8	175.9	119.2	181.7	230.8
10-94	286.3	271.0	216.1	279.0	254.8	292.0

TABLE 3
MEAN BLOOD FLUORINE LEVELS

Test Days	Negative Controls			Positive Controls		Test Substance	
	Deionized Water (ppm)	Corn Oil (ppm)	Corn Oil: Acetone (ppm)	H-24019 (ppm)	H-24020 (ppm)	H-24002 (ppm)	
1	<0.2	<0.2	<0.2	2.1 (0.9)	62.6 (3.2)	1.9 (0.4)	
5	<0.2	<0.2	<0.2	48.8 (17.6)	71.7 (6.2)	6.0 (0.4)	
10	<0.2	<0.2	0.3 ^a (0.1) ^b	61.7 (2.8)	54.2 (7.8)	7.3 (0.5)	
13	<0.2	0.2 ^a (0.1)	0.6 ^c (0.6)	64.5 (7.6)	26.6 (11.4)	3.1 (0.2)	
24	0.2 ^c	<0.2	0.2 ^d	42.2 (2.8)	10.5 (3.0)	1.8 (0.2)	
51/52	<0.2	0.3 ^a (0.1)	<0.2	26.9 (2.6)	0.9 (0.2)	0.6 (0.1)	
94	0.9 ^c	0.3 ^a (0.1)	<0.2	13.2 (2.1)	0.2 ^c (0.1)	0.3 (0.0)	

a Mean of 4 of the 5 values. One of the values was below the level of detection (LOD).

b Standard deviation is in parentheses.

c Mean of 3 of the 5 values. Two of the values were below the LOD.

d One value. Four of the values were below the LOD.

e Mean of 2 of the 5 values. Three of the values were below the LOD.

TABLE 4

MEAN BLOOD FLUORINE CONCENTRATION NORMALIZED TO DOSE

Test Days	<u>Positive Controls</u>		<u>Test Substance</u>
	H-24019	H-24020	H-24002
	$\mu\text{M F}$ Equivalents	$\mu\text{M F}$ Equivalents	$\mu\text{M F}$ Equivalents
1	28.92 (13.3) ^a	89.28 (23.4)	9.35 (2.0)
5	747.69 (271.5)	518.12 (44.9)	32.26 (2.4)
10	945.85 (43.5)	391.01 (56.8)	39.60 (2.6)
13	989.85 (116.9)	191.45 (82.7)	16.13 (1.3)
24	645.54 (42.9)	74.35 (22.1)	8.90 (0.9)
52	411.38 (40.6)	4.64 (1.1)	2.00 (0.6)
94	195.38 (32.5)	0.24 (0.4)	0.45 (0.3)

a Standard deviation is in parentheses.

FIGURES

FIGURE 1

MEAN BODY WEIGHTS (g)

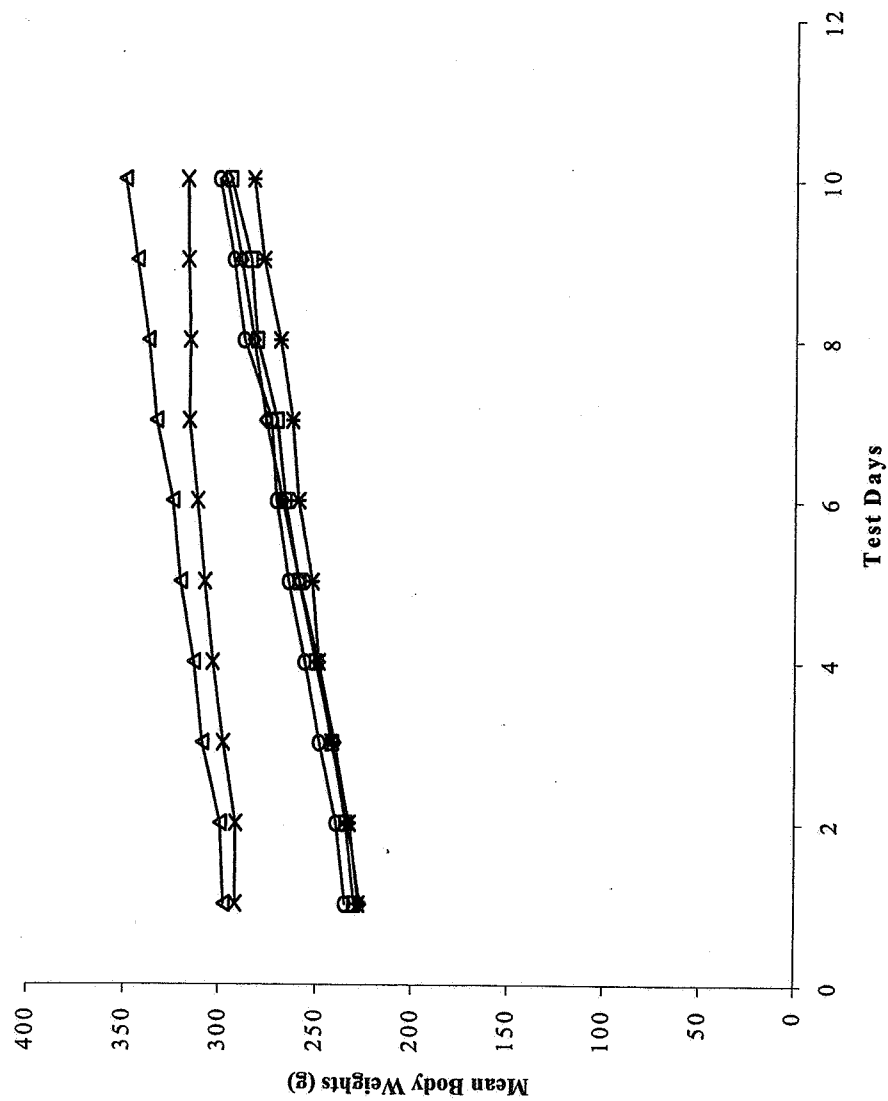
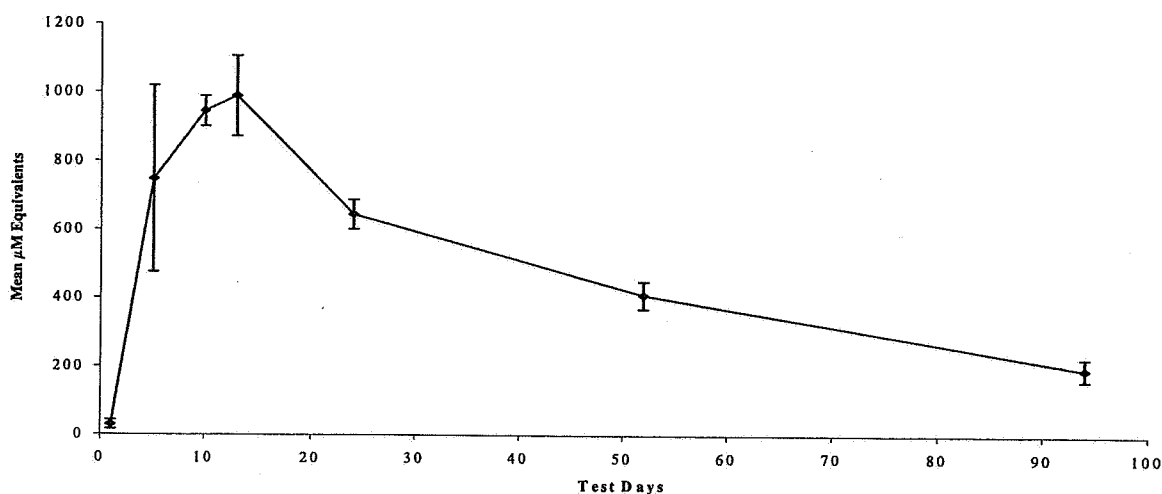


FIGURE 2

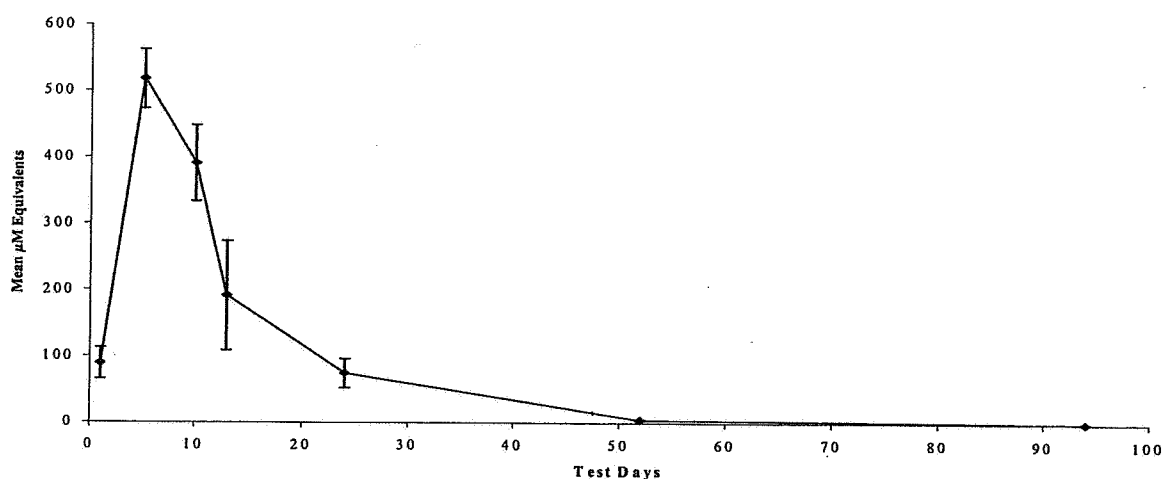
MICROMOLAR EQUIVALENTS IN RAT BLOOD

A. Normalized Rat Blood H-24019 μM Equivalents Resulting from a 10-Day Oral Gavage



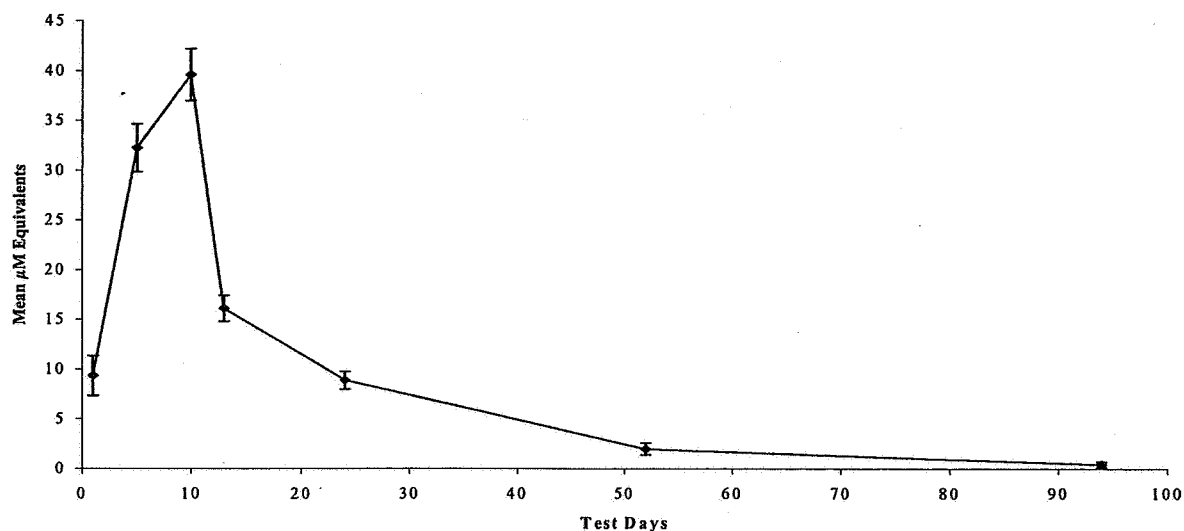
Micromolar (μM) equivalents of H-24019 (positive control) in rat blood resulting from a 10-day oral gavage exposure. Values are means and error bars are standard deviation.

B. Normalized Rat Blood H-24020 μM Equivalents Resulting from a 10-Day Oral Gavage



Micromolar (μM) equivalents of H-24020 (positive control) in rat blood resulting from a 10-day oral gavage exposure. Values are means and error bars are standard deviation.

C. Normalized Rat Blood H-24002 μ M Equivalents Resulting from a 10-Day Oral Gavage

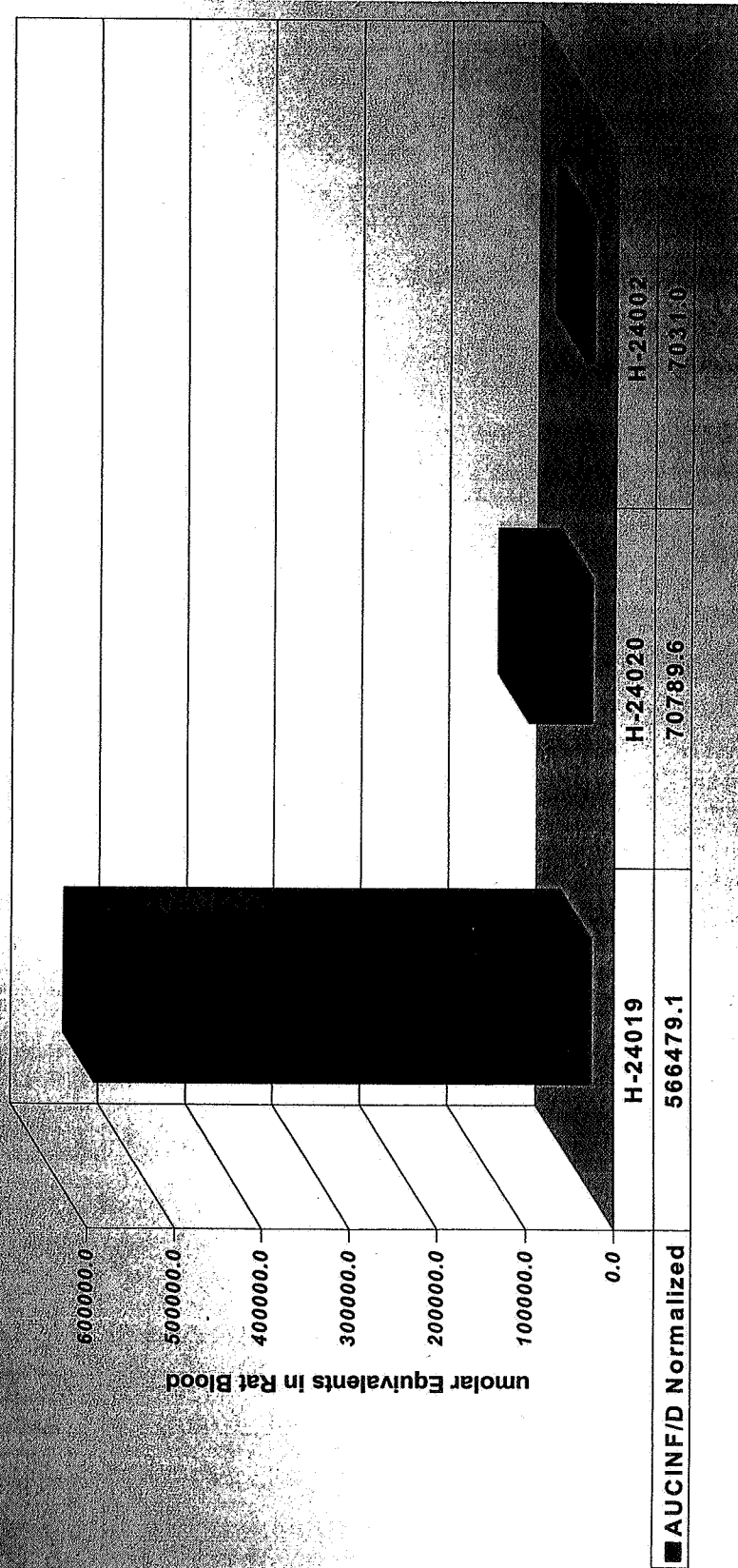


Micromolar (μ M) equivalents of H-24002 (test substance) in rat blood resulting from a 10-day oral gavage exposure. Values are means and error bars are standard deviation.

FIGURE 3

MICROMOLAR EQUIVALENTS IN TEST COMPOUND AND POSITIVE CONTROLS

H-24002 and Positive Control Normalized Blood AUCINF/D in Rats Resulting
from a 10-Day Oral Gavage



APPENDICES

APPENDIX A
Individual Body Weights

INDIVIDUAL BODY WEIGHTS

EXPLANATORY NOTES

ABBREVIATIONS:

SD - sacrificed by design

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

DuPont-2926

DEIONIZED WATER (NEGATIVE CONTROL)						
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS						
ANIMAL NUMBER	GROUP I					
	TEST DAYS					
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	
632649	208.8	208.2	219.8	225.1	240.4	SD test day 5
632650	223.3	231.1	239.3	243.7	261.7	SD test day 5
632651	238.6	243.1	253.6	260.8	276.7	SD test day 5
632652	243.4	240.0	253.0	257.3	272.4	SD test day 5
632653	210.5	210.5	217.6	223.0	236.0	SD test day 5

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

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DEIONIZED WATER (NEGATIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
632654	210.1	217.0	227.9	236.0	248.5	259.9	270.6
632655	234.4	238.1	248.1	258.7	265.7	278.0	289.3
632656	236.4	243.5	250.2	258.0	261.9	272.2	280.3
632657	251.5	255.0	265.0	277.0	292.0	297.3	308.0
632658	220.8	227.5	235.1	240.8	249.3	256.7	264.1

TEST DAYS

ANIMAL NUMBER	DAY 8	DAY 9	DAY 10	TEST DAYS
632654	282.8	286.6	303.1	SD test day 10
632655	295.4	307.1	315.8	SD test day 10
632656	286.5	286.1	294.5	SD test day 10
632657	317.0	324.3	329.6	SD test day 10
632658	274.3	278.2	286.0	SD test day 10

DEIONIZED WATER (NEGATIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP III

ANIMAL NUMBER	TEST DAYS						
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
632659	199.9	208.0	211.0	220.9	231.0	238.9	247.8
632660	232.6	238.9	240.7	251.8	260.8	268.0	275.7
632661	238.1	243.1	247.4	258.1	265.7	273.5	285.0
632662	248.1	255.5	261.5	269.7	279.8	286.2	292.8
632663	219.4	227.9	229.9	241.7	249.9	257.7	265.2

ANIMAL NUMBER	TEST DAYS			
	Day 8	Day 9	Day 10	Day 13
632659	254.1	261.5	270.0	293.1 SD test day 13
632660	279.4	286.1	296.3	309.1 SD test day 13
632661	291.8	302.4	304.5	334.9 SD test day 13
632662	297.0	302.4	309.2	331.1 SD test day 13
632663	272.0	276.4	285.1	299.9 SD test day 13

DEIONIZED WATER (NEGATIVE CONTROL)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP IV

ANIMAL NUMBER	TEST DAYS						
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
632664	208.2	213.9	219.9	226.1	236.6	242.9	252.6
632665	228.3	236.6	244.9	252.4	264.0	274.3	282.1
632666	245.8	251.0	263.4	273.8	282.8	297.4	310.0
632667	254.3	262.3	272.0	285.6	293.6	300.6	315.2
632668	218.7	226.8	238.5	249.3	260.3	270.1	282.0

ANIMAL NUMBER	TEST DAYS						
	Day 8	Day 9	Day 10	Day 13	Day 18	Day 24	
632664	256.0	262.8	273.2	- ^a	318.2	349.0	SD test day 24
632665	288.0	297.9	306.5	- ^a	367.1	408.5	SD test day 24
632666	314.6	326.9	334.0	- ^a	398.1	441.8	SD test day 24
632667	319.9	330.0	342.1	- ^a	414.4	460.4	SD test day 24
632668	291.6	301.7	314.7	- ^a	385.7	437.5	SD test day 24

a Rats not weighed.

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

DuPont-2926

DEIONIZED WATER (NEGATIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP V

ANIMAL NUMBER	TEST DAYS				
	Day 1	Day 2	Day 3	Day 4	Day 5
632669	194.4	197.8	202.5	209.5	215.1
632670	224.5	228.6	237.4	246.7	251.9
632671	226.8	230.9	237.2	243.5	249.0
632672	256.3	267.1	272.4	281.3	295.1
632673	217.3	224.8	230.8	241.3	248.2

ANIMAL NUMBER	TEST DAYS				
	Day 8	Day 9	Day 10	Day 13	Day 18
632669	234.3	232.6	239.6	- ^a	278.1
632670	271.0	271.0	280.9	- ^a	328.3
632671	268.0	273.6	276.0	- ^a	308.4
632672	319.4	328.4	334.8	- ^a	389.8
632673	268.9	276.4	285.2	- ^a	335.6

ANIMAL NUMBER	TEST DAYS				
	Day 32	Day 39	Day 46	Day 52	Day 52
632669	322.8	355.5	366.6	392.4	SD test day 52
632670	389.9	415.7	434.9	449.1	SD test day 52
632671	378.5	421.9	434.6	456.4	SD test day 52
632672	377.5	517.0	542.7	566.6	SD test day 52
632673	400.9	433.8	457.3	484.2	SD test day 52

a Rats not weighed.

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

DuPont-2926

DEIONIZED WATER (NEGATIVE CONTROL)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP VI

ANIMAL NUMBER	TEST DAYS						
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
632674	197.0	205.1	214.1	221.7	232.7	242.0	250.9
632675	228.8	239.3	243.1	255.3	264.9	271.8	278.0
632676	238.3	243.2	252.0	259.8	270.3	280.9	289.4
632677	238.1	240.7	248.2	255.9	261.7	276.0	282.0
632678	211.3	227.6	233.9	244.4	253.6	262.6	266.0

ANIMAL NUMBER	TEST DAYS						
	Day 8	Day 9	Day 10	Day 13	Day 18	Day 24	Day 25
632674	261.7	266.0	276.7	- ^a	336.2	- ^a	380.4
632675	285.7	291.6	296.7	- ^a	352.9	- ^a	389.6
632676	294.1	300.3	309.8	- ^a	368.3	- ^a	411.3
632677	289.0	298.0	302.7	- ^a	356.9	- ^a	397.5
632678	278.3	286.3	291.4	- ^a	351.4	- ^a	387.6

ANIMAL NUMBER	TEST DAYS						
	Day 32	Day 39	Day 46	Day 52	Day 53	Day 60	Day 67
632674	419.5	465.7	471.8	508.2	529.6	545.8	566.2
632675	433.4	482.3	485.0	536.0	540.7	584.8	592.2
632676	441.0	484.3	502.4	530.2	552.8	565.0	571.8
632677	423.9	458.8	472.8	492.8	514.7	525.1	536.4
632678	419.3	460.1	467.2	487.8	502.0	518.0	523.5

a Rats not weighed.

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

DuPont-2926

DEIONIZED WATER (NEGATIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS
GROUP VI

ANIMAL NUMBER	TEST DAYS			
	Day 74	Day 81	Day 88	Day 94
632674	581.9	- ^a	583.5	548.9 SD test day 94
632675	612.8	- ^a	645.4	652.9 SD test day 94
632676	587.0	- ^a	605.1	603.2 SD test day 94
632677	544.2	- ^a	562.0	569.4 SD test day 94
632678	539.3	- ^a	551.6	548.5 SD test day 94

a Rats not weighed.

CORN OIL (NEGATIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

ANIMAL NUMBER	GROUP I				
	DAY 1	DAY 2	TEST DAYS DAY 3	DAY 4	DAY 5
627789	222.6	220.7	223.5	236.9	247.7 SD test day 5
627801	215.9	209.1	223.5	233.5	240.1 SD test day 5
627805	249.4	250.1	263.3	273.6	283.7 SD test day 5
627810	230.5	231.6	241.9	254.4	265.0 SD test day 5
627818	229.7	228.6	239.1	252.4	260.2 SD test day 5

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

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CORN OIL (NEGATIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP II

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
627793	214.8	224.4	232.1	243.1	249.9	257.0	262.0
627797	239.9	245.9	257.3	267.5	280.7	288.0	290.9
627799	228.9	231.4	242.3	246.2	258.9	261.5	266.4
627800	246.9	252.8	265.2	279.3	283.6	295.5	300.1
627808	235.6	241.6	250.1	262.1	270.4	284.1	287.4

ANIMAL NUMBER	TEST DAYS	
	DAY 8	DAY 10

627793	270.6	283.5	SD	test	day	10
627797	303.9	305.1	324.2	SD	test	day 10
627799	280.2	284.3	294.7	SD	test	day 10
627800	312.0	315.4	331.3	SD	test	day 10
627808	303.6	305.7	321.8	SD	test	day 10

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

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CORN OIL (NEGATIVE CONTROL)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP III

ANIMAL NUMBER	DAY 1	DAY 2	TEST DAYS				DAY 6	DAY 7
			DAY 3	DAY 4	DAY 5	DAY 6		
627796	239.8	249.7	253.6	252.5	267.7	277.2	289.8	
627806	227.3	234.2	239.4	242.9	258.5	270.4	275.2	
627807	221.5	225.9	237.1	244.1	254.9	257.7	260.3	
627809	234.2	240.4	252.5	260.3	272.8	277.9	282.6	
627816	235.0	238.6	250.0	258.9	265.1	274.5	278.6	

ANIMAL NUMBER	DAY 8	DAY 9	TEST DAYS		DAY 13
			DAY 10	DAY 13	

627796	285.9	290.1	300.0	322.7	SD test day 13
627806	282.8	285.8	302.8	320.3	SD test day 13
627807	270.7	274.7	280.7	305.2	SD test day 13
627809	297.9	300.2	311.9	336.2	SD test day 13
627816	291.8	296.4	305.7	330.2	SD test day 13

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

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CORN OIL (NEGATIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP IV

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
627791	231.1	235.4	241.2	246.8	255.9	262.6	268.4
627794	224.4	233.0	238.1	247.8	260.0	267.4	270.1
627804	224.7	228.8	230.6	243.0	251.7	252.9	259.5
627812	221.9	231.5	236.3	245.7	255.5	264.9	269.5
627817	233.5	231.3	229.0	244.8	255.4	266.4	270.0

ANIMAL NUMBER	TEST DAYS						
	DAY 8	DAY 9	DAY 10	DAY 13	DAY 20	DAY 24	
627791	274.0	279.1	285.0	- ^a	334.4	365.6	SD test day 24
627794	286.1	289.5	295.4	- ^a	377.4	416.7	SD test day 24
627804	267.2	270.6	278.1	- ^a	345.8	378.1	SD test day 24
627812	278.2	282.7	294.3	- ^a	356.5	388.4	SD test day 24
627817	277.8	280.4	294.6	- ^a	368.7	407.3	SD test day 24

a Rats not weighed.

CORN OIL (NEGATIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS
GROUP V

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
627792	235.8	240.8	244.3	247.9	252.5	264.4	268.1
627798	241.1	253.4	257.6	266.1	272.9	281.9	286.2
627813	214.8	219.2	220.5	233.2	239.8	243.2	246.8
627814	217.5	220.5	223.7	225.2	233.8	236.7	240.6
627815	230.1	242.2	243.8	255.7	265.0	270.0	274.1

ANIMAL NUMBER	TEST DAYS						
	DAY 8	DAY 9	DAY 10	DAY 13	DAY 20	DAY 24	DAY 34
627792	282.4	286.4	295.2	- ^a	360.0	389.2	426.1
627798	294.3	296.3	315.7	- ^a	380.2	403.5	443.1
627813	258.7	259.2	267.9	- ^a	323.6	342.3	367.9
627814	248.0	250.7	257.3	- ^a	299.3	319.4	343.7
627815	289.2	293.4	303.3	- ^a	368.3	396.5	434.9

ANIMAL NUMBER	TEST DAYS				
	DAY 41	DAY 47	DAY 52	SD	test day 52
627792	456.5	482.3	496.8	SD	test day 52
627798	470.7	496.9	517.3	SD	test day 52
627813	395.0	407.2	416.8	SD	test day 52
627814	358.7	372.7	386.9	SD	test day 52
627815	462.6	487.3	505.9	SD	test day 52

a Rats not weighed.

CORN OIL (NEGATIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP VI

ANIMAL NUMBER	TEST DAYS				
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
627795	218.0	219.5	225.3	234.3	239.4
627811	228.6	226.3	236.7	246.1	251.5
627819	248.8	255.3	264.9	274.4	280.4
627820	225.5	228.9	239.2	247.9	255.6
627821	227.5	233.2	240.7	246.1	251.2

ANIMAL NUMBER	TEST DAYS				
	DAY 8	DAY 9	DAY 10	DAY 13	DAY 20
627795	261.4	265.0	270.7	- ^a	308.0
627811	273.0	276.7	285.6	- ^a	337.8
627819	304.5	308.0	324.3	- ^a	399.7
627820	281.3	282.9	292.4	- ^a	367.2
627821	272.6	275.3	281.8	- ^a	330.1

ANIMAL NUMBER	TEST DAYS				
	DAY 41	DAY 47	DAY 52	DAY 55	DAY 61
627795	384.2	398.0	- ^a	411.1	435.7
627811	422.0	439.3	- ^a	455.4	463.0
627819	505.9	534.9	- ^a	551.7	574.4
627820	478.0	504.1	- ^a	529.7	547.1
627821	411.8	426.1	- ^a	439.1	459.0

a Rats not weighed.

Company Sanitized. Does not contain TSCA CBI

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

DuPont-2926

CORN OIL (NEGATIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP VI

ANIMAL NUMBER	DAY 90	DAY 94	TEST DAYS
627795	474.6	485.0	SD test day 94
627811	503.6	511.6	SD test day 94
627819	638.1	653.1	SD test day 94
627820	608.6	618.0	SD test day 94
627821	509.0	521.5	SD test day 94

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

DuPont-2926

CORN OIL:ACETONE (NEGATIVE CONTROL)						
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS						
ANIMAL NUMBER	GROUP I					
	TEST DAYS					
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	
625361	322.6	325.0	337.6	340.3	349.7	SD test day 5
625363	273.7	271.4	278.4	281.7	286.7	SD test day 5
625364	291.1	290.9	299.9	306.0	312.0	SD test day 5
625380	289.4	286.2	291.5	300.1	305.5	SD test day 5
625383	304.7	299.7	302.7	310.7	313.1	SD test day 5

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

DuPont-2926

CORN OIL:ACETONE (NEGATIVE CONTROL)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP II

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
625355	280.0	282.0	293.0	297.9	306.1	311.2	315.7
625362	290.3	294.1	303.5	308.9	313.8	315.8	323.8
625367	301.5	307.8	315.6	320.1	327.7	333.7	345.6
625368	312.3	318.0	326.0	336.4	343.7	347.5	360.8
625378	309.6	306.4	327.3	328.4	333.7	336.6	346.9

ANIMAL NUMBER	TEST DAYS	
	DAY 8	DAY 9

625355	321.7	320.9	333.6	SD test day 10
625362	323.9	332.3	332.9	SD test day 10
625367	349.1	352.4	363.8	SD test day 10
625368	364.2	380.8	386.7	SD test day 10
625378	350.1	354.2	365.4	SD test day 10

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

DuPont-2926

CORN OIL:ACETONE (NEGATIVE Control)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP III

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
625357	311.9	308.8	320.3	328.4	340.5	343.3	361.1
625358	285.7	286.3	295.5	296.4	306.0	302.7	309.2
625370	307.9	316.7	329.5	337.9	346.9	349.8	364.1
625384	294.2	300.0	312.0	309.3	316.3	314.1	321.4
625385	297.6	304.6	313.0	320.4	331.9	334.0	345.4

ANIMAL NUMBER	TEST DAYS			
	DAY 8	DAY 9	DAY 10	DAY 13
625357	364.2	370.3	376.9	405.6 SD test day 13
625358	319.8	321.6	320.3	340.7 SD test day 13
625370	373.4	374.7	385.6	407.0 SD test day 13
625384	325.6	331.0	340.6	357.1 SD test day 13
625385	347.0	349.5	358.9	377.6 SD test day 13

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

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CORN OIL:ACETONE (NEGATIVE CONTROL)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP IV

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
625354	303.0	304.1	310.5	312.2	319.3	324.7	331.2
625365	327.7	328.7	337.9	343.6	357.7	357.2	364.3
625371	294.5	299.0	313.4	318.3	321.8	329.6	338.5
625376	289.7	289.9	302.2	304.9	313.2	317.0	322.8
625381	297.8	297.5	301.7	305.6	314.4	314.4	321.0

ANIMAL NUMBER	TEST DAYS						
	DAY 8	DAY 9	DAY 10	DAY 13	DAY 20	DAY 24	
625354	336.2	337.0	348.8	355.8	377.7	396.1	SD test day 24
625365	370.5	379.3	381.2	407.1	438.2	459.6	SD test day 24
625371	340.3	345.9	351.2	372.6	413.0	447.3	SD test day 24
625376	331.5	339.0	345.2	363.2	399.7	432.9	SD test day 24
625381	321.6	329.1	331.6	341.2	358.2	381.8	SD test day 24

CORN OIL:ACETONE (NEGATIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP V

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
625356	291.7	291.2	304.5	307.0	316.9	319.8	323.9
625359	297.9	303.3	314.0	315.0	323.5	323.5	333.9
625360	296.8	300.7	308.5	312.7	319.1	332.2	339.5
625372	294.8	298.8	310.6	317.4	324.0	329.0	335.6
625374	295.9	302.2	312.1	321.7	323.4	328.3	337.2

ANIMAL NUMBER	TEST DAYS						
	DAY 8	DAY 9	DAY 10	DAY 13	DAY 20	DAY 24	DAY 27
625356	328.8	334.7	341.3	361.9	396.7	- ^a	431.3
625359	339.1	346.2	353.6	372.9	410.0	- ^a	440.9
625360	347.9	354.3	363.4	381.7	419.8	- ^a	465.9
625372	344.7	348.8	355.1	373.1	395.1	- ^a	432.1
625374	338.0	344.6	350.8	371.5	401.3	- ^a	447.2

ANIMAL NUMBER	TEST DAYS	
	DAY 34	DAY 52
625356	466.2	533.7 SD test day 52
625359	467.7	530.3 SD test day 52
625360	484.1	555.4 SD test day 52
625372	454.7	506.2 SD test day 52
625374	466.8	512.3 SD test day 52

a Rats not weighed.

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

DuPont-2926

CORN OIL:ACETONE (NEGATIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP VI

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
625353	305.9	307.3	316.8	325.0	331.7	330.1	342.5
625369	281.7	279.9	289.7	286.9	292.8	295.3	303.8
625373	294.6	301.3	312.7	317.0	325.4	329.0	334.6
625375	289.1	291.0	298.0	307.0	309.6	314.2	323.5
625377	293.9	294.8	302.9	312.0	318.0	317.4	325.0

ANIMAL NUMBER	TEST DAYS						
	DAY 8	DAY 9	DAY 10	DAY 13	DAY 20	DAY 24	DAY 27
625353	344.7	352.7	358.1	371.7	399.1	- ^a	427.7
625369	307.3	311.9	317.2	331.1	347.6	- ^a	374.9
625373	340.6	348.2	352.6	371.5	402.3	- ^a	444.6
625375	324.7	336.0	336.9	350.1	387.9	- ^a	432.3
625377	325.0	333.7	340.7	353.5	376.3	- ^a	405.2

ANIMAL NUMBER	TEST DAYS						
	DAY 34	DAY 52	DAY 76	DAY 90	DAY 94		
625353	453.3	- ^a	544.9	562.8	565.3	SD test day 94	
625369	388.2	- ^a	483.8	505.3	514.8	SD test day 94	
625373	477.1	- ^a	628.8	661.3	673.7	SD test day 94	
625375	455.6	- ^a	567.3	589.8	588.8	SD test day 94	
625377	419.1	- ^a	470.3	492.0	496.6	SD test day 94	

a Rats not weighed.

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

DuPont-2926

H-24019 (POSITIVE CONTROL)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP I

ANIMAL NUMBER	TEST DAYS				
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
625322	290.3	283.7	291.5	298.9	298.0 SD test day 5
625323	285.0	285.5	290.2	290.9	294.0 SD test day 5
625336	316.5	313.5	320.1	327.1	329.0 SD test day 5
625343	288.2	281.9	286.8	291.0	293.7 SD test day 5
625349	303.6	295.9	308.2	310.1	318.1 SD test day 5

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

DuPont-2926

H-24019 (POSITIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP II

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
625320	279.3	283.0	287.7	288.4	295.9	299.4	300.6
625330	286.7	286.1	291.1	296.5	304.0	302.3	306.7
625332	300.0	295.9	304.1	308.8	315.0	322.4	320.7
625341	304.9	309.0	317.5	320.0	325.1	327.5	327.4
625350	257.1	268.5	267.3	272.2	272.6	276.3	283.6

ANIMAL NUMBER	TEST DAYS						
	DAY 8	DAY 9	DAY 10	SD	test	day	10
625320	308.5	306.3	312.1	SD	test	day	10
625330	314.0	312.6	310.1	SD	test	day	10
625332	324.1	321.8	318.3	SD	test	day	10
625341	332.4	320.3	325.6	SD	test	day	10
625350	279.8	282.5	284.3	SD	test	day	10

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

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H-24019 (POSITIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP III

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
625321	307.0	307.8	311.4	319.6	322.3	328.4	335.2
625327	311.4	306.6	312.5	317.8	318.3	319.3	327.6
625342	273.7	275.5	282.3	285.8	290.8	294.2	326.6
625345	291.2	291.7	297.3	303.3	306.4	310.4	316.1
625348	265.5	258.6	268.0	275.2	280.1	285.2	290.6

ANIMAL NUMBER	TEST DAYS		
	DAY 8	DAY 9	DAY 13

625321	337.8	339.6	371.2	SD test day 13
625327	334.3	337.0	355.3	SD test day 13
625342	304.3	305.9	324.4	SD test day 13
625345	317.3	312.9	336.9	SD test day 13
625348	302.7	306.5	336.4	SD test day 13

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

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H-24019 (POSITIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

ANIMAL NUMBER	GROUP IV						
	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
625325	282.8	285.9	291.7	295.5	303.2	309.2	308.3
625328	315.6	315.2	323.9	327.7	335.0	340.4	340.1
625338	264.6	261.9	268.5	272.6	275.7	281.9	284.4
625340	304.0	309.2	316.9	326.0	329.8	334.1	338.4
625352	285.5	283.9	289.1	299.6	307.9	308.2	312.4

ANIMAL NUMBER	TEST DAYS						
	DAY 8	DAY 9	DAY 10	DAY 13	DAY 20	DAY 24	
625325	318.6	321.9	327.4	331.6	355.8	381.3	SD test day 24
625328	352.0	351.7	357.5	367.4	400.2	423.9	SD test day 24
625338	287.4	291.3	290.2	291.1	320.4	339.9	SD test day 24
625340	347.0	352.2	359.2	368.1	389.3	419.0	SD test day 24
625352	316.9	322.3	321.0	329.6	355.7	375.3	SD test day 24

H-24019 (POSITIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP V

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
625324	303.0	298.5	305.8	312.1	320.1	322.8	326.8
625329	318.9	316.3	326.5	335.4	338.3	346.7	351.6
625333	292.4	291.2	297.8	304.1	307.7	312.0	313.5
625334	274.6	277.0	286.4	290.6	292.0	300.1	304.2
625344	262.9	262.2	269.0	273.5	274.5	284.1	-

ANIMAL NUMBER	TEST DAYS						
	DAY 8	DAY 9	DAY 10	DAY 13	DAY 20	DAY 24	DAY 27
625324	332.5	337.9	336.1	299.6	336.0	- ^a	380.3
625329	352.5	360.1	357.0	364.3	396.4	- ^a	423.3
625333	315.8	316.7	319.3	325.8	349.2	- ^a	375.2
625334	292.6	302.2	305.8	312.0	338.6	- ^a	368.8
625344	280.7	285.2	289.3	295.8	309.7	- ^a	330.4

ANIMAL NUMBER	TEST DAYS	
	DAY 34	DAY 52
625324	397.3	447.4 SD test day 52
625329	442.7	498.1 SD test day 52
625333	384.6	427.4 SD test day 52
625334	384.2	426.5 SD test day 52
625344	348.3	391.0 SD test day 52

^a Rats not weighed.

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

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H-24019 (POSITIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP VI

ANIMAL NUMBER	DAY 1	DAY 2	TEST DAYS				DAY 6	DAY 7
			DAY 3	DAY 4	DAY 5	DAY 6		
625326	313.2	317.1	325.5	330.9	336.2	336.0	-	
625335	301.0	303.6	302.3	310.4	315.1	299.6	293.6	
625346	290.2	293.4	300.2	309.5	313.5	318.6	326.0	
625347	266.0	275.6	287.7	300.0	308.5	316.6	326.9	
625351	310.6	310.9	321.1	329.6	338.2	341.6	340.7	

ANIMAL NUMBER	DAY 8	DAY 9	TEST DAYS				DAY 24	DAY 27
			DAY 10	DAY 13	DAY 20	DAY 24		
625326	311.5	308.9	297.5	274.2	335.4	- ^a	390.7	
625335	294.2	285.3	274.0	266.3	340.1	- ^a	393.8	
625346	292.9	290.8	288.4	296.9	352.5	- ^a	388.2	
625347	330.5	330.1	333.0	355.7	402.1	- ^a	436.2	
625351	351.1	357.8	350.5	380.0	413.7	- ^a	452.4	

ANIMAL NUMBER	DAY 34	DAY 52	TEST DAYS				DAY 80	DAY 90	DAY 94
			DAY 62	DAY 76	DAY 80	DAY 90			
625326	427.5	- ^a	497.5	540.0	547.9	565.2	577.5	SD test day 94	
625335	427.0	- ^a	506.0	538.6	547.7	562.1	579.5	SD test day 94	
625346	407.4	- ^a	485.8	523.7	532.8	542.4	556.9	SD test day 94	
625347	466.4	- ^a	568.6	617.8	618.1	632.6	638.9	SD test day 94	
625351	483.3	- ^a	559.0	596.8	607.2	624.0	636.8	SD test day 94	

^a Rats not weighed.

H-24020 (POSITIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

ANIMAL NUMBER	GROUP I				
	DAY 1	DAY 2	TEST DAYS		
			DAY 3	DAY 4	DAY 5
627756	227.2	226.4	233.4	238.6	237.5 SD test day 5
627767	227.0	231.8	237.9	245.8	248.6 SD test day 5
627771	219.5	214.7	226.1	233.5	239.6 SD test day 5
627773	246.8	244.4	252.7	263.8	262.3 SD test day 5
627777	225.4	221.4	232.9	239.4	236.0 SD test day 5

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

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H-24020 (POSITIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP II

ANIMAL NUMBER	DAY 1	DAY 2	TEST DAYS		DAY 5	DAY 6	DAY 7
			DAY 3	DAY 4			
627768	236.9	244.1	245.2	256.5	256.2	265.5	271.4
627774	258.6	261.6	275.8	283.4	289.3	301.5	303.2
627776	212.0	216.3	223.7	226.6	229.6	233.7	236.9
627782	221.6	228.3	237.3	239.0	238.8	244.7	246.7
627785	220.3	221.7	234.7	238.4	241.8	250.5	255.6

ANIMAL NUMBER	DAY 8	DAY 9	TEST DAYS		DAY 10
			DAY 10	DAY 10	
627768	272.3	291.9	293.5	SD test day 10	
627774	319.8	326.3	338.2	SD test day 10	
627776	246.1	252.3	254.4	SD test day 10	
627782	251.0	264.0	268.2	SD test day 10	
627785	260.7	268.5	267.9	SD test day 10	

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

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H-24020 (POSITIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP III

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
627758	235.1	240.3	248.6	255.8	261.2	272.0	276.1
627763	212.1	218.3	226.5	234.3	230.8	235.5	238.0
627764	230.0	235.0	246.1	251.3	254.8	261.7	264.7
627787	235.1	241.0	250.1	257.2	258.6	237.6	240.3
627788	219.4	222.3	232.2	239.6	247.6	256.7	257.9

ANIMAL NUMBER	TEST DAYS			
	DAY 8	DAY 9	DAY 10	DAY 13
627758	280.6	283.6	295.8	SD test day 13
627763	255.2	261.2	272.5	SD test day 13
627764	275.8	281.9	288.0	SD test day 13
627787	221.7	235.7	234.7	SD test day 13
627788	274.1	276.9	309.4	SD test day 13

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

DuPont-2926

H-24020 (POSITIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP IV

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
627759	226.6	232.9	241.4	250.9	254.2	262.1	265.4
627761	240.7	247.4	257.1	262.5	266.7	259.2	262.6
627770	235.6	244.3	253.6	260.1	267.7	277.3	279.8
627779	231.5	237.9	252.6	261.4	262.3	273.8	277.5
627786	211.6	218.2	222.5	230.4	230.6	240.6	244.1

ANIMAL NUMBER	TEST DAYS						
	DAY 8	DAY 9	DAY 10	DAY 13	DAY 20	DAY 24	
627759	277.8	284.9	288.0	- ^a	348.0	380.1	SD test day 24
627761	240.1	257.4	266.9	- ^a	335.7	359.4	SD test day 24
627770	291.4	301.3	306.4	- ^a	355.8	379.8	SD test day 24
627779	289.0	293.4	301.0	- ^a	374.4	406.2	SD test day 24
627786	251.3	255.8	257.0	- ^a	304.4	326.1	SD test day 24

a Rats not weighed.

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

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H-24020 (POSITIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS
GROUP V

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
627757	221.2	225.4	236.3	241.1	247.9	252.2	254.4
627760	226.2	232.0	244.4	251.7	260.2	254.5	258.3
627765	228.3	235.3	247.1	251.6	256.4	261.1	264.7
627772	245.2	256.4	266.2	277.0	276.9	285.0	291.0
627781	219.0	226.3	236.5	242.9	247.2	251.6	256.1

ANIMAL NUMBER	TEST DAYS						
	DAY 8	DAY 9	DAY 10	DAY 13	DAY 20	DAY 24	DAY 34
627757	269.1	276.7	279.7	- ^a	324.3	343.0	372.3
627760	262.6	280.3	287.3	- ^a	348.6	379.9	419.4
627765	271.5	282.4	288.1	- ^a	349.8	382.7	400.9
627772	300.9	307.5	317.0	- ^a	375.5	404.0	446.9
627781	258.1	266.8	271.2	- ^a	315.1	338.8	372.0

ANIMAL NUMBER	TEST DAYS						
	DAY 41	DAY 47	DAY 52	SD	test	day	52
627757	402.8	419.7	436.7	436.7	SD	test	day 52
627760	437.7	448.9	456.5	456.5	SD	test	day 52
627765	422.9	444.8	455.6	455.6	SD	test	day 52
627772	478.4	494.3	513.5	513.5	SD	test	day 52
627781	389.9	408.2	421.0	421.0	SD	test	day 52

a Rats not weighed.

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

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H-24020 (POSITIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP VI

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
627762	227.2	235.0	248.7	257.3	263.0	275.1	279.7
627769	231.1	241.1	255.9	264.2	272.3	286.3	289.9
627775	224.7	235.7	246.8	254.7	265.7	276.7	280.2
627778	213.1	217.4	221.3	225.5	230.1	236.9	240.4
627783	216.4	218.2	226.6	232.0	238.0	243.9	247.6

ANIMAL NUMBER	TEST DAYS						
	DAY 8	DAY 9	DAY 10	DAY 13	DAY 20	DAY 24	DAY 34
627762	285.9	299.1	301.5	- ^a	356.5	381.5	419.6
627769	302.0	309.6	312.5	- ^a	386.6	414.4	456.5
627775	286.6	296.0	304.5	- ^a	353.3	377.4	413.9
627778	244.8	250.8	255.1	- ^a	294.0	320.0	347.1
627783	256.6	259.2	264.3	- ^a	311.3	340.9	380.0

ANIMAL NUMBER	TEST DAYS						
	DAY 41	DAY 47	DAY 52	DAY 55	DAY 61	DAY 68	
627762	438.7	439.9	- ^a	453.5	473.0	471.6	
627769	479.7	474.6	- ^a	512.2	511.4	531.4	
627775	433.2	451.1	- ^a	460.8	477.4	478.6	
627778	356.8	373.5	- ^a	386.0	393.3	398.3	
627783	409.6	426.9	- ^a	449.0	473.8	474.8	

a Rats not weighed.

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

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H-24020 (POSITIVE CONTROL)
INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS
GROUP VI

ANIMAL NUMBER	TEST DAYS	
	DAY 81	DAY 90
627762	500.3	523.3
627769	566.2	603.2
627775	510.4	537.5
627778	410.1	436.5
627783	508.8	538.5
		SD test day 94
		528.6
		SD test day 94
		609.6
		SD test day 94
		552.8
		SD test day 94
		445.3
		SD test day 94
		557.2
		SD test day 94

H-24002 (TEST SUBSTANCE)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP I

ANIMAL NUMBER	TEST DAYS				
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
628192	227.2	224.9	236.5	244.2	251.3 SD test day 5
628195	245.6	250.7	261.4	265.9	279.5 SD test day 5
628207	238.0	241.3	253.4	261.0	269.9 SD test day 5
628211	220.1	224.3	233.4	239.6	250.9 SD test day 5
628212	252.0	250.9	267.8	271.0	281.1 SD test day 5

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

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H-24002 (TEST SUBSTANCE)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP II

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
628187	240.1	246.4	258.3	266.1	277.4	284.5	287.8
628188	258.1	261.5	269.2	279.0	292.3	299.3	302.6
628199	253.4	255.3	263.6	274.6	273.6	284.1	289.4
628209	229.5	238.2	247.6	253.9	259.5	268.7	272.5
628217	218.0	224.4	234.1	239.2	250.6	256.5	260.1

ANIMAL NUMBER	TEST DAYS			
	DAY 8	DAY 9	DAY 10	
628187	306.5	311.2	314.4	SD test day 10
628188	313.4	320.9	328.1	SD test day 10
628199	302.3	306.6	315.3	SD test day 10
628209	285.3	291.2	299.3	SD test day 10
628217	270.7	272.5	283.4	SD test day 10

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

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H-24002 (TEST SUBSTANCE)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP III

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
628190	230.1	235.0	241.3	249.5	256.2	269.3	273.0
628202	220.2	223.8	233.7	238.7	250.6	252.2	255.3
628204	255.6	257.2	267.7	277.4	283.8	293.9	296.4
628206	236.8	238.8	244.6	254.3	261.5	267.4	269.6
628214	239.6	243.7	249.8	254.2	262.0	265.1	268.1

ANIMAL NUMBER	TEST DAYS			
	DAY 8	DAY 9	DAY 10	DAY 13
628190	281.5	287.1	291.3	314.2 SD test day 13
628202	280.4	283.9	294.7	318.6 SD test day 13
628204	318.2	325.6	330.8	361.0 SD test day 13
628206	284.9	290.0	296.5	320.0 SD test day 13
628214	275.8	276.7	285.4	296.9 SD test day 13

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

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H-24002 (TEST SUBSTANCE)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP IV

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
628197	229.5	233.5	240.7	249.5	258.3	258.5	260.9
628198	238.3	239.0	247.1	259.0	266.0	277.7	281.1
628201	216.6	226.1	233.5	239.7	246.5	250.5	254.3
628203	234.0	239.2	251.0	263.7	271.4	275.6	278.1
628216	223.9	224.9	231.9	238.1	245.3	246.2	249.6

ANIMAL NUMBER	TEST DAYS						
	DAY 8	DAY 9	DAY 10	DAY 13	DAY 20	DAY 24	
628197	273.9	277.0	283.0	- ^a	328.0	345.6	SD test day 24
628198	287.8	298.0	302.7	- ^a	352.9	378.8	SD test day 24
628201	266.5	269.2	277.5	- ^a	337.0	362.8	SD test day 24
628203	297.6	300.9	311.3	- ^a	390.2	423.4	SD test day 24
628216	263.6	267.2	271.2	- ^a	323.5	348.9	SD test day 24

a Rats not weighed.

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

DuPont-2926

H-24002 (TEST SUBSTANCE)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP V

ANIMAL NUMBER	DAY 1	DAY 2	TEST DAYS				DAY 5	DAY 6	DAY 7
			DAY 3	DAY 4	DAY 5	DAY 6			
628191	222.1	225.8	233.3	241.8	249.6	253.6	257.3		
628196	233.7	239.7	246.0	260.5	266.8	275.0	276.9		
628208	253.7	258.5	264.8	270.8	279.9	288.8	291.5		
628210	238.8	244.2	254.6	263.4	274.5	280.8	283.1		
628215	224.3	234.3	242.5	249.0	259.2	266.7	269.4		

ANIMAL NUMBER	DAY 8	DAY 9	TEST DAYS				DAY 20	DAY 24	DAY 27
			DAY 10	DAY 13	DAY 20	DAY 24			
628191	275.0	283.5	291.6	- ^a	352.6	- ^a	396.6		
628196	299.9	309.9	316.6	- ^a	403.0	- ^a	451.0		
628208	300.2	304.5	316.2	- ^a	394.1	- ^a	437.6		
628210	298.8	306.8	314.5	- ^a	389.4	- ^a	435.2		
628215	283.3	293.4	301.1	- ^a	367.0	- ^a	404.9		

ANIMAL NUMBER	DAY 33	DAY 41	TEST DAYS				SD test day 51
			DAY 47	DAY 51	DAY 51	DAY 51	
628191	425.3	457.1	482.5	498.3	SD test day 51	SD test day 51	
628196	479.0	509.5	539.6	565.9	SD test day 51	SD test day 51	
628208	462.2	490.1	516.9	543.3	SD test day 51	SD test day 51	
628210	470.0	501.1	523.5	542.0	SD test day 51	SD test day 51	
628215	435.2	469.6	493.2	514.0	SD test day 51	SD test day 51	

a Rats not weighed.

H-24002 (TEST SUBSTANCE)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP VI

ANIMAL NUMBER	TEST DAYS						
	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
628194	221.3	229.5	236.4	242.5	253.2	262.2	266.1
628200	222.5	229.3	238.4	243.8	251.1	258.5	260.4
628213	250.9	259.9	271.6	280.0	289.9	297.8	300.2
628218	236.4	245.1	256.0	264.6	274.9	280.9	283.4
628219	228.5	232.1	241.0	248.7	256.0	266.7	268.7

ANIMAL NUMBER	TEST DAYS						
	DAY 8	DAY 9	DAY 10	DAY 13	DAY 20	DAY 24	DAY 27
628194	282.5	287.6	292.9	- ^a	363.1	- ^a	403.5
628200	271.3	281.8	289.6	- ^a	348.2	- ^a	385.3
628213	315.4	322.8	332.0	- ^a	401.1	- ^a	441.5
628218	303.1	304.7	313.8	- ^a	374.7	- ^a	415.4
628219	278.0	285.4	295.3	- ^a	346.0	- ^a	388.6

ANIMAL NUMBER	TEST DAYS						
	DAY 33	DAY 41	DAY 47	DAY 51	DAY 54	DAY 60	
628194	434.1	460.6	487.0	- ^a	501.0	522.8	
628200	416.8	444.6	465.1	- ^a	469.5	488.3	
628213	458.6	478.3	501.6	- ^a	525.5	539.5	
628218	446.7	472.1	506.8	- ^a	535.6	552.1	
628219	420.8	454.1	478.9	- ^a	501.2	526.8	

a Rats not weighed.

H-24002: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

DuPont-2926

H-24002 (TEST SUBSTANCE)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP VI

ANIMAL NUMBER	TEST DAYS			
	DAY 76	DAY 82	DAY 88	DAY 94
628194	556.5	567.5	567.8	578.2 SD test day 94
628200	521.9	534.2	547.2	556.4 SD test day 94
628213	584.2	597.3	605.2	609.7 SD test day 94
628218	586.6	610.6	625.4	633.8 SD test day 94
628219	562.4	581.1	586.4	591.2 SD test day 94

APPENDIX B

Individual Clinical Observations

DEIONIZED WATER (NEGATIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP I

Animal Number	Observation	Test Day
632649	No abnormalities detected	1-5
632650	No abnormalities detected	1-5
632651	No abnormalities detected	1-5
632652	No abnormalities detected	1-5
632653	No abnormalities detected	1-5

GROUP II

Animal Number	Observation	Test Day
632654	No abnormalities detected	1-10
632655	No abnormalities detected	1-10
632656	No abnormalities detected	1-10
632657	No abnormalities detected	1-10
632658	No abnormalities detected	1-10

GROUP III

Animal Number	Observation	Test Day
632659	No abnormalities detected	1-13
632660	No abnormalities detected	1-13
632661	No abnormalities detected	1-13
632662	No abnormalities detected	1-13
632663	No abnormalities detected	1-13

DEIONIZED WATER (NEGATIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP IV

Animal Number	Observation	Test Day
632664	No abnormalities detected	1-24
632665	No abnormalities detected	1-24
632666	No abnormalities detected	1-24
632667	No abnormalities detected	1-24
632668	No abnormalities detected	1-24

GROUP V

Animal Number	Observation	Test Day
632669	No abnormalities detected	1-52
632670	No abnormalities detected	1-52
632671	No abnormalities detected	1-52
632672	No abnormalities detected	1-52
632673	No abnormalities detected	1-52

GROUP VI

Animal Number	Observation	Test Day
632674	No abnormalities detected	1-88
	Hair Loss, Forelimb, Bilateral	94
632675	No abnormalities detected	1-81
	Hair Loss, Forepaw, Bilateral	88-94
632676	No abnormalities detected	1-94
632677	No abnormalities detected	1-53
	Hair Loss, Forepaw, Bilateral	60-94
632678	No abnormalities detected	1-94

CORN OIL (NEGATIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP I

Animal Number	Observation	Test Day
627789	No abnormalities detected	1-5
627801	No abnormalities detected	1-5
627805	No abnormalities detected	1-5
627810	No abnormalities detected	1-5
627818	No abnormalities detected	1-5

GROUP II

Animal Number	Observation	Test Day
627793	No abnormalities detected	1-10
627797	No abnormalities detected	1-10
627799	No abnormalities detected	1-10
627800	No abnormalities detected	1-10
627808	No abnormalities detected	1-10

GROUP III

Animal Number	Observation	Test Day
627796	No abnormalities detected	1-13
627806	No abnormalities detected	1-13
627807	No abnormalities detected	1-13
627809	No abnormalities detected	1-13
627816	No abnormalities detected	1-13

CORN OIL (NEGATIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP IV

Animal Number	Observation	Test Day
627791	No abnormalities detected	1-24
627794	No abnormalities detected	1-24
627804	No abnormalities detected	1-24
627812	No abnormalities detected	1-24
627817	No abnormalities detected	1-24

GROUP V

Animal Number	Observation	Test Day
627792	No abnormalities detected	1-52
627798	No abnormalities detected	1-52
627813	No abnormalities detected	1-52
627814	No abnormalities detected	1-52
627815	No abnormalities detected	1-52

GROUP VI

Animal Number	Observation	Test Day
627795	No abnormalities detected	1-94
627811	No abnormalities detected	1-94
627819	No abnormalities detected	1-94
627820	No abnormalities detected	1-94
627821	No abnormalities detected	1-94

CORN OIL:ACETONE (NEGATIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP I

Animal Number.	Observation	Test Day
625361	No abnormalities detected	1-5
625363	No abnormalities detected	1-5
625364	No abnormalities detected	1-5
625380	No abnormalities detected	1-5
625383	No abnormalities detected	1-5

GROUP II

Animal Number	Observation	Test Day
625355	No abnormalities detected	1-10
625362	No abnormalities detected	1-10
625367	No abnormalities detected	1-10
625368	No abnormalities detected	1-10
625378	No abnormalities detected	1-10

GROUP III

Animal Number	Observation	Test Day
625357	No abnormalities detected	1-13
625358	No abnormalities detected	1-13
625370	No abnormalities detected	1-13
625384	No abnormalities detected	1-13
625385	No abnormalities detected	1-13

CORN OIL:ACETONE (NEGATIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP IV

Animal Number	Observation	Test Day
625354	No abnormalities detected	1-24
625365	No abnormalities detected	1-24
625371	No abnormalities detected	1-24
625376	No abnormalities detected	1-24
625381	No abnormalities detected	1-24

GROUP V

Animal Number	Observation	Test Day
625356	No abnormalities detected	1-52
625359	No abnormalities detected	1-52
625360	No abnormalities detected	1-52
625372	No abnormalities detected	1-52
625374	No abnormalities detected	1-52

GROUP VI

Animal Number	Observation	Test Day
625353	No abnormalities detected	1-94
625369	No abnormalities detected	1-94
625373	No abnormalities detected	1-94
625375	No abnormalities detected	1-94
625377	No abnormalities detected	1-94

H-24019 (POSITIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP I

Animal Number	Observation	Test Day
625322	No abnormalities detected	1-5
625323	No abnormalities detected	1-5
625336	No abnormalities detected	1-5
625343	No abnormalities detected	1-5
625349	No abnormalities detected	1-5

GROUP II

Animal Number	Observation	Test Day
625320	No abnormalities detected	1-10
625330	No abnormalities detected	1-10
625332	No abnormalities detected	1-10
625341	No abnormalities detected	1-4, 6-10
	Diarrhea	5
625350	No abnormalities detected	1-10

GROUP III

Animal Number	Observation	Test Day
625321	No abnormalities detected	1-4, 6-13
	Diarrhea	5
625327	No abnormalities detected	1-13
625342	No abnormalities detected	1-13
625345	No abnormalities detected	1-13
625348	No abnormalities detected	1-13

H-24019 (POSITIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP IV

Animal Number	Observation	Test Day
625325	No abnormalities detected	1-24
625328	No abnormalities detected	1-24
625338	No abnormalities detected	1-6, 8-24
	Salivation	7
625340	No abnormalities detected	1-24
625352	No abnormalities detected	1-24

GROUP V

Animal Number	Observation	Test Day
625324	No abnormalities detected	1-52
625329	No abnormalities detected	1-6, 8-52
	Salivation	7
625333	No abnormalities detected	1-6, 8-52
	Salivation	7
625334	No abnormalities detected	1-52
625344	No abnormalities detected	1-52

GROUP VI

Animal Number	Observation	Test Day
625326	No abnormalities detected	1-6, 9-76, 77-94
	Salivation	7-8
	Alopecia both front legs	76
625335	Alopecia abdomen	7, 8, 9, 10, 13, 20, 27
625346	No abnormalities detected	1-6, 11-94
	Salivation	7-8
	Black ocular discharge	8
	Yellow-stained perineum	8
	Red-stained chin	8
	Brown-stained chin	9-10
625347	No abnormalities detected	1-94
625351	No abnormalities detected	1-6, 8-94
	Salivation	7

H-24020 (POSITIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP I		
Animal Number	Observation	Test Day
627756	No abnormalities detected	1-5
627767	No abnormalities detected	1-5
627771	No abnormalities detected	1-5
627773	No abnormalities detected	1-5
627777	No abnormalities detected	1-5

GROUP II		
Animal Number	Observation	Test Day
627768	No abnormalities detected	1-10
627774	No abnormalities detected	1-10
627776	No abnormalities detected	1-10
627782	No abnormalities detected	1-10
627785	No abnormalities detected	1-10

GROUP III		
Animal Number	Observation	Test Day
627758	No abnormalities detected	1-13
627763	No abnormalities detected	1-13
627764	No abnormalities detected	1-13
627787	No abnormalities detected	1-5, 7-13
	Wet perineum	6
627788	No abnormalities detected	1-8, 10-13
	Diarrhea	9

H-24020 (POSITIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP IV

Animal Number	Observation	Test Day
627759	No abnormalities detected	1-24
627761	No abnormalities detected	1-24
627770	No abnormalities detected	1-24
627779	No abnormalities detected	1-24
627786	No abnormalities detected	1-24

GROUP V

Animal Number	Observation	Test Day
627757	No abnormalities detected	1-52
627760	No abnormalities detected	1-52
627765	No abnormalities detected	1, 3-52
	Wet perineum	2
627772	No abnormalities detected	1, 3-52
	Wet perineum	2
627781	No abnormalities detected	1-52

GROUP VI

Animal Number	Observation	Test Day
627762	No abnormalities detected	1-8, 10-94
	Diarrhea	9
627769	No abnormalities detected	1-94
627775	No abnormalities detected	1-94
627778	Alopecia perineum	81, 90, 94
627783	No abnormalities detected	1-23, 94
	Alopecia both front paws	24, 34, 41, 47,
		55, 61,
	Alopecia right front leg	74, 81, 90

H-24002 (TEST SUBSTANCE)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP I

Animal Number	Observation	Test Day
628192	No abnormalities detected	1-5
628195	No abnormalities detected	1-5
628207	No abnormalities detected	1-5
628211	No abnormalities detected	1-5
628212	No abnormalities detected	1-5

GROUP II

Animal Number	Observation	Test Day
628187	No abnormalities detected	1-10
628188	No abnormalities detected	1-10
628199	No abnormalities detected	1-10
628209	No abnormalities detected	1-10
628217	No abnormalities detected	1-10

GROUP III

Animal Number	Observation	Test Day
628190	No abnormalities detected	1-13
628202	No abnormalities detected	1-13
628204	No abnormalities detected	1-13
628206	No abnormalities detected	1-13
628214	No abnormalities detected	1-13

H-24002 (TEST SUBSTANCE)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP IV

Animal Number	Observation	Test Day
628197	No abnormalities detected	1-24
628198	No abnormalities detected	1-24
628201	No abnormalities detected	1-10
	Alopecia right front paw	20, 24
628203	No abnormalities detected	1-24
628216	No abnormalities detected	1-24

GROUP V

Animal Number	Observation	Test Day
628191	No abnormalities detected	1-51
628196	No abnormalities detected	1-51
628208	No abnormalities detected	1-51
628210	No abnormalities detected	1-51
628215	No abnormalities detected	1-51

GROUP VI

Animal Number	Observation	Test Day
628194	No abnormalities detected	1-94
628200	No abnormalities detected	1-94
628213	No abnormalities detected	1-94
628218	No abnormalities detected	1-94
628219	No abnormalities detected	1-94

APPENDIX C

Individual Fluorine Levels

TERMS AND CALCULATIONS

Terms:

Active	Fluorine containing compound
% Active	The % of formulation that is made up of fluorine containing components
Mol Wt Active	The molecular weight of the fluorine containing components (g/mole)
Formulation Dose	The mg of formulation given per kg of animal body weight
% F in Active	The % fluorine in the fluorine containing components of the formulation (weight basis)
Mol Wt F	The molecular weight of fluorine g/mol

Compound Calculations:

Dose Active (mg/kg)	The mg of fluorine containing compound administered per kg of animal body weight. = (% active/100) x Formulation Dose
Dose Active (mmole/kg)	The mmole of fluorine containing compound administered per kg of animal body weight = dose [mg/kg] / Mol Wt Active [mg/mmol]
Dose F (mg/kg)	The mg Fluorine administered per kg of animal body weight = (% F in active/100) x Dose Active [mg/kg]
Dose F (mmol/kg)	The mmole of fluorine administered per kg of animal body weight = Dose F [mg/kg] / Mol Wt F [mg/mmol]
Molar Ratio (Active/F)	The moles of fluorine containing compound per mole of fluorine = Dose Active [mmol/kg] / Dose F [mmol/kg]
Formulation Dose Normalization Factor	The formulation dose that would be required to administer the amount of active needed to achieve the normalized dose = (Normalized dose of Active [mmol/kg] / Dose Active [mmol/kg]) x Formulation Dose

TERMS AND CALCULATIONS

Individual Animal Measurement:

ppm F in blood The ppm fluoride measured in blood

Individual Animal Calculations:

ppm F in Blood minus
Bkg 0.2 ppm The ppm fluoride measured in plasma minus the background fluoride
measured in control animal blood. In this case the value was
established at 0.2 ppm.

ppm F in Blood
normalized to
0.1 mmol/kg Dose The ppm fluoride minus background that would be expected if the
active dose was 0.1 mmol/kg instead of the actual active dose. This
assumes linearity between administered dose and blood fluorine
levels, but is needed because different doses of active were used in the
study.
= (0.1 [mmol/kg] / Active dose [mmol/kg]) x (ppm F in blood
minus background)

μmolar equivalents of
active in blood The μmolar [μmol/L] concentration of fluorine containing compound
in plasma based on the ppm fluorine in plasma normalized to
0.1 mmol/kg active dose. This assumes that all plasma fluorine is
derived from the fluorine-containing component in the formulation.
Note: 1 ppm – 1 mg/L
= (Normalized ppm [mg/L] fluorine in blood / Mol Wt F
[mg/mmol]) x molar ratio active/F [mmol active/mmol F] x
1000 μmol/mmol

FACTORS INFLUENCING INTERPRETATION OF KINETIC ANALYSIS

Considerations:

- The data used for kinetic analysis was from a limited screen and extrapolation should be done cautiously.
- Sample size is low
- Analytical data used without validation
- Steady-state not reached
- Terminal phase may not be reached
- Some compounds are mixtures of fluorinated compounds
- Different active and formulation doses were used
- Different vehicles were used to deliver formulations
- The kinetics apply only to plasma, not to specific tissues or the whole body
- Each compound may have very different potency for producing toxicity

Assumptions: (May or may not be justified in all cases)

- Plasma fluorine concentrations are linear with respect to dose
- Analytical method is appropriate for all types of compounds
- Elimination kinetics can be determined based on total fluorine rather than on concentrations of individual components
- Background plasma Fluorine is 0.2 ppm
- % F data is the % Fluorine of the active (Fluorine containing component(s) in the formulation
- Molecular weight is the molecular weight of the active component in the formulation

Data for H- 24019

Given:

Mol Wt. Active (g/mole):	497	% F in Active:	65
Formulation Dose (mg/kg):	10	Mol Wt. F (g/mol):	19
% Active (F Containing) in Formulation:	100		

Calculated Values:

Dose Active (mg/kg):	10	Dose F (mmol/kg):	0.342
Dose Active (mmole/kg):	0.020	Molar Ratio (Active/F):	0.059
Formulation Dose Normalization Factor:	49.7	Dose F (mg/kg):	6.5

Rat Number	Test Day Sample	ppm F in Blood	ppm F in Blood Minus Bkg 0.2 ppm	ppm F in Blood Normalized to 0.1 mmoles/kg Dose	μmolar Equivalents of Active in Blood
Group I					
625322	1	1.0	0.8	3.98	12.31
625323	1	1.3	1.1	5.47	16.92
625336	1	2.6	2.4	11.93	36.92
625343	1	2.6	2.4	11.93	36.92
625349	1	2.9	2.7	13.42	41.54
Group I					
625322	5	51.7	51.5	255.96	792.31
625323	5	38.0	37.8	187.87	581.54
625336	5	38.7	38.5	191.35	592.31
625343	5	78.5	78.3	389.15	1204.62
625349	5	37.1	36.9	183.39	567.69
Group II					
625320	10	65.6	65.4	325.04	1006.15
625330	10	61.1	60.9	302.67	936.92
625332	10	60.5	60.3	299.69	927.69
625341	10	63.1	62.9	312.61	967.69
625350	10	58.1	57.9	287.76	890.77

Rat Number	Test Day Sample	ppm F in Blood	ppm F in Blood Minus Bkg 0.2 ppm	ppm F in Blood Normalized to 0.1 mmoles/kg Dose	μmolar Equivalents of Active in Blood
Group III					
625321	13	77.2	77.0	382.69	1184.62
625327	13	61.5	61.3	304.66	943.08
625342	13	64.6	64.4	320.07	990.77
625345	13	57.0	56.8	282.30	873.85
625348	13	62.4	62.2	309.13	956.92
Group IV					
625325	24	40.3	40.1	199.30	616.92
625328	24	46.3	46.1	229.12	709.23
625338	24	43.2	43.0	213.71	661.54
625340	24	39.1	38.9	193.33	598.46
625352	24	41.9	41.7	207.25	641.54
Group V					
625324	52	24.7	24.5	121.77	376.92
625329	52	29.8	29.6	147.11	455.38
625333	52	27.3	27.1	134.69	416.92
625334	52	29.1	28.9	143.63	444.62
625344	52	23.8	23.6	117.29	363.08
Group VI					
625326	94	12.4	12.2	60.63	187.69
625335	94	16.4	16.2	80.51	249.23
625346	94	13.1	12.9	64.11	198.46
625347	94	11.0	10.8	53.68	166.15
625351	94	11.6	11.4	56.66	175.38

Data for H- 24020

Given:

Mol Wt. Active (g/mole):	426	% F in Active:	69
Formulation Dose (mg/kg):	20	Mol Wt. F (g/mol):	19
% Active (F Containing) in Formulation:	100		

Calculated Values:

Dose Active (mg/kg):	20	Dose F (mmol/kg):	0.726
Dose Active (mmole/kg):	0.047	Molar Ratio (Active/F):	0.065
Formulation Dose Normalization Factor:	42.6	Dose F (mg/kg):	13.8

Rat Number	Test Day Sample	ppm F in Blood	ppm F in Blood Minus Bkg 0.2 ppm	ppm F in Blood Normalized to 0.1 mmoles/kg Dose	μmolar Equivalents of Active in Blood
Group I					
627773	1	13.2	13.0	27.69	94.20
627771	1	8.1	7.9	16.83	57.25
627767	1	16.5	16.3	34.72	118.12
627756	1	14.1	13.9	29.61	100.72
627777	1	10.7	10.5	22.37	76.09
Group I					
627773	5	75.3	75.1	159.96	544.20
627771	5	66.8	66.6	141.86	482.61
627767	5	64.8	64.6	137.60	468.12
627756	5	80.0	79.8	169.97	578.26
627777	5	71.6	71.4	152.08	517.39
Group II					
627768	10	56.3	56.1	119.49	406.52
627774	10	51.0	50.8	108.20	368.12
627776	10	54.8	54.6	116.30	395.65
627782	10	43.6	43.4	92.44	314.49
627785	10	65.1	64.9	138.24	470.29

Rat Number	Test Day Sample	ppm F in Blood	ppm F in Blood Minus Bkg 0.2 ppm	ppm F in Blood Normalized to 0.1 mmoles/kg Dose	μmolar Equivalents of Active in Blood
Group III					
627758	13	43.5	43.3	92.23	313.77
627764	13	20.7	20.5	43.67	148.55
627787	13	13.2	13.0	27.69	94.20
627763	13	30.8	30.6	65.18	221.74
627788	13	24.9	24.7	52.61	178.99
Group IV					
627759	24	9.2	9.0	19.17	65.22
627779	24	14.9	14.7	31.31	106.52
627770	24	11.6	11.4	24.28	82.61
627761	24	9.9	9.7	20.66	70.29
627786	24	6.7	6.5	13.85	47.10
Group V					
627757	52	0.9	0.7	1.49	5.07
627781	52	0.6	0.4	0.85	2.90
627760	52	1.0	0.8	1.70	5.80
627765	52	0.9	0.7	1.49	5.07
627772	52	0.8	0.6	1.28	4.35
Group VI					
627778	94	0.3	0.1	0.21	0.72
627783	94	<0.2	*	*	*
627762	94	0.2	0.0	0.00	0.00
627775	94	0.2	0.0	0.00	0.00
627769	94	<0.2	*	*	*

* = Below LOD (Level of Detection)

Data for H-24002

Given:

Mol Wt. Active (g/mole):	570	% F in Active:	51
Formulation Dose (mg/kg):	75	Mol Wt. F (g/mol):	19
% Active (F Containing) in Formulation:	47		

Calculated Values:

Dose Active (mg/kg):	35.25	Dose F (mmol/kg):	0.946
Dose Active (mmole/kg):	0.062	Molar Ratio (Active/F):	0.065
Formulation Dose Normalization Factor:	121.3	Dose F (mg/kg):	17.9775

Rat Number	Test Day Sample	ppm F in Blood	ppm F in Blood Minus Bkg 0.2 ppm	ppm F in Blood Normalized to 0.1 mmoles/kg Dose	μ molar Equivalents of Active in Blood
Group I					
628207	1	2.0	1.8	2.91	10.01
628195	1	1.6	1.4	2.26	7.79
628212	1	1.9	1.7	2.75	9.46
628211	1	2.4	2.2	3.56	12.24
628192	1	1.5	1.3	2.10	7.23
Group I					
628207	5	6.1	5.9	9.54	32.82
628195	5	6.1	5.9	9.54	32.82
628212	5	6.0	5.8	9.38	32.26
628211	5	6.5	6.3	10.19	35.04
628192	5	5.3	5.1	8.25	28.37
Group II					
628209	10	7.1	6.9	11.16	38.38
628187	10	8.1	7.9	12.77	43.94
628199	10	7.4	7.2	11.64	40.05
628188	10	6.9	6.7	10.83	37.27
628217	10	7.1	6.9	11.16	38.38

Rat Number	Test Day Sample	ppm F in Blood	ppm F in Blood Minus Bkg 0.2 ppm	ppm F in Blood Normalized to 0.1 mmoles/kg Dose	μ molar Equivalents of Active in Blood
Group III					
628202	13	3.3	3.1	5.01	17.24
628190	13	2.8	2.6	4.20	14.46
628206	13	3.3	3.1	5.01	17.24
628214	13	3.2	3.0	4.85	16.69
628204	13	2.9	2.7	4.37	15.02
Group IV					
628201	24	1.8	1.6	2.59	8.90
628216	24	1.6	1.4	2.26	7.79
628197	24	2.0	1.8	2.91	10.01
628198	24	1.9	1.7	2.75	9.46
628203	24	1.7	1.5	2.43	8.34
Group V					
628208	52	0.7	0.5	0.81	2.78
628191	52	0.4	0.2	0.32	1.11
628215	52	0.6	0.4	0.65	2.23
628196	52	0.6	0.4	0.65	2.23
628210	52	0.5	0.3	0.49	1.67
Group VI					
628218	94	0.2	0.0	0.00	0.00
628213	94	0.3	0.1	0.16	0.56
628194	94	0.3	0.1	0.16	0.56
628200	94	0.3	0.1	0.16	0.56
628219	94	0.3	0.1	0.16	0.56