TRADE SECRET

Study Title

H-24949: Biopersistence Screening
10-Dose Oral Gavage Study in Rats

Laboratory Project ID: DuPont-6543

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STUDY COMPLETED ON: November 26, 2001

PERFORMING LABORATORY: E.I. du Pont de Nemours and Company
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WORK REQUEST NUMBER: [redacted]

SERVICE CODE NUMBER: [redacted]

CERTIFICATION

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

Reviewed by: _____ 26-Nov-2001
Paul Hinderliter, Ph.D.
Postdoctoral Fellow
Date

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STUDY INFORMATION

TEST SUBSTANCE:

Substance Tested: [redacted]

Synonyms/Codes: [redacted]
- H-24949
[redacted]

Haskell Number: 24949

CAS Registry Number: [redacted]

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: Octanoic acid, pentadecafluoro-, ammonium salt

Synonyms/Codes:
- H-24020
- [redacted]
- C-8
- Perfluorooctanoate, ammonium salt
- APFO
- 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: May 22, 2001 / (see report cover page)

In-Life Initiated/Completed: May 22, 2001 / August 23, 2001

STUDY PERSONNEL

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Laboratory Veterinarian: William Singleton, D.V.M., A.C.L.A.M

SUMMARY

The objective of this study was to evaluate the potential for H-24949, when administered by gavage, to be absorbed and to accumulate in a mammalian system. Two groups of 5 male Crl:CD®(SD)IGS BR rats each were exposed to 1000 mg/kg/day of H-24949 for 10 consecutive days. Blood was collected from the orbital sinus of 5 rats (group I) approximately 2 hours after dosing on test days 1 and 5. Approximately 2 hours after the last dose, these rats were euthanized and blood, livers, and fat were collected. Blood was collected from the orbital sinus of the remaining 5 rats (group III) on test days 13, 24, and 52. These rats were euthanized on test day 94 and blood, livers, and fat were collected. Body weights and clinical signs were recorded on each day of dosing and then weekly during the recovery period. Additionally, a negative control, deionized water, and 2 positive controls, H-24019 (10 mg/kg/day) and H-24020 (20 mg/kg/day), were tested as described for H-24949.

No deaths occurred. No test substance-related clinical signs were observed.

Comparison of body weights was complicated by the fact that there was a difference in age on test day 1 between the rats dosed with the test substance and those dosed with the positive controls or negative control. This difference resulted in differences in mean body weights on test day 1. Accounting for the age difference at study start and the expected rate of body weight gain, the mean body weights and mean body weight gains of the rats dosed with H-24949 were lower than the weights of the negative and positive controls.

The mean relative liver weight (liver/body weight) of rats dosed with the test substance, H-24949, was 19% higher than the weight of the negative control rats on day 10. The weights were similar by day 94. The mean relative liver weight of rats dosed with the positive control H-24019 was 38% higher at day 10 than the negative control group. The mean relative liver weight of rats dosed with the positive control H-24020 was 88% higher on day 10 than the negative control group. By day 94, the mean relative liver weights of rats dosed with H-24019 and H-24020 were similar to the negative control group.

A steady-state for fluorine levels in whole blood was not achieved during 10 consecutive days of dosing with 1000 mg/kg H-24949. 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-24949, was 2.68×10^2 compared to AUCINF/D values of 5.22×10^5 and 8.15×10^4 for H-24019 and H-24020, respectively.

The concentration of fluorine in the livers from rats dosed with the test substance, H-24949, was 21.71 μM equivalents on day 10 and 1.01 μM equivalents on day 94. On day 10, mean μM equivalent concentrations of fluorine in the livers from rats dosed with the positive control materials were approximately 220-fold (H-24019) and 40-fold (H-24020) greater than the fluorine concentration in livers from rats treated with the test substance. By day 94, the concentrations were approximately 1280x and 17x the fluorine concentration in rats treated with H-24949.

The fluorine concentration in the fat from rats dosed with the test substance was 105.95 μM equivalents on day 10. On day 94, the concentration was 1.92 μM equivalents. The fluorine concentration of the positive control H-24019 was approximately 2x higher than H-24949 on day 10. However, the fluorine concentration of the test substance was approximately 2x higher at day 10 than the concentration in the other positive control, H-24020. By day 94, the μM equivalent concentration of fluorine in the fat from rats dosed with the positive control H-24019 was approximately 8x higher than H-24949. There was no detectable fluorine by day 94 in the fat from rats dosed with H-24020.

The μM equivalents of fluorine in the liver and fat of animals dosed with the test substance were higher than levels in the blood.

Under the conditions of this study, there was minimal absorption and no retention of fluorine in the blood in rats dosed with H-24949. Administration of the test substance, H-24949, to male rats for 10 consecutive days resulted in some absorption and retention of fluorine in the liver and fat. However, levels in blood and liver in rats dosed with H-24949 were significantly lower than the fluorine levels in rats dosed with the positive control materials, H-24019 and H-24020. Fluorine levels in the fat from rats dosed with the test substance were lower than the levels in fat from rats dosed with the positive control H-24019 but higher than the levels in rats dosed with the positive control H-24020. Liver weights were elevated in rats dosed with the test substance, H-24949 at the end of the dosing period, but not at the end of the recovery period.

INTRODUCTION

The objective of this study was to define the potential of H-24949 to be absorbed and to bioaccumulate in a mammalian system, as indicated by analytical determination of total fluorine in blood, liver, and fat. The test substance was compared to 2 positive controls that were materials previously shown to bioaccumulate in mammals.

The daily dosage of 1000 mg/kg for the test substance was selected based on available toxicity data. The dosage of 1000 mg/kg was selected for the limit dosage for this project. The limit dosage of 1000 mg/kg was chosen for the study and was expected to produce less than a 10% difference in mean body weight over 10 days when compared to the negative control.

MATERIALS AND METHODS

A. Test Substance and Positive Controls

The test substance, H-24949, was supplied by the sponsor as a [redacted] The positive controls, H-24019 and H-24020, were supplied by the sponsor as [redacted] 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 Crl:CD®(SD)IGS BR rats were received from Charles River Laboratories, Inc., Raleigh, North Carolina. The Crl: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 ± 1°C and a relative humidity of 50 ± 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

Each rat was assigned a unique identification number which was recorded on a card affixed to the cage. The last 3 digits of the number were tattooed on the tail of 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 ensure 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. Evaluation of these data did not indicate any conditions that affected the validity of the study.

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 designee of the laboratory animal veterinarian.

E. Study Design

Substance	Vehicle	Dosage (mg/kg)	Number of Animals
Negative Control Deionized water	Not applicable	0	10
Positive Controls H-24019 H-24020	 Acetone/Corn Oil Acetone/Corn Oil	 10 20	 10 10
Test Substance H-24949	Not applicable	1000	10

F. Assignment to Groups and Study Start

After the quarantine period, the rats were selected on the bases of adequate body weight gain and freedom from any clinical signs of disease or injury. The selected rats were arbitrarily assigned to each group.

After assignment to groups, each rat was housed individually. The rats were 7 or 8 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 pathology evaluation.

G. Dosing Material Preparation and Administration

1. Test Substance

H-24949 was dosed as received. The amount of test substance each rat received was based on the body weight collected on each day of dosing and the test substance density of 1.8 g/mL. The test substance was stirred on a magnetic stir plate throughout the dosing procedure to maintain homogeneity.

2. Positive Controls

It was necessary to dissolve H-24019 and H-24020 in acetone before suspending them 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 rats were dosed at a volume of 1 mL/100 g of body weight. The dosing preparations were stirred on a magnetic stir plate throughout the dosing procedure to maintain homogeneity.

3. Negative Control

Deionized water was chosen as the negative control. The rats were dosed at a volume of 1 mL/100 g of body weight. 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 weekly 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 was individually handled and examined for abnormal behavior and appearance.

J. Collection and Analysis of Blood, Livers, and Fat

At time points selected for blood sampling other than sacrifice days, approximately 1 mL of blood was collected into EDTA tubes from the orbital sinus of each rat. Rats designated for sacrifice were euthanized by carbon dioxide anesthesia and exsanguination and blood, livers, and fat were collected according to the following schedules:

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

As much blood as possible was collected into EDTA tubes at sacrifice. The livers and fat were weighed. The fat weights were used only for the calculation of fluorine levels. The liver weights were used for the calculation of fluorine levels and for the calculation of liver weight relative to total body weight. The blood from all rats was refrigerated and the livers were frozen. The livers and fat were appropriately packaged and shipped refrigerated to Jackson Laboratory, Deepwater, New Jersey where they were analyzed for total fluorine. The liver and fat samples remained frozen while shipped.

The total fluorine content of the samples was determined by using a Wickbold torch combustion method, followed by analysis with a fluoride ion selective electrode. The samples were 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 with a fluoride ion selective electrode. Kinetic analysis of the data received (ppm F in each sample) was performed by Haskell Laboratory personnel for evaluation of fluorine biopersistence.

K. Treatment of Fluorine Data

Since the test substance and positive control materals had different toxicity profiles, it was not possible to administer a uniform mg/kg dose for all test materials. Properly conducted kinetic comparisons in situations with varied doses required the use of a normalized dose. The dose-normalization was conducted in μmolar units to accommodate test material molecular weight differences and was adjusted to an arbitrary normalized dose of 0.1 mmoles/kg.

H-24019 and H-24020 were used as positive controls and a dosing diluent was used as the negative control. The percent of fluorine and molecular weight of the test substance and positive controls were used as provided by the sponsor. The measured total fluorine values were used as received (ppm F) from Jackson Laboratory. For the Wickbold torch method, the background fluorine level is 0.2 ppm. This is the limit of detection (LOD) of this method and was subtracted from each sample. The limit of quantification (LOQ) for this method is 0.5 ppm, and any values listed as less than 0.5 ppm were excluded from further treatment.

Since the dosages and molecular weight for positive controls and test material differed, the data were converted from a mass to a molar basis. In addition, the data were standardized to a single reference dose to allow comparison between compounds of differing fluorine content. The doses were first converted from a mg of test material basis to millimoles of fluorine. Raw fluoride ion data (ppm F) were then normalized to a 0.1 millimole dose of active component. Finally the molar dosage and normalized concentration were combined to yield the μmolar (μM) equivalents of active component in the tissue. Detailed calculations can be found in Appendix C. The μM equivalents can be compared across compounds provided the considerations listed in Appendix C are observed.

Noncompartmental analysis was conducted on fluorine data derived from rats dosed with H-24949 and the positive controls using WinNonlin Version 3.1 software (Pharsight Corp, Mountain View, CA). WinNonlin software provided a means of computing derived pharmacokinetic parameters from experimental data. All analysis was calculated using the μM equivalent in the data.

The maximum observed concentration in blood was C_{max} (μM equivalent). Biopersistence was assessed by quantifying terminal elimination blood half-life ($T_{½}$, days). The points included in determination of the $T_{½}$ were selected manually and included only points after apparent log-linear elimination was achieved. Internal exposure was determined by calculating the blood area-under-the-curve (AUC). AUC, which is simply the integral of blood concentration over time, is the most common means for expressing internal dose. With the calculated half-life, the AUC can be extrapolated to infinity (AUCINF) to reflect the elimination of the compound. AUCINF normalized to dose (AUCINF/D) can be used to compare the relative exposures of different compounds and dosages.

L. Statistical Methods

Descriptive statistics (e.g. mean, standard deviation) were used.

RESULTS AND DISCUSSION

A. In-Life Toxicology
(Tables 1-2, Figure 1, Appendices A-B)

No deaths occurred. Hair loss observed in 4 rats and staining observed in one rat dosed with the test substance were considered spurious. A swollen mouth was observed during the dosing period in a negative control rat. One negative control rat exhibited black nasal discharge during the recovery period. Hair loss was observed in rats dosed with H-24019 and H-24020, and a wound was observed in a rat dosed with H-24020. Ocular discharge, dark eyes, corneal opacity, enophthalmus, and exophthalmus observed in several rats are considered to be a result of orbital sinus bleeding.

Comparison of body weights was complicated by the fact that there was a difference in age on test day 1 between the rats dosed with the test substance and those dosed with the positive controls or negative control. This difference resulted in differences in mean body weights on test day 1. The rats dosed with the test substance, H-24949, were older and heavier in weight than the positive and negative control rats. Accounting for the age difference at study start and the expected rate of body weight gain, the mean body weights and mean body weight gains of the rats dosed with H-24949 were lower than the negative and positive controls.

B. Liver Weights
(Table 3, Figures 2, 3, and 7)

1. Test Substance

The mean relative liver weight (liver/body weight) of rats dosed with the test substance, H-24949, was 19% higher than the weights of the negative control group on day 10. The weights were similar by day 94.

2. Positive Controls

The mean relative liver weight of rats dosed with one of the positive controls, H-24019, was 16% higher at day 10 than the liver weight of rats dosed with the test substance, H-24949. By day 94, the weights were similar.

The mean relative liver weight of rats dosed with the other positive control, H-24020, was 58% higher at day 10 than the liver weight of rats dosed with H-24949. By day 94, the weights were similar.

The mean relative liver weight of rats dosed with H-24019 was 38% higher at day 10 than the negative control group. By day 94, the mean relative liver weight of rats dosed with H-24019 was similar to the negative control group. The mean relative liver weight of rats dosed with

H-24020 was 88% higher on day 10 than the negative control group. By day 94, the weights were similar.

Therefore, liver weights of rats dosed with the test substance, H-24949, were elevated at the end of the 10-day dosing period. The mean relative liver weight by the end of recovery in rats dosed with the test substance was similar to the weights in rats dosed with the positive control materials, H-24019 and H-24020.

C. Fluorine Data

(Tables 4-9, Figures 4-9, Appendices C-F)

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 dosage 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 and H-24020 normalized μM equivalents in rat blood continued to rise throughout the dosing period and may not have reached steady-state (Figures 4A and 4B). The Cmax for H-24019 was 541.45 ± 50.37 μM equivalents (Mean ± SD) with a terminal half-life of 42.2 days. The Cmax for H-24020 was 1043.08 ±54.57 μM equivalents (Mean ± SD) with a terminal half-life of 15.1 days. 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 substance. The AUCINF/D for the fluorine component was 5.22×10^5 for H-24019 and 8.15×10^4 for H-24020.

The concentrations of fluorine in the livers on day 10 from rats dosed with the positive control materials were 4802.15 and 866.67 μM equivalents for H-24019 and H-24020, respectively. By day 94, the concentrations were 1292.92 and 17.10 μM equivalents.

The concentrations of fluorine in the fat on day 10 from rats dosed with the positive control materials were 194.46 and 57.25 μM equivalents for H-24019 and H-24020, respectively. By day 94, the concentration of fluorine in the fat from rats dosed with H-24019 was 15.38 μM equivalents. There was no detectable fluorine by day 94 in the fat from rats dosed with H-24020.

3. Test Substance

The H-24949 normalized μM equivalents in rat blood rose rapidly and did not reach steady-state (Figure 4C). The Cmax for H-24949 was 1.77 ± 0.07 μM equivalents (Mean ± SD). Blood was sampled at seven time points throughout the study, with only four of them occurring post-dose. Elimination of H-24949 from the blood showed biphasic behavior. The initial distribution phase half-life was 4.5 days. The terminal elimination half-life could not be accurately calculated because only two points (days 24 and 52) were available and would yield an artificially long half-life. The total internal exposure resulting from a normalized dose was described by AUCINF/D and was the basis for comparison between H-24949 and the positive controls. The AUCINF/D for the fluorine component of H-24949 was $2.68x10^2$ as compared to AUCINF/D values of $5.22x10^5$ and $8.15x10^4$ for H-24019 and H-24020, respectively.

Levels of total fluorine in livers from rats dosed with the test substance, H-24949, were lower than the levels in livers from rats dosed with the positive control materials. The total fluorine concentration in the liver from rats dosed with H-24949 was 21.71 μM equivalents at day 10 and 1.01 μM equivalents at day 94. For the positive control H-24019, the liver concentrations were approximately 220x higher (day 10) and approximately 1280x higher (end of study) than H-24949. For H-24020, the liver concentrations were approximately 40x higher (end of dosing) and 17x higher (end of study) than H-24949.

Levels of total fluorine in fat from rats dosed with the test substance were lower than the levels in fat from rats dosed with the positive control H-24019 but higher than the levels in fat from rats dosed with the positive control H-24020. The fluorine concentration in the fat from rats dosed with the test substance was 105.95 on day 10 and 1.92 μM equivalents on day 94. The fluorine concentration in the fat from rats dosed with the positive control H-24019 was approximately 2x higher than H-24949 at day 10 and 8x higher on day 94. The fluorine concentration in the fat from rats dosed with the test substance was approximately 2x higher than the concentration in fat from rats dosed with the other positive control, H-24020. By day 94, there was no detectable fluorine the fat from rats dosed with H-24020.

The μM equivalents of fluorine in the liver and fat of animals dosed with the test substance were higher than levels in the blood.

CONCLUSIONS

Rats dosed for 10 consecutive days with 1000 mg/kg H-24949 exhibited no mortality or test substance-related clinical signs. Body weight effects occurred, and liver weights were elevated at the end of the dosing period, but not at the end of the recovery period in rats dosed with the test substance. A steady-state for fluorine in the blood was not achieved during the 10-day dosing period with the test substance. Dose-adjusted areas under the curve (AUCINF/D) for positive controls, H-24019 and H-24020, were approximately 1950x and 305x the AUCINF/D for the test substance.

Under the conditions of this study, there was minimal absorption and no retention of fluorine in the blood following dosing with H-24949. Administration of the test substance, H-24949, to male rats for 10 consecutive days resulted in some absorption and retention of fluorine in the liver and fat. However, levels in blood and liver in rats dosed with H-24949 were significantly lower than the fluorine levels in rats dosed with the positive control materials, H-24019 and H-24020. Fluorine levels in the fat from rats dosed with the test substance were lower than the levels in fat from rats dosed with the positive control H-24019 but higher than the levels in rats dosed with the positive control H-24020.

RECORDS AND SAMPLE STORAGE

All original records will be retained at Haskell Laboratory, E. I. du Pont de Nemours and Company, Newark, Delaware or at Iron Mountain Records Management, 200 Todds Lane, Wilmington, Delaware.

TABLES

TABLE 1

MEAN BODY WEIGHTS (g)

	Negative Control	Positive Controls		Test Substance
Test Days	Deionized Water	H-24019	H-24020	H-24949
1	189.6	184.4	184.1	254.7
2	195.5	189.2	187.8	256.6
3	204.6	199.5	197.8	263.4
4	211.7	206.4	204.8	264.7
5	222.1	216.2	212.5	266.8
6	225.0	222.0	216.0	267.0
7	235.2	229.4	223.6	271.3
8	242.3	233.7	226.9	274.1
9	248.3	240.4	234.2	283.0
10	257.0	246.5	243.0	285.1
17	293.3	290.1	297.4	344.8
24	325.5	313.3	338.6	375.1
31	359.3	348.4	381.9	400.1
38	380.9	370.8	404.9	423.1
45	407.4	403.2	434.4	438.8
52	420.5	422.8	460.6	472.3
59	436.4	439.6	483.1	486.0
66	-	-	-	507.3
67	452.8	455.6	502.7	-
73	472.6	480.1	525.6	515.6
80	489.6	496.5	542.1	536.4
87	497.7	512.2	546.2	561.0
94	511.7	524.6	570.5	571.3

- Indicates the animals were not weighed.

TABLE 2

MEAN BODY WEIGHT GAINS (g)

Dosing

Test Days	Negative Control Deionized Water	Positive Controls H-24019	Positive Controls H-24020	Test Substance H-24949
1-5	32.5	31.8	28.4	12.1
5-10	34.9	30.3	30.5	18.3
1-10	67.4	62.1	58.9	30.4

Recovery

Test Days	Negative Control Deionized Water	Positive Controls H-24019	Positive Controls H-24020	Test Substance H-24949
10-17	36.3	43.6	54.4	59.7
17-24	32.2	23.2	41.2	30.3
24-52	95.0	109.5	122.0	97.2
52-94	91.2	101.8	109.9	99.0
10-94	254.7	278.1	327.5	286.2

TABLE 3

MEAN BODY AND LIVER WEIGHTS (g)

DEIONIZED WATER (NEGATIVE CONTROL)

	Absolute		Mean Relative
Test Days	Body Weight	Liver Weight	Liver Weight (Liver/Body Weight)
10	258.8	10.814	0.042
94	511.7	17.868	0.035

H-24019 (POSITIVE CONTROL)

	Absolute		Mean Relative
Test Days	Body Weight	Liver Weight	Liver Weight (Liver/Body Weight)
10	243.9	14.205	0.058
94	524.6	19.296	0.037

H-24020 (POSITIVE CONTROL)

	Absolute		Mean Relative
Test Days	Body Weight	Liver Weight	Liver Weight (Liver/Body Weight)
10	243.1	19.174	0.079
94	570.5	19.590	0.034

H-24949 (TEST SUBSTANCE)

	Absolute		Mean Relative
Test Days	Body Weight	Liver Weight	Liver Weight (Liver/Body Weight)
10	281.9	14.183	0.050
94	571.3	20.159	0.035

TABLE 4

MEAN BLOOD FLUORINE LEVELS

Test Days	Negative Control Deionized Water (ppm)	Positive Controls H-24019 (ppm)	Positive Controls H-24020 (ppm)	Test Substance H-24949 (ppm)
1	0.60[a]	2.60 (0.1)[b]	9.40 (2.4)	3.00 (1.6)
5	-[c]	31.32 (1.1)	74.92 (7.0)	5.72 (0.9)
10	1.10[a]	68.00 (3.5)	61.76 (5.5)	10.70 (0.4)
13	-[c]	53.98 (1.2)	29.52 (4.9)	4.62 (0.5)
24	0.5[a]	39.62 (3.4)	11.18 (2.9)	1.28 (0.3)
52	-[c]	23.56 (2.1)	2.26 (1.1)	1.18 (0.3)
94	-[c]	12.60 (1.2)	0.85[d] (0.1)	-[c]

a One of 5 values. Four of the values were below the limit of quantification (LOQ) or non-detectable.
b Standard deviation is in parentheses.
c All values were below the LOQ or non-detectable.
d Mean of 2 of the 5 values. Three of the values were below the LOQ.

TABLE 5

MEAN BLOOD FLUORINE CONCENTRATION NORMALIZED TO DOSE

Test Days	Positive Controls H-24019 μM F Equivalents	Positive Controls H-24020 μM F Equivalents	Test Substance H-24949 μM F Equivalents
1	36.92 (1.1)[a]	66.67 (17.5)	0.47 (0.3)
5	478.77 (17.6)	541.45 (50.4)	0.93 (0.2)
10	1043.08 (54.6)	446.09 (39.7)	1.77 (0.1)
13	827.38 (19.0)	212.46 (35.6)	0.74 (0.1)
24	606.46 (53.1)	79.57 (20.8)	0.18 (0.0)
52	359.38 (32.7)	14.93 (7.7)	0.16 (0.1)
94	190.77 (19.2)	4.71[b] (0.5)	-[c]

a Standard deviation is in parentheses.
b Mean of 2 of the 5 values. Three of the values were below the limit of quantification (LOQ).
c All values were below the LOQ.

TABLE 6

MEAN LIVER FLUORINE LEVELS

Test Days	Negative Control Deionized Water (ppm)	Positive Controls H-24019 (ppm)	Positive Controls H-24020 (ppm)	Test Substance H-24949 (ppm)
10	0.90 (0.2)[a]	312.34 (19.7)	119.80 (3.5)	129.36 (25.7)
94	0.78 (0.0)	84.24 (7.4)	2.56 (1.3)	6.20 (1.1)

a Standard deviation is in parentheses.

TABLE 7

MEAN LIVER FLUORINE CONCENTRATION
NORMALIZED TO DOSE

Test Days	Positive Controls H-24019 μM Equivalents	Positive Controls H-24020 μM Equivalents	Test Substance H-24949 μM Equivalents
10	4802.15 (303.8)[a]	866.67 (25.5)	21.71 (4.3)
94	1292.92 (114.1)	17.10 (9.8)	1.01 (0.2)

a Standard deviation is in parentheses.

TABLE 8

MEAN FAT FLUORINE LEVELS

Test Days	Negative Control Deionized Water (ppm)	Positive Controls H-24019 (ppm)	Positive Controls H-24020 (ppm)	Test Substance H-24949 (ppm)
10	-[a]	12.84 (1.7)[b]	8.10 (1.1)	630.52 (250.2)
94	-[a]	1.20 (0.3)	-[a]	11.64 (6.3)

a All values were below the limit of quantification (LOQ) or non-detectable.
b Standard deviation is in parentheses.

TABLE 9

MEAN FAT FLUORINE CONCENTRATION
NORMALIZED TO DOSE

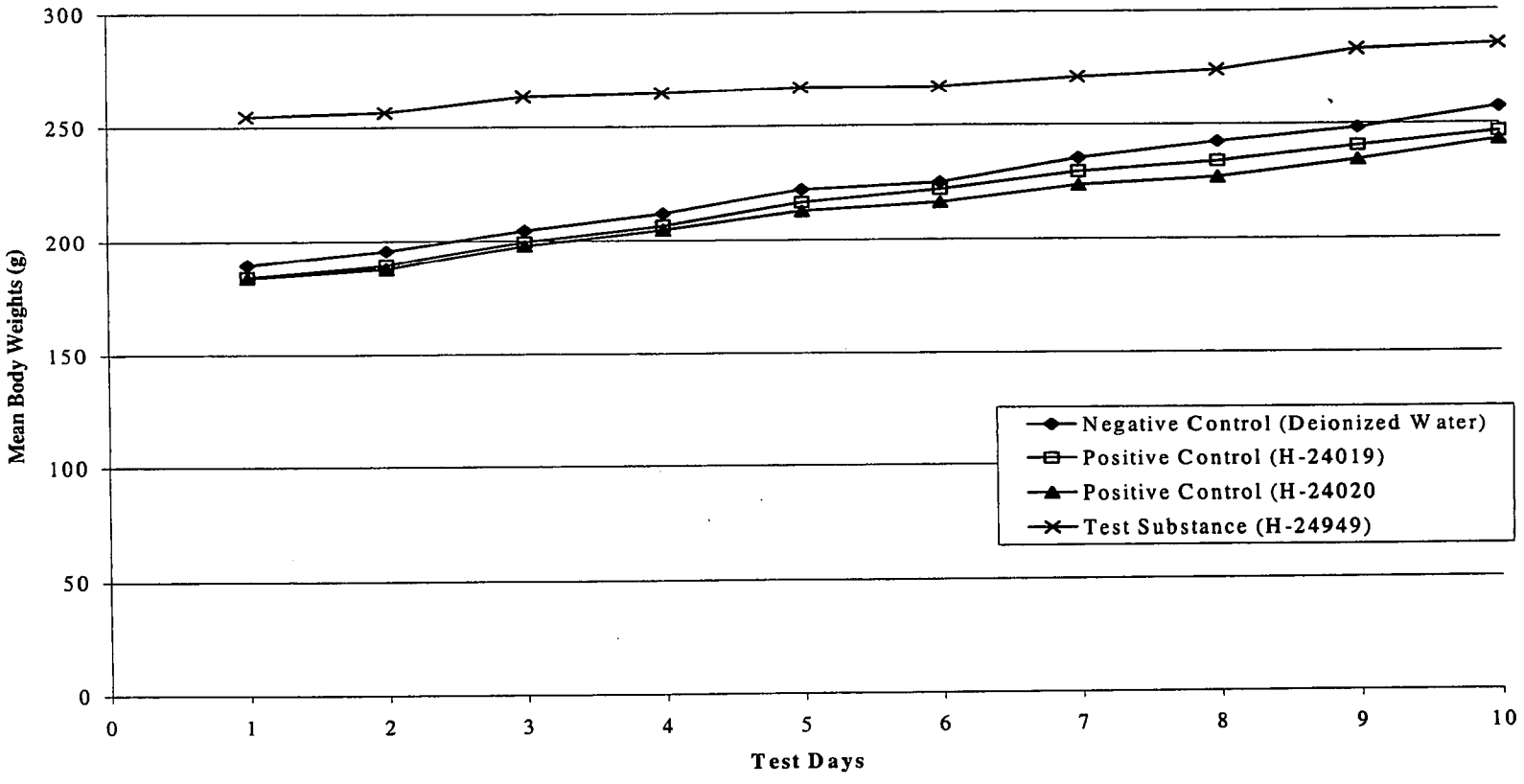
Test Days	Positive Controls H-24019 μM Equivalents	Positive Controls H-24020 μM Equivalents	Test Substance H-24949 μM Equivalents
10	194.46 (26.8)[a]	57.25 (7.8)	105.95 (42.1)
94	15.38 (4.1)	-[b]	1.92 (1.1)

a Standard deviation is in parentheses.
b All values were non-detectable.

FIGURES

FIGURE 1

MEAN BODY WEIGHTS (g)



Company Sanitized. Does not contain TSCA CBI

FIGURE 2

COMPARISON OF MEAN RELATIVE LIVER WEIGHTS:
TEST SUBSTANCE AND NEGATIVE CONTROL

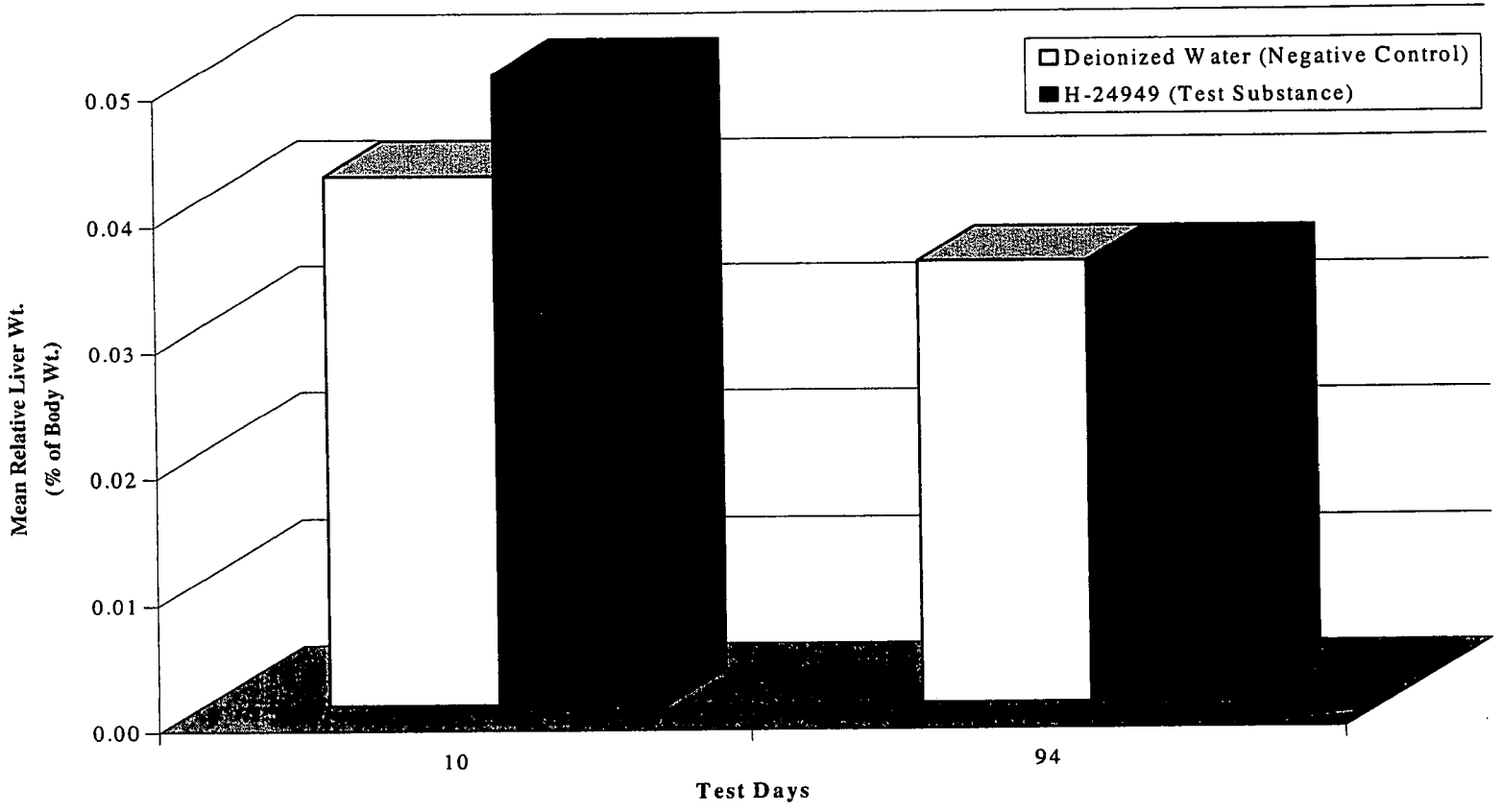


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FIGURE 3

COMPARISON OF MEAN RELATIVE LIVER WEIGHTS:
TEST SUBSTANCE AND POSITIVE CONTROLS

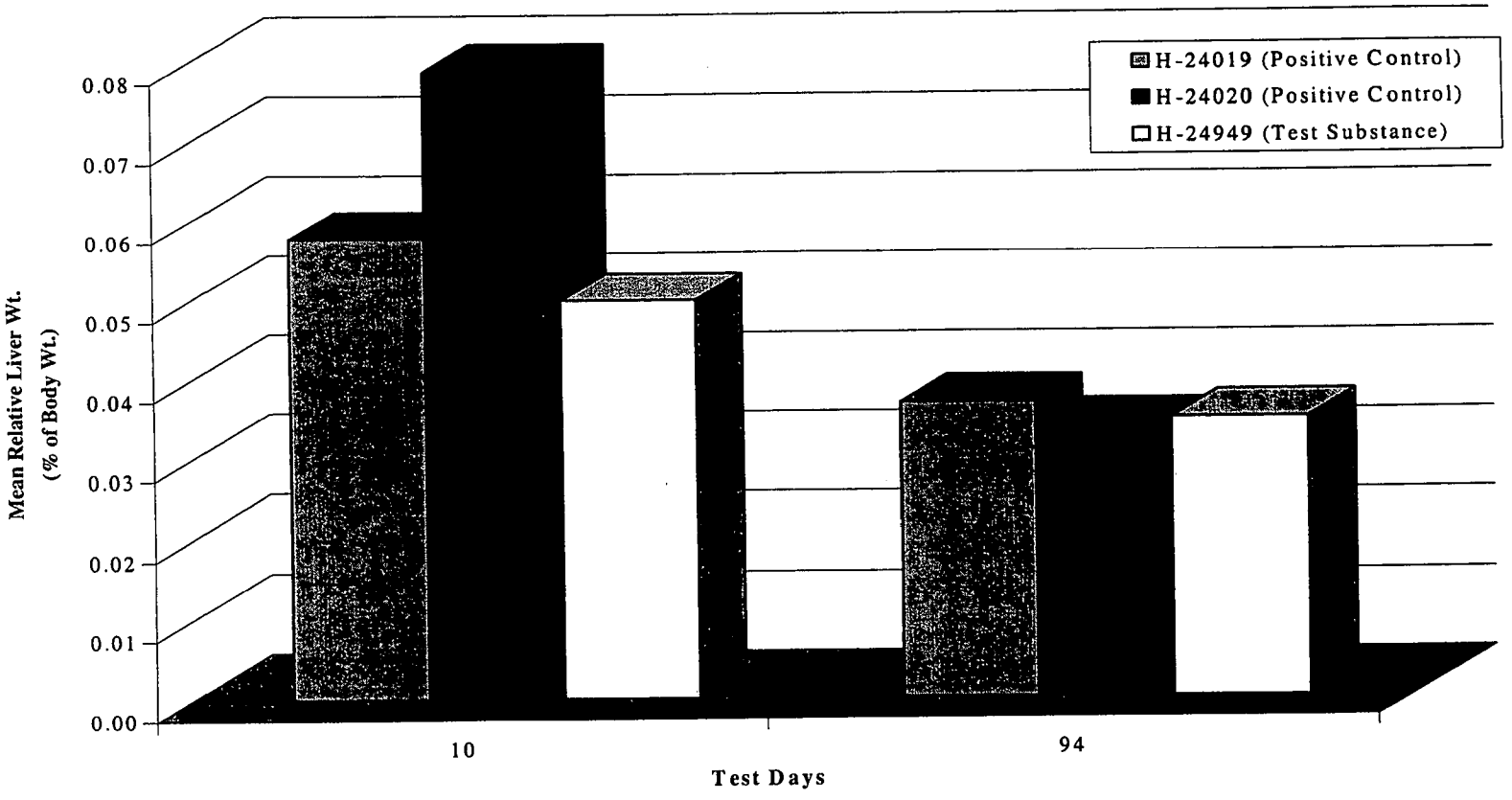

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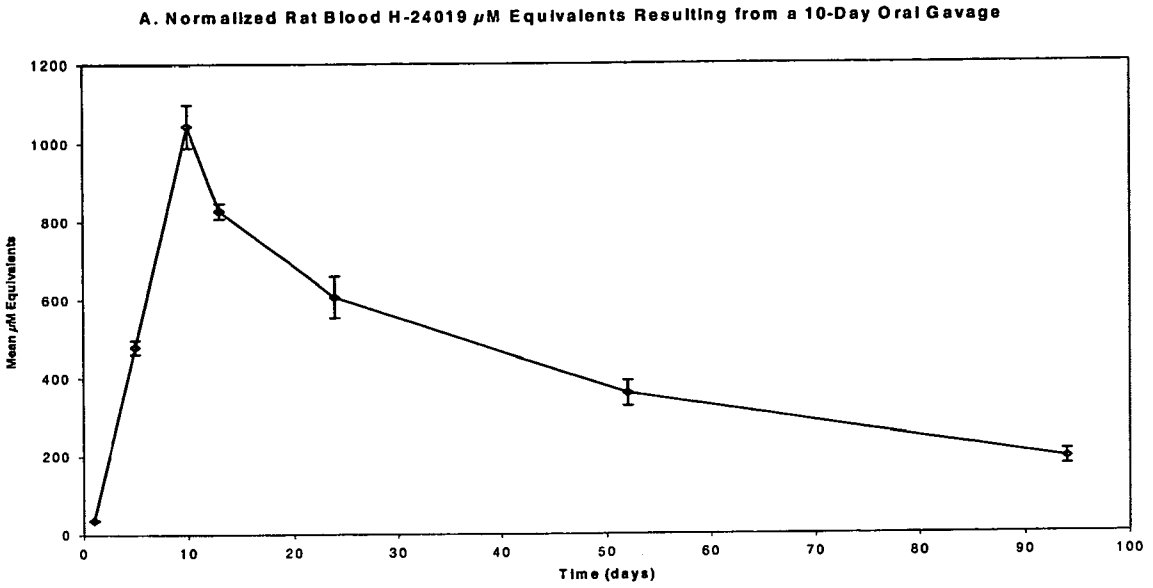
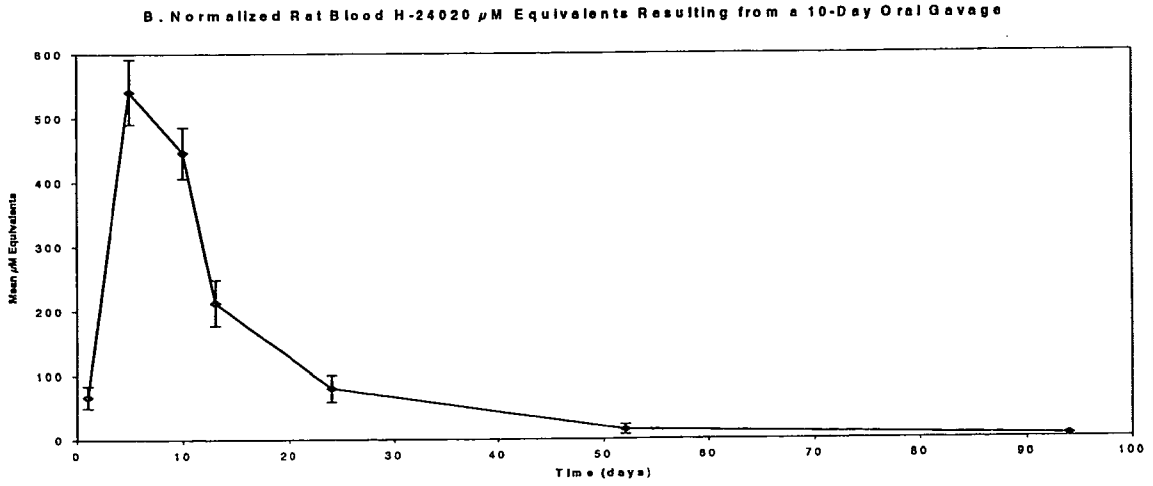
FIGURE 4

MICROMOLAR EQUIVALENTS IN RAT BLOOD

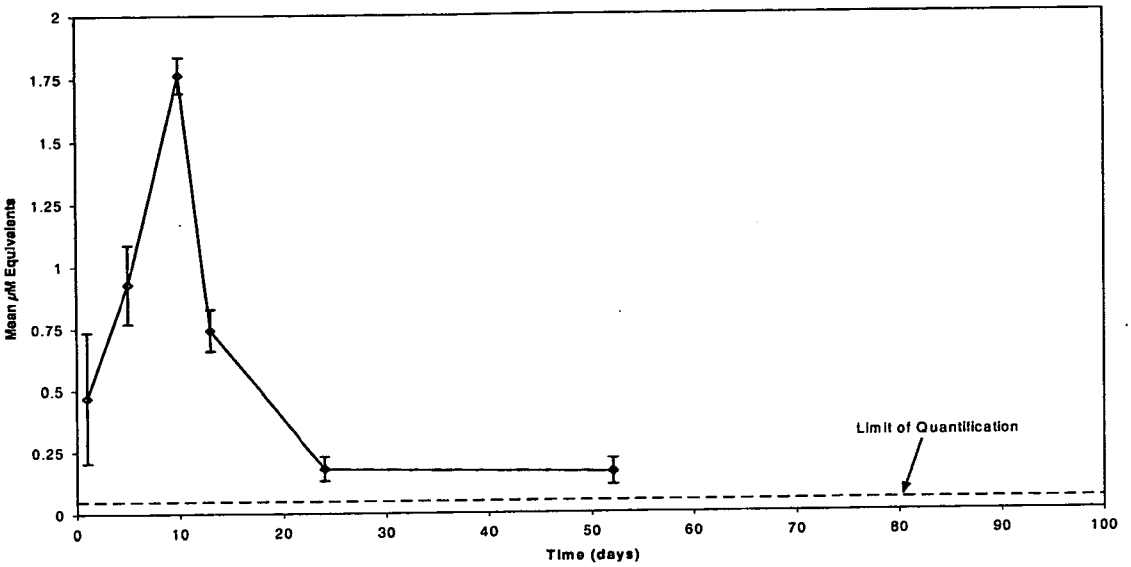


Micromolar (μM) equivalents of H-24019 (positive control) in rat blood resulting from a 10-day oral gavage exposure. Values are means and error bars are standard deviation.



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.

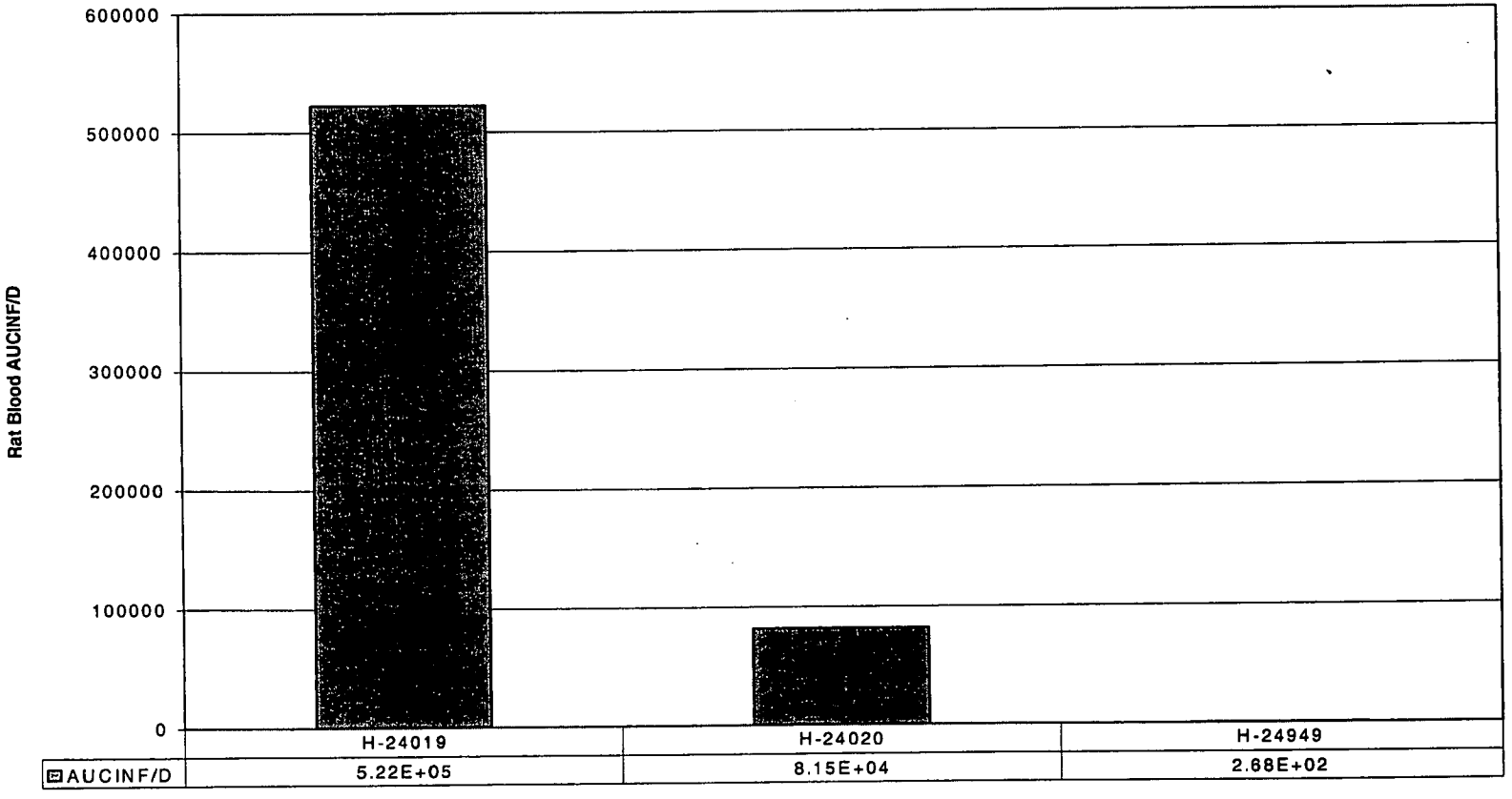
C. Normalized Rat Blood H-24949 μM Equivalents Resulting from a 10-Day Oral Gavage



Micromolar (μM) equivalents of H-24949 (test substance) in rat blood resulting from a 10-day oral gavage exposure. Values are means and error bars are standard deviation.

FIGURE 5

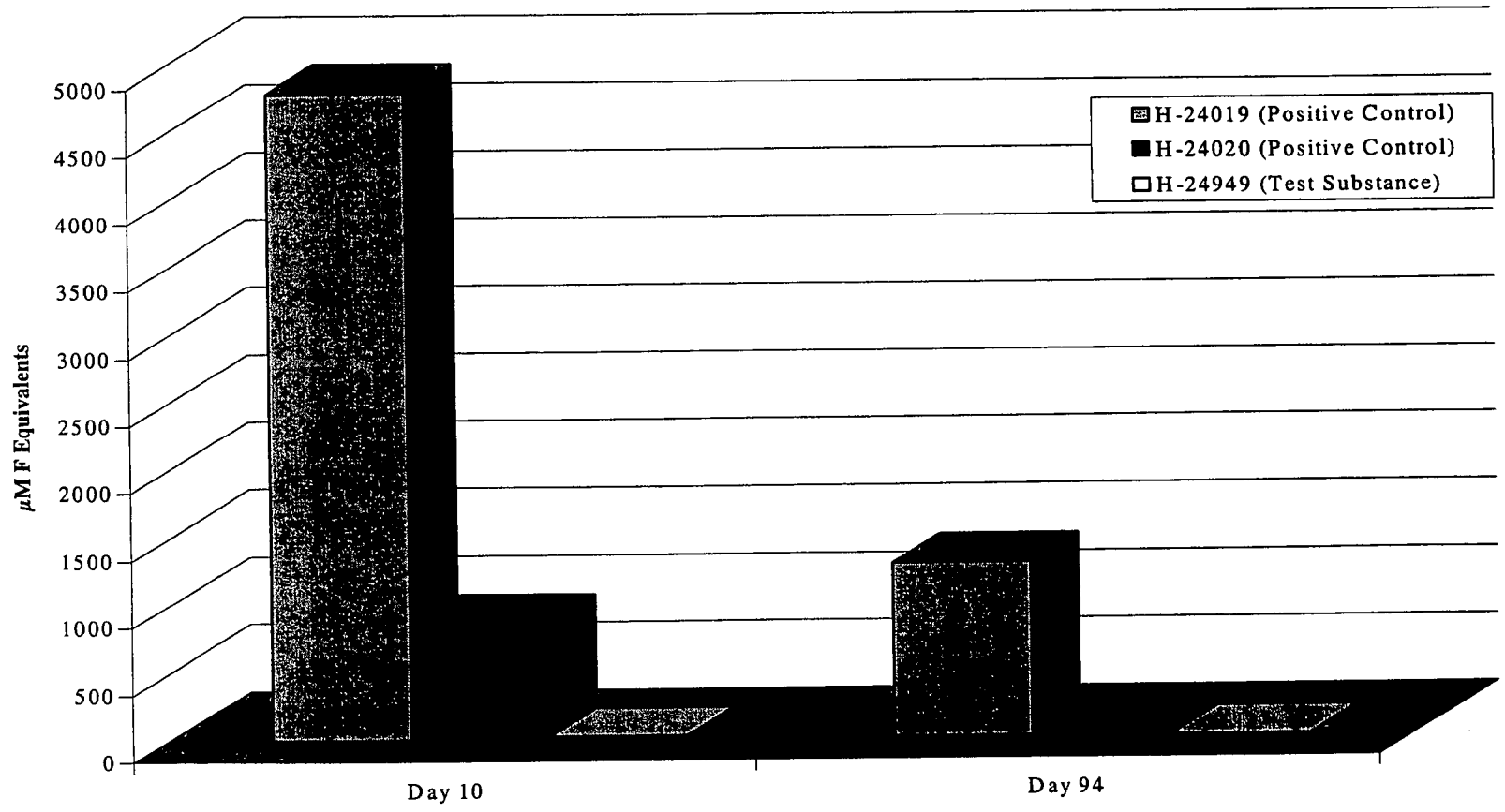
NORMALIZED H-24949 AND POSITIVE CONTROL BLOOD AUCINF/D
RESULTING FROM A 10-DAY ORAL GAVAGE



Company Sanitized. Does not contain TSCA CBI

FIGURE 6

MEAN LIVER FLUORINE CONCENTRATION NORMALIZED TO DOSE



Company Sanitized. Does not contain TSCA CBI

FIGURE 7

COMPARISON OF RELATIVE LIVER WEIGHT AND MEAN LIVER FLUORINE CONCENTRATION FOR H-24949 AND NEGATIVE CONTROL

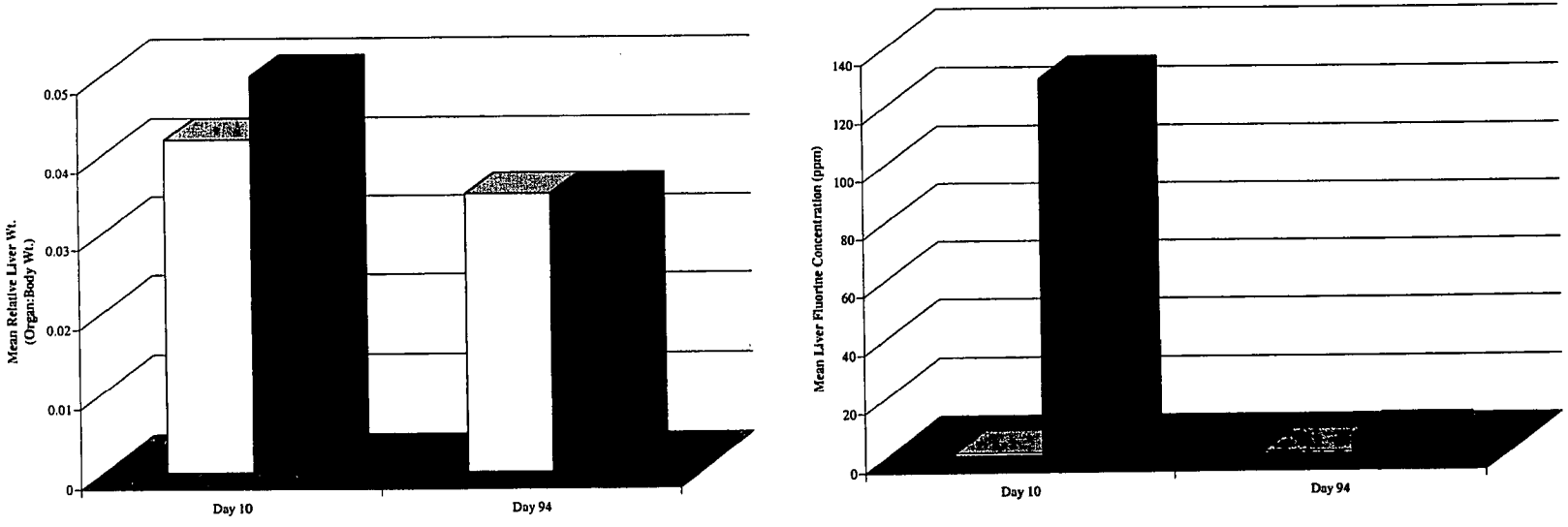


FIGURE 8

MEAN FAT FLUORINE CONCENTRATION NORMALIZED TO DOSE

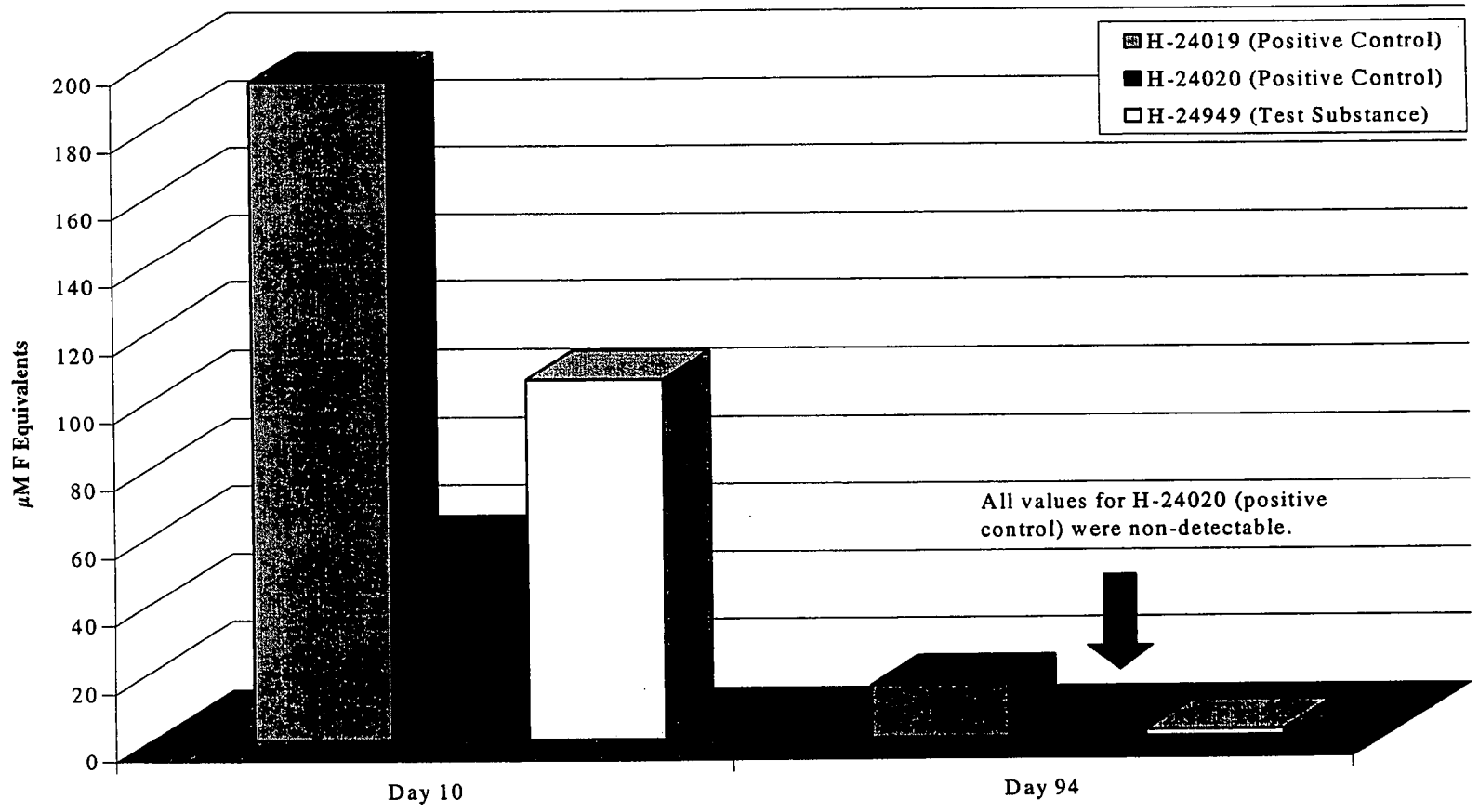


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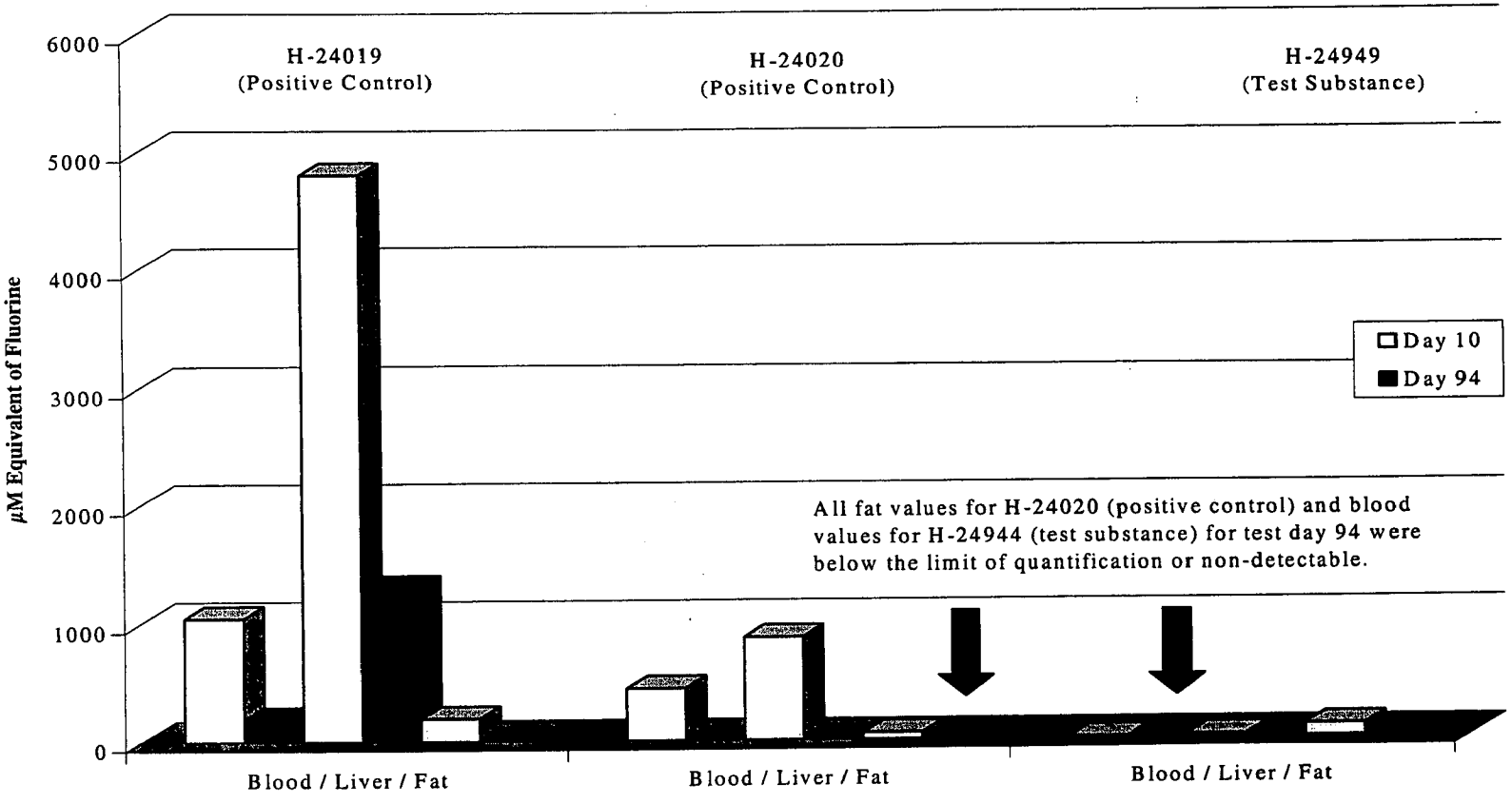
FIGURE 9

COMPARISON OF MEAN BLOOD, MEAN LIVER, AND MEAN FAT FLUORINE CONCENTRATION NORMALIZED TO DOSE



Company Sanitized. Does not contain TSCA CBI

APPENDICES

APPENDIX A

Individual Body Weights

INDIVIDUAL BODY WEIGHTS

EXPLANATORY NOTES

ABBREVIATIONS:

SD - sacrificed by design

DEIONIZED WATER (NEGATIVE CONTROL)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP I

ANIMAL NUMBER	TEST DAY Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
646932	197.1	202.1	212.9	221.5	233.6	234.1	242.4	251.1	256.1
646933	191.9	195.4	205.0	213.2	226.5	219.3	232.9	239.5	246.4
646934	182.6	188.9	195.4	207.0	213.9	215.9	224.2	230.9	238.1
646935	203.0	208.9	218.0	228.1	239.7	243.0	257.2	265.7	270.5
646936	196.8	201.4	208.6	204.0	216.7	218.6	229.9	234.9	240.3

ANIMAL NUMBER	TEST DAY Day 10	
646932	264.7	SD test day 10
646933	254.4	SD test day 10
646934	248.6	SD test day 10
646935	278.0	SD test day 10
646936	248.1	SD test day 10

DEIONIZED WATER (NEGATIVE CONTROL)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP III

ANIMAL NUMBER	TEST DAY Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
646937	184.5	186.8	199.0	205.9	213.6	221.0	229.6	238.7	241.4
646938	163.7	173.8	180.9	189.3	200.6	204.1	215.9	221.8	228.3
646939	193.3	204.2	214.6	221.1	234.4	240.7	248.9	259.2	267.3
646940	191.5	197.1	203.8	209.8	218.5	222.1	229.3	232.0	237.5
646941	191.6	195.9	207.9	216.8	223.1	231.2	241.3	249.1	257.0

ANIMAL NUMBER	TEST DAY Day 10	Day 17	Day 24	Day 31	Day 38	Day 45	Day 52	Day 59	Day 67
646937	249.8	282.6	322.3	366.1	395.0	425.0	443.9	461.7	478.7
646938	237.2	270.4	296.5	325.8	342.9	367.5	373.7	378.7	401.3
646939	277.9	329.7	372.8	415.2	443.2	475.2	484.1	505.7	516.4
646940	244.5	271.5	291.3	317.9	332.8	356.3	367.0	380.3	392.5
646941	266.3	312.4	344.8	371.6	390.7	412.8	433.6	455.8	475.3

ANIMAL NUMBER	TEST DAY Day 73	Day 80	Day 87	Day 94	
646937	504.3	520.5	533.7	545.7	SD test day 94
646938	417.4	431.0	432.1	450.6	SD test day 94
646939	540.1	568.9	578.1	586.9	SD test day 94
646940	407.3	424.0	430.8	449.4	SD test day 94
646941	493.7	503.5	513.8	525.8	SD test day 94

H-24019 (POSITIVE CONTROL)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP I

ANIMAL NUMBER	TEST DAY Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
646910	184.3	185.3	197.3	204.8	212.7	216.3	226.4	232.3	237.5
646911	184.4	187.1	195.7	202.0	211.7	217.2	225.2	225.6	231.9
646912	180.5	185.9	195.9	202.5	211.9	217.7	227.2	232.4	238.5
646913	186.4	189.7	198.1	205.7	221.8	225.0	228.6	238.4	245.8
646914	185.5	189.6	198.8	203.8	215.4	222.7	226.7	231.5	238.8

ANIMAL NUMBER	TEST DAY Day 10	
646910	241.1	SD test day 10
646911	236.6	SD test day 10
646912	241.9	SD test day 10
646913	257.0	SD test day 10
646914	243.0	SD test day 10

H-24019 (POSITIVE CONTROL)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP III

ANIMAL NUMBER	TEST DAY Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
646915	182.7	188.3	200.1	206.3	211.1	220.6	225.8	231.1	236.8
646916	185.0	192.7	205.5	211.6	220.0	226.9	239.5	240.1	249.3
646917	187.8	194.3	205.8	210.4	221.8	227.5	233.9	235.8	244.3
646918	175.5	181.9	189.8	197.6	207.0	212.4	220.2	224.1	228.2
646919	192.0	196.9	207.9	218.9	228.3	234.0	240.8	245.8	252.9

ANIMAL NUMBER	TEST DAY Day 10	Day 17	Day 24	Day 31	Day 38	Day 45	Day 52	Day 59	Day 67
646915	240.4	283.4	302.9	326.7	337.9	371.1	399.7	412.5	433.1
646916	257.0	310.0	334.4	383.2	411.9	450.3	469.8	494.8	511.8
646917	250.2	280.3	308.2	339.7	362.8	387.9	409.0	420.0	441.5
646918	237.1	270.6	292.7	323.2	350.8	379.4	396.7	418.8	433.8
646919	260.2	306.1	328.5	369.2	390.4	427.3	439.0	451.7	457.6

ANIMAL NUMBER	TEST DAY Day 73	Day 80	Day 87	Day 94	
646915	461.2	475.0	498.1	513.3	SD test day 94
646916	544.2	565.5	578.5	590.9	SD test day 94
646917	457.5	464.7	479.5	495.7	SD test day 94
646918	448.1	472.5	480.8	500.3	SD test day 94
646919	489.5	504.8	524.2	522.9	SD test day 94

H-24020 (POSITIVE CONTROL)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP I

ANIMAL NUMBER	TEST DAY Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
646921	204.5	204.9	215.7	222.2	233.3	238.8	244.3	244.9	252.2
646922	178.3	180.9	188.9	197.4	197.7	202.4	202.4	204.0	207.7
646923	185.9	185.1	196.0	202.3	203.5	204.9	219.1	224.9	231.7
646924	188.7	194.6	209.5	212.6	230.4	225.9	236.2	236.5	250.9
646925	172.2	176.0	183.9	193.4	202.7	202.7	215.1	221.5	228.7

ANIMAL NUMBER	TEST DAY Day 10	
646921	262.6	SD test day 10
646922	218.6	SD test day 10
646923	240.6	SD test day 10
646924	259.1	SD test day 10
646925	234.8	SD test day 10

H-24020 (POSITIVE CONTROL)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP III

ANIMAL NUMBER	TEST DAY Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
646926	182.0	187.8	197.0	203.6	206.0	213.2	222.9	229.9	239.7
646927	172.2	178.8	191.1	195.1	206.6	213.2	218.2	228.7	233.1
646928	190.4	195.3	204.5	212.3	222.1	230.1	236.1	235.8	243.4
646929	178.6	182.5	190.7	198.3	203.5	204.2	214.6	210.3	219.2
646930	187.9	191.6	201.0	210.4	219.6	224.4	226.7	232.6	235.3

ANIMAL NUMBER	TEST DAY Day 10	Day 17	Day 24	Day 31	Day 38	Day 45	Day 52	Day 59	Day 67
646926	250.8	297.2	349.3	383.8	412.1	432.1	467.8	493.2	509.5
646927	243.3	306.2	355.1	404.0	424.8	463.2	484.0	511.7	527.2
646928	254.1	310.6	349.4	392.8	422.4	443.5	464.8	492.2	518.6
646929	225.5	280.9	323.2	376.0	396.8	426.4	450.2	463.8	484.2
646930	240.3	292.3	316.2	352.7	368.4	406.8	436.0	454.7	474.2

ANIMAL NUMBER	TEST DAY Day 73	Day 80	Day 87	Day 94	
646926	535.3	551.9	564.4	580.6	SD test day 94
646927	551.2	574.5	541.3	602.5	SD test day 94
646928	540.3	557.0	568.3	581.9	SD test day 94
646929	502.6	509.6	526.7	544.0	SD test day 94
646930	498.5	517.6	530.3	543.4	SD test day 94

H-24949 (TEST SUBSTANCE)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP I

ANIMAL NUMBER	TEST DAY Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
648916	268.8	265.5	262.0	273.9	274.5	271.6	271.7	275.1	280.7
648917	246.4	252.5	261.3	264.4	257.5	259.4	259.2	254.6	258.5
648918	243.2	236.7	244.4	239.0	248.0	244.0	241.1	245.0	245.0
648919	272.5	272.4	279.6	271.8	275.6	269.1	283.6	287.9	301.4
648920	249.7	254.8	272.1	271.6	284.8	282.7	293.6	296.1	307.8

ANIMAL NUMBER	TEST DAY Day 10	
648916	284.0	SD test day 10
648917	258.9	SD test day 10
648918	247.1	SD test day 10
648919	311.7	SD test day 10
648920	307.6	SD test day 10

H-24949 (TEST SUBSTANCE)

INDIVIDUAL BODY WEIGHTS (g) OF MALE RATS

GROUP III

ANIMAL NUMBER	TEST DAY Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
648921	248.0	254.8	260.9	263.2	263.8	262.4	274.3	273.8	286.8
648922	262.1	256.5	271.6	273.1	276.1	282.9	284.9	280.8	299.4
648923	245.2	251.3	255.0	255.7	262.7	265.1	265.9	268.7	273.7
648924	261.2	269.0	276.3	282.4	281.5	291.9	299.7	303.3	313.6
648925	249.6	252.9	250.6	251.7	243.7	240.4	238.7	256.1	263.4

ANIMAL NUMBER	TEST DAY Day 10	Day 17	Day 24	Day 31	Day 38	Day 45	Day 52	Day 59	Day 66
648921	285.1	341.4	379.2	401.9	429.6	453.6	482.9	488.5	508.0
648922	298.5	363.0	395.5	419.9	439.7	474.6	504.6	525.4	552.9
648923	278.8	329.9	351.4	368.0	384.9	400.0	423.8	431.1	451.6
648924	319.4	373.6	405.5	432.5	452.9	422.8	482.8	497.0	515.1
648925	260.0	316.2	343.8	378.0	408.2	442.9	467.3	487.9	509.0

ANIMAL NUMBER	TEST DAY Day 73	Day 80	Day 87	Day 94	
648921	515.6	544.2	563.7	573.9	SD test day 94
648922	561.2	587.8	622.1	630.7	SD test day 94
648923	461.9	474.8	492.8	504.3	SD test day 94
648924	524.9	548.6	574.8	588.7	SD test day 94
648925	514.2	526.6	551.8	558.7	SD test day 94

APPENDIX B

Individual Clinical Observations

DEIONIZED WATER (NEGATIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP I

Animal	Observation	Days
646932	General observation, No Abnormality Detected	1
	Eye Observations, Exophthalmus, Left	2-9
	Eye Observations, Bled via Orbital for Clin Path, Left	1,5
	Discharge, Eye left, Black	10
	Sacrificed by design	10
646933	General observation, No Abnormality Detected	1-5
	Eye Observations, Bled via Orbital for Clin Path, Left	1,5
	Eye Observations, Dark, Left	6-10
	Discharge, Eye left, Black	6-7
	Swollen Observations, Mouth	10
	Sacrificed by design	10
646934	General observation, No Abnormality Detected	1-5,10
	Eye Observations, Bled via Orbital for Clin Path, Left	1,5
	Discharge, Eye left, Black	6-9
	Sacrificed by design	10

DEIONIZED WATER (NEGATIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP I (Continued)

Animal	Observation	Days
646935	General observation, No Abnormality Detected	1-10
	Eye Observations, Bled via Orbital for Clin Path, Left	1,5
	Sacrificed by design	10
646936	General observation, No Abnormality Detected	1-10
	Eye Observations, Bled via Orbital for Clin Path, Left	1,5
	Sacrificed by design	10

DEIONIZED WATER (NEGATIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP III

Animal	Observation	Days
646937	General observation, No Abnormality Detected	1-10,17-94
	Eye Observations, Bled via Orbital for Clin Path, Left	13
	Eye Observations, Bled via Orbital for Clin Path, Right	24,52
	Sacrificed by design	94
646938	General observation, No Abnormality Detected	1-10,17-45
	Eye Observations, Enophthalmus, Right	80-94
	Eye Observations, Exophthalmus, Right	52-73
	Eye Observations, Bled via Orbital for Clin Path, Bilateral	13,52
	Eye Observations, Bled via Orbital for Clin Path, Right	24
	Eye Observations, Corneal Opacity, Right	80-94
	Discharge, Eye right, Black	59
	Sacrificed by design	94
646939	General observation, No Abnormality Detected	1-10,17-94
	Eye Observations, Bled via Orbital for Clin Path, Left	13
	Eye Observations, Bled via Orbital for Clin Path, Right	24,52
	Sacrificed by design	94

DEIONIZED WATER (NEGATIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP III (Continued)

Animal	Observation	Days
646940	General observation, No Abnormality Detected	1-10,17-80,94
	Eye Observations, Bled via Orbital for Clin Path, Left	13
	Eye Observations, Bled via Orbital for Clin Path, Right	24,52
	Discharge, Nose, Black	87
	Sacrificed by design	94
646941	General observation, No Abnormality Detected	1-10,17-94
	Eye Observations, Bled via Orbital for Clin Path, Bilateral	52
	Eye Observations, Bled via Orbital for Clin Path, Left	13
	Eye Observations, Bled via Orbital for Clin Path, Right	24
	Sacrificed by design	94

H-24019 (POSITIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP I

Animal	Observation	Days
646910	General observation, No Abnormality Detected	1-10
	Eye Observations, Bled via Orbital for Clin Path, Left	1,5
	Sacrificed by design	10
646911	General observation, No Abnormality Detected	1,10
	Eye Observations, Bled via Orbital for Clin Path, Left	1,5
	Eye Observations, Dark, Left	2-9
	Sacrificed by design	10
646912	General observation, No Abnormality Detected	1-10
	Eye Observations, Bled via Orbital for Clin Path, Left	1
	Eye Observations, Bled via Orbital for Clin Path, Right	5
	Sacrificed by design	10
646913	General observation, No Abnormality Detected	1-10
	Eye Observations, Bled via Orbital for Clin Path, Left	1,5
	Sacrificed by design	10
646914	General observation, No Abnormality Detected	1-10
	Eye Observations, Bled via Orbital for Clin Path, Left	1,5
	Sacrificed by design	10

H-24019 (POSITIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP III

Animal	Observation	Days
646915	General observation, No Abnormality Detected	1,17-38,73
	Eye Observations, Bled via Orbital for Clin Path, Left	13,24,52
	Discharge, Eye right, Red	2-10
	Hair Loss, Forelimb, Right	80
	Hair Loss, Forepaw, Right	45-67,87-94
	Sacrificed by design	94
646916	General observation, No Abnormality Detected	1-10,17-94
	Eye Observations, Bled via Orbital for Clin Path, Bilateral	24
	Eye Observations, Bled via Orbital for Clin Path, Left	13
	Eye Observations, Bled via Orbital for Clin Path, Right	52
	Sacrificed by design	94
646917	General observation, No Abnormality Detected	1-10,17-94
	Eye Observations, Bled via Orbital for Clin Path, Left	13,24
	Eye Observations, Bled via Orbital for Clin Path, Right	52
	Sacrificed by design	94

H-24019 (POSITIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP III (Continued)

Animal	Observation	Days
646918	General observation, No Abnormality Detected	1-10,17-94
	Eye Observations, Bled via Orbital for Clin Path, Left	13,24
	Eye Observations, Bled via Orbital for Clin Path, Right	52
	Sacrificed by design	94
646919	General observation, No Abnormality Detected	1-10,17-94
	Eye Observations, Bled via Orbital for Clin Path, Left	13,24
	Eye Observations, Bled via Orbital for Clin Path, Right	52
	Sacrificed by design	94

H-24020 (POSITIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP I

Animal	Observation	Days
646921	General observation, No Abnormality Detected	1,5-10
	Eye Observations, Bled via Orbital for Clin Path, Left	1,5
	Eye Observations, Dark, Left	2-4
	Sacrificed by design	10
646922	General observation, No Abnormality Detected	1-10
	Eye Observations, Bled via Orbital for Clin Path, Left	1
	Eye Observations, Bled via Orbital for Clin Path, Right	5
	Sacrificed by design	10
646923	General observation, No Abnormality Detected	1,7-10
	Eye Observations, Exophthalmus, Left	4-6
	Eye Observations, Bled via Orbital for Clin Path, Left	1
	Eye Observations, Bled via Orbital for Clin Path, Right	5
	Eye Observations, Dark, Left	2-6
	Sacrificed by design	10

H-24020 (POSITIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP I (Continued)

Animal	Observation	Days
646924	General observation, No Abnormality Detected	1-10
	Eye Observations, Bled via Orbital for Clin Path, Left	1
	Eye Observations, Bled via Orbital for Clin Path, Right	5
	Sacrificed by design	10
646925	General observation, No Abnormality Detected	1-10
	Eye Observations, Bled via Orbital for Clin Path, Left	1
	Eye Observations, Bled via Orbital for Clin Path, Right	5
	Sacrificed by design	10

H-24020(POSITIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP III.

Animal	Observation	Days
646926	General observation, No Abnormality Detected	1-10,17-94
	Eye Observations, Bled via Orbital for Clin Path, Bilateral	52
	Eye Observations, Bled via Orbital for Clin Path, Left	13,24
	Sacrificed by design	94
646927	General observation, No Abnormality Detected	1-10,17-94
	Eye Observations, Bled via Orbital for Clin Path, Bilateral	52
	Eye Observations, Bled via Orbital for Clin Path, Left	13,24
	Sacrificed by design	94
646928	General observation, No Abnormality Detected	1-10,17-94
	Eye Observations, Bled via Orbital for Clin Path, Left	13,24,52
	Sacrificed by design	94

H-24020(POSITIVE CONTROL)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP III (Continued)

Animal	Observation	Days
646929	General observation, No Abnormality Detected	1-10,17-31
	Eye Observations, Bled via Orbital for Clin Path, Left	13,24
	Eye Observations, Bled via Orbital for Clin Path, Right	52
	Hair Loss, Forelimb, Bilateral	52-73
	Hair Loss, Neck, Left	73
	Hair Loss, Neck, Ventral	38-67,80-94
	Wound, Superficial, Face	59
	Sacrificed by design	94
646930	General observation, No Abnormality Detected	1-10,17-94
	Eye Observations, Bled via Orbital for Clin Path, Left	13,24
	Eye Observations, Bled via Orbital for Clin Path, Right	52
	Sacrificed by design	94

H-24949 (TEST SUBSTANCE)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP I

Animal	Observation	Days
648916	General observation, No Abnormality Detected	1-4
	Eye Observations, Bled via Orbital for Clin Path, Bilateral	1
	Eye Observations, Bled via Orbital for Clin Path, Left	5
	Hair Loss, Abdomen, Ventral	5-10
	Sacrificed by design	10
648917	General observation, No Abnormality Detected	1-10
	Eye Observations, Bled via Orbital for Clin Path, Left	5
	Eye Observations, Bled via Orbital for Clin Path, Right	1
	Sacrificed by design	10
648918	General observation, No Abnormality Detected	1-10
	Eye Observations, Bled via Orbital for Clin Path, Left	5
	Eye Observations, Bled via Orbital for Clin Path, Right	1
	Sacrificed by design	10

H-24949 (TEST SUBSTANCE)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP I (Continued)

Animal	Observation	Days
648919	General observation, No Abnormality Detected	1-5,7-10
	Eye Observations, Bled via Orbital for Clin Path, Left	5
	Eye Observations, Bled via Orbital for Clin Path, Right	1
	Discharge, Eye left, Black	6
	Sacrificed by design	10
648920	General observation, No Abnormality Detected	1-4
	Eye Observations, Bled via Orbital for Clin Path, Left	5
	Eye Observations, Bled via Orbital for Clin Path, Right	1
	Hair Loss, Thoracic, Ventral	5-10
	Sacrificed by design	10

H-24949 (TEST SUBSTANCE)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP III

Animal	Observation	Days
648921	General observation, No Abnormality Detected	1-10,17-52,94
	Eye Observations, Bled via Orbital for Clin Path, Bilateral	53
	Eye Observations, Bled via Orbital for Clin Path, Left	13,24,52
	Eye Observations, Bled via Orbital for Clin Path, Right	24
	Eye Observations, Corneal Opacity, Right	59-87
	Sacrificed by design	94
648922	General observation, No Abnormality Detected	1-9,24-94
	Eye Observations, Bled via Orbital for Clin Path, Left	13,24,52
	Eye Observations, Bled via Orbital for Clin Path, Right	24
	Hair Loss, Ventral body, Medial	10,17
	Sacrificed by design	94
648923	General observation, No Abnormality Detected	1-10,17-94
	Eye Observations, Bled via Orbital for Clin Path, Left	13,24,52
	Eye Observations, Bled via Orbital for Clin Path, Right	24
	Sacrificed by design	94

H-24949 (TEST SUBSTANCE)

INDIVIDUAL CLINICAL OBSERVATIONS IN MALE RATS

GROUP III (Continued)

Animal	Observation	Days
648924	General observation, No Abnormality Detected	1-10,17-38,52-94
	Eye Observations, Bled via Orbital for Clin Path, Left	13,24
	Eye Observations, Bled via Orbital for Clin Path, Right	24,52
	Stain Fur/Skin, Face, Red	45
	Sacrificed by design	94
648925	General observation, No Abnormality Detected	1-4,24-94
	Eye Observations, Bled via Orbital for Clin Path, Left	13,24
	Eye Observations, Bled via Orbital for Clin Path, Right	24,52
	Hair Loss, Abdomen, Medial	17
	Hair Loss, Abdomen, Ventral	5-10
	Sacrificed by design	94

APPENDIX C

Terms and Calculations
Factors Influencing Interpretation of Kinetic Analysis

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	The ppm fluoride measured

Individual Animal Calculations:

ppm F minus Bkg 0.2 ppm	The ppm fluoride measured minus the background fluoride measured in control animal. In this case the value was established at 0.2 ppm.
ppm F 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	The μmolar [μmol/L] concentration of fluorine containing compound based on the ppm fluorine normalized to 0.1 mmol/kg active dose. This assumes that all fluorine is derived from the fluorine-containing component in the formulation. Note: 1 ppm – 1 mg/L = (Normalized ppm [mg/L] fluorine / 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
- Each compound may have very different potency for producing toxicity

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

- 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 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

APPENDIX D

Individual Fluorine Levels in Blood

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	Molar Ratio (Active/F):	0.059
Dose Active (mmole/kg):	0.020	Dose F (mg/kg):	6.5
Dose F (mmol/kg):	0.342		

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					
646910	1	2.6	2.4	11.93	36.92
646911	1	2.7	2.5	12.43	38.46
646912	1	2.5	2.3	11.43	35.38
646913	1	2.6	2.4	11.93	36.92
646914	1	2.6	2.4	11.93	36.92
Group I					
646910	5	30.1	29.9	148.60	460.00
646911	5	30.3	30.1	149.60	463.08
646912	5	31.3	31.1	154.57	478.46
646913	5	32.2	32.0	159.04	492.31
646914	5	32.7	32.5	161.53	500.00
Group I					
646910	10	71.5	71.3	354.36	1096.92
646911	10	70.5	70.3	349.39	1081.54
646912	10	66.9	66.7	331.50	1026.15
646913	10	62.5	62.3	309.63	958.46
646914	10	68.4	68.4	339.95	1052.31

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					
646915	13	55.0	54.8	272.36	843.08
646916	13	55.3	55.1	273.85	847.69
646917	13	52.2	52.0	258.44	800.00
646918	13	53.8	53.6	266.39	824.62
646919	13	53.6	53.4	265.40	821.54
Group III					
646915	24	38.9	38.7	192.34	595.38
646916	24	43.8	43.6	216.69	670.77
646917	24	37.6	37.4	185.88	575.38
646918	24	35.4	35.2	174.94	541.54
646919	24	42.4	42.2	209.73	649.23
Group III					
646915	52	23.2	23.0	114.31	353.85
646916	52	20.3	20.1	99.90	309.23
646917	52	25.9	25.7	127.73	395.38
646918	52	24.9	24.7	122.76	380.00
646919	52	23.5	23.3	115.80	358.46
Group III					
646915	94	13.3	13.1	65.11	201.54
646916	94	11.7	11.5	57.16	176.92
646917	94	12.9	12.7	63.12	195.38
646918	94	11.0	10.8	53.68	166.15
646919	94	14.1	13.9	69.08	213.85

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	Molar Ratio (Active/F):	0.065
Dose Active (mmole/kg):	0.047	Dose F (mg/kg):	13.8
Dose F (mmol/kg):	0.726		

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					
646921	1	10.6	10.4	22.15	75.36
646922	1	10.7	10.5	22.37	76.09
646923	1	9.2	9.0	19.17	65.22
646924	1	5.3	5.1	10.86	36.96
646925	1	11.2	11.0	23.43	79.71
Group I					
646921	5	78.7	78.5	167.21	568.84
646922	5	83.2	83.0	176.79	601.45
646923	5	77.0	76.8	163.58	556.52
646924	5	66.1	65.9	140.37	477.54
646925	5	69.6	69.4	147.82	502.90
Group I					
646921	10	63.0	62.8	133.76	455.07
646922	10	69.1	68.9	146.76	499.28
646923	10	60.3	60.1	128.01	435.51
646924	10	62.5	62.3	132.70	451.45
646925	10	53.9	53.7	114.38	389.13

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					
646926	13	34.8	34.6	73.70	250.72
646927	13	30.0	29.8	63.47	215.94
646928	13	23.7	23.5	50.06	170.29
646929	13	33.7	33.5	71.36	242.75
646930	13	25.4	25.2	53.68	182.61
Group III					
646926	24	11.9	11.7	24.92	84.78
646927	24	10.4	10.2	21.73	73.91
646928	24	8.1	7.9	16.83	57.25
646929	24	15.7	15.5	33.02	112.32
646930	24	9.8	9.6	20.45	69.57
Group III					
646926	52	2.5	2.3	4.90	16.67
646927	52	1.7	1.5	3.20	10.87
646928	52	1.3	1.1	2.34	7.97
646929	52	4.0	3.8	8.09	27.54
646930	52	1.8	1.6	3.41	11.59
Group III					
646926	94	0.8	0.6	1.28	4.35
646927	94	<0.5	*	*	*
646928	94	<0.5	*	*	*
646929	94	0.9	0.7	1.49	5.07
646930	94	<0.5	*	*	*

* Below LOQ (Limit of Quantification)

Data for H-24949

Given:			
Mol Wt. Active (g/mole):	572	% F in Active:	59.49
Formulation Dose (mg/kg):	1000	Mol Wt. F (g/mol):	19
% Active (F Containing) in Formulation:	100		
Calculated Values:			
Dose Active (mg/kg):	1000	Molar Ratio (Active/F):	0.056
Dose Active (mmole/kg):	1.748	Dose F (mg/kg):	594.9
Dose F (mmol/kg):	31.311		

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					
648916	1	1.2	1.0	0.06	0.17
648917	1	3.0	2.8	0.16	0.47
648918	1	5.5	5.3	0.30	0.89
648919	1	3.0	2.8	0.16	0.47
648920	1	2.3	2.1	0.12	0.35
Group I					
648916	5	6.4	6.2	0.35	1.04
648917	5	6.3	6.1	0.35	1.03
648918	5	6.5	6.3	0.36	1.06
648919	5	4.6	4.4	0.25	0.74
648920	5	4.8	4.6	0.26	0.77
Group I					
648916	10	11.0	10.8	0.62	1.82
648917	10	10.9	10.7	0.61	1.80
648918	10	10.1	9.9	0.57	1.66
648919	10	10.4	10.2	0.58	1.71
648920	10	11.1	10.9	0.62	1.83

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					
648921	13	4.1	3.9	0.22	0.66
648922	13	4.2	4.0	0.23	0.67
648923	13	5.3	5.1	0.29	0.86
648924	13	4.9	4.7	0.27	0.79
648925	13	4.6	4.4	0.25	0.74
Group III					
648921	24	0.9	0.7	0.04	0.12
648922	24	1.3	1.1	0.06	0.18
648923	24	1.2	1.0	0.06	0.17
648924	24	1.3	1.1	0.06	0.18
648925	24	1.7	1.5	0.09	0.25
Group III					
648921	52	0.9	0.7	0.04	0.12
648922	52	1.7	1.5	0.09	0.25
648923	52	1.1	0.9	0.05	0.15
648924	52	1.2	1.0	0.06	0.17
648925	52	1.0	0.8	0.05	0.13
Group III					
648921	94	<0.5	*	*	*
648922	94	<0.5	*	*	*
648923	94	<0.5	*	*	*
648924	94	<0.5	*	*	*
648925	94	<0.5	*	*	*

* Below LOQ (Limit of Quantification)

APPENDIX E

Individual Fluorine Levels in Liver

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	Molar Ratio (Active/F):	0.059
Dose Active (mmole/kg):	0.020	Dose F (mg/kg):	6.5
Dose F (mmol/kg):	0.342		

Rat Number	Test Day Sample	ppm F in Liver	ppm F in Liver Minus Bkg 0.2 ppm	ppm F in Liver Normalized to 0.1 mmoles/kg Dose	µmolar Equivalents of Active in Liver
Group I					
646910	10	320.9	320.7	1593.88	4933.85
646911	10	334.0	333.8	1658.99	5135.38
646912	10	318.6	318.4	1582.45	4898.46
646913	10	281.6	281.4	1398.56	4329.23
646914	10	306.6	306.4	1522.81	4713.85
Group III					
646915	94	85.6	85.4	424.44	1313.85
646916	94	75.9	75.7	376.23	1164.62
646917	94	87.5	87.3	433.88	1343.08
646918	94	78.0	77.8	386.67	1196.92
646919	94	94.2	94.0	467.18	1446.15

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	Molar Ratio (Active/F):	0.065
Dose Active (mmole/kg):	0.047	Dose F (mg/kg):	13.8
Dose F (mmol/kg):	0.726		

Rat Number	Test Day Sample	ppm F in Liver	ppm F in Liver Minus Bkg 0.2 ppm	ppm F in Liver Normalized to 0.1 mmoles/kg Dose	µmolar Equivalents of Active in Liver
Group I					
646921	10	118.3	118.1	251.55	855.80
646922	10	122.7	122.5	260.93	887.68
646923	10	114.3	114.1	243.03	826.81
646924	10	121.6	121.4	258.58	879.71
646925	10	122.1	121.9	259.65	883.33
Group III					
646926	94	1.8	1.6	3.41	11.59
646927	94	1.2	1.0	2.13	7.25
646928	94	2.2	2.0	4.26	14.49
646929	94	4.7	4.5	9.59	32.61
646930	94	2.9	2.7	5.75	19.57

Data for H-24949

Given:			
Mol Wt. Active (g/mole):	572	% F in Active:	59.49
Formulation Dose (mg/kg):	1000	Mol Wt. F (g/mol):	19
% Active (F Containing) in Formulation:	100		
Calculated Values:			
Dose Active (mg/kg):	1000	Molar Ratio (Active/F):	0.056
Dose Active (mmole/kg):	1.748	Dose F (mg/kg):	594.9
Dose F (mmol/kg):	31.311		

Rat Number	Test Day Sample	ppm F in Liver	ppm F in Liver Minus Bkg 0.2 ppm	ppm F in Liver Normalized to 0.1 mmoles/kg Dose	μmolar Equivalents of Active in Liver
Group I					
648916	10	138.5	138.3	7.91	23.25
648917	10	168.4	168.2	9.62	28.27
648918	10	126.4	126.2	7.22	21.21
648919	10	106.5	106.3	6.08	17.87
648920	10	107.0	106.8	6.11	17.95
Group III					
648921	94	6.4	6.2	0.35	1.04
648922	94	6.6	6.4	0.37	1.08
648923	94	6.3	6.1	0.35	1.03
648924	94	4.4	4.2	0.24	0.71
648925	94	7.3	7.1	0.41	1.19

APPENDIX F

Individual Fluorine Levels in Fat

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	Molar Ratio (Active/F):	0.059
Dose Active (mmole/kg):	0.020	Dose F (mg/kg):	6.5
Dose F (mmol/kg):	0.342		

Rat Number	Test Day Sample	ppm F in Fat	ppm F in Fat Minus Bkg 0.2 ppm	ppm F in Fat Normalized to 0.1 mmoles/kg Dose	µmolar Equivalents of Active in Fat
Group I					
646910	10	14.4	14.2	70.57	218.46
646911	10	14.9	14.7	73.06	226.15
646912	10	10.9	10.7	53.18	164.62
646913	10	11.6	11.4	56.66	175.38
646914	10	12.4	12.2	60.63	187.69
Group III					
646915	94	1.3	1.1	5.47	16.92
646916	94	1.1	0.9	4.47	13.85
646917	94	1.3	1.1	5.47	16.92
646918	94	0.8	0.6	2.98	9.23
646919	94	1.5	1.3	6.46	20.00

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	Molar Ratio (Active/F):	0.065
Dose Active (mmole/kg):	0.047	Dose F (mg/kg):	13.8
Dose F (mmol/kg):	0.726		

Rat Number	Test Day Sample	ppm F in Fat	ppm F in Fat Minus Bkg 0.2 ppm	ppm F in Fat Normalized to 0.1 mmoles/kg Dose	µmolar Equivalents of Active in Fat
Group I					
646921	10	6.2	6.0	12.78	43.48
646922	10	8.5	8.3	17.68	60.14
646923	10	8.7	8.5	18.11	61.59
646924	10	8.8	8.6	18.32	62.32
646925	10	8.3	8.1	17.25	58.70
Group III					
646926	94	ND	ND	ND	ND
646927	94	ND	ND	ND	ND
646928	94	ND	ND	ND	ND
646929	94	ND	ND	ND	ND
646930	94	ND	ND	ND	ND

ND Non-detectable.

Data for H-24949

Given:			
Mol Wt. Active (g/mole):	572	% F in Active:	59.49
Formulation Dose (mg/kg):	1000	Mol Wt. F (g/mol):	19
% Active (F Containing) in Formulation:	100		
Calculated Values:			
Dose Active (mg/kg):	1000	Molar Ratio (Active/F):	0.056
Dose Active (mmole/kg):	1.748	Dose F (mg/kg):	594.9
Dose F (mmol/kg):	31.311		

Rat Number	Test Day Sample	ppm F in Fat	ppm F in Fat Minus Bkg 0.2 ppm	ppm F in Fat Normalized to 0.1 mmoles/kg Dose	µmolar Equivalents of Active in Fat
Group I					
646921	10	692.8	692.6	39.62	116.42
646922	10	1007.2	1007.0	57.60	169.27
646923	10	626.3	626.1	35.81	105.24
646924	10	341.7	341.5	19.53	57.40
646925	10	484.6	484.4	27.71	81.43
Group III					
646926	94	9.1	8.9	0.51	1.50
646927	94	4.0	3.8	0.22	0.64
646928	94	17.4	17.2	0.98	2.89
646929	94	8.9	8.7	0.50	1.46
646930	94	18.8	18.6	1.06	3.13