TRADE SECRET

Study Title

FRD-903: Acute Oral Toxicity Study in Rats - Up-and-Down Procedure

TEST GUIDELINES: U.S. EPA Health Effect Test Guidelines
OPPTS 870.1100 (2002)

OECD Guideline for the Testing of Chemicals
Section 4 (Part 425) (2001)

AUTHOR: Carol Carpenter, B.A.

STUDY COMPLETED ON: October 13, 2008

PERFORMING LABORATORY: E.I. du Pont de Nemours and Company
DuPont Haskell Global Centers
for Health & Environmental Sciences
P.O. Box 50
Newark, Delaware 19714
U.S.A.

LABORATORY PROJECT ID: DuPont-25875

WORK REQUEST NUMBER: 17644

SERVICE CODE NUMBER: 834

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

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted in compliance with U.S. EPA TSCA (40 CFR Part 792) Good Laboratory Practice Standards, which are compatible with current OECD Good Laboratory Practices, except for the item documented below. The item listed does not impact the validity of the study.

The diluted test substance was not characterized prior to initiation of the study. The dilution was prepared just prior to dosing by trained staff using graduated cylinders and calibrated pipettes.

Study Director: Carol Carpenter 13-Oct-2008

Carol Carpenter, B.A.
Senior Staff Toxicologist
Date

QUALITY ASSURANCE STATEMENT

Work Request Number: 17644
Service Code Number: 834

Phase Audited	*Audit Dates*	*Date Reported to Study Director*	*Date Reported to Management*
Protocol:	January 21, 2008	January 21, 2008	January 21, 2008
Conduct:	February 08, 2008	February 08, 2008	February 08, 2008
Report/Records:	May 29, June 03-04, 2008	Jun 04, 2008	Jun 10, 2008

Reported by: Donna M. Johnston 01 Oct 2008
Donna M. Johnston
Quality Assurance Auditor
Date

CERTIFICATION

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

Anatomic Pathology Evaluation Reported by: Lisa J. Lewis — 2-Oct-2008
Lisa J. Lewis
Associate Scientist
Date

Anatomic Pathology Evaluation Reviewed by: Steven R. Frame — 7 Oct 2008
Steven R. Frame, D.V.M., Ph.D., Diplomate A.C.V.P.
Research Fellow and Manager
Date

Reviewed by: Susan M. Munley — 6-Oct-2008
Susan M. Munley, M.A.
Research Toxicologist
Date

Issued by Study Director: Carol Carpenter — 13-Oct-2008
Carol Carpenter, B.A.
Senior Staff Toxicologist
Date

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STUDY INFORMATION

Substance Tested:
- FRD-903
- 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionic acid
- 13252-13-6 (CAS Number)
- H-28307

Haskell Number: 28307

Composition[a]:

98%	HFPO Dimer Acid
0.61%	Water
8.3 ppm	Perfluorooctanoic Acid

Purity[a]: 98%

Physical Characteristics: Clear and colorless liquid

Study Initiated/Completed: January 18, 2008 / (see report cover page)

Experimental Start/Termination: January 22, 2008 / October 7, 2008

[a] This is the composition and purity of FRD-903 as received. FRD-903 was diluted with deionized water at Haskell.

SUMMARY

A single dose of diluted FRD-903 was administered by oral gavage to fasted male and female rats. Male rats were dosed at 175 mg/kg (2 rats), 550 mg/kg (4 rats), 1750 mg/kg (6 rats), and 5000 mg/kg (3 rats). Female rats were dosed at 175 mg/kg (1 rat), 550 mg/kg (3 rats), 1750 mg/kg (4 rats), and 5000 mg/kg (1 rat). The rats were dosed 1 at a time at a minimum of 48-hour intervals. The rats were observed for mortality, body weight effects, and clinical signs for up to 14 days after dosing. All rats were necropsied to detect grossly observable evidence of organ or tissue damage.

In male rats, death occurred in 1 of 4 rats dosed at 550 mg/kg (sacrificed *in extremis* on test day 4 following a 23% reduction in body weight), in 2 of 6 rats dosed at 1750 mg/kg (found dead on test day 0 or 1), and in 3 of 3 rats dosed at 5000 mg/kg (found dead on test day 0). No clinical signs of toxicity were observed in the 2 male rats dosed at 175 mg/kg and in 1 surviving male rat dosed at 550 mg/kg. Clinical signs of toxicity were observed for up to 5 days after dosing in the remaining male rats and included lung noise, absent feces, lethargy, not eating, stained fur/skin, wet fur, labored breathing, lethargy, decreased muscle tone, prostrate posture, tremors, clear oral discharge, diarrhea, ataxia, and/or high posture. No biologically relevant body weight losses occurred in surviving male rats. Gross findings were present in 3 rats dosed at 5000 mg/kg, in 4 rats dosed at 1750 mg/kg, and 1 rat dosed at 550 mg/kg. These included stomach discoloration, stomach thick, skin stain, stomach distended with gas, and/or small testes and epididymides.

In female rats, death occurred in 3 of 4 rats dosed at 1750 mg/kg (found dead on test day 0 or 1) and in the single rat dosed at 5000 mg/kg (found dead on test day 0). Clinical signs of toxicity were observed up to 3 days after dosing in all female rats except the single rat dosed at 175 mg/kg and included wet fur, stained fur/skin, ataxia, labored breathing, cold to touch, clear ocular or oral discharge, lethargy, lung noise, absent feces, not eating, and/or rubbing face on bottom of cage. No body weight losses occurred in female rats. Gross findings were present in 1 rat dosed at 5000 mg/kg and in 3 rats dosed at 1750 mg/kg. These included stomach discoloration, stomach thick, esophagus fluid, skin wet, and/or mesenteric lymph nodes discoloration.

Under the conditions of this study, the estimated oral LD_{50} for diluted FRD-903 was 1730 mg/kg and 1750 mg/kg for male and female rats, respectively.

In accordance with the provisions of Directive 67/548/EEC, the test substance is classified as harmful and assigned the symbol Xn and the risk phrase R22 Harmful if swallowed.

According to the Globally Harmonized System (GHS) of classification and labeling of chemicals and under the conditions of this study, the test substance is classified in Category 4.

INTRODUCTION

The purpose of this study was to assess the acute oral toxicity of diluted FRD-903 when administered by oral gavage to male and female rats.

MATERIALS AND METHODS

A. Test Guidelines

The study design complied with the following test guidelines:

- U.S. EPA, OPPTS 870.1100: Acute Oral Toxicity, *Health Effects Test Guidelines* (2002)
- OECD, Section 4 (Part 425): Acute Oral Toxicity – Up-and-Down Procedure, *Guideline for the Testing of Chemicals* (2001)

B. Test Substance

The test substance, FRD-903, was supplied by the sponsor. The test substance 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.

The Certificate of Analysis for the undiluted test substance is presented in Appendix A.

C. Test System

Female Crl:CD(SD) rats were received from Charles River Laboratories, Inc., Raleigh, North Carolina.

The Crl:CD(SD) rat was selected based on consistently acceptable health status and on extensive experience with the strain at DuPont Haskell.

D. Animal Husbandry

1. Housing

All animals were housed singly in stainless steel, wire-mesh cages suspended above cage boards.

2. Environmental Conditions

Animal rooms were maintained at a temperature of 18-26°C and a relative humidity of 30-70%. Animal rooms were artificially illuminated (fluorescent light) on an approximate 12-hour light/dark cycle. Any excursions outside of these ranges were of insufficient magnitude and/or duration to have adversely affected the validity of the study.

3. Feed and Water

PMI® Nutrition International, LLC Certified Rodent LabDiet® 5002 and water were available *ad libitum* except as noted in section E. Dosing.

4. Identification

Each rat was assigned an identification number which was recorded on a card affixed to the cage. The rats were tail-marked, using a water-insoluble marker, with the identification number.

5. Quarantine

The rats were weighed and observed for general health during the quarantine period (at least 6 days).

6. Animal Health and Environmental Monitoring Program

As specified in the DuPont Haskell 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.
- 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.

E. Dosing

A single oral dose of diluted FRD-903 was administered by oral gavage to fasted male and female rats. Male rats were dosed at 175 mg/kg (2 rats), 550 mg/kg (4 rats), 1750 mg/kg (6 rats), and 5000 mg/kg (3 rats). Female rats were dosed at 175 mg/kg (1 rat), 550 mg/kg (3 rats), 1750 mg/kg (4 rats), and 5000 mg/kg (1 rat). The rats were dosed one at a time at a minimum of 48-hour intervals. A software package (AOT425StatPgm)[a] was used to determine the dose progression and the LD_{50}.

[a] Prepared for U.S. EPA by Westat, May 2001, Updated by U.S. EPA February 2002.

The rats were approximately 9-11 weeks old on the day of dosing. The rats were fasted approximately 16-18 hours prior to dosing, with food being returned to the rats approximately 3-4 hours after dosing. Individual dose volumes were calculated using the fasted body weights obtained prior to dosing and the diluted test substance density of 1.318 g/mL. The diluted test substance was stirred throughout the dosing procedure.

F. Observations, Body Weights, and Anatomic Pathology

Observations for mortality and signs of illness, injury, or abnormal behavior were made daily throughout the study. The rats were observed for clinical signs at the beginning of fasting, just before dosing (test day 0), once during the first 30 minutes after dosing and 2 more times on the day of dosing, and once each day thereafter. The rats were weighed on test days –1, 0, 7, and 14. On test day 14, the rats were euthanized and necropsied to detect grossly observable evidence of organ or tissue damage. The rats were anesthetized by carbon dioxide and euthanized by exsanguination. The rats that died or were sacrificed *in extremis* were also necropsied.

RESULTS AND DISCUSSION

In-life Toxicology

MALES

A. Dose Progression and Mortality

In male rats, death occurred in 1 rat dosed at 550 mg/kg (sacrificed *in extremis* on test day 4), in 2 rats dosed at 1750 mg/kg (found dead on test day 0 or 1), and in 3 rats dosed at 5000 mg/kg (found dead on test day 0). The dose progression and mortality are detailed below.

AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Test type: Main Test
Limit dose (mg/kg): 5000
Assumed LD_{50} (mg/kg): Default
Assumed sigma (mg/kg): 0.5
Recommended dose progression: 5000, 1750, 550, 175, 55, 17.5, 5.5, 1.75 mg/kg

1. Data

Test Sequence	Animal ID	Dose (mg/kg)	Short-Term Result	Long-Term Result
1	272	175	O	O
2	274	550	O	X
3	474	175	O	O
4	547	550	O	O
5	475	1750	X	X
6	591	550	O	O
7	592	1750	O	O
8	640	5000	X	X
9	641	1750	X	X
10	894	550	O	O
11	895	1750	O	O
12	796	5000	X	X
13	820	1750	O	O
14	821	5000	X	X
15	798	1750	O	O

X = Died, O = Survived
Short-term result = animal response within 48 hours of dosing
Long-term result = animal response at the end of the 14-day observation period

Dose recommendation: the main test is complete. Stopping criteria met: maximum number of animals tested.

2. Summary of Long-Term Results

Dose (mg/kg)	O	X	Total
175	2	0	2
550	3	1	4
1750	4	2	6
5000	0	3	3
All Doses	9	6	15

Statistical estimate based on long-term outcomes: estimated LD_{50} = 1730 mg/kg (based on maximum likelihood). 95% profile likelihood confidence interval is 678 to 12,800 mg/kg.

B. Body Weights

(Appendices B-C)

No biologically relevant body weight losses occurred in surviving male rats. A male rat dosed at 550 mg/kg exhibited body weight loss of approximately 23% of the fasted weight by test day 4 and was sacrificed *in extremis*.

C. Clinical Signs

(Appendix D)

No clinical signs of toxicity were observed in the 2 rats dosed at 175 mg/kg and in one rat dosed at 550 mg/kg. Lung noise, absent feces, lethargy, not eating, stained fur/skin, and wet fur were observed up to test day 4 in a rat dosed at 550 mg/kg. Because of these clinical signs and body weight loss of approximately 23%, this rat was sacrificed *in extremis* on test day 4. Another rat dosed at 550 mg/kg exhibited stained fur/skin and wet fur up to test day 1. Hair loss observed in this rat was considered to be incidental. Another rat dosed at 550 mg/kg exhibited diarrhea, stained fur/skin, and wet fur on the day of dosing.

Labored breathing, lethargy, decreased muscle tone, prostrate posture, and tremors were observed on the day of dosing in a rat dosed at 1750 mg/kg. This rat was found dead on test day 1. Decreased muscle tone, prostrate posture, stained fur/skin, and wet fur were observed on the day of dosing in another rat dosed at 1750 mg/kg. This rat was found dead on the day of dosing. A surviving rat dosed at 1750 mg/kg exhibited clear oral discharge, stained fur/skin, and wet fur up to 5 days after dosing. Two other surviving rats dosed at 1750 mg/kg exhibited stained fur/skin and wet fur up to 4 days after dosing. The remaining surviving rat dosed at 1750 mg/kg exhibited lethargy, high posture, stained fur/skin, and wet fur up to 3 days after dosing.

A rat dosed at 5000 mg/kg exhibited lethargy and wet fur on the day of dosing. Another rat dosed at 5000 mg/kg exhibited ataxia, lung noise, clear oral discharge, lethargy, stained fur/skin,

and wet fur on the day of dosing. The remaining rat dosed at 5000 mg/kg exhibited lethargy and decreased muscle tone on the day of dosing. These rats were found dead on the day of dosing.

FEMALES

A. Dose Progression and Mortality

AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Test type: Main Test
Limit dose (mg/kg): 5000
Assumed LD50 (mg/kg): Default
Assumed sigma (mg/kg): 0.5
Recommended dose progression: 5000, 1750, 550, 175, 55, 17.5, 5.5, 1.75 mg/kg

1. Data

Test Sequence	Animal ID	Dose (mg/kg)	Short-Term Result	Long-Term Result
1	254	175	O	O
2	263	550	O	O
3	478	1750	X	X
4	485	550	O	O
5	527	1750	X	X
6	532	550	O	O
7	594	1750	O	O
8	598	5000	X	X
9	626	1750	X	X

X = Died, O = Survived
Short-term result = animal response within 48 hours of dosing
Long-term result = animal response at the end of the 14-day observation period

Dose recommendation: the main test is complete. Stopping criteria met: likelihood ratio criterion.

2. Summary of Long-Term Results

Dose (mg/kg)	O	X	Total
175	1	0	1
550	3	0	3
1750	1	3	4
5000	0	1	1
All Doses	5	4	9

Statistical estimate based on long term outcomes: estimated LD_{50} = 1750 mg/kg (the one dose with partial response). 95% profile likelihood confidence interval is 652 to 2690 mg/kg.

B. Body Weights

(Appendices B-C)

No body weight losses occurred after dosing.

C. Clinical Signs

(Appendix D)

No clinical signs of toxicity were observed in the rat dosed at 175 mg/kg. One rat dosed at 550 mg/kg exhibited wet fur up to the day after dosing. Another rat dosed at 550 mg/kg exhibited stained fur/skin up to the day after dosing. Breathing noise, clear oral discharge, absent feces, not eating, stained fur/skin, and wet fur were observed up to 3 days after dosing in the remaining rat dosed at 550 mg/kg.

The surviving rat dosed at 1750 mg/kg exhibited stained fur/skin and wet fur on the day of dosing. Wet fur was observed on the day of dosing in a rat dosed at 1750 mg/kg. This rat was found dead on the day of dosing. Another rat dosed at 1750 mg/kg exhibited ataxia, labored breathing, clear ocular discharge, lethargy, wet fur, and was cold to touch on the day of dosing. This rat was found dead the day after dosing. The remaining rat dosed at 1750 mg/kg exhibited lung noise, lethargy, and wet fur and was observed rubbing its face on the bottom of the cage. This rat was found dead on the day of dosing.

Lethargy and wet fur were observed on the day of dosing in the rat dosed at 5000 mg/kg. This rat was found dead on the day of dosing.

Anatomic Pathology Evaluation

A. Gross Observations

(Appendix E)

MALES

Gross findings were present in 3 rats dosed at 5000 mg/kg, in 4 rats dosed at 1750 mg/kg, and 1 rat dosed at 550 mg/kg. These included stomach discoloration and stomach thick in rats 640, 796, and 821 (found dead, 5000 mg/kg); skin stain in rat 796 (5000 mg/kg); stomach discoloration and/or stomach thick in rats 475, 641, and 820 (1750 mg/kg); stomach distended with gas in rats 798 and 820 (1750 mg/kg); and small testes and epididymides in rat 274 (550 mg/kg). No other gross findings were observed in male rats.

FEMALES

Gross findings were present in 1 rat dosed at 5000 mg/kg and in 3 rats dosed at 1750 mg/kg. These included stomach discoloration and stomach thick in rat 598 (found dead, 5000 mg/kg); esophagus fluid and skin wet in rat 598 (found dead, 5000 mg/kg); stomach discoloration and/or

stomach thick in rats 478, 527, and 626 (found dead, 1750 mg/kg); skin discoloration in rat 527 (1750 mg/kg), and mesenteric lymph nodes discoloration in rat 527 (1750 mg/kg). No other gross findings were observed in female rats.

CONCLUSIONS

Under the conditions of this study, the estimated oral LD_{50} for diluted FRD-903 was 1730 mg/kg and 1750 mg/kg for male and female rats, respectively.

In accordance with the provisions of Directive 67/548/EEC, the test substance is classified as harmful and assigned the symbol Xn and the risk phrase R22 Harmful if swallowed.

According to the Globally Harmonized System (GHS) of classification and labeling of chemicals and under the conditions of this study, the test substance is classified in Category 4.

RECORDS AND SAMPLE STORAGE

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

APPENDICES

Appendix A
Certificate of Analysis

CERTIFICATE OF ANALYSIS

EXPLANATORY NOTE

This is the Certificate of Analysis for undiluted test substance (as received from the sponsor).

E. I. du Pont de Nemours and Company
Wilmington, DE 19898
USA

CERTIFICATE OF ANALYSIS

This Certificate of Analysis fulfills the requirement for characterization of a test substance prior to a study subject to GLP regulations. It documents the identity and content of the test substance. This work was conducted under EPA Good Laboratory Practice Standards (40 CFR 792).

Haskell Code Number	H-28307
Common Name	HFPO Dimer Acid
Purity Percent	98%
Other Components	Water – 0.61% Perfluorooctanoic acid – 8.3 ppm
Date of Analysis	October 4, 2007
Recommended reanalysis interval	1 year
Instructions for storage	NRT&H
Reference	DuPont-24003
Analysis performed at	E. I. DuPont de Nemours and Company DuPont Haskell Laboratories Newark, Delaware USA

Approver:

Peter A. Bloxham, Ph.D.
Senior Research Chemist

18-OCT-2007
Date

Appendix B
Individual Body Weights

Individual Body Weights (g)

MALES

Group Sex	Animal Number	Day numbers relative to Start Date -1	0	4	7	14
1m	272	329.4	307.2	.	368.9	406.2
2m	274	350.9	323.9	248.9	.	.
5m	474	347.7	320.8	.	393.1	433.7
6m	547	306.9	285.9	.	339.4	367.3
7m	475	374.0	352.7	.	.	.
11m	591	293.8	275.9	.	330.4	372.3
12m	592	354.6	325.5	.	361.7	403.7
14m	640	335.7	306.7	.	.	.
16m	641	353.1	322.0	.	.	.
17m	894	333.3	303.5	.	353.5	389.4
18m	895	336.7	310.8	.	366.1	405.5
19m	796	324.8	298.0	.	.	.
20m	820	319.7	298.6	.	299.2	303.7
21m	821	312.0	291.7	.	.	.
22m	798	355.8	332.3	.	326.9	387.8

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 5 - 175 mg/kg
Group 6 - 550 mg/kg Group 7 - 1750 mg/kg Group 11 - 550 mg/kg
Group 12 - 1750 mg/kg Group 14 - 5000 mg/kg Group 16 - 1750 mg/kg
Group 17 - 550 mg/kg Group 18 - 1750 mg/kg Group 19 - 5000 mg/kg
Group 20 - 1750 mg/kg Group 21 - 5000 mg/kg Group 22 - 1750 mg/kg

Individual Body Weights (g) – (Continued)

FEMALES

Group Sex	Animal Number	Day numbers relative to Start Date -1	0	7	14
1f	254	233.5	213.5	248.9	253.9
2f	263	234.1	210.8	250.3	270.5
3f	478	217.8	200.9	.	.
4f	485	248.9	229.0	272.0	300.5
8f	527	206.4	189.5	.	.
9f	532	240.1	215.8	240.7	245.9
10f	594	233.3	209.1	250.0	264.0
13f	598	212.8	198.2	.	.
15f	626	230.2	207.5	.	.

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 3 - 1750 mg/kg
Group 4 - 550 mg/kg Group 8 – 1750 mg/kg Group 9 - 550 mg/kg
Group 10 - 1750 mg/kg Group 13 - 5000 mg/kg Group 15 - 1750 mg/kg

Appendix C
Individual Body Weight Gains

Individual Body Weight Gains (g)

MALES

	Days 0-7	Days 7-14	Days 0-14
175 mg/kg			
272	61.7	37.3	99.0
550 mg/kg			
474	72.3	40.6	112.9
547	53.5	27.9	81.4
591	54.5	41.9	96.4
894	50.0	35.9	85.9
1750 mg/kg			
592	36.2	42.0	78.2
895	55.3	39.4	94.7
820	0.6	4.5	5.1
798	-5.4	60.9	55.5

FEMALES

	Days 0-7	Days 7-14	Days 0-14
175 mg/kg			
254	35.4	5.0	40.4
550 mg/kg			
263	39.5	20.2	59.7
485	43.0	28.5	71.5
532	24.9	5.2	30.1
1750 mg/kg			
594	40.9	14.0	54.9

Appendix D
Individual Clinical Observations and Mortality Records

INDIVIDUAL CLINICAL OBSERVATIONS AND MORTALITY RECORDS

EXPLANATORY NOTES

ABBREVIATIONS:

A - time slots for observations
Ts1 - postdose observation 1 (within 30 minutes of dosing)
Ts2 - postdose observation 2
Ts3 - postdose observation 3

Individual Clinical Observations in Male Rats

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
1m	272	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
1m	272	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 5 - 175 mg/kg Group 6 - 550 mg/kg
Group 7 - 1750 mg/kg Group 11 - 550 mg/kg Group 12 - 1750 mg/kg Group 14 - 5000 mg/kg
Group 16 - 1750 mg/kg Group 17 - 550 mg/kg Group 18 - 1750 mg/kg Group 19 - 5000 mg/kg
Group 20 - 1750 mg/kg Group 21 - 5000 mg/kg Group 22 - 1750 mg/kg

Individual Clinical Observations in Male Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
2m	274	No Abnormalities Detected		X	X	.	.	.	.	.	.	.	.
		Breathing - lung noise		.	.	.	X	X	X	X	X	X	.
		Feces absent		.	.	.	.	.	X	X	X	X	.
		Lethargic		.	.	.	.	X	X	X	X	X	.
		Not eating		.	.	.	.	.	X	X	X	X	.
		Stained skin/fur - brown	Chin	.	.	.	.	.	.	.	X	X	.
		Stained skin/fur - brown	Perineum	.	.	.	.	.	.	.	X	X	.
		Stained skin/fur - brown	Perioral	.	.	.	.	.	.	.	X	X	.
		Wet fur	Chin	.	.	X	X	X	X	X	.	.	.
		Wet fur	Underbody	.	.	.	X	.	.	.	.	.	.
		Wet fur	Perioral	.	.	.	.	X	X	X	.	.	.
		Sacrificed in extremis		.	.	.	.	.	.	.	.	X	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
2m	274	No Abnormalities Detected		.	.	.	.	.	.	.	.	.
		Breathing - lung noise		.	.	.	.	.	.	.	.	.
		Feces absent		.	.	.	.	.	.	.	.	.
		Lethargic		.	.	.	.	.	.	.	.	.
		Not eating		.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Chin	.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Perineum	.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Perioral	.	.	.	.	.	.	.	.	.
		Wet fur	Chin	.	.	.	.	.	.	.	.	.
		Wet fur	Underbody	.	.	.	.	.	.	.	.	.
		Wet fur	Perioral	.	.	.	.	.	.	.	.	.
		Sacrificed in extremis		.	.	.	.	.	.	.	.	.

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 5 - 175 mg/kg Group 6 - 550 mg/kg
Group 7 - 1750 mg/kg Group 11 - 550 mg/kg Group 12 - 1750 mg/kg Group 14 - 5000 mg/kg
Group 16 - 1750 mg/kg Group 17 - 550 mg/kg Group 18 - 1750 mg/kg Group 19 - 5000 mg/kg
Group 20 - 1750 mg/kg Group 21 - 5000 mg/kg Group 22 - 1750 mg/kg

Individual Clinical Observations in Male Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
5m	474	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
5m	474	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 5 - 175 mg/kg Group 6 - 550 mg/kg
Group 7 - 1750 mg/kg Group 11 - 550 mg/kg Group 12 - 1750 mg/kg Group 14 - 5000 mg/kg
Group 16 - 1750 mg/kg Group 17 - 550 mg/kg Group 18 - 1750 mg/kg Group 19 - 5000 mg/kg
Group 20 - 1750 mg/kg Group 21 - 5000 mg/kg Group 22 - 1750 mg/kg

Individual Clinical Observations in Male Rats – (Continued)

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
6m	547	No Abnormalities Detected		X	X	.	.	.	.	X	.	.	.
		Hair loss	Forelimb bilateral	.	.	.	.	.	.	.	X	X	X
		Stained skin/fur - brown	Chin	.	.	.	X	X	.	.	.	.	.
		Stained skin/fur - yellow	Perineum	.	.	.	.	.	X	.	.	.	.
		Wet fur	Chin	.	.	X	X	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	X	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
6m	547	No Abnormalities Detected		.	.	.	.	.	.	.	.	.
		Hair loss	Forelimb bilateral	X	X	X	X	X	X	X	X	X
		Stained skin/fur - brown	Chin	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Perineum	.	.	.	.	.	.	.	.	.
		Wet fur	Chin	.	.	.	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 5 - 175 mg/kg Group 6 - 550 mg/kg
Group 7 - 1750 mg/kg Group 11 - 550 mg/kg Group 12 - 1750 mg/kg Group 14 - 5000 mg/kg
Group 16 - 1750 mg/kg Group 17 - 550 mg/kg Group 18 - 1750 mg/kg Group 19 - 5000 mg/kg
Group 20 - 1750 mg/kg Group 21 - 5000 mg/kg Group 22 - 1750 mg/kg

Individual Clinical Observations in Male Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
7m	475	No Abnormalities Detected		X	X	X	.	.	.	.	.	.	.
		Breathing - labored		.	.	.	X	X	.	.	.	.	.
		Lethargic		.	.	.	X	X	.	.	.	.	.
		Muscle tone decreased		.	.	.	X	X	.	.	.	.	.
		Prostrate		.	.	.	X	X	.	.	.	.	.
		Tremors multiple site		.	.	.	.	X	.	.	.	.	.
		Found dead		.	.	.	.	.	X	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
7m	475	No Abnormalities Detected		.	.	.	.	.	.	.	.	.
		Breathing - labored		.	.	.	.	.	.	.	.	.
		Found dead		.	.	.	.	.	.	.	.	.
		Lethargic		.	.	.	.	.	.	.	.	.
		Muscle tone decreased		.	.	.	.	.	.	.	.	.
		Prostrate		.	.	.	.	.	.	.	.	.
		Tremors multiple site		.	.	.	.	.	.	.	.	.
		Found dead		.	.	.	.	.	.	.	.	.

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 5 - 175 mg/kg Group 6 - 550 mg/kg
Group 7 - 1750 mg/kg Group 11 - 550 mg/kg Group 12 - 1750 mg/kg Group 14 - 5000 mg/kg
Group 16 - 1750 mg/kg Group 17 - 550 mg/kg Group 18 - 1750 mg/kg Group 19 - 5000 mg/kg
Group 20 - 1750 mg/kg Group 21 - 5000 mg/kg Group 22 - 1750 mg/kg

Individual Clinical Observations in Male Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
11m	591	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
11m	591	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 5 - 175 mg/kg Group 6 - 550 mg/kg
Group 7 - 1750 mg/kg Group 11 - 550 mg/kg Group 12 - 1750 mg/kg Group 14 - 5000 mg/kg
Group 16 - 1750 mg/kg Group 17 - 550 mg/kg Group 18 - 1750 mg/kg Group 19 - 5000 mg/kg
Group 20 - 1750 mg/kg Group 21 - 5000 mg/kg Group 22 - 1750 mg/kg

Individual Clinical Observations in Male Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
12m	592	No Abnormalities Detected		X	X	.	.	.	.	.	.	.	.
		Discharge - clear	Mouth	.	.	.	X	.	.	.	.	.	.
		Stained skin/fur - brown	Chin	.	.	.	.	X	X	X	X	.	.
		Stained skin/fur - brown	Perioral	.	.	.	X	X	X	X	X	.	.
		Stained skin/fur - yellow	Abdomen	.	.	.	.	X	X	X	X	X	X
		Stained skin/fur - yellow	Inguen	.	.	.	.	X	X	X	X	X	X
		Stained skin/fur - yellow	Perineum	.	.	.	.	X	X	X	X	X	X
		Wet fur	Abdomen	.	.	.	.	X	X	X	X	.	.
		Wet fur	Inguen	.	.	.	X	X	X	X	X	.	.
		Wet fur	Perineum	.	.	.	X	X	X	X	X	.	.
		Wet fur	Perioral	.	.	X	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
12m	592	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		Discharge - clear	Mouth	.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Chin	.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Perioral	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Abdomen	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Inguen	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Perineum	.	.	.	.	.	.	.	.	.
		Wet fur	Abdomen	.	.	.	.	.	.	.	.	.
		Wet fur	Inguen	.	.	.	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	.	.	.	.	.
		Wet fur	Perioral	.	.	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 5 - 175 mg/kg Group 6 - 550 mg/kg
Group 7 - 1750 mg/kg Group 11 - 550 mg/kg Group 12 - 1750 mg/kg Group 14 - 5000 mg/kg
Group 16 - 1750 mg/kg Group 17 - 550 mg/kg Group 18 - 1750 mg/kg Group 19 - 5000 mg/kg
Group 20 - 1750 mg/kg Group 21 - 5000 mg/kg Group 22 - 1750 mg/kg

Individual Clinical Observations in Male Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
14m	640	No Abnormalities Detected		X	X	.	.	.	.	.	.	.	.
		Lethargic		.	.	X	.	.	.	.	.	.	.
		Wet fur	Chin	.	.	X	.	.	.	.	.	.	.
		Wet fur	Perioral	.	.	X	.	.	.	.	.	.	.
		Found dead		.	.	.	X	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
14m	640	No Abnormalities Detected		.	.	.	.	.	.	.	.	.
		Lethargic		.	.	.	.	.	.	.	.	.
		Wet fur	Chin	.	.	.	.	.	.	.	.	.
		Wet fur	Perioral	.	.	.	.	.	.	.	.	.
		Found dead		.	.	.	.	.	.	.	.	.

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 5 - 175 mg/kg Group 6 - 550 mg/kg
Group 7 - 1750 mg/kg Group 11 - 550 mg/kg Group 12 - 1750 mg/kg Group 14 - 5000 mg/kg
Group 16 - 1750 mg/kg Group 17 - 550 mg/kg Group 18 - 1750 mg/kg Group 19 - 5000 mg/kg
Group 20 - 1750 mg/kg Group 21 - 5000 mg/kg Group 22 - 1750 mg/kg

Individual Clinical Observations in Male Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
16m	641	No Abnormalities Detected		X	X	.	.	.	.	.	.	.	.
		Muscle tone decreased		.	.	X	X	.	.	.	.	.	.
		Prostrate		.	.	.	X	.	.	.	.	.	.
		Stained skin/fur - brown	Chin	.	.	.	X	.	.	.	.	.	.
		Wet fur	Chin	.	.	X	.	.	.	.	.	.	.
		Wet fur	Perioral	.	.	X	.	.	.	.	.	.	.
		Found dead		.	.	.	.	X	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
16m	641	No Abnormalities Detected		.	.	.	.	.	.	.	.	.
		Muscle tone decreased		.	.	.	.	.	.	.	.	.
		Prostrate		.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Chin	.	.	.	.	.	.	.	.	.
		Wet fur	Chin	.	.	.	.	.	.	.	.	.
		Wet fur	Perioral	.	.	.	.	.	.	.	.	.
		Found dead		.	.	.	.	.	.	.	.	.

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 5 - 175 mg/kg Group 6 - 550 mg/kg
Group 7 - 1750 mg/kg Group 11 - 550 mg/kg Group 12 - 1750 mg/kg Group 14 - 5000 mg/kg
Group 16 - 1750 mg/kg Group 17 - 550 mg/kg Group 18 - 1750 mg/kg Group 19 - 5000 mg/kg
Group 20 - 1750 mg/kg Group 21 - 5000 mg/kg Group 22 - 1750 mg/kg

Individual Clinical Observations in Male Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
17m	894	No Abnormalities Detected		X	X	.	.	.	X	X	X	X	X
		Diarrhea		.	.	X	.	.	.	.	.	.	.
		Stained skin/fur - brown	Chin	.	.	.	.	X	.	.	.	.	.
		Wet fur	Inguen	.	.	.	X	X	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
17m	894	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		Diarrhea		.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Chin	.	.	.	.	.	.	.	.	.
		Wet fur	Inguen	.	.	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 5 - 175 mg/kg Group 6 - 550 mg/kg
Group 7 - 1750 mg/kg Group 11 - 550 mg/kg Group 12 - 1750 mg/kg Group 14 - 5000 mg/kg
Group 16 - 1750 mg/kg Group 17 - 550 mg/kg Group 18 - 1750 mg/kg Group 19 - 5000 mg/kg
Group 20 - 1750 mg/kg Group 21 - 5000 mg/kg Group 22 - 1750 mg/kg

Individual Clinical Observations in Male Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
18m	895	No Abnormalities Detected		X	X	X	.	.	.	.	.	.	X
		Stained skin/fur - brown	Inguen	.	.	.	.	.	X	X	X	X	.
		Stained skin/fur - brown	Perineum	.	.	.	.	.	X	X	X	X	.
		Wet fur	Inguen	.	.	.	.	X	.	.	.	.	.
		Wet fur	Perineum	.	.	.	X	X	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
18m	895	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		Stained skin/fur - brown	Inguen	.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Perineum	.	.	.	.	.	.	.	.	.
		Wet fur	Inguen	.	.	.	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 5 - 175 mg/kg Group 6 - 550 mg/kg
Group 7 - 1750 mg/kg Group 11 - 550 mg/kg Group 12 - 1750 mg/kg Group 14 - 5000 mg/kg
Group 16 - 1750 mg/kg Group 17 - 550 mg/kg Group 18 - 1750 mg/kg Group 19 - 5000 mg/kg
Group 20 - 1750 mg/kg Group 21 - 5000 mg/kg Group 22 - 1750 mg/kg

Individual Clinical Observations in Male Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
19m	796	No Abnormalities Detected		X	X	.	.	.	.	.	.	.	.
		Ataxia		.	.	.	X	.	.	.	.	.	.
		Breathing - lung noise		.	.	X	.	.	.	.	.	.	.
		Discharge - clear	Mouth	.	.	X	.	.	.	.	.	.	.
		Lethargic		.	.	X	X	.	.	.	.	.	.
		Stained skin/fur - brown	Perinasal	.	.	.	X	.	.	.	.	.	.
		Wet fur	Chin	.	.	X	.	.	.	.	.	.	.
		Wet fur	Inguen	.	.	.	X	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	X	.	.	.	.	.	.
		Wet fur	Underbody	.	.	.	X	.	.	.	.	.	.
		Wet fur	Perioral	.	.	X	.	.	.	.	.	.	.
		Found dead		.	.	.	.	X	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
19m	796	No Abnormalities Detected		.	.	.	.	.	.	.	.	.
		Ataxia		.	.	.	.	.	.	.	.	.
		Breathing - lung noise		.	.	.	.	.	.	.	.	.
		Discharge - clear	Mouth	.	.	.	.	.	.	.	.	.
		Lethargic		.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Perinasal	.	.	.	.	.	.	.	.	.
		Wet fur	Chin	.	.	.	.	.	.	.	.	.
		Wet fur	Inguen	.	.	.	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	.	.	.	.	.
		Wet fur	Underbody	.	.	.	.	.	.	.	.	.
		Wet fur	Perioral	.	.	.	.	.	.	.	.	.
		Found dead		.	.	.	.	.	.	.	.	.

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 5 - 175 mg/kg Group 6 - 550 mg/kg
Group 7 - 1750 mg/kg Group 11 - 550 mg/kg Group 12 - 1750 mg/kg Group 14 - 5000 mg/kg
Group 16 - 1750 mg/kg Group 17 - 550 mg/kg Group 18 - 1750 mg/kg Group 19 - 5000 mg/kg
Group 20 - 1750 mg/kg Group 21 - 5000 mg/kg Group 22 - 1750 mg/kg

Individual Clinical Observations in Male Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
20m	820	No Abnormalities Detected		X	X	.	.	.	.	.	.	X	X
		Lethargic		.	.	X	X	X	.	.	.	.	.
		Posture - high		.	.	.	.	X	.	.	.	.	.
		Stained skin/fur - black	Forelimb bilateral	.	.	.	.	.	X	.	.	.	.
		Stained skin/fur - brown	Perioral	.	.	.	X	X	X	.	.	.	.
		Stained skin/fur - yellow	Hindlimb bilateral	.	.	.	.	.	X	.	.	.	.
		Stained skin/fur - yellow	Inguen	.	.	.	.	.	X	X	X	.	.
		Stained skin/fur - yellow	Perineum	.	.	.	.	.	X	X	.	.	.
		Wet fur	Inguen	.	.	.	X	X	.	.	.	.	.
		Wet fur	Perineum	.	.	.	X	X	.	.	.	.	.
		Wet fur	Perioral	.	.	X	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
20m	820	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		Lethargic		.	.	.	.	.	.	.	.	.
		Posture - high		.	.	.	.	.	.	.	.	.
		Stained skin/fur - black	Forelimb bilateral	.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Perioral	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Hindlimb bilateral	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Inguen	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Perineum	.	.	.	.	.	.	.	.	.
		Wet fur	Inguen	.	.	.	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	.	.	.	.	.
		Wet fur	Perioral	.	.	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 5 - 175 mg/kg Group 6 - 550 mg/kg
Group 7 - 1750 mg/kg Group 11 - 550 mg/kg Group 12 - 1750 mg/kg Group 14 - 5000 mg/kg
Group 16 - 1750 mg/kg Group 17 - 550 mg/kg Group 18 - 1750 mg/kg Group 19 - 5000 mg/kg
Group 20 - 1750 mg/kg Group 21 - 5000 mg/kg Group 22 - 1750 mg/kg

Individual Clinical Observations in Male Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
21m	821	No Abnormalities Detected		X	X	.	.	.	.	.	.	.	.
		Lethargic		.	.	X	.	.	.	.	.	.	.
		Muscle tone decreased		.	.	X	.	.	.	.	.	.	.
		Found dead		.	.	.	X	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
21m	821	No Abnormalities Detected		.	.	.	.	.	.	.	.	.
		Lethargic		.	.	.	.	.	.	.	.	.
		Muscle tone decreased		.	.	.	.	.	.	.	.	.
		Found dead		.	.	.	.	.	.	.	.	.

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 5 - 175 mg/kg Group 6 - 550 mg/kg
Group 7 - 1750 mg/kg Group 11 - 550 mg/kg Group 12 - 1750 mg/kg Group 14 - 5000 mg/kg
Group 16 - 1750 mg/kg Group 17 - 550 mg/kg Group 18 - 1750 mg/kg Group 19 - 5000 mg/kg
Group 20 - 1750 mg/kg Group 21 - 5000 mg/kg Group 22 - 1750 mg/kg

Individual Clinical Observations in Male Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
22m	798	No Abnormalities Detected		X	X	.	.	.	.	.	.	.	X
		Stained skin/fur - tan	Inguen	.	.	.	.	.	.	.	X	X	.
		Stained skin/fur - tan	Perineum	.	.	.	.	.	.	.	X	X	.
		Stained skin/fur - yellow	Chin	.	.	.	X	X	.	.	.	.	.
		Stained skin/fur - yellow	Inguen	.	.	.	.	X	X	X	.	.	.
		Stained skin/fur - yellow	Perineum	.	.	.	.	X	X	X	.	.	.
		Stained skin/fur - yellow	Perioral	.	.	.	X	X	X	X	.	.	.
		Wet fur	Inguen	.	.	.	.	X	X	.	.	.	.
		Wet fur	Perineum	.	.	.	X	X	X	X	.	.	.
		Wet fur	Perioral	.	.	X	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
22m	798	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		Stained skin/fur - tan	Inguen	.	.	.	.	.	.	.	.	.
		Stained skin/fur - tan	Perineum	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Chin	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Inguen	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Perineum	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Perioral	.	.	.	.	.	.	.	.	.
		Wet fur	Inguen	.	.	.	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	.	.	.	.	.
		Wet fur	Perioral	.	.	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 5 - 175 mg/kg Group 6 - 550 mg/kg
Group 7 - 1750 mg/kg Group 11 - 550 mg/kg Group 12 - 1750 mg/kg Group 14 - 5000 mg/kg
Group 16 - 1750 mg/kg Group 17 - 550 mg/kg Group 18 - 1750 mg/kg Group 19 - 5000 mg/kg
Group 20 - 1750 mg/kg Group 21 - 5000 mg/kg Group 22 - 1750 mg/kg

Individual Clinical Observations in Male Rats – (Continued)

Comments

Group Sex	Animal Number	Day Number	Time slot	Comment
12m	592	0	Ts2	discharge mouth is foamy

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 5 - 175 mg/kg Group 6 - 550 mg/kg
Group 7 - 1750 mg/kg Group 11 - 550 mg/kg Group 12 - 1750 mg/kg Group 14 - 5000 mg/kg
Group 16 - 1750 mg/kg Group 17 - 550 mg/kg Group 18 - 1750 mg/kg Group 19 - 5000 mg/kg
Group 20 - 1750 mg/kg Group 21 - 5000 mg/kg Group 22 - 1750 mg/kg

Individual Clinical Observations in Female Rats

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
1f	254	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
1f	254	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 3 - 1750 mg/kg Group 4 - 550 mg/kg
Group 8 – 1750 mg/kg Group 9 - 550 mg/kg Group 10 - 1750 mg/kg Group 13 - 5000 mg/kg
Group 15 - 1750 mg/kg

Individual Clinical Observations in Female Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
2f	263	No Abnormalities Detected		X	X	X	X	.	.	X	X	X	X
		Wet fur	Perineum	.	.	.	.	X	X	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
2f	263	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		Wet fur	Perineum	.	.	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 3 - 1750 mg/kg Group 4 - 550 mg/kg
Group 8 – 1750 mg/kg Group 9 - 550 mg/kg Group 10 - 1750 mg/kg Group 13 - 5000 mg/kg
Group 15 - 1750 mg/kg

Individual Clinical Observations in Female Rats – (Continued)

Group Sex	Animal Number	Clinical Sign	Site	Day numbers relative to Start Date: -1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
3f	478	No Abnormalities Detected		X	X	.	.	.	.	.	.	.	.
		Wet fur	Perioral	.	.	X	.	.	.	.	.	.	.
		Found dead		.	.	.	X	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
3f	478	No Abnormalities Detected		.	.	.	.	.	.	.	.	.
		Wet fur	Perioral	.	.	.	.	.	.	.	.	.
		Found dead		.	.	.	.	.	.	.	.	.

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 3 - 1750 mg/kg Group 4 - 550 mg/kg
Group 8 – 1750 mg/kg Group 9 - 550 mg/kg Group 10 - 1750 mg/kg Group 13 - 5000 mg/kg
Group 15 - 1750 mg/kg

Individual Clinical Observations in Female Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
4f	485	No Abnormalities Detected		X	X	X	X	.	.	X	X	X	X
		Stained skin/fur - brown	Chin	.	.	.	.	X	.	.	.	.	.
		Stained skin/fur - brown	Perioral	.	.	.	.	X	.	.	.	.	.
		Stained skin/fur - yellow	Inguen	.	.	.	.	.	X	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
4f	485	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		Stained skin/fur - brown	Chin	.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Perioral	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Inguen	.	.	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 3 - 1750 mg/kg Group 4 - 550 mg/kg
Group 8 – 1750 mg/kg Group 9 - 550 mg/kg Group 10 - 1750 mg/kg Group 13 - 5000 mg/kg
Group 15 - 1750 mg/kg

Individual Clinical Observations in Female Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
8f	527	No Abnormalities Detected		X	X	.	.	.	.	.	.	.	.
		Ataxia		.	.	X	X	X	.	.	.	.	.
		Breathing - labored		.	.	.	.	X	.	.	.	.	.
		Cold to touch		.	.	.	.	X	.	.	.	.	.
		Discharge - clear	Eye bilateral	.	.	.	.	X	.	.	.	.	.
		Lethargic		.	.	.	X	X	.	.	.	.	.
		Wet fur	Inguen	.	.	.	.	X	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	X	.	.	.	.	.
		Found dead		.	.	.	.	.	X	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
8f	527	No Abnormalities Detected		.	.	.	.	.	.	.	.	.
		Ataxia		.	.	.	.	.	.	.	.	.
		Breathing - labored		.	.	.	.	.	.	.	.	.
		Cold to touch		.	.	.	.	.	.	.	.	.
		Discharge - clear	Eye bilateral	.	.	.	.	.	.	.	.	.
		Lethargic		.	.	.	.	.	.	.	.	.
		Wet fur	Inguen	.	.	.	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	.	.	.	.	.
		Found dead		.	.	.	.	.	.	.	.	.

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 3 - 1750 mg/kg Group 4 - 550 mg/kg
Group 8 – 1750 mg/kg Group 9 - 550 mg/kg Group 10 - 1750 mg/kg Group 13 - 5000 mg/kg
Group 15 - 1750 mg/kg

Individual Clinical Observations in Female Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
9f	532	No Abnormalities Detected		X	X	.	.	.	.	.	.	X	X
		Breathing - lung noise		.	.	X	X	X	X	.	.	.	.
		Discharge - clear	Mouth	.	.	.	X	X	.	.	.	.	.
		Feces absent		.	.	.	.	.	X	X	.	.	.
		Not eating		.	.	.	.	.	X	X	.	.	.
		Stained skin/fur - brown	Chin	.	.	.	X	X	X	X	.	.	.
		Stained skin/fur - brown	Forelimb bilateral	.	.	.	.	.	.	X	.	.	.
		Stained skin/fur - yellow	Inguen	.	.	.	.	.	X	X	X	.	.
		Stained skin/fur - yellow	Perineum	.	.	.	.	.	X	X	X	.	.
		Wet fur	Chin	.	.	.	X	X	.	.	.	.	.
		Wet fur	Inguen	.	.	.	.	X	X	X	.	.	.
		Wet fur	Perineum	.	.	.	X	X	X	X	.	.	.
		Wet fur	Perioral	.	.	X	X	X	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
9f	532	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		Breathing - lung noise		.	.	.	.	.	.	.	.	.
		Discharge - clear	Mouth	.	.	.	.	.	.	.	.	.
		Feces absent		.	.	.	.	.	.	.	.	.
		Not eating		.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Chin	.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Forelimb bilateral	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Inguen	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Perineum	.	.	.	.	.	.	.	.	.
		Wet fur	Chin	.	.	.	.	.	.	.	.	.
		Wet fur	Inguen	.	.	.	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	.	.	.	.	.
		Wet fur	Perioral	.	.	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 3 - 1750 mg/kg Group 4 - 550 mg/kg
Group 8 – 1750 mg/kg Group 9 - 550 mg/kg Group 10 - 1750 mg/kg Group 13 - 5000 mg/kg
Group 15 - 1750 mg/kg

Individual Clinical Observations in Female Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
10f	594	No Abnormalities Detected		X	X	X	.	.	X	X	X	X	X
		Stained skin/fur - brown	Perioral	.	.	.	X	X	.	.	.	.	.
		Wet fur	Perineum	.	.	.	X	X	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
10f	594	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		Stained skin/fur - brown	Perioral	.	.	.	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 3 - 1750 mg/kg Group 4 - 550 mg/kg
Group 8 – 1750 mg/kg Group 9 - 550 mg/kg Group 10 - 1750 mg/kg Group 13 - 5000 mg/kg
Group 15 - 1750 mg/kg

Individual Clinical Observations in Female Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
13f	598	No Abnormalities Detected		X	X	.	.	.	.	.	.	.	.
		Lethargic		.	.	X	.	.	.	.	.	.	.
		Wet fur	Perioral	.	.	X	.	.	.	.	.	.	.
		Found dead		.	.	.	X	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
13f	598	No Abnormalities Detected		.	.	.	.	.	.	.	.	.
		Found dead		.	.	.	.	.	.	.	.	.
		Lethargic		.	.	.	.	.	.	.	.	.
		Wet fur	Perioral	.	.	.	.	.	.	.	.	.

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 3 - 1750 mg/kg Group 4 - 550 mg/kg
Group 8 – 1750 mg/kg Group 9 - 550 mg/kg Group 10 - 1750 mg/kg Group 13 - 5000 mg/kg
Group 15 - 1750 mg/kg

Individual Clinical Observations in Female Rats – (Continued)

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
15f	626	No Abnormalities Detected		X	X	.	.	.	.	.	.	.	.
		Breathing - lung noise		.	.	X	.	.	.	.	.	.	.
		Lethargic		.	.	X	.	.	.	.	.	.	.
		Wet fur	Chin	.	.	X	.	.	.	.	.	.	.
		Wet fur	Perioral	.	.	X	.	.	.	.	.	.	.
		Found dead		.	.	.	X	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
15f	626	No Abnormalities Detected		.	.	.	.	.	.	.	.	.
		Breathing - lung noise		.	.	.	.	.	.	.	.	.
		Lethargic		.	.	.	.	.	.	.	.	.
		Wet fur	Chin	.	.	.	.	.	.	.	.	.
		Wet fur	Perioral	.	.	.	.	.	.	.	.	.
		Found dead		.	.	.	.	.	.	.	.	.

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 3 - 1750 mg/kg Group 4 - 550 mg/kg
Group 8 – 1750 mg/kg Group 9 - 550 mg/kg Group 10 - 1750 mg/kg Group 13 - 5000 mg/kg
Group 15 - 1750 mg/kg

Individual Clinical Observations in Female Rats – (Continued)

Comments

Group Sex	Animal Number	Day Number	Time slot	Comment
9f	532	2	A	water bottle added
		3	A	water bottle added
		4	A	water bottle added
15f	626	0	Ts1	rubbing face on bottom of cage

X = Present

Nominal Dose: Group 1 - 175 mg/kg Group 2 - 550 mg/kg Group 3 - 1750 mg/kg Group 4 - 550 mg/kg
Group 8 – 1750 mg/kg Group 9 - 550 mg/kg Group 10 - 1750 mg/kg Group 13 - 5000 mg/kg
Group 15 - 1750 mg/kg

Appendix E
Individual Animal Gross Observations

Individual Gross Observations in Male Rats

Group: 1 Dose: 175 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
272	SACRIFICE BY DESIGN	14	(2)	No Visible Lesions

Group: 2 Dose: 550 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
274	SACRIFICED IN EXTREMIS	4	(0)	EPIDIDYMIDES; Small; bilateral TESTES; Small; bilateral Any remaining protocol required tissues, which have been examined, have no visible lesions

Group: 5 Dose: 175 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
474	SACRIFICE BY DESIGN	14	(2)	No Visible Lesions

Individual Gross Observations in Male Rats (Continued)

Group: 6 Dose: 550 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
547	SACRIFICE BY DESIGN	14	(2)	No Visible Lesions

Group: 7 Dose: 1750 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
475	FOUND DEAD	1	(0)	STOMACH; glandular; Discoloration; dark Any remaining protocol required tissues, which have been examined, have no visible lesions

Group: 11 Dose: 550 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
591	SACRIFICE BY DESIGN	14	(2)	No Visible Lesions

Group: 12 Dose: 1750 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
592	SACRIFICE BY DESIGN	14	(2)	No Visible Lesions

Individual Gross Observations in Male Rats (Continued)

Group: 14 Dose: 5000 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
640	FOUND DEAD	0	(0)	STOMACH; glandular; Discoloration; black STOMACH; glandular; Thick Any remaining protocol required tissues, which have been examined, have no visible lesions

Group: 16 Dose: 1750 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
641	FOUND DEAD	0	(0)	STOMACH; glandular; Discoloration; dark STOMACH; glandular; Thick Any remaining protocol required tissues, which have been examined, have no visible lesions

Group: 17 Dose: 550 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
894	SACRIFICE BY DESIGN	14	(2)	No Visible Lesions

Individual Gross Observations in Male Rats (Continued)

Group: 18 Dose: 1750 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
895	SACRIFICE BY DESIGN	14	(2)	No Visible Lesions

Group: 19 Dose: 5000 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
796	FOUND DEAD	0	(0)	SKIN; face; Stain; red STOMACH; glandular; Discoloration; dark STOMACH; glandular; Thick Any remaining protocol required tissues, which have been examined, have no visible lesions

Group: 20 Dose: 1750 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
820	SACRIFICE BY DESIGN	14	(2)	STOMACH; Distended with gas STOMACH; glandular; Thick Any remaining protocol required tissues, which have been examined, have no visible lesions

Individual Gross Observations in Male Rats (Continued)

Group: 21 Dose: 5000 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
821	FOUND DEAD	0	(0)	STOMACH; glandular; Discoloration; dark STOMACH; glandular; Thick Any remaining protocol required tissues, which have been examined, have no visible lesions

Group: 22 Dose: 1750 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
798	SACRIFICE BY DESIGN	14	(2)	STOMACH; Distended with gas Any remaining protocol required tissues, which have been examined, have no visible lesions

Individual Gross Observations in Female Rats

Group: 1 Dose: 175 mg/kg Sex: Female

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
254	SACRIFICE BY DESIGN	14	(2)	No Visible Lesions

Group: 2 Dose: 550 mg/kg Sex: Female

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
263	SACRIFICE BY DESIGN	14	(2)	No Visible Lesions

Group: 3 Dose: 1750 mg/kg Sex: Female

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
478	FOUND DEAD	0	(0)	STOMACH; glandular; Discoloration; dark Any remaining protocol required tissues, which have been examined, have no visible lesions

Individual Gross Observations in Female Rats (Continued)

Group: 4 Dose: 550 mg/kg Sex: Female

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
485	SACRIFICE BY DESIGN	14	(2)	No Visible Lesions

Group: 8 Dose: 1750 mg/kg Sex: Female

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
527	FOUND DEAD	1	(0)	MESENTERIC LYMPH NODES; Discoloration; dark SKIN; inguen; Discoloration; yellow SKIN; face; Discoloration; nose; red STOMACH; glandular; Discoloration; black; multiple: 1 cm linear Any remaining protocol required tissues, which have been examined, have no visible lesions

Group: 9 Dose: 550 mg/kg Sex: Female

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
532	SACRIFICE BY DESIGN	14	(2)	No Visible Lesions

Individual Gross Observations in Female Rats (Continued)

Group: 10 Dose: 1750 mg/kg Sex: Female

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
594	SACRIFICE BY DESIGN	14	(2)	No Visible Lesions

Group: 13 Dose: 5000 mg/kg Sex: Female

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
598	FOUND DEAD	0	(0)	ESOPHAGUS; Fluid; white: foamy SKIN; face; Wet STOMACH; glandular; Discoloration; dark: raised, 100% affected STOMACH; nonglandular; Discoloration; white STOMACH; nonglandular; Thick Any remaining protocol required tissues, which have been examined, have no visible lesions

Group: 15 Dose: 1750 mg/kg Sex: Female

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
626	FOUND DEAD	0	(0)	STOMACH; glandular; Discoloration; brown STOMACH; glandular; Thick Any remaining protocol required tissues, which have been examined, have no visible lesions