TRADE SECRET

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STUDY TITLE: H-28548: Subchronic Toxicity
90-Day Gavage Study in Mice

TEST GUIDELINES: OECD Guideline for the Testing of Chemicals
Section 4 (Part 408) (1998)

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STUDY COMPLETED ON: February 19, 2010

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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.

Study Director: Susan A. MacKenzie 19-FEB-2010

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QUALITY ASSURANCE STATEMENT

Work Request Number: 18405
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Key inspections for DuPont work request 18405, service code 1307 were completed by the Quality Assurance Unit of DuPont Haskell and the findings were submitted on the following dates.

Phase Audited	***Audit Dates***	***Date Reported to Principal Investigator (PI)/ PI Management***	***Date Reported to Study Director (SD)/ SD Management***
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Reported by: Donna M. Johnston 18 Feb. 2010
Donna M. Johnston Date
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CERTIFICATION

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

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STUDY INFORMATION

Substance Tested:
- HFPO Dimer Acid Ammonium Salt
- 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionic acid, ammonium salt
- 62037-80-3 (CAS Number)
- H-28548

Haskell Number: 28548

Composition: Proprietary

Purity: 84%

Physical Characteristics: Clear and colorless liquid

Stability: The test substance appeared to be stable under the conditions of the study; no evidence of instability was observed.

Study Initiated/Completed: July 17, 2009 / (see report cover page)

Experimental Start/Termination: July 23, 2009 / February 18, 2010

In-Life Initiated/Completed: July 23, 2009 / October 28, 2009

Notebook Number(s): E-98524-FP, E-113111-BI, E-113112-BI, E-113112-BQ

SUMMARY

The objective of this study was to evaluate the potential subchronic toxicity of H-28548 in mice. Four groups of young adult male and female Crl:CD1(ICR) mice (10/sex/group) were dosed by oral gavage for at least 90 days. Mice were dosed with the test substance at doses of 0 (control), 0.1, 0.5, or 5 mg/kg/day of H-28548. The control mice were dosed with deionized water.

Body weights, food consumption, and detailed clinical observations were evaluated weekly and acute clinical observations were evaluated daily. Ophthalmology and neurobehavioral (functional observational battery and motor activity) were evaluated prior to study start and near the end of the dosing period. Clinical pathology endpoints (hematology and clinical chemistry parameters) were evaluated at the end of the exposure period. After 96 (males) or 97 (females) days of dosing, the surviving mice designated for subchronic toxicity evaluation were sacrificed and given a gross and microscopic pathological examination.

An additional 15 mice/sex/dose were included in each group and were evaluated for plasma concentration of the test substance in samples collected approximately 2 hours after dosing on test days 0, 28, and 95 (5/sex/dose/timepoint). These mice were evaluated for body weight, food consumption, clinical signs, and ophthalmology (pretest only) but did not receive neurobehavioral or clinical or anatomic pathology evaluations.

Analysis of dosing formulations confirmed that the test substance was at the targeted concentrations for all dose levels and stable under relative storage conditions.

No test substance-related deaths occurred, and no clinical observations were attributed to exposure to the test substance. One male and 4 female mice died prior to scheduled sacrifice, due to gavage trauma. No adverse, test substance-related effects on body weight, body weight gain, food consumption, or food efficiency were observed. Non-adverse increases in body weight and nutritional parameters were observed in males in the 5 mg/kg/day group, but were attributed primarily to increased liver weights observed in this group. No test substance-related effect on any neurobehavioral parameter was observed in any dose group.

There were no adverse changes in hematology parameters that were attributed to H-28548 exposure. Increases in the level of multiple liver enzymes and total bile acids were observed in 5 mg/kg/day males and females and correlated with microscopic liver pathology effects observed at that dose. Minimal or mild increases in total protein and albumin and mildly reduced cholesterol levels were observed in males at 5 mg/kg/day. Minimally increased albumin was observed in females at 5 mg/kg/day. These protein and cholesterol changes were considered treatment related but non-adverse.

In 5 mg/kg/day male and female dose groups, increases were observed in the incidence of single cell necrosis, mitotic figures, and/or Kupffer cell pigment. The liver effects at 5 mg/kg/day correlated with clinical chemistry effects and were considered test substance related and adverse. Other test substance-related effects were observed in the livers of 0.5 and 5 mg/kg/day males and 5 mg/kg/day females, including increases in absolute and/or relative liver weight, enlarged and/or discolored livers, and centrilobular hepatocellular hypertrophy. The liver effects observed

in 0.5 mg/kg/day males were considered to be non-adverse adaptive responses as they were not correlated with clinical or microscopic pathology evidence of liver toxicity. Increased kidney weights and minimal tubular epithelial hypertrophy were observed in 5 mg/kg/day males but were considered to be non-adverse adaptive responses.

Results of analysis of plasma from multiple time points in females were consistent with a test substance that was cleared rapidly from the blood within one dosing interval, and that reached steady state on the first day of dosing. Compared to female mice, male mice took longer to clear the test substance from the blood, with steady state being achieved by test day 28. The plasma concentration was linear with dose, implying that absorption was not saturated over the range of doses tested in this study. Test substance was not present in plasma from control animals.

Under the conditions of this study, the no-observed-adverse-effect level (NOAEL) for H-28548 was 0.5 mg/kg/day in males and females, based on changes in clinical chemistry and histopathology indicative of liver toxicity in animals dosed with 5 mg/kg/day.

INTRODUCTION AND OBJECTIVE

The objective of this study was to evaluate the potential subchronic toxicity of H-28548 when administered by oral gavage to male and female mice for approximately 90 days. The oral route of administration was selected as the most efficient way to deliver an accurate dose.

In a previous study,[1] Crl:CD1(ICR) mice (10/sex/dose) were dosed with the test substance by oral gavage for 28 days at daily doses of 0, 0.1, 3, or 30 mg/kg/day. An additional 10 mice/sex/dose in the control and 30 mg/kg/day groups were dosed for 28 days then held for an additional 28 days without dosing (recovery group). No deaths or clinical observations were attributed to test substance exposure. Body weight and body weight gain in the 30 mg/kg/day groups were higher than in controls during the exposure period, and these increases were attributed to increased liver weights. Red blood cell mass parameters (RBC, hematocrit, hemoglobin) were slightly (< 10%) decreased relative to control in 30 mg/kg/day males, but were comparable to control in all other male and female dose groups.

Most changes in clinical pathology, pathology, and biochemical parameters were consistent with a peroxisome proliferator (PPARα agonist). Test substance-related effects on clinical chemistry were observed in males and females administered 3 and/or 30 mg/kg/day. Liver enzymes (alanine aminotransferase, alkaline phosphatase, sorbitol dehydrogenase, and aspartate aminotransferase (males only) were increased in males at 3 mg/kg/day and in both sexes at 30 mg/kg/day (not all statistically significant). These effects were associated with increased liver weights (males and females ≥ 3 mg/kg/day) and liver microscopic changes: hypertrophy (males and females ≥ 3 mg/kg/day), increased mitoses (males and females 30 mg/kg/day), necrosis (males ≥ 3 mg/kg/day), and single cell necrosis (males ≥ 3 mg/kg/day and females at 30 mg/kg/day). Biochemical changes were observed in the liver, including increased beta-oxidation at ≥ 0.1 mg/kg/day in males and ≥ 3 mg/kg/day in females, and reduced total cytochrome P450 content in males at ≥ 3 mg/kg/day. The following test substance-related effects on serum protein were observed in males and females: increased albumin and total protein (males only) at 30 mg/kg/day, reduced globulin and increased A/G ratio at ≥ 3 mg/kg/day.

Other observed differences of uncertain relationship to treatment included slightly increased adrenal weights with minimal adrenal cortical hypertrophy in 30 mg/kg/day males, a statistically significant increase in blood urea nitrogen in 30 mg/kg/day males with no associated increase in creatinine or kidney microscopic pathology, and increased number of 30 mg/kg/day females in the diestrus stage of the estrus cycle, compared to controls, with no other differences in ovarian morphology. Following the 28-day recovery period, all observed effects had reversed and were comparable to control except increased liver weights in males and females, which were mostly but not completely reversed in the 30 mg/kg/day dose group.

Based on the results of the 28-day study, doses of 0, 0.1, 0.5, and 5 mg/kg/day were selected for this study. The 5 mg/kg/day dose was expected to produce effects on clinical chemistry and liver biochemical parameters, organ weight, and/or histopathology in males and females. The 0.5 mg/kg/day dose was thought to possibly produce liver and clinical chemistry changes in

males but could be a no-observed-adverse-effect level (NOAEL) in females. The 0.1 mg/kg/day dose was expected to be a NOAEL in both males and females.

ANIMAL WELFARE ACT COMPLIANCE

This study complied with all applicable sections of the Final Rules of the Animal Welfare Act regulations (9 CFR) and the Guidelines from the Guide for the Care and Use of Laboratory Animals (NRC 1996). All studies conducted by or for DuPont Haskell adhere to the following principles:

- The sponsor and/or the study director ensures that the study described in this report does not unnecessarily duplicate previous experiments, and is in compliance with the DuPont Policy on Animal Testing.
- Whenever possible, procedures used in this study have been designed to implement a reduction, replacement, and/or refinement in the use of animals in an effort to avoid or minimize discomfort, distress or pain to animals. All methods are described in this study report or in written laboratory standard operating procedures.
- DuPont Haskell policy is that animals experiencing severe pain or distress that cannot be relieved are painlessly euthanized, as deemed appropriate by the veterinary staff and study director or appropriate designee.
- Methods of euthanasia used during this study were in conformance with the above referenced regulation and the recommendations of the American Veterinary Medical Association (AVMA), 2007 Guidelines on Euthanasia.
- Animals were provided with species-appropriate environmental enrichment.
- DuPont Haskell is accredited by the Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC) International.

STUDY DESIGN

Group		Number/Group[a]		Daily Dosage	Dose Formulation Concentration
Male	Female	Male	Female	(mg/kg)[b]	(mg/mL)[c]
1	1	25	25	0 (Control)	0
2	2	25	25	0.1	0.01
3	3	25	25	0.5	0.05
4	4	25	25	5	0.5

a First 10 animals/group designated for subchronic toxicity evaluation; remaining 15 animals/group designated for evaluation of plasma concentration of test substance (5/sex/dose/timepoint)
b Weight of test substance/kg animal body weight.
c Formulations were adjusted for purity (84%)

Study Parameters	Frequency[c]
Body Weight	Test day 0 and weekly thereafter
Food Consumption	Weekly
Daily Animal Health Observations	Twice daily
General Clinical Observations	Daily[a]
Detailed Clinical Observations	Test day 0 and weekly thereafter
Ophthalmology Evaluation	Pretest and week 12
Neurobehavioral Evaluation	Pretest and week 12
Clinical Pathology Evaluation	Week 13
Anatomic Pathology Evaluation	Week 13
Plasma Concentration of Test Substance[b]	Test day 0, week 3, and week 12

a A check for acute clinical signs of toxicity was conducted approximately 2 hours post-dosing.
b Evaluated in 5 animals/sex/dose/timepoint.
c Test day 0 was the first day of dosing and week 0 was the first week of dosing.

MATERIALS AND METHODS

A. Test Guidelines

The study design complied with the following test guidelines:

- OECD, Section 4 (Part 408): Repeated Dose Oral Toxicity Study in Rodents, *Guidelines for Testing of Chemicals* (1998)

B. Test Substance

The test substance, H-28548, was supplied by the sponsor as a clear and colorless liquid with a purity of 84%. The test batch used for this study was assigned Haskell number 28548.

C. Test System

On July 9, 2009, 110 male and 110 female Crl:CD1(ICR) mice, born approximately June 3, 2009, were received from Charles River Laboratories, Inc., Raleigh, North Carolina.

The Crl:CD1(ICR) mouse was selected based on consistently acceptable health status and on extensive experience with this strain at DuPont Haskell.

D. Animal Husbandry

1. Housing

Animals were housed individually in solid bottom caging with bedding and nestlets as enrichment. Each cage rack contained only animals of one sex.

2. Cage and Cage Rack Positioning

Cage racks were relocated within the animal room and cages on the racks were repositioned at least every 2 weeks.

3. Environmental Conditions

Animal rooms were maintained at a temperature of 18-26ºC (64-79ºF) and a relative humidity of 30-70%. Animal rooms were artificially illuminated (fluorescent light) on an approximate 12 hour light/dark cycle.

4. Feed and Water

All mice were provided tap water *ad libitum*. They were fed PMI® Nutritional International, LLC. Certified Rodent LabDiet® 5002 *ad libitum*.

5. 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. Pretest Period

Upon arrival at DuPont Haskell, all mice were housed in quarantine. They were:

- quarantined for at least 5 days.
- assigned an identification number, which was tattooed on the tail.
- weighed at least 3 times.

- given an ophthalmology evaluation (all animals) and an abbreviated neurobehavioral evaluation (all animals designated for subchronic toxicity evaluation plus spares).

The mice were released from quarantine based on body weights and clinical signs.

F. Assignment to Groups and Study Start

Mice of each sex were selected for use on study based on adequate body weight gain and freedom from any ophthalmology abnormalities or clinical signs of disease or injury. They were distributed by computerized, stratified randomization into study groups as designated in the Study Design, so that there were no statistically significant differences among group body weight means within a sex. The weight variation of selected mice did not exceed ± 20% of the mean weight for each sex. The first 10 mice in each group were designated for the subchronic toxicity evaluation. The next 15 mice assigned to each group were designated for analysis of concentration of the test substance in plasma (5/group/timepoint). If an animal designated for evaluation of subchronic toxicity died prior to scheduled sacrifice, it was replaced with an animal from the plasma concentration satellite group.

At study start (test day 0) the mice were approximately 7 weeks old.

Mice that were not assigned to a test group were released for other laboratory purposes.

G. Dose Formulation Preparation and Administration

H-28548 was formulated in deionized water. Dose formulations were prepared weekly with a correction for the sponsor-reported purity of 84%, and stored protected from light until used.

Animals were dosed daily by intragastric intubation at a dose volume of 10 mL/kg body weight. Animals were dosed at approximately the same time (± 2 hours) each day, except on the days of the end-of-study eye examination and neurobehavioral evaluations, when dosing was delayed due to these procedures. All animals were dosed for at least 90 days, except those designated for plasma concentration evaluation at earlier timepoints. The amount of test substance each mouse received was based on the most recently collected body weight and the formulation concentration. Control mice were dosed with deionized water at a volume of 10 mL/kg of body weight.

H. Dose Formulation Sampling and Analysis

Stability of the test substance formulations was established prior to study start.

Samples of each dosing formulation were collected 3 times during the study for verification of concentration of the test substance: near the beginning, middle, and end of the study. Analysis was performed by the DuPont Haskell Regulatory Analytical Chemistry group. At the time of analysis, the samples were diluted with an appropriate solvent and analyzed by a high-performance liquid chromatography method with mass spectrometry detection (LC/MS). Detailed methods, along with the sample preparation procedure are fully documented in the study records and are described in the final report (Appendix B).

On days samples were collected, the formulations remaining after dosing were saved and stored under conditions of established stability for possible additional analysis. These formulations were discarded as no additional analysis was necessary.

I. Body Weights

All mice were weighed once each week. In addition, mice designated for neurobehavioral evaluation were weighed on the days of those observations and mice designated for evaluation of plasma concentrations of test substance were weighed on the day of blood collection. All mice were weighed on the day of sacrifice.

J. Food Consumption and Food Efficiency

The amount of food consumed by each animal over each weighing interval was determined by weighing each feeder at the beginning and end of the interval and subtracting the final weight from the initial weight. From these measurements, mean daily food consumption over the interval was determined. From the food consumption and body weight data, the mean daily food efficiency was calculated.

K. Clinical Observations

1. Daily Animal Health Observations

Cage-site examinations to detect moribund or dead mice and abnormal behavior and/or appearance among mice were conducted at least twice daily throughout the study. Abnormal behavior/appearance was recorded by exception. Moribund mice were sacrificed and necropsied.

2. General Clinical Observations

An additional cage-site evaluation was conducted approximately 2 hours after the last animal was dosed to detect acute clinical signs of systemic toxicity. Only those animals exhibiting a sign were recorded in the study records.

3. Detailed Clinical Observations

At every weighing (excluding weights on days of neurobehavioral evaluations, blood collection for plasma concentration, and at scheduled sacrifice), each mouse was individually handled and examined for abnormal behavior and appearance. Detailed clinical observations in a standardized arena were also evaluated on all mice. The detailed clinical observations included (but were not limited to) evaluation of fur, skin, eyes, mucous membranes, occurrence of secretions and excretions, autonomic nervous system activity (lacrimation, piloerection, and unusual respiratory pattern), changes in gait, posture, response to handling, presence of clonic, tonic, stereotypical, or bizarre behavior. Any abnormal clinical signs noted were recorded.

L. Ophthalmology Evaluation

Two ophthalmology evaluations were conducted by a veterinary ophthalmologist. The pretest examination was performed on all mice received for the study, prior to assignment to groups. One mouse with preexisting ophthalmology abnormalities was eliminated from use in the study. All surviving mice designated for subchronic toxicity evaluation were examined prior to the final sacrifice.

Both eyes of each mouse were examined by focal illumination and indirect ophthalmoscopy. The eyes were examined in subdued light after mydriasis has been produced.

A report of findings from each ophthalmology evaluation was submitted by the examining veterinarian. The findings from the pretest examination were documented in the study records but not included in this report.

M. Neurobehavioral Evaluation

For all the following assessments, the experimenter was unaware of the group designation of the animal.

Prior to initiation of test substance administration (but after grouping) and then during week 13 of dose administration, an abbreviated functional observational battery (FOB) and motor activity (MA) were conducted on all surviving animals designated for subchronic toxicity evaluation. Spare mice were also evaluated for FOB and MA prior to study start.

For each evaluation, the FOB and MA assessments were conducted in 4 replicates over multiple days to minimize the influence of uncontrolled factors for each evaluation. Assignment to a given replicate was counterbalanced across all groups. Replicate designation was not reported in the final report, but was recorded in the study records.

Testing was conducted in a sound attenuated room equipped with a whit-noise generation system to minimize environmental variations in the test conditions. Animals were acclimated for at least 10 minutes in the FOB laboratory prior to initiation of the evaluation.

Animals were weighed on the day of the FOB assessment, however, these weights were not necessary for interpretation of the data, and therefore will be maintained in the study records, but not included in the final report..

1. Abbreviated Functional Observational Battery

Assessments of responses to approach/touch, sharp auditory stimulus, and tail pinch were made while the animal was in a standard arena.

Combined forelimb and hindlimb grip strength was measured by a strain gauge device (Chatillon® Digital Force gauge) by allowing the animal to grip the angled wire screen with all 4 paws. The animal was gently pulled across the screen with a fluid motion until it released all 4 paws. Each animal was given 4 trials per evaluation, and a mean value was calculated.

Pupillary constriction was measured immediately prior to removing the mice from the MA chambers (Section 2. below) because the darkened room in which the apparatus was located facilitated observing the response. The presence or absence of pupillary constriction was assessed after a beam of light was directed into each eye.

2. Motor Activity Evaluation

Following the evaluation of grip strength and sensory function, assessment of MA was conducted. Mice were individually tested in one of 30 identical, automated activity monitors (Coulbourn® Infrared Motor Activity System). Group and sex were counterbalanced across the monitors and time of day to the fullest extent possible. The infrared monitoring device enables measurement of 2 dependent variables: duration of movement and number of movements. A continuous movement was counted as 1 movement regardless of duration. The technical characteristics of the measurement system are such that duration of movement is analogous to "counts" in other types of devices that employ interruption of light beams. Duration of movement and number of movements were evaluated in 9 consecutive blocks of 10 minutes each as well as for the total 90-minute session.

Presence of diarrhea and polyuria on the cageboards below the MA monitor was also recorded following each MA session.

3. Test Facility Positive Control Data

Procedures and data describing the effects of positive control substances are presented in 3 separate reports.[2,3,4] These positive control studies are the basis of training certification for the people making judgments in the neurobehavioral and neuropathology tests. The data also document that the equipment and procedures are capable of detecting effects that may be seen in neurotoxicity studies of this type.

N. Clinical Pathology Evaluation

A clinical pathology evaluation was conducted on all animals designated for subchronic toxicity on test days 96 and 97 for males and females, respectively. These animals were not fasted prior to blood collection. Blood samples for hematology and clinical chemistry measurements were collected from the orbital sinus of each animal while the animal was under isoflurane anesthesia. Bone marrow smears were prepared at sacrifice from all surviving animals. Bone marrow smears were stained with Wright-Giemsa stain, but analysis was not necessary to support experimental findings. All blood samples were evaluated for quality by visual examination and results were included in the study records.

1. Hematology and Coagulation

Complete blood counts, including reticulocytes, were determined on a Bayer® Advia 120 hematology analyzer or determined from microscopic evaluation of the blood smear. Wright-Giemsa-stained blood smears from all animals were examined microscopically for confirmation of automated results and evaluation of cellular morphology.

The following parameters were determined:

red blood cell count	red cell distribution width
hemoglobin	absolute reticulocyte count
hematocrit	platelet count
mean corpuscular (cell) volume	white blood cell count
mean corpuscular (cell) hemoglobin	differential white blood cell count
mean corpuscular (cell) hemoglobin concentration	microscopic blood smear examination

2. Clinical Chemistry

Serum clinical chemistry parameters were determined on an Olympus® AU640 clinical chemistry analyzer.

The following parameters were determined (number indicates priority order if blood volume was limiting):

alanine aminotransferase[1]	aspartate aminotransferase[2]
sorbitol dehydrogenase	total bilirubin[2]
alkaline phosphatase[1]	glucose[2]
urea nitrogen[1]	bile acids[2]
creatinine[1]	
cholesterol[1]	calcium[3]
triglycerides[1]	inorganic phosphorus[3]
total protein[1]	sodium[3]
albumin[1]	potassium[3]
globulin[1]	chloride[3]
A/G ratio[1]	

O. Anatomic Pathology Evaluation

1. Mice Designated for the Subchronic Toxicity Evaluation

After approximately 90 days on study (test days 96 for males and 97 for females), the surviving mice from each exposure level (0, 0.1, 0.5, and 5 mg/kg/day) were weighed, sacrificed and necropsied for evaluation of subchronic toxicity. The order of sacrifice for scheduled deaths was stratified across treatment groups within a sex. Mice were euthanized by carbon dioxide anesthesia and exsanguination. Gross examinations were performed on all mice.

Of the 80 mice designated for the subchronic toxicity evaluation (10/sex/exposure level), 2 mice died before the terminal sacrifice. One group 3 female (mouse 355) and one group 4 female (mouse 456) were euthanized for humane reasons on test day 6 and 20 respectively. These animals received a gross and microscopic examination, although organs were not weighed.

The following tissues were collected from the 80 mice designated for the terminal sacrifice, including the 2 early decedents:

Digestive System	Cardiovascular System	Musculoskeletal System
liver	heart	skeletal muscle
esophagus	aorta	femur/knee joint
stomach		sternum
duodenum	Hematopoietic System	
jejunum	spleen	Reproductive System
ileum	thymus	Male
cecum	mandibular lymph node	testes
colon	mesenteric lymph node	epididymides
rectum	bone marrow[a]	prostate
salivary glands	Peyer's patches[b]	seminal vesicles
pancreas		Female
gall bladder	Endocrine System	ovaries (with oviducts)
	pituitary gland	uterus (with cervix)
Urinary System	thyroid gland	mammary glands
kidneys	parathyroid glands	vagina
urinary bladder	adrenal glands	
		Miscellaneous
Respiratory System	Nervous System	skin
lungs	brain (including cerebrum, cerebellum, medulla/pons)	eyes (including retina)
trachea	spinal cord (cervical, mid-thoracic, lumbar)	gross observations[c]
nose (4 sections)	sciatic nerve	
pharynx/larynx	optic nerves	

a Bone marrow was collected with the femur and sternum.
b Peyer's patches were collected from sections of the intestine.
c Gross observations made at necropsy for which histopathology was not appropriate (e.g., fluid, ruffled fur, and missing anatomic parts) were generally not collected.

The following tissues were weighed from mice sacrificed by design at the end of the subchronic toxicity study: liver, kidneys, adrenal glands, thymus, brain, spleen, heart, testes, epididymides, ovaries, and uterus. Relative organ weights (relative to final body weight; relative to brain weight) were calculated.

Testes, epididymides, and eyes were fixed in modified Davidson's solution. All other tissues were fixed in 10% neutral buffered formalin. Processed tissues were embedded in paraffin, sectioned approximately 5-6 microns thick, stained with hematoxylin and eosin (H&E), and examined microscopically by a veterinary pathologist.

All tissues collected from control and high-dose (5 mg/kg/day) mice at the terminal sacrifice (test days 96 and 97), and tissues collected from early decedents were processed to slides and evaluated microscopically. Potential target organs (liver in males and females; kidneys in males only) and gross observations (as recorded at necropsy) were examined microscopically for all animals designated for the subchronic toxicity evaluation.

2. Mice Designated for Plasma Concentration Evaluation

Of the 120 mice designated for plasma concentration evaluation (5/sex/exposure level/ time point), 3 mice died or were euthanized before their scheduled sacrifice.

One group 1 female (mouse 165) was found dead on day 16. One group 3 male (mouse 312) and one group 3 female (mouse 367) were euthanized for humane reasons on test day 3 and 6, respectively. These animals received a gross examination and tissues were collected (same as for main study mice), but organs were not weighed and a microscopic examination was not performed. The gross findings of these 3 animals were unrelated to test substance exposure and have been included in individual animal pathology data (Appendix M).

After collection of blood, the animals were euthanized by carbon dioxide asphyxiation and exsanguination and discarded without necropsy.

P. Plasma Concentration Evaluation

Plasma was evaluated for plasma concentration of H-28548 in 5 mice/sex/dose at the 0-, 28- and 95-day time points. The test substance was extracted and analyzed by liquid chromatography/ mass spectrometry.[5]

STATISTICAL ANALYSES

Significance was judged at $p < 0.05$. Separate analyses were performed on the data collected for each sex.

		Method of Statistical Analysis	
Parameter	Preliminary Test	If preliminary test is not significant	If preliminary test is significant
Body Weight Body Weight Gain Food Consumption Food Efficiency Clinical Pathology[a] Organ Weight	Levene's test for homogeneity[6] and Shapiro-Wilk test[7] for normality[b]	One-way analysis of variance[8] followed by Dunnett's test[9,10,11]	Kruskal-Wallis test[12] followed by Dunn's test[13]
Survival Incidence of FOB Descriptive Parameters	None	Cochran-Armitage test for trend[8][c]	

		Method of Statistical Analysis	
Parameter	Preliminary Test	If preliminary test is not significant	If preliminary test is significant
Motor Activity[d] Grip Strength	Levene's test for homogeneity[6] and Shapiro-Wilk test[7] for normality[b]	Repeated measures analysis of variance[14] followed by linear contrasts[15]	A normalizing, variance stabilizing transformation followed by repeated measures analysis of variance[14] or sequential application[16] of the Jonckheere-Terpstra trend test[e][17]

a When an individual observation was recorded as being less than a certain value, calculations were performed on half the recorded value. For example, if bilirubin was reported as < 0.1, 0.05 was used for any calculations performed with that data. When an individual observation was recorded as being greater than a certain value, calculations were performed on the recorded value. For example, if specific gravity was reported as > 1.083, 1.083 was used for any calculations performed with that data.

b If the Shapiro-Wilk test was not significant but Levene's test was significant, a robust version of Dunnett's test was used. If the Shapiro-Wilk test was significant, Kruskal-Wallis test was followed by Dunn's test.

c If the incidence was not significant, but a significant lack of fit occurred, then Fisher's Exact test with a Bonferroni-Holm correction was used.[18,19]

d Test day and 10-minute interval were used as repeated-measure factors.

e If there was a significant lack of monotonicity (i.e., Linear Trend:Dose was not significant, and Quadratic Trend:Dose was significant), Dunn's[13] test was used instead of Jonckheere-Terpstra

RESULTS AND DISCUSSION

Dose Formulations Analytical Evaluation

A. Dose Formulations Analytical Evaluation

(Appendix B)

The analytical results demonstrate that the test substance was at the targeted concentrations for all dose levels and stable for up to 15 days when stored at room temperature in the vehicle in the concentration range for the study. Test substance was not detected in the 0 mg/mL control samples. These results support that animals received the targeted dose of test substance.

In-Life Toxicology

A. Mean Body Weights and Body Weight Gains

(Tables 1-4, Figures 1-2, Appendix C)

No adverse, test substance-related effects on mean body weight or mean body weight gain were observed in any male or female group.

Statistically significant increases in mean final body weight (test day 91) and overall body weight gain (test days 0-91) were observed in the male 5 mg/kg/day group, relative to control. Mean final body weight and overall body weight gain were 108% and 136% of control, respectively. Mean body weight in this group was higher than control on all test days (variable statistically significance). Body weight gain was significantly higher than control over 2 weekly intervals (test days 49-56 and 84-91). No statistically significant differences in mean body weight or body weight gain were observed in any other male test group on any test day or over any test week. The difference in body weight and body weight gain in the high dose males was attributed primarily to increased liver weight, and was not considered adverse.

Mean final body weight and overall body weight gain in the 5 mg/kg/day female group were 101% and 98% of control, respectively (neither statistically significant). Mean body weight gain in the female 0.5 mg/kg/day group was significantly higher than control over test days 7-14 and significantly lower than control over test days 28-35, but these differences were considered spurious as overall body weight gain in this group was comparable to control. No other statistically significant differences in body weight or body weight gain were observed in any groups on any test day or over any test week.

B. Food Consumption and Food Efficiency

(Tables 5-8, Appendix D)

No adverse, test substance-related effects on mean food consumption or food efficiency were observed in any male or female group.

Statistically significant increases in mean overall (test days 0-91) food consumption and food efficiency were observed in the male 5 mg/kg/day group, relative to control. Mean overall food consumption and food efficiency were 111% and 127% of control, respectively. Mean weekly food consumption in this group was higher than control over all weeks except test days 0-7 (statistically significant over most intervals). Mean weekly food efficiency was higher than control over the first 6 weekly intervals, but none of the differences was statistically significant. Weekly food efficiency over the rest of the study was variable, with higher and lower mean values (variable statistical significance). The higher food efficiency is likely due to increased body weight due to enlarged livers in this group. No statistically significant differences in mean food consumption or food efficiency were observed in any other male test group on any test day or over any test week.

Mean overall food consumption and food efficiency in the 5 mg/kg/day female group were 102% and 100% of control, respectively (neither statistically significant). No statistically significant differences in food consumption were observed over any weekly interval in this group. Mean food efficiency in the female 0.5 mg/kg/day group was significantly higher than control over test days 7-14 and significantly lower than control over test days 28-35. These differences were correlated with differences in body weight gain over those intervals and were considered spurious as overall food efficiency in this group was comparable to control. No other statistically significant differences in food consumption or food efficiency were observed in any groups on any test day or over any test week.

C. Clinical Observations

(Tables 9-10, Appendix E)

There were no test substance-related deaths. One control female mouse was found dead on test day 16. One male mouse (0.5 mg/kg/day; test day 3) and 3 female mice (2 at 0.5 mg/kg/day on test day 6 and 1 at 5 mg/kg/day on test day 20) were euthanized due to clinical signs attributed to misdosing. These animals displayed clinical signs related to injury from the gavage misdosing (swollen neck and/or shoulder, abnormal breathing, cold, dehydrated, and/or lethargic; abnormal gait) prior to death.

One male in the 0.1 mg/kg/day group (201) exhibited aggressiveness and convulsions, each on one day, and hyperreactivity over multiple days, especially over the second half of the dosing period. These signs were not considered to be test substance related as they only occurred in one male mouse in the low dose group and were not associated with any correlative pathology findings.

One female in the 5 mg/kg/day group (451) exhibited intermittent signs of hyperactivity, hyperreactivity, and running in circles. Although this female was in the high dose group, these

signs were not attributed to test substance exposure as they only occurred in one mouse, they were not seen everyday, the observations were separated by hours and days when the mouse exhibited no abnormal signs, the signs were often observed prior to dosing (when test substance blood levels would have been expected to be at the lowest level) and they were not associated with any correlative pathology findings.

All other clinical observations were typical of those seen in mice of this age and were not considered to be test substance related.

D. Ophthalmology Evaluation

(Tables 11-12, Appendix F)

No ophthalmological signs were observed in any mouse in any group.

E. In-Life Conclusions

No adverse effects on any in-life parameter were observed in any male or female dose group. Increased body weight, body weight gain, food consumption, and food efficiency were observed in male mice at 5 mg/kg/day, but were not considered adverse as these parameters were greater than in control. The body weight and food efficiency differences were primarily attributed to an increase in liver weight in this group.

Neurobehavioral Evaluation

A. Abbreviated Functional Observational Battery

1. Grip Strength

(Tables 13-14, Appendix G)

There were no test substance-related effects on strength in males or females administered any dosage of the test substance. Mean values for the test groups were similar to the values of the control groups.

2. Observations

(Tables 15-16, Appendix H)

There were no test substance-related effects on any behavioral parameter evaluated in either males or females.

B. Motor Activity

(Tables 17-20, Appendices I-J)

There were no test substance-related effects on duration of movement or number of movements for males or females. Mean values of the test groups were similar to the values of the control groups.

C. Neurobehavioral Conclusions

Under the conditions of the study, the test substance had no effect on neurobehavioral parameters in either males or females.

Clinical Pathology Evaluation

A. Hematology

(Tables 21-22, Appendix K)

There were no adverse or treatment-related changes in group mean hematology parameters at test day 96 (males) or 97 (females). The following statistically significant changes were not considered to be test substance related or adverse.

- Mean corpuscular hemoglobin (MCHC) was minimally decreased in male mice dosed with 5 mg/kg/day (97% of control). MCHC is a calculated hematology parameter using values for hemoglobin, red blood cell and mean corpuscular volume ((hemoglobin/[red blood cell * mean corpuscular volume])* 100). There were no statistically significant decreases in red cell mass parameters (red blood cell, hemoglobin, hematocrit), mean corpuscular volume or changes in red cell morphology. Therefore, minimally decreased MCHC was considered to be spurious.

- Platelet count (PLT) was minimally increased in male mice dosed with 0.5 or 5 mg/kg/day (127% and 126% of control, respectively). Changes in platelet count did not show a dose response relationship despite the 10-fold increase in dose. There were no clinical signs or pathology or clinical pathology changes consistent with biological processes that might be associated with thrombocytosis (e.g., acute or chronic inflammation). In addition, higher platelet counts were not seen in a previous 28 day gavage study[(1)] with the same test substance. Therefore, the higher platelet counts in the 0.5 and 5.0 mg/kg/day male groups were considered to be unrelated to treatment and non-adverse.

- Absolute monocyte count (AMON) was minimally decreased in female mice dosed with 0.1 mg/kg (25% of control). This decrease was not dose related, as a similar change was not seen in the higher dose groups. Therefore the lower AMON in the 0.1 mg/kg/day female group was not considered to be test substance related or adverse.

B. Clinical Chemistry

(Tables 23-24, Appendix K)

Test substance-related increases in a number of liver-related clinical chemistry parameters were present in male and female mice administered 5 mg/kg/day. Increases were mild to severe, were consistently more severe in males compared to females, and included increases in aspartate aminotransferase (AST), alanine aminotransferase (ALT), sorbitol dehydrogenase (SDH), alkaline phosphatase (ALKP) and total bile acids (TBA) (Text Table 1). Changes in these parameters were consistent with hepatocellular damage and/or cholestasis, correlated microscopically with hepatocellular single cell necrosis in male (10/10) and female (1/10) mice at this dose, and thus were considered to be adverse effects.

There were no statistically significant changes in liver enzyme parameters in male or female mice administered 0.5 or 0.1 mg/kg/day.

Text Table 1

	Male Mice – Test Day 96				Female Mice – Test Day 97			
Group:	1	2	3	4	1	2	3	4
Dosage (mg/kg):	0	0.1	0.5	5	0	0.1	0.5	5
AST (U/L)	62	67[a] 108%[b]	84 135%	**128** **206%**	68	71 104%	69 101%	74 109%
ALT (U/L)	49	62 127%	66 135%	**255** **520%**	36	36 100%	32 89%	**51** **142%**
SDH (U/L)	26.6	26.0 98%	25.8 97%	**108.5** **408%**	25.3	22.9 91%	23.6 93%	**33.5** **132%**
ALKP (U/L)	50	55 110%	70 140%	**617** **1234%**	65	77 118%	72 111%	**158** **243%**
TBA (µmol/L)	1.2	1.2 100%	1.4 117%	**11.1** **925%**	4.3	2.3 53%	2.7 63%	13.2 307%

a mean
b % of control
Bold = statistically significant

There were no other adverse changes in group mean clinical chemistry parameters in male or female mice. The following statistically significant changes in mean clinical chemistry parameters were not adverse or not related to exposure to the test substance:

- Total protein (TP) and albumin (ALB) were minimally increased in male mice dosed with 5 mg/kg (110% and 114% of control, respectively). ALB was also minimally increased in female mice at the same dose (104% of control). These changes were considered to be treatment-related due to the consistency of change among individual animals. However, minimally increased total protein and albumin have no toxicologic significance; therefore, these changes were considered to be non-adverse.

- Cholesterol (CHOL) was mildly decreased in male mice dosed with 5 mg/kg (74% of control). There are no known adverse effects associated with minimal decreases in cholesterol. Therefore, these changes were considered test substance related but non-adverse.

- Bilirubin (BILI) was minimally decreased in female mice dosed with 5 mg/kg. However, this statistical difference was not considered treatment related or indicative of an adverse effect, The magnitude of difference in BILI was small (86% of control), the individual BILI values in all 5 mg/kg/day females except one were within the concurrent control range, and no changes in BILI were present in male mice, the more sensitive gender. In addition, the direction of change in BILI in 5 mg/kg/day females–decreased rather than increased–is not considered adverse. Therefore, these changes were not considered to be treatment related or adverse.

- Potassium (K) was decreased in male and female mice dosed with 5 mg/kg (87% and 91% of control, respectively). Decreased K typically occurs when there is a shift of K from extra cellular fluid to intracellular fluid (e.g., in metabolic alkalosis), a decreased dietary intake of K, or an increased loss of K via kidneys (e.g., polyuria), alimentary tract (e.g., diarrhea) or skin (e.g., sweating). In the present study, the relationship of this finding to test substance administration is uncertain. However, there were no clinical signs suggestive of hypokalemia and no test substance-related alterations in sodium (Na). Therefore, the minimal change in K was not considered to be adverse.

- Decreased bilirubin (BILI) in male mice dosed with 0.5 mg/kg (76% of control) was not dose related and was thus considered to be a spurious finding.

- Chloride (CL) was slightly higher (102% of control) in male mice dosed with 5 mg/kg. Based on the minimal nature of the change and lack of any correlative findings, this change was considered to be unrelated to treatment and nonadverse.

C. Clinical Pathology Conclusions

In conclusion, under the conditions of this study, adverse changes in liver-related parameters (AST, ALT, SDH, ALKP, TBA) were present in male and female mice dosed with 5 mg/kg/day. No adverse changes in clinical pathology parameters were present in male or female mice dosed with 0.5 or 0.1 mg/kg/day.

Anatomic Pathology Evaluation

A. Cause of Death

(Appendices M-N)

There were no test substance-related deaths among any mice on study. Two mice designated for subchronic toxicity evaluation and 3 mice designated for plasma concentration evaluation were either found dead or sacrificed for humane reasons prior to scheduled sacrifice.

One group 3 female (mouse 355) was euthanized on test day 6 because of respiratory signs. Gross examination revealed impacted esophagus and edema in the ventral neck region. Significant histopathological findings in this animal included necrosis and acute inflammation in pharynx and esophagus which were consistent with gavage injury. Lymphoid depletion/necrosis in thymus, spleen and lymph nodes (submandibular and mesenteric) was also observed in this animal, which were likely the result of stress.

One group 4 female (mouse 456) was also euthanized on test day 20 because of respiratory signs. Gross examination revealed discolored lungs, which had no microscopic correlate. Significant microscopic findings in this animal included hepatocellular hypertrophy associated with mild subcapsular necrosis. Lymphoid depletion of the thymus was also observed in this animal and was likely secondary to stress. The liver changes observed in this animal were not severe enough to explain the morbidity of this animal. Although a microscopic correlate was not observed in the sections examined, the gross findings in the lungs, as well as clinical signs suggestive of respiratory distress, suggest that the most likely cause of death in this animal was also gavage injury.

Gross findings in the 3 mice that died prior to scheduled sacrifice, in the plasma concentration subgroup, included lung discoloration, pleural adhesions, and foreign material in skin (axilla). Based on gross lesions, gavage injury is likely cause of morbidity and mortality in these animals. Microscopic pathology evaluation was not conducted in these animals.

B. Organ Weight Data

(Tables 25-26, Appendix L)

A test substance related increase in mean liver weight parameters was observed in mice exposed to ≥ 0.5 mg/kg/day in males and 5 mg/kg/day in females.

In the 5 mg/kg/day males, mean absolute and mean relative (% brain weight and % body weight) liver weights were increased to 263%, 242%, and 230% of control, respectively (Text table 2). These increases were statistically significant. In the 0.5 mg/kg/day males, mean absolute and mean relative (% brain weight and % body weight) liver weights were also increased (not statistically significant) to 112%, 113%, and 111% of control, respectively. In 5 mg/kg/day females, mean absolute and mean relative (% brain weight and % body weight) liver weights were increased (statistically significant) to 169% , 167% and 169% of control, respectively.

Increased liver weight parameters were considered test substance related in males given ≥ 0.5 mg/kg/day and in females given 5 mg/kg/day. The increase in liver weight parameters in both sexes correlated with a treatment-related increase in enlarged liver (see gross findings) and microscopic hepatic changes (see microscopic findings).

Text Table 2: Test Substance-Related Effects on Mean Absolute and Relative Liver Weights

Dose (mg/kg/day):	0	0.1	0.5	5
Male				
Number of Mice:	10	10	10	10
Mean final body weight (grams)	38.7	40.3	38.9	44.3*
Liver				
absolute weight (grams)	1.955	2.024	2.186	5.144*
Liver weight/body weight x 100	5.06	5.028	5.618	11.637*
Female				
Number of Mice:	10	10	9	9
Mean final body weight (grams)	32.2	32.1	32.6	32.4
Liver				
absolute weight (grams)	1.693	1.697	1.745	2.867*
Liver weight/body weight x 100	5.225	5.309	5.337	8.811*

* Statistically significant as compared to control value.
Underlined values were interpreted to be test-substance related increases, as compared to control values.

Mean relative (to brain) weight of kidneys was increased (statistically significant) in male mice given 5 mg/kg/day of test substance as compared to controls. Although minimal renal tubular hypertrophy was present in this group, the change in kidney weight relative to brain weight was not associated with changes in mean absolute or relative (% body weight) kidney weights. Therefore, the significance of the kidney weight change relative to test substance administration is uncertain.

Mean weights of brain and epididymides relative to body weight were lower, and mean weight of heart relative to brain weight was higher in male mice given 5 mg/kg/day of test substance as compared to controls (all statistically significant). These changes occurred without correlative changes in other weight parameters for these organs or with microscopic findings. Thus, these organ weight changes were not considered to be test substance related.

Mean spleen weight relative to brain and body weight were decreased relative to controls in the 0.5 and 5 mg/kg/day female mice respectively. These changes did not occur in a dose-related manner, were not associated with changes in mean absolute spleen weight, and were not associated with test substance-related microscopic changes in the spleen. In addition, no spleen weight changes occurred in male mice in any dose group. Therefore, the changes in mean spleen weight relative to brain and body weight in females were considered spurious and unrelated to treatment.

In females, mean absolute and mean relative (% brain and % body weight) ovarian weights were increased to 203%, 206%, and 208% of control, respectively. These ovarian weight changes did not occur in dose related manner. Ovaries of 3 female mice (357, 359 and 360) in the 0.5 mg/kg/day exposure group had cysts and their ovarian weights were outside the range of individual values in control or high dose animals. Therefore, the increase in mean ovarian

weights in the 0.5 mg/kg/day group is due to the influence of 3 female mice having ovarian cysts. Ovarian cysts in this exposure group were considered as background lesions and no dose-response for this lesion was observed. Therefore, the ovarian weight changes in 0.5 mg/kg/day female mice were considered spurious and unrelated to test substance administration.

C. Gross Observations

(Tables 27-28, Appendix M)

At the terminal sacrifice, enlarged and/ or discolored livers were observed in 4/10 and 9/10 male mice exposed to 0.5 mg/kg/day and 5 mg/kg/day of test substance respectively (Text Table 3). In the 5 mg/kg/day group 3/10 female mice had enlarged livers. These gross changes were considered test substance related. Liver enlargement and discoloration correlated with test substance related increases in liver weights (see Organ Weights) and microscopic hepatocellular hypertrophy and (see Microscopic Findings).

Text Table 3: Test Substance-Related Gross Observations in Mice

	Male				Female			
Dose (mg/kg/day):	0	0.1	0.5	5	0	0.1	0.5	5
mice/group:	10	10	10	10	10	10	10	10
Liver	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
Large	0	0	1	9	0	0	0	3
Discoloration	0	0	4	5	1	0	0	3

Numbers in parentheses are the number of tissues examined within each group.
Underlined values were interpreted to be test substance-related gross findings.

All other gross observations were consistent with normal background lesions in mice of this age and strain.

D. Microscopic Observations

(Tables 29-30, Appendix N)

1. Liver

Test substance-related and adverse microscopic findings were present in the liver of male and female mice administered 5 mg/kg/day of the test substance. At 0.5 mg/kg/day, test substance-related microscopic changes were limited to male mice which had minimal hepatocellular hypertrophy, without evidence of liver cell injury. Therefore, this change was considered to be test substance related but not adverse. There were no test substance-related changes in the liver of male or female mice administered 0.1 mg/kg/day or in female mice administered 0.5 mg/kg/day. Incidences of test substance-related microscopic findings in the liver are summarized in Text Table 4 and discussed in more detail below.

Text Table 4: Incidences of Test Substance-Related Microscopic Findings in the Liver of Male and Female Mice

	Male				Female			
Dose (mg/kg/day):	0	0.1	0.5	5	0	0.1	0.5	5
mice/group:	10	10	10	10	10	10	10	10
Liver	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
Hepatocellular hypertrophy	0	0	8	10	0	0	0	10
Hepatocellular single cell necrosis	0	0	0	10	0	0	0	1
Mitotic figures	0	0	0	9	0	0	0	0
Pigment increased, Kupffer cells	0	0	0	10	0	0	0	2

Numbers in parentheses are the number of tissues examined within each group.
Underlined values were interpreted to be test substance-related microscopic findings.

In the 5 mg/kg/day male and female groups, test substance-related hepatocellular hypertrophy was present in all animals. Hypertrophy was graded as mild (grade 2 out of 4) in males and minimal (grade 1 out of 4) or mild in females. The distribution of the hepatocellular hypertrophy was centrilobular when of minimal severity and diffuse when of mild severity. Hypertrophy was morphologically consistent with peroxisome proliferation and was characterized by increase in the size of hepatocytes due to increased amount of finely granular eosinophilic cytoplasm and enlarged nuclei with occasional binucleated cells. Additional liver changes in the 5 mg/kg/day group occurred most consistently in males and included increased numbers of mitotic figures (males only), increased pigment (likely lipofuchsin) in Kupffer cells, and single cell hepatocellular necrosis. The latter change was characterized by isolated eosinophilic bodies with occasional pyknotic nuclear fragments and unaccompanied by inflammation, and thus was consistent with apoptosis. Hepatic lesions correlated with increased absolute and relative liver weight and increased total bile acid and liver enzyme levels (AST, ALT, SDH, ALP) (see clinical pathology). Minimal bile duct hyperplasia was present in the liver of one male mouse in the 5 mg/kg/day group. Since similar changes were not seen in any other treated mice, the relationship of this finding to test substance administration is uncertain.

In the 0.5 mg/kg/day groups, liver changes were limited to minimal hepatocellular hypertrophy in males only. Hypertrophy was not associated with microscopic changes or changes in clinical chemistry parameters indicative of liver cell injury. Therefore, liver hypertrophy in the 0.5 mg/kg/day male group was considered test substance related but non-adverse.[20]

There were no other microscopic findings in liver considered to be test substance related. In females, focal necrosis was present in both treated and control mice with slightly increased incidence in the 5 mg/kg/day females (1/10, 0/10, 2/10, 3/10 in control, 0.1, 0.5, and 5 mg/kg/day groups, respectively). Focal hepatic necrosis is a common background lesion in mice,[21] and there was no difference in morphology or severity of this lesion in treated female mice as compared to controls. In addition, test substance-related focal necrosis did not occur in males, the more sensitive gender for liver effects. Therefore, the minimal increase in the incidence of this lesion in high dose females was considered spurious and unrelated to treatment. All other microscopic changes were consistent with background findings common to mice of this strain and age.

2. Kidney

Test substance related changes in the kidney were limited to minimal tubular epithelial hypertrophy in 9/10 male mice given 5 mg/kg/day of the test substance. Hypertrophy was characterized by slightly enlarged epithelial cells containing increased amounts of fine granular eosinophilic cytoplasm. Tubular epithelial hypertrophy was not associated with renal tubular cell degeneration/necrosis. Also there was no change in clinical pathology parameters indicative of renal injury. Therefore, the renal epithelial hypertrophy was considered a non-adverse adaptive response.

All other microscopic observations in treated and control animals were consistent with normal background lesions in mice of this age and strain.

E. Anatomic Pathology Conclusions

Under the conditions of this study, daily gavage administration of 5 mg/kg of test substance resulted in test substance-related and adverse effects in the liver of male and female mice. Incidences and severity of changes were greater in males compared to females. At 0.5 mg/kg/day, non-adverse liver effects were present in males only. No test substance-related changes were present in females given 0.5 mg/kg/day or in males or female given 0.1 mg/kg/day. An increase in kidney weight and minimal renal tubular epithelial cell hypertrophy was observed in 5 mg/kg/day males but was considered a non-adverse, adaptive response. No test substance-related effects on mortality were observed at any dose.

Plasma Concentration Evaluation

A. Plasma Concentration Evaluation

(Appendix O)

The test substance concentration in blood was similar on days 0, 28, and 95 in female mice, indicating that steady-state concentrations were achieved on the first day of dosing. This is consistent with a test substance that was cleared rapidly from the blood within one dosing interval. The test substance concentration in blood from male mice was slightly lower on day 0 than on day 28, but the day 28 and day 95 concentrations were similar, indicating steady state had been achieved by day 28. Compared to female mice, male mice took longer to achieve steady-state concentrations in blood. The plasma concentration was linear with dose, implying that absorption was not saturated over the range of doses tested in this study. Test substance was not present in plasma from control animals.

CONCLUSIONS

Under the conditions of this study, the no-observed-adverse-effect level (NOAEL) for H-28548 was 0.5 mg/kg/day in males and females, based on changes in clinical chemistry and histopathology indicative of liver toxicity in animals dosed with 5 mg/kg/day.

RECORDS AND SAMPLE STORAGE

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

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TABLES

TABLES

EXPLANATORY NOTES

ABBREVIATIONS:

Mean Grip Strength
Motor Activity Assessment: Duration of Movement
Motor Activity Assessment: Number of Movements

N - number of animals evaluated

Summary of Hematology Values

RBC	-	red blood cell count
HGB	-	hemoglobin
HCT	-	hematocrit
MCV	-	mean corpuscular (cell) volume
MCH	-	mean corpuscular (cell) hemoglobin
MCHC	-	mean corpuscular (cell) hemoglobin concentration
RDW	-	red cell distribution width
ARET	-	absolute reticulocyte count
PLT	-	platelet count
WBC	-	white blood cell count
ANEU	-	absolute neutrophil
ALYM	-	absolute lymphocyte
AMON	-	absolute monocyte
AEOS	-	absolute eosinophil
ABAS	-	absolute basophil
ALUC	-	absolute large unstained cell
ABAN	-	absolute neutrophil band
AATL	-	absolute atypical lymphocyte
AIL	-	absolute immature lymphocyte
-	-	no data
NC	-	not calculated or not calculable

TABLES

EXPLANATORY NOTES (Continued)

ABBREVIATIONS: (Continued)

Summary of Clinical Chemistry Values

AST	-	aspartate aminotransferase
ALT	-	alanine aminotransferase
SDH	-	sorbitol dehydrogenase
ALKP	-	alkaline phosphatase
BILI	-	total bilirubin
BUN	-	urea nitrogen
CREA	-	creatinine
CHOL	-	cholesterol
TRIG	-	triglycerides
GLUC	-	glucose
TP	-	total protein
ALB	-	albumin
GLOB	-	globulin
AG	-	albumin/globulin ratio
CALC	-	calcium
IPHS	-	inorganic phosphorous
NA	-	sodium
K	-	potassium
CL	-	chloride
TBA	-	total bile acids

NOTES:

Mean Grip Strength
Summary of Functional Observational Battery Findings
Motor Activity Assessment: Duration of Movement
Motor Activity Assessment: Number of Movements
N = 9 in female groups 3 and 4 due to unscheduled sacrifice prior to the week 13 evaluation. Baseline data for these mice are included in the report appendices, but were not used in the tables.

Summary of Hematology Values
Summary of Clinical Chemistry Values
Groups with identical values may vary in statistical significance, because tabulated statistics are rounded to fewer decimal places than the values used for statistical determination.

Table 1
Mean Body Weights of Male Mice

	MEAN BODY WEIGHTS (g)			
DAYS ON TEST	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
0	31.8 1.9(25)	32.1 1.9(25)	32.2 2.0(25)	32.2 1.8(25)
7	32.5 2.2(20)	32.4 2.1(20)	32.6 2.4(19)	33.6 1.9(20)
14	33.6 2.5(20)	33.2 2.3(20)	33.9 2.6(19)	35.2 2.4(20)
21	34.8 2.8(20)	34.3 2.7(20)	35.0 2.8(19)	36.7 2.3(20)
28	35.7 2.5(20)	35.6 2.4(20)	36.3 3.0(19)	38.0@ 2.2(20)
35	36.6 2.9(15)	36.6 2.9(15)	36.4 2.9(14)	38.6 2.0(15)
42	37.1 3.1(15)	37.6 2.6(15)	37.1 2.9(14)	39.6* 2.1(15)
49	38.3 3.3(15)	38.2 2.8(15)	37.8 3.1(14)	40.1 2.4(15)
56	38.5 2.9(15)	39.0 3.1(15)	38.4 3.3(14)	41.4* 2.2(15)
63	39.2 3.2(15)	39.8 3.2(15)	39.5 3.0(14)	42.1* 2.4(15)
70	39.4 3.8(15)	40.3 3.1(15)	39.7 3.4(14)	42.2 2.6(15)
77	39.8 3.9(15)	40.4 3.0(15)	39.8 3.5(14)	42.1 2.8(15)
84	40.4 3.8(15)	40.9 3.3(15)	40.1 3.6(14)	42.7 2.6(15)
91	39.7 4.0(15)	40.6 3.2(15)	39.9 3.6(14)	42.9* 2.3(15)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

* Statistically significant difference from control at $p < 0.05$ by Dunnett/Tamhane-Dunnett test.
@ Statistically significant difference from control at $p < 0.05$ by Dunn's test.
~ Due to lack of control group values or variability among group means, statistical analyses were unable to be performed.

Table 2
Mean Body Weights of Female Mice

	MEAN BODY WEIGHTS (g)			
DAYS ON TEST	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
0	25.9 1.7(25)	25.8 1.8(25)	25.8 1.7(25)	26.3 1.3(25)
7	26.5 2.0(20)	26.3 2.0(20)	25.9 1.8(18)	27.1 1.7(20)
14	27.0 1.9(20)	27.1 1.8(20)	27.1 1.7(18)	27.8 1.9(20)
21	28.1 2.3(19)	27.6 2.1(20)	28.1 1.9(18)	29.1 1.8(19)
28	28.4 2.2(19)	28.0 2.0(20)	28.8 1.9(18)	29.3 1.8(19)
35	29.7 3.1(14)	28.4 2.1(15)	29.4 2.7(14)	29.4 2.0(14)
42	29.8 2.9(14)	28.8 2.1(15)	29.7 3.0(14)	29.9 2.3(14)
49	29.9 3.6(14)	29.7 2.3(15)	29.7 2.5(14)	30.0 2.1(14)
56	30.4 3.5(14)	29.8 2.1(15)	30.5 2.8(14)	29.7 2.2(14)
63	31.2 3.7(14)	29.9 2.1(15)	31.3 4.0(14)	30.7 2.9(14)
70	31.4 4.1(14)	30.2 1.9(15)	31.4 3.6(14)	30.9 2.1(14)
77	31.2 3.7(14)	30.5 2.2(15)	31.6 3.4(14)	31.3 1.8(14)
84	31.6 4.3(14)	31.1 2.7(15)	32.1 4.3(14)	31.6 2.6(14)
91	31.3 3.8(14)	30.9 2.4(15)	31.7 3.5(14)	31.6 2.6(14)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

* Statistically significant difference from control at $p < 0.05$ by Dunnett/Tamhane-Dunnett test.
@ Statistically significant difference from control at $p < 0.05$ by Dunn's test.
~ Due to lack of control group values or variability among group means, statistical analyses were unable to be performed.

Table 3
Mean Body Weight Gains of Male Mice

	MEAN BODY WEIGHT GAINS (g)			
DAYS ON TEST	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
0-7	1.0 1.0(20)	0.6 1.0(20)	0.6 1.5(19)	1.5 1.0(20)
7-14	1.0 0.7(20)	0.8 1.0(20)	1.3 1.6(19)	1.6 1.0(20)
14-21	1.3 0.7(20)	1.1 1.1(20)	1.1 0.5(19)	1.6 0.6(20)
21-28	0.8 0.9(20)	1.3 1.0(20)	1.3 0.7(19)	1.2 1.0(20)
28-35	0.6 0.6(15)	0.8 0.7(15)	0.9 0.6(14)	0.9 0.7(15)
35-42	0.5 1.1(15)	1.0 0.8(15)	0.7 0.7(14)	1.0 0.8(15)
42-49	1.1 1.0(15)	0.6 0.6(15)	0.7 0.9(14)	0.5 0.8(15)
49-56	0.2 0.7(15)	0.8 1.0(15)	0.5 1.1(14)	1.3* 0.7(15)
56-63	0.7 0.7(15)	0.7 0.8(15)	1.1 1.0(14)	0.7 1.0(15)
63-70	0.2 1.2(15)	0.5 0.7(15)	0.2 0.9(14)	0.1 0.9(15)
70-77	0.4 0.8(15)	0.1 0.8(15)	0.1 0.9(14)	-0.1 0.8(15)
77-84	0.6 0.7(15)	0.5 0.8(15)	0.2 0.8(14)	0.6 1.0(15)
84-91	-0.7 1.0(15)	-0.3 0.9(15)	-0.2 0.8(14)	0.3* 0.8(15)
OVERALL 0-91	8.0 2.6(15)	8.8 2.0(15)	8.4 2.3(14)	10.9* 1.5(15)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

* Statistically significant difference from control at $p < 0.05$ by Dunnett/Tamhane-Dunnett test.
@ Statistically significant difference from control at $p < 0.05$ by Dunn's test.
~ Due to lack of control group values or variability among group means, statistical analyses were unable to be performed.

Table 4
Mean Body Weight Gains of Female Mice

	MEAN BODY WEIGHT GAINS (g)			
DAYS ON TEST	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
0-7	0.7 1.5(20)	0.6 0.9(20)	0.3 1.5(18)	1.0 1.7(20)
7-14	0.4 0.9(20)	0.7 0.8(20)	1.2@ 1.3(18)	0.7 1.0(20)
14-21	1.1 0.9(19)	0.5 1.2(20)	1.0 0.8(18)	1.4 0.9(19)
21-28	0.2 0.9(19)	0.4 1.3(20)	0.7 1.1(18)	0.2 0.9(19)
28-35	1.4 1.0(14)	0.8 1.1(15)	0.3@ 1.0(14)	0.5 1.0(14)
35-42	0.1 1.1(14)	0.4 1.1(15)	0.2 1.2(14)	0.5 1.2(14)
42-49	0.1 1.3(14)	0.9 1.3(15)	0.1 0.9(14)	0.1 0.9(14)
49-56	0.5 0.9(14)	0.0 1.8(15)	0.8 1.0(14)	-0.3 0.9(14)
56-63	0.8 0.7(14)	0.1 1.0(15)	0.8 1.5(14)	1.0 1.7(14)
63-70	0.2 1.3(14)	0.3 0.8(15)	0.1 1.3(14)	0.2 1.4(14)
70-77	-0.2 1.2(14)	0.3 1.2(15)	0.2 1.0(14)	0.4 1.4(14)
77-84	0.4 1.6(14)	0.6 2.1(15)	0.5 1.3(14)	0.3 1.3(14)
84-91	-0.2 1.3(14)	-0.2 1.6(15)	-0.4 1.5(14)	0.0 1.0(14)
OVERALL 0-91	5.8 2.6(14)	5.6 2.0(15)	6.0 2.6(14)	5.7 2.0(14)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

* Statistically significant difference from control at $p < 0.05$ by Dunnett/Tamhane-Dunnett test.
@ Statistically significant difference from control at $p < 0.05$ by Dunn's test.
~ Due to lack of control group values or variability among group means, statistical analyses were unable to be performed.

Table 5
Mean Daily Food Consumption by Male Mice

	MEAN DAILY FOOD CONSUMED PER ANIMAL (g)			
DAYS ON TEST	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
0-7	6.3 1.6(20)	5.9 1.0(20)	6.1 1.3(19)	5.8 0.5(20)
7-14	6.1 1.2(20)	6.2 1.3(20)	6.1 1.4(19)	6.3 1.0(20)
14-21	5.7 0.6(20)	5.9 0.6(20)	5.9 1.0(19)	6.3@ 0.8(20)
21-28	5.7 0.8(20)	5.9 0.6(20)	6.1 1.0(19)	6.2@ 0.7(20)
28-35	5.6 0.6(15)	6.0 0.6(15)	5.9 0.7(14)	6.3* 0.5(15)
35-42	5.6 0.6(15)	6.1 1.0(15)	6.1 1.2(14)	6.3@ 0.5(15)
42-49	5.5 0.7(15)	5.9 0.7(15)	5.8 0.7(14)	6.4@ 0.8(15)
49-56	5.5 0.5(15)	6.0 1.0(15)	6.0 1.5(14)	6.5@ 0.9(15)
56-63	5.8 1.0(15)	5.8 0.4(15)	6.2 1.3(14)	6.6@ 1.1(15)
63-70	5.6 0.7(15)	5.7 0.8(15)	5.9 0.6(14)	6.6@ 0.8(15)
70-77	5.2 0.7(15)	5.3 0.6(15)	5.5 0.4(14)	6.0@ 0.7(15)
77-84	5.3 0.6(15)	5.6 0.5(15)	5.4 0.5(14)	6.0* 0.4(15)
84-91	5.1 0.7(15)	5.2 0.4(15)	5.2 0.5(14)	5.9* 0.3(15)
OVERALL 0-91	5.6 0.6(15)	5.8 0.6(15)	5.9 0.8(14)	6.2@ 0.5(15)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

* Statistically significant difference from control at $p < 0.05$ by Dunnett/Tamhane-Dunnett test.
@ Statistically significant difference from control at $p < 0.05$ by Dunn's test.
~ Due to lack of control group values or variability among group means, statistical analyses were unable to be performed.

Table 6
Mean Daily Food Consumption by Female Mice

	MEAN DAILY FOOD CONSUMED PER ANIMAL (g)			
DAYS ON TEST	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
0-7	5.9 1.4(20)	6.0 1.5(20)	5.5 1.4(18)	5.7 1.6(20)
7-14	5.6 0.7(20)	5.8 0.9(20)	6.0 1.6(18)	5.8 1.2(20)
14-21	5.6 0.7(19)	6.0 1.1(20)	5.8 1.4(18)	5.6 0.7(19)
21-28	5.7 1.0(19)	6.0 1.3(20)	6.3 1.5(18)	5.9 0.8(19)
28-35	5.8 0.7(14)	5.8 1.2(15)	6.1 1.3(14)	5.7 0.6(14)
35-42	5.5 0.6(14)	5.5 0.6(15)	6.2 1.3(14)	5.7 0.7(14)
42-49	5.4 0.5(14)	5.8 0.8(15)	5.9 1.2(14)	5.7 1.1(14)
49-56	5.8 0.9(14)	5.7 0.8(15)	6.0 1.4(14)	5.8 1.0(14)
56-63	5.9 0.6(14)	5.8 0.9(15)	6.2 1.7(14)	5.8 1.2(14)
63-70	5.7 0.6(14)	5.5 0.6(15)	5.6 0.9(14)	6.1 1.1(14)
70-77	5.3 0.6(14)	5.1 0.5(15)	5.4 0.9(14)	5.6 1.4(14)
77-84	5.5 0.7(14)	5.5 0.7(15)	5.5 0.6(14)	5.6 0.7(14)
84-91	5.1 0.5(14)	5.2 0.7(15)	5.2 0.7(14)	5.5 0.8(14)
OVERALL 0-91	5.6 0.5(14)	5.6 0.6(15)	5.9 1.0(14)	5.7 0.7(14)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

* Statistically significant difference from control at $p < 0.05$ by Dunnett/Tamhane-Dunnett test.
@ Statistically significant difference from control at $p < 0.05$ by Dunn's test.
~ Due to lack of control group values or variability among group means, statistical analyses were unable to be performed.

Table 7
Mean Daily Food Efficiency of Male Mice

	MEAN DAILY FOOD EFFICIENCY (g weight gain/g food consumed)			
DAYS ON TEST	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
0-7	0.022 0.023(20)	0.013 0.030(20)	0.014 0.035(19)	0.036 0.025(20)
7-14	0.025 0.016(20)	0.019 0.023(20)	0.029 0.034(19)	0.034 0.023(20)
14-21	0.032 0.016(20)	0.024 0.030(20)	0.027 0.011(19)	0.036 0.013(20)
21-28	0.021 0.021(20)	0.032 0.025(20)	0.029 0.016(19)	0.028 0.024(20)
28-35	0.015 0.015(15)	0.021 0.016(15)	0.022 0.013(14)	0.021 0.014(15)
35-42	0.014 0.028(15)	0.024 0.019(15)	0.018 0.019(14)	0.021 0.017(15)
42-49	0.028 0.023(15)	0.016 0.014(15)	0.018 0.024(14)	0.009* 0.017(15)
49-56	0.006 0.018(15)	0.020 0.025(15)	0.011 0.025(14)	0.030* 0.018(15)
56-63	0.017 0.015(15)	0.018 0.020(15)	0.026 0.024(14)	0.016 0.022(15)
63-70	0.005 0.030(15)	0.013 0.018(15)	0.005 0.021(14)	0.001 0.019(15)
70-77	0.012 0.020(15)	0.002 0.022(15)	0.002 0.025(14)	-0.003 0.017(15)
77-84	0.014 0.017(15)	0.010 0.020(15)	0.007 0.022(14)	0.014 0.024(15)
84-91	-0.020 0.029(15)	-0.008 0.027(15)	-0.005 0.023(14)	0.007* 0.019(15)
OVERALL 0-91	0.015 0.004(15)	0.017 0.004(15)	0.016 0.003(14)	0.019* 0.002(15)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

* Statistically significant difference from control at $p < 0.05$ by Dunnett/Tamhane-Dunnett test.
@ Statistically significant difference from control at $p < 0.05$ by Dunn's test.
~ Due to lack of control group values or variability among group means, statistical analyses were unable to be performed.

Table 8
Mean Daily Food Efficiency of Female Mice

	MEAN DAILY FOOD EFFICIENCY (g weight gain/g food consumed)			
DAYS ON TEST	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
0-7	0.015 0.039(20)	0.013 0.019(20)	0.006 0.041(18)	0.025 0.045(20)
7-14	0.010 0.025(20)	0.018 0.018(20)	0.030@ 0.029(18)	0.016 0.025(20)
14-21	0.028 0.024(19)	0.014 0.026(20)	0.026 0.020(18)	0.038 0.027(19)
21-28	0.005 0.023(19)	0.009 0.032(20)	0.018 0.028(18)	0.003 0.024(19)
28-35	0.033 0.022(14)	0.020 0.027(15)	0.008@ 0.026(14)	0.012 0.026(14)
35-42	0.004 0.029(14)	0.011 0.027(15)	0.004 0.027(14)	0.013 0.030(14)
42-49	-0.000 0.031(14)	0.022 0.031(15)	0.004 0.022(14)	0.002 0.022(14)
49-56	0.013 0.024(14)	-0.000 0.045(15)	0.019 0.025(14)	-0.009 0.021(14)
56-63	0.020 0.017(14)	0.003 0.024(15)	0.017 0.025(14)	0.024 0.042(14)
63-70	0.003 0.029(14)	0.008 0.021(15)	0.004 0.033(14)	0.004 0.040(14)
70-77	-0.007 0.032(14)	0.008 0.030(15)	0.003 0.029(14)	0.010 0.034(14)
77-84	0.010 0.036(14)	0.012 0.049(15)	0.013 0.032(14)	0.006 0.033(14)
84-91	-0.008 0.037(14)	-0.007 0.045(15)	-0.013 0.040(14)	0.000 0.025(14)
OVERALL 0-91	0.011 0.005(14)	0.011 0.004(15)	0.011 0.005(14)	0.011 0.003(14)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

* Statistically significant difference from control at $p < 0.05$ by Dunnett/Tamhane-Dunnett test.
@ Statistically significant difference from control at $p < 0.05$ by Dunn's test.
~ Due to lack of control group values or variability among group means, statistical analyses were unable to be performed.

Table 9
Summary of Clinical Observations and Mortality in Male Mice

Day numbers relative to Start Date

Sex: Male

	Group 1	Group 2	Group 3	Group 4
Dosage (mg/kg)	0	0.1	0.5	5
Animal Count	25	25	25	25
Mechanistic sacrifice				
Number of Observations	15	15	14	15
Number of Animals	15	15	14	15
Days from - to	0 95	0 95	0 95	0 95
Scheduled sacrifice				
Number of Observations	10	10	10	10
Number of Animals	10	10	10	10
Days from - to	96 96	96 96	96 96	96 96
Unscheduled Sacrifice				
Number of Observations	.	.	1	.
Number of Animals	.	.	1	.
Days from - to	.	.	3 3	.
Aggressive				
Number of Observations	.	1	.	.
Number of Animals	.	1	.	.
Days from - to	.	52 52	.	.
Breathing - slow				
Number of Observations	.	.	1	.
Number of Animals	.	.	1	.
Days from - to	.	.	3 3	.

Table 9
Summary of Clinical Observations and Mortality in Male Mice (Continued)

Day numbers relative to Start Date

Sex: Male

	Group 1	Group 2	Group 3	Group 4
Dosage (mg/kg)	0	0.1	0.5	5
Animal Count	25	25	25	25
Cold to touch				
Number of Observations	.	.	1	.
Number of Animals	.	.	1	.
Days from - to	.	.	3 3	.
Convulsions - clonic				
Number of Observations	.	1	.	.
Number of Animals	.	1	.	.
Days from - to	.	51 51	.	.
Dehydrated				
Number of Observations	.	.	2	.
Number of Animals	.	.	1	.
Days from - to	.	.	2 3	.
Hyperreactive				
Number of Observations	.	11	.	.
Number of Animals	.	1	.	.
Days from - to	.	42 96	.	.
Lethargic				
Number of Observations	.	2	1	.
Number of Animals	.	1	1	.
Days from - to	.	51 52	3 3	.

Table 9
Summary of Clinical Observations and Mortality in Male Mice (Continued)

Day numbers relative to Start Date

Sex: Male

	Group 1	Group 2	Group 3	Group 4
Dosage (mg/kg)	0	0.1	0.5	5
Animal Count	25	25	25	25
Mass				
Number of Observations	.	4	2	4
Number of Animals	.	2	1	2
Days from - to	.	28 70	28 35	28 96
Misshapen				
Number of Observations	.	.	.	13
Number of Animals	.	.	.	1
Days from - to	.	.	.	14 96
Swollen				
Number of Observations	.	.	3	1
Number of Animals	.	.	1	1
Days from - to	.	.	1 3	91 91
Wound - superficial				
Number of Observations	.	.	.	3
Number of Animals	.	.	.	1
Days from - to	.	.	.	35 49

Table 10
Summary of Clinical Observations and Mortality in Female Mice

Day numbers relative to Start Date

Sex: Female

	Group 1	Group 2	Group 3	Group 4
Dosage (mg/kg)	0	0.1	0.5	5
Animal Count	25	25	25	25
Found dead				
Number of Observations	1	.	.	.
Number of Animals	1	.	.	.
Days from - to	16 16	.	.	.
Mechanistic sacrifice				
Number of Observations	14	15	14	15
Number of Animals	14	15	14	15
Days from - to	0 95	0 95	0 95	0 95
Scheduled sacrifice				
Number of Observations	10	10	9	9
Number of Animals	10	10	9	9
Days from - to	97 97	97 97	97 97	97 97
Unscheduled Sacrifice				
Number of Observations	.	.	2	1
Number of Animals	.	.	2	1
Days from - to	.	.	6 6	20 20
Abnormal gait				
Number of Observations	.	.	.	1
Number of Animals	.	.	.	1
Days from - to	.	.	.	20 20

Table 10
Summary of Clinical Observations and Mortality in Female Mice (Continued)

Day numbers relative to Start Date

Sex: Female

	Group 1	Group 2	Group 3	Group 4
Dosage (mg/kg)	0	0.1	0.5	5
Animal Count	25	25	25	25
Breathing - slow				
Number of Observations	.	.	3	1
Number of Animals	.	.	2	1
Days from - to	.	.	5 6	20 20
Cold to touch				
Number of Observations	.	.	1	.
Number of Animals	.	.	1	.
Days from - to	.	.	6 6	.
Dehydrated				
Number of Observations	2	.	5	.
Number of Animals	1	.	2	.
Days from - to	9 10	.	4 6	.
Eye enophthalmus				
Number of Observations	7	.	.	.
Number of Animals	1	.	.	.
Days from - to	9 15	.	.	.
Hyperactive				
Number of Observations	.	.	.	2
Number of Animals	.	.	.	1
Days from - to	.	.	.	42 49

Table 10
Summary of Clinical Observations and Mortality in Female Mice (Continued)

Day numbers relative to Start Date

Sex: Female

	Group 1	Group 2	Group 3	Group 4
Dosage (mg/kg)	0	0.1	0.5	5
Animal Count	25	25	25	25
Hyperreactive				
Number of Observations	.	.	.	2
Number of Animals	.	.	.	1
Days from - to	.	.	.	42 49
Leaning				
Number of Observations	.	.	.	1
Number of Animals	.	.	.	1
Days from - to	.	.	.	20 20
Mass				
Number of Observations	2	.	.	.
Number of Animals	1	.	.	.
Days from - to	14 15	.	.	.
Stained cageboard - red				
Number of Observations	.	.	.	2
Number of Animals	.	.	.	1
Days from - to	.	.	.	50 51
Swollen				
Number of Observations	7	2	1	.
Number of Animals	1	1	1	.
Days from - to	7 13	21 28	5 5	.

Table 10
Summary of Clinical Observations and Mortality in Female Mice (Continued)

Day numbers relative to Start Date

Sex: Female

	Group 1	Group 2	Group 3	Group 4
Dosage (mg/kg)	0	0.1	0.5	5
Animal Count	25	25	25	25
Wound - superficial				
Number of Observations	.	4	.	9
Number of Animals	.	1	.	1
Days from - to	.	7 28	.	50 91

Table 11
Summary of Ophthalmology Observations in Male Mice

Sex: Male

	Group 1	Group 2	Group 3	Group 4
Dosage (mg/kg)	0	0.1	0.5	5
Animal Count	25	25	25	25

No Abnormalities Detected

Table 12
Summary of Ophthalmology Observations in Female Mice

Sex: Female

	Group 1	Group 2	Group 3	Group 4
Dosage (mg/kg)	0	0.1	0.5	5
Animal Count	25	25	25	25

No Abnormalities Detected

Table 13
Mean Grip Strength for Male Mice

GROUP	DOSAGE (mg/kg)	GRIP STRENGTH (kg)
Baseline		
1	0	0.25(0.04)
2	0.1	0.26(0.04)
3	0.5	0.25(0.02)
4	5	0.26(0.02)
Week 13		
1	0	0.34(0.03)
2	0.1	0.33(0.03)
3	0.5	0.32(0.03)
4	5	0.34(0.04)

Data arranged as: Mean (Standard Deviation)
N = 10

No statistically significant differences compared to the control group at $p < 0.05$.

Table 14
Mean Grip Strength for Female Mice

GROUP	DOSAGE (mg/kg)	GRIP STRENGTH (kg)
Baseline		
1	0	0.21(0.02)
2	0.1	0.23(0.04)
3	0.5	0.24(0.04)
4	5	0.22(0.02)
Week 13		
1	0	0.28(0.05)
2	0.1	0.29(0.04)
3	0.5	0.29(0.04)
4	5	0.29(0.03)

Data arranged as: Mean (Standard Deviation)
N = 10 for Groups 1 and 2; N = 9 for Groups 3 and 4

No statistically significant differences compared to the control group at $p < 0.05$.

Table 15
Summary of Functional Observational Battery Findings for Male Mice

	Baseline				Week 13			
GROUP	1	2	3	4	1	2	3	4
DOSAGE (mg/kg)	0	0.1	0.5	5	0	0.1	0.5	5
NUMBER EXAMINED	10	10	10	10	10	10	10	10
MANIPULATIONS:								
APPROACH & TOUCH:								
no reaction	0	0	0	0	0	0	0	0
normal	10	10	10	10	10	10	10	10
increased reaction (jumps away or attacks)	0	0	0	0	0	0	0	0
AUDITORY STIMULUS:								
no reaction	0	0	0	0	1	0	0	0
normal reaction (mouse flinches or flicks ear)	10	10	10	10	9	10	10	10
exaggerated reaction (mouse jumps, flips)	0	0	0	0	0	0	0	0
TAIL PINCH:								
no response	0	0	0	0	0	0	0	0
normal (turns toward site)	10	10	10	10	10	10	10	10
exaggerated response	0	0	0	0	0	0	0	0
IN MOTOR ACTIVITY MONITOR:								
PUPILLARY RESPONSE:								
present	10	10	10	10	10	10	10	10
absent	0	0	0	0	0	0	0	0
DIARRHEA:								
absent	10	10	10	10	10	10	10	10
present	0	0	0	0	0	0	0	0
POLYURIA:								
absent	10	10	10	10	10	10	10	10
present	0	0	0	0	0	0	0	0
FOOTNOTES:								
c - High arousal								
absent	10	10	10	10	10	9	10	10
present	0	0	0	0	0	1	0	0
e - Corneal opacity, right								
absent	10	10	10	10	10	10	9	10
present	0	0	0	0	0	0	1	0
f - Swollen face and neck								
absent	10	10	10	10	10	10	10	9
present	0	0	0	0	0	0	0	1

No statistically significant differences compared to the control group at $p < 0.05$.

Table 16
Summary of Functional Observational Battery Findings for Female Mice

	Baseline				Week 13			
GROUP	1	2	3	4	1	2	3	4
DOSAGE (mg/kg)	0	0.1	0.5	5	0	0.1	0.5	5
NUMBER EXAMINED	10	10	9	9	10	10	9	9
MANIPULATIONS:								
APPROACH & TOUCH:								
no reaction	0	0	0	0	0	0	0	0
normal	10	10	9	9	10	10	9	9
increased reaction (jumps away or attacks)	0	0	0	0	0	0	0	0
AUDITORY STIMULUS:								
no reaction	0	0	0	0	0	0	0	0
normal reaction (mouse flinches or flicks ear)	10	10	9	9	10	10	9	9
exaggerated reaction (mouse jumps, flips)	0	0	0	0	0	0	0	0
TAIL PINCH:								
no response	0	0	0	0	0	0	0	0
normal (turns toward site)	10	10	9	9	10	10	9	9
exaggerated response	0	0	0	0	0	0	0	0
IN MOTOR ACTIVITY MONITOR:								
PUPILLARY RESPONSE:								
present	10	10	9	9	10	10	9	9
absent	0	0	0	0	0	0	0	0
DIARRHEA:								
absent	10	10	9	9	10	10	9	9
present	0	0	0	0	0	0	0	0
POLYURIA:								
absent	10	10	9	9	10	10	9	9
present	0	0	0	0	0	0	0	0
FOOTNOTES:								
b - Splayed rear limbs, slight								
absent	10	10	9	8	10	10	9	9
present	0	0	0	1	0	0	0	0
d - Wound, end of tail								
absent	10	10	9	9	10	9	9	9
present	0	0	0	0	0	1	0	0

No statistically significant differences compared to the control group at $p < 0.05$.

Table 17
Motor Activity Assessment: Mean Duration of Movement for Male Mice

GROUP	DOSAGE (mg/kg)	SUCCESSIVE 10-MINUTE INTERVALS 1	2	3	4	5	6	7	8	9	TOTAL
Baseline											
1	0	452(56)	370(71)	386(69)	351(56)	356(57)	343(70)	306(94)	294(98)	211(111)	3069(559)
2	0.1	438(77)	383(54)	382(41)	347(71)	334(77)	348(95)	300(104)	257(143)	206(149)	2995(649)
3	0.5	441(64)	361(78)	347(79)	340(64)	323(67)	301(50)	219(115)	181(149)	127(142)	2638(672)
4	5	458(68)	391(81)	395(63)	365(69)	364(64)	359(84)	333(56)	295(97)	255(131)	3213(522)
Week 13											
1	0	497(33)	435(43)	425(54)	401(50)	372(69)	379(79)	372(70)	351(63)	322(82)	3552(448)
2	0.1	476(67)	405(77)	413(65)	382(70)	398(90)	397(85)	366(91)	366(87)	317(91)	3520(634)
3	0.5	481(52)	400(63)	386(62)	388(59)	362(71)	367(88)	351(87)	318(104)	298(96)	3351(613)
4	5	510(36)	428(60)	410(58)	379(67)	386(103)	375(80)	375(93)	383(74)	321(106)	3567(623)

Data arranged as: Mean (Standard Deviation)
N = 10

Statistical Methods: Shapiro-Wilk test for homogeneity and Levene's test for normality were performed. Repeated measures analysis of variance with linear contrasts or Jonckheere-Terpstra trend test was used to identify which groups, if any, were significantly different from the control group. These tests were applied to Interval data and Total data.

No statistically significant differences compared to the control group at $p < 0.05$.

Table 18
Motor Activity Assessment: Mean Duration of Movement for Female Mice

GROUP	DOSAGE (mg/kg)	SUCCESSIVE 10-MINUTE INTERVALS[a] 1	2	3	4	5	6	7	8	9	TOTAL
Baseline											
1	0	413(55)	344(78)	333(58)	341(85)	328(80)	295(77)	220(126)	189(153)	182(147)	2646(666)
2	0.1	442(59)	362(63)	365(61)	345(59)	312(66)	342(42)	327(54)	258(86)	245(115)	2997(404)
3	0.5	414(83)	355(60)	333(65)	344(74)	316(87)	251(113)	218(130)	166(75)	132(113)	2527(484)
4	5	418(55)	360(71)	332(65)	329(85)	264(90)	247(127)	247(75)	197(139)	158(152)	2551(574)
Week 13											
1	0	453(42)	391(73)	365(89)	379(100)	381(61)	353(68)	349(88)	318(75)	312(96)	3301(571)
2	0.1	482(46)	416(54)	395(54)	393(70)	392(59)	391(46)	370(36)	315(123)	261(125)	3414(400)
3	0.5	465(62)	382(57)	385(58)	354(63)	346(51)	314(50)	278(100)	281(79)	216(106)	3021(505)
4	5	472(72)	404(96)	418(61)	420(27)	413(69)	418(75)	401(75)	363(89)	309(139)	3619(568)

Data arranged as: Mean (Standard Deviation)
N = 10 for Groups 1 and 2; N = 9 for Groups 3 and 4

Statistical Methods: Shapiro-Wilk test for homogeneity and Levene's test for normality were performed. Repeated measures analysis of variance with linear contrasts or Jonckheere-Terpstra trend test was used to identify which groups, if any, were significantly different from the control group. These tests were applied to Interval data and Total data.

No statistically significant differences compared to the control group at $p < 0.05$.

Table 19
Motor Activity Assessment: Mean Number of Movements for Male Mice

GROUP	DOSAGE (mg/kg)	SUCCESSIVE 10-MINUTE INTERVALS 1	2	3	4	5	6	7	8	9	TOTAL
Baseline											
1	0	128(31)	139(23)	136(23)	141(21)	138(20)	146(17)	142(31)	140(24)	112(37)	1223(137)
2	0.1	134(30)	146(26)	142(24)	140(20)	140(22)	146(15)	141(26)	121(53)	101(58)	1210(191)
3	0.5	136(25)	139(18)	142(8)	137(10)	147(12)	151(21)	121(41)	97(59)	68(64)	1138(166)
4	5	125(33)	134(22)	131(17)	133(19)	138(12)	142(22)	143(16)	135(26)	127(56)	1209(159)
Week 13											
1	0	113(24)	134(21)	130(17)	140(22)	142(26)	136(24)	143(24)	146(17)	144(17)	1228(156)
2	0.1	120(38)	139(23)	131(29)	136(21)	136(20)	133(16)	137(17)	143(18)	140(18)	1215(157)
3	0.5	116(28)	141(21)	140(18)	141(19)	140(11)	146(17)	149(13)	152(18)	143(26)	1266(91)
4	5	103(23)	131(18)	141(24)	132(19)	131(13)	138(15)	141(19)	144(23)	138(20)	1199(137)

Data arranged as: Mean (Standard Deviation)
N = 10

Statistical Methods: Shapiro-Wilk test for homogeneity and Levene's test for normality were performed. Repeated measures analysis of variance with linear contrasts or Jonckheere-Terpstra trend test was used to identify which groups, if any, were significantly different from the control group. These tests were applied to Interval data and Total data.

No statistically significant differences compared to the control group at $p < 0.05$.

Table 20
Motor Activity Assessment: Mean Number of Movements for Female Mice

GROUP	DOSAGE (mg/kg)	SUCCESSIVE 10-MINUTE INTERVALS[a] 1	2	3	4	5	6	7	8	9	TOTAL
Baseline											
1	0	145(15)	132(18)	140(25)	130(16)	136(16)	135(27)	114(55)	95(64)	96(62)	1123(209)
2	0.1	134(27)	144(19)	139(17)	136(20)	135(18)	148(18)	144(20)	136(32)	118(42)	1234(149)
3	0.5	133(27)	141(16)	144(14)	138(15)	140(22)	125(34)	104(43)	98(36)	78(56)	1103(130)
4	5	141(19)	135(13)	134(10)	129(23)	127(34)	121(43)	129(29)	106(57)	75(67)	1097(142)
Week 13											
1	0	131(26)	139(18)	142(22)	135(27)	140(20)	137(16)	139(18)	136(17)	129(18)	1228(132)
2	0.1	118(27)	137(22)	138(23)	132(19)	141(25)	145(24)	137(24)	127(44)	122(38)	1196(200)
3	0.5	123(34)	144(19)	149(25)	149(16)	143(12)	148(11)	134(25)	135(18)	118(48)	1243(80)
4	5	110(32)	125(22)	133(33)	148(16)	133(29)	135(28)	133(28)	135(37)	131(51)	1181(230)

Data arranged as: Mean (Standard Deviation)
N = 10 for Groups 1 and 2; N = 9 for Groups 3 and 4

Statistical Methods: Shapiro-Wilk test for homogeneity and Levene's test for normality were performed. Repeated measures analysis of variance with linear contrasts or Jonckheere-Terpstra trend test was used to identify which groups, if any, were significantly different from the control group. These tests were applied to Interval data and Total data.

No statistically significant differences compared to the control group at $p < 0.05$.

Table 21
Summary of Hematology Values for Male Mice

	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
RBC ($x10^6/\mu L$)				
DAY 96	9.41	9.32	9.46	9.10
	0.39(10)	0.45(9)	0.44(10)	0.50(9)
HGB (g/dL)				
DAY 96	15.1	14.5	14.6	14.5
	0.6(10)	0.8(9)	0.6(10)	0.7(9)
HCT (%)				
DAY 96	46.6	45.3	45.8	45.9
	1.9(10)	2.3(9)	1.7(10)	2.1(9)
MCV (fL)				
DAY 96	49.5	48.6	48.5	50.6
	1.6(10)	1.3(9)	1.0(10)	2.2(9)
MCH (pg)				
DAY 96	16.0	15.6	15.5	15.9
	0.5(10)	0.5(9)	0.4(10)	0.7(9)
MCHC (g/dL)				
DAY 96	32.4	32.0	31.9	31.5*
	0.6(10)	0.7(9)	0.6(10)	0.4(9)
RDW (%)				
DAY 96	12.6	12.7	12.8	12.9
	0.6(10)	1.1(9)	0.5(10)	0.7(9)
ARET ($x10^3/\mu L$)				
DAY 96	262.4	237.1	263.2	284.0
	21.8(10)	28.0(9)	26.7(10)	24.4(9)
PLT ($x10^3/\mu L$)				
DAY 96	998	1124	1263*	1257*
	124(5)	80(5)	160(7)	240(6)
WBC ($x10^3/\mu L$)				
DAY 96	4.43	3.56	3.20	4.28
	2.96(10)	1.05(9)	1.58(10)	2.46(9)
ANEU ($x10^3/\mu L$)				
DAY 96	1.13	0.81	0.75	1.29
	0.82(10)	0.33(9)	0.50(10)	0.97(9)
ALYM ($x10^3/\mu L$)				
DAY 96	2.98	2.53	2.29	2.71
	2.12(10)	0.73(9)	1.14(10)	1.42(9)
AMON ($x10^3/\mu L$)				
DAY 96	0.13	0.07	0.07	0.15
	0.12(10)	0.04(9)	0.05(10)	0.10(9)
AEOS ($x10^3/\mu L$)				
DAY 96	0.16	0.13	0.09	0.08
	0.12(10)	0.12(9)	0.04(10)	0.08(9)
ABAS ($x10^3/\mu L$)				
DAY 96	0.00	0.00	0.00	0.00
	0.00(10)	0.01(9)	0.00(10)	0.01(9)

Table 21
Summary of Hematology Values for Male Mice (Continued)

	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
ALUC ($x10^3/\mu L$)				
DAY 96	0.01 0.02(10)	0.01 0.01(9)	0.01 0.01(10)	0.04 0.05(9)
ABAN ($x10^3/\mu L$)				
DAY 96	0.06 NC(1)	-	-	0.02 0.01(3)
AIL ($x10^3/\mu L$)				
DAY 96	-	-	0.02~ NC(1)	-

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

* Statistically significant difference from control at $p < 0.05$ by Dunnett/Tamhane-Dunnett test.
@ Statistically significant difference from control at $p < 0.05$ by Dunn's test.
~ Due to lack of control values or variability among group means, statistical analyses were unable to be performed.

Table 22
Summary of Hematology Values for Female Mice

	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
RBC ($x10^6/\mu L$)				
DAY 97	9.22	9.39	9.20	9.51
	0.57(10)	0.51(10)	0.64(9)	0.61(9)
HGB (g/dL)				
DAY 97	14.7	15.4	15.0	14.9
	0.8(10)	0.6(10)	0.7(9)	0.9(9)
HCT (%)				
DAY 97	45.4	47.1	46.6	46.7
	2.4(10)	2.1(10)	2.4(9)	2.3(9)
MCV (fL)				
DAY 97	49.3	50.2	50.7	49.3
	1.4(10)	1.4(10)	1.6(9)	2.3(9)
MCH (pg)				
DAY 97	16.0	16.5	16.4	15.7
	0.4(10)	0.5(10)	0.5(9)	0.7(9)
MCHC (g/dL)				
DAY 97	32.4	32.8	32.2	31.9
	0.8(10)	0.9(10)	0.7(9)	0.9(9)
RDW (%)				
DAY 97	13.2	12.9	12.7	12.6
	0.8(10)	0.5(10)	0.5(9)	0.6(9)
ARET ($x10^3/\mu L$)				
DAY 97	279.9	248.4	233.9	241.3
	73.2(10)	57.6(10)	47.5(9)	48.8(9)
PLT ($x10^3/\mu L$)				
DAY 97	1050	1072	1087	964
	103(5)	94(4)	132(4)	235(5)
WBC ($x10^3/\mu L$)				
DAY 97	2.76	2.44	2.56	2.27
	1.89(10)	1.19(10)	1.40(9)	0.99(9)
ANEU ($x10^3/\mu L$)				
DAY 97	0.48	0.52	0.41	0.48
	0.14(10)	0.32(10)	0.30(9)	0.31(9)
ALYM ($x10^3/\mu L$)				
DAY 97	2.09	1.83	1.99	1.63
	1.70(10)	0.94(10)	1.15(9)	0.70(9)
AMON ($x10^3/\mu L$)				
DAY 97	0.08	0.02@	0.05	0.07
	0.10(10)	0.02(10)	0.02(9)	0.07(9)
AEOS ($x10^3/\mu L$)				
DAY 97	0.09	0.06	0.08	0.06
	0.06(10)	0.02(10)	0.04(9)	0.06(9)
ABAS ($x10^3/\mu L$)				
DAY 97	0.00	0.00	0.00	0.00
	0.01(10)	0.00(10)	0.00(9)	0.00(9)

Table 22
Summary of Hematology Values for Female Mice

	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
ALUC ($x10^3/\mu L$)				
DAY 97	0.01 0.02(10)	0.01 0.01(10)	0.00 0.01(9)	0.01 0.02(9)
ABAN ($x10^3/\mu L$)				
DAY 97	0.02~ 0.00(2)	0.03~ NC(1)	0.02~ NC(1)	0.01~ 0.00(2)
AATL ($x10^3/\mu L$)				
DAY 97	-	-	0.05~ NC(1)	-
AIL ($x10^3/\mu L$)				
DAY 97	-	0.02~ NC(1)	0.03~ 0.01(2)	0.04~ 0.01(3)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

* Statistically significant difference from control at $p < 0.05$ by Dunnett/Tamhane-Dunnett test.
@ Statistically significant difference from control at $p < 0.05$ by Dunn's test.
~ Due to lack of control values or variability among group means, statistical analyses were unable to be performed.

Table 23
Summary of Clinical Chemistry Values for Male Mice

	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
AST (U/L)				
DAY 96	62	67	84	128@
	11(10)	21(10)	21(10)	80(10)
ALT (U/L)				
DAY 96	49	62	66	255@
	16(10)	22(10)	48(10)	114(10)
SDH (U/L)				
DAY 96	26.6	26.0	25.8	108.5@
	2.5(10)	2.4(10)	5.4(10)	47.2(10)
ALKP (U/L)				
DAY 96	50	55	70	617@
	12(10)	22(10)	30(10)	339(10)
BILI (mg/dL)				
DAY 96	0.17	0.16	0.13@	0.17
	0.03(10)	0.02(10)	0.02(10)	0.06(10)
BUN (mg/dL)				
DAY 96	28	28	30	29
	8(10)	6(10)	5(10)	6(10)
CREA (mg/dL)				
DAY 96	0.12	0.12	0.12	0.12
	0.03(10)	0.02(10)	0.02(10)	0.03(10)
CHOL (mg/dL)				
DAY 96	133	125	134	98*
	25(10)	22(10)	26(10)	30(10)
TRIG (mg/dL)				
DAY 96	99	111	101	108
	26(10)	38(10)	28(10)	57(10)
GLUC (mg/dL)				
DAY 96	172	187	170	152
	32(10)	25(10)	34(10)	26(10)
TP (g/dL)				
DAY 96	4.9	5.0	5.0	5.4*
	0.2(10)	0.3(10)	0.3(10)	0.3(10)
ALB (g/dL)				
DAY 96	2.8	2.8	2.9	3.2*
	0.2(10)	0.2(10)	0.2(10)	0.2(10)
GLOB (g/dL)				
DAY 96	2.1	2.2	2.2	2.2
	0.2(10)	0.2(10)	0.2(10)	0.2(10)
AG				
DAY 96	1.3	1.3	1.3	1.5
	0.2(10)	0.1(10)	0.1(10)	0.2(10)
CALC (mg/dL)				
DAY 96	8.2	8.3	8.4	8.5
	0.2(9)	0.2(10)	0.3(10)	0.4(10)

Table 23
Summary of Clinical Chemistry Values for Male Mice (Continued)

	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
IPHS (mg/dL)				
DAY 96	6.0	6.1	6.5	6.3
	0.5(9)	1.0(10)	0.5(10)	0.7(10)
NA (mmol/L)				
DAY 96	145.7	144.8	145.4	145.1
	1.2(9)	1.1(10)	1.8(9)	1.2(10)
K (mmol/L)				
DAY 96	5.17	4.84	4.99	4.50*
	0.56(9)	0.50(10)	0.49(9)	0.37(10)
CL (mmol/L)				
DAY 96	109.6	109.3	109.9	111.5@
	2.0(9)	1.0(10)	1.7(9)	1.3(10)
TBA (µmol/L)				
DAY 96	1.2	1.2	1.4	11.1@
	0.3(10)	0.3(10)	0.5(10)	6.0(10)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

* Statistically significant difference from control at $p < 0.05$ by Dunnett/Tamhane-Dunnett test.
@ Statistically significant difference from control at $p < 0.05$ by Dunn's test.
~ Due to lack of control values or variability among group means, statistical analyses were unable to be performed.

Table 24
Summary of Clinical Chemistry Values for Female Mice

	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
AST (U/L)				
DAY 97	68	71	69	74
	18(10)	12(9)	15(9)	12(9)
ALT (U/L)				
DAY 97	36	36	32	51@
	12(10)	8(10)	6(9)	20(9)
SDH (U/L)				
DAY 97	25.3	22.9	23.6	33.5@
	11.7(10)	2.0(9)	3.6(9)	9.3(9)
ALKP (U/L)				
DAY 97	65	77	72	158*
	19(10)	25(10)	18(9)	38(9)
BILI (mg/dL)				
DAY 97	0.14	0.14	0.14	0.12*
	0.01(9)	0.01(9)	0.02(9)	0.02(9)
BUN (mg/dL)				
DAY 97	21	19	20	21
	6(10)	3(10)	5(9)	6(9)
CREA (mg/dL)				
DAY 97	0.10	0.10	0.12	0.11
	0.02(10)	0.01(10)	0.02(9)	0.02(9)
CHOL (mg/dL)				
DAY 97	81	95	88	92
	20(10)	19(10)	19(9)	29(9)
TRIG (mg/dL)				
DAY 97	104	97	93	69
	53(10)	33(9)	36(9)	25(9)
GLUC (mg/dL)				
DAY 97	178	173	171	169
	29(9)	30(9)	28(9)	13(9)
TP (g/dL)				
DAY 97	4.7	4.7	4.8	4.7
	0.2(10)	0.2(9)	0.2(9)	0.2(9)
ALB (g/dL)				
DAY 97	2.8	2.8	2.9	2.9*
	0.1(10)	0.2(10)	0.1(9)	0.2(9)
GLOB (g/dL)				
DAY 97	1.9	2.0	1.9	1.8
	0.1(10)	0.2(9)	0.2(9)	0.2(9)
AG				
DAY 97	1.5	1.4	1.6	1.7
	0.1(10)	0.2(9)	0.3(9)	0.2(9)
CALC (mg/dL)				
DAY 97	8.7	8.7	8.7	8.7
	0.3(9)	0.1(9)	0.2(9)	0.3(9)

Table 24
Summary of Clinical Chemistry Values for Female Mice (Continued)

	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
IPHS (mg/dL)				
DAY 97	6.4	6.8	7.0	6.8
	0.7(9)	0.7(9)	1.1(9)	1.3(9)
NA (mmol/L)				
DAY 97	148.0	148.0	148.3	147.7
	0.9(9)	0.8(9)	1.7(9)	1.4(9)
K (mmol/L)				
DAY 97	4.39	4.46	4.68	3.98*
	0.40(9)	0.18(9)	0.35(9)	0.21(9)
CL (mmol/L)				
DAY 97	114.5	114.0	113.8	114.4
	1.5(9)	1.2(9)	1.4(9)	1.8(9)
TBA (µmol/L)				
DAY 97	4.3	2.3	2.7	13.2
	2.8(9)	1.0(9)	1.6(9)	28.4(9)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

* Statistically significant difference from control at $p < 0.05$ by Dunnett/Tamhane-Dunnett test.
@ Statistically significant difference from control at $p < 0.05$ by Dunn's test.
~ Due to lack of control values or variability among group means, statistical analyses were unable to be performed.

Table 25
Mean Final Body and Organ Weights from Male Mice

	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
FINAL BODY WEIGHT (grams)				
	38.7	40.3	38.9	44.3*
	3.4(10)	3.2(10)	2.4(10)	2.0(10)
MEAN FINAL BODY AND ABSOLUTE ORGAN WEIGHTS (grams)				
ADRENAL GLANDS	0.008	0.008	0.008	0.015
	0.004(10)	0.004(10)	0.003(10)	0.016(10)
BRAIN	0.506	0.498	0.503	0.497
	0.033(10)	0.028(10)	0.030(10)	0.025(9)[a]
EPIDIDYMIDES	0.131	0.170	0.123	0.119
	0.019(10)	0.159(10)	0.017(10)	0.028(10)
HEART	0.194	0.202	0.198	0.215
	0.018(10)	0.033(10)	0.016(10)	0.029(10)
KIDNEYS	0.622	0.594	0.614	0.692
	0.088(10)	0.071(10)	0.050(10)	0.074(10)
LIVER	1.955	2.024	2.186	5.144@
	0.265(10)	0.169(10)	0.267(10)	1.806(10)
SPLEEN	0.105	0.093	0.087	0.126
	0.026(10)	0.019(10)	0.018(10)	0.045(10)
TESTES	0.229	0.236	0.222	0.226
	0.026(10)	0.039(10)	0.029(10)	0.038(10)
THYMUS	0.030	0.033	0.033	0.037
	0.009(10)	0.007(10)	0.016(10)	0.012(10)

Table 25
Mean Final Body and Organ Weights from Male Mice (Continued)

	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
MEAN RELATIVE ORGAN WEIGHTS (% of body weight)				
ADRENAL GLANDS/	0.020	0.019	0.020	0.034
FINAL BODY * 100	0.008(10)	0.011(10)	0.007(10)	0.035(10)
BRAIN/	1.312	1.242	1.298	1.125*
FINAL BODY * 100	0.092(10)	0.111(10)	0.120(10)	0.073(9)[a]
EPIDIDYMIDES/	0.338	0.424	0.315	0.268@
FINAL BODY * 100	0.031(10)	0.395(10)	0.039(10)	0.060(10)
HEART/	0.503	0.500	0.510	0.485
FINAL BODY * 100	0.034(10)	0.062(10)	0.037(10)	0.054(10)
KIDNEYS/	1.604	1.473	1.581	1.568
FINAL BODY * 100	0.152(10)	0.134(10)	0.148(10)	0.201(10)
LIVER/	5.060	5.028	5.618	11.637@
FINAL BODY * 100	0.583(10)	0.272(10)	0.616(10)	4.113(10)
SPLEEN/	0.270	0.230	0.221	0.286
FINAL BODY * 100	0.052(10)	0.036(10)	0.035(10)	0.102(10)
TESTES/	0.598	0.591	0.572	0.509
FINAL BODY * 100	0.103(10)	0.126(10)	0.074(10)	0.079(10)
THYMUS/	0.077	0.083	0.085	0.084
FINAL BODY * 100	0.023(10)	0.021(10)	0.042(10)	0.027(10)

Table 25
Mean Final Body and Organ Weights from Male Mice (Continued)

	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
MEAN RELATIVE ORGAN WEIGHTS (% of brain weight)				
ADRENAL GLANDS/	1.532	1.540	1.575	3.197
BRAIN * 100	0.675(10)	0.809(10)	0.606(10)	3.716(9)[a]
EPIDIDYMIDES/	25.954	33.974	24.525	25.020
BRAIN * 100	3.644(10)	30.945(10)	4.186(10)	5.183(9)[a]
HEART/	38.416	40.694	39.552	43.988*
BRAIN * 100	2.275(10)	6.963(10)	3.998(10)	4.361(9)[a]
KIDNEYS/	122.786	119.221	122.402	139.565*
BRAIN * 100	14.395(10)	12.956(10)	13.474(10)	17.752(9)[a]
LIVER/	386.366	407.101	437.100	935.966@
BRAIN * 100	45.011(10)	36.407(10)	69.385(10)	193.179(9)[a]
SPLEEN/	20.716	18.696	17.309	22.818
BRAIN * 100	4.677(10)	3.723(10)	3.956(10)	3.633(9)[a]
TESTES/	45.435	47.456	44.249	46.112
BRAIN * 100	6.154(10)	8.818(10)	5.809(10)	7.459(9)[a]
THYMUS/	5.950	6.667	6.625	7.784
BRAIN * 100	1.834(10)	1.394(10)	3.328(10)	2.695(9)[a]

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

a Weight removed due to weighing error.

* Statistically significant difference from control at $p < 0.05$ by Dunnett/Tamhane-Dunnett test.

@ Statistically significant difference from control at $p < 0.05$ by Dunn's test.

Table 26
Mean Final Body and Organ Weights from Female Mice

	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
FINAL BODY WEIGHT (grams)				
	32.2	32.1	32.6	32.4
	4.6(10)	1.7(10)	3.7(9)	2.2(9)
MEAN FINAL BODY AND ABSOLUTE ORGAN WEIGHTS (grams)				
ADRENAL GLANDS	0.014	0.017	0.016	0.016
	0.003(10)	0.005(10)	0.004(9)	0.004(9)
BRAIN	0.507	0.508	0.499	0.518
	0.024(10)	0.021(10)	0.019(9)	0.023(9)
HEART	0.170	0.177	0.169	0.191
	0.018(10)	0.018(10)	0.022(9)	0.030(9)
KIDNEYS	0.436	0.445	0.417	0.493
	0.057(10)	0.036(10)	0.039(9)	0.081(9)
LIVER	1.693	1.697	1.745	2.867@
	0.385(10)	0.139(10)	0.288(9)	0.993(9)
OVARIES	0.036	0.040	0.073@	0.043
	0.010(10)	0.010(10)	0.041(9)	0.012(9)
SPLEEN	0.119	0.106	0.095	0.097
	0.023(10)	0.019(10)	0.021(9)	0.020(7)[a]
THYMUS	0.041	0.040	0.056	0.047
	0.009(10)	0.011(10)	0.038(9)	0.011(9)
UTERUS	0.254	0.276	0.261	0.214
	0.093(10)	0.112(10)	0.103(9)	0.058(9)

Table 26
Mean Final Body and Organ Weights from Female Mice (Continued)

	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
MEAN RELATIVE ORGAN WEIGHTS (% of body weight)				
ADRENAL GLANDS/	0.043	0.054	0.048	0.048
FINAL BODY * 100	0.008(10)	0.018(10)	0.011(9)	0.010(9)
BRAIN/	1.602	1.589	1.546	1.607
FINAL BODY * 100	0.205(10)	0.117(10)	0.168(9)	0.152(9)
HEART/	0.537	0.555	0.522	0.592
FINAL BODY * 100	0.082(10)	0.064(10)	0.066(9)	0.089(9)
KIDNEYS/	1.362	1.388	1.285	1.525
FINAL BODY * 100	0.122(10)	0.114(10)	0.110(9)	0.236(9)
LIVER/	5.225	5.309	5.337	8.811@
FINAL BODY * 100	0.542(10)	0.602(10)	0.440(9)	2.837(9)
OVARIES/	0.112	0.124	0.233@	0.133
FINAL BODY * 100	0.028(10)	0.032(10)	0.143(9)	0.040(9)
SPLEEN/	0.369	0.332	0.292*	0.301*
FINAL BODY * 100	0.035(10)	0.059(10)	0.055(9)	0.050(7)[a]
THYMUS/	0.127	0.123	0.175	0.144
FINAL BODY * 100	0.026(10)	0.032(10)	0.119(9)	0.030(9)
UTERUS/	0.807	0.872	0.824	0.667
FINAL BODY * 100	0.335(10)	0.386(10)	0.356(9)	0.199(9)

Table 26
Mean Final Body and Organ Weights from Female Mice (Continued)

	Group 1 0 mg/kg	Group 2 0.1 mg/kg	Group 3 0.5 mg/kg	Group 4 5 mg/kg
MEAN RELATIVE ORGAN WEIGHTS (% of brain weight)				
ADRENAL GLANDS/	2.745	3.355	3.107	3.030
BRAIN * 100	0.531(10)	0.984(10)	0.701(9)	0.693(9)
HEART/	33.626	34.892	33.927	36.994
BRAIN * 100	3.659(10)	3.182(10)	3.959(9)	5.747(9)
KIDNEYS/	86.000	87.562	83.561	95.374
BRAIN * 100	11.320(10)	7.804(10)	6.773(9)	15.405(9)
LIVER/	332.826	334.248	350.216	555.330@
BRAIN * 100	66.340(10)	30.441(10)	59.323(9)	193.239(9)
OVARIES/	7.100	7.749	14.618@	8.300
BRAIN * 100	1.999(10)	1.765(10)	8.110(9)	2.534(9)
SPLEEN/	23.395	20.898	19.004*	18.672*
BRAIN * 100	3.760(10)	3.522(10)	3.721(9)	4.223(7)[a]
THYMUS/	8.019	7.808	11.193	9.068
BRAIN * 100	1.975(10)	2.169(10)	7.013(9)	2.392(9)
UTERUS/	50.066	54.046	52.243	41.205
BRAIN * 100	18.439(10)	21.619(10)	20.411(9)	10.595(9)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

a Weight removed due to weighing error.

* Statistically significant difference from control at $p < 0.05$ by Dunnett/Tamhane-Dunnett test.

@ Statistically significant difference from control at $p < 0.05$ by Dunn's test.

Table 27
Incidences of Gross Observations in Male Mice

Group:	1	2	3	4
Dosage (mg/kg):	0	0.1	0.5	5
Number of Animals on Study :	10	10	10	10
LIVER;				
No Visible Lesions	10	10	6	1
Discoloration	0	0	4	5
Large	0	0	1	9

Table 28
Incidences of Gross Observations in Female Mice

Group:	1	2	3	4
Dosage (mg/kg):	0	0.1	0.5	5
Number of Animals on Study :	10	10	10	10
ESOPHAGUS;				
No Visible Lesions	10	10	9	10
Impaction	0	0	1	0
JEJUNUM;				
No Visible Lesions	9	10	10	10
Deformity	1	0	0	0
LIVER;				
No Visible Lesions	9	10	10	7
Discoloration	1	0	0	3
Large	0	0	0	3
LUNGS;				
No Visible Lesions	10	10	10	9
Discoloration	0	0	0	1
OVARIES;				
No Visible Lesions	10	10	7	9
Cyst	0	0	3	1
SKIN;				
No Visible Lesions	10	10	9	10
Foreign body	0	0	1	0
Edema	0	0	1	0

Table 29
Incidences and Lesion Grades of Microscopic Findings in Male Mice

Group:	1	2	3	4
Dosage (mg/kg):	0	0.1	0.5	5
Number of Animals on Study :	10	10	10	10
ADRENAL GLANDS;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	8	0	0	6
Accessory cortical tissue; capsule	(0)	(0)	(0)	(1)
minimal	0	0	0	1
Hyperplasia; subcapular cell; focal/multifocal	(1)	(0)	(0)	(3)
minimal	1	0	0	3
Pigment; lipogenic; zona fasciculata; multifocal	(1)	(0)	(0)	(0)
mild	1	0	0	0
Pigment; lipogenic; zona reticularis; multifocal	(1)	(0)	(0)	(1)
minimal	1	0	0	1
AORTA;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
BONE MARROW;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
BRAIN;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
CECUM;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
COLON;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
DUODENUM;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10

Table 29
Incidences and Lesion Grades of Microscopic Findings in Male Mice (Continued)

Group:	1	2	3	4
Dosage (mg/kg):	0	0.1	0.5	5
Number of Animals on Study :	10	10	10	10
EPIDIDYMIDES;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
ESOPHAGUS;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	9	0	0	10
Inflammation; subacute/chronic; submucosa; focal	(1)	(0)	(0)	(0)
minimal	1	0	0	0
EYES;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	9	0	0	10
Rosette; retinal; unilateral	(1)	(0)	(0)	(0)
minimal	1	0	0	0
FEMUR/KNEE JOINT;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
GALLBLADDER;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
HEART;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	9	0	0	8
Cardiomyopathy; focal/multifocal	(1)	(0)	(0)	(2)
minimal	1	0	0	2
ILEUM;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
JEJUNUM;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10

Table 29
Incidences and Lesion Grades of Microscopic Findings in Male Mice (Continued)

Group:	1	2	3	4
Dosage (mg/kg):	0	0.1	0.5	5
Number of Animals on Study :	10	10	10	10
KIDNEYS;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	6	6	7	0
Aggregates; lymphocyte/plasmacyte; focal/multifocal	(1)	(1)	(3)	(0)
minimal	0	1	3	0
mild	1	0	0	0
Chronic progressive nephropathy	(2)	(3)	(0)	(2)
minimal	2	3	0	2
Dilated tubule(s); focal/multifocal	(1)	(2)	(0)	(2)
minimal	1	2	0	2
Hydronephrosis; bilateral	(1)	(0)	(0)	(0)
minimal	1	0	0	0
Hypertrophy; tubular epithelium	(0)	(0)	(0)	(9)
minimal	0	0	0	9
Microvesiculation; epithelium; tubule; diffuse	(1)	(0)	(0)	(0)
moderate	1	0	0	0
LIVER;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	6	4	1	0
Hepatocellular hypertrophy	(0)	(0)	(8)	(10)
minimal	0	0	8	1
mild	0	0	0	9
Hyperplasia; bile duct	(0)	(0)	(0)	(1)
minimal	0	0	0	1
Mitotic figures	(0)	(0)	(0)	(9)
minimal	0	0	0	6
mild	0	0	0	3
Mononuclear cell infiltrate	(4)	(6)	(4)	(7)
minimal	4	6	3	7
mild	0	0	1	0
Pigment increased; kupffer cells	(0)	(0)	(0)	(10)
minimal	0	0	0	10
Single cell necrosis; hepatocellular	(0)	(0)	(0)	(10)
minimal	0	0	0	10

Table 29
Incidences and Lesion Grades of Microscopic Findings in Male Mice (Continued)

Group:	1	2	3	4
Dosage (mg/kg):	0	0.1	0.5	5
Number of Animals on Study :	10	10	10	10
LUNGS;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
MANDIBULAR LYMPH NODES;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	9	0	0	10
Erythrocytosis/erythrophagocytosis; sinus	(1)	(0)	(0)	(0)
minimal	1	0	0	0
MESENTERIC LYMPH NODES;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
NOSE;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	9	0	0	9
Inflammation; turbinate; focal/multifocal	(1)	(0)	(0)	(1)
minimal	1	0	0	1
OPTIC NERVES;				
Examined	(8)	(0)	(0)	(9)
Within Normal Limits	8	0	0	9
Not Examined: MISSING	2	0	0	1
PANCREAS;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
PARATHYROID GLANDS;				
Examined	(8)	(0)	(0)	(9)
Within Normal Limits	8	0	0	9
Not Examined: MISSING	2	0	0	1
PEYERS PATCH;				
Examined	(8)	(0)	(0)	(9)
Within Normal Limits	8	0	0	9
Not Examined: MISSING	2	0	0	1

Table 29
Incidences and Lesion Grades of Microscopic Findings in Male Mice (Continued)

Group:	1	2	3	4
Dosage (mg/kg):	0	0.1	0.5	5
Number of Animals on Study :	10	10	10	10
PHARYNX/LARYNX;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
PITUITARY GLAND;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
PROSTATE;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	9	0	0	10
Aggregates; lymphoid; focal/multifocal	(1)	(0)	(0)	(0)
minimal	1	0	0	0
RECTUM;				
Examined	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	9
Not Examined: MISSING	0	0	0	1
SALIVARY GLANDS;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	8	0	0	7
Aggregates; lymphoid; focal/multifocal	(2)	(0)	(0)	(3)
minimal	2	0	0	3
SCIATIC NERVE;				
Examined	(9)	(0)	(0)	(10)
Within Normal Limits	9	0	0	10
Not Examined: MISSING	1	0	0	0
SEMINAL VESICLES;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
SKELETAL MUSCLE;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10

Table 29
Incidences and Lesion Grades of Microscopic Findings in Male Mice (Continued)

Group:	1	2	3	4
Dosage (mg/kg):	0	0.1	0.5	5
Number of Animals on Study :	10	10	10	10
SKIN;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
SPINAL CORD;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
SPLEEN;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
STERNUM;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	9
Inflammation; granulomatous; focal	(0)	(0)	(0)	(1)
mild	0	0	0	1
STOMACH;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
TESTES;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	9	0	0	9
Degeneration/atrophy; unilateral	(1)	(0)	(0)	(1)
minimal	1	0	0	1
THYMUS;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
THYROID GLAND;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	6	0	0	8
Dilated follicle(s); focal/multifocal	(4)	(0)	(0)	(2)
minimal	4	0	0	2
Ectopic thymus tissue	(1)	(0)	(0)	(0)
present	1	0	0	0

Table 29
Incidences and Lesion Grades of Microscopic Findings in Male Mice (Continued)

Group:	1	2	3	4
Dosage (mg/kg):	0	0.1	0.5	5
Number of Animals on Study :	10	10	10	10
TRACHEA;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10
URINARY BLADDER;				
Examined	(10)	(0)	(0)	(10)
Within Normal Limits	10	0	0	10

Table 30
Incidences and Lesion Grades of Microscopic Findings in Female Mice

Group:	1	2	3	4
Dosage (mg/kg):	0	0.1	0.5	5
Number of Animals on Study :	10	10	10	10
ADRENAL GLANDS;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	3	0	1	5
Accessory cortical tissue; capsule	(2)	(0)	(0)	(1)
minimal	2	0	0	1
Hyperplasia; subcapular cell; focal/multifocal	(6)	(0)	(0)	(5)
minimal	4	0	0	5
mild	2	0	0	0
AORTA;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	9
Inflammation; subacute/chronic; tunica media; focal	(0)	(0)	(0)	(1)
minimal	0	0	0	1
Mineralization; tunica media; focal	(0)	(0)	(0)	(1)
minimal	0	0	0	1
BONE MARROW;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	0	10
Hyperplasia; granulocytic	(0)	(0)	(1)	(0)
moderate	0	0	1	0
BRAIN;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10
CECUM;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10
CERVIX;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10
COLON;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10

Table 30
Incidences and Lesion Grades of Microscopic Findings in Female Mice (Continued)

Group:	1	2	3	4
Dosage (mg/kg):	0	0.1	0.5	5
Number of Animals on Study :	10	10	10	10
DUODENUM;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10
ESOPHAGUS;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	9	0	0	10
Degeneration/inflammation; muscularis; myofiber; focal	(1)	(0)	(0)	(0)
minimal	1	0	0	0
Inflammation; acute; transmural; focal	(0)	(0)	(1)	(0)
moderate	0	0	1	0
EYES;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10
FEMUR/KNEE JOINT;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10
GALLBLADDER;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10
HEART;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10
ILEUM;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10
JEJUNUM;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	9	0	1	10
Diverticulum	(1)	(0)	(0)	(0)
present	1	0	0	0

Table 30
Incidences and Lesion Grades of Microscopic Findings in Female Mice (Continued)

Group:	1	2	3	4
Dosage (mg/kg):	0	0.1	0.5	5
Number of Animals on Study :	10	10	10	10
KIDNEYS;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	6	0	1	6
Aggregates; lymphocyte/plasmacyte; focal/multifocal	(1)	(0)	(0)	(1)
minimal	0	0	0	1
mild	1	0	0	0
Chronic progressive nephropathy	(1)	(0)	(0)	(2)
minimal	1	0	0	2
Dilated tubule(s); focal/multifocal	(2)	(0)	(0)	(4)
minimal	2	0	0	4
LIVER;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	6	8	7	0
Focal necrosis	(1)	(0)	(2)	(3)
minimal	0	0	2	0
mild	0	0	0	3
moderate	1	0	0	0
Hepatocellular hypertrophy	(0)	(0)	(0)	(10)
minimal	0	0	0	6
mild	0	0	0	4
Mononuclear cell infiltrate	(3)	(2)	(3)	(6)
minimal	3	2	3	5
mild	0	0	0	1
Pigment increased; kupffer cells	(0)	(0)	(0)	(2)
minimal	0	0	0	2
Single cell necrosis; hepatocellular	(0)	(0)	(0)	(1)
minimal	0	0	0	1
LUNGS;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	9
Inflammation; subacute/chronic; focal	(0)	(0)	(0)	(1)
minimal	0	0	0	1
MAMMARY GLANDS;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10

Table 30
Incidences and Lesion Grades of Microscopic Findings in Female Mice (Continued)

Group:	1	2	3	4
Dosage (mg/kg):	0	0.1	0.5	5
Number of Animals on Study :	10	10	10	10
MANDIBULAR LYMPH NODES;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	0	10
Necrosis; lymphoid; diffuse	(0)	(0)	(1)	(0)
moderate	0	0	1	0
MESENTERIC LYMPH NODES;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	0	10
Necrosis; lymphoid; diffuse	(0)	(0)	(1)	(0)
moderate	0	0	1	0
NOSE;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	8	0	0	8
Cyst; turbinate; mucosa	(0)	(0)	(0)	(1)
mild	0	0	0	1
Exudate; lumen; unilateral	(0)	(0)	(0)	(1)
moderate	0	0	0	1
Exudate; maxillary sinus; unilateral	(0)	(0)	(0)	(1)
moderate	0	0	0	1
Inclusions/crystals; hyaline; respiratory epithelium	(0)	(0)	(0)	(1)
mild	0	0	0	1
Inflammation; turbinate; focal/multifocal	(2)	(0)	(1)	(1)
minimal	2	0	0	1
moderate	0	0	1	0
OPTIC NERVES;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10
OVARIES;				
Examined	(10)	(0)	(4)	(10)
Within Normal Limits	9	0	1	10
Cyst; bilateral	(0)	(0)	(2)	(0)
present	0	0	2	0
Cyst; unilateral	(1)	(0)	(1)	(0)
present	1	0	1	0

Table 30
Incidences and Lesion Grades of Microscopic Findings in Female Mice (Continued)

Group:	1	2	3	4
Dosage (mg/kg):	0	0.1	0.5	5
Number of Animals on Study :	10	10	10	10
OVIDUCTS;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10
PANCREAS;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	9
Inflammation; chronic; focal	(0)	(0)	(0)	(1)
minimal	0	0	0	1
PARATHYROID GLANDS;				
Examined	(10)	(0)	(1)	(9)
Within Normal Limits	10	0	1	9
Not Examined: MISSING	0	0	0	1
PEYERS PATCH;				
Examined	(9)	(0)	(0)	(9)
Within Normal Limits	9	0	0	9
Not Examined: MISSING	1	0	1	1
PHARYNX/LARYNX;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	0	10
Inflammation; acute; focal	(0)	(0)	(1)	(0)
moderate	0	0	1	0
PITUITARY GLAND;				
Examined	(9)	(0)	(1)	(9)
Within Normal Limits	9	0	1	9
Not Examined: MISSING	1	0	0	1
RECTUM;				
Examined	(10)	(0)	(1)	(9)
Within Normal Limits	10	0	1	9
Not Examined: MISSING	0	0	0	1

Table 30
Incidences and Lesion Grades of Microscopic Findings in Female Mice (Continued)

Group:	1	2	3	4
Dosage (mg/kg):	0	0.1	0.5	5
Number of Animals on Study :	10	10	10	10
SALIVARY GLANDS;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	8	0	0	7
Aggregates; lymphoid; focal/multifocal	(2)	(0)	(0)	(2)
minimal	2	0	0	2
Hypertrophy; acinar cell; diffuse	(0)	(0)	(1)	(1)
minimal	0	0	1	0
mild	0	0	0	1
SCIATIC NERVE;				
Examined	(9)	(0)	(1)	(10)
Within Normal Limits	9	0	1	10
Not Examined: MISSING	1	0	0	0
SKELETAL MUSCLE;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10
SKIN;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10
SPINAL CORD;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10
SPLEEN;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	0	10
Necrosis; lymphoid; white pulp; diffuse	(0)	(0)	(1)	(0)
moderate	0	0	1	0
STERNUM;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	9	0	0	10
Atrophy; marrow; focal/multifocal	(1)	(0)	(0)	(0)
mild	1	0	0	0
Hyperplasia; granulocytic; marrow	(0)	(0)	(1)	(0)
moderate	0	0	1	0

Table 30
Incidences and Lesion Grades of Microscopic Findings in Female Mice (Continued)

Group:	1	2	3	4
Dosage (mg/kg):	0	0.1	0.5	5
Number of Animals on Study :	10	10	10	10
STOMACH;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	9	0	1	10
Inflammation; subacute/chronic; glandular; serosa	(1)	(0)	(0)	(0)
mild	1	0	0	0
THYMUS;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	0	9
Necrosis; lymphoid; cortex; diffuse	(0)	(0)	(1)	(1)
severe	0	0	1	1
THYROID GLAND;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	7	0	1	9
Dilated follicle(s); focal/multifocal	(3)	(0)	(0)	(1)
minimal	3	0	0	1
TRACHEA;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10
URINARY BLADDER;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	9
Aggregates; lymphoid; lamina propria; focal/multifocal	(0)	(0)	(0)	(1)
minimal	0	0	0	1
UTERUS;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10
VAGINA;				
Examined	(10)	(0)	(1)	(10)
Within Normal Limits	10	0	1	10

FIGURES

Figure 1
Mean Body Weights of Male Mice

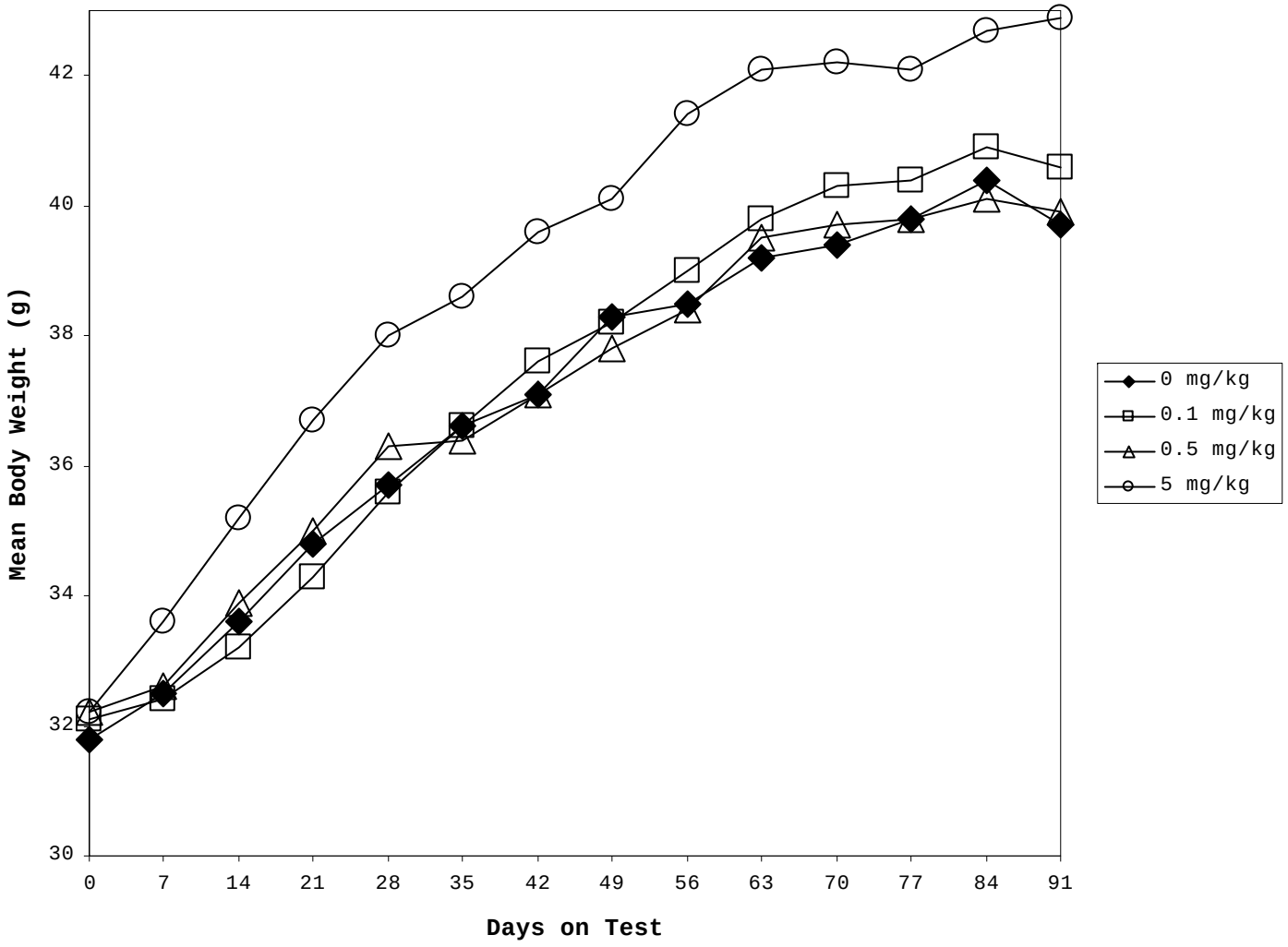
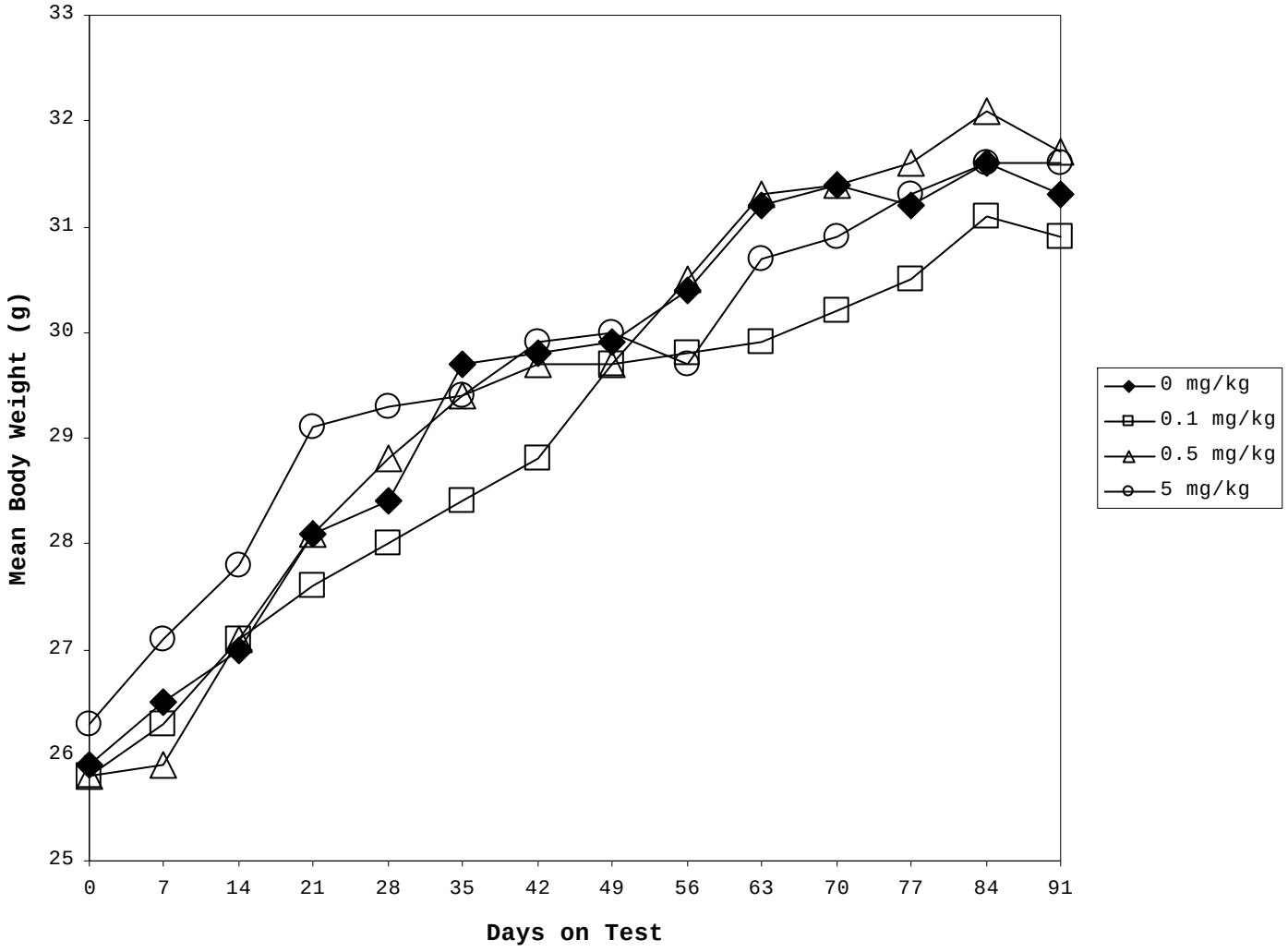


Figure 2
Mean Body Weights of Female Mice



APPENDICES

Appendix A
Certificate of Analysis

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-28548
Common Name	HFPO Dimer Acid Ammonium Salt
Purity Percent	84%
Other Components	Water – 12.7% Perfluorooctanoic acid – 150 ppm
Date of Analysis	June 13, 2008
Expiration Date	June 13, 2011
Instructions for storage	NRT&H
Reference	DuPont-25455
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

24-JUN-2009
Date

Revision #1: Revised COA expiration date based on compound stability assessment. 6/23/09

Appendix B
Dose Formulation Analysis Data

ANALYSIS FOR H-28548 IN DOSE SAMPLES

for

H-28548: Subchronic Toxicity
90-Day Gavage Study in Mice

Work Request Number:	18405
Service Code:	1307
Haskell Sample Number:	28548
Analytical Report Number:	DuPont-18405-1307-AN
DuPont Study Number	DuPont-18405-1307

SUMMARY

Dose samples of H-28548 at the concentrations of 0.01, 0.05, and 0.5 mg/mL prepared on July 22, 2009, September 10, 2009, and October 14, 2009 were submitted for concentration verification and room temperature stability analyses. A 0 mg/mL control sample containing the vehicle only, deionized water, was included and analyzed together with each set of samples.

Samples were diluted with water and concentrations of H-28548 in the diluted samples were determined by high-performance liquid chromatography (HPLC) with mass spectrometry detection (LC/MS).

The analysis results show that the test substance was at the targeted concentrations for all dose levels and stable for up to 15 days when stored at room temperature in the vehicle in the concentration range for the study.

Test substance was not detected in the 0 mg/mL control samples.

MATERIALS AND METHODS

All solvents used were HPLC grade.

1. Dose Sample Preparation

An aliquot of each dose sample was diluted with water to a nominal concentration of 0.005 or 0.0045 mg/mL. The control sample was prepared by diluting 0.5 mL to 1 mL with water. These diluted samples were analyzed by LC/MS.

2. Chromatographic Conditions

Concentrations of H-28548 in diluted dose samples were determined by LC/MS.

LC Parameters

Instrument:	Agilent 1100 liquid chromatograph
Column:	Agilent Zorbax® SB-C8, 2.1 x 100 mm, 3.5 µm
Column Temperature:	35°C
Injection Volume:	5 µL
Mobile Phase:	75% of 0.15% Formic acid in water/25% Acetonitrile (ACN)
Flow Rate:	0.400 mL/min
Stop Time:	5.5 min

MS Parameters

Instrument:	Waters Micromass ZQ
Ionization Source:	Electrospray, negative (ES-)
Capillary Voltage:	3.20 kV
Cone Voltage:	9.00 V
Source Temperature:	120°C
Desolvation Temperature:	300°C
Scan Function:	SIR mass: 329 m/z

3. Calibration and Quantitation

The test substance (H-28548, 84%) was used as the analytical reference standard to make a stock solution in water. The stock solution was further diluted with water to make a set of standard solutions. These standard solutions were then used to generate a calibration curve that covered the targeted concentrations of the diluted samples.

Peak areas from the HPLC analysis of these standard solutions were used to construct a calibration curve by Waters Masslynx software (see Figure 1 for a representative curve). Measured concentrations for the diluted dose samples were determined by applying the peak areas from replicate injections of each sample to the calibration curve.

Concentration verification of the test substance in the dose samples were evaluated by the average results of the duplicate sample analyses for each respective dose level. Relative

standard deviation (RSD = standard deviation/average x 100) was calculated to confirm the concentrations.

Stability of the test substance in the dose samples were evaluated by using the average result of the duplicate sample analyses for the respective dose levels as the baseline for comparing the corresponding stability results.

RESULTS AND DISCUSSION

1. Chromatography

H-28548 eluted from the HPLC column as a resolved peak within a retention time window from approximately 3 to 4 minutes. Representative HPLC chromatograms are shown in Figures 2a - c. Test substance was not detected in the control dose samples.

2. Sample Analysis Results

Detailed results for the concentration verification and stability analyses of the dose samples are shown in Table 1.

The data for the dose samples prepared on July 22, 2009 show that the test substance was at the targeted concentrations (± 8.2% of nominal and RSDs ≤ 2%) and stable when stored at room temperature for up to 15 days in the vehicle for all dose levels. Test substance was not detected in the control sample.

The data for the dose samples prepared on September 10, 2009, and October 14, 2009 show that the test substance was at the targeted concentrations (± 13.2% of nominal) in the vehicle. Test substance was not detected in the control samples.

3. Conclusions

The analytical results show that the test substance was at the targeted concentrations and stable in the vehicle for all dose levels under the storage conditions for the study. Test substance was not detected in the 0 mg/mL control samples.

Table 1: Analysis Results of H-28548 in Dose Samples

Sample Type / Formulation Preparation Date	H-28548 (mg/mL) Nominal	H-28548 (mg/mL) Measured	Percent Nominal
Concentration Verification			
22-July-2009			
Control	0	ND[A]	---
1	0.01	0.0102	102.0
2	0.01	0.0105	105.0
	Average ± SD[B]:	***0.0104 ± 0.0002***	***(104.0)[B]***
	RSD[B]:	***2%***	
1	0.05	0.0540	108.0
2	0.05	0.0542	108.4
	Average ± SD:	***0.0541 ± 0.0001***	***(108.2)***
	RSD:	***0.2%***	
1	0.5	0.532	106.4
2	0.5	0.540	108.0
	Average ± SD:	***0.536 ± 0.006***	***(107.2)***
	RSD:	***1%***	
Stability[C]			
8-Day RT	0.01	0.0103	103.0
	0.05	0.0544	108.8
	0.5	0.561	112.1
15-Day RT	0.01	0.0106	106.0
	0.05	0.0540	108.0
	0.5	0.536	107.2
Concentration Verification[D]			
10-September-2009			
Control	0	ND	---
	0.01	0.0112	112.0
	0.05	0.0566	113.2
	0.5	0.561	112.1
14-October-2009			
Control	0	ND	---
	0.01	0.00941	94.1
	0.05	0.0480	96.0
	0.5	0.474	94.8

[A] ND = Not Detected.
[B] Concentration for each dose level is the average of the duplicate analysis results; SD (standard deviation) and RSD calculated to confirm concentrations. The percent nominal of the average is shown in parenthesis.
[C] Samples stored at room temperature (RT) for 8 or 15 days before duplicate analyses.
[D] Average of duplicate analysis results.

Figure 1
Representative Calibration Curve

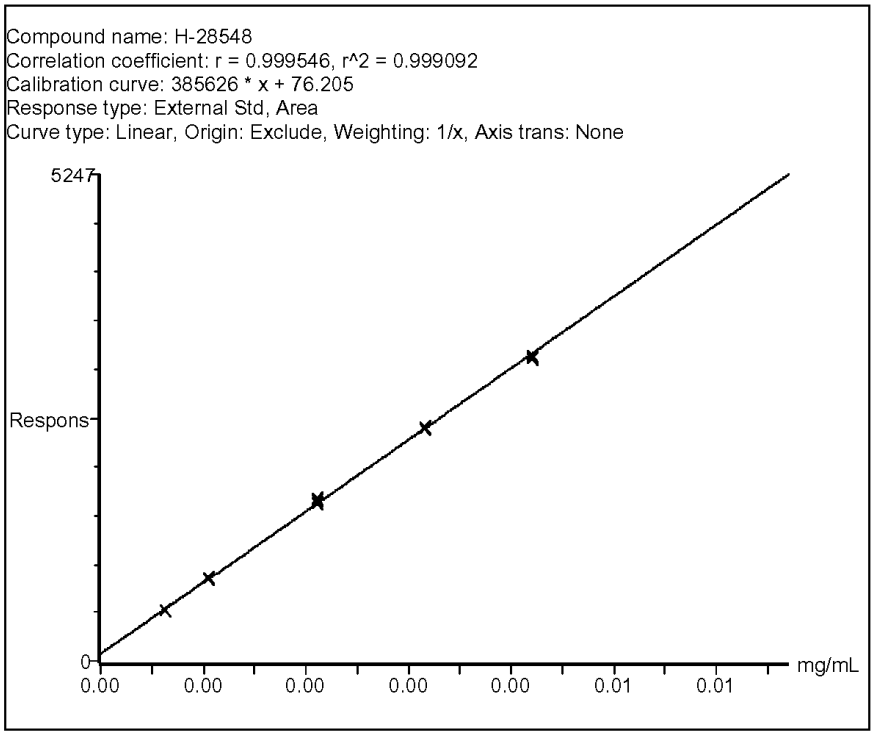


Figure 1. Representative calibration curve showing linear fit to replicate peak area measurements for calibration standard solutions of H-28548 over the concentration range from 0.00126 to 0.00841 mg/mL.

Figure 2
Representative LC/MS Chromatograms

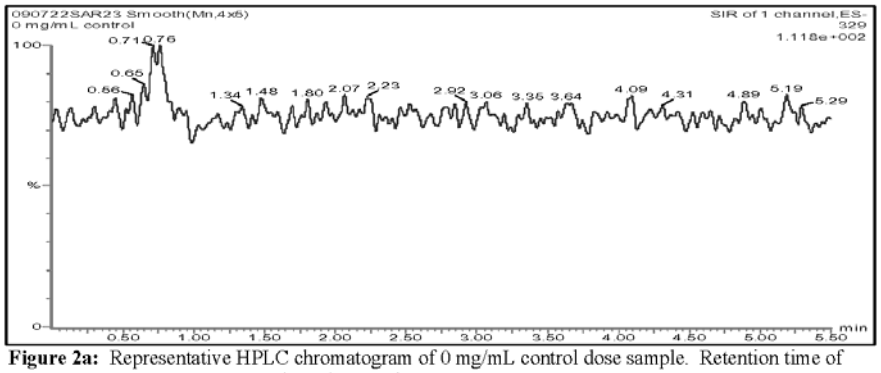


Figure 2a: Representative HPLC chromatogram of 0 mg/mL control dose sample. Retention time of H-28548 was approximately 3.1 minutes.

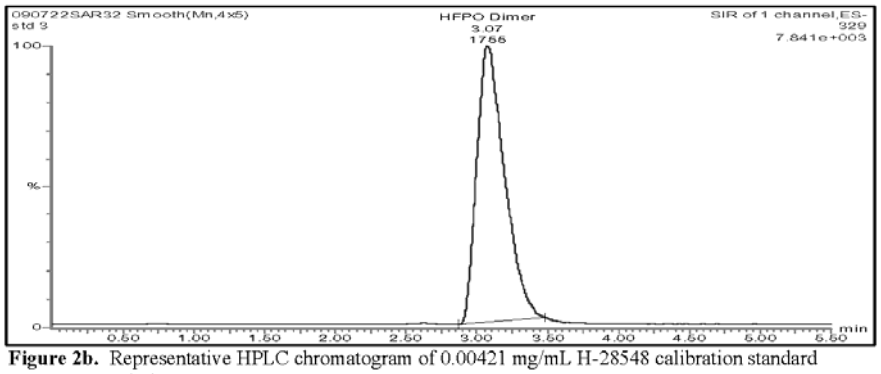


Figure 2b. Representative HPLC chromatogram of 0.00421 mg/mL H-28548 calibration standard solution.

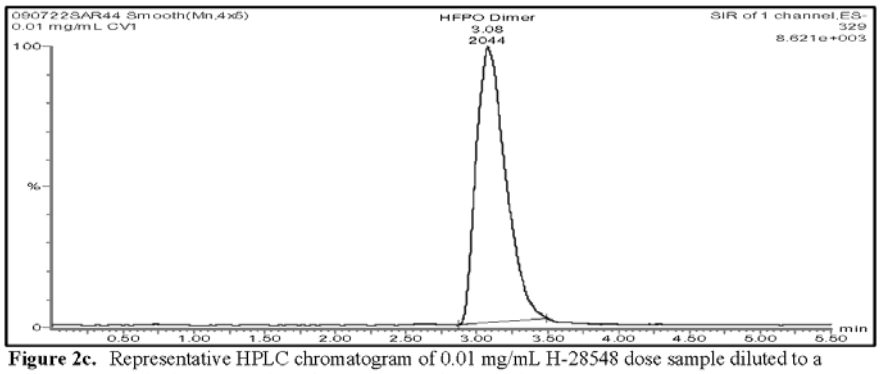


Figure 2c. Representative HPLC chromatogram of 0.01 mg/mL H-28548 dose sample diluted to a nominal concentration of 0.005 mg/mL for analysis.

Appendix C
Individual Body Weights

INDIVIDUAL BODY WEIGHTS

EXPLANATORY NOTES

ABBREVIATIONS:

g - grams

Individual Body Weights

Bodyweights (g)

Day numbers relative to Start Date

Group Sex	Animal Number	0	3	7	14	21	28	35	42	49	56	63	70	77	84	91
1m	101	31.8	.	31.5	31.6	32.5	33.7	34.4	35.1	35.9	37.5	37.5	36.7	36.8	38.8	36.9
	102	30.1	.	31.1	31.3	32.4	34.0	33.7	34.9	35.0	35.6	36.3	35.1	35.4	35.7	34.5
	103	33.4	.	34.5	36.1	37.4	38.1	38.9	39.2	40.1	40.6	41.1	40.9	42.5	42.6	41.4
	104	31.0	.	31.5	31.8	32.6	33.4	33.0	33.9	34.5	35.2	35.9	35.8	35.7	36.7	35.2
	105	29.1	.	30.3	31.5	32.5	34.1	34.6	35.0	36.0	36.3	36.7	36.8	37.2	37.6	35.7
	106	33.1	.	32.7	34.7	35.6	36.8	37.2	38.3	40.7	40.1	42.3	42.4	44.0	45.1	43.4
	107	32.2	.	33.7	35.3	37.6	36.3	38.3	39.4	40.2	39.5	39.2	42.0	41.0	41.8	42.3
	108	30.7	.	31.4	32.8	33.6	34.1	34.6	36.4	37.9	38.0	39.2	40.0	42.0	42.8	41.6
	109	29.9	.	31.8	31.8	32.6	34.5	34.7	35.4	36.0	36.6	37.7	36.2	37.0	36.3	37.5
	110	32.7	.	34.9	35.7	38.5	39.2	40.2	40.3	41.4	41.4	41.6	41.2	41.5	41.2	40.6
	111	32.9	.	35.8	37.4	38.1	37.5	38.7	38.9	39.5	39.8	40.3	40.0	39.7	40.2	40.3
	113	35.5	.	37.1	39.1	41.1	41.4	42.4	44.2	44.9	45.2	47.0	48.4	48.6	48.6	48.5
	114	32.1	.	34.8	35.4	36.8	37.1	37.7	38.7	40.2	39.5	39.7	41.0	41.2	41.6	42.4
	115	31.4	.	32.3	34.0	35.3	37.9	38.1	35.2	39.3	38.6	39.0	40.6	40.6	41.7	40.8
	116	28.8	.	30.1	30.7	32.2	33.1	.	.	.	.	.	.	.	.	.
	117	31.9	.	32.8	34.0	35.8	36.1	.	.	.	.	.	.	.	.	.
	118	31.1	.	30.9	30.9	33.1	33.9	.	.	.	.	.	.	.	.	.
	119	32.4	.	34.2	34.9	35.9	37.4	.	.	.	.	.	.	.	.	.
	120	31.3	.	30.8	32.0	32.1	32.8	.	.	.	.	.	.	.	.	.
	121	29.0	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	122	34.2	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	123	32.4	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	124	33.3	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	125	35.0	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	127	28.7	.	28.1	30.2	30.9	31.9	32.7	32.3	32.3	33.2	33.8	33.5	33.9	34.8	34.0

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Body Weights

Bodyweights (g)

Day numbers relative to Start Date

Group Sex	Animal Number	0	3	7	14	21	28	35	42	49	56	63	70	77	84	91
2m	201	30.1	.	31.6	33.1	33.7	34.5	33.8	35.4	34.8	34.4	36.7	38.6	37.1	36.9	37.0
	202	30.8	.	31.0	32.0	32.4	32.8	34.3	36.5	37.2	37.0	36.6	36.6	36.8	36.8	36.0
	203	30.1	.	30.5	30.8	33.0	36.0	37.1	38.1	39.1	40.4	41.0	41.5	41.4	42.0	40.9
	204	30.9	.	31.8	31.9	32.4	35.1	35.0	36.3	36.0	37.4	38.0	38.3	39.4	40.8	38.9
	205	33.4	.	33.9	35.2	36.3	37.6	38.6	39.2	39.7	42.2	41.5	41.2	41.6	42.4	42.3
	206	31.3	.	32.4	32.6	34.6	34.1	34.6	37.0	38.1	37.1	37.8	37.8	37.6	36.8	38.2
	207	33.3	.	35.4	37.0	39.4	39.2	41.7	41.2	41.4	42.3	42.4	43.0	42.9	45.2	43.3
	208	32.7	.	33.1	34.9	35.7	36.9	37.3	38.6	39.4	40.5	41.3	41.3	42.3	42.8	42.1
	209	33.0	.	34.2	35.1	36.1	35.7	37.1	38.7	39.6	41.3	42.6	43.5	42.9	43.1	43.3
	210	29.8	.	29.8	30.9	28.3	31.5	32.2	33.0	34.0	35.1	35.8	37.3	38.8	39.6	39.2
	211	34.0	.	33.7	34.1	36.8	38.6	39.3	39.4	41.5	41.4	42.3	43.2	43.9	43.8	44.5
	212	30.3	.	32.2	31.7	32.6	34.6	35.6	36.5	37.0	38.2	39.5	41.0	40.2	41.7	41.7
	213	35.4	.	37.0	38.6	39.6	40.9	41.9	42.5	43.2	44.9	46.9	47.0	46.3	46.2	46.7
	214	29.1	.	29.6	29.5	30.5	32.0	32.8	33.4	33.8	35.2	35.5	35.1	35.8	35.3	35.4
	215	32.9	.	34.4	32.3	34.4	36.2	37.1	37.8	38.3	38.3	38.9	39.4	39.1	39.5	39.3
	216	33.7	.	33.6	34.9	36.3	37.4	.	.	.	.	.	.	.	.	.
	217	30.7	.	28.2	30.5	32.4	33.4	.	.	.	.	.	.	.	.	.
	218	30.8	.	31.4	32.1	33.1	34.8	.	.	.	.	.	.	.	.	.
	219	33.2	.	33.3	34.5	35.0	36.1	.	.	.	.	.	.	.	.	.
	220	30.8	.	31.7	33.1	33.3	35.1	.	.	.	.	.	.	.	.	.
	221	29.1	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	222	34.5	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	223	34.4	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	224	34.0	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	225	34.6	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Body Weights

Bodyweights (g)

Day numbers relative to Start Date

Group Sex	Animal Number	0	3	7	14	21	28	35	42	49	56	63	70	77	84	91
3m	301	30.6	.	31.3	32.4	32.7	33.8	35.0	34.5	34.7	36.0	37.0	38.0	38.7	38.4	37.1
	302	30.4	.	31.6	32.9	33.4	35.3	35.5	36.3	37.2	38.3	39.3	39.9	40.3	40.1	40.7
	303	29.3	.	29.5	30.3	31.4	31.6	31.7	34.0	34.0	34.5	37.4	37.1	38.5	36.8	37.3
	304	31.5	.	31.0	31.6	32.4	33.9	35.0	35.2	36.7	37.8	37.3	36.3	36.3	37.0	36.9
	305	33.2	.	33.7	35.3	37.0	38.2	39.8	40.7	41.4	41.7	43.8	44.5	44.4	45.0	42.8
	306	31.4	.	31.1	33.8	35.4	36.2	37.2	38.0	39.7	39.5	40.2	39.7	40.0	40.1	40.2
	307	32.1	.	33.3	33.8	34.3	35.0	35.4	36.4	35.2	36.2	36.3	38.0	35.9	37.3	38.0
	308	30.9	.	32.3	33.0	34.2	35.9	36.4	35.9	37.3	37.6	38.4	38.0	37.9	38.5	37.4
	309	29.0	.	29.9	30.5	32.1	32.3	33.5	34.4	34.6	35.6	37.5	37.6	36.7	37.0	36.9
	310	31.9	.	31.8	32.6	33.6	34.4	35.0	35.9	36.6	37.2	38.4	38.9	38.5	39.4	39.4
	311	32.1	.	33.2	34.6	35.4	36.4	38.1	38.6	40.6	38.9	40.4	39.8	40.5	40.9	41.0
	312	33.2	24.8	.	.	.	.	.	.	.	.	.	.	.	.	.
	313	29.2	.	30.2	31.3	32.1	33.6	34.3	34.9	36.4	35.1	37.5	36.8	37.8	37.3	37.3
	314	34.2	.	29.6	36.6	38.7	39.7	40.2	41.5	40.8	41.8	42.7	43.3	44.3	44.3	44.1
	315	35.1	.	36.5	38.0	38.6	40.5	42.3	43.3	44.4	46.9	46.7	48.4	47.9	48.9	49.4
	316	34.7	.	37.1	38.4	39.7	41.4	.	.	.	.	.	.	.	.	.
	317	31.7	.	32.6	33.1	34.4	35.6	.	.	.	.	.	.	.	.	.
	318	34.8	.	36.3	37.3	38.2	41.4	.	.	.	.	.	.	.	.	.
	319	30.7	.	32.5	31.0	32.1	34.2	.	.	.	.	.	.	.	.	.
	320	35.0	.	35.9	37.3	39.3	39.9	.	.	.	.	.	.	.	.	.
	321	30.2	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	322	33.5	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	323	30.2	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	324	35.7	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	325	33.2	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Body Weights

Bodyweights (g)

Day numbers relative to Start Date

Group Sex	Animal Number	0	3	7	14	21	28	35	42	49	56	63	70	77	84	91
4m	401	31.8	.	33.7	35.8	37.8	38.5	39.1	40.1	42.1	43.9	43.5	44.9	43.1	44.7	43.5
	402	30.4	.	32.7	34.9	37.0	37.9	40.1	41.6	41.8	42.1	42.8	44.3	44.3	44.1	43.2
	403	33.5	.	34.8	37.3	38.9	41.0	41.0	42.1	42.1	43.9	44.1	44.4	44.3	44.2	44.5
	404	34.0	.	36.3	37.6	39.0	40.2	42.1	41.3	41.7	42.5	44.4	44.1	44.0	45.5	45.5
	405	30.8	.	34.1	35.2	36.1	35.7	35.9	36.3	35.6	38.4	39.8	37.8	37.0	38.5	38.6
	406	31.8	.	32.6	34.9	35.7	37.8	38.4	39.2	39.9	41.6	41.2	41.7	40.7	41.6	43.2
	407	32.8	.	32.3	34.8	36.7	37.3	38.7	40.5	41.5	42.5	45.3	44.8	46.3	45.2	45.7
	408	32.7	.	34.9	37.6	39.2	39.3	39.8	40.9	40.6	42.2	42.6	42.7	42.6	43.7	43.6
	409	33.7	.	35.1	36.0	36.7	39.0	39.9	40.4	41.3	42.7	43.8	43.7	43.8	42.7	44.1
	410	35.5	.	37.2	38.7	39.9	38.9	40.6	43.0	43.8	44.7	45.6	45.6	45.7	46.8	46.5
	411	29.3	.	31.3	32.5	33.7	35.6	35.8	37.1	36.7	37.0	37.2	37.9	37.9	37.6	38.6
	412	31.4	.	31.9	32.6	33.5	36.3	36.8	37.1	37.9	38.7	39.7	39.4	40.2	40.5	41.4
	413	32.7	.	33.1	34.5	35.6	37.1	38.3	38.8	39.4	40.6	40.0	40.1	40.1	40.5	41.2
	414	30.2	.	30.2	30.8	33.3	35.3	36.2	38.1	39.7	40.9	40.4	41.1	41.1	42.1	42.4
	415	30.3	.	31.6	32.2	34.2	35.4	36.8	37.4	36.7	39.2	41.2	40.6	39.9	42.1	41.9
	416	31.0	.	31.3	32.1	34.6	35.6	.	.	.	.	.	.	.	.	.
	417	32.7	.	34.8	37.9	39.1	39.3	.	.	.	.	.	.	.	.	.
	418	33.2	.	36.6	39.2	41.1	43.6	.	.	.	.	.	.	.	.	.
	419	32.2	.	32.8	35.2	36.7	38.9	.	.	.	.	.	.	.	.	.
	420	32.5	.	34.5	33.3	35.8	36.6	.	.	.	.	.	.	.	.	.
	421	31.1	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	422	35.0	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	423	30.6	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	425	29.5	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	427	35.7	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Body Weights

Bodyweights (g)

Day numbers relative to Start Date

Group Sex	Animal Number	0	6	7	14	20	21	28	35	42	49	56	63	70	77	84	91
1f	151	26.0	.	26.8	28.2	.	29.6	30.1	32.8	31.2	33.1	33.4	34.6	33.2	35.0	35.0	33.0
	152	23.8	.	25.8	25.8	.	26.9	26.8	27.9	28.9	28.4	28.0	28.2	27.9	29.0	28.8	31.5
	153	24.3	.	24.4	24.4	.	24.3	25.6	27.3	26.0	25.9	27.2	28.2	27.4	27.8	28.6	28.1
	154	24.2	.	24.5	25.4	.	25.3	25.1	24.8	24.7	25.1	25.5	26.4	26.2	26.8	26.0	26.0
	155	25.1	.	25.8	26.1	.	27.0	26.4	27.3	28.7	27.1	27.7	27.6	27.7	28.4	27.5	28.3
	156	27.4	.	28.2	28.7	.	29.2	28.6	29.5	31.0	31.3	30.5	32.0	31.8	31.8	31.0	31.9
	157	22.4	.	24.5	25.6	.	26.7	27.9	28.1	28.8	27.6	29.1	30.3	30.2	30.4	29.7	30.2
	158	25.2	.	26.9	29.0	.	29.1	28.1	29.1	30.9	30.9	30.8	31.8	32.5	31.9	31.6	30.6
	159	28.9	.	29.8	30.3	.	32.3	33.1	35.9	34.3	37.4	36.6	36.8	39.5	36.6	41.5	39.2
	160	27.4	.	29.0	28.9	.	31.2	30.9	34.1	33.6	33.2	34.4	34.4	37.1	36.9	35.9	35.2
	161	24.6	.	25.6	25.3	.	26.7	26.1	27.7	27.3	27.5	27.0	27.3	28.3	26.9	28.4	28.5
	162	24.9	.	25.3	25.2	.	26.4	27.5	29.2	28.7	28.3	30.0	30.2	29.2	28.4	29.9	28.9
	163	25.8	.	27.8	26.2	.	29.5	28.7	29.0	29.6	28.1	29.1	30.9	30.9	30.2	31.1	29.5
	164	28.2	.	30.3	30.6	.	31.7	31.6	33.2	34.0	34.5	36.3	38.5	37.4	36.4	37.3	37.9
	165	27.9	.	22.9	25.4	.	.	.	.	.	.	.	.	.	.	.	.
	166	28.8	.	29.7	29.1	.	30.2	32.0	.	.	.	.	.	.	.	.	.
	167	25.7	.	25.6	25.5	.	26.8	26.8	.	.	.	.	.	.	.	.	.
	168	25.0	.	26.1	26.6	.	26.2	27.1	.	.	.	.	.	.	.	.	.
	169	25.1	.	24.9	25.1	.	26.3	28.1	.	.	.	.	.	.	.	.	.
	170	27.0	.	27.0	27.7	.	29.0	28.2	.	.	.	.	.	.	.	.	.
	171	27.2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	172	26.2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	173	26.4	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	174	25.1	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	175	24.1	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Body Weights

Bodyweights (g)

Day numbers relative to Start Date

Group Sex	Animal Number	0	6	7	14	20	21	28	35	42	49	56	63	70	77	84	91
2f	251	23.1	.	24.4	27.2	.	27.2	25.7	27.9	28.5	31.7	30.4	30.7	30.7	29.6	35.8	31.9
	252	25.2	.	26.2	26.5	.	28.3	27.7	28.1	28.2	30.1	30.8	30.8	30.4	31.0	33.6	30.6
	253	27.2	.	27.2	28.1	.	29.1	27.3	29.3	28.6	29.8	30.7	29.8	31.2	30.7	31.0	32.7
	254	25.5	.	28.2	28.2	.	27.4	29.7	29.3	32.0	30.9	30.7	30.3	30.5	34.4	31.5	32.5
	255	22.1	.	22.6	23.8	.	22.4	24.3	26.1	24.6	25.8	25.2	25.5	26.2	26.1	26.9	26.9
	256	27.9	.	27.2	27.9	.	28.8	28.3	29.7	30.2	31.3	30.2	30.0	31.8	32.2	31.0	31.4
	257	25.6	.	26.4	27.6	.	27.5	27.1	27.6	28.7	28.9	32.7	30.4	31.0	31.9	34.0	35.7
	258	28.3	.	27.8	29.3	.	28.1	29.9	29.7	30.5	32.6	29.3	30.9	31.0	30.8	32.4	31.4
	259	25.4	.	26.6	26.8	.	30.9	29.9	30.6	30.7	33.3	30.5	31.1	30.7	31.8	31.9	31.2
	260	24.3	.	24.9	25.4	.	26.6	25.9	28.4	28.6	30.3	29.7	31.5	30.8	29.9	28.6	29.4
	261	27.7	.	29.6	28.8	.	29.0	29.7	31.7	30.5	31.2	32.0	32.1	33.1	32.8	32.6	32.9
	262	22.8	.	23.4	24.1	.	25.6	25.9	26.2	28.0	27.5	28.6	28.4	29.1	29.6	29.9	29.7
	263	25.3	.	26.3	26.7	.	27.2	29.2	29.1	29.6	28.6	30.8	31.7	31.1	30.6	31.8	31.1
	264	22.9	.	22.7	22.8	.	23.8	23.7	23.0	24.0	25.0	25.3	24.8	25.8	26.1	25.6	25.5
	265	27.1	.	26.9	27.7	.	28.0	29.6	29.0	29.3	29.1	29.7	30.7	30.1	30.7	30.1	31.1
	266	26.6	.	27.0	27.7	.	28.3	29.7	.	.	.	.	.	.	.	.	.
	267	26.6	.	25.6	27.7	.	27.0	27.7	.	.	.	.	.	.	.	.	.
	268	29.2	.	29.7	30.1	.	31.8	31.0	.	.	.	.	.	.	.	.	.
	269	26.4	.	27.5	27.6	.	27.5	27.7	.	.	.	.	.	.	.	.	.
	270	26.3	.	26.6	27.3	.	27.5	29.3	.	.	.	.	.	.	.	.	.
	271	25.5	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	272	24.6	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	273	24.8	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	274	26.9	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	275	27.6	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Body Weights

Bodyweights (g)

Day numbers relative to Start Date

Group Sex	Animal Number	0	6	7	14	20	21	28	35	42	49	56	63	70	77	84	91
3f	351	25.5	.	27.9	28.6	.	29.2	27.6	28.8	29.8	29.1	30.5	29.2	30.7	30.1	29.9	31.0
	352	23.1	.	24.7	26.2	.	27.0	29.2	29.0	29.6	29.7	31.8	31.9	31.9	32.5	32.6	31.2
	353	27.5	.	28.2	28.9	.	31.6	33.4	34.8	37.7	35.8	38.0	43.1	40.5	41.0	45.1	41.0
	354	24.5	.	24.5	25.3	.	25.8	28.4	27.5	27.5	28.0	29.2	29.2	28.9	28.8	30.5	29.9
	355	26.2	18.9	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	356	26.8	.	26.7	27.6	.	29.7	30.9	30.1	30.5	31.9	31.5	32.5	33.3	33.7	34.0	32.7
	357	23.5	.	24.3	24.3	.	24.9	26.0	26.0	25.2	26.4	26.8	26.8	26.9	28.0	27.7	27.1
	358	25.8	.	26.9	28.4	.	29.6	28.6	30.0	28.4	29.6	29.7	29.8	31.3	31.5	31.3	32.3
	359	26.2	.	26.4	28.4	.	29.0	29.0	29.4	29.1	29.0	29.5	31.4	30.9	31.9	31.9	31.9
	360	24.5	.	24.8	26.2	.	28.3	28.8	28.3	28.2	28.9	28.4	28.7	29.0	29.2	29.7	28.3
	361	26.6	.	28.1	28.4	.	29.6	30.4	29.9	30.5	30.5	32.7	33.0	32.1	33.2	31.6	32.9
	362	27.5	.	28.6	29.2	.	28.9	31.1	33.7	32.4	31.7	32.0	33.3	36.3	33.3	35.1	34.2
	363	27.3	.	22.4	28.2	.	29.7	29.3	29.8	29.2	29.3	29.7	30.4	30.0	30.5	31.3	33.3
	364	23.5	.	24.5	23.6	.	24.5	25.1	24.3	26.1	25.4	26.5	26.9	26.3	26.8	26.9	26.7
	365	28.0	.	27.7	28.5	.	29.1	29.6	30.4	30.9	30.9	30.5	32.1	31.8	31.6	31.8	31.1
	366	25.5	.	24.5	25.7	.	25.8	27.3	.	.	.	.	.	.	.	.	.
	367	27.1	17.4	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	368	24.4	.	24.8	25.7	.	27.5	28.0	.	.	.	.	.	.	.	.	.
	369	25.3	.	24.9	26.7	.	27.7	28.2	.	.	.	.	.	.	.	.	.
	370	25.3	.	26.4	28.0	.	28.7	28.2	.	.	.	.	.	.	.	.	.
	371	24.9	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	372	30.2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	373	24.5	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	374	27.5	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	375	23.6	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Body Weights

Bodyweights (g)

Day numbers relative to Start Date

Group Sex	Animal Number	0	6	7	14	20	21	28	35	42	49	56	63	70	77	84	91
4f	451	23.5	.	26.4	27.7	.	28.2	27.3	27.3	26.5	28.3	26.8	28.4	28.7	30.5	28.5	27.5
	452	25.6	.	27.7	29.0	.	31.1	30.9	32.5	34.3	34.0	32.3	33.6	33.4	33.9	34.4	34.0
	453	26.5	.	26.7	27.4	.	30.0	29.7	29.5	29.6	30.9	30.8	30.3	31.1	31.5	33.2	31.9
	454	27.2	.	28.5	29.9	.	30.2	31.0	32.3	31.8	32.9	32.6	32.8	32.7	33.5	35.3	34.0
	455	27.5	.	30.1	30.8	.	30.9	30.7	31.9	31.4	31.8	31.4	32.8	33.0	32.1	33.8	32.8
	456	26.2	.	27.1	28.7	22.5	.	.	.	.	.	.	.	.	.	.	.
	457	25.9	.	27.5	26.9	.	27.5	27.7	29.0	32.5	31.8	32.0	33.9	32.7	31.6	33.9	35.6
	458	25.2	.	27.0	26.4	.	28.9	26.9	28.4	30.6	29.3	28.8	34.7	31.2	30.7	29.4	29.9
	459	25.6	.	26.1	25.5	.	27.7	28.1	27.6	28.4	27.9	27.9	28.6	29.2	33.6	32.5	33.9
	460	24.7	.	25.3	24.9	.	26.1	26.9	26.2	27.0	27.6	27.2	26.5	28.6	29.2	28.5	28.3
	461	25.6	.	28.1	28.5	.	28.5	29.2	29.2	29.8	28.9	29.1	28.4	30.3	30.2	29.7	30.0
	462	25.1	.	26.1	26.9	.	29.4	31.2	30.5	29.9	29.4	31.6	32.6	32.0	31.0	30.9	32.1
	463	24.2	.	24.0	23.8	.	26.5	27.4	26.5	26.0	26.5	25.4	25.2	26.2	27.1	27.0	27.6
	464	26.6	.	26.7	28.3	.	28.9	28.8	30.5	30.7	30.5	29.7	31.3	32.2	31.9	32.3	31.9
	465	28.7	.	23.7	26.2	.	27.7	28.7	29.9	30.0	30.1	29.9	30.7	30.7	31.5	32.5	32.5
	466	27.7	.	29.5	31.3	.	33.0	32.6	.	.	.	.	.	.	.	.	.
	467	25.6	.	26.9	28.4	.	29.8	30.3	.	.	.	.	.	.	.	.	.
	468	27.7	.	30.1	29.4	.	31.4	30.8	.	.	.	.	.	.	.	.	.
	469	27.9	.	28.0	28.1	.	29.7	31.1	.	.	.	.	.	.	.	.	.
	470	25.8	.	26.8	27.3	.	27.9	27.3	.	.	.	.	.	.	.	.	.
	471	27.3	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	472	26.6	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	473	25.4	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	474	25.8	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	475	28.9	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Appendix D
Individual Food Consumption

Individual Food Consumption (g)

Day numbers relative to Start Date

Group Sex	Cage Number	No in Cage	From: To:	0 7	7 14	14 21	21 28	28 35	35 42	42 49	49 56	56 63	63 70	70 77	77 84	84 91
1m	101	1		5.9	5.6	5.1	5.0	4.9	4.9	4.5	5.4	8.8	6.9	4.5	6.3	6.2
	102	1		5.3	5.0	4.8	5.0	4.9	4.9	4.8	4.8	5.0	4.9	4.5	4.6	4.2
	103	1		5.4	5.7	5.9	5.4	5.4	5.7	5.6	5.5	5.3	5.2	5.3	5.1	4.8
	104	1		4.9	5.2	5.3	4.9	4.9	4.8	4.5	4.7	4.6	4.7	4.5	4.5	3.9
	105	1		5.2	5.3	5.4	5.7	5.8	5.7	5.2	5.3	5.3	5.4	5.0	5.1	4.7
	106	1		7.9	7.0	6.5	6.2	6.4	6.1	6.3	6.1	6.7	5.8	5.8	6.0	5.2
	107	1		5.6	6.2	6.3	5.6	5.8	5.8	5.8	5.2	5.6	5.5	5.3	5.3	5.6
	108	1		5.0	6.2	5.6	6.1	5.2	5.6	5.6	5.4	5.5	5.8	6.0	6.2	5.1
	109	1		8.9	9.3	5.8	5.6	5.2	5.3	5.4	5.8	5.1	4.9	4.6	4.7	4.9
	110	1		6.0	5.8	6.0	5.7	6.2	6.1	6.1	5.9	5.8	5.8	5.8	5.3	4.9
	111	1		10.6	6.7	6.4	6.4	6.5	6.5	6.1	6.3	6.5	6.7	7.0	6.2	6.3
	113	1		7.6	7.9	7.3	6.8	6.4	6.7	6.7	6.5	6.7	6.3	5.9	5.8	6.0
	114	1		5.4	5.6	5.5	5.3	5.2	5.4	5.7	5.1	5.4	5.2	4.8	4.8	5.0
	115	1		6.1	6.2	6.1	5.9	6.1	5.8	6.1	5.5	5.6	5.6	5.1	5.5	5.3
	116	1		8.5	4.9	5.1	5.1	.	.	.	.	.	.	.	.	.
	117	1		5.2	5.4	5.6	5.5	.	.	.	.	.	.	.	.	.
	118	1		5.8	4.7	5.1	5.6	.	.	.	.	.	.	.	.	.
	119	1		6.1	5.3	5.4	8.4	.	.	.	.	.	.	.	.	.
	120	1		5.4	8.1	5.1	5.3	.	.	.	.	.	.	.	.	.
	127	1		5.1	4.9	4.9	4.9	5.2	5.2	4.7	5.1	5.2	4.7	4.5	4.8	4.9

Food Consumption Units are grams/animal/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Food Consumption (g)

Day numbers relative to Start Date

Group Sex	Cage Number	No in Cage	From: To:	0 7	7 14	14 21	21 28	28 35	35 42	42 49	49 56	56 63	63 70	70 77	77 84	84 91
2m	201	1		5.8	7.7	6.5	6.7	7.5	6.7	6.4	6.0	5.9	5.5	4.9	5.0	5.3
	202	1		7.2	6.8	5.6	5.5	5.7	6.1	5.5	5.5	5.7	5.1	4.7	5.0	4.9
	203	1		6.0	6.0	6.0	6.1	6.3	6.4	6.6	5.9	6.2	5.6	5.5	6.0	5.6
	204	1		7.7	10.9	6.6	7.4	6.0	7.5	7.7	6.8	6.3	6.3	6.5	6.4	4.3
	205	1		5.6	5.9	5.6	5.3	5.8	5.7	5.4	5.5	5.4	5.0	4.9	5.3	5.0
	206	1		5.0	5.4	5.5	5.1	5.2	5.4	5.6	4.8	4.9	4.7	4.4	4.8	4.6
	207	1		6.1	7.3	6.9	6.0	6.5	5.7	5.6	5.9	5.6	5.8	5.7	6.0	5.1
	208	1		5.8	6.2	6.6	6.4	6.2	6.2	6.1	6.5	6.3	5.6	5.5	5.9	5.4
	209	1		5.7	5.8	5.8	5.4	6.1	5.9	5.8	5.8	6.3	5.6	5.4	5.6	5.4
	210	1		4.2	4.8	4.6	5.1	5.0	4.9	5.0	5.0	5.2	5.4	5.1	5.6	5.1
	211	1		5.6	5.3	6.0	6.1	6.8	6.0	6.3	5.8	6.0	6.1	6.1	6.1	6.1
	212	1		7.0	5.6	5.7	5.9	6.1	5.5	5.3	6.4	6.1	6.5	4.9	6.6	5.4
	213	1		5.6	6.1	5.7	5.3	5.4	5.6	5.7	5.8	5.5	5.6	5.1	5.3	5.1
	214	1		4.9	5.3	5.1	5.5	5.4	5.1	5.1	5.5	5.4	5.1	5.0	5.1	4.9
	215	1		7.8	5.9	7.0	6.7	6.2	9.0	7.0	9.1	6.1	7.9	5.9	5.7	5.3
	216	1		5.5	5.7	6.0	5.9	.	.	.	.	.	.	.	.	.
	217	1		3.7	5.6	5.6	5.3	.	.	.	.	.	.	.	.	.
	218	1		5.6	5.6	5.9	5.6	.	.	.	.	.	.	.	.	.
	219	1		6.1	6.2	6.0	6.1	.	.	.	.	.	.	.	.	.
	220	1		6.7	6.6	6.1	6.6	.	.	.	.	.	.	.	.	.

Food Consumption Units are grams/animal/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Food Consumption (g)

Day numbers relative to Start Date

Group Sex	Cage Number	No in Cage	From: To:	0 7	7 14	14 21	21 28	28 35	35 42	42 49	49 56	56 63	63 70	70 77	77 84	84 91
3m	301	1		5.7	6.2	5.4	5.5	5.3	5.4	5.3	6.7	5.6	5.9	5.3	5.4	4.9
	302	1		8.0	10.7	9.1	9.1	6.6	9.7	7.6	9.5	10.1	7.0	6.0	6.2	5.7
	303	1		4.6	4.9	5.0	4.8	4.8	5.0	4.9	5.1	5.4	5.4	5.3	5.0	4.8
	304	1		5.2	5.2	5.1	5.3	5.4	5.3	5.0	5.5	5.5	5.2	4.7	4.4	4.6
	305	1		5.9	6.1	6.3	6.4	6.1	6.5	6.3	6.3	6.5	6.0	5.9	5.8	5.1
	306	1		4.5	5.0	5.5	5.7	5.8	5.4	5.5	5.4	5.4	5.7	5.6	5.3	5.3
	307	1		7.1	5.3	5.1	5.2	5.1	4.9	4.9	4.9	4.6	5.2	4.8	4.8	4.4
	308	1		6.2	7.2	7.0	6.6	6.0	6.6	5.7	2.6	5.8	5.7	5.1	4.9	4.9
	309	1		5.5	5.9	6.0	5.5	5.6	5.9	5.8	6.3	6.3	5.9	5.5	5.3	5.1
	310	1		6.0	5.6	5.6	6.2	5.6	5.8	5.6	6.5	6.3	5.6	5.5	5.9	5.5
	311	1		5.3	5.5	5.2	5.5	5.8	5.8	5.5	5.3	5.5	5.3	5.2	4.9	5.0
	313	1		5.2	5.1	5.7	5.8	6.2	6.3	5.7	5.6	6.5	6.1	5.7	5.4	6.2
	314	1		6.1	7.4	7.1	6.7	6.8	6.8	6.6	6.4	6.8	6.6	5.8	5.9	5.8
	315	1		7.1	7.2	6.2	7.3	7.1	6.7	6.4	7.6	6.8	7.3	6.2	5.7	5.8
	316	1		5.6	6.5	5.8	5.7	.	.	.	.	.	.	.	.	.
	317	1		6.9	6.4	5.8	6.0	.	.	.	.	.	.	.	.	.
	318	1		5.3	5.8	5.3	7.1	.	.	.	.	.	.	.	.	.
	319	1		5.4	4.6	4.6	5.2	.	.	.	.	.	.	.	.	.
	320	1		10.2	6.0	6.8	6.7	.	.	.	.	.	.	.	.	.

Food Consumption Units are grams/animal/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Food Consumption (g)

Day numbers relative to Start Date

Group Sex	Cage Number	No in Cage	From: To:	0 7	7 14	14 21	21 28	28 35	35 42	42 49	49 56	56 63	63 70	70 77	77 84	84 91
4m	401	1		5.6	9.1	8.8	6.5	5.9	7.1	9.0	9.4	10.0	8.8	7.8	6.1	5.7
	402	1		5.6	5.9	6.0	6.2	7.1	6.7	6.8	6.8	7.4	7.4	6.5	6.6	6.2
	403	1		5.8	7.4	6.4	6.6	6.4	6.3	6.2	6.6	6.8	6.7	6.1	6.0	5.3
	404	1		5.9	6.0	5.8	6.0	6.3	6.0	6.2	6.6	6.3	6.8	5.5	5.7	5.4
	405	1		5.4	5.9	5.8	5.5	5.4	5.2	4.9	5.3	5.8	5.6	5.2	5.5	5.5
	406	1		6.1	6.3	5.9	6.2	6.4	6.3	6.2	6.4	6.5	6.4	5.3	5.5	5.7
	407	1		5.5	6.1	6.3	6.2	6.5	6.8	6.8	6.6	7.0	7.0	7.0	6.4	6.3
	408	1		6.6	7.0	7.0	6.6	6.7	6.9	6.7	6.5	6.4	6.4	6.0	6.5	5.7
	409	1		5.7	6.1	6.1	6.5	6.6	6.6	6.2	6.4	6.3	6.5	6.2	5.6	5.9
	410	1		5.6	6.2	5.8	5.6	5.9	6.6	6.5	6.5	6.5	6.5	6.1	6.2	6.3
	411	1		5.8	6.3	6.2	5.7	5.8	6.0	6.1	5.9	5.9	5.7	5.4	5.4	5.9
	412	1		5.1	5.7	5.6	5.5	6.0	5.6	6.0	5.5	5.8	5.6	5.4	5.9	5.5
	413	1		5.6	6.9	6.0	6.2	6.8	6.6	6.4	6.7	5.8	7.2	5.9	6.6	6.4
	414	1		4.8	4.9	6.2	5.6	6.6	6.5	7.0	6.3	6.1	6.2	6.1	6.2	5.9
	415	1		5.9	5.4	5.6	5.6	5.9	5.9	5.9	6.1	6.9	6.4	5.9	6.2	6.0
	416	1		6.4	5.6	7.6	7.0	.	.	.	.	.	.	.	.	.
	417	1		5.8	6.6	6.7	7.1	.	.	.	.	.	.	.	.	.
	418	1		6.9	7.2	7.3	8.1	.	.	.	.	.	.	.	.	.
	419	1		5.9	6.3	5.9	6.2	.	.	.	.	.	.	.	.	.
	420	1		5.4	4.8	5.7	5.6	.	.	.	.	.	.	.	.	.

Food Consumption Units are grams/animal/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Food Consumption (g)

Day numbers relative to Start Date

Group Sex	Cage Number	No in Cage	From: To:	0 7	7 14	14 21	21 28	28 35	35 42	42 49	49 56	56 63	63 70	70 77	77 84	84 91
1f	151	1		5.7	7.0	7.4	8.9	6.4	7.1	5.9	8.6	6.7	6.3	6.0	6.3	5.4
	152	1		7.9	5.4	5.3	6.0	5.7	5.9	5.7	5.5	5.9	6.2	6.1	6.1	5.9
	153	1		5.0	6.0	5.5	5.5	5.7	5.4	5.3	6.0	5.8	5.7	5.3	5.4	5.0
	154	1		5.0	5.6	5.6	5.3	5.2	5.1	5.3	5.4	5.4	5.4	5.8	5.8	5.6
	155	1		5.2	6.5	5.5	5.5	5.2	5.5	5.6	5.8	5.8	5.3	5.3	5.2	4.9
	156	1		5.4	5.9	5.9	5.1	5.6	5.3	5.4	5.7	5.5	5.3	5.1	5.0	4.9
	157	1		8.9	5.8	5.6	5.5	5.3	5.7	4.9	5.3	5.6	5.2	4.7	4.9	4.5
	158	1		5.9	6.3	5.9	6.0	6.4	5.7	5.4	6.2	6.4	6.3	5.2	5.5	5.3
	159	1		5.4	5.1	5.2	5.2	6.3	5.2	6.5	5.3	6.3	6.8	5.2	7.1	4.3
	160	1		6.4	6.8	6.3	6.9	7.4	6.2	6.0	6.2	6.4	6.7	6.3	6.1	5.9
	161	1		4.4	4.3	5.0	4.5	4.8	4.7	4.5	4.6	4.6	4.8	4.4	4.6	4.5
	162	1		6.6	5.9	5.9	6.8	6.4	5.6	5.3	5.7	6.5	6.0	5.6	5.7	5.4
	163	1		5.3	4.9	5.1	5.0	5.1	4.9	4.6	5.1	5.5	4.9	4.4	4.8	4.7
	164	1		5.2	5.4	5.2	5.1	5.3	5.3	5.3	5.5	6.3	5.2	5.2	5.0	5.2
	165	1		5.3	4.5	.	.	.	.	.	.	.	.	.	.	.
	166	1		9.7	6.6	6.8	6.3	.	.	.	.	.	.	.	.	.
	167	1		6.0	5.4	5.3	5.3	.	.	.	.	.	.	.	.	.
	168	1		4.6	5.0	5.0	5.0	.	.	.	.	.	.	.	.	.
	169	1		5.4	5.1	4.3	5.6	.	.	.	.	.	.	.	.	.
	170	1		5.4	5.3	5.5	5.2	.	.	.	.	.	.	.	.	.

Food Consumption Units are grams/animal/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Food Consumption (g)

Day numbers relative to Start Date

Group Sex	Cage Number	No in Cage	From: To:	0 7	7 14	14 21	21 28	28 35	35 42	42 49	49 56	56 63	63 70	70 77	77 84	84 91
2f	251	1		5.9	5.7	7.1	5.7	5.4	5.7	5.8	5.8	5.8	6.2	5.2	6.9	4.7
	252	1		5.9	5.2	6.5	5.4	5.1	5.7	6.7	7.0	5.9	5.4	4.7	5.4	4.8
	253	1		5.2	5.2	5.4	5.8	6.2	5.6	5.9	6.1	5.8	6.3	5.8	5.6	5.5
	254	1		7.8	6.3	6.1	6.0	6.4	6.6	7.2	6.0	6.3	5.9	5.9	5.2	5.6
	255	1		5.2	7.1	6.5	5.2	5.7	5.3	5.6	5.1	5.6	5.7	5.4	5.9	6.7
	256	1		6.4	5.3	4.7	5.2	5.5	5.2	5.2	4.9	4.9	4.8	4.8	4.9	4.8
	257	1		5.2	5.8	5.4	5.3	5.5	5.5	5.4	6.6	5.8	6.1	5.5	6.3	5.9
	258	1		7.1	5.8	7.9	8.7	9.5	5.8	7.2	6.9	8.0	5.8	5.6	5.7	5.5
	259	1		10.1	7.1	8.0	9.1	4.7	4.7	6.0	4.6	5.1	4.7	4.6	5.1	4.6
	260	1		5.2	5.2	4.9	5.1	5.8	6.1	6.0	6.1	7.0	6.0	4.6	5.9	4.7
	261	1		5.9	6.1	6.0	6.2	6.2	6.1	6.2	6.4	6.5	6.2	5.7	6.4	6.3
	262	1		4.9	5.1	5.0	5.1	5.4	4.9	5.5	5.9	5.6	5.3	5.4	5.3	5.2
	263	1		4.2	4.6	4.5	4.7	4.6	4.6	4.6	4.8	5.2	4.6	4.6	4.7	4.2
	264	1		4.3	4.8	4.8	4.9	4.9	4.9	4.7	4.9	4.9	4.8	4.3	4.6	4.5
	265	1		4.9	5.3	5.3	5.7	5.7	5.0	5.1	4.9	5.1	5.2	5.0	5.0	5.2
	266	1		5.3	5.6	5.4	5.3	.	.	.	.	.	.	.	.	.
	267	1		8.2	8.5	8.2	8.2	.	.	.	.	.	.	.	.	.
	268	1		5.4	6.4	5.9	6.5	.	.	.	.	.	.	.	.	.
	269	1		7.8	5.9	5.3	6.5	.	.	.	.	.	.	.	.	.
	270	1		5.1	5.2	6.2	5.5	.	.	.	.	.	.	.	.	.

Food Consumption Units are grams/animal/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Food Consumption (g)

Day numbers relative to Start Date

Group Sex	Cage Number	No in Cage	From: To:	0 7	7 14	14 21	21 28	28 35	35 42	42 49	49 56	56 63	63 70	70 77	77 84	84 91
3f	351	1		7.8	9.6	7.6	7.5	6.2	8.4	7.7	6.3	7.2	4.9	4.9	5.3	5.0
	352	1		4.8	4.7	4.8	6.0	6.0	4.8	4.5	5.9	4.6	4.6	4.3	4.8	4.2
	353	1		6.5	6.3	6.0	6.9	6.8	6.9	6.6	4.8	9.6	6.3	5.2	6.3	5.6
	354	1		4.7	5.3	5.1	5.8	5.6	5.3	5.2	5.1	4.9	5.1	5.0	5.1	4.7
	356	1		5.5	6.3	5.4	5.6	5.0	5.5	6.6	9.0	5.6	6.2	5.3	6.3	5.1
	357	1		4.4	4.6	4.7	5.1	4.9	4.9	4.8	4.7	4.9	4.9	5.0	4.7	4.3
	358	1		4.8	5.5	5.4	5.4	5.4	5.2	5.0	5.3	5.2	5.0	5.8	5.3	5.9
	359	1		9.1	8.7	8.3	10.2	9.2	7.7	8.9	7.5	9.7	5.1	7.9	6.2	6.2
	360	1		4.5	4.9	5.0	5.2	5.1	5.1	4.8	4.6	4.6	4.9	4.7	4.9	4.6
	361	1		6.6	8.7	9.4	9.4	8.4	7.5	5.9	6.3	6.7	5.9	5.9	5.5	5.5
	362	1		5.1	5.4	5.4	5.2	5.6	5.6	5.3	5.1	4.9	5.6	5.0	5.2	5.2
	363	1		5.3	6.8	6.9	6.9	6.7	7.9	6.1	8.5	6.9	7.6	6.0	6.7	6.3
	364	1		7.6	7.4	6.2	7.9	5.9	6.6	6.1	6.1	6.4	7.0	5.8	5.9	5.9
	365	1		4.0	4.4	4.7	5.4	4.9	4.8	4.9	4.9	5.0	5.1	4.8	5.3	4.9
	366	1		4.0	4.4	4.6	4.7	.	.	.	.	.	.	.	.	.
	368	1		4.2	4.8	5.0	5.1	.	.	.	.	.	.	.	.	.
	369	1		4.8	5.1	5.1	5.5	.	.	.	.	.	.	.	.	.
	370	1		5.0	5.6	5.4	6.0	.	.	.	.	.	.	.	.	.

Food Consumption Units are grams/animal/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Food Consumption (g)

Day numbers relative to Start Date

Group Sex	Cage Number	No in Cage	From: To:	0 7	7 14	14 21	21 28	28 35	35 42	42 49	49 56	56 63	63 70	70 77	77 84	84 91
4f	451	1		5.9	6.4	6.2	5.6	6.8	5.6	8.0	6.2	6.9	7.9	10.2	6.8	7.0
	452	1		5.0	5.2	5.8	7.1	6.0	5.5	6.1	6.3	5.4	8.0	5.1	6.1	5.2
	453	1		5.6	5.4	5.3	5.6	5.9	5.5	5.0	5.6	5.7	5.5	5.6	5.4	5.3
	454	1		5.8	6.0	6.0	6.0	5.8	5.5	5.5	5.9	5.2	5.4	5.3	5.3	5.0
	455	1		6.5	6.3	6.5	6.8	5.6	5.8	5.7	5.6	5.9	6.4	5.6	6.0	5.7
	456	1		4.4	5.0	.	.	.	.	.	.	.	.	.	.	.
	457	1		6.7	6.2	5.8	5.7	5.8	6.6	5.6	7.2	6.6	6.6	5.3	5.9	6.9
	458	1		4.8	4.5	4.5	4.4	4.5	4.9	5.3	4.8	5.7	4.6	4.7	4.7	4.9
	459	1		5.5	5.9	5.9	6.5	5.7	5.8	6.1	5.7	5.6	5.9	6.0	5.5	5.3
	460	1		4.9	4.8	4.9	5.0	5.1	5.3	5.0	4.8	4.7	5.3	4.8	4.9	4.9
	461	1		5.4	6.4	5.9	6.0	6.2	5.2	4.9	4.8	4.7	5.1	4.8	5.1	4.7
	462	1		8.9	7.7	6.5	6.5	5.7	7.3	7.8	7.2	9.2	6.0	5.5	5.4	5.4
	463	1		4.0	4.2	4.1	4.5	4.6	4.3	4.1	3.9	4.4	4.6	4.5	4.3	4.6
	464	1		5.1	5.6	5.7	5.9	5.9	5.7	5.6	5.7	5.7	6.3	5.7	6.0	6.3
	465	1		5.1	5.4	5.4	6.6	6.4	6.5	5.5	7.1	4.8	7.6	5.5	6.4	5.4
	466	1		5.4	5.9	5.9	6.2	.	.	.	.	.	.	.	.	.
	467	1		4.2	4.9	4.7	5.0	.	.	.	.	.	.	.	.	.
	468	1		5.7	5.9	5.8	6.0	.	.	.	.	.	.	.	.	.
	469	1		10.7	9.6	5.7	6.9	.	.	.	.	.	.	.	.	.
	470	1		5.0	4.9	5.0	4.8	.	.	.	.	.	.	.	.	.

Food Consumption Units are grams/animal/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Appendix E
Individual Clinical Observations and Mortality Records

INDIVIDUAL CLINICAL OBSERVATIONS AND MORTALITY RECORDS

EXPLANATORY NOTES

ABBREVIATIONS:

X - present

NOTES:

Clinical observations and fates are recorded in the following time slots:

A - daily animal health observations (recorded by exception) and mode of death
C - general clinical observations (post dosing; recorded by exception)
D - detailed clinical observations

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	0 A	0 D	1 C	2 C	3 A	7 D	14 D	21 D	28 A	28 D	35 D	42 D
1m	101	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	102	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	103	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	104	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	105	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	106	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	107	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	108	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	109	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	110	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	111	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	113	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	114	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	115	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	Site	49 D	51 C	52 C	56 D	63 D	70 D	77 D	84 D	91 D	95 A	96 A
1m	101	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	102	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	103	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	104	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	105	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	106	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	107	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	108	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	109	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	110	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	111	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.
	113	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.
	114	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.
	115	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	0 A	0 D	1 C	2 C	3 A	7 D	14 D	21 D	28 A	28 D	35 D	42 D
1m	116	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	117	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	118	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	119	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	120	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	121	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.
	122	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.
	123	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.
	124	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.
	125	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.
	127	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	Site	49 D	51 C	52 C	56 D	63 D	70 D	77 D	84 D	91 D	95 A	96 A
1m	116	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	117	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	118	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	119	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	120	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	121	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	122	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	123	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	124	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	125	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	127	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	0 A	0 D	1 C	2 C	3 A	7 D	14 D	21 D	28 A	28 D	35 D	42 D
2m	201	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
		Aggressive		.	.	.	.	.	.	.	.	.	.	.	.
		Convulsions - clonic		.	.	.	.	.	.	.	.	.	.	.	.
		Hyperreactive		.	.	.	.	.	.	.	.	.	.	.	X
		Lethargic		.	.	.	.	.	.	.	.	.	.	.	.
		Mass	Inguen	.	.	.	.	.	.	.	.	.	.	.	.
	202	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	203	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	204	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	205	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	206	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	207	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	208	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	209	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	210	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	211	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	212	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	Site	49 D	51 C	52 C	56 D	63 D	70 D	77 D	84 D	91 D	95 A	96 A
2m	201	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
		Aggressive		.	.	X	.	.	.	.	.	.	.	.
		Convulsions - clonic		.	X	.	.	.	.	.	.	.	.	.
		Hyperreactive		X	X	X	X	X	X	X	X	X	.	X
		Lethargic		.	X	X	.	.	.	.	.	.	.	.
		Mass	Inguen	.	.	.	.	X	X	.	.	.	.	.
	202	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	203	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	204	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	205	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	206	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	207	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	208	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	209	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	210	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	211	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.
	212	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	0 A	0 D	1 C	2 C	3 A	7 D	14 D	21 D	28 A	28 D	35 D	42 D
2m	213	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	214	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	215	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
		Mass	Inguen	.	.	.	.	.	.	.	.	.	X	X	.
	216	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	217	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	218	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	219	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	220	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	221	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.
	222	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.
	223	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.
	224	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.
	225	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	Site	49 D	51 C	52 C	56 D	63 D	70 D	77 D	84 D	91 D	95 A	96 A
2m	213	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.
	214	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.
	215	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.
		Mass	Inguen	.	.	.	.	.	.	.	.	.	.	.
	216	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	217	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	218	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	219	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	220	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	221	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	222	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	223	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	224	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	225	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	0 A	0 D	1 C	2 C	3 A	7 D	14 D	21 D	28 A	28 D	35 D	42 D
3m	301	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	302	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	303	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	304	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	305	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	306	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	307	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	308	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	309	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
		Mass	Inguen	.	.	.	.	.	.	.	.	.	X	X	.
	310	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	311	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	Site	49 D	51 C	52 C	56 D	63 D	70 D	77 D	84 D	91 D	95 A	96 A
3m	301	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	302	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	303	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	304	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	305	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	306	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	307	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	308	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	309	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
		Mass	Inguen	.	.	.	.	.	.	.	.	.	.	.
	310	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	311	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	0 A	0 D	1 C	2 C	3 A	7 D	14 D	21 D	28 A	28 D	35 D	42 D
3m	312	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Unscheduled Sacrifice		.	.	.	.	X	.	.	.	.	.	.	.
		Breathing - slow		.	.	.	.	X	.	.	.	.	.	.	.
		Cold to touch		.	.	.	.	X	.	.	.	.	.	.	.
		Dehydrated		.	.	.	X	X	.	.	.	.	.	.	.
		Lethargic		.	.	.	.	X	.	.	.	.	.	.	.
		Swollen	Neck	.	.	X	.	.	.	.	.	.	.	.	.
		Swollen	Shoulder right	.	.	X	X	X	.	.	.	.	.	.	.
	313	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	314	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	315	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	316	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	317	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	318	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	319	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	320	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	321	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.
	322	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.
	323	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.
	324	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.
	325	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	Site	49 D	51 C	52 C	56 D	63 D	70 D	77 D	84 D	91 D	95 A	96 A
3m	312	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Unscheduled Sacrifice		.	.	.	.	.	.	.	.	.	.	.
		Breathing - slow		.	.	.	.	.	.	.	.	.	.	.
		Cold to touch		.	.	.	.	.	.	.	.	.	.	.
		Dehydrated		.	.	.	.	.	.	.	.	.	.	.
		Lethargic		.	.	.	.	.	.	.	.	.	.	.
		Swollen	Neck	.	.	.	.	.	.	.	.	.	.	.
		Swollen	Shoulder right	.	.	.	.	.	.	.	.	.	.	.
	313	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.
	314	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.
	315	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.
	316	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	317	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	318	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	319	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	320	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	321	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	322	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	323	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	324	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	325	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	0 A	0 D	1 C	2 C	3 A	7 D	14 D	21 D	28 A	28 D	35 D	42 D
4m	401	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	402	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	403	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	404	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	405	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	406	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	407	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	408	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	409	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
		Mass	Inguen	.	.	.	.	.	.	.	.	.	.	.	.
		Swollen	Testes	.	.	.	.	.	.	.	.	.	.	.	.
	410	No Abnormalities Detected		.	X	.	.	.	X	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
		Mass	Inguen	.	.	.	.	.	.	.	.	.	X	.	.
		Misshapen	Tail	.	.	.	.	.	.	X	X	.	X	X	X
		Wound - superficial	Inguen	.	.	.	.	.	.	.	.	.	.	X	X
	411	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	412	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	Site	49 D	51 C	52 C	56 D	63 D	70 D	77 D	84 D	91 D	95 A	96 A
4m	401	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	402	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	403	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	404	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	405	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	406	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	407	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	408	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
	409	No Abnormalities Detected		X	.	.	X	X	X	X	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
		Mass	Inguen	.	.	.	.	.	.	.	X	X	.	X
		Swollen	Testes	.	.	.	.	.	.	.	.	X	.	.
	410	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	X
		Mass	Inguen	.	.	.	.	.	.	.	.	.	.	.
		Misshapen	Tail	X	.	.	X	X	X	X	X	X	.	X
		Wound - superficial	Inguen	X	.	.	.	.	.	.	.	.	.	.
	411	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.
	412	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	0 A	0 D	1 C	2 C	3 A	7 D	14 D	21 D	28 A	28 D	35 D	42 D
4m	413	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	414	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	415	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	X	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.
	416	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	417	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	418	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	419	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	420	No Abnormalities Detected		.	X	.	.	.	X	X	X	.	X	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	X	.	.	.
	421	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.
	422	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.
	423	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.
	425	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.
	427	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	Site	49 D	51 C	52 C	56 D	63 D	70 D	77 D	84 D	91 D	95 A	96 A
4m	413	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.
	414	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.
	415	No Abnormalities Detected		X	.	.	X	X	X	X	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	X	.
	416	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	417	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	418	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	419	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	420	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	421	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	422	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	423	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	425	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.
	427	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	0 A	0 D	4 C	5 C	6 A	7 C	7 D	8 C	9 C	10 C	11 C	12 C	13 C	14 C	14 D	15 C	16 A	20 A	21 D
1f	151	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	152	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	153	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	154	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	155	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	156	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	157	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	158	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	159	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	160	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	161	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	162	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	163	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	164	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	Site	28 A	28 D	35 D	42 C	42 D	49 D	50 C	51 C	56 D	63 D	70 D	77 D	80 C	81 C	84 D	91 D	95 A	97 A
1f	151	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	152	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	153	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	154	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	155	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	156	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	157	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	158	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	159	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	160	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	161	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
	162	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
	163	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
	164	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	0 A	0 D	4 C	5 C	6 A	7 C	7 D	8 C	9 C	10 C	11 C	12 C	13 C	14 C	14 D	15 C	16 A	20 A	21 D
1f	165	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Found dead		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Dehydrated		.	.	.	.	.	.	.	.	X	X	.	.	.	.	.	.	.	.	.
		Eye enophthalmus	Left	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	.	.	.
		Mass	Shoulder left	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	.	.	.
		Swollen	Shoulder left	.	.	.	.	.	X	X	X	X	X	X	X	X	.	.	.	.	.	.
	166	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	167	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	168	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	169	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	170	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	171	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	172	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	173	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	174	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	175	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	Site	28 A	28 D	35 D	42 C	42 D	49 D	50 C	51 C	56 D	63 D	70 D	77 D	80 C	81 C	84 D	91 D	95 A	97 A
1f	165	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Found dead		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Dehydrated		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Eye enophthalmus	Left	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mass	Shoulder left	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Swollen	Shoulder left	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	166	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	167	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	168	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	169	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	170	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	171	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	172	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	173	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	174	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	175	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	0 A	0 D	4 C	5 C	6 A	7 C	7 D	8 C	9 C	10 C	11 C	12 C	13 C	14 C	14 D	15 C	16 A	20 A	21 D
2f	251	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	252	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	253	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	254	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	255	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	256	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	257	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	258	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	259	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	260	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	261	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	262	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	263	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	264	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	Site	28 A	28 D	35 D	42 C	42 D	49 D	50 C	51 C	56 D	63 D	70 D	77 D	80 C	81 C	84 D	91 D	95 A	97 A
2f	251	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	252	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	253	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	254	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	255	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	256	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	257	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	258	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	259	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	260	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	261	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
	262	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
	263	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
	264	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	0 A	0 D	4 C	5 C	6 A	7 C	7 D	8 C	9 C	10 C	11 C	12 C	13 C	14 C	14 D	15 C	16 A	20 A	21 D
2f	265	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	266	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	267	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Swollen	Tail	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Wound - superficial	Tail	.	.	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
	268	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	269	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	270	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	271	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	272	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	273	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	274	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	275	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	Site	28 A	28 D	35 D	42 C	42 D	49 D	50 C	51 C	56 D	63 D	70 D	77 D	80 C	81 C	84 D	91 D	95 A	97 A
2f	265	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
	266	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	267	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Swollen	Tail	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Wound - superficial	Tail	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	268	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	269	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	270	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	271	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	272	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	273	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	274	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	275	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	0 A	0 D	4 C	5 C	6 A	7 C	7 D	8 C	9 C	10 C	11 C	12 C	13 C	14 C	14 D	15 C	16 A	20 A	21 D
3f	351	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	352	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	353	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	354	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	355	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Unscheduled Sacrifice		.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Breathing - slow		.	.	.	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Cold to touch		.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Dehydrated		.	.	.	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Swollen	Shoulder right	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	356	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	357	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	358	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	359	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	360	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	361	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	362	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	Site	28 A	28 D	35 D	42 C	42 D	49 D	50 C	51 C	56 D	63 D	70 D	77 D	80 C	81 C	84 D	91 D	95 A	97 A
3f	351	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	352	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	353	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	354	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	355	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Unscheduled Sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Breathing - slow		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Cold to touch		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Dehydrated		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Swollen	Shoulder right	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	356	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	357	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	358	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	359	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	360	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	361	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
	362	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	0 A	0 D	4 C	5 C	6 A	7 C	7 D	8 C	9 C	10 C	11 C	12 C	13 C	14 C	14 D	15 C	16 A	20 A	21 D
3f	363	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	364	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	365	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	366	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	367	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Unscheduled Sacrifice		.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Breathing - slow		.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Dehydrated		.	.	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	368	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	369	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	370	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	371	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	372	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	373	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	374	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	375	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	Site	28 A	28 D	35 D	42 C	42 D	49 D	50 C	51 C	56 D	63 D	70 D	77 D	80 C	81 C	84 D	91 D	95 A	97 A
3f	363	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
	364	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
	365	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
	366	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	367	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Unscheduled Sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Breathing - slow		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Dehydrated		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	368	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	369	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	370	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	371	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	372	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	373	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	374	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	375	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	0 A	0 D	4 C	5 C	6 A	7 C	7 D	8 C	9 C	10 C	11 C	12 C	13 C	14 C	14 D	15 C	16 A	20 A	21 D
4f	451	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Hyperactive		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Hyperreactive		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Stained cageboard - red		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Wound - superficial	End of tail	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Wound - superficial	Tail	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	452	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	453	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	454	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	455	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	456	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	.
		Unscheduled Sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Abnormal gait		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Breathing - slow		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Leaning		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
	457	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	458	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	459	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	460	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	Site	28 A	28 D	35 D	42 C	42 D	49 D	50 C	51 C	56 D	63 D	70 D	77 D	80 C	81 C	84 D	91 D	95 A	97 A
4f	451	No Abnormalities Detected		.	X	X	.	X	.	.	.	.	.	.	.	.	.	.	.	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Hyperactive		.	.	.	X	.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Hyperreactive		.	.	.	X	.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Stained cageboard - red		.	.	.	.	.	.	X	X	.	.	.	.	.	.	.	.	.	.
		Wound - superficial	End of tail	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	.	.
		Wound - superficial	Tail	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.
	452	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	453	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	454	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	455	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	456	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Unscheduled Sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Abnormal gait		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Breathing - slow		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Leaning		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	457	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	458	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	459	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	460	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	.	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	0 A	0 D	4 C	5 C	6 A	7 C	7 D	8 C	9 C	10 C	11 C	12 C	13 C	14 C	14 D	15 C	16 A	20 A	21 D
4f	461	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	462	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	463	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	464	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	465	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	466	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	467	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	468	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	469	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	470	No Abnormalities Detected		.	X	.	.	.	.	X	.	.	.	.	.	.	.	X	.	.	.	X
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	471	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	472	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	473	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	474	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	475	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	Site	28 A	28 D	35 D	42 C	42 D	49 D	50 C	51 C	56 D	63 D	70 D	77 D	80 C	81 C	84 D	91 D	95 A	97 A
4f	461	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
	462	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
	463	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
	464	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
	465	No Abnormalities Detected		.	X	X	.	X	X	.	.	X	X	X	X	.	.	X	X	X	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.
	466	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	467	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	468	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	469	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	470	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	471	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	472	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	473	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	474	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
4f	475	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Mechanistic sacrifice		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Clinical Observations and Mortality Records

Group Sex	Animal Number	Day Number	Time slot	Comments: Comment
2m	201	51	C	ruffled fur - observations made prior to dosing
		52	C	ruffled fur - observations made prior to dosing and at postdose obs
4f	451	42	C	animal running in circles to the left; observation made upon entering room
		50	C	stained bedding red (no cageboard)
		51	C	stained bedding red (no cageboard)
		80	C	running fast in tight circles to the left - first observed prior to dosing
		81	C	running fast in tight circles to the left - first observed prior to dosing
		84	D	running fast in tight circles to the left - first observed prior to dosing
		91	D	running fast in tight circles to the left - first observed prior to dosing
		97	A	running fast in tight circles to the left - first observed prior to dosing
	456	20	A	Noticed before dosing in morning.

Appendix F
Individual Ophthalmology Observations

INDIVIDUAL OPHTHALMOLOGY OBSERVATIONS

EXPLANATORY NOTES

ABBREVIATIONS:

X - present

NANCY M. BROMBERG, VMD, MS, DACVO
EYE CLINIC FOR ANIMALS
6119 MASSACHUSETTS AVE
BETHESDA, MD 20816

STUDY INFORMATION: **Study No. 18405 1307**
Species: Mouse
Study Director: Sue MacKenzie

OPHTHALMOLOGICAL EXAMINATION SUMMARY
Examination Date: October 16, 2009

METHODS: Indirect Ophthalmoscopy following 1% Tropicamide mydriasis

COMMENTS/DISCUSSION
All animals examined had no visible ophthalmoscopic lesions.

Nancy M Bromberg VMD October 19, 2009

Nancy M. Bromberg, VMD, MS **Date**
Diplomate, ACVO

Individual Ophthalmology Observations

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	8 5
1m	101	No Abnormalities Detected		X
	102	No Abnormalities Detected		X
	103	No Abnormalities Detected		X
	104	No Abnormalities Detected		X
	105	No Abnormalities Detected		X
	106	No Abnormalities Detected		X
	107	No Abnormalities Detected		X
	108	No Abnormalities Detected		X
	109	No Abnormalities Detected		X
	110	No Abnormalities Detected		X
2m	201	No Abnormalities Detected		X
	202	No Abnormalities Detected		X
	203	No Abnormalities Detected		X
	204	No Abnormalities Detected		X
	205	No Abnormalities Detected		X
	206	No Abnormalities Detected		X
	207	No Abnormalities Detected		X
	208	No Abnormalities Detected		X
	209	No Abnormalities Detected		X
	210	No Abnormalities Detected		X

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Ophthalmology Observations

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	8 5
3m	301	No Abnormalities Detected		X
	302	No Abnormalities Detected		X
	303	No Abnormalities Detected		X
	304	No Abnormalities Detected		X
	305	No Abnormalities Detected		X
	306	No Abnormalities Detected		X
	307	No Abnormalities Detected		X
	308	No Abnormalities Detected		X
	309	No Abnormalities Detected		X
	310	No Abnormalities Detected		X
4m	401	No Abnormalities Detected		X
	402	No Abnormalities Detected		X
	403	No Abnormalities Detected		X
	404	No Abnormalities Detected		X
	405	No Abnormalities Detected		X
	406	No Abnormalities Detected		X
	407	No Abnormalities Detected		X
	408	No Abnormalities Detected		X
	409	No Abnormalities Detected		X
	410	No Abnormalities Detected		X

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Ophthalmology Observations

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	8 5
1f	151	No Abnormalities Detected		X
	152	No Abnormalities Detected		X
	153	No Abnormalities Detected		X
	154	No Abnormalities Detected		X
	155	No Abnormalities Detected		X
	156	No Abnormalities Detected		X
	157	No Abnormalities Detected		X
	158	No Abnormalities Detected		X
	159	No Abnormalities Detected		X
	160	No Abnormalities Detected		X
2f	251	No Abnormalities Detected		X
	252	No Abnormalities Detected		X
	253	No Abnormalities Detected		X
	254	No Abnormalities Detected		X
	255	No Abnormalities Detected		X
	256	No Abnormalities Detected		X
	257	No Abnormalities Detected		X
	258	No Abnormalities Detected		X
	259	No Abnormalities Detected		X
	260	No Abnormalities Detected		X

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Ophthalmology Observations

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	8 5
3f	351	No Abnormalities Detected		X
	352	No Abnormalities Detected		X
	353	No Abnormalities Detected		X
	354	No Abnormalities Detected		X
	356	No Abnormalities Detected		X
	357	No Abnormalities Detected		X
	358	No Abnormalities Detected		X
	359	No Abnormalities Detected		X
	360	No Abnormalities Detected		X
4f	451	No Abnormalities Detected		X
	452	No Abnormalities Detected		X
	453	No Abnormalities Detected		X
	454	No Abnormalities Detected		X
	455	No Abnormalities Detected		X
	457	No Abnormalities Detected		X
	458	No Abnormalities Detected		X
	459	No Abnormalities Detected		X
	460	No Abnormalities Detected		X

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Appendix G
Individual Grip Strength

INDIVIDUAL GRIP STRENGTH

EXPLANATORY NOTES

ABBREVIATIONS:

… - no data collected due to unscheduled mortality

NOTES:

Mice 355 and 456 died prior to the week 13 evaluation.

Individual Grip Strength

Animal Number	Grip Strength (kg) Trial 1	Trial 2	Trial 3	Trial 4	Mean of 4 Trials
Male, Group 1 - 0 mg/kg - Baseline					
101	0.33	0.26	0.35	0.27	0.30
102	0.24	0.21	0.23	0.22	0.23
103	0.25	0.38	0.25	0.22	0.28
104	0.24	0.19	0.28	0.25	0.24
105	0.35	0.26	0.36	0.31	0.32
106	0.28	0.30	0.19	0.25	0.26
107	0.22	0.25	0.20	0.21	0.22
108	0.22	0.22	0.21	0.21	0.22
109	0.22	0.23	0.23	0.22	0.23
110	0.27	0.26	0.22	0.24	0.25
Male, Group 2 - 0.1 mg/kg - Baseline					
201	0.20	0.19	0.27	0.19	0.21
202	0.30	0.30	0.24	0.26	0.28
203	0.27	0.31	0.27	0.27	0.28
204	0.33	0.33	0.23	0.28	0.29
205	0.27	0.27	0.20	0.27	0.25
206	0.26	0.18	0.23	0.20	0.22
207	0.28	0.31	0.31	0.34	0.31
208	0.28	0.20	0.28	0.25	0.25
209	0.27	0.29	0.28	0.26	0.28
210	0.19	0.21	0.20	0.23	0.21
Male, Group 3 - 0.5 mg/kg - Baseline					
301	0.27	0.26	0.23	0.31	0.27
302	0.22	0.27	0.28	0.25	0.26
303	0.20	0.28	0.20	0.23	0.23
304	0.26	0.23	0.21	0.27	0.24
305	0.30	0.21	0.23	0.31	0.26
306	0.22	0.32	0.23	0.29	0.27
307	0.24	0.19	0.25	0.21	0.22
308	0.26	0.23	0.22	0.26	0.24
309	0.26	0.22	0.30	0.24	0.26
310	0.24	0.21	0.20	0.23	0.22
Male, Group 4 - 5 mg/kg - Baseline					
401	0.28	0.26	0.22	0.24	0.25
402	0.27	0.22	0.21	0.22	0.23
403	0.25	0.28	0.21	0.25	0.25
404	0.29	0.28	0.24	0.26	0.27
405	0.27	0.30	0.22	0.29	0.27
406	0.24	0.23	0.20	0.21	0.22
407	0.26	0.28	0.24	0.27	0.26
408	0.29	0.31	0.27	0.27	0.29
409	0.27	0.31	0.23	0.27	0.27
410	0.25	0.28	0.29	0.23	0.26

Individual Grip Strength

Animal Number	Grip Strength (kg) Trial 1	Trial 2	Trial 3	Trial 4	Mean of 4 Trials
Male, Group 1 - 0 mg/kg - Week 13					
101	0.42	0.42	0.34	0.42	0.40
102	0.30	0.31	0.38	0.37	0.34
103	0.25	0.37	0.40	0.38	0.35
104	0.29	0.43	0.28	0.40	0.35
105	0.31	0.27	0.34	0.35	0.32
106	0.32	0.29	0.35	0.41	0.34
107	0.35	0.37	0.29	0.27	0.32
108	0.30	0.31	0.38	0.33	0.33
109	0.40	0.31	0.33	0.30	0.34
110	0.26	0.24	0.28	0.31	0.27
Male, Group 2 - 0.1 mg/kg - Week 13					
201	0.28	0.38	0.32	0.32	0.33
202	0.37	0.35	0.37	0.37	0.37
203	0.30	0.39	0.38	0.34	0.35
204	0.29	0.42	0.32	0.32	0.34
205	0.40	0.40	0.37	0.37	0.39
206	0.25	0.27	0.32	0.33	0.29
207	0.29	0.35	0.35	0.34	0.33
208	0.35	0.28	0.26	0.32	0.30
209	0.34	0.39	0.32	0.28	0.33
210	0.21	0.29	0.30	0.33	0.28
Male, Group 3 - 0.5 mg/kg - Week 13					
301	0.27	0.34	0.36	0.39	0.34
302	0.30	0.33	0.41	0.34	0.35
303	0.28	0.28	0.32	0.32	0.30
304	0.21	0.35	0.44	0.33	0.33
305	0.24	0.41	0.28	0.42	0.34
306	0.40	0.34	0.38	0.33	0.36
307	0.26	0.23	0.34	0.26	0.27
308	0.23	0.27	0.26	0.26	0.26
309	0.33	0.29	0.29	0.33	0.31
310	0.36	0.25	0.36	0.25	0.31
Male, Group 4 - 5 mg/kg - Week 13					
401	0.29	0.36	0.37	0.46	0.37
402	0.38	0.26	0.36	0.32	0.33
403	0.33	0.44	0.46	0.37	0.40
404	0.35	0.29	0.29	0.29	0.31
405	0.37	0.36	0.38	0.36	0.37
406	0.27	0.38	0.28	0.36	0.32
407	0.41	0.25	0.40	0.29	0.34
408	0.47	0.31	0.27	0.31	0.34
409	0.41	0.36	0.37	0.31	0.36
410	0.30	0.26	0.24	0.23	0.26

Individual Grip Strength

Animal Number	Grip Strength (kg) Trial 1	Trial 2	Trial 3	Trial 4	Mean of 4 Trials
Female, Group 1 - 0 mg/kg - Baseline					
151	0.25	0.28	0.23	0.20	0.24
152	0.16	0.15	0.21	0.21	0.18
153	0.22	0.17	0.17	0.15	0.18
154	0.21	0.23	0.17	0.15	0.19
155	0.18	0.17	0.24	0.28	0.22
156	0.23	0.20	0.16	0.20	0.20
157	0.18	0.17	0.18	0.21	0.19
158	0.27	0.24	0.24	0.24	0.25
159	0.23	0.25	0.20	0.20	0.22
160	0.21	0.25	0.22	0.20	0.22
Female, Group 2 - 0.1 mg/kg - Baseline					
251	0.31	0.33	0.33	0.25	0.31
252	0.22	0.19	0.19	0.17	0.19
253	0.25	0.22	0.19	0.24	0.23
254	0.33	0.26	0.27	0.25	0.28
255	0.20	0.18	0.23	0.19	0.20
256	0.30	0.20	0.20	0.20	0.23
257	0.26	0.22	0.26	0.27	0.25
258	0.26	0.20	0.23	0.21	0.23
259	0.20	0.27	0.27	0.18	0.23
260	0.21	0.22	0.19	0.19	0.20
Female, Group 3 - 0.5 mg/kg - Baseline					
351	0.25	0.25	0.18	0.24	0.23
352	0.33	0.26	0.19	0.34	0.28
353	0.21	0.22	0.15	0.23	0.20
354	0.32	0.23	0.23	0.21	0.25
355	0.18	0.18	0.17	0.17	0.18
356	0.26	0.44	0.22	0.27	0.30
357	0.19	0.19	0.19	0.23	0.20
358	0.22	0.19	0.22	0.28	0.23
359	0.24	0.30	0.23	0.29	0.27
360	0.20	0.25	0.17	0.17	0.20
Female, Group 4 - 5 mg/kg - Baseline					
451	0.21	0.27	0.21	0.17	0.22
452	0.24	0.28	0.21	0.28	0.25
453	0.25	0.21	0.19	0.25	0.23
454	0.23	0.22	0.19	0.20	0.21
455	0.25	0.26	0.27	0.18	0.24
456	0.23	0.21	0.28	0.23	0.24
457	0.20	0.18	0.19	0.14	0.18
458	0.24	0.22	0.25	0.25	0.24
459	0.23	0.22	0.20	0.20	0.21
460	0.23	0.22	0.19	0.17	0.20

Individual Grip Strength

Animal Number	Grip Strength (kg) Trial 1	Trial 2	Trial 3	Trial 4	Mean of 4 Trials
Female, Group 1 - 0 mg/kg - Week 13					
151	0.35	0.26	0.37	0.35	0.33
152	0.22	0.20	0.29	0.25	0.24
153	0.33	0.22	0.25	0.32	0.28
154	0.24	0.22	0.22	0.20	0.22
155	0.27	0.28	0.26	0.26	0.27
156	0.32	0.29	0.29	0.22	0.28
157	0.36	0.32	0.31	0.25	0.31
158	0.45	0.36	0.37	0.31	0.37
159	0.24	0.31	0.37	0.26	0.30
160	0.21	0.23	0.29	0.26	0.25
Female, Group 2 - 0.1 mg/kg - Week 13					
251	0.34	0.31	0.27	0.29	0.30
252	0.35	0.37	0.22	0.25	0.30
253	0.33	0.33	0.23	0.31	0.30
254	0.33	0.33	0.36	0.33	0.34
255	0.31	0.22	0.22	0.33	0.27
256	0.29	0.24	0.27	0.29	0.27
257	0.31	0.37	0.32	0.33	0.33
258	0.33	0.29	0.27	0.29	0.30
259	0.25	0.23	0.19	0.25	0.23
260	0.23	0.24	0.20	0.26	0.23
Female, Group 3 - 0.5 mg/kg - Week 13					
351	0.33	0.33	0.37	0.28	0.33
352	0.35	0.33	0.31	0.38	0.34
353	0.44	0.32	0.28	0.31	0.34
354	0.22	0.35	0.13	0.15	0.21
355	…	…	…	…	…
356	0.21	0.19	0.38	0.32	0.28
357	0.35	0.36	0.23	0.36	0.33
358	0.23	0.27	0.29	0.35	0.29
359	0.25	0.25	0.33	0.30	0.28
360	0.23	0.30	0.25	0.22	0.25
Female, Group 4 - 5 mg/kg - Week 13					
451	0.37	0.28	0.31	0.46	0.36
452	0.32	0.24	0.23	0.24	0.26
453	0.26	0.27	0.30	0.25	0.27
454	0.27	0.34	0.28	0.28	0.29
455	0.22	0.29	0.35	0.35	0.30
456	…	…	…	…	…
457	0.22	0.26	0.32	0.32	0.28
458	0.29	0.25	0.37	0.27	0.30
459	0.29	0.22	0.34	0.27	0.28
460	0.27	0.28	0.30	0.31	0.29

Appendix H
Individual Functional Observational Battery Assessment

INDIVIDUAL FUNCTIONAL OBSERVATIONAL BATTERY ASSESSMENT

EXPLANATORY NOTES

INDIVIDUAL FUNCTIONAL OBSERVATIONAL BATTERY SCORING SYSTEM

AUDITORY STIMULUS:	-1	=	no reaction
	0	=	normal reaction (animal flinches or flicks ear)
	1	=	exaggerated reaction (animal jumps, flips)
APPROACH & TOUCH:	-1	=	no reaction
	0	=	normal
	1	=	increased reaction (jumps away or attacks)
TAIL PINCH:	-1	=	no response
	0	=	normal (turns toward site)
	1	=	exaggerated response (vocalizations, rapid turning)
DIARRHEA:	0	=	absent
	1	=	present
POLYURIA:	0	=	absent
	1	=	present
PUPILLARY RESPONSE:	0	=	present
	1	=	absent

ABBREVIATIONS:

… - no data collected

FOOTNOTES:

a - hyerreactive
b - splayed rear limbs, slight
c - high arousal
e - corneal opacity, right
d - wound, end of tail
f - swollen face and neck

NOTES:

Mice 355 and 456 died prior to the week 13 evaluation.

Individual Functional Observational Battery Assessment

ANIMAL NUMBER	FOOTNOTES	AUDITORY STIMULUS (-1,0,1)	APPROACH & TOUCH (-1,0,1)	TAIL PINCH (-1,0,1)	DIARRHEA (0,1)	POLYURIA (0,1)	PUPILLARY RESPONSE (0,1)
Male, Group 1 - 0 mg/kg - Baseline							
101		0	0	0	0	0	0
102		0	0	0	0	0	0
103		0	0	0	0	0	0
104		0	0	0	0	0	0
105		0	0	0	0	0	0
106		0	0	0	0	0	0
107		0	0	0	0	0	0
108		0	0	0	0	0	0
109		0	0	0	0	0	0
110		0	0	0	0	0	0
Male, Group 2 - 0.1 mg/kg- Baseline							
201		0	0	0	0	0	0
202		0	0	0	0	0	0
203		0	0	0	0	0	0
204		0	0	0	0	0	0
205		0	0	0	0	0	0
206		0	0	0	0	0	0
207		0	0	0	0	0	0
208		0	0	0	0	0	0
209		0	0	0	0	0	0
210		0	0	0	0	0	0
Male, Group 3 - 0.5 mg/kg- Baseline							
301		0	0	0	0	0	0
302		0	0	0	0	0	0
303		0	0	0	0	0	0
304		0	0	0	0	0	0
305		0	0	0	0	0	0
306		0	0	0	0	0	0
307		0	0	0	0	0	0
308		0	0	0	0	0	0
309		0	0	0	0	0	0
310		0	0	0	0	0	0
Male, Group 4 - 5 mg/kg- Baseline							
401		0	0	0	0	0	0
402		0	0	0	0	0	0
403		0	0	0	0	0	0
404		0	0	0	0	0	0
405		0	0	0	0	0	0
406		0	0	0	0	0	0
407		0	0	0	0	0	0
408		0	0	0	0	0	0
409		0	0	0	0	0	0
410		0	0	0	0	0	0

Individual Functional Observational Battery Assessment

ANIMAL NUMBER	FOOTNOTES	AUDITORY STIMULUS (-1,0,1)	APPROACH & TOUCH (-1,0,1)	TAIL PINCH (-1,0,1)	DIARRHEA (0,1)	POLYURIA (0,1)	PUPILLARY RESPONSE (0,1)
Male, Group 1 - 0 mg/kg - Week 13							
101		0	0	0	0	0	0
102		0	0	0	0	0	0
103		0	0	0	0	0	0
104		0	0	0	0	0	0
105		0	0	0	0	0	0
106		0	0	0	0	0	0
107		-1	0	0	0	0	0
108		0	0	0	0	0	0
109		0	0	0	0	0	0
110		0	0	0	0	0	0
Male, Group 2 - 0.1 mg/kg- Week 13							
201	c	0	0	0	0	0	0
202		0	0	0	0	0	0
203		0	0	0	0	0	0
204		0	0	0	0	0	0
205		0	0	0	0	0	0
206		0	0	0	0	0	0
207		0	0	0	0	0	0
208		0	0	0	0	0	0
209		0	0	0	0	0	0
210		0	0	0	0	0	0
Male, Group 3 - 0.5 mg/kg- Week 13							
301		0	0	0	0	0	0
302		0	0	0	0	0	0
303	e	0	0	0	0	0	…
304		0	0	0	0	0	0
305		0	0	0	0	0	0
306		0	0	0	0	0	0
307		0	0	0	0	0	0
308		0	0	0	0	0	0
309		0	0	0	0	0	0
310		0	0	0	0	0	0
Male, Group 4 - 5 mg/kg- Week 13							
401		0	0	0	0	0	0
402		0	0	0	0	0	0
403		0	0	0	0	0	0
404		0	0	0	0	0	0
405		0	0	0	0	0	0
406	f	0	0	0	0	0	0
407		0	0	0	0	0	0
408		0	0	0	0	0	0
409		0	0	0	0	0	0
410		0	0	0	0	0	0

Individual Functional Observational Battery Assessment

ANIMAL NUMBER	FOOTNOTES	AUDITORY STIMULUS (-1,0,1)	APPROACH & TOUCH (-1,0,1)	TAIL PINCH (-1,0,1)	DIARRHEA (0,1)	POLYURIA (0,1)	PUPILLARY RESPONSE (0,1)
Female, Group 1 - 0 mg/kg - Baseline							
151		0	0	0	0	0	0
152		0	0	0	0	0	0
153		0	0	0	0	0	0
154		0	0	0	0	0	0
155		0	0	0	0	0	0
156		0	0	0	0	0	0
157		0	0	0	0	0	0
158		0	0	0	0	0	0
159		0	0	0	0	0	0
160		0	0	0	0	0	0
Female, Group 2 - 0.1 mg/kg- Baseline							
251		0	0	0	0	0	0
252		0	0	0	0	0	0
253		0	0	0	0	0	0
254		0	0	0	0	0	0
255		0	0	0	0	0	0
256		0	0	0	0	0	0
257		0	0	0	0	0	0
258		0	0	0	0	0	0
259		0	0	0	0	0	0
260		0	0	0	0	0	0
Female, Group 3 - 0.5 mg/kg- Baseline							
351		0	0	0	0	0	0
352		0	0	0	0	0	0
353		0	0	0	0	0	0
354		0	0	0	0	0	0
355		0	0	0	0	0	0
356		0	0	0	0	0	0
357		0	0	0	0	0	0
358		0	0	0	0	0	0
359		0	0	0	0	0	0
360		0	0	0	0	0	0
Female, Group 4 - 5 mg/kg- Baseline							
451		0	0	0	0	0	0
452		0	0	0	0	0	0
453		0	0	0	0	0	0
454		0	0	0	0	0	0
455		0	0	0	0	0	0
456		0	0	0	0	0	0
457		0	0	0	0	0	0
458		0	0	0	0	0	0
459	b	0	0	0	0	0	0
460		0	0	0	0	0	0

Individual Functional Observational Battery Assessment

ANIMAL NUMBER	FOOTNOTES	AUDITORY STIMULUS (-1,0,1)	APPROACH & TOUCH (-1,0,1)	TAIL PINCH (-1,0,1)	DIARRHEA (0,1)	POLYURIA (0,1)	PUPILLARY RESPONSE (0,1)
Female, Group 1 - 0 mg/kg - Week 13							
151		0	0	0	0	0	0
152		0	0	0	0	0	0
153		0	0	0	0	0	0
154		0	0	0	0	0	0
155		0	0	0	0	0	0
156		0	0	0	0	0	0
157		0	0	0	0	0	0
158		0	0	0	0	0	0
159		0	0	0	0	0	0
160		0	0	0	0	0	0
Female, Group 2 - 0.1 mg/kg- Week 13							
251		0	0	0	0	0	0
252		0	0	0	0	0	0
253		0	0	0	0	0	0
254		0	0	0	0	0	0
255	d	0	0	0	0	0	0
256		0	0	0	0	0	0
257		0	0	0	0	0	0
258		0	0	0	0	0	0
259		0	0	0	0	0	0
260		0	0	0	0	0	0
Female, Group 3 - 0.5 mg/kg- Week 13							
351		0	0	0	0	0	0
352		0	0	0	0	0	0
353		0	0	0	0	0	0
354		0	0	0	0	0	0
355		…	…	…	…	…	…
356		0	0	0	0	0	0
357		0	0	0	0	0	0
358		0	0	0	0	0	0
359		0	0	0	0	0	0
360		0	0	0	0	0	0
Female, Group 4 - 5 mg/kg- Week 13							
451		0	0	0	0	0	0
452		0	0	0	0	0	0
453		0	0	0	0	0	0
454		0	0	0	0	0	0
455		0	0	0	0	0	0
456		…	…	…	…	…	…
457		0	0	0	0	0	0
458		0	0	0	0	0	0
459		0	0	0	0	0	0
460		0	0	0	0	0	0

Appendix I
Individual Motor Activity: Duration of Movement

INDIVIDUAL MOTOR ACTIVITY: DURATION OF MOVEMENT

EXPLANATORY NOTES

ABBREVIATIONS:

… - no data collected

NOTES:

Mice 355 and 456 died prior to the week 13 evaluation.

Individual Motor Activity: Duration of Movement (sec)

Animal Number	Successive 10-Minute Intervals 1	2	3	4	5	6	7	8	9	Total
Male, Group 1 - 0 mg/kg - Baseline										
101	419	344	448	314	373	329	340	278	91	2936
102	517	472	453	425	425	369	344	318	279	3602
103	510	434	431	412	369	403	261	344	82	3246
104	403	310	258	290	249	200	79	88	207	2084
105	393	305	320	332	370	322	300	333	214	2889
106	491	420	374	359	343	424	367	371	283	3432
107	541	472	482	439	443	435	433	432	343	4020
108	417	327	354	284	289	292	276	177	38	2454
109	412	305	358	315	350	308	294	296	208	2846
110	415	315	386	336	349	350	363	307	364	3185
Male, Group 2 - 0.1 mg/kg - Baseline										
201	391	353	324	248	264	272	249	245	155	2501
202	508	451	451	393	421	392	375	327	317	3635
203	457	368	375	389	370	364	336	342	316	3317
204	451	364	366	342	277	347	273	155	0	2575
205	370	317	405	384	408	459	396	430	222	3391
206	437	389	386	353	330	321	384	337	297	3234
207	494	390	406	351	271	324	314	290	263	3103
208	265	301	310	207	206	135	103	57	52	1636
209	501	453	404	453	359	432	412	387	435	3836
210	501	446	397	349	430	434	160	0	1	2718
Male, Group 3 - 0.5 mg/kg - Baseline										
301	535	444	450	407	391	400	379	392	398	3796
302	464	351	312	305	286	323	191	265	188	2685
303	487	396	376	376	409	353	346	312	307	3362
304	391	329	278	320	277	276	107	12	0	1990
305	480	402	379	304	399	299	275	149	0	2687
306	442	421	417	411	317	277	179	22	56	2542
307	326	162	224	206	190	216	54	45	0	1423
308	435	357	376	398	292	282	75	12	0	2227
309	364	354	236	308	342	303	291	314	176	2688
310	481	392	418	361	325	280	291	283	147	2978
Male, Group 4 - 5 mg/kg - Baseline										
401	403	363	430	427	372	366	295	359	278	3293
402	503	447	441	425	379	339	294	105	1	2934
403	391	284	268	314	273	274	254	229	218	2505
404	419	405	345	400	334	425	349	349	127	3153
405	527	450	452	403	428	458	419	370	398	3905
406	487	424	435	424	447	304	414	410	313	3658
407	571	524	468	334	432	457	306	337	436	3865
408	357	248	343	211	291	201	285	286	161	2383
409	434	389	402	330	291	339	372	175	299	3031
410	492	371	363	379	392	422	339	333	315	3406

Individual Motor Activity: Duration of Movement (sec)

Animal Number	Successive 10-Minute Intervals 1	2	3	4	5	6	7	8	9	Total
Male, Group 1 - 0 mg/kg - Week 13										
101	444	416	411	355	308	228	287	359	322	3130
102	496	433	455	424	354	299	322	254	207	3244
103	527	425	440	385	386	395	395	417	342	3712
104	455	372	311	323	289	341	306	308	185	2890
105	471	367	352	359	355	370	330	314	352	3270
106	534	492	465	469	497	523	500	462	391	4333
107	533	490	452	451	439	422	461	395	424	4067
108	519	436	460	434	411	417	373	315	377	3742
109	480	442	429	363	402	388	327	301	243	3375
110	509	473	476	445	279	407	415	384	373	3761
Male, Group 2 - 0.1 mg/kg - Week 13										
201	407	359	335	290	258	226	198	188	148	2409
202	541	464	468	409	399	476	421	412	339	3929
203	509	420	491	450	461	473	395	320	433	3952
204	440	346	369	361	374	349	318	316	230	3103
205	435	454	392	418	525	467	449	495	423	4058
206	442	304	380	346	313	367	367	353	321	3193
207	552	447	449	371	405	451	258	414	274	3621
208	364	277	311	261	289	295	324	311	247	2679
209	549	481	494	442	469	442	450	445	387	4159
210	521	493	445	476	489	426	482	404	365	4101
Male, Group 3 - 0.5 mg/kg - Week 13										
301	533	480	467	470	445	456	449	471	381	4152
302	459	381	355	357	388	282	269	264	217	2972
303	523	482	461	441	428	410	403	372	350	3870
304	485	356	347	394	354	392	324	260	305	3217
305	502	396	397	424	326	366	336	197	243	3187
306	489	439	420	398	389	410	423	363	333	3664
307	372	274	281	267	188	152	161	138	74	1907
308	444	428	437	386	338	390	427	429	329	3608
309	456	358	313	327	385	427	375	378	396	3415
310	551	407	386	415	376	385	347	305	348	3520
Male, Group 4 - 5 mg/kg - Week 13										
401	512	432	414	350	446	385	467	337	387	3730
402	540	481	428	397	432	313	361	394	273	3619
403	473	381	364	336	324	312	306	312	270	3078
404	507	392	402	330	417	371	321	420	270	3430
405	519	464	446	456	495	423	457	461	441	4162
406	475	423	382	342	281	311	317	384	305	3220
407	560	506	498	448	477	491	495	470	470	4415
408	490	335	360	370	338	387	375	326	222	3203
409	460	362	314	274	179	259	199	255	146	2448
410	563	502	487	486	475	502	452	466	427	4360

Individual Motor Activity: Duration of Movement (sec)

Animal Number	Successive 10-Minute Intervals 1	2	3	4	5	6	7	8	9	Total
Female, Group 1 - 0 mg/kg - Baseline										
151	455	380	366	444	411	342	318	252	211	3179
152	518	443	374	463	496	422	394	477	418	4005
153	369	200	234	233	283	251	216	169	11	1966
154	397	313	268	215	278	203	34	0	0	1708
155	368	271	286	284	316	312	241	242	266	2586
156	450	443	413	386	345	320	234	206	16	2813
157	408	361	350	366	366	357	198	0	96	2502
158	328	277	303	340	243	282	192	213	184	2362
159	396	393	394	285	311	302	366	320	337	3104
160	443	361	340	397	234	156	6	13	280	2230
Female, Group 2 - 0.1 mg/kg - Baseline										
251	397	307	349	328	225	310	329	342	307	2894
252	399	327	301	337	305	294	329	266	120	2678
253	465	412	388	409	385	359	317	223	247	3205
254	384	294	327	258	280	325	231	134	329	2562
255	483	391	401	400	373	408	403	148	3	3010
256	530	468	446	437	377	388	404	359	376	3785
257	366	291	327	260	217	298	316	232	228	2535
258	526	432	478	357	388	382	365	274	310	3512
259	457	380	296	347	307	302	277	389	188	2943
260	408	320	336	315	260	352	299	213	339	2842
Female, Group 3 - 0.5 mg/kg - Baseline										
351	407	338	293	308	234	291	277	244	155	2547
352	452	401	417	457	416	339	357	274	179	3292
353	537	452	343	441	446	336	368	108	1	3032
354	316	341	333	308	258	43	67	206	230	2102
355	509	381	384	367	325	293	448	281	411	3399
356	366	287	259	245	338	109	6	207	333	2150
357	306	261	225	256	211	245	161	128	119	1912
358	404	336	341	357	338	294	262	167	152	2651
359	404	378	379	337	226	213	142	38	15	2132
360	533	400	410	385	373	387	321	119	0	2928
Female, Group 4 - 5 mg/kg - Baseline										
451	407	298	302	375	299	344	311	361	335	3032
452	419	420	342	389	331	333	220	288	27	2769
453	461	419	430	380	127	17	248	371	368	2821
454	386	378	260	295	262	180	107	0	0	1868
455	470	400	369	380	286	168	193	36	58	2360
456	356	287	288	225	211	43	167	218	72	1867
457	426	350	347	205	287	410	347	258	260	2890
458	430	312	289	231	158	206	250	78	88	2042
459	293	224	239	251	205	192	213	132	0	1749
460	467	440	407	451	419	377	331	251	284	3427

Individual Motor Activity: Duration of Movement (sec)

Animal Number	Successive 10-Minute Intervals 1	2	3	4	5	6	7	8	9	Total
Female, Group 1 - 0 mg/kg - Week 13										
151	457	436	423	421	347	229	375	307	247	3242
152	520	508	512	505	478	412	455	336	445	4171
153	405	286	230	304	252	328	162	265	173	2405
154	431	361	301	430	412	376	415	271	367	3364
155	372	266	244	154	361	321	310	233	306	2567
156	456	408	389	366	354	320	295	263	219	3070
157	454	389	327	443	391	370	345	367	302	3388
158	469	450	441	458	443	480	451	473	412	4077
159	497	424	375	384	367	387	386	396	427	3643
160	466	381	410	329	400	310	299	264	226	3085
Female, Group 2 - 0.1 mg/kg - Week 13										
251	466	391	309	296	386	310	361	373	243	3135
252	414	359	383	316	350	348	348	331	267	3116
253	529	444	450	455	443	369	373	354	307	3724
254	414	331	328	422	358	410	331	333	112	3039
255	540	517	445	355	305	445	347	18	36	3008
256	530	451	422	487	471	378	448	446	365	3998
257	489	402	338	306	309	358	363	218	210	2993
258	475	452	462	461	417	450	376	425	390	3908
259	509	433	418	422	447	402	343	286	232	3492
260	457	379	392	408	429	437	414	365	449	3730
Female, Group 3 - 0.5 mg/kg - Week 13										
351	456	355	356	372	354	274	299	340	254	3060
352	484	423	386	305	342	335	257	274	241	3047
353	573	487	482	437	428	320	383	382	308	3800
354	395	332	386	424	342	335	84	150	8	2456
355	…	…	…	…	…	…	…	…	…	…
356	456	321	306	256	248	221	193	164	79	2244
357	368	311	348	309	347	297	283	307	263	2833
358	500	408	444	374	311	397	355	344	310	3443
359	439	398	326	302	339	299	245	260	189	2797
360	514	405	430	406	403	349	406	308	291	3512
Female, Group 4 - 5 mg/kg - Week 13										
451	514	463	552	454	523	535	552	561	541	4695
452	537	438	427	412	455	415	335	357	308	3684
453	500	413	435	441	450	421	400	295	52	3407
454	434	396	407	396	398	377	343	283	209	3243
455	468	451	405	410	394	278	369	325	356	3456
456	…	…	…	…	…	…	…	…	…	…
457	517	445	406	427	453	487	405	391	344	3875
458	467	391	394	421	357	419	429	369	433	3680
459	299	161	315	368	279	366	310	271	232	2601
460	513	482	420	447	410	468	469	416	305	3930

Appendix J
Individual Motor Activity: Number of Movements

INDIVIDUAL MOTOR ACTIVITY: NUMBER OF MOVEMENTS

EXPLANATORY NOTES

ABBREVIATIONS:

… - no data collected

NOTES:

Mice 355 and 456 died prior to the week 13 evaluation.

Individual Motor Activity: Number of Movements

Animal Number	Successive 10-Minute Intervals 1	2	3	4	5	6	7	8	9	Total
Male, Group 1 - 0 mg/kg - Baseline										
101	129	130	110	143	142	144	157	134	68	1157
102	105	137	121	113	126	155	150	148	144	1199
103	100	119	115	142	109	130	98	145	77	1035
104	147	144	150	151	129	124	83	86	120	1134
105	190	172	177	168	175	163	177	159	119	1500
106	122	158	151	161	131	135	152	155	147	1312
107	88	92	113	98	130	130	130	140	153	1074
108	160	157	161	152	158	162	175	116	44	1285
109	132	151	124	143	156	173	151	174	115	1319
110	111	130	140	140	122	147	150	140	137	1217
Male, Group 2 - 0.1 mg/kg - Baseline										
201	188	178	174	143	154	151	168	148	120	1424
202	97	125	111	108	125	148	153	140	142	1149
203	140	178	143	170	142	164	177	158	152	1424
204	133	154	123	138	157	154	156	103	0	1118
205	167	182	159	175	175	169	136	165	127	1455
206	136	131	165	127	127	148	136	167	136	1273
207	96	109	121	131	97	145	131	107	136	1073
208	155	149	150	132	123	126	99	67	67	1068
209	113	126	163	134	156	126	152	150	131	1251
210	111	129	108	138	143	130	103	0	1	863
Male, Group 3 - 0.5 mg/kg - Baseline										
301	86	140	147	130	144	147	165	134	139	1232
302	127	151	150	144	164	174	132	143	118	1303
303	123	132	136	133	150	117	131	144	145	1211
304	140	138	152	138	156	158	82	13	0	977
305	139	131	145	132	141	139	153	99	0	1079
306	129	126	137	124	136	129	100	25	48	954
307	183	106	142	136	132	156	70	75	0	1000
308	157	155	143	137	153	152	59	22	1	979
309	148	174	136	160	164	189	177	164	137	1449
310	128	136	127	137	133	152	142	151	88	1194
Male, Group 4 - 5 mg/kg - Baseline										
401	186	173	151	157	155	162	155	155	185	1479
402	119	132	148	114	137	135	122	74	2	983
403	133	150	136	164	144	154	154	131	153	1319
404	127	132	127	113	139	145	152	122	73	1130
405	96	120	111	111	129	105	127	147	132	1078
406	111	128	144	129	127	161	139	140	148	1227
407	70	99	95	133	116	103	118	129	149	1012
408	156	106	128	131	143	139	151	149	93	1196
409	144	148	132	151	144	166	166	129	154	1334
410	106	151	141	131	150	152	147	174	176	1328

Individual Motor Activity: Number of Movements

Animal Number	Successive 10-Minute Intervals 1	2	3	4	5	6	7	8	9	Total
Male, Group 1 - 0 mg/kg - Week 13										
101	125	138	132	142	136	99	123	127	137	1159
102	126	141	137	148	164	157	156	160	134	1323
103	70	111	105	112	107	109	114	124	129	981
104	133	147	141	149	153	127	140	155	111	1256
105	143	159	155	182	177	155	190	173	164	1498
106	97	129	133	128	115	116	120	121	171	1130
107	93	115	124	133	123	121	136	144	149	1138
108	96	146	127	144	163	159	152	153	152	1292
109	141	159	147	155	167	164	168	156	147	1404
110	107	96	100	104	113	152	129	150	144	1095
Male, Group 2 - 0.1 mg/kg - Week 13										
201	171	185	182	171	176	155	164	164	147	1515
202	89	142	135	148	149	111	133	145	149	1201
203	111	146	123	153	140	142	157	123	160	1255
204	132	126	104	111	135	144	142	135	133	1162
205	147	152	158	130	109	127	137	145	160	1265
206	151	149	158	164	141	150	140	132	151	1336
207	73	108	96	127	116	125	113	130	108	996
208	163	148	142	124	147	142	144	174	124	1308
209	83	123	92	124	123	130	119	160	148	1102
210	75	112	122	110	122	106	117	125	121	1010
Male, Group 3 - 0.5 mg/kg - Week 13										
301	93	131	131	136	141	135	150	145	148	1210
302	136	163	173	165	143	155	149	168	163	1415
303	84	108	122	122	120	154	152	146	141	1149
304	112	155	144	135	152	167	161	155	154	1335
305	99	139	143	118	129	153	152	121	137	1191
306	109	141	115	140	129	135	134	159	140	1202
307	167	166	147	173	151	112	125	130	72	1243
308	142	159	161	147	150	159	160	145	160	1383
309	131	140	134	120	146	156	167	182	150	1326
310	82	109	128	150	143	132	136	168	161	1209
Male, Group 4 - 5 mg/kg - Week 13										
401	111	151	172	161	139	133	145	164	165	1341
402	98	121	133	117	134	148	151	155	121	1178
403	128	137	161	155	148	156	152	141	154	1332
404	118	129	119	116	131	139	126	111	116	1105
405	87	116	145	133	131	125	130	124	151	1142
406	111	141	161	133	146	162	158	169	167	1348
407	67	95	94	99	106	132	103	111	119	926
408	116	139	144	141	136	138	165	155	131	1265
409	129	157	159	138	121	140	131	175	115	1265
410	68	120	120	124	117	109	153	133	144	1088

Individual Motor Activity: Number of Movements

Animal Number	Successive 10-Minute Intervals 1	2	3	4	5	6	7	8	9	Total
Female, Group 1 - 0 mg/kg - Baseline										
151	157	162	183	140	170	182	182	172	138	1486
152	107	122	109	143	107	106	140	116	142	1092
153	143	94	113	108	144	153	134	121	17	1027
154	149	153	122	95	136	112	39	0	0	806
155	156	132	156	134	136	149	133	143	144	1283
156	157	132	130	135	132	129	136	119	21	1091
157	143	130	150	130	138	136	109	2	76	1014
158	154	134	164	133	127	150	98	139	135	1234
159	146	134	153	146	145	145	167	127	158	1321
160	136	127	120	135	125	88	4	13	130	878
Female, Group 2 - 0.1 mg/kg - Baseline										
251	170	150	147	137	99	163	139	157	133	1295
252	160	168	148	171	153	168	185	177	99	1429
253	138	162	163	158	143	151	156	162	136	1369
254	135	134	132	111	134	155	126	84	128	1139
255	99	133	125	120	129	127	123	84	7	947
256	95	102	123	112	115	109	140	129	127	1052
257	146	155	163	145	155	161	120	121	133	1299
258	109	153	116	147	144	158	156	137	136	1256
259	121	138	128	129	129	145	140	161	124	1215
260	166	145	144	133	151	141	155	143	157	1335
Female, Group 3 - 0.5 mg/kg - Baseline										
351	148	160	129	138	117	140	116	123	107	1178
352	124	140	156	137	149	134	131	137	86	1194
353	86	144	133	136	121	146	134	70	1	971
354	151	135	175	169	171	60	52	102	130	1145
355	111	131	114	135	146	102	120	155	156	1170
356	144	128	138	126	164	73	17	101	139	1030
357	157	156	143	148	122	144	125	128	121	1244
358	153	162	150	126	158	158	129	129	103	1268
359	139	134	140	149	116	140	93	36	16	963
360	92	112	136	117	143	133	141	55	2	931
Female, Group 4 - 5 mg/kg - Baseline										
451	156	140	126	148	137	136	132	165	141	1281
452	156	123	136	153	163	166	140	121	21	1179
453	111	139	123	118	55	18	86	122	138	910
454	140	131	133	122	123	129	85	0	0	863
455	158	149	155	163	164	101	121	42	37	1090
456	179	171	155	130	141	30	108	130	63	1107
457	115	117	130	87	123	130	125	148	161	1136
458	146	160	128	123	97	118	142	61	46	1021
459	161	129	136	127	140	145	169	142	0	1149
460	127	127	140	117	144	147	159	149	135	1245

Individual Motor Activity: Number of Movements

Animal Number	Successive 10-Minute Intervals 1	2	3	4	5	6	7	8	9	Total
Female, Group 1 - 0 mg/kg - Week 13										
151	146	144	184	166	159	119	163	160	135	1376
152	82	113	111	106	105	126	119	115	114	991
153	149	134	144	174	174	142	151	162	124	1354
154	153	138	134	124	143	130	118	120	131	1191
155	161	134	145	92	136	141	133	131	150	1223
156	109	130	141	135	121	137	124	129	114	1140
157	107	146	121	114	135	122	125	133	122	1125
158	155	185	154	146	147	135	160	122	148	1352
159	123	137	166	159	149	176	160	154	152	1376
160	124	132	122	130	128	146	140	131	96	1149
Female, Group 2 - 0.1 mg/kg - Week 13										
251	126	137	149	113	139	129	144	139	110	1186
252	169	177	168	154	190	201	178	181	143	1561
253	104	142	145	138	127	155	168	154	143	1276
254	122	126	117	149	129	134	131	142	101	1151
255	77	102	124	113	124	122	117	20	26	825
256	92	109	123	123	115	139	122	99	115	1037
257	130	148	167	130	166	133	132	131	145	1282
258	104	140	100	103	109	124	95	130	155	1060
259	109	126	123	139	159	161	142	121	138	1218
260	146	159	160	158	148	154	143	155	139	1362
Female, Group 3 - 0.5 mg/kg - Week 13										
351	126	149	147	149	134	141	140	146	132	1264
352	123	136	148	138	138	156	123	138	109	1209
353	62	110	137	149	136	161	167	145	159	1226
354	162	182	204	160	146	158	75	104	16	1207
355	…	…	…	…	…	…	…	…	…	…
356	139	140	166	147	152	135	146	106	65	1196
357	171	141	155	148	159	142	137	153	158	1364
358	105	156	131	178	148	156	145	149	150	1318
359	127	151	139	150	152	154	141	145	144	1303
360	90	134	116	120	119	132	130	128	127	1096
Female, Group 4 - 5 mg/kg - Week 13										
451	68	82	60	128	64	76	74	43	74	669
452	89	136	140	160	150	138	153	148	149	1263
453	99	110	124	116	118	151	123	122	33	996
454	101	153	147	144	129	139	157	140	109	1219
455	143	146	153	158	160	156	154	160	156	1386
456	…	…	…	…	…	…	…	…	…	…
457	95	140	149	158	137	107	129	130	147	1192
458	117	125	133	148	155	136	141	154	138	1247
459	175	117	178	160	152	167	157	162	181	1449
460	102	112	109	157	130	145	108	153	192	1208

Appendix K
Individual Animal Clinical Pathology Data

INDIVIDUAL ANIMAL CLINICAL PATHOLOGY DATA

EXPLANATORY NOTES

ABBREVIATIONS:

General:

Adeq	-	adequate
CLOT or Clot	-	sample clotted
Decr	-	decreased
OK	-	sample condition OK for testing
UTD	-	unable to determine
-	-	not observed
.	-	not taken, not performed, not observed, or results not valid

Individual Hematology Values:

WB	-	whole blood condition
RBC	-	red blood cell count
HGB	-	hemoglobin
HCT	-	hematocrit
MCV	-	mean corpuscular (cell) volume
MCH	-	mean corpuscular (cell) hemoglobin
MCHC	-	mean corpuscular (cell) hemoglobin concentration
RDW	-	red cell distribution width
ARET	-	absolute reticulocyte count
PLT	-	platelet count
WBC	-	white blood cell count
ANEU	-	absolute neutrophil
ALYM	-	absolute lymphocyte
AMON	-	absolute monocyte
AEOS	-	absolute eosinophil
ABAS	-	absolute basophil
ALUC	-	absolute large unstained cell
ABAN	-	absolute neutrophil band
AATL	-	absoulute atypical lymphocyte
AIL	-	absolute immature lymphocyte

Individual Red Blood Cell / White Blood Cell / Platelet Morphology Values:

ANIS	-	anisocytosis
MIC	-	microcytes
MAC	-	macrocytes
POLY	-	polychromasia
HYPO	-	hypochromasia
ECHI	-	echinocytes
ACAN	-	acanthocytes
TARG	-	target cells
RX	-	rouleaux
HJB	-	Howell-Jolly body
SM	-	smudge white blood cells
TOX	-	toxic granulation
DB	-	Döhle bodies
VC	-	vacuolated cytoplasm
BC	-	basophilic cytoplasm
PCE	-	platelet clumps / estimate
GP	-	giant platelets
BP	-	bizarre platelets

INDIVIDUAL ANIMAL CLINICAL PATHOLOGY DATA

EXPLANATORY NOTES (Continued)

ABBREVIATIONS: (Continued)

Individual Clinical Chemistry Values:

HEM	-	hemolysis
LIP	-	lipemia
ICT	-	icterus
AST	-	aspartate aminotransferase
ALT	-	alanine aminotransferase
SDH	-	sorbitol dehydrogenase
ALKP	-	alkaline phosphatase
BILI	-	total bilirubin
BUN	-	urea nitrogen
CREA	-	creatinine
CHOL	-	cholesterol
TRIG	-	triglycerides
GLUC	-	glucose
TP	-	total protein
ALB	-	albumin
GLOB	-	globulin
AG	-	albumin/globulin ratio
CALC	-	calcium
IPHS	-	inorganic phosphorous
NA	-	sodium
K	-	potassium
CL	-	chloride
TBA	-	total bile acids

NOTES:

When individual animal data are not reported, it may be due to one of the following reasons or other reasons, all of which are explained in the study records:
the sample was clotted (CLOT)
there was insufficient sample for testing (QNS)
a valid result could not be obtained (RNV)
the sample was not suitable for testing
the animal died prior to sample collection
no sample was available for testing (NSR)

Only positive findings were recorded for special observations (e.g., additional cell types) or observations marked other.

Individual Animal Clinical Pathology Data

Group Sex	Animal Number	Day Number	WB	RBC x10^6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	ARET x10^3/uL	PLT x10^3/uL
1m	101	96	OK	9.17	15.6	47.9	52.2	17.0	32.5	12.2	220.1	.
	102	96	OK	9.70	15.9	49.6	51.1	16.4	32.0	12.2	272.4	.
	103	96	OK	9.12	14.6	44.1	48.4	16.0	33.2	12.0	248.4	.
	104	96	OK	9.38	15.0	45.0	47.9	16.0	33.4	12.6	271.0	1060
	105	96	OK	10.09	15.4	47.9	47.5	15.3	32.1	12.9	247.5	793
	106	96	OK	9.01	14.7	45.0	50.0	16.3	32.6	12.4	284.9	1037
	107	96	OK	9.41	15.5	47.9	50.9	16.5	32.4	13.5	265.7	1115
	108	96	OK	9.12	14.1	45.2	49.5	15.5	31.2	13.2	245.2	985
	109	96	OK	9.12	14.4	44.9	49.2	15.8	32.1	13.0	292.2	.
	110	96	OK	10.01	15.4	48.0	47.9	15.4	32.2	11.8	276.3	.
2m	201	96	OK	8.68	13.0	42.2	48.6	15.0	30.8	15.3	195.3	.
	202	96	OK	9.18	14.4	44.2	48.1	15.7	32.7	11.7	252.6	.
	203	96	OK	8.86	14.0	43.1	48.6	15.8	32.5	12.6	267.3	1212
	204	96	OK	9.54	15.0	45.6	47.8	15.7	32.9	12.2	253.7	.
	205	96	OK	8.90	13.9	43.6	49.0	15.6	31.7	12.9	260.8	.
	206	96	OK	9.45	15.3	48.5	51.3	16.2	31.6	12.0	191.5	1138
	207	96	OK	9.85	14.3	45.6	46.3	14.5	31.3	12.6	238.0	1003
	208	96	OK	9.48	15.2	46.4	49.0	16.0	32.7	12.1	222.1	1171
	209	96	OK	9.96	15.5	48.9	49.1	15.5	31.7	13.1	252.6	1096
	210	96	CLOT	.	.	.	.	.	.	.	.	.
3m	301	96	OK	9.45	14.3	45.6	48.3	15.1	31.3	12.7	297.0	1255
	302	96	OK	9.11	14.5	44.1	48.4	15.9	32.8	12.4	263.1	.
	303	96	OK	9.14	14.5	43.9	48.1	15.8	32.9	12.9	276.9	1191
	304	96	OK	9.63	14.5	45.5	47.3	15.1	31.9	12.2	253.1	1034
	305	96	OK	9.07	13.6	43.8	48.3	15.0	31.1	12.9	248.0	1134
	306	96	OK	8.82	14.0	44.5	50.5	15.9	31.4	13.5	227.6	.
	307	96	OK	10.30	15.2	48.3	46.9	14.7	31.4	12.6	259.3	1321
	308	96	OK	9.58	14.9	46.5	48.5	15.6	32.2	12.5	309.1	1417
	309	96	OK	9.66	15.3	47.9	49.6	15.8	32.0	12.6	270.9	1490
	310	96	OK	9.84	15.5	47.8	48.6	15.7	32.4	13.7	227.1	.
4m	401	96	OK	9.27	15.0	47.3	51.0	16.2	31.7	13.0	289.3	1337
	402	96	OK	8.29	14.0	43.7	52.7	16.8	31.9	13.2	302.3	.
	403	96	CLOT	.	.	.	.	.	.	.	.	.
	404	96	OK	8.97	14.3	46.1	51.5	16.0	31.1	12.5	255.9	1218
	405	96	OK	9.53	14.9	46.7	49.0	15.7	32.0	12.3	256.1	.
	406	96	OK	9.29	15.3	48.2	52.0	16.5	31.8	12.0	298.5	.
	407	96	OK	9.77	15.4	48.7	49.9	15.8	31.6	13.1	263.8	897
	408	96	OK	8.72	14.5	46.1	52.8	16.6	31.5	12.8	269.3	1236
	409	96	OK	8.52	13.2	43.3	50.8	15.5	30.6	14.4	327.8	1641
	410	96	OK	9.51	13.7	43.4	45.7	14.4	31.5	12.9	293.4	1213

Individual Animal Clinical Pathology Data

Group Sex	Animal Number	Day Number	WBC x10^3/uL	ANEU x10^3/uL	ALYM x10^3/uL	AMON x10^3/uL	AEOS x10^3/uL	ABAS x10^3/uL	ALUC x10^3/uL	ABAN x10^3/uL	AATL x10^3/uL	AIL x10^3/uL
1m	101	96	5.26	1.26	3.84	0.05	0.11	0.00	0.00	.	.	.
	102	96	9.41	2.89	5.95	0.23	0.27	0.01	0.05	.	.	.
	103	96	10.12	1.92	7.50	0.40	0.30	0.00	0.00	.	.	.
	104	96	2.86	0.43	1.94	0.09	0.34	0.00	0.00	0.06	.	.
	105	96	4.00	1.76	2.00	0.24	0.00	0.00	0.00	.	.	.
	106	96	2.60	0.69	1.76	0.03	0.10	0.00	0.02	.	.	.
	107	96	3.01	0.68	2.24	0.02	0.05	0.00	0.02	.	.	.
	108	96	2.46	0.74	1.45	0.15	0.12	0.00	0.00	.	.	.
	109	96	2.24	0.45	1.41	0.11	0.27	0.00	0.00	.	.	.
	110	96	2.37	0.49	1.75	0.02	0.08	0.00	0.02	.	.	.
2m	201	96	4.53	1.43	2.84	0.06	0.16	0.01	0.03	.	.	.
	202	96	5.28	1.06	3.64	0.16	0.42	0.00	0.00	.	.	.
	203	96	2.97	0.68	2.12	0.10	0.06	0.00	0.00	.	.	.
	204	96	3.19	0.83	2.27	0.06	0.03	0.00	0.00	.	.	.
	205	96	2.82	0.49	2.21	0.04	0.06	0.00	0.02	.	.	.
	206	96	3.30	1.02	2.16	0.03	0.07	0.01	0.01	.	.	.
	207	96	1.76	0.32	1.25	0.05	0.14	0.00	0.00	.	.	.
	208	96	4.20	0.64	3.34	0.06	0.13	0.01	0.02	.	.	.
	209	96	3.98	0.84	2.96	0.07	0.10	0.00	0.01	.	.	.
	210	96	.	.	.	.	.	.	.	.	.	.
3m	301	96	3.09	0.99	1.98	0.06	0.06	0.00	0.00	.	.	.
	302	96	3.98	0.48	3.18	0.20	0.12	0.00	0.00	.	.	.
	303	96	2.11	0.47	1.49	0.06	0.08	0.00	0.01	.	.	.
	304	96	3.94	1.22	2.56	0.04	0.12	0.00	0.00	.	.	.
	305	96	4.19	0.62	3.31	0.09	0.16	0.01	0.01	.	.	.
	306	96	1.35	0.36	0.98	0.00	0.01	0.00	0.00	.	.	.
	307	96	0.75	0.15	0.46	0.09	0.03	0.00	0.00	.	.	0.02
	308	96	3.80	0.96	2.70	0.04	0.09	0.00	0.01	.	.	.
	309	96	6.19	1.81	4.20	0.07	0.09	0.00	0.03	.	.	.
	310	96	2.56	0.42	2.00	0.04	0.10	0.01	0.00	.	.	.
4m	401	96	5.66	1.98	3.12	0.28	0.28	0.00	0.00	.	.	.
	402	96	3.95	1.08	2.58	0.20	0.07	0.01	0.02	.	.	.
	403	96	.	.	.	.	.	.	.	.	.	.
	404	96	2.88	0.63	2.10	0.03	0.09	0.00	0.00	0.03	.	.
	405	96	2.39	0.47	1.74	0.10	0.06	0.00	0.02	.	.	.
	406	96	1.70	0.49	1.09	0.07	0.03	0.00	0.00	0.02	.	.
	407	96	1.46	0.29	1.10	0.06	0.00	0.00	0.00	0.01	.	.
	408	96	6.34	1.45	4.56	0.13	0.09	0.01	0.09	.	.	.
	409	96	8.85	3.19	5.14	0.32	0.06	0.01	0.13	.	.	.
	410	96	5.26	2.05	2.93	0.15	0.06	0.00	0.06	.	.	.

Individual Animal Clinical Pathology Data

Group Sex	Animal Number	Day Number	WB	RBC x10^6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	ARET x10^3/uL	PLT x10^3/uL
1f	151	97	OK	9.26	15.0	45.8	49.4	16.2	32.9	12.3	149.2	.
	152	97	OK	8.41	13.4	41.9	49.8	16.0	32.1	14.2	357.3	.
	153	97	OK	9.30	15.2	48.7	52.4	16.4	31.3	14.6	288.7	1026
	154	97	OK	8.58	13.8	41.9	48.8	16.0	32.9	12.7	296.1	925
	155	97	OK	8.89	15.0	44.3	49.8	16.9	33.9	12.6	222.0	997
	156	97	OK	9.09	14.5	44.5	48.9	15.9	32.5	12.8	220.7	.
	157	97	OK	8.98	14.1	44.6	49.7	15.7	31.5	13.4	331.7	.
	158	97	OK	10.36	16.2	48.6	46.9	15.6	33.3	13.0	258.0	.
	159	97	OK	9.62	15.0	47.2	49.1	15.6	31.8	13.6	401.6	1193
	160	97	OK	9.67	15.0	46.9	48.5	15.5	32.1	12.3	273.4	1108
2f	251	97	OK	9.78	15.2	46.9	47.9	15.5	32.4	12.6	196.7	.
	252	97	OK	9.16	15.3	45.1	49.2	16.7	33.9	13.2	174.0	1097
	253	97	OK	8.84	14.7	45.2	51.2	16.6	32.4	12.9	329.4	1026
	254	97	OK	8.88	15.1	44.9	50.6	17.0	33.7	13.4	297.9	974
	255	97	OK	8.54	14.4	44.9	52.6	16.9	32.1	13.9	327.1	.
	256	97	OK	9.83	15.8	49.3	50.1	16.1	32.1	12.4	196.1	1190
	257	97	OK	10.04	16.3	51.2	51.0	16.3	31.9	12.7	203.0	.
	258	97	OK	9.54	16.4	48.3	50.6	17.2	33.9	12.4	226.0	.
	259	97	OK	9.50	15.2	48.0	50.5	16.0	31.7	13.4	281.9	.
	260	97	OK	9.80	15.8	47.2	48.2	16.2	33.5	12.2	252.0	.
3f	351	97	OK	9.03	15.1	45.8	50.8	16.7	33.0	12.8	249.6	.
	352	97	OK	8.09	13.7	43.0	53.2	17.0	32.0	12.1	192.4	1189
	353	97	OK	8.51	14.3	45.3	53.2	16.8	31.6	12.5	160.5	953
	354	97	OK	9.49	15.3	48.0	50.6	16.2	31.9	13.2	274.4	995
	356	97	OK	8.96	14.5	44.6	49.8	16.2	32.5	12.5	235.0	.
	357	97	OK	9.39	15.2	47.1	50.2	16.2	32.3	13.3	260.2	.
	358	97	OK	9.90	15.3	48.3	48.8	15.5	31.7	13.4	184.9	.
	359	97	OK	10.11	16.3	51.3	50.7	16.1	31.7	12.6	310.8	.
	360	97	OK	9.31	15.3	45.7	49.1	16.5	33.5	12.3	236.9	1211
4f	451	97	OK	8.69	13.1	41.1	47.3	15.1	31.9	13.7	266.8	.
	452	97	OK	9.38	16.0	48.2	51.4	17.0	33.1	12.4	226.7	588
	453	97	OK	10.20	16.0	48.6	47.6	15.7	33.0	12.3	235.1	933
	454	97	OK	8.87	14.5	45.6	51.4	16.3	31.8	12.4	238.7	1028
	455	97	OK	9.10	14.9	46.2	50.8	16.4	32.3	12.9	312.2	.
	457	97	OK	9.04	14.3	47.6	52.7	15.8	30.1	13.3	131.1	.
	458	97	OK	10.18	15.3	47.8	47.0	15.1	32.1	11.9	234.9	1224
	459	97	OK	10.04	14.8	47.9	47.7	14.7	30.9	12.8	260.9	.
	460	97	OK	10.06	15.4	47.7	47.4	15.3	32.2	11.7	265.3	1045

Individual Animal Clinical Pathology Data

Group Sex	Animal Number	Day Number	WBC x10^3/uL	ANEU x10^3/uL	ALYM x10^3/uL	AMON x10^3/uL	AEOS x10^3/uL	ABAS x10^3/uL	ALUC x10^3/uL	ABAN x10^3/uL	AATL x10^3/uL	AIL x10^3/uL
1f	151	97	3.96	0.48	2.96	0.36	0.16	0.00	0.00	.	.	.
	152	97	1.45	0.41	0.97	0.02	0.05	0.01	0.00	.	.	.
	153	97	2.50	0.45	1.85	0.08	0.12	0.00	0.00	.	.	.
	154	97	1.82	0.33	1.29	0.09	0.09	0.00	0.00	0.02	.	.
	155	97	1.25	0.37	0.82	0.01	0.05	0.00	0.00	.	.	.
	156	97	2.41	0.56	1.76	0.03	0.06	0.00	0.01	.	.	.
	157	97	2.62	0.66	1.86	0.02	0.06	0.00	0.02	.	.	.
	158	97	1.68	0.29	1.29	0.05	0.03	0.00	0.00	0.02	.	.
	159	97	7.69	0.69	6.62	0.09	0.21	0.02	0.07	.	.	.
	160	97	2.22	0.55	1.51	0.09	0.06	0.00	0.01	.	.	.
2f	251	97	2.97	0.89	2.02	0.00	0.06	0.00	0.00	.	.	.
	252	97	3.98	0.96	2.92	0.03	0.06	0.00	0.02	.	.	.
	253	97	1.34	0.20	1.07	0.01	0.05	0.00	0.00	.	.	.
	254	97	2.57	0.77	1.68	0.02	0.09	0.00	0.01	.	.	.
	255	97	2.06	0.21	1.71	0.06	0.06	0.00	0.00	.	.	0.02
	256	97	1.73	0.38	1.26	0.02	0.06	0.00	0.01	.	.	.
	257	97	1.12	0.10	0.99	0.00	0.03	0.00	0.00	.	.	.
	258	97	2.20	0.66	1.45	0.02	0.07	0.00	0.00	.	.	.
	259	97	1.58	0.27	1.20	0.00	0.08	0.00	0.00	0.03	.	.
	260	97	4.84	0.75	3.96	0.03	0.07	0.01	0.02	.	.	.
3f	351	97	4.84	1.10	3.56	0.05	0.10	0.00	0.02	.	.	.
	352	97	2.17	0.20	1.74	0.04	0.13	0.00	0.00	0.02	.	0.04
	353	97	2.07	0.38	1.57	0.04	0.07	0.00	0.01	.	.	.
	354	97	2.16	0.24	1.73	0.06	0.11	0.00	0.00	.	.	0.02
	356	97	0.60	0.11	0.45	0.02	0.02	0.00	0.00	.	.	.
	357	97	1.22	0.28	0.83	0.06	0.05	0.00	0.00	.	.	.
	358	97	4.60	0.46	3.86	0.09	0.14	0.00	0.00	.	0.05	.
	359	97	2.97	0.27	2.61	0.06	0.03	0.00	0.00	.	.	.
	360	97	2.37	0.65	1.60	0.03	0.08	0.00	0.01	.	.	.
4f	451	97	1.37	0.37	0.86	0.05	0.05	0.00	0.00	0.01	.	0.03
	452	97	4.09	1.26	2.47	0.22	0.06	0.01	0.07	.	.	.
	453	97	2.31	0.51	1.45	0.14	0.21	0.00	0.00	.	.	.
	454	97	1.77	0.39	1.33	0.01	0.02	0.00	0.00	.	.	.
	455	97	1.97	0.28	1.53	0.08	0.04	0.00	0.00	.	.	0.04
	457	97	3.80	0.57	3.03	0.08	0.08	0.00	0.00	.	.	0.04
	458	97	1.79	0.30	1.43	0.04	0.02	0.00	0.00	.	.	.
	459	97	1.40	0.38	0.92	0.03	0.06	0.00	0.00	0.01	.	.
	460	97	1.96	0.27	1.65	0.01	0.02	0.00	0.01	.	.	.

Individual Animal Clinical Pathology Data

Group Sex	Animal Number	Day Number	ANIS	MIC	MAC	POLY	HYPO	ECHI	ACAN	TARG	RX
1m	101	96	-	-	-	-	-	-	-	-	-
	102	96	-	-	-	-	-	-	-	-	-
	103	96	-	-	-	-	-	-	-	-	-
	104	96	-	-	-	-	-	-	-	-	-
	105	96	-	-	-	-	-	-	-	-	-
	106	96	-	-	-	-	-	-	-	-	-
	107	96	-	-	-	-	-	-	-	-	-
	108	96	-	-	-	-	-	-	-	-	-
	109	96	-	-	-	-	-	-	-	-	-
	110	96	-	-	-	-	-	-	-	-	-
2m	201	96	-	-	-	-	-	-	-	-	-
	202	96	-	-	-	-	-	-	-	-	-
	203	96	-	-	-	-	-	-	-	-	-
	204	96	-	-	-	-	-	-	-	-	-
	205	96	-	-	-	-	-	-	-	-	-
	206	96	-	-	-	-	-	-	-	-	-
	207	96	-	-	-	-	-	-	-	-	-
	208	96	-	-	-	-	-	-	-	-	-
	209	96	Trace	Trace	-	-	-	-	-	-	-
	210	96	CLOT	.	.	.	.	.	.	.	.
3m	301	96	-	-	-	-	-	-	-	-	-
	302	96	-	-	-	-	-	-	-	-	-
	303	96	-	-	-	-	-	-	-	-	-
	304	96	-	-	-	-	-	-	-	-	-
	305	96	-	-	-	-	-	-	-	-	-
	306	96	-	-	-	-	-	-	-	-	-
	307	96	-	-	-	-	-	-	-	-	-
	308	96	-	-	-	-	-	-	-	-	-
	309	96	-	-	-	-	-	-	-	-	-
	310	96	-	-	-	-	-	-	-	-	-
4m	401	96	-	-	-	-	-	-	-	-	-
	402	96	-	-	-	-	-	-	-	-	-
	403	96	CLOT	.	.	.	.	.	.	.	.
	404	96	-	-	-	-	-	-	-	-	-
	405	96	-	-	-	-	-	-	-	-	-
	406	96	-	-	-	-	-	-	-	-	-
	407	96	-	-	-	-	-	-	-	-	-
	408	96	-	-	-	-	-	-	-	-	-
	409	96	-	-	-	-	-	-	-	-	-
	410	96	-	-	-	-	-	-	-	-	-

Individual Animal Clinical Pathology Data

Group Sex	Animal Number	Day Number	HJB	SM	TOX	DB	VC	BC	PCE	GP	BP
1m	101	96	-	-	-	-	-	-	Adeq	-	-
	102	96	-	-	-	-	-	-	Adeq	-	-
	103	96	-	-	-	-	-	-	UTD	-	-
	104	96	Trace	-	-	-	-	-	-	Trace	-
	105	96	-	-	-	-	-	-	-	-	-
	106	96	-	-	-	-	-	-	-	-	-
	107	96	-	-	-	-	-	-	-	-	-
	108	96	-	-	-	-	-	-	-	-	-
	109	96	Trace	-	-	-	-	-	Decr	-	-
	110	96	-	-	-	-	-	-	Adeq	-	-
2m	201	96	-	-	-	-	-	-	Adeq	-	-
	202	96	-	-	-	-	-	-	Adeq	-	-
	203	96	-	-	-	-	-	-	-	-	-
	204	96	-	-	-	-	-	-	Adeq	-	-
	205	96	-	-	-	-	-	-	Adeq	-	-
	206	96	-	-	-	-	-	-	-	-	-
	207	96	-	-	-	-	-	-	-	-	-
	208	96	-	-	-	-	-	-	-	-	-
	209	96	-	-	-	-	-	-	-	-	-
	210	96	.	.	.	.	.	.	.	.	.
3m	301	96	-	-	-	-	-	-	-	-	-
	302	96	-	-	-	-	-	-	Adeq	-	-
	303	96	-	-	-	-	-	-	-	-	-
	304	96	-	-	-	-	-	-	-	-	-
	305	96	Trace	-	-	-	-	-	-	-	-
	306	96	-	-	-	-	-	-	Adeq	-	-
	307	96	-	-	-	-	-	-	-	-	-
	308	96	Trace	-	-	-	-	-	-	-	-
	309	96	-	-	-	-	-	-	-	-	-
	310	96	-	-	-	-	-	-	Adeq	-	-
4m	401	96	-	-	-	-	-	-	-	-	-
	402	96	-	-	-	-	-	-	Adeq	-	-
	403	96	.	.	.	.	.	.	.	.	.
	404	96	-	-	-	-	-	-	-	-	-
	405	96	-	-	-	-	-	-	Adeq	-	-
	406	96	-	-	-	-	-	-	Adeq	-	-
	407	96	Trace	-	-	-	-	-	-	-	-
	408	96	Trace	-	-	-	-	-	-	-	-
	409	96	-	-	-	-	-	-	-	Trace	-
	410	96	-	-	-	-	-	-	-	-	-

Individual Animal Clinical Pathology Data

Group Sex	Animal Number	Day Number	ANIS	MIC	MAC	POLY	HYPO	ECHI	ACAN	TARG	RX
1f	151	97	-	-	-	-	-	-	-	-	-
	152	97	-	-	-	-	-	-	-	-	-
	153	97	-	-	-	-	-	-	-	-	-
	154	97	-	-	-	-	-	-	-	-	-
	155	97	-	-	-	-	-	-	-	-	-
	156	97	-	-	-	-	-	Few	-	-	-
	157	97	-	-	-	-	-	-	-	-	-
	158	97	Trace	Trace	-	-	-	-	-	-	-
	159	97	-	-	-	-	-	-	-	-	-
	160	97	-	-	-	-	-	-	-	-	-
2f	251	97	Trace	Trace	-	-	-	-	-	-	-
	252	97	-	-	-	-	-	-	-	-	-
	253	97	-	-	-	-	-	-	-	-	-
	254	97	Trace	Trace	-	-	-	-	-	-	-
	255	97	-	-	-	-	-	-	-	-	-
	256	97	-	-	-	-	-	-	-	-	-
	257	97	Trace	Trace	-	-	-	-	-	-	-
	258	97	-	-	-	-	-	-	-	-	-
	259	97	-	-	-	-	-	-	-	-	-
	260	97	-	-	-	-	-	-	-	-	-
3f	351	97	-	-	-	-	-	-	-	-	-
	352	97	-	-	-	-	-	-	-	-	-
	353	97	-	-	-	-	-	-	-	-	-
	354	97	-	-	-	-	-	-	-	-	-
	356	97	-	-	-	-	-	-	-	-	-
	357	97	-	-	-	-	-	-	-	-	-
	358	97	-	-	-	-	-	-	-	-	-
	359	97	-	-	-	-	-	-	-	-	-
	360	97	-	-	-	-	-	-	-	-	-
4f	451	97	-	-	-	-	-	-	-	-	-
	452	97	-	-	-	-	-	-	-	-	-
	453	97	-	-	-	-	-	-	-	-	-
	454	97	-	-	-	-	-	-	-	-	-
	455	97	Trace	Trace	-	-	-	-	-	-	-
	457	97	-	-	-	-	-	-	-	-	-
	458	97	-	-	-	-	-	-	-	-	-
	459	97	Trace	Trace	-	-	-	-	-	-	-
	460	97	-	-	-	-	-	-	-	-	-

Individual Animal Clinical Pathology Data

Group Sex	Animal Number	Day Number	HJB	SM	TOX	DB	VC	BC	PCE	GP	BP
1f	151	97	-	-	-	-	-	-	Adeq	-	-
	152	97	-	-	-	-	-	-	Adeq	-	-
	153	97	-	-	-	-	-	-	-	-	-
	154	97	-	-	-	-	-	-	-	-	-
	155	97	-	-	-	-	-	-	-	-	-
	156	97	-	-	-	-	-	-	Adeq	-	-
	157	97	-	-	-	-	-	-	Adeq	-	-
	158	97	-	-	-	-	-	-	Adeq	-	-
	159	97	-	-	-	-	-	-	-	-	-
	160	97	-	-	-	-	-	-	-	-	-
2f	251	97	-	-	-	-	-	-	UTD	-	-
	252	97	-	-	-	-	-	-	-	-	-
	253	97	-	-	-	-	-	-	-	-	-
	254	97	Trace	-	-	-	-	-	-	-	-
	255	97	Trace	-	-	-	-	-	Adeq	-	-
	256	97	-	-	-	-	-	-	-	-	-
	257	97	-	-	-	-	-	-	Adeq	-	-
	258	97	-	-	-	-	-	-	Adeq	-	-
	259	97	-	-	-	-	-	-	Adeq	-	-
	260	97	-	-	-	-	-	-	Adeq	-	-
3f	351	97	-	-	-	-	-	-	Adeq	-	-
	352	97	-	-	-	-	-	-	-	-	-
	353	97	-	-	-	-	-	-	-	-	-
	354	97	-	-	-	-	-	-	-	-	-
	356	97	Trace	-	-	-	-	-	Adeq	-	-
	357	97	-	-	-	-	-	-	Adeq	-	-
	358	97	-	-	-	-	-	-	UTD	-	-
	359	97	-	-	-	-	-	-	Adeq	-	-
	360	97	-	-	-	-	-	-	-	-	-
4f	451	97	-	-	-	-	-	-	Adeq	-	-
	452	97	Trace	-	-	-	-	-	-	-	-
	453	97	-	-	-	-	-	-	-	-	-
	454	97	-	-	-	-	-	-	-	-	-
	455	97	-	-	-	-	-	-	Adeq	-	-
	457	97	-	-	-	-	-	-	Adeq	-	-
	458	97	-	-	-	-	-	-	-	-	-
	459	97	Trace	-	-	-	-	-	Adeq	-	-
	460	97	-	-	-	-	-	-	-	-	-

Individual Animal Clinical Pathology Data

Group Sex	Animal Number	Day Number	HEM	LIP	ICT	AST U/L	ALT U/L	SDH U/L
1m	101	96	Trace	None	None	81	65	26.1
	102	96	None	None	None	73	76	29.5
	103	96	None	None	None	60	47	28.0
	104	96	None	None	None	54	32	26.0
	105	96	None	None	None	61	42	25.3
	106	96	None	None	None	47	40	30.2
	107	96	None	None	None	70	57	25.0
	108	96	None	None	None	60	41	25.0
	109	96	None	None	None	68	62	28.5
	110	96	None	None	None	47	25	21.9
2m	201	96	None	None	None	59	50	29.9
	202	96	None	None	None	88	106	24.0
	203	96	None	None	None	71	63	24.5
	204	96	None	None	None	67	48	25.9
	205	96	None	None	None	71	79	28.3
	206	96	None	None	None	45	52	28.6
	207	96	None	None	None	42	35	22.4
	208	96	None	None	None	39	40	26.5
	209	96	None	None	None	96	79	26.5
	210	96	None	None	None	96	72	23.5
3m	301	96	None	None	None	88	64	25.1
	302	96	None	None	None	70	44	23.9
	303	96	None	None	None	69	44	23.4
	304	96	None	None	None	116	63	28.4
	305	96	None	None	None	51	61	39.9
	306	96	None	None	None	70	41	25.2
	307	96	None	None	None	93	34	21.6
	308	96	None	None	None	116	58	26.6
	309	96	None	None	None	73	200	22.7
	310	96	None	None	None	91	51	21.6
4m	401	96	None	None	None	151	264	69.7
	402	96	None	None	None	325	382	180.0
	403	96	None	None	None	101	199	77.9
	404	96	None	None	None	64	167	108.0
	405	96	None	None	None	154	415	196.0
	406	96	None	None	None	99	422	109.0
	407	96	None	None	None	167	245	121.0
	408	96	None	None	None	61	117	57.9
	409	96	None	None	None	68	126	62.6
	410	96	None	None	None	86	216	103.0

Individual Animal Clinical Pathology Data

Group Sex	Animal Number	Day Number	ALKP U/L	BILI mg/dL	BUN mg/dL	CREA mg/dL	CHOL mg/dL	TRIG mg/dL
1m	101	96	56	0.24	27	0.15	129	130
	102	96	55	0.17	25	0.14	101	70
	103	96	29	0.18	24	0.09	160	96
	104	96	55	0.20	23	0.11	115	81
	105	96	48	0.15	26	0.10	132	107
	106	96	33	0.14	37	0.14	168	110
	107	96	67	0.19	25	0.08	93	67
	108	96	59	0.15	18	0.11	152	82
	109	96	51	0.15	47	0.15	123	148
	110	96	44	0.14	25	0.09	154	96
2m	201	96	58	0.18	25	0.14	103	116
	202	96	41	0.13	39	0.15	101	74
	203	96	31	0.15	30	0.10	128	147
	204	96	55	0.14	23	0.12	151	199
	205	96	53	0.16	25	0.12	136	108
	206	96	45	0.15	28	0.13	110	110
	207	96	41	0.14	26	0.12	126	86
	208	96	36	0.18	19	0.08	100	92
	209	96	98	0.15	26	0.13	163	68
	210	96	90	0.18	34	0.12	131	110
3m	301	96	74	0.16	24	0.17	190	104
	302	96	45	0.14	35	0.12	125	132
	303	96	68	0.12	27	0.12	120	93
	304	96	61	0.14	24	0.11	98	78
	305	96	118	0.10	35	0.12	133	87
	306	96	72	0.10	27	0.10	143	111
	307	96	125	0.13	28	0.10	152	77
	308	96	34	0.14	39	0.12	108	156
	309	96	56	0.12	28	0.12	122	112
	310	96	50	0.14	29	0.09	148	62
4m	401	96	590	0.18	27	0.16	96	86
	402	96	1535	0.30	35	0.15	152	79
	403	96	393	0.15	33	0.14	68	65
	404	96	380	0.14	30	0.11	85	110
	405	96	590	0.24	24	0.10	89	72
	406	96	381	0.11	24	0.10	59	106
	407	96	701	0.17	27	0.10	103	116
	408	96	510	0.16	39	0.14	70	99
	409	96	525	0.10	22	0.13	117	263
	410	96	568	0.12	24	0.08	138	84

Individual Animal Clinical Pathology Data

Group Sex	Animal Number	Day Number	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	CALC mg/dL	IPHS mg/dL	NA mmol/L	K mmol/L	CL mmol/L	A/G	TBA umol/L
1m	101	96	142	5.1	2.9	2.2	.	.	146.1	6.42	107.8	1.3	1.9
	102	96	155	4.9	2.7	2.2	8.4	5.8	145.7	5.32	110.9	1.2	1.1
	103	96	173	4.8	2.6	2.2	8.3	6.2	145.8	5.24	108.0	1.2	1.3
	104	96	173	5.0	3.0	2.0	8.0	5.3	144.6	4.63	108.3	1.5	1.4
	105	96	173	5.0	2.5	2.5	7.9	5.5	.	.	.	1.0	1.1
	106	96	207	5.0	2.7	2.3	8.0	5.5	144.1	4.74	108.7	1.2	1.1
	107	96	124	4.8	2.8	2.0	8.5	6.7	145.8	5.16	109.0	1.4	1.0
	108	96	235	4.9	2.9	2.0	8.4	6.4	147.7	5.36	114.2	1.5	0.8
	109	96	188	4.6	2.7	1.9	8.0	6.2	144.3	5.12	110.7	1.4	1.2
	110	96	154	5.1	3.0	2.1	8.3	6.1	146.9	4.57	109.2	1.4	0.8
2m	201	96	225	5.4	2.7	2.7	8.4	4.4	145.0	4.80	107.3	1.0	1.6
	202	96	190	4.4	2.4	2.0	8.0	5.5	143.1	5.18	109.7	1.2	0.7
	203	96	170	5.0	2.7	2.3	8.7	6.3	147.1	4.68	109.8	1.2	1.5
	204	96	174	5.2	3.0	2.2	8.0	7.0	144.9	4.94	109.6	1.4	1.0
	205	96	211	4.9	2.8	2.1	8.2	6.7	144.9	4.63	109.3	1.3	1.0
	206	96	170	5.1	3.0	2.1	8.4	5.6	145.0	4.54	109.9	1.4	1.0
	207	96	182	5.1	2.8	2.3	8.1	5.0	144.0	3.84	108.1	1.2	1.6
	208	96	216	4.9	2.8	2.1	8.2	5.8	143.7	5.21	108.5	1.3	1.3
	209	96	195	5.0	2.9	2.1	8.5	7.8	146.0	4.81	109.7	1.4	0.8
	210	96	141	4.9	2.7	2.2	8.6	6.6	144.7	5.77	110.6	1.2	1.2
3m	301	96	201	5.4	3.0	2.4	9.2	6.3	145.3	5.99	108.3	1.3	1.8
	302	96	179	4.5	2.4	2.1	8.1	6.4	148.0	5.01	113.1	1.1	1.9
	303	96	180	5.4	3.0	2.4	8.1	6.2	141.9	4.51	107.6	1.3	1.0
	304	96	192	4.8	2.9	1.9	8.3	6.3	.	.	.	1.5	1.2
	305	96	179	5.1	2.9	2.2	8.3	5.5	145.7	4.62	108.8	1.3	2.4
	306	96	107	4.8	2.8	2.0	8.2	6.8	145.3	4.66	110.7	1.4	1.0
	307	96	131	5.5	3.2	2.3	8.3	6.2	144.9	4.48	110.5	1.4	1.4
	308	96	176	4.7	2.7	2.0	8.3	7.0	144.2	5.33	108.4	1.4	1.6
	309	96	216	5.1	2.8	2.3	8.3	7.3	145.5	5.18	110.8	1.2	1.0
	310	96	139	4.9	2.9	2.0	8.5	7.0	147.8	5.10	110.6	1.5	1.1
4m	401	96	187	5.3	3.1	2.2	8.4	6.0	145.7	4.58	111.1	1.4	13.5
	402	96	110	5.7	3.4	2.3	9.1	7.1	145.5	5.06	110.4	1.5	25.2
	403	96	153	5.1	3.2	1.9	8.4	6.0	143.2	4.17	110.8	1.7	9.2
	404	96	159	5.1	3.2	1.9	8.3	5.5	144.3	3.92	110.9	1.7	8.5
	405	96	146	5.6	3.4	2.2	8.3	5.7	144.8	4.82	109.9	1.5	14.5
	406	96	126	5.3	3.1	2.2	8.2	7.0	143.9	4.91	111.8	1.4	4.1
	407	96	124	5.7	3.4	2.3	8.5	5.7	144.5	4.20	111.6	1.5	7.2
	408	96	164	5.2	3.1	2.1	9.0	5.9	145.8	4.61	112.1	1.5	14.4
	409	96	174	5.7	3.0	2.7	9.0	7.1	146.4	4.24	112.3	1.1	7.8
	410	96	180	5.2	2.8	2.4	8.2	6.9	147.0	4.44	114.4	1.2	7.0

Individual Animal Clinical Pathology Data

Group Sex	Animal Number	Day Number	HEM	LIP	ICT	AST U/L	ALT U/L	SDH U/L
1f	151	97	Trace	None	None	67	25	26.0
	152	97	None	None	None	77	32	20.8
	153	97	None	None	None	91	42	19.5
	154	97	None	None	None	68	31	18.2
	155	97	None	None	None	57	28	22.3
	156	97	None	None	None	48	31	20.3
	157	97	None	None	None	104	63	57.6
	158	97	None	None	None	59	30	23.1
	159	97	None	None	None	45	25	25.9
	160	97	None	None	None	66	49	19.4
2f	251	97	None	None	None	92	41	21.5
	252	97	None	None	None	83	36	26.4
	253	97	Trace	None	None	69	43	22.4
	254	97	None	None	None	57	32	21.1
	255	97	None	None	None	74	30	21.1
	256	97	None	None	None	76	37	22.5
	257	97	None	None	None	54	25	24.4
	258	97	None	None	None	69	34	21.5
	259	97	None	None	None	.	26	.
	260	97	None	None	None	67	52	25.6
3f	351	97	None	None	None	60	29	26.9
	352	97	None	None	None	62	27	27.9
	353	97	None	None	None	99	44	24.1
	354	97	None	None	None	58	30	23.7
	356	97	None	None	None	48	30	23.3
	357	97	None	None	None	67	26	21.5
	358	97	None	None	None	71	39	27.4
	359	97	None	None	None	77	34	21.2
	360	97	None	None	None	76	29	16.6
4f	451	97	None	None	None	59	32	25.4
	452	97	None	None	None	92	89	48.1
	453	97	None	None	None	92	37	24.7
	454	97	None	None	None	66	58	36.7
	455	97	None	None	None	71	42	30.9
	457	97	None	None	None	66	37	35.9
	458	97	None	None	None	71	50	29.8
	459	97	None	None	None	65	76	47.3
	460	97	None	None	None	80	38	23.1

Individual Animal Clinical Pathology Data

Group Sex	Animal Number	Day Number	ALKP U/L	BILI mg/dL	BUN mg/dL	CREA mg/dL	CHOL mg/dL	TRIG mg/dL
1f	151	97	46	0.14	32	0.16	92	193
	152	97	91	0.13	29	0.12	71	50
	153	97	94	.	15	0.10	120	60
	154	97	68	0.14	23	0.09	46	69
	155	97	51	0.11	17	0.08	96	101
	156	97	62	0.14	18	0.10	75	80
	157	97	45	0.14	20	0.09	73	79
	158	97	67	0.13	17	0.10	77	117
	159	97	44	0.15	18	0.08	95	204
	160	97	78	0.15	19	0.12	66	90
2f	251	97	69	0.14	20	0.10	85	70
	252	97	65	0.13	24	0.13	107	167
	253	97	76	0.15	17	0.11	80	62
	254	97	65	0.13	18	0.09	113	101
	255	97	139	0.16	25	0.10	78	100
	256	97	72	0.14	19	0.12	72	110
	257	97	92	0.13	17	0.09	130	73
	258	97	72	0.16	15	0.09	77	75
	259	97	46	.	18	0.10	95	.
	260	97	71	0.13	19	0.09	111	117
3f	351	97	70	0.15	25	0.15	90	74
	352	97	108	0.13	27	0.15	78	132
	353	97	65	0.14	25	0.14	67	133
	354	97	79	0.11	16	0.10	106	55
	356	97	70	0.13	18	0.12	104	82
	357	97	59	0.14	14	0.08	51	70
	358	97	90	0.16	17	0.10	97	152
	359	97	55	0.16	20	0.12	101	81
	360	97	53	0.14	21	0.11	95	57
4f	451	97	98	0.12	28	0.13	94	46
	452	97	123	0.12	27	0.12	64	109
	453	97	136	0.11	13	0.09	90	48
	454	97	135	0.12	24	0.12	135	74
	455	97	181	0.12	23	0.12	68	47
	457	97	151	0.13	14	0.11	69	67
	458	97	208	0.13	13	0.07	71	43
	459	97	189	0.11	22	0.10	98	98
	460	97	197	0.08	22	0.09	140	85

Individual Animal Clinical Pathology Data

Group Sex	Animal Number	Day Number	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	CALC mg/dL	IPHS mg/dL	NA mmol/L	K mmol/L	CL mmol/L	A/G	TBA umol/L
1f	151	97	155	4.8	2.7	2.1	8.9	5.8	149.6	4.67	113.2	1.3	4.7
	152	97	148	4.6	2.8	1.8	8.3	6.4	147.4	4.29	115.3	1.6	5.2
	153	97	.	4.5	2.6	1.9	.	.	.	.	.	1.4	.
	154	97	158	4.3	2.7	1.6	8.7	6.3	147.2	3.78	116.3	1.7	3.7
	155	97	172	4.6	2.7	1.9	8.2	5.1	147.5	4.36	114.9	1.4	3.3
	156	97	192	4.7	2.8	1.9	8.7	6.2	149.1	4.54	114.9	1.5	1.2
	157	97	151	4.7	2.8	1.9	8.7	6.4	147.3	4.99	114.4	1.5	2.9
	158	97	233	4.6	2.6	2.0	8.8	6.8	148.5	3.87	116.0	1.3	10.4
	159	97	180	4.9	2.8	2.1	9.1	7.2	147.5	4.24	111.3	1.3	6.0
	160	97	210	5.0	3.0	2.0	9.0	7.5	148.0	4.79	114.5	1.5	1.6
2f	251	97	141	4.8	2.7	2.1	8.7	5.6	148.6	4.58	112.4	1.3	1.6
	252	97	149	4.9	2.7	2.2	8.7	7.7	147.5	4.65	112.7	1.2	2.6
	253	97	167	4.8	2.8	2.0	8.8	7.9	147.1	4.44	113.7	1.4	1.8
	254	97	145	5.0	3.0	2.0	8.8	6.9	147.0	4.53	114.1	1.5	1.0
	255	97	205	4.3	2.7	1.6	8.4	6.4	148.1	4.37	116.5	1.7	1.6
	256	97	184	4.8	2.8	2.0	8.6	7.2	149.2	4.71	114.0	1.4	3.6
	257	97	179	4.5	2.6	1.9	8.7	6.3	147.3	4.24	114.2	1.4	4.2
	258	97	154	4.7	2.9	1.8	8.6	6.2	148.5	4.18	114.7	1.6	1.8
	259	97	.	.	2.9	.	.	.	.	.	.	.	.
	260	97	230	4.5	2.4	2.1	8.8	6.9	148.4	4.48	113.3	1.1	2.7
3f	351	97	147	5.0	2.8	2.2	8.7	5.7	148.7	4.43	111.7	1.3	3.3
	352	97	201	4.6	2.8	1.8	8.3	5.9	146.8	4.64	113.9	1.6	1.7
	353	97	190	5.0	2.9	2.1	8.8	7.4	147.8	4.52	115.8	1.4	2.3
	354	97	203	4.8	3.0	1.8	8.9	5.7	146.9	4.52	114.2	1.7	6.4
	356	97	184	4.6	2.7	1.9	8.7	7.1	151.0	4.28	114.4	1.4	2.1
	357	97	137	4.8	2.8	2.0	8.6	7.9	150.9	4.75	113.2	1.4	2.0
	358	97	160	4.9	3.1	1.8	8.8	7.0	147.1	4.72	111.6	1.7	2.7
	359	97	189	4.8	2.8	2.0	9.1	8.9	146.8	5.52	114.4	1.4	2.9
	360	97	128	4.6	3.1	1.5	8.6	7.5	148.3	4.70	115.1	2.1	0.9
4f	451	97	187	4.3	2.6	1.7	8.3	5.6	146.5	4.05	115.6	1.5	2.8
	452	97	149	4.7	2.9	1.8	8.4	5.1	146.2	4.20	111.4	1.6	2.4
	453	97	165	4.9	3.0	1.9	8.8	5.1	146.9	4.01	113.6	1.6	2.9
	454	97	154	4.9	3.3	1.6	9.0	7.0	147.4	4.02	112.5	2.1	4.1
	455	97	167	5.0	3.0	2.0	8.9	6.7	148.7	3.61	115.5	1.5	9.3
	457	97	185	4.8	2.9	1.9	9.0	7.3	147.4	4.18	113.8	1.5	88.7
	458	97	161	4.6	2.9	1.7	8.7	8.5	150.6	4.16	116.7	1.7	1.5
	459	97	180	4.8	2.9	1.9	9.0	8.2	148.5	3.91	116.7	1.5	6.2
	460	97	172	4.5	3.0	1.5	8.6	7.3	146.9	3.68	113.9	2.0	1.1

Appendix L
Individual Animal Final Body and Organ Weights

INDIVIDUAL ANIMAL FINAL BODY AND ORGAN WEIGHTS

KEY TO APPENDIX

COLUMN HEADINGS USED:

Bodywt	-	Body Weight
Adrenal Glands	-	Adrenal Glands Weight
Brain	-	Brain Weight
Epididym	-	Epididymides Weight
Heart	-	Heart Weight
Kidneys	-	Kidneys Weight
Liver	-	Liver Weight
Ovaries	-	Ovaries Weight
Spleen	-	Spleen Weight
Testes	-	Testes Weight
Thymus	-	Thymus Weight
Uterus	-	Uterus Weight
Adren Gl %FBW	-	Adrenal Glands/Body Weight
Brain %FBW	-	Brain/Body Weight
Epididym %FBW	-	Epididymides/Body Weight
Heart %FBW	-	Heart/Body Weight
Kidney %FBW	-	Kidney/Body Weight
Liver %FBW	-	Liver/Body Weight
Ovaries %FBW	-	Ovaries/Body Weight
Spleen %FBW	-	Spleen/Body Weight
Testes %FBW	-	Testes/Body Weight
Thymus %FBW	-	Thymus/Body Weight
Uterus %FBW	-	Uterus/Body Weight
Adren Gl %Brain	-	Adrenal Glands/Brain Weight
Epididym %Brain	-	Epididymides/Brain Weight
Heart %Brain	-	Heart/Brain Weight
Kidney %Brain	-	Kidney/Brain Weight
Liver %Brain	-	Liver/Brain Weight
Ovaries %Brain	-	Ovaries/Brain Weight
Spleen %Brain	-	Spleen/Brain Weight
Testes %Brain	-	Testes/Brain Weight
Thymus %Brain	-	Thymus/Brain Weight
Uterus %Brain	-	Uterus/Brain Weight

CALCULATED MEASUREMENT FORMULAE:

Organ/Body Weight = Organ Weight (g)/Body Weight (g) x 100
Organ/Brain Weight = Organ Weight (g)/Brain Weight (g) x 100

ABBREVIATIONS:

g - gram
WE - weighing error

Individual Animal Final Body and Organ Weights

Group Sex	Animal Number	Bodywt g	Adrenal Glands g	Brain g	Epididym g	Heart g	Kidneys g	Liver g	Spleen g	Testes g	Thymus g
1m	101	36.6	0.007	0.486	0.126	0.191	0.562	1.856	0.092	0.237	0.048
	102	34.8	0.006	0.475	0.123	0.171	0.487	1.776	0.087	0.255	0.024
	103	41.3	0.010	0.482	0.150	0.189	0.721	2.237	0.087	0.233	0.028
	104	34.9	0.009	0.479	0.117	0.187	0.518	1.854	0.093	0.211	0.022
	105	35.0	0.004	0.515	0.105	0.174	0.608	1.763	0.091	0.248	0.017
	106	43.3	0.011	0.581	0.150	0.234	0.713	2.203	0.137	0.221	0.029
	107	40.4	0.010	0.536	0.140	0.203	0.708	2.498	0.097	0.242	0.031
	108	41.9	0.014	0.515	0.118	0.210	0.709	1.845	0.097	0.205	0.040
	109	36.9	0.003	0.489	0.118	0.200	0.630	1.846	0.104	0.259	0.027
	110	41.9	0.004	0.500	0.164	0.185	0.563	1.667	0.165	0.177	0.034
	Mean	38.70	0.0078	0.5058	0.1311	0.1944	0.6219	1.9545	0.1050	0.2288	0.0300
	S.D.	3.37	0.0036	0.0328	0.0188	0.0185	0.0878	0.2649	0.0256	0.0255	0.0090
	N	10	10	10	10	10	10	10	10	10	10
2m	201	38.1	0.014	0.533	0.121	0.167	0.647	2.052	0.108	0.216	0.041
	202	35.7	0.005	0.459	0.121	0.193	0.490	1.883	0.071	0.300	0.033
	203	41.3	0.014	0.529	0.144	0.192	0.657	2.142	0.113	0.242	0.026
	204	40.1	0.009	0.509	0.618	0.171	0.658	1.840	0.086	0.223	0.036
	205	42.8	0.004	0.516	0.102	0.233	0.564	2.310	0.088	0.179	0.023
	206	35.9	0.003	0.478	0.108	0.155	0.516	1.801	0.070	0.237	0.032
	207	44.0	0.004	0.456	0.103	0.226	0.622	2.155	0.115	0.178	0.035
	208	42.5	0.007	0.482	0.131	0.201	0.609	2.057	0.094	0.241	0.034
	209	44.4	0.013	0.507	0.157	0.256	0.674	2.139	0.115	0.280	0.026
	210	38.2	0.005	0.512	0.097	0.227	0.500	1.862	0.071	0.259	0.045
	Mean	40.30	0.0078	0.4981	0.1702	0.2021	0.5937	2.0241	0.0931	0.2355	0.0331
	S.D.	3.20	0.0044	0.0276	0.1585	0.0328	0.0706	0.1692	0.0188	0.0392	0.0068
	N	10	10	10	10	10	10	10	10	10	10

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Animal Final Body and Organ Weights

Group Sex	Animal Number	Bodywt g	Adrenal Glands g	Brain g	Epididym g	Heart g	Kidneys g	Liver g	Spleen g	Testes g	Thymus g
3m	301	36.3	0.008	0.517	0.108	0.188	0.649	1.976	0.061	0.237	0.025
	302	40.6	0.004	0.502	0.114	0.176	0.570	2.193	0.081	0.267	0.013
	303	37.5	0.006	0.559	0.114	0.208	0.642	2.261	0.090	0.209	0.031
	304	37.6	0.009	0.487	0.151	0.197	0.561	2.329	0.085	0.211	0.071
	305	44.6	0.013	0.493	0.149	0.221	0.644	2.489	0.124	0.226	0.040
	306	39.7	0.005	0.518	0.102	0.223	0.624	2.220	0.100	0.209	0.036
	307	36.9	0.009	0.523	0.113	0.175	0.513	1.628	0.066	0.194	0.024
	308	38.8	0.005	0.456	0.122	0.203	0.631	2.284	0.098	0.190	0.030
	309	38.1	0.008	0.467	0.131	0.195	0.678	2.515	0.081	0.204	0.039
	310	39.0	0.012	0.510	0.122	0.198	0.623	1.964	0.080	0.276	0.021
	Mean	38.91	0.0079	0.5032	0.1226	0.1984	0.6135	2.1859	0.0866	0.2223	0.0330
	S.D.	2.38	0.0030	0.0296	0.0165	0.0163	0.0499	0.2670	0.0180	0.0294	0.0158
	N	10	10	10	10	10	10	10	10	10	10
4m	401	44.3	0.013	0.528	0.165	0.233	0.698	4.837	0.120	0.307	0.025
	402	43.7	0.011	0.492	0.114	0.206	0.706	6.673	0.142	0.190	0.044
	403	44.6	0.006	0.481	0.127	0.196	0.628	4.767	0.097	0.208	0.038
	404	45.5	0.007	0.490	0.119	0.219	0.551	3.651	0.108	0.230	0.055
	405	39.4	0.009	0.483	0.096	0.187	0.737	3.940	0.100	0.185	0.045
	406	43.0	0.008	0.512	0.098	0.207	0.711	3.985	0.103	0.230	0.022
	407	46.8	0.017	0.543	0.103	0.274	0.676	4.247	0.099	0.207	0.028
	408	44.1	0.012	WE	0.074	0.180	0.687	9.674	0.246	0.194	0.026
	409	45.3	0.009	0.485	0.151	0.249	0.843	5.189	0.135	0.252	0.034
	410	46.0	0.060	0.462	0.143	0.201	0.682	4.477	0.114	0.253	0.053
	Mean	44.27	0.0152	0.4973	0.1190	0.2152	0.6919	5.1440	0.1264	0.2256	0.0370
	S.D.	2.05	0.0161	0.0255	0.0280	0.0292	0.0744	1.8064	0.0447	0.0375	0.0119
	N	10	10	9	10	10	10	10	10	10	10

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Animal Final Body and Organ Weights

Group Sex	Animal Number	Adren Gl %FBW	Brain %FBW	Epididym %FBW	Heart %FBW	Kidney %FBW	Liver %FBW	Spleen %FBW	Testes %FBW	Thymus %FBW
1m	101	0.0191	1.3279	0.3443	0.5219	1.5355	5.0710	0.2514	0.6475	0.1311
	102	0.0172	1.3649	0.3534	0.4914	1.3994	5.1034	0.2500	0.7328	0.0690
	103	0.0242	1.1671	0.3632	0.4576	1.7458	5.4165	0.2107	0.5642	0.0678
	104	0.0258	1.3725	0.3352	0.5358	1.4842	5.3123	0.2665	0.6046	0.0630
	105	0.0114	1.4714	0.3000	0.4971	1.7371	5.0371	0.2600	0.7086	0.0486
	106	0.0254	1.3418	0.3464	0.5404	1.6467	5.0878	0.3164	0.5104	0.0670
	107	0.0248	1.3267	0.3465	0.5025	1.7525	6.1832	0.2401	0.5990	0.0767
	108	0.0334	1.2291	0.2816	0.5012	1.6921	4.4033	0.2315	0.4893	0.0955
	109	0.0081	1.3252	0.3198	0.5420	1.7073	5.0027	0.2818	0.7019	0.0732
	110	0.0095	1.1933	0.3914	0.4415	1.3437	3.9785	0.3938	0.4224	0.0811
	Mean	0.01989	1.31199	0.33818	0.50314	1.60443	5.05958	0.27022	0.59807	0.07730
	S.D.	0.00828	0.09150	0.03139	0.03394	0.15231	0.58308	0.05204	0.10283	0.02249
	N	10	10	10	10	10	10	10	10	10
2m	201	0.0367	1.3990	0.3176	0.4383	1.6982	5.3858	0.2835	0.5669	0.1076
	202	0.0140	1.2857	0.3389	0.5406	1.3725	5.2745	0.1989	0.8403	0.0924
	203	0.0339	1.2809	0.3487	0.4649	1.5908	5.1864	0.2736	0.5860	0.0630
	204	0.0224	1.2693	1.5411	0.4264	1.6409	4.5885	0.2145	0.5561	0.0898
	205	0.0093	1.2056	0.2383	0.5444	1.3178	5.3972	0.2056	0.4182	0.0537
	206	0.0084	1.3315	0.3008	0.4318	1.4373	5.0167	0.1950	0.6602	0.0891
	207	0.0091	1.0364	0.2341	0.5136	1.4136	4.8977	0.2614	0.4045	0.0795
	208	0.0165	1.1341	0.3082	0.4729	1.4329	4.8400	0.2212	0.5671	0.0800
	209	0.0293	1.1419	0.3536	0.5766	1.5180	4.8176	0.2590	0.6306	0.0586
	210	0.0131	1.3403	0.2539	0.5942	1.3089	4.8743	0.1859	0.6780	0.1178
	Mean	0.01927	1.24247	0.42352	0.50037	1.47309	5.02787	0.22986	0.59079	0.08315
	S.D.	0.01066	0.11143	0.39513	0.06181	0.13430	0.27156	0.03596	0.12610	0.02072
	N	10	10	10	10	10	10	10	10	10

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Animal Final Body and Organ Weights

Group Sex	Animal Number	Adren Gl %FBW	Brain %FBW	Epididym %FBW	Heart %FBW	Kidney %FBW	Liver %FBW	Spleen %FBW	Testes %FBW	Thymus %FBW
3m	301	0.0220	1.4242	0.2975	0.5179	1.7879	5.4435	0.1680	0.6529	0.0689
	302	0.0099	1.2365	0.2808	0.4335	1.4039	5.4015	0.1995	0.6576	0.0320
	303	0.0160	1.4907	0.3040	0.5547	1.7120	6.0293	0.2400	0.5573	0.0827
	304	0.0239	1.2952	0.4016	0.5239	1.4920	6.1941	0.2261	0.5612	0.1888
	305	0.0291	1.1054	0.3341	0.4955	1.4439	5.5807	0.2780	0.5067	0.0897
	306	0.0126	1.3048	0.2569	0.5617	1.5718	5.5919	0.2519	0.5264	0.0907
	307	0.0244	1.4173	0.3062	0.4743	1.3902	4.4119	0.1789	0.5257	0.0650
	308	0.0129	1.1753	0.3144	0.5232	1.6263	5.8866	0.2526	0.4897	0.0773
	309	0.0210	1.2257	0.3438	0.5118	1.7795	6.6010	0.2126	0.5354	0.1024
	310	0.0308	1.3077	0.3128	0.5077	1.5974	5.0359	0.2051	0.7077	0.0538
	Mean	0.02026	1.29828	0.31521	0.51042	1.58049	5.61764	0.22127	0.57206	0.08513
	S.D.	0.00716	0.11954	0.03908	0.03719	0.14767	0.61576	0.03489	0.07395	0.04168
	N	10	10	10	10	10	10	10	10	10
4m	401	0.0293	1.1919	0.3725	0.5260	1.5756	10.9187	0.2709	0.6930	0.0564
	402	0.0252	1.1259	0.2609	0.4714	1.6156	15.2700	0.3249	0.4348	0.1007
	403	0.0135	1.0785	0.2848	0.4395	1.4081	10.6883	0.2175	0.4664	0.0852
	404	0.0154	1.0769	0.2615	0.4813	1.2110	8.0242	0.2374	0.5055	0.1209
	405	0.0228	1.2259	0.2437	0.4746	1.8706	10.0000	0.2538	0.4695	0.1142
	406	0.0186	1.1907	0.2279	0.4814	1.6535	9.2674	0.2395	0.5349	0.0512
	407	0.0363	1.1603	0.2201	0.5855	1.4444	9.0748	0.2115	0.4423	0.0598
	408	0.0272	WE	0.1678	0.4082	1.5578	21.9365	0.5578	0.4399	0.0590
	409	0.0199	1.0706	0.3333	0.5497	1.8609	11.4547	0.2980	0.5563	0.0751
	410	0.1304	1.0043	0.3109	0.4370	1.4826	9.7326	0.2478	0.5500	0.1152
	Mean	0.03386	1.12500	0.26834	0.48546	1.56801	11.63672	0.28591	0.50926	0.08377
	S.D.	0.03460	0.07265	0.05956	0.05432	0.20074	4.11321	0.10167	0.07928	0.02719
	N	10	9	10	10	10	10	10	10	10

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Animal Final Body and Organ Weights

Group Sex	Animal Number	Adren Gl %Brain	Epididym %Brain	Heart %Brain	Kidney %Brain	Liver %Brain	Spleen %Brain	Testes %Brain	Thymus %Brain
1m	101	1.4403	25.9259	39.3004	115.6379	381.8930	18.9300	48.7654	9.8765
	102	1.2632	25.8947	36.0000	102.5263	373.8947	18.3158	53.6842	5.0526
	103	2.0747	31.1203	39.2116	149.5851	464.1079	18.0498	48.3402	5.8091
	104	1.8789	24.4259	39.0397	108.1420	387.0564	19.4154	44.0501	4.5929
	105	0.7767	20.3883	33.7864	118.0583	342.3301	17.6699	48.1553	3.3010
	106	1.8933	25.8176	40.2754	122.7194	379.1738	23.5800	38.0379	4.9914
	107	1.8657	26.1194	37.8731	132.0896	466.0448	18.0970	45.1493	5.7836
	108	2.7184	22.9126	40.7767	137.6699	358.2524	18.8350	39.8058	7.7670
	109	0.6135	24.1309	40.8998	128.8344	377.5051	21.2679	52.9652	5.5215
	110	0.8000	32.8000	37.0000	112.6000	333.4000	33.0000	35.4000	6.8000
	Mean	1.53247	25.95356	38.41631	122.78629	386.36582	20.71608	45.43534	5.94956
	S.D.	0.67453	3.64379	2.27483	14.39510	45.01075	4.67655	6.15351	1.83351
	N	10	10	10	10	10	10	10	10
2m	201	2.6266	22.7017	31.3321	121.3884	384.9906	20.2627	40.5253	7.6923
	202	1.0893	26.3617	42.0479	106.7538	410.2397	15.4684	65.3595	7.1895
	203	2.6465	27.2212	36.2949	124.1966	404.9149	21.3611	45.7467	4.9149
	204	1.7682	121.4145	33.5953	129.2731	361.4931	16.8959	43.8114	7.0727
	205	0.7752	19.7674	45.1550	109.3023	447.6744	17.0543	34.6899	4.4574
	206	0.6276	22.5941	32.4268	107.9498	376.7782	14.6444	49.5816	6.6946
	207	0.8772	22.5877	49.5614	136.4035	472.5877	25.2193	39.0351	7.6754
	208	1.4523	27.1784	41.7012	126.3485	426.7635	19.5021	50.0000	7.0539
	209	2.5641	30.9665	50.4931	132.9389	421.8935	22.6824	55.2268	5.1282
	210	0.9766	18.9453	44.3359	97.6563	363.6719	13.8672	50.5859	8.7891
	Mean	1.54036	33.97385	40.69436	119.22112	407.10075	18.69578	47.45622	6.66680
	S.D.	0.80903	30.94532	6.96340	12.95551	36.40708	3.72287	8.81811	1.39362
	N	10	10	10	10	10	10	10	10

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Animal Final Body and Organ Weights

Group Sex	Animal Number	Adren Gl %Brain	Epididym %Brain	Heart %Brain	Kidney %Brain	Liver %Brain	Spleen %Brain	Testes %Brain	Thymus %Brain
3m	301	1.5474	20.8897	36.3636	125.5319	382.2050	11.7988	45.8414	4.8356
	302	0.7968	22.7092	35.0598	113.5458	436.8526	16.1355	53.1873	2.5896
	303	1.0733	20.3936	37.2093	114.8479	404.4723	16.1002	37.3882	5.5456
	304	1.8480	31.0062	40.4517	115.1951	478.2341	17.4538	43.3265	14.5791
	305	2.6369	30.2231	44.8276	130.6288	504.8682	25.1521	45.8418	8.1136
	306	0.9653	19.6911	43.0502	120.4633	428.5714	19.3050	40.3475	6.9498
	307	1.7208	21.6061	33.4608	98.0880	311.2811	12.6195	37.0937	4.5889
	308	1.0965	26.7544	44.5175	138.3772	500.8772	21.4912	41.6667	6.5789
	309	1.7131	28.0514	41.7559	145.1820	538.5439	17.3448	43.6831	8.3512
	310	2.3529	23.9216	38.8235	122.1569	385.0980	15.6863	54.1176	4.1176
	Mean	1.57510	24.52464	39.55199	122.40169	437.10038	17.30872	44.24938	6.62499
	S.D.	0.60611	4.18611	3.99805	13.47441	69.38489	3.95582	5.80886	3.32758
	N	10	10	10	10	10	10	10	10
4m	401	2.4621	31.2500	44.1288	132.1970	916.0985	22.7273	58.1439	4.7348
	402	2.2358	23.1707	41.8699	143.4959	1356.3008	28.8618	38.6179	8.9431
	403	1.2474	26.4033	40.7484	130.5613	991.0603	20.1663	43.2432	7.9002
	404	1.4286	24.2857	44.6939	112.4490	745.1020	22.0408	46.9388	11.2245
	405	1.8634	19.8758	38.7164	152.5880	815.7350	20.7039	38.3023	9.3168
	406	1.5625	19.1406	40.4297	138.8672	778.3203	20.1172	44.9219	4.2969
	407	3.1308	18.9687	50.4604	124.4936	782.1363	18.2320	38.1215	5.1565
	408	WE	WE	WE	WE	WE	WE	WE	WE
	409	1.8557	31.1340	51.3402	173.8144	1069.8969	27.8351	51.9588	7.0103
	410	12.9870	30.9524	43.5065	147.6190	969.0476	24.6753	54.7619	11.4719
	Mean	3.19703	25.02013	43.98824	139.56504	935.96641	22.81774	46.11224	7.78389
	S.D.	3.71635	5.18300	4.36075	17.75248	193.17855	3.63296	7.45908	2.69500
	N	9	9	9	9	9	9	9	9

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Animal Final Body and Organ Weights

Group Sex	Animal Number	Bodywt g	Adrenal Glands g	Brain g	Heart g	Kidneys g	Liver g	Ovaries g	Spleen g	Thymus g	Uterus g
1f	151	34.1	0.013	0.518	0.182	0.396	1.831	0.054	0.112	0.043	0.157
	152	28.7	0.014	0.506	0.172	0.416	1.424	0.047	0.103	0.030	0.401
	153	28.3	0.014	0.499	0.198	0.433	1.467	0.027	0.107	0.033	0.181
	154	27.3	0.009	0.518	0.162	0.399	1.424	0.024	0.100	0.049	0.174
	155	29.1	0.013	0.516	0.149	0.406	1.262	0.032	0.113	0.038	0.357
	156	32.6	0.017	0.499	0.190	0.477	1.723	0.032	0.137	0.042	0.390
	157	30.3	0.012	0.502	0.142	0.384	1.539	0.027	0.111	0.035	0.209
	158	32.4	0.018	0.492	0.161	0.389	1.912	0.030	0.113	0.029	0.236
	159	42.1	0.016	0.559	0.183	0.554	2.621	0.043	0.178	0.049	0.232
	160	36.7	0.013	0.465	0.165	0.505	1.723	0.044	0.116	0.058	0.199
	Mean	32.16	0.0139	0.5074	0.1704	0.4359	1.6926	0.0360	0.1190	0.0406	0.2536
	S.D.	4.56	0.0026	0.0240	0.0179	0.0573	0.3852	0.0102	0.0230	0.0094	0.0929
	N	10	10	10	10	10	10	10	10	10	10
2f	251	30.9	0.024	0.498	0.170	0.455	1.624	0.037	0.088	0.039	0.470
	252	32.6	0.014	0.518	0.181	0.409	1.819	0.028	0.092	0.038	0.201
	253	32.6	0.026	0.534	0.192	0.484	1.515	0.049	0.120	0.042	0.407
	254	31.5	0.013	0.528	0.198	0.462	1.745	0.050	0.138	0.051	0.259
	255	27.7	0.021	0.506	0.178	0.413	1.817	0.039	0.095	0.029	0.381
	256	33.8	0.011	0.495	0.200	0.495	1.800	0.041	0.102	0.031	0.204
	257	32.7	0.018	0.532	0.181	0.420	1.809	0.045	0.120	0.048	0.219
	258	32.9	0.011	0.480	0.148	0.386	1.484	0.023	0.077	0.047	0.201
	259	33.1	0.017	0.516	0.151	0.449	1.545	0.053	0.106	0.019	0.300
	260	33.1	0.016	0.477	0.175	0.473	1.811	0.031	0.126	0.052	0.116
	Mean	32.09	0.0171	0.5084	0.1774	0.4446	1.6969	0.0396	0.1064	0.0396	0.2758
	S.D.	1.75	0.0052	0.0206	0.0176	0.0360	0.1393	0.0100	0.0192	0.0107	0.1115
	N	10	10	10	10	10	10	10	10	10	10

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Animal Final Body and Organ Weights

Group Sex	Animal Number	Bodywt g	Adrenal Glands g	Brain g	Heart g	Kidneys g	Liver g	Ovaries g	Spleen g	Thymus g	Uterus g
3f	351	31.3	0.013	0.493	0.153	0.388	1.803	0.046	0.081	0.046	0.411
	352	33.0	0.016	0.474	0.148	0.379	1.649	0.024	0.070	0.036	0.197
	353	40.9	0.013	0.479	0.193	0.451	2.284	0.047	0.106	0.047	0.110
	354	29.5	0.013	0.498	0.171	0.377	1.571	0.055	0.080	0.043	0.213
	356	34.5	0.022	0.514	0.150	0.458	1.825	0.052	0.112	0.058	0.336
	357	28.6	0.012	0.479	0.145	0.394	1.296	0.137	0.085	0.036	0.245
	358	34.0	0.022	0.523	0.206	0.484	2.046	0.069	0.134	0.044	0.182
	359	31.7	0.016	0.523	0.187	0.403	1.611	0.139	0.109	0.155	0.249
	360	29.8	0.013	0.505	0.171	0.417	1.622	0.090	0.079	0.043	0.407
	Mean	32.59	0.0156	0.4987	0.1693	0.4168	1.7452	0.0732	0.0951	0.0564	0.2611
	S.D.	3.72	0.0039	0.0190	0.0221	0.0386	0.2883	0.0408	0.0210	0.0375	0.1032
	N	9	9	9	9	9	9	9	9	9	9
4f	451	29.1	0.015	0.517	0.187	0.475	2.561	0.029	0.075	0.029	0.167
	452	34.7	0.015	0.471	0.197	0.427	3.176*	0.054	0.117	0.063	0.151
	453	32.3	0.020	0.521	0.145	0.443	1.840	0.040	0.091	0.034	0.191
	454	33.6	0.017	0.550	0.225	0.473	2.992*	0.040	0.124	0.049	0.247
	455	33.2	0.020	0.525	0.173	0.680	5.244*	0.036	WE	0.047	0.244
	457	34.0	0.013	0.526	0.246	0.518	2.734	0.035	0.090	0.043	0.143
	458	31.0	0.009	0.518	0.202	0.510	2.419	0.070	0.108	0.044	0.323
	459	34.4	0.018	0.495	0.174	0.512	2.842*	0.037	WE	0.058	0.210
	460	29.2	0.014	0.538	0.174	0.403	1.998	0.044	0.072	0.053	0.250
	Mean	32.39	0.0157	0.5179	0.1914	0.4934	2.8673	0.0428	0.0967	0.0467	0.2140
	S.D.	2.15	0.0035	0.0231	0.0304	0.0806	0.9927	0.0123	0.0202	0.0108	0.0580
	N	9	9	9	9	9	9	9	7	9	9

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Animal Final Body and Organ Weights

Group Sex	Animal Number	Adren Gl %FBW	Brain %FBW	Heart %FBW	Kidney %FBW	Liver %FBW	Ovaries %FBW	Spleen %FBW	Thymus %FBW	Uterus %FBW
1f	151	0.0381	1.5191	0.5337	1.1613	5.3695	0.1584	0.3284	0.1261	0.4604
	152	0.0488	1.7631	0.5993	1.4495	4.9617	0.1638	0.3589	0.1045	1.3972
	153	0.0495	1.7633	0.6996	1.5300	5.1837	0.0954	0.3781	0.1166	0.6396
	154	0.0330	1.8974	0.5934	1.4615	5.2161	0.0879	0.3663	0.1795	0.6374
	155	0.0447	1.7732	0.5120	1.3952	4.3368	0.1100	0.3883	0.1306	1.2268
	156	0.0521	1.5307	0.5828	1.4632	5.2853	0.0982	0.4202	0.1288	1.1963
	157	0.0396	1.6568	0.4686	1.2673	5.0792	0.0891	0.3663	0.1155	0.6898
	158	0.0556	1.5185	0.4969	1.2006	5.9012	0.0926	0.3488	0.0895	0.7284
	159	0.0380	1.3278	0.4347	1.3159	6.2257	0.1021	0.4228	0.1164	0.5511
	160	0.0354	1.2670	0.4496	1.3760	4.6948	0.1199	0.3161	0.1580	0.5422
	Mean	0.04348	1.60169	0.53706	1.36205	5.22540	0.11174	0.36942	0.12655	0.80692
	S.D.	0.00772	0.20491	0.08207	0.12236	0.54217	0.02778	0.03487	0.02581	0.33476
	N	10	10	10	10	10	10	10	10	10
2f	251	0.0777	1.6117	0.5502	1.4725	5.2557	0.1197	0.2848	0.1262	1.5210
	252	0.0429	1.5890	0.5552	1.2546	5.5798	0.0859	0.2822	0.1166	0.6166
	253	0.0798	1.6380	0.5890	1.4847	4.6472	0.1503	0.3681	0.1288	1.2485
	254	0.0413	1.6762	0.6286	1.4667	5.5397	0.1587	0.4381	0.1619	0.8222
	255	0.0758	1.8267	0.6426	1.4910	6.5596	0.1408	0.3430	0.1047	1.3755
	256	0.0325	1.4645	0.5917	1.4645	5.3254	0.1213	0.3018	0.0917	0.6036
	257	0.0550	1.6269	0.5535	1.2844	5.5321	0.1376	0.3670	0.1468	0.6697
	258	0.0334	1.4590	0.4498	1.1733	4.5106	0.0699	0.2340	0.1429	0.6109
	259	0.0514	1.5589	0.4562	1.3565	4.6677	0.1601	0.3202	0.0574	0.9063
	260	0.0483	1.4411	0.5287	1.4290	5.4713	0.0937	0.3807	0.1571	0.3505
	Mean	0.05381	1.58920	0.55455	1.38772	5.30891	0.12380	0.33199	0.12341	0.87248
	S.D.	0.01799	0.11721	0.06424	0.11375	0.60152	0.03160	0.05929	0.03221	0.38564
	N	10	10	10	10	10	10	10	10	10

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Animal Final Body and Organ Weights

Group Sex	Animal Number	Adren Gl %FBW	Brain %FBW	Heart %FBW	Kidney %FBW	Liver %FBW	Ovaries %FBW	Spleen %FBW	Thymus %FBW	Uterus %FBW
3f	351	0.0415	1.5751	0.4888	1.2396	5.7604	0.1470	0.2588	0.1470	1.3131
	352	0.0485	1.4364	0.4485	1.1485	4.9970	0.0727	0.2121	0.1091	0.5970
	353	0.0318	1.1711	0.4719	1.1027	5.5844	0.1149	0.2592	0.1149	0.2689
	354	0.0441	1.6881	0.5797	1.2780	5.3254	0.1864	0.2712	0.1458	0.7220
	356	0.0638	1.4899	0.4348	1.3275	5.2899	0.1507	0.3246	0.1681	0.9739
	357	0.0420	1.6748	0.5070	1.3776	4.5315	0.4790	0.2972	0.1259	0.8566
	358	0.0647	1.5382	0.6059	1.4235	6.0176	0.2029	0.3941	0.1294	0.5353
	359	0.0505	1.6498	0.5899	1.2713	5.0820	0.4385	0.3438	0.4890	0.7855
	360	0.0436	1.6946	0.5738	1.3993	5.4430	0.3020	0.2651	0.1443	1.3658
	Mean	0.04783	1.54644	0.52226	1.28533	5.33680	0.23268	0.29179	0.17483	0.82423
	S.D.	0.01067	0.16817	0.06567	0.10999	0.43971	0.14335	0.05468	0.11920	0.35553
	N	9	9	9	9	9	9	9	9	9
4f	451	0.0515	1.7766	0.6426	1.6323	8.8007	0.0997	0.2577	0.0997	0.5739
	452	0.0432	1.3573	0.5677	1.2305	9.1527	0.1556	0.3372	0.1816	0.4352
	453	0.0619	1.6130	0.4489	1.3715	5.6966	0.1238	0.2817	0.1053	0.5913
	454	0.0506	1.6369	0.6696	1.4077	8.9048	0.1190	0.3690	0.1458	0.7351
	455	0.0602	1.5813	0.5211	2.0482	15.7952	0.1084	WE	0.1416	0.7349
	457	0.0382	1.5471	0.7235	1.5235	8.0412	0.1029	0.2647	0.1265	0.4206
	458	0.0290	1.6710	0.6516	1.6452	7.8032	0.2258	0.3484	0.1419	1.0419
	459	0.0523	1.4390	0.5058	1.4884	8.2616	0.1076	WE	0.1686	0.6105
	460	0.0479	1.8425	0.5959	1.3801	6.8425	0.1507	0.2466	0.1815	0.8562
	Mean	0.04831	1.60719	0.59186	1.52527	8.81094	0.13261	0.30076	0.14361	0.66662
	S.D.	0.01036	0.15169	0.08872	0.23614	2.83702	0.04028	0.04951	0.03001	0.19926
	N	9	9	9	9	9	9	7	9	9

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Animal Final Body and Organ Weights

Group Sex	Animal Number	Adren Gl %Brain	Heart %Brain	Kidney %Brain	Liver %Brain	Ovaries %Brain	Spleen %Brain	Thymus %Brain	Uterus %Brain
1f	151	2.5097	35.1351	76.4479	353.4749	10.4247	21.6216	8.3012	30.3089
	152	2.7668	33.9921	82.2134	281.4229	9.2885	20.3557	5.9289	79.2490
	153	2.8056	39.6794	86.7735	293.9880	5.4108	21.4429	6.6132	36.2725
	154	1.7375	31.2741	77.0270	274.9035	4.6332	19.3050	9.4595	33.5907
	155	2.5194	28.8760	78.6822	244.5736	6.2016	21.8992	7.3643	69.1860
	156	3.4068	38.0762	95.5912	345.2906	6.4128	27.4549	8.4168	78.1563
	157	2.3904	28.2869	76.4940	306.5737	5.3785	22.1116	6.9721	41.6335
	158	3.6585	32.7236	79.0650	388.6179	6.0976	22.9675	5.8943	47.9675
	159	2.8623	32.7370	99.1055	468.8730	7.6923	31.8426	8.7657	41.5027
	160	2.7957	35.4839	108.6022	370.5376	9.4624	24.9462	12.4731	42.7957
	Mean	2.74527	33.62643	86.00019	332.82557	7.10024	23.39472	8.01891	50.06628
	S.D.	0.53125	3.65932	11.32013	66.33985	1.99892	3.76001	1.97465	18.43916
	N	10	10	10	10	10	10	10	10
2f	251	4.8193	34.1365	91.3655	326.1044	7.4297	17.6707	7.8313	94.3775
	252	2.7027	34.9421	78.9575	351.1583	5.4054	17.7606	7.3359	38.8031
	253	4.8689	35.9551	90.6367	283.7079	9.1760	22.4719	7.8652	76.2172
	254	2.4621	37.5000	87.5000	330.4924	9.4697	26.1364	9.6591	49.0530
	255	4.1502	35.1779	81.6206	359.0909	7.7075	18.7747	5.7312	75.2964
	256	2.2222	40.4040	100.0000	363.6364	8.2828	20.6061	6.2626	41.2121
	257	3.3835	34.0226	78.9474	340.0376	8.4586	22.5564	9.0226	41.1654
	258	2.2917	30.8333	80.4167	309.1667	4.7917	16.0417	9.7917	41.8750
	259	3.2946	29.2636	87.0155	299.4186	10.2713	20.5426	3.6822	58.1395
	260	3.3543	36.6876	99.1614	379.6646	6.4990	26.4151	10.9015	24.3187
	Mean	3.35495	34.89227	87.56213	334.24778	7.74917	20.89762	7.80833	54.04579
	S.D.	0.98373	3.18156	7.80368	30.44097	1.76547	3.52245	2.16941	21.61858
	N	10	10	10	10	10	10	10	10

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Individual Animal Final Body and Organ Weights

Group Sex	Animal Number	Adren Gl %Brain	Heart %Brain	Kidney %Brain	Liver %Brain	Ovaries %Brain	Spleen %Brain	Thymus %Brain	Uterus %Brain
3f	351	2.6369	31.0345	78.7018	365.7201	9.3306	16.4300	9.3306	83.3671
	352	3.3755	31.2236	79.9578	347.8903	5.0633	14.7679	7.5949	41.5612
	353	2.7140	40.2923	94.1545	476.8267	9.8121	22.1294	9.8121	22.9645
	354	2.6104	34.3373	75.7028	315.4618	11.0442	16.0643	8.6345	42.7711
	356	4.2802	29.1829	89.1051	355.0584	10.1167	21.7899	11.2840	65.3696
	357	2.5052	30.2714	82.2547	270.5637	28.6013	17.7453	7.5157	51.1482
	358	4.2065	39.3881	92.5430	391.2046	13.1931	25.6214	8.4130	34.7992
	359	3.0593	35.7553	77.0554	308.0306	26.5774	20.8413	29.6367	47.6099
	360	2.5743	33.8614	82.5743	321.1881	17.8218	15.6436	8.5149	80.5941
	Mean	3.10692	33.92742	83.56104	350.21603	14.61783	19.00368	11.19293	52.24277
	S.D.	0.70068	3.95918	6.77297	59.32341	8.11044	3.72128	7.01311	20.41078
	N	9	9	9	9	9	9	9	9
4f	451	2.9014	36.1702	91.8762	495.3578	5.6093	14.5068	5.6093	32.3017
	452	3.1847	41.8259	90.6582	674.3100	11.4650	24.8408	13.3758	32.0594
	453	3.8388	27.8311	85.0288	353.1670	7.6775	17.4664	6.5259	36.6603
	454	3.0909	40.9091	86.0000	544.0000	7.2727	22.5455	8.9091	44.9091
	455	3.8095	32.9524	129.5238	998.8571	6.8571	WE	8.9524	46.4762
	457	2.4715	46.7681	98.4791	519.7719	6.6540	17.1103	8.1749	27.1863
	458	1.7375	38.9961	98.4556	466.9884	13.5135	20.8494	8.4942	62.3552
	459	3.6364	35.1515	103.4343	574.1414	7.4747	WE	11.7172	42.4242
	460	2.6022	32.3420	74.9071	371.3755	8.1784	13.3829	9.8513	46.4684
	Mean	3.03032	36.99404	95.37368	555.32990	8.30024	18.67173	9.06779	41.20453
	S.D.	0.69275	5.74700	15.40527	193.23858	2.53396	4.22325	2.39216	10.59549
	N	9	9	9	9	9	7	9	9

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 0.1 mg/kg Group 3 - 0.5 mg/kg Group 4 - 5 mg/kg

Appendix M
Individual Animal Gross Pathology Observations - Animals Designated for Plasma Concentration Evaluation

Individual Animal Gross Pathology Observations - Animals Designated for Plasma Concentration Evaluation

Group: 1 Dose: 0 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
111	MECHANISTIC SACRIFICE	95	(13)	
113	MECHANISTIC SACRIFICE	95	(13)	
114	MECHANISTIC SACRIFICE	95	(13)	
115	MECHANISTIC SACRIFICE	95	(13)	
116	MECHANISTIC SACRIFICE	28	(4)	
117	MECHANISTIC SACRIFICE	28	(4)	
118	MECHANISTIC SACRIFICE	28	(4)	
119	MECHANISTIC SACRIFICE	28	(4)	
120	MECHANISTIC SACRIFICE	28	(4)	
121	MECHANISTIC SACRIFICE	0	(0)	
122	MECHANISTIC SACRIFICE	0	(0)	
123	MECHANISTIC SACRIFICE	0	(0)	
124	MECHANISTIC SACRIFICE	0	(0)	
125	MECHANISTIC SACRIFICE	0	(0)	
127	MECHANISTIC SACRIFICE	95	(13)	

Individual Animal Gross Pathology Observations - Animals Designated for Plasma Concentration Evaluation

Group: 2 Dose: 0.1 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
211	MECHANISTIC SACRIFICE	95	(13)	
212	MECHANISTIC SACRIFICE	95	(13)	
213	MECHANISTIC SACRIFICE	95	(13)	
214	MECHANISTIC SACRIFICE	95	(13)	
215	MECHANISTIC SACRIFICE	95	(13)	
216	MECHANISTIC SACRIFICE	28	(4)	
217	MECHANISTIC SACRIFICE	28	(4)	
218	MECHANISTIC SACRIFICE	28	(4)	
219	MECHANISTIC SACRIFICE	28	(4)	
220	MECHANISTIC SACRIFICE	28	(4)	
221	MECHANISTIC SACRIFICE	0	(0)	
222	MECHANISTIC SACRIFICE	0	(0)	
223	MECHANISTIC SACRIFICE	0	(0)	
224	MECHANISTIC SACRIFICE	0	(0)	
225	MECHANISTIC SACRIFICE	0	(0)	

Individual Animal Gross Pathology Observations - Animals Designated for Plasma Concentration Evaluation

Group: 3 Dose: 0.5 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
311	MECHANISTIC SACRIFICE	95	(13)	
312	UNSCHEDULED SACRIFICE	3	(0)	STOMACH; Lesion other: Empty of ingesta
313	MECHANISTIC SACRIFICE	95	(13)	
314	MECHANISTIC SACRIFICE	95	(13)	
315	MECHANISTIC SACRIFICE	95	(13)	
316	MECHANISTIC SACRIFICE	28	(4)	
317	MECHANISTIC SACRIFICE	28	(4)	
318	MECHANISTIC SACRIFICE	28	(4)	
319	MECHANISTIC SACRIFICE	28	(4)	
320	MECHANISTIC SACRIFICE	28	(4)	
321	MECHANISTIC SACRIFICE	0	(0)	
322	MECHANISTIC SACRIFICE	0	(0)	
323	MECHANISTIC SACRIFICE	0	(0)	
324	MECHANISTIC SACRIFICE	0	(0)	
325	MECHANISTIC SACRIFICE	0	(0)	

Individual Animal Gross Pathology Observations - Animals Designated for Plasma Concentration Evaluation

Group: 4 Dose: 5 mg/kg Sex: Male

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
411	MECHANISTIC SACRIFICE	95	(13)	
412	MECHANISTIC SACRIFICE	95	(13)	
413	MECHANISTIC SACRIFICE	95	(13)	
414	MECHANISTIC SACRIFICE	95	(13)	
415	MECHANISTIC SACRIFICE	95	(13)	
416	MECHANISTIC SACRIFICE	28	(4)	
417	MECHANISTIC SACRIFICE	28	(4)	
418	MECHANISTIC SACRIFICE	28	(4)	
419	MECHANISTIC SACRIFICE	28	(4)	
420	MECHANISTIC SACRIFICE	28	(4)	
421	MECHANISTIC SACRIFICE	0	(0)	
422	MECHANISTIC SACRIFICE	0	(0)	
423	MECHANISTIC SACRIFICE	0	(0)	
425	MECHANISTIC SACRIFICE	0	(0)	
427	MECHANISTIC SACRIFICE	0	(0)	

Individual Animal Gross Pathology Observations - Animals Designated for Plasma Concentration Evaluation

Group: 1 Dose: 0 mg/kg Sex: Female

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
161	MECHANISTIC SACRIFICE	95	(13)	
162	MECHANISTIC SACRIFICE	95	(13)	
163	MECHANISTIC SACRIFICE	95	(13)	
164	MECHANISTIC SACRIFICE	95	(13)	
165	FOUND DEAD	16	(2)	BRAIN; Autolysis; mild SPLEEN; Large STOMACH; Lesion other; red: ingesta VAGINA; Thick
166	MECHANISTIC SACRIFICE	28	(4)	
167	MECHANISTIC SACRIFICE	28	(4)	
168	MECHANISTIC SACRIFICE	28	(4)	
169	MECHANISTIC SACRIFICE	28	(4)	
170	MECHANISTIC SACRIFICE	28	(4)	
171	MECHANISTIC SACRIFICE	0	(0)	
172	MECHANISTIC SACRIFICE	0	(0)	
173	MECHANISTIC SACRIFICE	0	(0)	
174	MECHANISTIC SACRIFICE	0	(0)	
175	MECHANISTIC SACRIFICE	0	(0)	

Individual Animal Gross Pathology Observations - Animals Designated for Plasma Concentration Evaluation

Group: 2 Dose: 0.1 mg/kg Sex: Female

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
261	MECHANISTIC SACRIFICE	95	(13)	
262	MECHANISTIC SACRIFICE	95	(13)	
263	MECHANISTIC SACRIFICE	95	(13)	
264	MECHANISTIC SACRIFICE	95	(13)	
265	MECHANISTIC SACRIFICE	95	(13)	
266	MECHANISTIC SACRIFICE	28	(4)	
267	MECHANISTIC SACRIFICE	28	(4)	
268	MECHANISTIC SACRIFICE	28	(4)	
269	MECHANISTIC SACRIFICE	28	(4)	
270	MECHANISTIC SACRIFICE	28	(4)	
271	MECHANISTIC SACRIFICE	0	(0)	
272	MECHANISTIC SACRIFICE	0	(0)	
273	MECHANISTIC SACRIFICE	0	(0)	
274	MECHANISTIC SACRIFICE	0	(0)	
275	MECHANISTIC SACRIFICE	0	(0)	

Individual Animal Gross Pathology Observations - Animals Designated for Plasma Concentration Evaluation

Group: 3 Dose: 0.5 mg/kg Sex: Female

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
361	MECHANISTIC SACRIFICE	95	(13)	
362	MECHANISTIC SACRIFICE	95	(13)	
363	MECHANISTIC SACRIFICE	95	(13)	
364	MECHANISTIC SACRIFICE	95	(13)	
365	MECHANISTIC SACRIFICE	95	(13)	
366	MECHANISTIC SACRIFICE	28	(4)	
367	UNSCHEDULED SACRIFICE - MECHANISTIC	6	(0)	LUNGS; Not expanded LUNGS; right; Discoloration; dark PLEURAL CAVITY; Adhesion SKIN; left; Foreign body; axilla
368	MECHANISTIC SACRIFICE	28	(4)	
369	MECHANISTIC SACRIFICE	28	(4)	
370	MECHANISTIC SACRIFICE	28	(4)	
371	MECHANISTIC SACRIFICE	0	(0)	
372	MECHANISTIC SACRIFICE	0	(0)	
373	MECHANISTIC SACRIFICE	0	(0)	
374	MECHANISTIC SACRIFICE	0	(0)	
375	MECHANISTIC SACRIFICE	0	(0)	

Individual Animal Gross Pathology Observations - Animals Designated for Plasma Concentration Evaluation

Group: 4 Dose: 5 mg/kg Sex: Female

Animal Ref.	Mode Of Death	Death Day	(Week)	Observation(s)
461	MECHANISTIC SACRIFICE	95	(13)	
462	MECHANISTIC SACRIFICE	95	(13)	
463	MECHANISTIC SACRIFICE	95	(13)	
464	MECHANISTIC SACRIFICE	95	(13)	
465	MECHANISTIC SACRIFICE	95	(13)	
466	MECHANISTIC SACRIFICE	28	(4)	
467	MECHANISTIC SACRIFICE	28	(4)	
468	MECHANISTIC SACRIFICE	28	(4)	
469	MECHANISTIC SACRIFICE	28	(4)	
470	MECHANISTIC SACRIFICE	28	(4)	
471	MECHANISTIC SACRIFICE	0	(0)	
472	MECHANISTIC SACRIFICE	0	(0)	
473	MECHANISTIC SACRIFICE	0	(0)	
474	MECHANISTIC SACRIFICE	0	(0)	
475	MECHANISTIC SACRIFICE	0	(0)	

Appendix N
Individual Animal Pathology Data

INDIVIDUAL ANIMAL PATHOLOGY DATA

EXPLANATORY NOTES

LESION GRADING:

Histopathology changes are described according to their morphologic character, distribution and severity. The distribution (extent of tissue involvement) is indicated, where appropriate, by modifiers such as focal, multifocal, diffuse, unilateral, bilateral, etc. A severity score, if appropriate, is also assigned as follows:

PRESENT: Lesion present; severity not graded.

MINIMAL: The amount of change present barely exceeds that which is considered to be within normal limits.

MILD: In general, the lesion is easily identified but of limited severity. The lesion probably does not produce any functional impairment.

MODERATE: The lesion is prominent but there is significant potential for increased severity. Limited tissue or organ dysfunction is possible.

SEVERE: The degree of change is either as complete as considered possible or great enough in intensity or extent to expect significant tissue or organ dysfunction.

COMMENTS:

Grades minimal through severe represent progressive involvement/severity along a continuum with minimal lesions being the least severe and severe lesions being the most severe. While the grades refer to the morphologic characteristics of lesions, they also indicate their relative biologic significance.

Gross observations listing multiple masses for a tissue are distinguished with letters (i.e., a, b, c, d, etc.).

The microscopic correlate for selected gross observations, primarily masses, is provided to the right of the respective gross observation.

ABBREVIATIONS:

E - excluded from all calculations

Individual Animal Pathology Data

Animal Ref.: 101 Group: 1 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 36.6g

Organ Weights:

ADRENAL GLANDS	0.007g	BRAIN	0.486g	EPIDIDYMIDES	0.126g
HEART	0.191g	KIDNEYS	0.562g	LIVER	1.856g
SPLEEN	0.092g	TESTES	0.237g	THYMUS	0.048g

Gross Pathology Observations: None

Histo Pathology Observations:

MANDIBULAR LYMPH NODES;
Erythrocytosis/erythrophagocytosis; sinus; minimal

SALIVARY GLANDS;
Aggregates; lymphoid; focal/multifocal; minimal: submandibular glands

THYROID GLAND;
Dilated follicle(s); focal/multifocal; minimal

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM
EPIDIDYMIDES	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	KIDNEYS	LIVER	LUNGS	MESENTERIC LYMPH NODES		NOSE
PANCREAS	PARATHYROID GLANDS	PHARYNX/LARYNX	PITUITARY GLAND	PROSTATE	RECTUM	SCIATIC NERVE
SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN	STERNUM	STOMACH
TESTES	THYMUS	TRACHEA	URINARY BLADDER			

The following tissues have not been examined:

OPTIC NERVES; MISSING
PEYERS PATCH; MISSING

Individual Animal Pathology Data

Animal Ref.: 102 Group: 1 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 34.8g

Organ Weights:

ADRENAL GLANDS	0.006g	BRAIN	0.475g	EPIDIDYMIDES	0.123g
HEART	0.171g	KIDNEYS	0.487g	LIVER	1.776g
SPLEEN	0.087g	TESTES	0.255g	THYMUS	0.024g

Gross Pathology Observations: None

Histo Pathology Observations:

OPTIC NERVES;
ONE OF A PAIR PRESENT

SALIVARY GLANDS;
Aggregates; lymphoid; focal/multifocal; minimal: submandibular gland

THYROID GLAND;
Dilated follicle(s); focal/multifocal; minimal
Ectopic thymus tissue; present

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM
EPIDIDYMIDES	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	KIDNEYS	LIVER	LUNGS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES
NOSE	OPTIC NERVES	PANCREAS	PARATHYROID GLANDS	PHARYNX/LARYNX	PITUITARY GLAND	PROSTATE
RECTUM	SCIATIC NERVE	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN
STERNUM	STOMACH	TESTES	THYMUS	TRACHEA	URINARY BLADDER	

The following tissues have not been examined:

PEYERS PATCH; MISSING

Individual Animal Pathology Data

Animal Ref.: 103 Group: 1 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 41.3g

Organ Weights:

ADRENAL GLANDS	: 0.010g	BRAIN	: 0.482g	EPIDIDYMIDES	: 0.150g
HEART	: 0.189g	KIDNEYS	: 0.721g	LIVER	: 2.237g
SPLEEN	: 0.087g	TESTES	: 0.233g	THYMUS	: 0.028g

Gross Pathology Observations: None

Histo Pathology Observations:

ADRENAL GLANDS;
Pigment; zona reticularis; lipogenic; multifocal; minimal
Hyperplasia; subcapular cell; focal/multifocal; minimal

EYES;
Rosette; retinal; unilateral; minimal

KIDNEYS;
Chronic progressive nephropathy; minimal

LIVER;
Mononuclear cell infiltrate; minimal

The following tissues were within normal limits:

AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM	EPIDIDYMIDES
ESOPHAGUS	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM	LUNGS
MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		NOSE	OPTIC NERVES	PANCREAS
PARATHYROID GLANDS						
PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND	PROSTATE	RECTUM	SALIVARY GLANDS	SCIATIC NERVE
SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN	STERNUM	STOMACH
TESTES	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER		

Individual Animal Pathology Data

Animal Ref.: 104 Group: 1 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 34.9g

Organ Weights:

ADRENAL GLANDS	0.009g	BRAIN	0.479g	EPIDIDYMIDES	0.117g
HEART	0.187g	KIDNEYS	0.518g	LIVER	1.854g
SPLEEN	0.093g	TESTES	0.211g	THYMUS	0.022g

Gross Pathology Observations: None

Histo Pathology Observations:

ESOPHAGUS;
Inflammation; submucosa; subacute/chronic; focal; minimal

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM
EPIDIDYMIDES	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM
KIDNEYS	LIVER	LUNGS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES	
NOSE	OPTIC NERVES	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND
PROSTATE	RECTUM	SALIVARY GLANDS	SCIATIC NERVE	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN
SPINAL CORD	SPLEEN	STERNUM	STOMACH	TESTES	THYMUS	THYROID GLAND
TRACHEA	URINARY BLADDER					

Individual Animal Pathology Data

Animal Ref.: 105 Group: 1 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 35g

Organ Weights:

ADRENAL GLANDS	: 0.004g	BRAIN	: 0.515g	EPIDIDYMIDES	: 0.105g
HEART	: 0.174g	KIDNEYS	: 0.608g	LIVER	: 1.763g
SPLEEN	: 0.091g	TESTES	: 0.248g	THYMUS	: 0.017g

Gross Pathology Observations: None

Histo Pathology Observations:

HEART;
Cardiomyopathy; focal/multifocal; minimal

OPTIC NERVES;
ONE OF A PAIR PRESENT

PROSTATE;
Aggregates; lymphoid; focal/multifocal; minimal

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM
EPIDIDYMIDES	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	ILEUM	JEJUNUM
KIDNEYS	LIVER	LUNGS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES	
NOSE	OPTIC NERVES	PANCREAS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND	RECTUM
SALIVARY GLANDS	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN	STERNUM
STOMACH	TESTES	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER	

The following tissues have not been examined:

PARATHYROID GLANDS; MISSING
SCIATIC NERVE; MISSING

Individual Animal Pathology Data

Animal Ref.: 106 Group: 1 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 43.3g

Organ Weights:

ADRENAL GLANDS	0.011g	BRAIN	0.581g	EPIDIDYMIDES	0.150g
HEART	0.234g	KIDNEYS	0.713g	LIVER	2.203g
SPLEEN	0.137g	TESTES	0.221g	THYMUS	0.029g

Gross Pathology Observations: None

Histo Pathology Observations:

KIDNEYS;
Hydronephrosis; bilateral; minimal

LIVER;
Mononuclear cell infiltrate; minimal

TESTES;
Degeneration/atrophy; unilateral; minimal

THYROID GLAND;
Dilated follicle(s); focal/multifocal; minimal

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM
EPIDIDYMIDES	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	LUNGS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		NOSE
PANCREAS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND	PROSTATE	RECTUM	SALIVARY GLANDS
SCIATIC NERVE						
SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN	STERNUM	STOMACH
THYMUS	TRACHEA	URINARY BLADDER				

The following tissues have not been examined:

OPTIC NERVES; MISSING
PARATHYROID GLANDS; MISSING

Individual Animal Pathology Data

Animal Ref.: 107 Group: 1 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 40.4g

Organ Weights:

ADRENAL GLANDS	0.010g	BRAIN	0.536g	EPIDIDYMIDES	0.140g
HEART	0.203g	KIDNEYS	0.708g	LIVER	2.498g
SPLEEN	0.097g	TESTES	0.242g	THYMUS	0.031g

Gross Pathology Observations: None

Histo Pathology Observations:

PITUITARY GLAND;
pars nervosa and pars intermedia missing from the section

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM
EPIDIDYMIDES	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	KIDNEYS	LIVER	LUNGS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES
NOSE	OPTIC NERVES	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND
PROSTATE	RECTUM	SALIVARY GLANDS	SCIATIC NERVE	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN
SPINAL CORD	SPLEEN	STERNUM	STOMACH	TESTES	THYMUS	THYROID GLAND
TRACHEA	URINARY BLADDER					

Individual Animal Pathology Data

Animal Ref.: 108 Group: 1 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 41.9g

Organ Weights:

ADRENAL GLANDS	0.014g	BRAIN	0.515g	EPIDIDYMIDES	0.118g
HEART	0.210g	KIDNEYS	0.709g	LIVER	1.845g
SPLEEN	0.097g	TESTES	0.205g	THYMUS	0.040g

Gross Pathology Observations: None

Histo Pathology Observations:

KIDNEYS;
Microvesiculation; tubule; epithelium; diffuse; moderate
Aggregates; lymphocyte/plasmacyte; focal/multifocal; mild
Dilated tubule(s); focal/multifocal; minimal

LIVER;
Mononuclear cell infiltrate; minimal

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM
EPIDIDYMIDES	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	LUNGS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		NOSE
OPTIC NERVES	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND	PROSTATE
RECTUM	SALIVARY GLANDS	SCIATIC NERVE	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD
SPLEEN	STERNUM	STOMACH	TESTES	THYMUS	THYROID GLAND	TRACHEA
URINARY BLADDER						

Individual Animal Pathology Data

Animal Ref.: 109 Group: 1 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 36.9g

Organ Weights:

ADRENAL GLANDS	: 0.003g	BRAIN	: 0.489g	EPIDIDYMIDES	: 0.118g
HEART	: 0.200g	KIDNEYS	: 0.630g	LIVER	: 1.846g
SPLEEN	: 0.104g	TESTES	: 0.259g	THYMUS	: 0.027g

Gross Pathology Observations: None

Histo Pathology Observations:

ADRENAL GLANDS;
Pigment; zona fasciculata; lipogenic; multifocal; mild

KIDNEYS;
Chronic progressive nephropathy; minimal

NOSE;
Inflammation; turbinate; focal/multifocal; minimal: L2

The following tissues were within normal limits:

AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM	EPIDIDYMIDES
ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM
LIVER	LUNGS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		OPTIC NERVES
PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND	PROSTATE	RECTUM
SALIVARY GLANDS	SCIATIC NERVE	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN
STERNUM	STOMACH	TESTES	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER

Individual Animal Pathology Data

Animal Ref.: 110 Group: 1 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 41.9g

Organ Weights:

ADRENAL GLANDS	0.004g	BRAIN	0.500g	EPIDIDYMIDES	0.164g
HEART	0.185g	KIDNEYS	0.563g	LIVER	1.667g
SPLEEN	0.165g	TESTES	0.177g	THYMUS	0.034g

Gross Pathology Observations: None

Histo Pathology Observations:

EYES;
ONE OF A PAIR PRESENT

LIVER;
Mononuclear cell infiltrate; minimal

OPTIC NERVES;
ONE OF A PAIR PRESENT

THYROID GLAND;
Dilated follicle(s); focal/multifocal; minimal

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM
EPIDIDYMIDES	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	KIDNEYS	LUNGS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES	
NOSE	OPTIC NERVES	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND
PROSTATE						
RECTUM	SALIVARY GLANDS	SCIATIC NERVE	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD
SPLEEN	STERNUM	STOMACH	TESTES	THYMUS	TRACHEA	URINARY BLADDER

Individual Animal Pathology Data

Animal Ref.: 201 Group: 2 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 38.1g

Organ Weights:

ADRENAL GLANDS	0.014g	BRAIN	0.533g	EPIDIDYMIDES	0.121g
HEART	0.167g	KIDNEYS	0.647g	LIVER	2.052g
SPLEEN	0.108g	TESTES	0.216g	THYMUS	0.041g

Gross Pathology Observations: None

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

Individual Animal Pathology Data

Animal Ref.: 202 Group: 2 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 35.7g

Organ Weights:

ADRENAL GLANDS	0.005g	BRAIN	0.459g	EPIDIDYMIDES	0.121g
HEART	0.193g	KIDNEYS	0.490g	LIVER	1.883g
SPLEEN	0.071g	TESTES	0.300g	THYMUS	0.033g

Gross Pathology Observations: None

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

Individual Animal Pathology Data

Animal Ref.: 203 Group: 2 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 41.3g

Organ Weights:

ADRENAL GLANDS	0.014g	BRAIN	0.529g	EPIDIDYMIDES	0.144g
HEART	0.192g	KIDNEYS	0.657g	LIVER	2.142g
SPLEEN	0.113g	TESTES	0.242g	THYMUS	0.026g

Gross Pathology Observations: None

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

Individual Animal Pathology Data

Animal Ref.: 204 Group: 2 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 40.1g

Organ Weights:

ADRENAL GLANDS	0.009g	BRAIN	0.509g	EPIDIDYMIDES	0.618g
HEART	0.171g	KIDNEYS	0.658g	LIVER	1.840g
SPLEEN	0.086g	TESTES	0.223g	THYMUS	0.036g

Gross Pathology Observations: None

Histo Pathology Observations:

KIDNEYS;
Dilated tubule(s); focal/multifocal; minimal

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 205 Group: 2 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 42.8g

Organ Weights:

ADRENAL GLANDS	0.004g	BRAIN	0.516g	EPIDIDYMIDES	0.102g
HEART	0.233g	KIDNEYS	0.564g	LIVER	2.310g
SPLEEN	0.088g	TESTES	0.179g	THYMUS	0.023g

Gross Pathology Observations: None

Histo Pathology Observations:

KIDNEYS;
Chronic progressive nephropathy; minimal

LIVER;
Mononuclear cell infiltrate; minimal

Individual Animal Pathology Data

Animal Ref.: 206 Group: 2 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 35.9g

Organ Weights:

ADRENAL GLANDS	0.003g	BRAIN	0.478g	EPIDIDYMIDES	0.108g
HEART	0.155g	KIDNEYS	0.516g	LIVER	1.801g
SPLEEN	0.070g	TESTES	0.237g	THYMUS	0.032g

Gross Pathology Observations: None

Histo Pathology Observations:

KIDNEYS;
Aggregates; lymphocyte/plasmacyte; focal/multifocal; minimal
Chronic progressive nephropathy; minimal
Dilated tubule(s); focal/multifocal; minimal

LIVER;
Mononuclear cell infiltrate; minimal

Individual Animal Pathology Data

Animal Ref.: 207 Group: 2 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 44g

Organ Weights:

ADRENAL GLANDS	0.004g	BRAIN	0.456g	EPIDIDYMIDES	0.103g
HEART	0.226g	KIDNEYS	0.622g	LIVER	2.155g
SPLEEN	0.115g	TESTES	0.178g	THYMUS	0.035g

Gross Pathology Observations: None

Histo Pathology Observations:

KIDNEYS;
Chronic progressive nephropathy; minimal

LIVER;
Mononuclear cell infiltrate; minimal

Individual Animal Pathology Data

Animal Ref.: 208 Group: 2 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 42.5g

Organ Weights:

ADRENAL GLANDS	0.007g	BRAIN	0.482g	EPIDIDYMIDES	0.131g
HEART	0.201g	KIDNEYS	0.609g	LIVER	2.057g
SPLEEN	0.094g	TESTES	0.241g	THYMUS	0.034g

Gross Pathology Observations: None

Histo Pathology Observations:

LIVER;
Mononuclear cell infiltrate; minimal

The following tissues were within normal limits:

KIDNEYS

Individual Animal Pathology Data

Animal Ref.: 209 Group: 2 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 44.4g

Organ Weights:

ADRENAL GLANDS	0.013g	BRAIN	0.507g	EPIDIDYMIDES	0.157g
HEART	0.256g	KIDNEYS	0.674g	LIVER	2.139g
SPLEEN	0.115g	TESTES	0.280g	THYMUS	0.026g

Gross Pathology Observations: None

Histo Pathology Observations:

LIVER;
Mononuclear cell infiltrate; minimal

The following tissues were within normal limits:

KIDNEYS

Individual Animal Pathology Data

Animal Ref.: 210 Group: 2 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 38.2g

Organ Weights:

ADRENAL GLANDS	0.005g	BRAIN	0.512g	EPIDIDYMIDES	0.097g
HEART	0.227g	KIDNEYS	0.500g	LIVER	1.862g
SPLEEN	0.071g	TESTES	0.259g	THYMUS	0.045g

Gross Pathology Observations: None

Histo Pathology Observations:

LIVER;
Mononuclear cell infiltrate; minimal

The following tissues were within normal limits:

KIDNEYS

Individual Animal Pathology Data

Animal Ref.: 301 Group: 3 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 36.3g

Organ Weights:

ADRENAL GLANDS	0.008g	BRAIN	0.517g	EPIDIDYMIDES	0.108g
HEART	0.188g	KIDNEYS	0.649g	LIVER	1.976g
SPLEEN	0.061g	TESTES	0.237g	THYMUS	0.025g

Gross Pathology Observations: None

Histo Pathology Observations:

KIDNEYS;
Aggregates; lymphocyte/plasmacyte; focal/multifocal; minimal

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 302 Group: 3 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 40.6g

Organ Weights:

ADRENAL GLANDS	0.004g	BRAIN	0.502g	EPIDIDYMIDES	0.114g
HEART	0.176g	KIDNEYS	0.570g	LIVER	2.193g
SPLEEN	0.081g	TESTES	0.267g	THYMUS	0.013g

Gross Pathology Observations: None

Histo Pathology Observations:

LIVER;
Hepatocellular hypertrophy; minimal

The following tissues were within normal limits:

KIDNEYS

Individual Animal Pathology Data

Animal Ref.: 303 Group: 3 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 37.5g

Organ Weights:

ADRENAL GLANDS	0.006g	BRAIN	0.559g	EPIDIDYMIDES	0.114g
HEART	0.208g	KIDNEYS	0.642g	LIVER	2.261g
SPLEEN	0.090g	TESTES	0.209g	THYMUS	0.031g

Gross Pathology Observations:

LIVER;
Discoloration; pale

Histo Pathology Observations:

LIVER;
Hepatocellular hypertrophy; minimal

The following tissues were within normal limits:

KIDNEYS

Individual Animal Pathology Data

Animal Ref.: 304 Group: 3 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 37.6g

Organ Weights:

ADRENAL GLANDS	0.009g	BRAIN	0.487g	EPIDIDYMIDES	0.151g
HEART	0.197g	KIDNEYS	0.561g	LIVER	2.329g
SPLEEN	0.085g	TESTES	0.211g	THYMUS	0.071g

Gross Pathology Observations: None

Histo Pathology Observations:

LIVER;
Hepatocellular hypertrophy; minimal
Mononuclear cell infiltrate; mild

The following tissues were within normal limits:

KIDNEYS

Individual Animal Pathology Data

Animal Ref.: 305 Group: 3 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 44.6g

Organ Weights:

ADRENAL GLANDS	: 0.013g	BRAIN	: 0.493g	EPIDIDYMIDES	: 0.149g
HEART	: 0.221g	KIDNEYS	: 0.644g	LIVER	: 2.489g
SPLEEN	: 0.124g	TESTES	: 0.226g	THYMUS	: 0.040g

Gross Pathology Observations:

LIVER;
Discoloration; pale

Histo Pathology Observations:

LIVER;
Hepatocellular hypertrophy; minimal

The following tissues were within normal limits:

KIDNEYS

Individual Animal Pathology Data

Animal Ref.: 306 Group: 3 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 39.7g

Organ Weights:

ADRENAL GLANDS	0.005g	BRAIN	0.518g	EPIDIDYMIDES	0.102g
HEART	0.223g	KIDNEYS	0.624g	LIVER	2.220g
SPLEEN	0.100g	TESTES	0.209g	THYMUS	0.036g

Gross Pathology Observations: None

Histo Pathology Observations:

KIDNEYS;
Aggregates; lymphocyte/plasmacyte; focal/multifocal; minimal: perivascular

LIVER;
Hepatocellular hypertrophy; minimal

Individual Animal Pathology Data

Animal Ref.: 307 Group: 3 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 36.9g

Organ Weights:

ADRENAL GLANDS	0.009g	BRAIN	0.523g	EPIDIDYMIDES	0.113g
HEART	0.175g	KIDNEYS	0.513g	LIVER	1.628g
SPLEEN	0.066g	TESTES	0.194g	THYMUS	0.024g

Gross Pathology Observations: None

Histo Pathology Observations:

LIVER;
Hepatocellular hypertrophy; minimal

The following tissues were within normal limits:

KIDNEYS

Individual Animal Pathology Data

Animal Ref.: 308 Group: 3 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 38.8g

Organ Weights:

ADRENAL GLANDS	0.005g	BRAIN	0.456g	EPIDIDYMIDES	0.122g
HEART	0.203g	KIDNEYS	0.631g	LIVER	2.284g
SPLEEN	0.098g	TESTES	0.190g	THYMUS	0.030g

Gross Pathology Observations:

LIVER;
Discoloration; pale

Histo Pathology Observations:

KIDNEYS;
Aggregates; lymphocyte/plasmacyte; focal/multifocal; minimal: perivascular

LIVER;
Hepatocellular hypertrophy; minimal
Mononuclear cell infiltrate; minimal

Individual Animal Pathology Data

Animal Ref.: 309 Group: 3 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 38.1g

Organ Weights:

ADRENAL GLANDS	0.008g	BRAIN	0.467g	EPIDIDYMIDES	0.131g
HEART	0.195g	KIDNEYS	0.678g	LIVER	2.515g
SPLEEN	0.081g	TESTES	0.204g	THYMUS	0.039g

Gross Pathology Observations:

LIVER;
Discoloration; pale
Large

Histo Pathology Observations:

LIVER;
Hepatocellular hypertrophy; minimal
Mononuclear cell infiltrate; minimal

The following tissues were within normal limits:

KIDNEYS

Individual Animal Pathology Data

Animal Ref.: 310 Group: 3 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 39g

Organ Weights:

ADRENAL GLANDS	0.012g	BRAIN	0.510g	EPIDIDYMIDES	0.122g
HEART	0.198g	KIDNEYS	0.623g	LIVER	1.964g
SPLEEN	0.080g	TESTES	0.276g	THYMUS	0.021g

Gross Pathology Observations: None

Histo Pathology Observations:

LIVER;
Mononuclear cell infiltrate; minimal

The following tissues were within normal limits:

KIDNEYS

Individual Animal Pathology Data

Animal Ref.: 401 Group: 4 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 44.3g

Organ Weights:

ADRENAL GLANDS	0.013g	BRAIN	0.528g	EPIDIDYMIDES	0.165g
HEART	0.233g	KIDNEYS	0.698g	LIVER	4.837g
SPLEEN	0.120g	TESTES	0.307g	THYMUS	0.025g

Gross Pathology Observations: None

Histo Pathology Observations:

HEART;
Cardiomyopathy; focal/multifocal; minimal

KIDNEYS;
Hypertrophy; tubular epithelium; minimal

LIVER;
Single cell necrosis; hepatocellular; minimal
Pigment increased; kupffer cells; minimal
Hepatocellular hypertrophy; mild
Mitotic figures; minimal

SALIVARY GLANDS;
Aggregates; lymphoid; focal/multifocal; minimal: submandibular salivary gland

Individual Animal Pathology Data

Animal Ref.: 401 Group: 4 Sex: Male (continued)

Histo Pathology Observations:

STERNUM;
Inflammation; granulomatous; focal; mild: with fibrosis

THYROID GLAND;
Dilated follicle(s); focal/multifocal; minimal

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM
EPIDIDYMIDES	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	ILEUM	JEJUNUM
LUNGS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		NOSE	OPTIC NERVES
PANCREAS	PARATHYROID GLANDS	PHARYNX/LARYNX	PITUITARY GLAND	PROSTATE	RECTUM	SCIATIC NERVE
SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN	STOMACH	TESTES
THYMUS	TRACHEA	URINARY BLADDER				

The following tissues have not been examined:

PEYERS PATCH; MISSING

Individual Animal Pathology Data

Animal Ref.: 402 Group: 4 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 43.7g

Organ Weights:

ADRENAL GLANDS	: 0.011g	BRAIN	: 0.492g	EPIDIDYMIDES	: 0.114g
HEART	: 0.206g	KIDNEYS	: 0.706g	LIVER	: 6.673g
SPLEEN	: 0.142g	TESTES	: 0.190g	THYMUS	: 0.044g

Gross Pathology Observations:

LIVER;
Discoloration; pale
Large

Histo Pathology Observations:

KIDNEYS;
Hypertrophy; tubular epithelium; minimal
Chronic progressive nephropathy; minimal

LIVER;
Single cell necrosis; hepatocellular; minimal
Pigment increased; kupffer cells; minimal
Hyperplasia; bile duct; minimal
Hepatocellular hypertrophy; mild
Mitotic figures; minimal

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM
EPIDIDYMIDES	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	LUNGS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		NOSE
OPTIC NERVES						
PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND	PROSTATE	RECTUM
SALIVARY GLANDS	SCIATIC NERVE	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN
STERNUM	STOMACH	TESTES	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER

Individual Animal Pathology Data

Animal Ref.: 403 Group: 4 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 44.6g

Organ Weights:

ADRENAL GLANDS	0.006g	BRAIN	0.481g	EPIDIDYMIDES	0.127g
HEART	0.196g	KIDNEYS	0.628g	LIVER	4.767g
SPLEEN	0.097g	TESTES	0.208g	THYMUS	0.038g

Gross Pathology Observations:

LIVER;
Large

Histo Pathology Observations:

ADRENAL GLANDS;
Hyperplasia; subcapular cell; focal/multifocal; minimal

KIDNEYS;
Hypertrophy; tubular epithelium; minimal
Chronic progressive nephropathy; minimal
Dilated tubule(s); focal/multifocal; minimal

LIVER;
Single cell necrosis; hepatocellular; minimal
Pigment increased; kupffer cells; minimal
Hepatocellular hypertrophy; mild
Mitotic figures; minimal
Mononuclear cell infiltrate; minimal

PITUITARY GLAND;
pars intermedia and pars nervosa not present in the section

The following tissues were within normal limits:

AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM	EPIDIDYMIDES
ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM
LUNGS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		NOSE	OPTIC NERVES
PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND	PROSTATE	RECTUM
SALIVARY GLANDS	SCIATIC NERVE	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN
STERNUM	STOMACH	TESTES	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER

Individual Animal Pathology Data

Animal Ref.: 404 Group: 4 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 45.5g

Organ Weights:

ADRENAL GLANDS	0.007g	BRAIN	0.490g	EPIDIDYMIDES	0.119g
HEART	0.219g	KIDNEYS	0.551g	LIVER	3.651g
SPLEEN	0.108g	TESTES	0.230g	THYMUS	0.055g

Gross Pathology Observations:

LIVER;
Discoloration; pale
Large

Histo Pathology Observations:

ADRENAL GLANDS;
Accessory cortical tissue; capsule; minimal

KIDNEYS;
Hypertrophy; tubular epithelium; minimal

LIVER;
Single cell necrosis; hepatocellular; minimal
Pigment increased; kupffer cells; minimal
Hepatocellular hypertrophy; mild
Mitotic figures; mild
Mononuclear cell infiltrate; minimal

SALIVARY GLANDS;
Aggregates; lymphoid; focal/multifocal; minimal: parotid gland

Individual Animal Pathology Data

Animal Ref.: 404 Group: 4 Sex: Male (continued)

Histo Pathology Observations:

TESTES;
Degeneration/atrophy; unilateral; minimal: vacuolation in sertoli cells/seminiferous tubular epithelium

The following tissues were within normal limits:

AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM	EPIDIDYMIDES
ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM
LUNGS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		NOSE	OPTIC NERVES
PANCREAS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND	PROSTATE	RECTUM	SCIATIC NERVE
SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN	STERNUM	STOMACH
THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER			

The following tissues have not been examined:

PARATHYROID GLANDS; MISSING

Individual Animal Pathology Data

Animal Ref.: 405 Group: 4 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 39.4g

Organ Weights:

ADRENAL GLANDS	: 0.009g	BRAIN	: 0.483g	EPIDIDYMIDES	: 0.096g
HEART	: 0.187g	KIDNEYS	: 0.737g	LIVER	: 3.940g
SPLEEN	: 0.100g	TESTES	: 0.185g	THYMUS	: 0.045g

Gross Pathology Observations:

LIVER;
Discoloration; pale
Large

Histo Pathology Observations:

KIDNEYS;
Hypertrophy; tubular epithelium; minimal

LIVER;
Single cell necrosis; hepatocellular; minimal
Pigment increased; kupffer cells; minimal
Hepatocellular hypertrophy; mild
Mitotic figures; mild

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM
EPIDIDYMIDES	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	LUNGS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		NOSE
OPTIC NERVES	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND	PROSTATE
RECTUM	SALIVARY GLANDS	SCIATIC NERVE	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD
SPLEEN						
STERNUM	STOMACH	TESTES	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER

Individual Animal Pathology Data

Animal Ref.: 406 Group: 4 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 43g

Organ Weights:

ADRENAL GLANDS	: 0.008g	BRAIN	: 0.512g	EPIDIDYMIDES	: 0.098g
HEART	: 0.207g	KIDNEYS	: 0.711g	LIVER	: 3.985g
SPLEEN	: 0.103g	TESTES	: 0.230g	THYMUS	: 0.022g

Gross Pathology Observations:

LIVER;
Large

Histo Pathology Observations:

ADRENAL GLANDS;
ONE OF A PAIR PRESENT

KIDNEYS;
Hypertrophy; tubular epithelium; minimal

LIVER;
Single cell necrosis; hepatocellular; minimal
Pigment increased; kupffer cells; minimal
Hepatocellular hypertrophy; minimal
Mononuclear cell infiltrate; minimal

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM
EPIDIDYMIDES	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	LUNGS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		NOSE
OPTIC NERVES						
PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND	PROSTATE	SALIVARY GLANDS
SCIATIC NERVE	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN	STERNUM
STOMACH	TESTES	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER	

The following tissues have not been examined:

RECTUM; MISSING

Individual Animal Pathology Data

Animal Ref.: 407 Group: 4 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 46.8g

Organ Weights:

ADRENAL GLANDS	0.017g	BRAIN	0.543g	EPIDIDYMIDES	0.103g
HEART	0.274g	KIDNEYS	0.676g	LIVER	4.247g
SPLEEN	0.099g	TESTES	0.207g	THYMUS	0.028g

Gross Pathology Observations:

LIVER;
Large

Histo Pathology Observations:

ADRENAL GLANDS;
Pigment; zona reticularis; lipogenic; multifocal; minimal
Hyperplasia; subcapular cell; focal/multifocal; minimal

KIDNEYS;
Dilated tubule(s); focal/multifocal; minimal

LIVER;
Single cell necrosis; hepatocellular; minimal
Pigment increased; kupffer cells; minimal
Hepatocellular hypertrophy; mild
Mitotic figures; minimal
Mononuclear cell infiltrate; minimal

The following tissues were within normal limits:

AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM	EPIDIDYMIDES
ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM
LUNGS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		NOSE	OPTIC NERVES
PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND	PROSTATE	RECTUM
SALIVARY GLANDS	SCIATIC NERVE	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN
STERNUM	STOMACH	TESTES	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER

Individual Animal Pathology Data

Animal Ref.: 408 Group: 4 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 44.1g

Organ Weights:

ADRENAL GLANDS	0.012g	BRAIN	1.748g E	EPIDIDYMIDES	0.074g
HEART	0.180g	KIDNEYS	0.687g	LIVER	9.674g
SPLEEN	0.246g	TESTES	0.194g	THYMUS	0.026g

Gross Pathology Observations:

LIVER;
Large

Histo Pathology Observations:

ADRENAL GLANDS;
Hyperplasia; subcapular cell; focal/multifocal; minimal

HEART;
Cardiomyopathy; focal/multifocal; minimal

KIDNEYS;
Hypertrophy; tubular epithelium; minimal

LIVER;
Single cell necrosis; hepatocellular; minimal
Pigment increased; kupffer cells; minimal
Hepatocellular hypertrophy; mild
Mitotic figures; minimal
Mononuclear cell infiltrate; minimal

Codes Used: (E) - Excluded from all calculations

Individual Animal Pathology Data

Animal Ref.: 408 Group: 4 Sex: Male (continued)

Histo Pathology Observations:

NOSE;
Inflammation; turbinate; focal/multifocal; minimal: L2

THYROID GLAND;
Dilated follicle(s); focal/multifocal; minimal

The following tissues were within normal limits:

AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM	EPIDIDYMIDES
ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	ILEUM	JEJUNUM	LUNGS
MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		OPTIC NERVES	PANCREAS	PARATHYROID GLANDS
PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND	PROSTATE	RECTUM	SALIVARY GLANDS	SCIATIC NERVE
SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN	STERNUM	STOMACH
TESTES	THYMUS	TRACHEA	URINARY BLADDER			

Individual Animal Pathology Data

Animal Ref.: 409 Group: 4 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 45.3g

Organ Weights:

ADRENAL GLANDS	0.009g	BRAIN	0.485g	EPIDIDYMIDES	0.151g
HEART	0.249g	KIDNEYS	0.843g	LIVER	5.189g
SPLEEN	0.135g	TESTES	0.252g	THYMUS	0.034g

Gross Pathology Observations:

LIVER;
Discoloration; pale
Large

Histo Pathology Observations:

KIDNEYS;
Hypertrophy; tubular epithelium; minimal

LIVER;
Single cell necrosis; hepatocellular; minimal
Pigment increased; kupffer cells; minimal
Hepatocellular hypertrophy; mild
Mitotic figures; mild
Mononuclear cell infiltrate; minimal

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM
EPIDIDYMIDES	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	LUNGS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		NOSE
OPTIC NERVES	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND	PROSTATE
RECTUM						
SALIVARY GLANDS	SCIATIC NERVE	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN
STERNUM	STOMACH	TESTES	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER

Individual Animal Pathology Data

Animal Ref.: 410 Group: 4 Sex: Male Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/27/09 Study Day No. (Week): 96 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/27/09

Terminal Body Weight: 46g

Organ Weights:

ADRENAL GLANDS	0.060g	BRAIN	0.462g	EPIDIDYMIDES	0.143g
HEART	0.201g	KIDNEYS	0.682g	LIVER	4.477g
SPLEEN	0.114g	TESTES	0.253g	THYMUS	0.053g

Gross Pathology Observations:

LIVER;
Discoloration; pale
Large

Histo Pathology Observations:

KIDNEYS;
Hypertrophy; tubular epithelium; minimal

LIVER;
Single cell necrosis; hepatocellular; minimal
Pigment increased; kupffer cells; minimal
Hepatocellular hypertrophy; mild
Mitotic figures; minimal
Mononuclear cell infiltrate; minimal

SALIVARY GLANDS;
Aggregates; lymphoid; focal/multifocal; minimal

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	COLON	DUODENUM
EPIDIDYMIDES	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	LUNGS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		NOSE
PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND	PROSTATE	RECTUM
SCIATIC NERVE	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN	STERNUM
STOMACH	TESTES	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER	

The following tissues have not been examined:

OPTIC NERVES; MISSING

Individual Animal Pathology Data

Animal Ref.: 151 Group: 1 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 34.1g

Organ Weights:

ADRENAL GLANDS	: 0.013g	BRAIN	: 0.518g	HEART	: 0.182g
KIDNEYS	: 0.396g	LIVER	: 1.831g	OVARIES	: 0.054g
SPLEEN	: 0.112g	THYMUS	: 0.043g	UTERUS	: 0.157g

Gross Pathology Observations: None

Histo Pathology Observations:

ADRENAL GLANDS;
Hyperplasia; subcapular cell; focal/multifocal; minimal

OPTIC NERVES;
ONE OF A PAIR PRESENT

STERNUM;
Atrophy; marrow; focal/multifocal; mild

THYROID GLAND;
Dilated follicle(s); focal/multifocal; minimal

The following tissues were within normal limits:

AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON	DUODENUM
ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM
KIDNEYS	LIVER	LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES
NOSE	OPTIC NERVES	OVARIES	OVIDUCTS	PANCREAS	PARATHYROID GLANDS	PHARYNX/LARYNX
PITUITARY GLAND						
RECTUM	SALIVARY GLANDS	SCIATIC NERVE	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN
STOMACH	THYMUS	TRACHEA	URINARY BLADDER	UTERUS	VAGINA	

The following tissues have not been examined:

PEYERS PATCH; MISSING

Individual Animal Pathology Data

Animal Ref.: 152 Group: 1 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 28.7g

Organ Weights:

ADRENAL GLANDS	0.014g	BRAIN	0.506g	HEART	0.172g
KIDNEYS	0.416g	LIVER	1.424g	OVARIES	0.047g
SPLEEN	0.103g	THYMUS	0.030g	UTERUS	0.401g

Gross Pathology Observations: None

Histo Pathology Observations:

ADRENAL GLANDS;
Accessory cortical tissue; capsule; minimal

ESOPHAGUS;
Degeneration/inflammation; muscularis; myofiber; focal; minimal

EYES;
lens missing in one eye section

OVARIES;
Cyst; unilateral; present

The following tissues were within normal limits:

AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON	DUODENUM
EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM	KIDNEYS
LIVER	LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES	
NOSE	OPTIC NERVES	OVIDUCTS	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX
PITUITARY GLAND						
RECTUM	SALIVARY GLANDS	SCIATIC NERVE	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN
STERNUM	STOMACH	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS
VAGINA						

Individual Animal Pathology Data

Animal Ref.: 153 Group: 1 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 28.3g

Organ Weights:

ADRENAL GLANDS	: 0.014g	BRAIN	: 0.499g	HEART	: 0.198g
KIDNEYS	: 0.433g	LIVER	: 1.467g	OVARIES	: 0.027g
SPLEEN	: 0.107g	THYMUS	: 0.033g	UTERUS	: 0.181g

Gross Pathology Observations:

JEJUNUM;
Deformity: diverticulum

Histo Pathology Observations:

ADRENAL GLANDS;
Hyperplasia; subcapular cell; focal/multifocal; mild

JEJUNUM;
Diverticulum; present

KIDNEYS;
Dilated tubule(s); focal/multifocal; minimal

NOSE;
Inflammation; turbinate; focal/multifocal; minimal: L2

The following tissues were within normal limits:

AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON	DUODENUM
ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	LIVER
LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		OPTIC NERVES
OVARIES						
OVIDUCTS	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND	RECTUM
SALIVARY GLANDS	SCIATIC NERVE	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN	STERNUM
STOMACH	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS	VAGINA

Individual Animal Pathology Data

Animal Ref.: 154 Group: 1 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 27.3g

Organ Weights:

ADRENAL GLANDS	: 0.009g	BRAIN	: 0.518g	HEART	: 0.162g
KIDNEYS	: 0.399g	LIVER	: 1.424g	OVARIES	: 0.024g
SPLEEN	: 0.100g	THYMUS	: 0.049g	UTERUS	: 0.174g

Gross Pathology Observations: None

Histo Pathology Observations:

ADRENAL GLANDS;
Hyperplasia; subcapular cell; focal/multifocal; minimal

KIDNEYS;
Dilated tubule(s); focal/multifocal; minimal

LIVER;
Mononuclear cell infiltrate; minimal

NOSE;
Inflammation; turbinate; focal/multifocal; minimal: L2

The following tissues were within normal limits:

AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON	DUODENUM
ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM
LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		OPTIC NERVES
OVARIES	OVIDUCTS	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND
RECTUM						
SALIVARY GLANDS	SCIATIC NERVE	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN	STERNUM
STOMACH	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS	VAGINA

Individual Animal Pathology Data

Animal Ref.: 155 Group: 1 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 29.1g

Organ Weights:

ADRENAL GLANDS	0.013g	BRAIN	0.516g	HEART	0.149g
KIDNEYS	0.406g	LIVER	1.262g	OVARIES	0.032g
SPLEEN	0.113g	THYMUS	0.038g	UTERUS	0.357g

Gross Pathology Observations: None

Histo Pathology Observations:

ADRENAL GLANDS;
Hyperplasia; subcapular cell; focal/multifocal; minimal

LIVER;
Mononuclear cell infiltrate; minimal

The following tissues were within normal limits:

AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON	DUODENUM
ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM
KIDNEYS	LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES	
NOSE	OPTIC NERVES	OVARIES	OVIDUCTS	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH
PHARYNX/LARYNX	RECTUM	SALIVARY GLANDS	SCIATIC NERVE	SKELETAL MUSCLE	SKIN	SPINAL CORD
SPLEEN	STERNUM	STOMACH	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER
UTERUS	VAGINA					

The following tissues have not been examined:

PITUITARY GLAND; MISSING

Individual Animal Pathology Data

Animal Ref.: 156 Group: 1 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 32.6g

Organ Weights:

ADRENAL GLANDS	0.017g	BRAIN	0.499g	HEART	0.190g
KIDNEYS	0.477g	LIVER	1.723g	OVARIES	0.032g
SPLEEN	0.137g	THYMUS	0.042g	UTERUS	0.390g

Gross Pathology Observations: None

Histo Pathology Observations:

SALIVARY GLANDS;
Aggregates; lymphoid; focal/multifocal; minimal: submandibular gland

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON
DUODENUM	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	KIDNEYS	LIVER	LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES	
MESENTERIC LYMPH NODES		NOSE	OPTIC NERVES	OVARIES	OVIDUCTS	PANCREAS
PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND	RECTUM	SCIATIC NERVE	SKELETAL MUSCLE
SKIN	SPINAL CORD	SPLEEN	STERNUM	STOMACH	THYMUS	THYROID GLAND
TRACHEA	URINARY BLADDER	UTERUS	VAGINA			

Individual Animal Pathology Data

Animal Ref.: 157 Group: 1 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 30.3g

Organ Weights:

ADRENAL GLANDS	0.012g	BRAIN	0.502g	HEART	0.142g
KIDNEYS	0.384g	LIVER	1.539g	OVARIES	0.027g
SPLEEN	0.111g	THYMUS	0.035g	UTERUS	0.209g

Gross Pathology Observations:

LIVER;
Discoloration; caudate; lobe: ventral red, dorsal tan

Histo Pathology Observations:

LIVER;
Focal necrosis; moderate: diffuse and restricted to one lobe (likely due to lobular torsion)

OPTIC NERVES;
ONE OF A PAIR PRESENT

STOMACH;
Inflammation; glandular; serosa; subacute/chronic; mild: focal and extended into adjacent mesenteric adipose tissue

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON
DUODENUM	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	KIDNEYS	LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES
NOSE	OPTIC NERVES	OVARIES	OVIDUCTS	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH
PHARYNX/LARYNX						
PITUITARY GLAND	RECTUM	SALIVARY GLANDS	SCIATIC NERVE	SKELETAL MUSCLE	SKIN	SPINAL CORD
SPLEEN	STERNUM	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS
VAGINA						

Individual Animal Pathology Data

Animal Ref.: 158 Group: 1 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 32.4g

Organ Weights:

ADRENAL GLANDS	0.018g	BRAIN	0.492g	HEART	0.161g
KIDNEYS	0.389g	LIVER	1.912g	OVARIES	0.030g
SPLEEN	0.113g	THYMUS	0.029g	UTERUS	0.236g

Gross Pathology Observations: None

Histo Pathology Observations:

OPTIC NERVES;
ONE OF A PAIR PRESENT

PITUITARY GLAND;
pars nervosa and pars intermedia not present in the section

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON
DUODENUM	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	KIDNEYS	LIVER	LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES	
MESENTERIC LYMPH NODES		NOSE	OPTIC NERVES	OVARIES	OVIDUCTS	PANCREAS
PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND	RECTUM	SALIVARY GLANDS	SCIATIC NERVE
SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN	STERNUM	STOMACH	THYMUS
THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS	VAGINA		

Individual Animal Pathology Data

Animal Ref.: 159 Group: 1 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 42.1g

Organ Weights:

ADRENAL GLANDS	: 0.016g	BRAIN	: 0.559g	HEART	: 0.183g
KIDNEYS	: 0.554g	LIVER	: 2.621g	OVARIES	: 0.043g
SPLEEN	: 0.178g	THYMUS	: 0.049g	UTERUS	: 0.232g

Gross Pathology Observations: None

Histo Pathology Observations:

ADRENAL GLANDS;
Hyperplasia; subcapular cell; focal/multifocal; minimal

KIDNEYS;
Chronic progressive nephropathy; minimal

LIVER;
Mononuclear cell infiltrate; minimal

THYROID GLAND;
Dilated follicle(s); focal/multifocal; minimal

The following tissues were within normal limits:

AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON	DUODENUM
ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM
LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		NOSE
OPTIC NERVES	OVARIES	OVIDUCTS	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX
PITUITARY GLAND						
RECTUM	SALIVARY GLANDS	SCIATIC NERVE	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN
STERNUM	STOMACH	THYMUS	TRACHEA	URINARY BLADDER	UTERUS	VAGINA

Individual Animal Pathology Data

Animal Ref.: 160 Group: 1 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 36.7g

Organ Weights:

ADRENAL GLANDS	: 0.013g	BRAIN	: 0.465g	HEART	: 0.165g
KIDNEYS	: 0.505g	LIVER	: 1.723g	OVARIES	: 0.044g
SPLEEN	: 0.116g	THYMUS	: 0.058g	UTERUS	: 0.199g

Gross Pathology Observations: None

Histo Pathology Observations:

ADRENAL GLANDS;
Accessory cortical tissue; capsule; minimal
Hyperplasia; subcapular cell; focal/multifocal; mild

KIDNEYS;
Aggregates; lymphocyte/plasmacyte; focal/multifocal; mild: perivascular

OPTIC NERVES;
ONE OF A PAIR PRESENT

SALIVARY GLANDS;
Aggregates; lymphoid; focal/multifocal; minimal: submandibular salivary gland

THYROID GLAND;
Dilated follicle(s); focal/multifocal; minimal

Individual Animal Pathology Data

Animal Ref.: 160 Group: 1 Sex: Female (continued)

The following tissues were within normal limits:

AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON	DUODENUM
ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM
LIVER	LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES	
NOSE	OPTIC NERVES	OVARIES	OVIDUCTS	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH
PHARYNX/LARYNX	PITUITARY GLAND	RECTUM	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN
STERNUM	STOMACH	THYMUS	TRACHEA	URINARY BLADDER	UTERUS	VAGINA

The following tissues have not been examined:

SCIATIC NERVE; MISSING

Individual Animal Pathology Data

Animal Ref.: 251 Group: 2 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 30.9g

Organ Weights:

ADRENAL GLANDS	0.024g	BRAIN	0.498g	HEART	0.170g
KIDNEYS	0.455g	LIVER	1.624g	OVARIES	0.037g
SPLEEN	0.088g	THYMUS	0.039g	UTERUS	0.470g

Gross Pathology Observations: None

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 252 Group: 2 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 32.6g

Organ Weights:

ADRENAL GLANDS	0.014g	BRAIN	0.518g	HEART	0.181g
KIDNEYS	0.409g	LIVER	1.819g	OVARIES	0.028g
SPLEEN	0.092g	THYMUS	0.038g	UTERUS	0.201g

Gross Pathology Observations: None

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 253 Group: 2 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 32.6g

Organ Weights:

ADRENAL GLANDS	: 0.026g	BRAIN	: 0.534g	HEART	: 0.192g
KIDNEYS	: 0.484g	LIVER	: 1.515g	OVARIES	: 0.049g
SPLEEN	: 0.120g	THYMUS	: 0.042g	UTERUS	: 0.407g

Gross Pathology Observations: None

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 254 Group: 2 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 31.5g

Organ Weights:

ADRENAL GLANDS	0.013g	BRAIN	0.528g	HEART	0.198g
KIDNEYS	0.462g	LIVER	1.745g	OVARIES	0.050g
SPLEEN	0.138g	THYMUS	0.051g	UTERUS	0.259g

Gross Pathology Observations: None

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 255 Group: 2 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 27.7g

Organ Weights:

ADRENAL GLANDS	: 0.021g	BRAIN	: 0.506g	HEART	: 0.178g
KIDNEYS	: 0.413g	LIVER	: 1.817g	OVARIES	: 0.039g
SPLEEN	: 0.095g	THYMUS	: 0.029g	UTERUS	: 0.381g

Gross Pathology Observations: None

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 256 Group: 2 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 33.8g

Organ Weights:

ADRENAL GLANDS	0.011g	BRAIN	0.495g	HEART	0.200g
KIDNEYS	0.495g	LIVER	1.800g	OVARIES	0.041g
SPLEEN	0.102g	THYMUS	0.031g	UTERUS	0.204g

Gross Pathology Observations: None

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 257 Group: 2 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 32.7g

Organ Weights:

ADRENAL GLANDS	0.018g	BRAIN	0.532g	HEART	0.181g
KIDNEYS	0.420g	LIVER	1.809g	OVARIES	0.045g
SPLEEN	0.120g	THYMUS	0.048g	UTERUS	0.219g

Gross Pathology Observations: None

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 258 Group: 2 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 32.9g

Organ Weights:

ADRENAL GLANDS	0.011g	BRAIN	0.480g	HEART	0.148g
KIDNEYS	0.386g	LIVER	1.484g	OVARIES	0.023g
SPLEEN	0.077g	THYMUS	0.047g	UTERUS	0.201g

Gross Pathology Observations: None

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 259 Group: 2 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 33.1g

Organ Weights:

ADRENAL GLANDS	: 0.017g	BRAIN	: 0.516g	HEART	: 0.151g
KIDNEYS	: 0.449g	LIVER	: 1.545g	OVARIES	: 0.053g
SPLEEN	: 0.106g	THYMUS	: 0.019g	UTERUS	: 0.300g

Gross Pathology Observations: None

Histo Pathology Observations:

LIVER;
Mononuclear cell infiltrate; minimal

Individual Animal Pathology Data

Animal Ref.: 260 Group: 2 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.1 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 33.1g

Organ Weights:

ADRENAL GLANDS	0.016g	BRAIN	0.477g	HEART	0.175g
KIDNEYS	0.473g	LIVER	1.811g	OVARIES	0.031g
SPLEEN	0.126g	THYMUS	0.052g	UTERUS	0.116g

Gross Pathology Observations: None

Histo Pathology Observations:

LIVER;
Mononuclear cell infiltrate; minimal

Individual Animal Pathology Data

Animal Ref.: 351 Group: 3 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 31.3g

Organ Weights:

ADRENAL GLANDS	: 0.013g	BRAIN	: 0.493g	HEART	: 0.153g
KIDNEYS	: 0.388g	LIVER	: 1.803g	OVARIES	: 0.046g
SPLEEN	: 0.081g	THYMUS	: 0.046g	UTERUS	: 0.411g

Gross Pathology Observations: None

Histo Pathology Observations:

LIVER;
Mononuclear cell infiltrate; minimal

Individual Animal Pathology Data

Animal Ref.: 352 Group: 3 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 33g

Organ Weights:

ADRENAL GLANDS	0.016g	BRAIN	0.474g	HEART	0.148g
KIDNEYS	0.379g	LIVER	1.649g	OVARIES	0.024g
SPLEEN	0.070g	THYMUS	0.036g	UTERUS	0.197g

Gross Pathology Observations: None

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 353 Group: 3 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 40.9g

Organ Weights:

ADRENAL GLANDS	: 0.013g	BRAIN	: 0.479g	HEART	: 0.193g
KIDNEYS	: 0.451g	LIVER	: 2.284g	OVARIES	: 0.047g
SPLEEN	: 0.106g	THYMUS	: 0.047g	UTERUS	: 0.110g

Gross Pathology Observations: None

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 354 Group: 3 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 29.5g

Organ Weights:

ADRENAL GLANDS	0.013g	BRAIN	0.498g	HEART	0.171g
KIDNEYS	0.377g	LIVER	1.571g	OVARIES	0.055g
SPLEEN	0.080g	THYMUS	0.043g	UTERUS	0.213g

Gross Pathology Observations: None

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 355 Group: 3 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 07/29/09 Study Day No. (Week): 6 (0) Mode of Death: UNSCHEDULED SACRIFICE
Date of Necropsy: 07/29/09

Terminal Body Weight: None

Gross Pathology Observations:

ESOPHAGUS;
Impaction

SKIN;
Foreign body; axilla; subcutaneous; right
Edema; ventral body; neck

Histo Pathology Observations:

BONE MARROW;
Hyperplasia; granulocytic; moderate: Increased M:E ratio, Shift in maturation sequence (increase in mature granulopoietic cells)

ESOPHAGUS;
Inflammation; transmural; acute; focal; moderate: ulcerative and necrotic lesion admixed with neutrophils and bacterial colonies

MANDIBULAR LYMPH NODES;
Necrosis; lymphoid; diffuse; moderate

MESENTERIC LYMPH NODES;
Necrosis; lymphoid; diffuse; moderate

NOSE;
Inflammation; turbinate; focal/multifocal; moderate: L2 at the base of nasala turbinate, exudate admixed with foreign body. small amount of exudate present in the nasal cavity lumen of L3 and L4 sections

Individual Animal Pathology Data

Animal Ref.: 355 Group: 3 Sex: Female (continued)

Histo Pathology Observations:

OPTIC NERVES;
ONE OF A PAIR PRESENT

PHARYNX/LARYNX;
Inflammation; acute; focal; moderate: focally extensive lesion in pharynx.
ulcerative and necrotic admixed with neutrophils and bacterial colonies

SALIVARY GLANDS;
Hypertrophy; acinar cell; diffuse; minimal: submandibular and sublingual
salivary glands

SPLEEN;
Necrosis; white pulp; lymphoid; diffuse; moderate

STERNUM;
Hyperplasia; marrow; granulocytic; moderate: Increased M:E ratio, Shift in
maturation sequence (increase in mature granulopoietic cells)

THYMUS;
Necrosis; cortex; lymphoid; diffuse; severe

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BRAIN	CECUM	CERVIX	COLON	DUODENUM
EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM	KIDNEYS
LIVER	LUNGS	MAMMARY GLANDS	OPTIC NERVES	OVARIES	OVIDUCTS	PANCREAS
PARATHYROID GLANDS	PITUITARY GLAND	RECTUM	SCIATIC NERVE	SKELETAL MUSCLE	SKIN	SPINAL CORD
STOMACH	THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS	VAGINA	

The following tissues have not been examined:

PEYERS PATCH; MISSING

Individual Animal Pathology Data

Animal Ref.: 356 Group: 3 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 34.5g

Organ Weights:

ADRENAL GLANDS	: 0.022g	BRAIN	: 0.514g	HEART	: 0.150g
KIDNEYS	: 0.458g	LIVER	: 1.825g	OVARIES	: 0.052g
SPLEEN	: 0.112g	THYMUS	: 0.058g	UTERUS	: 0.336g

Gross Pathology Observations: None

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 357 Group: 3 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 28.6g

Organ Weights:

ADRENAL GLANDS	0.012g	BRAIN	0.479g	HEART	0.145g
KIDNEYS	0.394g	LIVER	1.296g	OVARIES	0.137g
SPLEEN	0.085g	THYMUS	0.036g	UTERUS	0.245g

Gross Pathology Observations:

OVARIES;
Cyst; red; bilateral: 3mm

Histo Pathology Observations:

LIVER;
Focal necrosis; minimal
Mononuclear cell infiltrate; minimal

OVARIES;
Cyst; bilateral; present: cyst contains blood, foamy macrophages and hemosi-
derin laden macropahges

Individual Animal Pathology Data

Animal Ref.: 358 Group: 3 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 34g

Organ Weights:

ADRENAL GLANDS	: 0.022g	BRAIN	: 0.523g	HEART	: 0.206g
KIDNEYS	: 0.484g	LIVER	: 2.046g	OVARIES	: 0.069g
SPLEEN	: 0.134g	THYMUS	: 0.044g	UTERUS	: 0.182g

Gross Pathology Observations: None

Histo Pathology Observations:

LIVER;
Focal necrosis; minimal
Mononuclear cell infiltrate; minimal

Individual Animal Pathology Data

Animal Ref.: 359 Group: 3 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 31.7g

Organ Weights:

ADRENAL GLANDS	0.016g	BRAIN	0.523g	HEART	0.187g
KIDNEYS	0.403g	LIVER	1.611g	OVARIES	0.139g
SPLEEN	0.109g	THYMUS	0.155g	UTERUS	0.249g

Gross Pathology Observations:

OVARIES;
Cyst; red; bilateral: 4mm

Histo Pathology Observations:

OVARIES;
Cyst; bilateral; present: cyst contains blood, foamy macrophages and hemosi-
derin laden macropahges

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 360 Group: 3 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 0.5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 29.8g

Organ Weights:

ADRENAL GLANDS	0.013g	BRAIN	0.505g	HEART	0.171g
KIDNEYS	0.417g	LIVER	1.622g	OVARIES	0.090g
SPLEEN	0.079g	THYMUS	0.043g	UTERUS	0.407g

Gross Pathology Observations:

OVARIES;
Cyst; left; red: 3 mm dia.

Histo Pathology Observations:

OVARIES;
Cyst; unilateral; present: cyst contains blood, foamy macrophages and hemosiderin laden macropahges

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 451 Group: 4 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 29.1g

Organ Weights:

ADRENAL GLANDS	: 0.015g	BRAIN	: 0.517g	HEART	: 0.187g
KIDNEYS	: 0.475g	LIVER	: 2.561g	OVARIES	: 0.029g
SPLEEN	: 0.075g	THYMUS	: 0.029g	UTERUS	: 0.167g

Gross Pathology Observations: None

Histo Pathology Observations:

ADRENAL GLANDS;
Accessory cortical tissue; capsule; minimal
Hyperplasia; subcapular cell; focal/multifocal; minimal

LIVER;
Hepatocellular hypertrophy; minimal

The following tissues were within normal limits:

AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON	DUODENUM
ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM
KIDNEYS	LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES	
NOSE	OPTIC NERVES	OVARIES	OVIDUCTS	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH
PHARYNX/LARYNX	PITUITARY GLAND	RECTUM	SALIVARY GLANDS	SCIATIC NERVE	SKELETAL MUSCLE	SKIN
SPINAL CORD	SPLEEN	STERNUM	STOMACH	THYMUS	THYROID GLAND	TRACHEA
URINARY BLADDER	UTERUS	VAGINA				

Individual Animal Pathology Data

Animal Ref.: 452 Group: 4 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 34.7g

Organ Weights:

ADRENAL GLANDS	0.015g	BRAIN	0.471g	HEART	0.197g
KIDNEYS	0.427g	LIVER	3.176g	OVARIES	0.054g
SPLEEN	0.117g	THYMUS	0.063g	UTERUS	0.151g

Gross Pathology Observations: None

Histo Pathology Observations:

ADRENAL GLANDS;
Hyperplasia; subcapular cell; focal/multifocal; minimal

AORTA;
Inflammation; tunica media; subacute/chronic; focal; minimal: lesion present in the section of heart
Mineralization; tunica media; focal; minimal: lesion present in the section of heart

LIVER;
Pigment increased; kupffer cells; minimal
Hepatocellular hypertrophy; mild
Mononuclear cell infiltrate; minimal

PANCREAS;
Inflammation; chronic; focal; minimal: small number of scattered pigmented macrophages are present in the lesion

The following tissues were within normal limits:

BONE MARROW	BRAIN	CECUM	CERVIX	COLON	DUODENUM	ESOPHAGUS
EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM	KIDNEYS
LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		NOSE
OPTIC NERVES	OVARIES	OVIDUCTS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX	PITUITARY GLAND
RECTUM	SALIVARY GLANDS	SCIATIC NERVE	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN
STERNUM	STOMACH	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS
VAGINA						

Individual Animal Pathology Data

Animal Ref.: 453 Group: 4 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 32.3g

Organ Weights:

ADRENAL GLANDS	: 0.020g	BRAIN	: 0.521g	HEART	: 0.145g
KIDNEYS	: 0.443g	LIVER	: 1.840g	OVARIES	: 0.040g
SPLEEN	: 0.091g	THYMUS	: 0.034g	UTERUS	: 0.191g

Gross Pathology Observations: None

Histo Pathology Observations:

ADRENAL GLANDS;
Hyperplasia; subcapular cell; focal/multifocal; minimal

KIDNEYS;
Dilated tubule(s); focal/multifocal; minimal

LIVER;
Hepatocellular hypertrophy; minimal
Mononuclear cell infiltrate; minimal

SALIVARY GLANDS;
Aggregates; lymphoid; focal/multifocal; minimal: submandibular salivary gland

The following tissues were within normal limits:

AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON	DUODENUM
ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM
LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		NOSE
OPTIC NERVES	OVARIES	OVIDUCTS	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX
PITUITARY GLAND	RECTUM	SCIATIC NERVE	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN
STERNUM	STOMACH	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS
VAGINA						

Individual Animal Pathology Data

Animal Ref.: 454 Group: 4 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 33.6g

Organ Weights:

ADRENAL GLANDS	: 0.017g	BRAIN	: 0.550g	HEART	: 0.225g
KIDNEYS	: 0.473g	LIVER	: 2.992g	OVARIES	: 0.040g
SPLEEN	: 0.124g	THYMUS	: 0.049g	UTERUS	: 0.247g

Gross Pathology Observations: None

Histo Pathology Observations:

KIDNEYS;
Chronic progressive nephropathy; minimal
Dilated tubule(s); focal/multifocal; minimal

LIVER;
Hepatocellular hypertrophy; mild
Mononuclear cell infiltrate; minimal

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON
DUODENUM	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES	
NOSE	OPTIC NERVES	OVARIES	OVIDUCTS	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH
PHARYNX/LARYNX	PITUITARY GLAND	RECTUM	SALIVARY GLANDS	SCIATIC NERVE	SKELETAL MUSCLE	SKIN
SPINAL CORD	SPLEEN	STERNUM	STOMACH	THYMUS	THYROID GLAND	TRACHEA
URINARY BLADDER	UTERUS	VAGINA				

Individual Animal Pathology Data

Animal Ref.: 455 Group: 4 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 33.2g

Organ Weights:

ADRENAL GLANDS	0.020g	BRAIN	0.525g	HEART	0.173g
KIDNEYS	0.680g	LIVER	5.244g	OVARIES	0.036g
SPLEEN	2.608gE	THYMUS	0.047g	UTERUS	0.244g

Gross Pathology Observations:

LIVER;
Discoloration; pale
Large

Histo Pathology Observations:

ADRENAL GLANDS;
Hyperplasia; subcapular cell; focal/multifocal; minimal

KIDNEYS;
Dilated tubule(s); focal/multifocal; minimal

LIVER;
Hepatocellular hypertrophy; minimal

URINARY BLADDER;
Aggregates; lamina propria; lymphoid; focal/multifocal; minimal

Codes Used: (E) - Excluded from all calculations

Individual Animal Pathology Data

Animal Ref.: 455 Group: 4 Sex: Female (continued)

The following tissues were within normal limits:

AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON	DUODENUM
ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM
LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		NOSE
OPTIC NERVES	OVARIES	OVIDUCTS	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX
SALIVARY GLANDS	SCIATIC NERVE	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN	STERNUM
STOMACH	THYMUS	THYROID GLAND	TRACHEA	UTERUS	VAGINA	

The following tissues have not been examined:

PITUITARY GLAND; MISSING
RECTUM; MISSING

Individual Animal Pathology Data

Animal Ref.: 456 Group: 4 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 08/12/09 Study Day No. (Week): 20 (2) Mode of Death: UNSCHEDULED SACRIFICE
Date of Necropsy: 08/12/09

Terminal Body Weight: None

Gross Pathology Observations:

LUNGS;
Discoloration; dark: mild, mottled

Histo Pathology Observations:

LIVER;
Focal necrosis; mild: sub-capsular
Hepatocellular hypertrophy; minimal
Mononuclear cell infiltrate; minimal

SALIVARY GLANDS;
Hypertrophy; acinar cell; diffuse; mild: submandibular and sublingual salivary glands

THYMUS;
Necrosis; cortex; lymphoid; diffuse; severe

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON
DUODENUM	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	KIDNEYS	LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES
NOSE	OPTIC NERVES	OVARIES	OVIDUCTS	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH
PHARYNX/LARYNX	PITUITARY GLAND	RECTUM	SCIATIC NERVE	SKELETAL MUSCLE	SKIN	SPINAL CORD
SPLEEN	STERNUM	STOMACH	THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS
VAGINA						

Individual Animal Pathology Data

Animal Ref.: 457 Group: 4 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 34g

Organ Weights:

ADRENAL GLANDS	: 0.013g	BRAIN	: 0.526g	HEART	: 0.246g
KIDNEYS	: 0.518g	LIVER	: 2.734g	OVARIES	: 0.035g
SPLEEN	: 0.090g	THYMUS	: 0.043g	UTERUS	: 0.143g

Gross Pathology Observations: None

Histo Pathology Observations:

ADRENAL GLANDS;
Hyperplasia; subcapular cell; focal/multifocal; minimal

KIDNEYS;
Aggregates; lymphocyte/plasmacyte; focal/multifocal; minimal: perivascular
Chronic progressive nephropathy; minimal
Dilated tubule(s); focal/multifocal; minimal

LIVER;
Hepatocellular hypertrophy; mild

LUNGS;
Inflammation; subacute/chronic; focal; minimal

NOSE;
Inflammation; turbinate; focal/multifocal; minimal
Cyst; turbinate; mucosa; mild: L2

Individual Animal Pathology Data

Animal Ref.: 457 Group: 4 Sex: Female (continued)

Histo Pathology Observations:

Inclusions/crystals; respiratory epithelium; hyaline; mild: L2

SALIVARY GLANDS;
Aggregates; lymphoid; focal/multifocal; minimal: submandibular salivary gland

The following tissues were within normal limits:

AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON	DUODENUM
ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM	JEJUNUM
MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES		OPTIC NERVES	OVARIES
OVIDUCTS	PANCREAS	PARATHYROID GLANDS	PHARYNX/LARYNX	PITUITARY GLAND	RECTUM	SCIATIC NERVE
SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN	STERNUM	STOMACH	THYMUS
THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS	VAGINA		

The following tissues have not been examined:

PEYERS PATCH; MISSING

Individual Animal Pathology Data

Animal Ref.: 458 Group: 4 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 31g

Organ Weights:

ADRENAL GLANDS	0.009g	BRAIN	0.518g	HEART	0.202g
KIDNEYS	0.510g	LIVER	2.419g	OVARIES	0.070g
SPLEEN	0.108g	THYMUS	0.044g	UTERUS	0.323g

Gross Pathology Observations:

LIVER;
Discoloration; pale
Large

OVARIES;
Cyst; right; red: 2 mm dia.

Histo Pathology Observations:

LIVER;
Hepatocellular hypertrophy; minimal

OPTIC NERVES;
ONE OF A PAIR PRESENT

THYROID GLAND;
Dilated follicle(s); focal/multifocal; minimal

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON
DUODENUM	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	KIDNEYS	LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES
NOSE	OPTIC NERVES	OVARIES	OVIDUCTS	PANCREAS	PEYERS PATCH	PHARYNX/LARYNX
PITUITARY GLAND	RECTUM	SALIVARY GLANDS	SCIATIC NERVE	SKELETAL MUSCLE	SKIN	SPINAL CORD
SPLEEN	STERNUM	STOMACH	THYMUS	TRACHEA	URINARY BLADDER	UTERUS
VAGINA						

The following tissues have not been examined:

PARATHYROID GLANDS; MISSING

Individual Animal Pathology Data

Animal Ref.: 459 Group: 4 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 34.4g

Organ Weights:

ADRENAL GLANDS	: 0.018g	BRAIN	: 0.495g	HEART	: 0.174g
KIDNEYS	: 0.512g	LIVER	: 2.842g	OVARIES	: 0.037g
SPLEEN	: 3.003gE	THYMUS	: 0.058g	UTERUS	: 0.210g

Gross Pathology Observations:

LIVER;
Discoloration; pale
Large

Histo Pathology Observations:

LIVER;
Single cell necrosis; hepatocellular; minimal
Pigment increased; kupffer cells; minimal
Focal necrosis; mild
Hepatocellular hypertrophy; mild
Mononuclear cell infiltrate; mild

NOSE;
Exudate; lumen; unilateral; moderate: proteinaceous, present in all the sections (L1, L2, L3, L4)
Exudate; maxillary sinus; unilateral; moderate: proteinaceous, present in all the sections (L1, L2, L3, L4)

Codes Used: (E) - Excluded from all calculations

Individual Animal Pathology Data

Animal Ref.: 459 Group: 4 Sex: Female (continued)

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON
DUODENUM	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	KIDNEYS	LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES
OPTIC NERVES	OVARIES	OVIDUCTS	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH	PHARYNX/LARYNX
PITUITARY GLAND	RECTUM	SALIVARY GLANDS	SCIATIC NERVE	SKELETAL MUSCLE	SKIN	SPINAL CORD
SPLEEN	STERNUM	STOMACH	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER
UTERUS	VAGINA					

Individual Animal Pathology Data

Animal Ref.: 460 Group: 4 Sex: Female Species: Mouse Strain: Crl:CD1(ICR)

Test Material: H-28548 Dose: 5 mg/kg Route: Gavage-CV Study Type: 90 Day Subchronic
Date of Death : 10/28/09 Study Day No. (Week): 97 (13) Mode of Death: SCHEDULED SACRIFICE
Date of Necropsy: 10/28/09

Terminal Body Weight: 29.2g

Organ Weights:

ADRENAL GLANDS	: 0.014g	BRAIN	: 0.538g	HEART	: 0.174g
KIDNEYS	: 0.403g	LIVER	: 1.998g	OVARIES	: 0.044g
SPLEEN	: 0.072g	THYMUS	: 0.053g	UTERUS	: 0.250g

Gross Pathology Observations: None

Histo Pathology Observations:

LIVER;
Focal necrosis; mild
Hepatocellular hypertrophy; minimal
Mononuclear cell infiltrate; minimal

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE MARROW	BRAIN	CECUM	CERVIX	COLON
DUODENUM	ESOPHAGUS	EYES	FEMUR/KNEE JOINT	GALLBLADDER	HEART	ILEUM
JEJUNUM	KIDNEYS	LUNGS	MAMMARY GLANDS	MANDIBULAR LYMPH NODES		MESENTERIC LYMPH NODES
NOSE	OPTIC NERVES	OVARIES	OVIDUCTS	PANCREAS	PARATHYROID GLANDS	PEYERS PATCH
PHARYNX/LARYNX	PITUITARY GLAND	RECTUM	SALIVARY GLANDS	SCIATIC NERVE	SKELETAL MUSCLE	SKIN
SPINAL CORD	SPLEEN	STERNUM	STOMACH	THYMUS	THYROID GLAND	TRACHEA
URINARY BLADDER	UTERUS	VAGINA				

Appendix O
Plasma Analysis Data

ANALYSIS FOR H-28548 IN PLASMA SAMPLES

for

H-28548: Subchronic Toxicity
90-Day Gavage Study in Mice

Work Request Number:	18405
Service Code:	1307
Haskell Sample Number:	28548
DuPont Study Number	DuPont-18405-1307

MATERIALS AND METHODS

A. Sample Preparation and Chemical Analysis

1. Sample Collection and Treatment

The plasma samples from test days 0, 28, and 95 were received and stored frozen upon laboratory receipt, and when not in use. The plasma samples consisted of the following groupings.

Group		Daily Dosage
Male	Female	(mg/kg)[a]
1	1	0 (Control)
2	2	0.1
3	3	0.5
4	4	5

a Weight of test substance/kg animal body weight

2. Sample Preparation Procedure

The frozen plasma study samples were thawed to room temperature and mixed prior to sampling. A pipette was used to transfer 50-µL of plasma sample and 150 µL acetonitrile into a 96 well microtiter plate (2-mL well volume). The microtiter plate was vortexed to mix homogenously, and then centrifuged at 4150 rpm for 10 minutes at 20 ºC. The pipette was used to add 400 µL HPLC grade water into empty wells, and 100 µL sample supernatant. The plate was vortexed to mix homogenously. Additional sample dilutions were performed using a dilution solvent containing 15% acetonitrile in HPLC grade water. Finally, a 10 µL aliquot of internal standard stock solution was added to all prepared samples and QC samples prior to LC/MS/MS analysis. The final concentration of the ^{13}C-PFHxA internal standard was 10 ng/mL.

3. Stock Solutions and Calibration Standards

A stock solution of H-28548 (HFPO Dimer Acid, Ammonium Salt, purity = 84.0%) in HPLC grade water was prepared at 1650 ppm concentration. The stock solution was then used to prepare calibration standards in the dilution solvent at 0.00, 1.00, 2.00, 5.00, 15.0, 40.0, 120, and 196 ng/mL concentration with ^{13}C-PFHxA internal standard at 10 ng/mL concentration.

B. Instrument and Conditions

The prepared study samples, QC samples, and calibration standards were analyzed by LC/MS/MS to quantify the levels of H-28548. The instrument and conditions were as follows:

HPLC Instrument: Agilent Model 1100
MS Instrument: Quattro Micro, Micromass
Software: MassLynx and QuanLynx version 4.1.

LC Parameters:
Column: Zorbax RX-C8 2.1x150mm with 5 µm particle size
Mobile Phase: A: 0.15% acetic acid in HPLC grade water
B: 0.15% acetic acid in Acetonitrile

Gradient:

Time (min)	% A	%B	Flow (mL/min)
0.00	90.0	10.0	0.600
0.50	90.0	10.0	0.600
0.60	50.0	50.0	0.600
4.00	50.0	50.0	0.600
4.10	5.0	95.0	0.600
7.00	5.0	95.0	0.600
7.10	90.0	10.0	0.600
10.00	90.0	10.0	0.600

Column Temperature: 40 °C
Injection Volume: 25 µL

MS Parameters:
Capillary Voltage: 3.2 kV
Source Temperature: 120 °C
Desolvation Temperature: 400 °C
Cone Gas Flow: 40 L/Hr
Desolvation Gas Flow: 400 L/Hr
Quadrupole Resolution: Quad. 1: LM and HM = 15
Quad. 2: LM and HM = 15
Collision Gas and Pressure: Argon .00366 mbar
Ionization Mode: Electrospray, Negative Ion
Divert Valve: 0-2.75 min to waste. 2.75 min to end to source

MRM Data Acquisition:	Analyte	MRM Transition
	H-28548	329 → 285
	^{13}C-PFHxA Internal Standard	315 → 270
Collision Energy:	5.00 eV	
Dwell	0.100 seconds	
Cone Voltage:	9.00 V	

C. Quantitation

The calibration standard curve was generated by regression analysis using the chromatographic peak areas of the calibration standard solutions analyzed in duplicate. Sample concentrations were calculated using an external standard technique. The dual isotopically labeled perfluorohexanoic acid internal standard (^{13}C-PFHxA) has the following structure: $CF_3CF_2CF_2CF_2{}^{13}CF_2{}^{13}C(O)OH$. Additional sample dilutions were performed as necessary to ensure that the peak area responses were within the calibration curve.

RESULTS AND DISCUSSION

A. Calibration Standards and Curves

The calibration curves were generated based on resulting peak areas of the parent compound H-28548 using an internal standard technique with a quadratic equation and 1/x weighting.

B. Limit of Detection and Limit of Quantitation

The limit of detection (LOD) and limit of quantitation (LOQ) for H-28548 was 5 ng/mL and 20 ng/mL in plasma, respectively. The limit of detection was based on a concentration that provides a peak-to-peak intensity that is 3x the noise multiplied by the sample preparation dilution factor of 20x. The LOQ was determined by multiplying the lowest level calibration standard of 1 ng/mL by the sample preparation dilution factor of 20x. The lowest calibration standard had a peak-to-peak intensity that was at least 10x the noise of a control plasma sample.

C. Plasma Sample Results

The H-28548 eluted as a well resolved chromatographic peak at a retention time of approximately 3.5 minutes. The ^{13}C-PFHxA internal standard had a retention time of approximately 3.45 minutes.

The individual male mouse plasma results from Appendix A are summarized in Table 1 and plotted in Figure 1.

The individual female mouse plasma results from Appendix B are summarized in Table 2 and plotted in Figure 2.

The test substance concentration in blood was similar on days 0, 28, and 95 in female mice, indicating that steady-state concentrations were achieved on the first day of dosing. This is consistent with a test substance that was cleared rapidly from the blood within one dosing interval (24 hours for this study). The test substance concentration in blood from male mice was slightly lower on day 0 than on day 28, but the day 28 and day 95 concentrations were similar, indicating steady state had been achieved by day 28. Compared to female mice, male mice took longer to achieve steady-state concentrations in blood. The plasma concentration was linear with dose (Figure 3), implying that absorption was not saturated over the range of doses tested in this study. Test substance was not present in plasma from control animals.

TABLES

TABLE 1
SUMMARY OF PLASMA CONCENTRATIONS FOR PARENT COMPOUND H-28548 IN MALE MICE

Day	Dosage (mg/kg/day)	Average Conc. (ng/mL)[a]	SD	n
Day 0	0 (Control)	ND[b]	N/A	5
Day 0	0.1	736	99	5
Day 0	0.5	3806	1197	5
Day 0	5	42580	5214	5
Day 28	0 (Control)	ND	N/A	5
Day 28	0.1	1124	238	5
Day 28	0.5	7182	3055	5
Day 28	5	52240	16725	5
Day 95	0 (Control)	ND	N/A	5
Day 95	0.1	1276	309	5
Day 95	0.5	7068	2398	4
Day 95	5	67980	13717	5

a) Plasma results are reported in units of ng/mL of H-28548.
b) Not Detected. The detection limit of the method was 5 ng/mL H-28548 in plasma.

TABLE 2
SUMMARY OF PLASMA CONCENTRATIONS FOR PARENT COMPOUND H-28548 IN FEMALE MICE

Day	Dosage (mg/kg/day)	Average Conc. (ng/mL)[a]	SD	n
Day 0	0 (Control)	ND[b]	N/A	5
Day 0	0.1	824	72	5
Day 0	0.5	3606	1308	5
Day 0	5	35340	9262	5
Day 28	0 (Control)	ND	N/A	5
Day 28	0.1	704	350	5
Day 28	0.5	4198	1239	4
Day 28	5	46580	16842	5
Day 95	0 (Control)	ND	N/A	4
Day 95	0.1	740	282	5
Day 95	0.5	5438	1696	5
Day 95	5	45580	5741	5

a) Plasma results are reported in units of ng/mL of H-28548.
b) Not Detected. The detection limit of the method was 5 ng/mL H-28548 in plasma.

FIGURES

FIGURE 1
CONCENTRATION OF H-28548 IN PLASMA FROM MALE MICE ON DAY 0, 28, AND 95

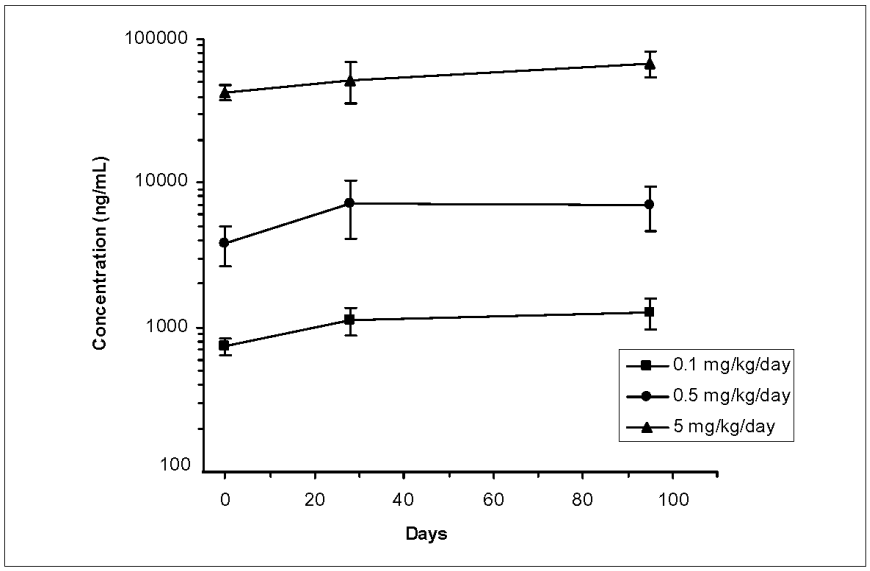


FIGURE 2
CONCENTRATION OF H-28548 IN PLASMA FROM FEMALE MICE ON DAY 0, 28, AND 95

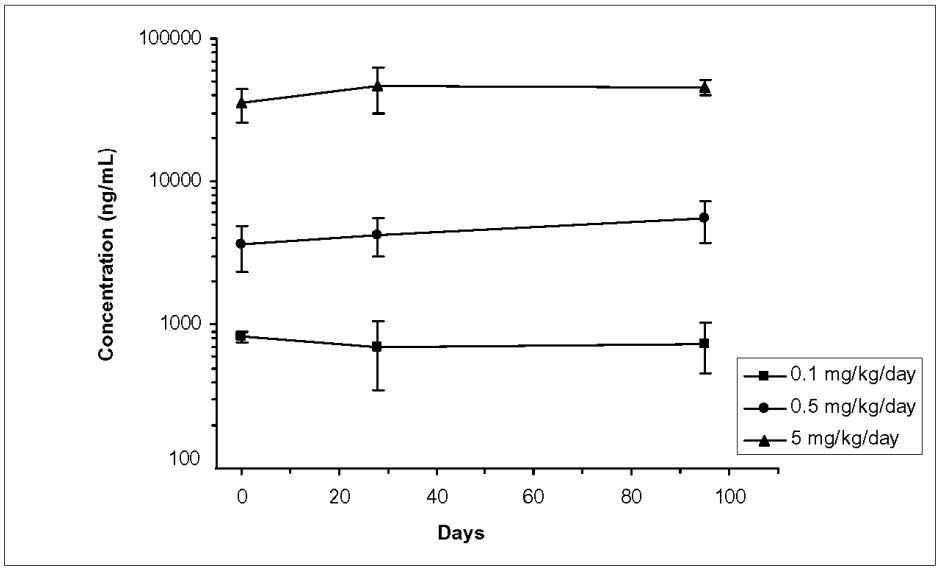
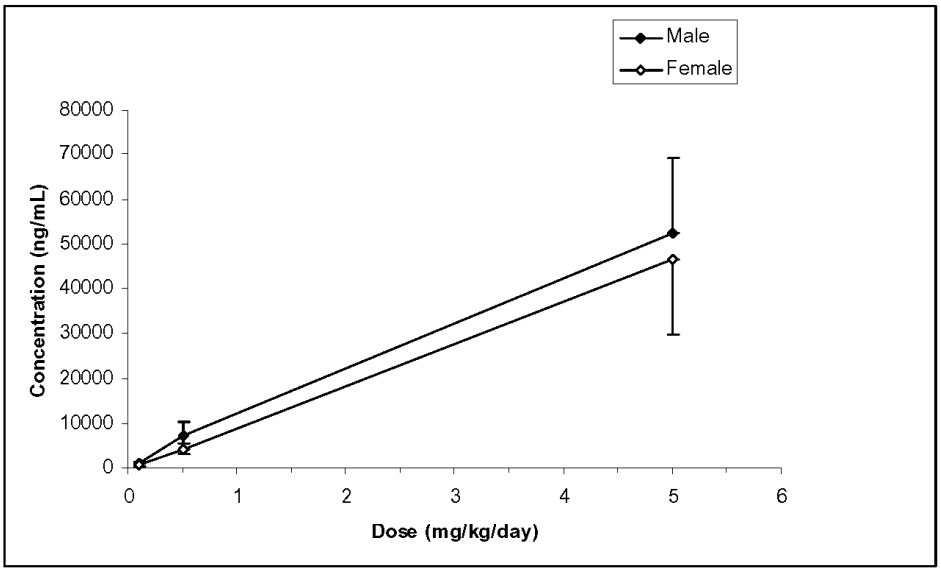


FIGURE 3
CONCENTRATION OF H-28548 IN PLASMA FROM MALE AND FEMALE MICE ON DAY 28



APPENDICES

APPENDIX A
Individual Plasma Concentrations of Parent Compound H-28548 in Male Mice

Sample Name	Day	Sex	Group	Dosage (mg/kg/day)	H-28548 (ng/mL Plasma)
Plasma, Day 0, Male 121__	Day 0	M	1	0 (Control)	ND
Plasma, Day 0, Male 122__	Day 0	M	1	0 (Control)	ND
Plasma, Day 0, Male 123__	Day 0	M	1	0 (Control)	ND
Plasma, Day 0, Male 124__	Day 0	M	1	0 (Control)	ND
Plasma, Day 0, Male 125__	Day 0	M	1	0 (Control)	ND
Plasma, Day 0, Male 221__	Day 0	M	2	0.1	794
Plasma, Day 0, Male 222__	Day 0	M	2	0.1	595
Plasma, Day 0, Male 223__	Day 0	M	2	0.1	775
Plasma, Day 0, Male 224__	Day 0	M	2	0.1	839
Plasma, Day 0, Male 225__	Day 0	M	2	0.1	676
Plasma, Day 0, Male 321__	Day 0	M	3	0.5	4480
Plasma, Day 0, Male 322__	Day 0	M	3	0.5	3860
Plasma, Day 0, Male 323__	Day 0	M	3	0.5	1720
Plasma, Day 0, Male 324__	Day 0	M	3	0.5	4530
Plasma, Day 0, Male 325__	Day 0	M	3	0.5	4440
Plasma, Day 0, Male 421__	Day 0	M	4	5	39700
Plasma, Day 0, Male 422__	Day 0	M	4	5	45500
Plasma, Day 0, Male 423__	Day 0	M	4	5	47300
Plasma, Day 0, Male 425__	Day 0	M	4	5	45600
Plasma, Day 0, Male 427__	Day 0	M	4	5	34800
Plasma, Day 28, Male 116_	Day 28	M	1	0 (Control)	ND
Plasma, Day 28, Male 117_	Day 28	M	1	0 (Control)	ND
Plasma, Day 28, Male 118_	Day 28	M	1	0 (Control)	ND
Plasma, Day 28, Male 119_	Day 28	M	1	0 (Control)	ND
Plasma, Day 28, Male 120_	Day 28	M	1	0 (Control)	ND
Plasma, Day 28, Male 216_	Day 28	M	2	0.1	1350
Plasma, Day 28, Male 217_	Day 28	M	2	0.1	770
Plasma, Day 28, Male 218_	Day 28	M	2	0.1	998
Plasma, Day 28, Male 219_	Day 28	M	2	0.1	1290
Plasma, Day 28, Male 220_	Day 28	M	2	0.1	1210
Plasma, Day 28, Male 316_	Day 28	M	3	0.5	11500
Plasma, Day 28, Male 317_	Day 28	M	3	0.5	6170
Plasma, Day 28, Male 318_	Day 28	M	3	0.5	8560
Plasma, Day 28, Male 319_	Day 28	M	3	0.5	6390
Plasma, Day 28, Male 320_	Day 28	M	3	0.5	3290
Plasma, Day 28, Male 416_	Day 28	M	4	5	28800
Plasma, Day 28, Male 417_	Day 28	M	4	5	50500
Plasma, Day 28, Male 418_	Day 28	M	4	5	65800
Plasma, Day 28, Male 419_	Day 28	M	4	5	70600
Plasma, Day 28, Male 420_	Day 28	M	4	5	45500
Plasma, Day 95, Male 111_	Day 95	M	1	0 (Control)	ND
Plasma, Day 95, Male 113_	Day 95	M	1	0 (Control)	ND
Plasma, Day 95, Male 114_	Day 95	M	1	0 (Control)	ND
Plasma, Day 95, Male 115_	Day 95	M	1	0 (Control)	ND
Plasma, Day 95, Male 127_	Day 95	M	1	0 (Control)	ND
Plasma, Day 95, Male 211_	Day 95	M	2	0.1	1160
Plasma, Day 95, Male 212_	Day 95	M	2	0.1	1460

Sample Name	Day	Sex	Group	Dosage (mg/kg/day)	H-28548 (ng/mL Plasma)
Plasma, Day 95, Male 213_	Day 95	M	2	0.1	899
Plasma, Day 95, Male 214_	Day 95	M	2	0.1	1160
Plasma, Day 95, Male 215_	Day 95	M	2	0.1	1700
Plasma, Day 95, Male 311_	Day 95	M	3	0.5	8130
Plasma, Day 95, Male 313_	Day 95	M	3	0.5	5210
Plasma, Day 95, Male 314_	Day 95	M	3	0.5	4980
Plasma, Day 95, Male 315_	Day 95	M	3	0.5	9950
Plasma, Day 95, Male 411_	Day 95	M	4	5	60800
Plasma, Day 95, Male 412_	Day 95	M	4	5	64000
Plasma, Day 95, Male 413_	Day 95	M	4	5	91400
Plasma, Day 95, Male 414_	Day 95	M	4	5	67400
Plasma, Day 95, Male 415_	Day 95	M	4	5	56300

Note: ND = Not Detected. The detection limit of the method was 5 ng/mL in plasma.

APPENDIX B
Individual Plasma Concentrations of Parent Compound H-28548 in Female Mice

Sample Name	Day	Sex	Group	Dosage (mg/kg/day)	H-28548 (ng/mL Plasma)
Plasma, Day 0, Female 171	Day 0	F	1	0 (Control)	ND
Plasma, Day 0, Female 172	Day 0	F	1	0 (Control)	ND
Plasma, Day 0, Female 173	Day 0	F	1	0 (Control)	ND
Plasma, Day 0, Female 174	Day 0	F	1	0 (Control)	ND
Plasma, Day 0, Female 175	Day 0	F	1	0 (Control)	ND
Plasma, Day 0, Female 271	Day 0	F	2	0.1	701
Plasma, Day 0, Female 272	Day 0	F	2	0.1	834
Plasma, Day 0, Female 273	Day 0	F	2	0.1	889
Plasma, Day 0, Female 274	Day 0	F	2	0.1	854
Plasma, Day 0, Female 275	Day 0	F	2	0.1	840
Plasma, Day 0, Female 371	Day 0	F	3	0.5	3810
Plasma, Day 0, Female 372	Day 0	F	3	0.5	4150
Plasma, Day 0, Female 373	Day 0	F	3	0.5	1490
Plasma, Day 0, Female 374	Day 0	F	3	0.5	3550
Plasma, Day 0, Female 375	Day 0	F	3	0.5	5030
Plasma, Day 0, Female 471	Day 0	F	4	5	40300
Plasma, Day 0, Female 472	Day 0	F	4	5	42900
Plasma, Day 0, Female 473	Day 0	F	4	5	27100
Plasma, Day 0, Female 474	Day 0	F	4	5	23600
Plasma, Day 0, Female 475	Day 0	F	4	5	42800
Plasma, Day 28, Female 166	Day 28	F	1	0 (Control)	ND
Plasma, Day 28, Female 167	Day 28	F	1	0 (Control)	ND
Plasma, Day 28, Female 168	Day 28	F	1	0 (Control)	ND
Plasma, Day 28, Female 169	Day 28	F	1	0 (Control)	ND
Plasma, Day 28, Female 170	Day 28	F	1	0 (Control)	ND
Plasma, Day 28, Female 266	Day 28	F	2	0.1	944
Plasma, Day 28, Female 267	Day 28	F	2	0.1	207
Plasma, Day 28, Female 268	Day 28	F	2	0.1	473
Plasma, Day 28, Female 269	Day 28	F	2	0.1	1030
Plasma, Day 28, Female 270	Day 28	F	2	0.1	866
Plasma, Day 28, Female 366	Day 28	F	3	0.5	4290
Plasma, Day 28, Female 368	Day 28	F	3	0.5	5320
Plasma, Day 28, Female 369	Day 28	F	3	0.5	4730
Plasma, Day 28, Female 370	Day 28	F	3	0.5	2450
Plasma, Day 28, Female 466	Day 28	F	4	5	75600
Plasma, Day 28, Female 467	Day 28	F	4	5	46500
Plasma, Day 28, Female 468	Day 28	F	4	5	35400
Plasma, Day 28, Female 469	Day 28	F	4	5	35500
Plasma, Day 28, Female 470	Day 28	F	4	5	39900
Plasma, Day 95, Female 161	Day 95	F	1	0 (Control)	ND
Plasma, Day 95, Female 162	Day 95	F	1	0 (Control)	ND
Plasma, Day 95, Female 163	Day 95	F	1	0 (Control)	ND
Plasma, Day 95, Female 164	Day 95	F	1	0 (Control)	ND
Plasma, Day 95, Female 261	Day 95	F	2	0.1	504
Plasma, Day 95, Female 262	Day 95	F	2	0.1	841
Plasma, Day 95, Female 263	Day 95	F	2	0.1	440
Plasma, Day 95, Female 264	Day 95	F	2	0.1	1140
Plasma, Day 95, Female 265	Day 95	F	2	0.1	777

Sample Name	Day	Sex	Group	Dosage (mg/kg/day)	H-28548 (ng/mL Plasma)
Plasma, Day 95, Female 361	Day 95	F	3	0.5	7050
Plasma, Day 95, Female 362	Day 95	F	3	0.5	4020
Plasma, Day 95, Female 363	Day 95	F	3	0.5	7260
Plasma, Day 95, Female 364	Day 95	F	3	0.5	5310
Plasma, Day 95, Female 365	Day 95	F	3	0.5	3550
Plasma, Day 95, Female 461	Day 95	F	4	5	39800
Plasma, Day 95, Female 462	Day 95	F	4	5	51700
Plasma, Day 95, Female 463	Day 95	F	4	5	51700
Plasma, Day 95, Female 464	Day 95	F	4	5	43500
Plasma, Day 95, Female 465	Day 95	F	4	5	41200

Note: ND = Not Detected. The detection limit of the method was 5 ng/mL in plasma.