APPENDIX A: PROTOCOL AND PROTOCOL AMENDMENTS

PRODUCT IDENTIFICATION

Silk Fibroin

SILK FIBROIN: A 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS

PRODUCT IDENTIFICATION

Silk Fibroin

PSL PROTOCOL NO.

P713.01 CMR

PERFORMING LABORATORY

Product Safety Labs
2394 US Highway 130
Dayton, New Jersey 08810

PSL STUDY NUMBER

51651

STUDY DIRECTOR

SPONSOR

Cambridge Crops, Inc.
444 Somerville Ave.
Somerville, MA 02143

Product Safety Labs

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1. TITLE OF STUDY: SILK FIBROIN: A 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS

2. OBJECTIVE

The objective of this study is to evaluate the potential subchronic toxicity of Silk Fibroin in male and female rats likely to arise from repeated exposure, via oral gavage, over a test period of at least 28 days. A no-observed-adverse-effect-level (NOAEL) will be determined.

3. STUDY DIRECTOR

Raghavendra Gowda Ph.D
Study Director
Tel: 732-438-5100 x1542
Email: RaghavendraGowda@ProductSafetyLabs.com

4. NAME AND ADDRESS OF THE TESTING FACILITY

5. SPONSOR

Cambridge Crops, Inc
444 Somerville Ave.
Somerville, MA 02143

6. SPONSOR REPRESENTATIVE

Laith Abu-Taleb
Cambridge Crops, Inc.
444 Somerville Ave.
Somerville, MA 02143
Tel: 301-580-3965
Email: laith@cambridgecrops.com

7. DATES

Proposed In-Life Start Date: November 5, 2019

Proposed Experimental Termination Date: December 4, 2019

8. TEST SUBSTANCE

9. NAME AND ADDRESS OF THE TESTING FACILITY

Product Safety Labs (PSL)
2394 US Highway 130
Dayton, NJ 08810
Tel: 732 438 5100

9.A Source

The test substance will be provided by the Sponsor.

9.B Identification

The test substance is identified using the following information provided by the Sponsor:

Product Identifier: Silk Fibroin
Composition: 5.0% Silk Fibroin (CAS# 9007-76-5) & 95% Water

Documentation of the methods of synthesis, fabrication, or derivation of the test substance is retained by the Sponsor.

Sponsor has provided vials of a solution of the test substance at the highest dose concentration:

Identity: Silk fibroin solution
PSL ID: 191015-2D
Batch #: 215
Concentration: 50 mg/mL, aqueous
Physical Description: Slightly yellow liquid
Storage Conditions: -20°C (thawed in refrigerator before use)
Expiration Date: Stable at 4 °C for one month. Upon thawing, please use in one month

9.C Analysis

The test substance, as received, is expected to be stable for the duration of the study. The stability of the test substance and verification of the test substance in the dose preparations will be determined as part of this study (Section 10.C).

9.D Hazards

Appropriate routine safety precautions will be exercised in the handling of the test and control substances unless otherwise indicated by the Sponsor.

10. GENERAL TEST SYSTEM PARAMETERS

10.A Animal Requirements

10.A.1 Number of Animals: 80

10.A.2 Number of Groups: 4 (3 dose levels + 1 control group)

10.A.3 Number of Animals per Group: 20 (10 males, 10 females)

10.A.4 Sex: Male and Female; females will be nulliparous and non-pregnant

10.A.5 Species/Strain: CRL Sprague-Dawley CD® IGS rats

10.A.6 Age/Weight: Seven to eight weeks at initiation; the weight variation will not exceed ± 20% of the mean weight for each sex.

10.A.7 Supplier: Charles River Laboratories, Inc. Rats will be shipped in filtered cartons by airfreight and/or truck.

10.B Test System Justification

The Sprague Dawley® rat is the system of choice because, historically, it has been a preferred and commonly used species for oral toxicity tests. The current state of scientific knowledge does not provide acceptable alternatives to the use of live animals to accomplish the objective of this study.

PSL is AAALAC (Association for Assessment and Accreditation of Laboratory Animal Care) accredited and certified in the appropriate care of all live experimental animals and maintains current staff training, ensuring animals will be handled humanely during the experimental phase of this study, and will meet all guideline standards[1].

10.C Husbandry

10.C.1 Housing

The animals will be housed in cages which conform to the size recommendations in the latest *Guide for the Care and Use of Laboratory Animal*[1]. Litter paper placed beneath the cage will be changed at least three times/week. The animal room will have a 12-hour light/dark cycle and will be kept clean and vermin free. Environmental controls are set to maintain temperature and relative humidity ranges of 23 ± 3°C and 30-70%, respectively. Observed ranges will be documented in the raw data.

10.C.2 Acclimation

The animals will be conditioned to the housing facilities for a minimum of five days prior to testing. Body weights and clinical observations will be recorded at least two times prior to study start.

10.C.3 Feed

2016 Certified Envigo Teklad Global Rodent Diet® will be stored in a dedicated temperature and humidity monitored feed storage site and will be available *ad libitum* during acclimation and throughout the study except for times of fasting.

10.C.4 Water

Filtered tap water will be available *ad libitum* from individual bottles attached to the cages or from an automatic watering access system. Water analysis is conducted by Precision Analytical Services, Inc., Toms River, NJ and South Brunswick Municipal Water Supply, South Brunswick, NJ.

10.C.5 Contaminants

There are no known contaminants reasonably expected to be found in the food or water that would interfere with the results of this study. Routine analysis consisting of each lot of feed used in this study will be received from Envigo Teklad, Madison, WI. Water analysis is conducted periodically and the records are kept on file at Product Safety Labs. The date(s) of the most recent analyses will be reported in the final report.

10.C.6 Viral Screen

Serum samples from naïve rats housed in the same room as test animals, as part of PSL's sentinel health monitoring program, will be evaluated for the absence of viruses near the end of the in-life portion of the study (PSL SOP #755).

[1] National Research Council (2011). *Guide for the Care and use of Laboratory Animals (8th ed)*. Washington, DC: The National Academies Press.

10.D Identification

10.D.1 Cage

Each cage will be identified by a cage card indicating at least the study number, dose level, group assignment, individual animal identification and sex of the animal.

10.D.2 Animal

Each animal will be given a sequential number in addition to being uniquely identified with a Monel® self-piercing stainless steel ear tag.

11. EXPERIMENTAL DESIGN

11.A Route of Administration

The test substance will be administered by oral gavage.

11.B Justification of Route of Administration

The oral route of administration will be used because it is recommended in the referenced guidelines (Section 14.C.), and because human exposure may occur via this route.

11.C Control of Bias

Animals will be randomly assigned to test groups according to PSL SOP # 714.

11.D Dose Levels

Ten male and ten female test animals will be randomly assigned to each of the following test groups:

Group	No. Animals/ Group (M/F)	Oral Gavage Dose of Test Substance (mg/kg/day)	Dose Volume (mL/kg)	Concentration (mg/mL)[b]
1	10/10	0 (Vehicle Control)[a]	10	0
2	10/10	125		12.5
3	10/10	250		25
4	10/10	500		50

[a] Distilled Water
[b] Appropriate concentrations of the test substance as received in vehicle to achieve the target dose level

11.E Justification of Dose Level Selection

The dose levels of 0, (vehicle control), 125, 250, and 500 mg/kg/day of Silk Fibroin were selected by the Sponsor in consultation with the Study Director and was based on a previous 14-Day range-

finding study (PSL Study#50725)[1]. The high dose was previously selected because of solubility limitations. The high dose is a tolerable dose and is not expected to cause marked toxicity. The intermediate and low dose levels were selected to derive a dose-response for any effects observed.

12. GENERAL PROCEDURES

12.A Selection of Animals

Eighty healthy male and female rats will be used on test. Animals will be selected for this study on the basis of adequate body weight gain, freedom from clinical signs of disease or injury, and a body weight within ±20% of the mean within a sex. Selected rats will be distributed by randomization according to stratification by body weight so that there will be no statistically significant difference among group body weight means.

12.B Dose Preparations and Procedures

12.B.1 Test Substance Preparation

The test substance has been provided by the Sponsor at the highest concentration (50 mg/mL). Vials will be thawed overnight in refrigerator before use, and vortexed two (2) times in five (5) second intervals, with a ten (10) second waiting period between each vortex before use. Further dilutions will be made with distilled water to produce formulations containing 25 (intermediate dose) and 12.5 (low dose) concentrations of the test substance. These will be prepared daily. Formulations will be mixed until a visually homogeneous mixture is achieved. Preparations of the test substance will be documented in the raw data.

12.B.2 Dose Calculations

Individual doses will be calculated based on the most recent weekly body weights and will be adjusted to maintain the targeted dose level for all rats (i.e. mg/kg). All doses will be administered volumetrically at 10 mL/kg. The control group will receive vehicle only, at the same dose volume as the test animals.

12.B.3 Dosing

Each animal will be dosed by oral intubation, using a stainless steel ball-tipped gavage needle attached to an appropriate syringe. Dose administration will be once daily (7 days/week). The first day of administration will be considered Day 1 of the study. Dosing will be at approximately the same time each day (± 2 hours) with an exception on the day(s) hematology and/or clinical chemistry, and urinalysis samples are collected. Prepared dosing formulations remaining will be discarded following each administration and sampling (as required).

12.C Analysis of Test Substance and Dose Preparations

12.C.1 Sampling

The prepared dosing mixtures will be sampled in duplicate. Additional samples may be collected and analyzed, at the discretion of the Study Director, to ensure stability, accuracy, and homogeneity of the dosing concentrations over the course of the study. Samples not requiring analysis will be discarded at study termination.

[1] Silk Fibroin: A 14-day repeat dose oral gavage ranger finder study in rats; PSL#50725 (report in preparation).

12.C.2 Homogeneity

At the beginning of the study, formulation of each concentration will be prepared according to the procedures as will be used on test (Section 11.B). Samples from these preparations will be collected from the top, middle, and bottom of each concentration of test substance that was prepared in the vehicle. Sample of the vehicle control will be collected from the middle of the container only.

12.C.3 Concentration Verification

Dose preparations will be sampled at the beginning (as part of the homogeneity assessment, Section 12.C.2), near the middle, and again at the end of the study for verification of dose concentration. Samples will be collected from preparations of each concentration of test substance and one sample from the control (middle).

12.C.4 Sample Preservation

Samples of dose preparations will be stored frozen. Samples will be considered stable from the point at which they are frozen.

12.C.5 Sample Analysis

The frozen samples described above will be sent to Product Safety Labs Clinical Pathology Lab for analysis of dose preparations.

12.D Analytical Chemistry

12.D.1 Sample Storage

Upon receipt, all samples will be stored and maintained frozen (approximately -20°C) prior to analysis.

12.D.2 Method Validation

Prior to sample analysis, the suitability of the Pierce BCA Protein assay (Catalog # 23225; Thermo Scientific) will be demonstrated. Method validation will include, but is not limited to determination of linearity, precision, and accuracy. In addition, QC samples will be prepared in the vehicle at the low, middle, and high dose concentrations. These samples will be analyzed the day they are prepared and then stored frozen. The frozen QC samples will be re-analyzed after a storage period of at least the maximum number of days that the dose solutions samples were stored prior to analysis.

12.D.3 Reference Substance

A Sponsor-provided AB Silk Fibroin solution (Catalog #5154; Advanced Biomatrix, Carlsbad, CA) will serve as the reference standard.

12.D.4 Chemical Analysis

Samples will be analyzed in replicate. A detailed description of the analytical test method(s) will be documented. Any remaining sample material will be retained until the issuance of the final report.

12.D.5 Data Reporting

Data will be captured on standard raw data sheets and as instrument output, as necessary, and summarized in tabular form.

12.D.6 Analytical Report and Records to be Maintained

A signed, analytical report will be provided to the Study Director. This report will include the methodology, pertinent measurements, study results, and tabulated results. The finalized analytical chemistry report will be provided to the Study Director, to be incorporated into the main study report.

12.E Clinical Observations

All animals will be observed at least twice daily for viability. Cage-side observations of all animals will be performed daily during the study. All findings will be recorded.

On Day 1, prior to test substance administration, and approximately weekly thereafter, a detailed observation will be conducted (PSL SOP #726) while handling the animal, generally on days that the animals are weighed and food consumption measurements are taken. Potential signs noted should include, but not be limited to: changes in skin, fur, eyes, and mucous membranes, occurrence of secretions and excretions and autonomic activity (e.g., lacrimation, piloerection, pupil size, unusual respiratory pattern). Likewise, changes in gait, posture and response to handling as well as the presence of clonic or tonic movements, stereotypes (e.g., excessive grooming, repetitive circling), or bizarre behavior (e.g., self-mutilation, walking backwards) should also be recorded. The date and clock time of all observations and/or mortality checks will be recorded.

The Study Director will be promptly notified of severe/remarkable clinical observations and will be advised when an animal is found in a moribund condition and may authorize euthanasia and necropsy as necessary to avoid the loss of quality data. All such authorizations will be recorded in the raw data.

12.F Body Weight and Body Weight Gain

Individual body weights will be recorded at least two times during acclimation. Test animals will be weighed on Day 1 (prior to study start) and approximately weekly thereafter (intervals of 7 days ± 1) for all animals. Decedents need not be weighed. Body weight gain will be calculated for selected intervals and for the study overall. A final fasted body weight will also be obtained prior to scheduled terminal sacrifice.

12.G Food Consumption and Food Efficiency

Individual food consumption will be measured and recorded to coincide with weekly body weight measurements for all animals. Food efficiency will be calculated and reported, if warranted

12.H Clinical Pathology

Clinical pathology will be performed on all surviving animals for clinical chemistry, hematology, and coagulation once, prior to or at necropsy. Blood will be collected via the inferior vena cava, under isoflurane anesthesia at terminal sacrifice. All clinical pathology samples will be evaluated for quality by visual examination. The animals will be fasted overnight prior to blood collection.

12.H.1 Hematology

Approximately 500 µL of blood will be collected in a pre-calibrated tube containing K_2EDTA for hematology assessments. Whole blood samples will be stored under refrigeration or on ice and transferred to the clinical pathology department at Product Safety Labs on cold packs. The following parameters will be evaluated.

erythrocyte count (RBC)	hemoglobin concentration (HGB)
hematocrit (HCT)	mean corpuscular volume (MCV)
mean corpuscular hemoglobin (MCH)	red cell distribution width (RDW)
absolute reticulocyte count (ARET)	platelet count (PLT)

total white blood cell (WBC) and differential leukocyte count

Mean corpuscular hemoglobin concentration (MCHC) will be calculated.

In addition, separate, blood smears, stained with New Methylene Blue or Wright-Giemsa stain, will be prepared from each animal undergoing hematological evaluation and will be examined, if required, to substantiate or clarify the results of hematology findings.

12.H.1 Clinical chemistry

Approximately 1000 µL of blood will be collected into a tube containing no preservative for clinical chemistry assessments. These samples will be centrifuged in a refrigerated centrifuge and the serum will be transferred to a labeled tube. Serum samples will be stored in a -80°C freezer until analysis. The following parameters will be evaluated.

serum aspartate amino transferase (AST)	serum alanine aminotransferase (ALT)
sorbitol dehydrogenase (SDH)	alkaline phosphatase (ALKP)
total bilirubin (BILI)	urea nitrogen (BUN)
blood creatinine (CREA)	total cholesterol (CHOL)
triglycerides (TRIG)	fasting glucose (GLUC)
total serum protein (TP)	albumin (ALB)
globulin (GLOB)	calcium (CALC)
inorganic phosphorus (IPHS)	sodium (NA)
potassium (K)	chloride (CL)

12.H.1 Urinalysis:

The day before their respective collection of samples for the clinical pathology evaluation, animals will be placed in metabolism cages. Animals will be fasted overnight and urine will be collected from each animal. Urine samples will be stored on ice or under refrigeration until analysis.

quality (QUAL)	pH	ketone (KET)
color (COL)	glucose (UGLC)	bilirubin (UBIL)
clarity (CLAR)	specific gravity (SG)	blood (BLD)
volume (UVOL)	protein (UMTP)	urobilinogen (URO)

microscopic urine sediment examination

12.H.1 Coagulation

Approximately 1.8 mL of blood will be collected in a pre-calibrated tube containing 3.2% sodium citrate. These samples will be centrifuged in a refrigerated centrifuge and the plasma will be transferred to labeled tubes. Plasma samples will be stored in a -80°C freezer until analysis. In possible, a second blood sample will be retained during the exsanguination procedure for future possible evaluation if treatment-related effects are identified. Details of this evaluation will be added by amendment. The following parameters will be evaluated.

prothrombin time (PT)

activated partial thromboplastin time (APTT)

12.H.2 Clinical Pathology Report

A signed, clinical pathology report will be provided to the Study Director. This report will include, but not be limited to the methodology, pertinent measurements, study results, a GLP compliance statement signed by the Principal Investigator (Section 13.B), a Quality Assurance statement, and tabulated results. The finalized clinical pathology report will be provided to the Study Director, to be incorporated into the main study report.

Any remaining serum samples will be maintained frozen at approximately -80°C and discarded upon approval of the Sponsor at finalization.

12.I Terminal Sacrifice and Histopathology

12.I.1 Scheduled Sacrifice

At respective terminal sacrifice, all survivors will be euthanized by exsanguination from the abdominal aorta under isoflurane anesthesia. All animals in the study (including decedents) will be subjected to a gross necropsy, which will include examination of the external surface of the body, all orifices, musculoskeletal system, and the cranial, thoracic, abdominal, and pelvic cavities, with their associated organs and tissues. All gross lesions will be recorded.

The following tissues (of all animals sacrificed by design) will be weighed wet as soon as possible after dissection to avoid drying:

adrenals (combined)	kidneys (combined)	spleen
brain	liver	thymus
epididymides (combined)	heart	testes (combined)
Uterus	Ovaries w/o oviducts	

The following tissues will be weighed at least 24 hours after preservation in 10% neutral buffered formalin

ventral prostate	thyroid/parathyroid
seminal vesicles with coagulating gland (combined)	

The following organs and tissues from all animals will be preserved in 10% neutral buffered formalin for possible future histopathological examination:

accessory genital organs (prostate and seminal vesicles)	ileum with Peyer's patches	rectum
adrenals	jejunum	salivary glands (sublingual submandibular, and parotid)
all gross lesions	kidneys	skeletal muscle
aorta	larynx	skin
bone (femur)	liver	spinal cord – 3 levels: cervical, mid- thoracic, and lumbar
bone marrow (from femur & sternum)	lungs	spleen
brain –sections including medulla/pons, cerebellar, and cerebral cortex	lymph node mandibular	sternum
	lymph node mesenteric	
	mammary gland	
	nasal turbinates	
	nose	

cecum	ovaries	stomach
cervix	oviducts	thymus
colon	pancreas	thyroid
duodenum	parathyroid	trachea
esophagus	peripheral nerve (sciatic)	urinary bladder
Harderian gland	pharynx	uterus
heart	pituitary gland	vagina

The following organs and tissues will be preserved in modified Davidson's fixative and then stored in ethanol, for possible future histopathological examination:

eyes	optic nerve
epididymides	testes

Additional tissues will be preserved if indicated by signs of toxicity or target organ involvement. All tissues collected and preserved at terminal sacrifice will be scheduled for pick-up by courier and delivered to Histo-Scientific Research Laboratories (HSRL).

12.1.2 Unscheduled Sacrifice

Any rat that dies or is sacrificed because of a moribund condition will be examined for the cause of death or moribund condition on the day the observation is made. Rats will be evaluated for gross lesions. Organs and tissues will be excised, weighed (except for animals found dead), and preserved as described for those animals sacrificed at the scheduled terminal sacrifices. Blood need not be collected from animals sacrificed prior to study termination unless requested by the Study Director.

12.1.3 Histopathology

Histological examination will be performed on the preserved organs and tissues of the animals from both the control and high dose groups (Groups 1 and 4, respectively) as well as from any animal that dies during the course of the study. In addition, gross lesions noted in any test groups at the time of terminal sacrifice will also be examined. These examinations may be extended to other tissues and organs from the low and intermediate groups at the request of Pathologist in consultation with the Study Director and Sponsor to further investigate changes observed in the high dose group. The fixed tissues will be trimmed, processed, embedded in paraffin, sectioned with a microtome, placed on glass microscope slides, stained with hematoxylin and eosin and examined by light microscopy. Slide preparation and histological assessment, by a board-certified veterinary pathologist, will be performed at HSRL (Section 15.A).

13. STATISTICAL ANALYSIS

Product Safety Labs will perform statistical analysis of all data collected during the in-life phase of the study, as well as clinical pathology and organ weight data. The use of the word "significant" or "significantly" indicates a statistically significant difference between the control and the experimental groups. Significance will be judged at a probability value of $p < 0.05$. Mean and standard deviations will be calculated for all quantitative data. Male and female rats will be evaluated separately.

Statistical analysis will be conducted by using one or more of the following software applications: Provantis® version 9, Tables and Statistics, Instem LSS, Staffordshire UK; Pristima® version 7.2.0, Statistical Analysis, Xybion Corporation, Lawrenceville, NJ; INSTAT or Prism Biostatistics,

GraphPad Software, San Diego, CA; Statview, version 5. SAS Institute Inc., Cary, NC; Pheonix 8.1, Certara USA, Inc., Princeton, NJ; and SigmaStat, version 2, Systat Software, San Jose, CA. Other statistical methods will be used if appropriate, at the time of analysis and described in the final report.

13.A Statistical Methods

In-Life Data

For all in-life endpoints that are identified as multiple measurements of continuous data over time (e.g. body weight, food consumption, and food efficiency), treatment and control groups will be compared using a two-way analysis of variance (ANOVA), testing the effects of both time and treatment, with methods accounting for repeated measures in one independent variable (time)[1]. Further analysis of the p value for each individual factor may be conducted and ultimately by a *post hoc* multiple comparisons test (e.g. Dunnett's test) of the individual treated groups to control.

Organ Weight Data

If warranted by sufficient group sizes, all endpoints with single measurements of continuous data within groups (e.g. organ weight, relative organ weight, etc) will be evaluated for homogeneity of variances[2] and normality. Where homogeneous variances and normal distribution is observed, treatment and control groups will be compared using a one-way ANOVA. A comparison of the treated groups to control will be performed with a multiple comparisons test (e.g. Dunnett's test)[3,4]. Where variances are considered significantly different, groups will be compared using a non-parametric method (e.g. Kruskal-Wallis non-parametric analysis of variance[5]). When non-parametric analysis of variance is significant, a comparison of treated groups to control will be performed (e.g. Dunn's test[6]).

If warranted by sufficient group sizes, the incidence of clinical observations may be evaluated through sequential application of a trend test[7]. Other procedures will be used if appropriate, following consultation with the Sponsor, and will be described in the final report.

[1] Motulsky,H (2014). Intuitive biostatistics, a nonmathematical guide to statistical thinking (3rd Edition). Oxford University Press. New York, NJ.

[2] Bartlett, MS. (1937). Properties of sufficiency and statistical tests. *Proceeding of the Royal Statistical Society Series A*, 160, 268-82.

[3] Dunnett, C.W. (1980). Pairwise multiple comparisons in the unequal variance case. *J. Amer. Statist. Assoc.* 75, 796-800.

[4] Dunnett, C.W. (1964). New tables for multiple comparisons with control. *Biometrics*, 482-491.

[5] Kruskal, W.H. and Wallis W.A. (1952). Use of ranks in one-criterion analysis of variance. *J. Amer. Statist. Assoc.* 47, 583-621.

[6] Dunn, O.J. (1964). Multiple contrasts using rank sums. *Technometrics*, 6, 241-252.

[7] Agresti, Alan (2013). Categorical Data Analysis (3rd Edition). John Wiley & Sons, Inc. Hoboken, NJ.

13.B Statistical Methods (Clinical Pathology)

Significance will be judged at a probability value of $p < 0.05$. Males and females will be analyzed separately.

		Method of Statistical Analysis	
Parameter	Preliminary Test	If preliminary test is not significant	If preliminary test is significant
Clinical Pathology*	Bartlett's test for homogeneity and Shapiro-Wilk[1] test for normality	One-way analysis of variance followed with Dunnett's test	Log transforms of the data to achieve normality and variance homogeneity may be used. If the log transform fails, a non-parametric method (Kruskal-Wallis non-parametric analysis of variance) will be used. When non-parametric analysis of variance is significant, a comparison of treated groups to control will be performed (e.g. Dunn's test).

* When an individual observation is recorded as being less than a certain value (e.g. below the lower limit of quantitation), calculations are performed on half the recorded value. For example, if bilirubin is reported as <0.1, 0.05 is used for any calculations performed with that bilirubin data. When an individual observation is recorded as being greater than a certain value, calculations are performed on the recorded value. For example, if specific gravity was reported as ≥1.100, 1.100 is used for any calculation performed with that specific gravity data.

Other statistical methods will be used if appropriate, at the time of analysis. The statistical methods used will be described in the final report.

14. FINAL REPORT

A report of the results of this study will accurately describe all methods used for generation and analysis of the data. This report will include, but not be limited to, the following information:

- individual animal data (and averages where appropriate) for actual concentration of test substance received; time of observation of each abnormal sign and its subsequent course;
- body weights food consumption, and food efficiency values (if applicable);
- hematology, clinical chemistry, coagulation, and urinalysis results;
- organ weights, organ to body weight and organ to brain weight ratios;
- necropsy and pathology findings;
- dose preparation analysis;
- a compliance statement signed by the Study Director that states whether or not all applicable GLP regulations were followed in the conduct of the study;
- a Quality Assurance statement summarizing QA activities performed for the study;
- a certification statement signed by the Study Director and test facility management that states whether or not the report accurately reflects the raw data obtained during the performance of the study.

[1] Shapiro, S.S. & Wilk, M.B. (1965). An analysis of variance test for normality (complete samples). *Biometrika*, 52(3-4), 591–611.

Product Safety Labs

15. STUDY CONDUCT

15.A Laboratory

Test Facility

In-life portion	Product Safety Labs 2394 US Highway 130 Dayton, NJ 08810
Clinical pathology and Dose analysis (clinical chemistry, hematology, coagulation, and urinalysis), and dose formulation analysis	Product Safety Labs 2394 US Highway 130 Dayton, NJ 08810 P.I.: Victor Ansah-Johnson, BS

Test Site

Clinical pathology data evaluation	Eurofins Advinus 21 & 22, Phase II, Peenya Industrial Area Bengaluru, 560 058, India Prospective P.I.(s): Dr. Jayachandra, K.C, M.V.Sc., DABT Dr. K.V. Lakshmisha, B.V.Sc, M.V.Sc, DABT Dr. K. Kamala, B.V.Sc, M.V.Sc, IBTP
Test Site QA for Clinical Pathology Evaluation	Muktha Bhagavan, M.Sc., RQAP-GLP
Test Site Management for Clinical Pathology Evaluation	Rajiv Malik
Histological slide preparation	Histo-Scientific Research Laboratories (HSRL) 5930 Main Street Mount Jackson, VA 22842 P.I. (histology): Craig Zook
Histological slide evaluation	Histo-Scientific Research Laboratories (HSRL) 5930 Main Street Mount Jackson, VA 22842 Prospective P.I.(s) (pathology): David Garlick, DVM, DACVP Laura E. Elcock, DVM, PhD, DACVP Katherine A.B. Knostman, DVM, PhD, DACVP Matthew A. Buccellato, DVM, PhD, DACVP Earl F. Meierhenry, DVM, PhD, DACVP Allen Singer, DVM, DACVP, DABT

15.B GLP Compliance

This study will be conducted in compliance with the following regulations:

- U.S. FDA GLP: 21 CFR Part 58, 1987,

  which is compatible with

- OECD Principles of Good Laboratory Practice (as revised in 1997) published in ENV/MC/CHEM (98)17, OECD, Paris, 1998.

15.C Test Procedure Guidelines

This study design is based on the following guidelines:

- OECD Guidelines for Testing of Chemicals, Section 4, Test No. 407: Health Effects, Repeated Dose 28-Day Oral Toxicity Study in Rodents (adopted 1995; updated October 2008). US EPA Health Effects Test Guidelines: OPPTS 870.3050 Repeated Dose 28-day Oral Toxicity Study in Rodents (2000).
- US FDA Toxicological Principles for the Safety Assessment of Food Ingredients, Redbook 2000, Revised 2007 IV.C. 4. a. *Subchronic Toxicity Studies with Rodents* (2003).

16. QUALITY ASSURANCE

The Quality Assurance Unit (QAU) of PSL has reviewed this protocol for GLP compliance and will conduct in-process inspections of selected procedures during the study. The analytical phase report, clinical pathology phase report, and final report will be audited for agreement with the raw data records and for compliance with the protocol and PSL SOPs.

In addition, PSL QAU will function as lead QA for this study and will monitor QA activities at HSRL and Eurofins Advinus Ltd. For portions of the study conducted by a subcontractor, the QAU for that facility will conduct necessary critical phase inspections and audit respective results and reports for the study phase according to the SOPs of that facility.

The QA Unit from HSRL and Eurofins Advinus Ltd will send all GLP audit reports to the Study Director, Study Director's management, and PSL QAU as soon as they are issued.

17. RECORDS TO BE MAINTAINED

An electronic signed copy of the report, will be sent to the Sponsor. The original signed report, together with the protocol and all raw data generated at Product Safety Labs, will be maintained in the Product Safety Labs Archives. PSL will maintain these records for a period of at least five years. After this time, the Sponsor of the study will be offered the opportunity to take possession of the records or will be charged an archiving fee for continued archiving by PSL.

The following records will be maintained:

A. Information on test substance will include but not be limited to the following:

Storage	Dose preparation analysis
Usage	Disposition

B. Information on animals will include, but not be limited to the following:

Receipt, date of birth	Clinical observations
Initial health assessment	Histopathology data
Dosing	Individual necropsy records
Body weights	Organ weights
Food consumption	

Hematology, clinical chemistry, coagulation, urinalysis data

C. All other records that would demonstrate adherence to the protocol.

Raw data related to clinical pathology evaluations will be maintained by Product Safety Labs. Prepared slides and pathology data will be maintained by Product Safety Labs and/or by HSRL, 5930 Main Street, Mount Jackson, VA, 22842. Dose preparation analysis data will be maintained by Product Safety Labs, 2394 US Highway 130, Dayton, NJ 08810.

Any electronic raw data generated by the Test Site will be maintained by the Test Site in accordance with their GLP archiving procedures.

18. PROTOCOL AMENDMENTS AND DEVIATIONS

All amendments and/or deviations to this protocol and the reasons therefore, shall be appropriately documented, signed by the Study Director, and described in the final report.

19. DISPOSITION OF TEST SUBSTANCE

A reserve sample of the test substance and records of sample disposition will be maintained at Product Safety Labs. All remaining test substance will be retained for at least one year from receipt, unless otherwise specified by the Sponsor. All remaining test substance will be returned to the Sponsor unless otherwise directed.

Product Safety Labs

20. PROTOCOL APPROVAL

Signature: [redacted]
Laith Abu-Taleb
Sponsor Representative
Cambridge Crops, Inc.

Date: November 1, 2019

Signature: [redacted]
Raghavendra Gowda PhD
Study Director
Product Safety Labs

Date: Nov 1, 2019

Signature: [redacted]
Daniel J. Merkel
President
Product Safety Labs

Date: Nov 1, 2019

21. PROTOCOL REVIEW:

Signature: [redacted]
Rhonda S. Krick, BS
Director, Quality Assurance
Product Safety Labs

Date: Nov 1, 2019

Product Safety Labs

PROTOCOL AMENDMENT

SILK FIBROIN: A 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS

PROTOCOL NO.: P713.01 CMR **AMENDMENT NO.:** 1 - 3

STUDY NO.: 51651 **PSL NO.:** 191015-2D

Amendment # 1

Protocol Section: 9.C Analysis

Change from: The test substance, as received, is expected to be stable for the duration of the study. The stability of the test substance and verification of the test substance in the dose preparations will be determined as part of this study (Section 10.C).

Change to: The test substance, as received, is expected to be stable for the duration of the study. Verification of the test substance concentration in the dose preparations will be determined as part of this study (Section 12.C).

Amendment # 2

Protocol Section: 10.C.0 Housing

Change from: The animals will be housed in cages which conform to the size recommendations in the latest Guide for the Care and Use of Laboratory Animal1. Litter paper placed beneath the cage will be changed at least three times/week. The animal room will have a 12-hour light/dark cycle and will be kept clean and vermin free. Environmental controls are set to maintain temperature and relative humidity ranges of 23 ± 3°C and 30-70%, respectively. Observed ranges will be documented in the raw data

Change to: The animals will be housed in regularly cleaned cages which conform to the size recommendations in the latest Guide for the Care and Use of Laboratory Animals. The animal room will have a 12-hour light/dark cycle and will be kept clean and vermin free. Environmental controls are set to maintain temperature and relative humidity ranges of 21 ± 2°C and 30-70%, respectively. Observed ranges will be documented in the raw data. In addition, airflow in the animal room will be maintained at or above 10 air changes per hour.

Amendment # 3

Protocol Section: 12.I.1 Scheduled Sacrifice

Change from: At respective terminal sacrifice, all survivors will be euthanized by exsanguination from the abdominal aorta under isoflurane anesthesia. All animals in the study (including decedents) will be subjected to a gross necropsy, which will include examination of the external surface of the body, all orifices, musculoskeletal system, and the cranial, thoracic, abdominal, and pelvic cavities, with their associated organs and tissues. All gross lesions will be recorded.

The following tissues (of all animals sacrificed by design) will be weighed wet as soon as possible after dissection to avoid drying:

adrenals (combined)	kidneys (combined)	spleen
brain	liver	thymus
epididymides (combined)	heart	testes (combined)
Uterus	Ovaries w/o oviducts	

Product Safety Labs

Change to: At respective terminal sacrifice, all survivors will be euthanized by exsanguination from the abdominal aorta under isoflurane anesthesia. All animals in the study (including decedents) will be subjected to a gross necropsy, which will include examination of the external surface of the body, all orifices, musculoskeletal system, and the cranial, thoracic, abdominal, and pelvic cavities, with their associated organs and tissues. All gross lesions will be recorded.

The following tissues (of all animals sacrificed by design) will be weighed wet as soon as possible after dissection to avoid drying:

adrenals (combined)	kidneys (combined)	spleen
brain	liver	thymus
epididymides (combined)	heart	testes (combined)
Uterus	**Ovaries with oviducts**	

REASON: Clarification of Protocol and study requirements

Effective Date: November 5th, 2019

[redacted]
Raghavendra Gowda Ph.D
Study Director
Product Safety Labs

11/05/2019
Date

Product Safety Labs

PROTOCOL AMENDMENT

SILK FIBROIN: A 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS

PROTOCOL NO.: P713.01 CMR AMENDMENT NO.: 4

STUDY NO.: 51651 PSL NO.: 191015-2D

PROTOCOL SECTION: **10.C.6 Viral Screen**

Change from
Serum samples from naive rats housed in the same room as test animals, as part of PSL's sentinel health monitoring program, will be evaluated for the absence of viruses near the end of the in-life portion of the study (PSL SOP #755).

Change to: (change in bold)
Serum samples from **few representative control animals**, as part of PSL's sentinel health monitoring program, will be evaluated for the absence of viruses near the end of the in-life portion of the study (PSL SOP #755).

Reason:

Use serum from control animals for viral screen.

EFFECTIVE DATE: 2/17/2020

[redacted]

Raghavendra Gowda
Study Director
Product Safety Laboratories

2/17/2020
Date

Product Safety Labs

PROTOCOL AMENDMENT

SILK FIBROIN: A 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS

PROTOCOL NO.: P713.01 CMR **AMENDMENT NO.:** 5

STUDY NO.: 51651 **PSL NO.:** 191015-2D

AMENDMENT (various sections): Additional method validation will be done to improve upon the method as it currently exists. Method validation will include samples of unused test substance to evaluate differences specific to the test substance use with this kit. Other modifications may be made as deemed necessary and will be documented. If improvements in the method can be achieved, the additional set of samples that were collected ("B" samples) will be analyzed and the results will be used to replace the original results ("A" Samples).

REASON: The results of the original analysis were below the concentrations expected by the Sponsor based on qualification of the samples prior to being shipped to PSL. As a result, it is believed that the original method validation may not have been sufficiently robust and therefore additional method validation is expected to improve upon the method being used and to yield more accurate results.

Effective Date: March 04, 2020

[redacted]

Raghavendra Gowda Ph.D
Study Director
Product Safety Labs

03/04/2020
Date

Product Safety Labs

PROTOCOL AMENDMENT

SILK FIBROIN: A 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS

PROTOCOL NO.: P713.01 CMR **AMENDMENT NO** 6

STUDY NO.: 51651 **PSL NO.:** 191015-2D

PROTOCOL SECTION: 16 Study Conduct

Change From:

Histological slide evaluation	Histo-Scientific Research Laboratories (HSRL) 5930 Main Street Mount Jackson, VA 22842 Prospective P I.(s) (pathology) David Garlick, DVM, DACVP Laura E. Elcock, DVM, PhD, DACVP Katherine A B. Knostman, DVM, PhD, DACVP Matthew A. Buccellato, DVM, PhD, DACVP Earl F. Meierhenry, DVM, PhD, DACVP Allen Singer, DVM, DACVP, DABT

Change To:

Histological slide evaluation	Histo-Scientific Research Laboratories (HSRL) 5930 Main Street Mount Jackson, VA 22842 Prospective P I.(s) (pathology) David Garlick, DVM, DACVP Laura E. Elcock, DVM, PhD, DACVP Katherine A B. Knostman, DVM, PhD, DACVP Matthew A. Buccellato, DVM, PhD, DACVP Earl F. Meierhenry, DVM, PhD, DACVP Allen Singer, DVM, DACVP, DABT **Christine E. Watson, MS, BVMS, MRCVS, DACVP**

REASON: Addition of a Prospective P I and clarification of responsibilities

Effective Date: March 30, 2020

[redacted]
Ragnavendra Gowda Ph.D
Study Director
Product Safety Labs

3/31/2020
Date

APPENDIX B: FEED, WATER, AND SEROLOGY ANALYSES

PRODUCT IDENTIFICATION

Silk Fibroin

APPENDIX B: FEED

+++
ENVIGO

Teklad Certified Global 16% Protein Rodent Diet

Lot Number	2016C-080619MA
Date of Manufacture	06Sep2019
Report Date	16Sep2019

Laboratory Diet Certification Report

The following data is a consolidation of results obtained from one or more independent testing laboratories. The actual laboratory results are available upon request.

2019.09.16
13:40:02 -05'00'

Analysis	Result (%)
Protein	16.80
Fat	3.02
Fiber	3.87
Moisture	11.38
Ash	5.11
Calcium	0.94
Phosphorus	0.79

Analysis	Result	Units	Established Maximum Concentration
Heavy Metals			
Arsenic	< 0.10	ppm	1.00
Cadmium	< 0.10	ppm	0.50
Lead	< 0.20	ppm	1.50
Mercury	< 0.05	ppm	0.20
Selenium	0.29	ppm	0.50
Mycotoxins			
Aflatoxin B1, B2, G1, G2	< 5.00	ppb	5.00
Chlorinated Hydrocarbons			
Aldrin	< 0.01	ppm	0.03
Lindane	< 0.01	ppm	0.05
Chlordane	< 0.01	ppm	0.05
DDT & related substances	< 0.03	ppm	0.15
Dieldrin	< 0.02	ppm	0.03
Endrin	< 0.02	ppm	0.03
Heptachlor	< 0.01	ppm	0.03
Heptachlor Epoxide	< 0.01	ppm	0.03
Toxaphene	< 0.10	ppm	0.15
PCBs	< 0.10	ppm	0.15
a-BHC	< 0.01	ppm	0.05
b-BHC	< 0.01	ppm	0.05
d-BHC	< 0.01	ppm	0.05
Hexachlorobenzene	< 0.01	ppm	0.03
Mirex	< 0.01	ppm	0.02
Methoxychlor	< 0.05	ppm	0.50
Organophosphates			
Thimet	< 0.15	ppm	0.50
Diazinon	< 0.14	ppm	0.50
Disulfoton	< 0.10	ppm	0.50
Methyl Parathion	< 0.14	ppm	0.50
Malathion	< 0.14	ppm	0.50
Parathion	< 0.12	ppm	0.50
Thiodan	< 0.02	ppm	0.50
Ethion	< 0.14	ppm	0.50
Trithion	< 0.15	ppm	0.50

Envigo Teklad Diets • Madison WI • [illegible] • tekladinfo@envigo.com • (800) 483-5523

APPENDIX B (cont.): WATER

In December 2019, water was analyzed for contaminants.

LABORATORY: PRECISION ANALYTICAL SERVICES, INC.
2161 Whitesville Road
Toms River, NJ 08755

Results of water analysis for possible contaminants were acceptable within regulatory standards.

PRECISION ANALYTICAL SERVICES, INC.

CERTIFICATE OF ANALYSIS

Customer: [illegible]

Project Title: Quarterly Sampling [illegible]
PAS Project ID: P19-11584
Purpose of Test: Regulatory Samples
Conditions: [illegible]

Report Date: [illegible]

PAS Sample ID	Sample Location	Analyte	Results	Units	DF	PQL	MDL	MCL	Method	Date Sampled	Date Analyzed
[illegible]	Cage Wash [illegible]	Copper	[illegible]	mg/L	1	0.050	[illegible]	1.30*	[illegible]	[illegible]	[illegible]
[illegible]	Cage Wash [illegible]	Zinc	[illegible]	mg/L	1	0.020	[illegible]	5.00	[illegible]	[illegible]	[illegible]
[illegible]	Cage Wash [illegible]	Lead	ND	mg/L	1	0.002	[illegible]	0.015*	[illegible]	[illegible]	[illegible]
[illegible]	Cage Wash [illegible]	E. Coli / Coliform	Absent	[illegible]	1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Cage Wash [illegible]	Total Coliform / Coliform	Absent	[illegible]	1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Room 13 [illegible]	Copper	ND	mg/L	1	0.050	[illegible]	1.30*	[illegible]	[illegible]	[illegible]
[illegible]	Room 13 [illegible]	Zinc	ND	mg/L	1	[illegible]	[illegible]	5.00	[illegible]	[illegible]	[illegible]
[illegible]	Room 13 [illegible]	Lead	ND	mg/L	1	[illegible]	[illegible]	0.015*	[illegible]	[illegible]	[illegible]
[illegible]	Room 13 [illegible]	E. Coli / Coliform	Absent	[illegible]	1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Room 13 [illegible]	Total Coliform / Coliform	Absent	[illegible]	1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Room 29 Pressure [illegible]	Copper	[illegible]	mg/L	1	[illegible]	[illegible]	1.30*	[illegible]	[illegible]	[illegible]
[illegible]	Room 29 Pressure [illegible]	Zinc	[illegible]	mg/L	1	[illegible]	[illegible]	5.00	[illegible]	[illegible]	[illegible]
[illegible]	Room 29 Pressure [illegible]	Lead	ND	mg/L	1	[illegible]	[illegible]	0.015*	[illegible]	[illegible]	[illegible]
[illegible]	Room 29 Pressure [illegible]	E. Coli / Coliform	Absent	[illegible]	1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Room 29 Pressure [illegible]	Total Coliform / Coliform	Absent	[illegible]	1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Sipper Bottle	E. Coli	Absent	[illegible]	1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Sipper Bottle	[illegible]	[illegible]	[illegible]	1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Sipper Tap	E. Coli	Absent	[illegible]	1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Sipper Tap	Total Coliform	[illegible]	[illegible]	1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

[illegible]

All samples are analyzed in accordance with [illegible]

[illegible], Lab Director

APPENDIX B (cont.): SEROLOGY

In December 2019, serology from representative control animals residing in Room #48, was obtained from collected blood serum for a battery of common viral and microbiologic pathogens.

The representative control animals were in Room #48 from November 6 – December 6, 2019, for the duration of the study. Blood samples were collected on December 6, 2019.

LABORATORY: IDEXX BioAnalytics
4011 Discovery Drive
Columbia, MO 65201

Results of the serology analyses for the representative control animals corresponding with this study are reported as samples 7004M 9/13/19, 7005M 9/13/19, and 7009M 9/13/19. All samples were negative for microbial antibodies.

IDEXX BioAnalytics

FINAL REPORT OF LABORATORY EXAMINATION

4011 Discovery Drive, Columbia, MO 65201
1-800-669-0825 1-573-499-5700
idexxbioanalytics@idexx.com www.idexxbioanalytics.com

IDEXX BioAnalytics Case # 6643-2020

Received: 2/20/2020
Completed: 2/21/2020

Submitted By

Mithila Rao
Product Safety Labs
2394 US Highway 130
Dayton, NJ 08810

Phone: 732-438-5100 ext 1558
Email: Mithilarao@productsafetylabs.com

Specimen Description

Species rat
Breed/Strain: CD/CRL
Description Opti-Spot; Opti-Spot strip(s)
Number of Specimens/Animals. 3

Purchase Order #: US003456567

Client ID	Investigator	Room #	Species	Strain /Breed	Sex	Study #	Age
7004M 9 13 19	Raghu Gowda	48	rat	CD/CRL	M	51651	3M
7005M 9 13 19	Raghu Gowda	48	rat	CD/CRL	M	51651	3M
7009M 9 13 19	Raghu Gowda	48	rat	CD/CRL	M	51651	3M

Services/Tests Performed: Primary Serology Profile (1-3)

Serologic evaluation for antibodies to: H1, KRV, RCV/SDAV, RMV, RPV RTV

Summary: All test results were negative

SEROLOGY SUMMARY

	7004M 2.18.20	7005M 2.18.20	7006M 2.18.20
RPV	-	-	-
RMV	-	-	-
RRV	-	-	-
H1	-	-	-
RCV/SDAV	-	-	-
RTV	-	-	-
Rat IgG	N	N	N

Legend: + = positive - = negative Blank = test not performed EQ = equivocal HE = hemolysis precluded testing I = insufficient W = weak positive WB = Western Blot confirmatory analyses pending NS = non-specific reactivity N = normal IgG L = less than normal IgG

IDEXX BioAnalytics

FINAL REPORT OF LABORATORY EXAMINATION
4011 Discovery Drive, Columbia, MO 65201
1-800-669-0825 1-573-499-5700
idexxbioanalytics@idexx.com www.idexxbioanalytics.com

IDEXX BioAnalytics Case # 6643-2020

Received: 2/20/2020
Completed: 2/21/2020

SEROLOGY DETAILS

	Baseline	7004M 2.19.20	7005M 2.19.20	7006M 2.19.20
RPV				
RPV purified virus	MFI > 2,500	-	-	-
NS1[1]	MFI > 3,750	-	-	-
RMV				
RMV VP2 recombinant	MFI > 2,000	-	-	-
NS1[1]	MFI > 3,750	-	-	-
KRV				
KRV purified virus	MFI > 3,250	-	-	-
NS1[1]	MFI > 3,750	-	-	-
H1				
H1 purified virus	MFI > 1,750	-	-	-
NS1[1]	MFI > 3,750	-	-	-
RCV/SDAV				
RCV/SDAV purified virus	MFI > 3,750		-	-
RCV/SDAV Spike	MFI > 3,750	-	-	-
RTV				
RTV purified virus	MFI > 2,000	-	-	-
TMEV purified virus	MFI > 2,000	-	-	-

NS1[1]: NS1 protein is highly conserved among rodent parvoviruses and thus serves as a generic assay for parvovirus seroconversion

Legend: + = positive - = negative Blank = test not performed EQ = equivocal HE = hemolysis precluded testing I = insufficient W = weak positive WB = Western Blot confirmatory analysis pending NS = non-specific reactivity N = normal IgG L = less than normal IgG

Positive MFI results are reported as "+" followed by a number from 1 to 33 in thousands rounded off to the nearest thousand

APPENDIX C: CHEMICAL ANALYSIS

PRODUCT IDENTIFICATION

Silk Fibroin

Product Safety Labs

Project Title:

Analysis of Samples from Study
Silk Fibroin
A 28-Day Oral Gavage Toxicity Study in Rats

SPONSOR

Cambridge Crops, Inc
444 Somerville Ave
Somerville, MA 02143

ANALYTICAL REPORT

TEST SUBSTANCE

Silk Fibroin

AUTHOR

Victor Ansale-Johnson, BS

REPORT COMPLETION DATE

April 3, 2020

PERFORMING LABORATORY

Analytical Services
Product Safety Labs
2394 US Highway 130
Dayton, NJ 08810

PROJECT IDENTIFICATION NUMBER

Product Safety Labs Study Number 51651

Product Safety Labs

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

Silk Fibroin

The analytical phase of this study meets the requirements of 21 CFR Part 58 U.S. FDA GLP Standards, 1987, which are compatible with OECD Principles of GLP (as revised in 1997) published in ENV/MC/CHEM(98)17 OECD Paris, 1998

Principal Investigator [redacted] Date 9/5/2018

Name of Signer Victor Anoja-Johnson, HS

Name of Company Product Safety Labs

Product Safety Labs

QUALITY ASSURANCE STATEMENT

The Product Safety Labs' Quality Assurance Unit has reviewed this analytical report to assure the report accurately describes the methods and standard operating procedures, and that the reported results accurately reflect the raw data of the study.

QA activities for this study

QA Activity	Performed By	Date Conducted	Date Findings Reported To Study Director And Management
Protocol review	R. Krick, M. Zakrzewski	Oct 31, 2019 Mar 20, 2020;	Oct 31, 2019 Mar 23, 2020,
Critical phase inspection *Standard and sample preparation for BCA Protein Assay*	M. Zakrzewski	Feb 14, 2020	Feb 14, 2020
Raw data audit	M. Zakrzewski	Mar 20 & 23, 2020	Mar 23, 2020
Draft report review	M. Zakrzewski	Mar 20 & 23, 2020	Mar 23, 2020

Final Analytical report reviewed by

[redacted]

for Mervyn Zakrzewski
Quality Assurance Auditor
Product Safety Labs

April 2, 2020
Date

Product Safety Labs

SIGNATURE

Silk Fibroin

I, the undersigned, declare that the methods, results and data contained in this report faithfully reflect the procedures used and raw data collected during the study.

[redacted]

Victor Ansah-Johnson, BS
Principal Investigator
Product Safety Labs

4/6/18
Date

Product Safety Labs

TABLE OF CONTENTS

Product Safety Labs

STUDY INFORMATION

Protocol No	P71330 CMR
Test Substance	Silk Fibroin
Physical Description	Slightly yellow liquid
Dates Test Substance Received	October 15, 2019
PSL IDs	191015-2D
PSL Study Number	51651
Sponsor	Cambridge Crops, Inc 444 Somerville Ave Somerville, MA 02143
Dates of Analysis	February 18 - March 6, 2020
Analytical Principal Investigator	Victor Ansah-Johnson, BS
Primary Chemist	Jeanette Paez, MS
Study Director	Raghavendra Gowda, PhD

Product Safety Labs

1. SUMMARY

This report presents the dose analysis phase of PSL Study Number 51651 Silk Fibroin A 28-Day Oral Gavage Toxicity Study in Rats. Dose mixture samples were collected from all dose concentrations for homogeneity (HO) on Day 1. Concentration verification (CV) samples were collected on Days 16 and 30. All samples were transferred to the Analytical Services laboratory of Product Safety Labs. The active ingredients (as % or mg/mL) were determined in each of the samples using the BCA protein assay. This method was validated in terms of linearity. All samples were stored refrigerated prior to testing and thawed just prior to analysis.

Samples

Samples for Homogeneity (HO, T = top, M = middle, B = bottom; Day 1)

HO 1 BM
HO 2 BT
HO 3 BM
HO 4 BB
HO 5 BT
HO 6 BM
HO 7 BB
HO 8 BT
HO 9 BM
HO 10 BB

Samples Concentration Verification (CV, Days 16 and 30)

CV 1 A
CV 2 A
CV 3 A
CV 4 A
CV 5 A
CV 5 A
CV 7 A
CV 8 A

2. PROCEDURE

A. Reference Standard(s)

Name: Silk
PSL ID: 191015-2D
Batch #: 215
Concentration: 50 mg/mL, aqueous
Physical Description: Slightly yellow liquid
Expiration Date: Stable at 4 °C for one month. Upon thawing, please use in one month.

Note: The neat test substance was used as the reference standard. No purity correction was applied in order to report results as percent test substance (versus percent active ingredient).

Product Safety Labs

B. Chemical Analysis

2 B 1 Standard Preparation

Three sets of 6 microcentrifuge tubes were labeled from #1 to #6 and prepared as noted below (for all three repheates) The tubes were vortexed five times in 1 second intervals to mix well The standards were used for linearity determination

Tube #1, 50 µL of silk + 150 µL of deionized
Tube #2, 100 µL from Tube #1 + 400 µL of deionized water
Tube #3, 375 µL from Tube #2 + 225 µL of deionized water
Tube #4, 400 µL from Tube #3 + 100 µL of deionized water
Tube #5, 200 µL from Tube #4 + 300 µL of deionized water
Tube #6, 125 µL from Tube #5 + 375 µL of deionized water

Final Silk Concentrations Prepared from Serial Dilutions

Tube Number	1	2	3	4	5	6
Silk Concentration mg/mL	5.0	1.0	0.625	0.5	0.2	0.05

2 B 2 QC Preparation

QCs were prepared using Albumin Standard provided in the Pierce BCA Protein Assay Kit (Lot #UI289347, Ref 23225) in a 1:5 dilution

- 3 microcentrifuge tubes were labeled QC-1, QC-2, QC-3
- 100 µL of the Albumin Standard was added to 400 µL of deionized water in tube QC-1 and repeated for QC-2 and QC-3 The tubes were vortexed

2 B 3 BCA Protein Assay

All dose mixture samples were brought to room temperature and prepared for testing using the below two steps Results from the initial and repeat samples were averaged and reported

A 1:10 dilution was prepared using a deep well plate One line of wells was labeled "1:10" A volume of 450 µL of deionized water was added to 3 wells The samples were inverted 5 times and 50 µL was added to the 3 wells. The plate was covered and vortex five times 2-second intervals

A 1:100 Dilution was prepared from the stock The next line of wells was labeled "1:100" A volume of 450 µL of deionized water was added to 3 wells and 50 µL was added from 1:10 to 1:100 The plate was covered and vortex five times 2-second intervals

Working Reagent (WR) Preparation

The following formula was used to determine the total volume of WR required

0.3 mL x 96 x # of Plates Needed = Total WR Required

Round to nearest whole number

Total WR Required / 50 Volume of Reagent B

Total WR Required Volume of Reagent B Volume of Reagent A

The volume of BCA Reagent A was added to a centrifuge tube of appropriate size. The volume of BCA Reagent B was added to the same centrifuge tube. The WR was gently inverted 10 times or until well mixed.

Assay

A volume of 9 µL of each silk standard, deionized water, and 1:100 dilutions were pipetted into the appropriate microplate wells and 260 µL of WR was added to each well. The plates were placed into an incubator set to 37°C for 30 minutes on a slow shaker. The plates were allowed to cool to room temperature for 5 minutes. The absorbance was then measured on a plate reader at 562 nm.

2.B.4 Method Performance

Linearity. In triplicate, reference standards 1-6 were assayed using the BCA assay and the wavelengths were recorded. The correlation coefficient, r, was ≥ 0.995 for all three linearity curves.

2.B.5 Calculations

All calculations were performed using Excel with full precision. Minor differences may be found between the values reported and those obtained if calculated manually.

Calc. Conc. (ug/mL) = (Value - Intercept) / Slope

Note: Intercept and Slope being specific to the standard curve of each plate.

Dose Conc. (mg/mL) = Calc. Conc.*(Final Vol. First/Dilution First)*(Final Vol. Second/Dilution Second)

% Target = Average (mg/mL) / Dose level (mg/mL) *100

3. RESULTS

Summaries of results are presented in Tables 1A-1B. Instrument conditions are presented in Table 2. Linearity results are reported in Table 3. Results of homogeneity and concentration verification of the test substance in the dosing solutions are presented in Tables 4 and 5, respectively.

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TABLE 1A: CHEMICAL ANALYSIS RESULTS[1]

Results for Homogeneity

Group	Target Dose Level (mg/mL)	Sampling Location	Average Conc. (mg/mL)	Overall Average Conc. (mg/mL)	% of Target[2]	Average % of Target	%RSD
1	0	Middle	0	NA	NA	NA	NA
2	12.5	Top	12.7	13.1	101.5	104.8	10.4
		Middle	11.9		95.3		
		Bottom	14.6		116.8		
3	25	Top	22.1	22.8	88.2	91.0	2.7
		Middle	23.1		92.3		
		Bottom	23.1		92.6		
4	50	Top	42.5	42.7	85.0	85.5	3.5
		Middle	41.3		82.7		
		Bottom	44.4		88.7		

NA = Not Applicable

ND = None Detected

See Amendment 5

[2] % of Target = [Average Test Substance in dose (mg/mL)/Target Dose Concentration (mg/mL)] x 100

Product Safety Labs

TABLE 1B: CHEMICAL ANALYSIS RESULTS[1]

Results for Concentration Verification

Study Day	Group	Dose Level (mg/mL)	Average Conc. (mg/mL)	% of Target
1	1	0	0	NA
	2	12.5	13.1	104.4
	3	25	22.8	91.0
	4	50	42.7	85.5
16	1	0	0	NA
	2	12.5	12.0	96.2
	3	25	24.9	99.8
	4	50	45.1	90.2
30	1	0	0	NA
	2	12.5	16.1	128.9
	3	25	22.7	90.7
	4	50	44.8	89.6

[1] See Amendment 3

Product Safety Labs

TABLE 2: INSTRUMENT PARAMETERS

Instrument	Molecular Devices Spectramax M3
UV Wavelength (nm)	562

Product Safety Labs

Plate B1

	Concentration	Mean Value
STD2	1	0.901
STD3	0.25	0.055
STD4	0.5	0.524
STD5	0.2	0.225
STD6	0.05	0.051

Intercept	0.0883
Slope	1.0076

TABLE 3: LINEARITY

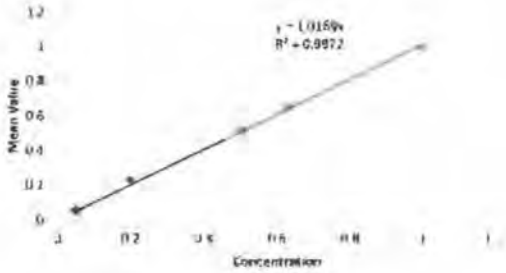

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TABLE 3 (cont.): LINEARITY

Plate B2

	Concentration	Mean Value
STD2	[illegible]	[illegible]
STD3	[illegible]	[illegible]
STD4	[illegible]	[illegible]
STD5	[illegible]	[illegible]
STD6	[illegible]	[illegible]

[illegible]	[illegible]
Slope	[illegible]

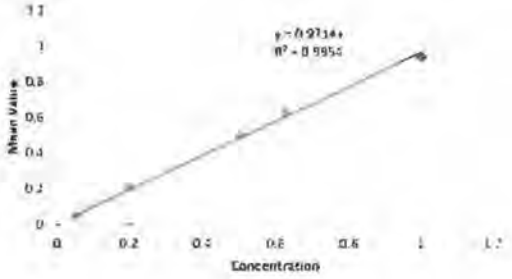

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TABLE 3 (cont.). LINEARITY

Plate B3

	[illegible]	[illegible]
[illegible]		[illegible]
[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]

Intercept	[illegible]
Slope	[illegible]

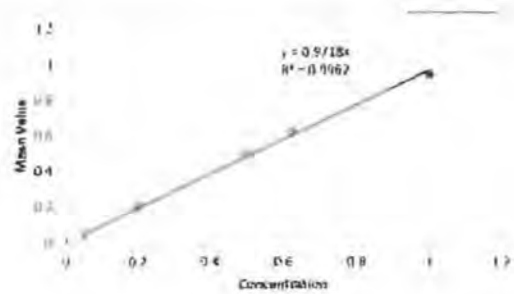

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TABLE 4: RESULTS OF HOMOGENEITY SAMPLES

Plate	Sample ID	Value	Calc. Conc (mg/mL)	Dose Concentration (mg/mL)	Average (mg/mL)	STDEV	%RSD	% Target	Average % Target Of samples	%Target between the strains
	[illegible]	[illegible]	[illegible]	[illegible]						
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]					
	[illegible]	[illegible]	[illegible]	[illegible]						
	[illegible]	[illegible]	[illegible]	[illegible]						Average
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		104.8
	[illegible]	[illegible]	[illegible]	[illegible]					[illegible]	
	[illegible]	[illegible]	[illegible]	[illegible]						
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		
	[illegible]	[illegible]	[illegible]	[illegible]						
	HO 3 BM-1	0.101	0.099	9.92						
Plate B1	HO 3 BM-2	0.096	0.096	9.61	9.7	0.25	2.56	77.4		%RSD
	HO 3 BM-3	0.096	0.094	9.41						13.8
	HO 3 BM-1	0.142	0.146	14.62						
Plate B2	HO 3 BM-2	0.131	0.135	13.50	13.9	0.65	4.72	110.9	95.3	
	HO 3 BM-3	0.131	0.135	13.44						
	HO 3 BM-1	0.115	0.118	11.83						
Plate B3	HO 3 BM-2	0.129	0.133	13.27	12.2	0.93	7.65	97.7		
	HO 3 BM-3	0.112	0.115	11.51						
	HO 4 BB-1	0.170	0.175	17.50						
Plate B4	HO 4 BB-2	0.139	0.137	13.67	15.6	2.71	17.40	124.5		
	HO 4 BB-3	[1]							118.4	
	HO 4 BB-1	0.143	0.147	14.72						
Plate B5	HO 4 BB-2	0.144	0.148	14.83	14.6	0.31	2.17	116.7		
	HO 4 BB-3	0.138	0.142	14.23						

[1] Result is not reported because it was an outlier

Product Safety Labs

Plate	Sample ID	Value	Calc. Conc. (mg/mL)	Dose Concentration (mg/mL)	Average (mg/mL)	STDEV	%RSD	% Target	Average % Target (3 sample means)	% Target between the strata
Plate B4	HO + BB-1	0.144	0.140	14.02	13.[illegible]	1.1[illegible]	8.67	107.8		
	HO + BB-2	0.123	0.127	12.66						
	HO + BB-3	0.126	0.130	12.91						
Plate [illegible]	[illegible]	[illegible]	[illegible]	22.[illegible]	22	[illegible]	[illegible]	[illegible]		Average 91.8
	[illegible]	[illegible]	[illegible]	[illegible]						
	[illegible]	[illegible]	[illegible]	[illegible]						% RSD 2.16
Plate [illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		
	[illegible]	[illegible]	[illegible]	[illegible]						
	[illegible]	[illegible]	[illegible]	[illegible]						
Plate [illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		
	[illegible]	[illegible]	[illegible]	[illegible]						
	[illegible]	[illegible]	[illegible]	[illegible]						
Plate [illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		Average 85.2
	[illegible]	[illegible]	[illegible]	[illegible]						
	[illegible]	[illegible]	[illegible]	[illegible]						% RSD 3.56
Plate [illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		
	[illegible]	[illegible]	[illegible]	[illegible]						
	[illegible]	[illegible]	[illegible]	[illegible]						
Plate [illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		
	[illegible]	[illegible]	[illegible]	[illegible]						
	[illegible]	[illegible]	[illegible]	[illegible]						

Product Safety Labs

TABLE 5: RESULTS OF CONCENTRATION VERIFICATION SAMPLES

Plate	Sample ID	Value	Calc. Conc. (ug/mL)	Dose Concentration (ug/mL)	Average (ug/mL)	STDEV	%RSD	% Target	Average % Target (of sample serum)
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]				
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]				
Plate (b)	CV-6B-1 CV-6B-2 CV-6B-3	**0.154** **0.158** **0.159**	0.151 0.155 0.156	15.11 15.54 15.64	15.1	0.26	1.69	123.5	129.9
Plate (b2	CV-6B-1 CV-6B-2 CV-6B-3	0.163 **0.156** **0.170**	0.160 0.154 0.172	16.29 16.06 17.50	16.6	0.72	4.29	135.2	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	

APPENDIX D: INDIVIDUAL ANIMAL IN-LIFE CLINICAL OBSERVATIONS[1]

PRODUCT IDENTIFICATION

Silk Fibroin

[1] If no observations are listed on the day the animals were necropsied, animals were normal upon observation.

Individual Animal In-Life Clinical Observations
PSL Study Number 51651 A 28 Day Oral Gavage Toxicity Study In Rats

Sex: Male	Animal	Observation Type: All Types	From Day 1 (Start Date) to 31 (Start Date)
Vehicle	7001	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7002	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7003	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7004	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7005	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7006	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7007	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7008	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7009	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7010	Normal	1 to 29
		Scheduled Removal (Terminal)	30

Values = Clin Obs (Range)

[illegible]

Individual Animal In-Life Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male	Animal	Observation Type: All Types	From Day 1 (Start Date) to 31 (Start Date)
Low Dose	7021	Normal	1 to 29
From Day 1 (Start Date) to 31 (Start Date)		Scheduled Removal (Terminal)	30
	7022	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7023	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7024	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7025	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7026	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7027	Normal	1 to 28
		Scheduled Removal (Terminal)	90
	7028	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7029	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7030	Normal	1 to 29
		Scheduled Removal (Terminal)	30

Values = Day Date Range

If no observations are present for an animal on the day of scheduled necropsy, the animal was normal upon examination.

Sex: Male	Animal	Observation Type: All Types	
Mid Dose	7051	Normal	
		Scheduled Removal (Terminal)	
	7047	Normal	
		Scheduled Removal (Terminal)	
	7043	Normal	
		Scheduled Removal (Terminal)	
	7044	Normal	
		Scheduled Removal (Terminal)	
	7048	Normal	
		Scheduled Removal (Terminal)	
	7049	Normal	
		Scheduled Removal (Terminal)	
	7047	Normal	
		Scheduled Removal (Terminal)	
	7046	Normal	
		Scheduled Removal (Terminal)	
		Ectopic Head: Superficial	
	7049	Normal	
		Scheduled Removal (Terminal)	
	7050	Normal	
		Scheduled Removal (Terminal)	

Values = Day Low Range

[1] If no observations are present for an animal on the day of scheduled necropsy, the animal was normal upon examination.

Individual Animal In-Life Clinical Observations
PSI Study Number 51651 A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male	Animal	Observation Type: All Types	(From Day 1 (Start Date) to 31 (End Date))
High Dose	7063	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7062	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7052	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7054	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7068	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7069	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7057	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7058	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7059	Normal	1 to 29
		Scheduled Removal (Terminal)	30
	7061	Normal	1 to 29
		Scheduled Removal (Terminal)	30

Values = Clinical Range

If no observations are present for an animal on the day of scheduled removal, the animal was found moribund

Individual Animal In-Life Clinical Observations
PSI Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex, Female	Animal	Observation Type: All Types	From Day 1 (Start Date) to 31 (End Date)
Vehicle	7001	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7002	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7003	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7004	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7005	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7006	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7007	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7008	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7009	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7010	Normal	1 to 30
		Scheduled Removal (Terminal)	31

Values = Min, Max Range

[illegible] observations are present for an animal on the day of scheduled necropsy, the animal was removed upon examination.

Individual Animal In-Life Clinical Observations
PSI Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female	Animal	Observation Type: All Types	From Day 1 (Start Date) to 31 (Start Date)
Low Dose	[illegible]21	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	[illegible]22	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	[illegible]23	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	[illegible]24	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	[illegible]25	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	[illegible]	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	[illegible]27	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	[illegible]28	Normal	1 to 2, 4 to 30
		Scheduled Removal (Terminal)	31
		Swelling, Right Eye: Slight	3
	[illegible]29	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	[illegible]30	Normal	1 to 30
		Scheduled Removal (Terminal)	31

Values = Cm Use Range

If no observations are present for an animal on the day of scheduled necropsy, the animal was normal upon examination.

Individual Animal In-Life Clinical Observations
PSI Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female	Animal	Observation Type: All Types	(From Day 1 (Start Date) to 31 (Start Date))
Mid Dose	1E1	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7(6)	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7(5)	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	1E4	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7(3)	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	1E	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	1E7	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	1E8	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	1E9	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7(10)	Normal	1 to 30
		Scheduled Removal (Terminal)	31

Values = Clinician Range

If no observations are present for an animal on the day of scheduled necropsy, the animal was normal upon examination.

Individual Animal In-Life Clinical Observations
PSI Study Number 51651: A 28-Day Oral Gavage Toxicity Study in Rats

Sex, Female	Animal	Observation Type: All Types	From Day 1 (Start Date) to 31 (Last Day)
High Dose	7071	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7072	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7073	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7074	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7075	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7076	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7077	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7078	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7079	Normal	1 to 30
		Scheduled Removal (Terminal)	31
	7080	Normal	1 to 30
		Scheduled Removal (Terminal)	31

[1] No observations are present for an animal on the day of scheduled necropsy. The animal was normal upon examination.

APPENDIX E: DETAILED CLINICAL OBSERVATIONS ASSESSMENT METHODS SCORING KEY

PRODUCT IDENTIFICATION

Silk Fibroin

Removal from Cage/Hand-held Observations	
Ease of Removal/Handling	0. Slight/moderate resistance – animal is easy to handle, may squirm or vocalize occasionally 1. No resistance – animal is flaccid when being handled 2. High resistance – animal is difficult to handle, and/or squirms continuously 3. Aggressive – biting or lunging behavior specifically directed at handler
Emaciation	0. Absent 1. Present (confirmed using body weights)
Eyes	0. Normal 1. Exophthalmos – abnormal protrusion of eyeball present 2. Enophthalmus – posterior displacement of the eye (sunken eyeball) 3. Eye lesion – mechanical damage or other (e.g., orbital bleeding)
Fur/Skin Appearance	0. Normal 1. Unkempt – coat rough or ungroomed, may be slightly stained 2. Stained/wetness (e.g., ano-genital staining) 3. Hair loss 4. Other – includes but is not limited; eschar, wound, laceration or other skin lesions
Lacrimation	0. Absent 1. Present – lacrimation noticeable 2. Excessive – animal has excessive amount of tearing
Mucous Membranes (color)	0. Normal 1. Blanch to pink tone 2. Dusky rose to deep flush 3. Cyanosis (blue) 4. Excessive or abnormal secretion
Muscle Tone	0. Normal – muscles are resilient and firm and the hind legs go through their full range of motion 1. Increased – muscles are rigid; hind limbs will not go through their full range of motion 2. Decreased – muscles are flaccid; hind limbs have little or no resistance to movement
Palpebral Closure	0. Eyes wide open 1. Eyes halfway shut 2. Eyes completely shut
Piloerection	0. Absent 1. Present
Pupillary reflex	0. Normal 1. Slow or absent- pupil reaction is slow or absent.
Respiratory Pattern	0. Normal 1. Slow 2. Rapid 3. Rales (Moist or Dry) 4. Gasping 5. Labored - Dyspnea
Salivation	0. None 1. Present - salivation is noticeable around the edge of the mouth 2. Excessive - salivation extends to the fur around the jaw
Vocalization	0. Absent 1. Present - animal vocalizes unprovoked or continuously vocalizes when being handled.

Open Field Observations	
Activity/Arousal	0. Alternating behaviors – animal goes through normal repertoire of behaviors during observation period; these consist of exploring, sniffing, grooming, rearing, etc. 1. Inactive/Alert – animal sits in one place during the observation period but appears to be aware of its surroundings. It may go through its normal repertoire of activities but the majority of the observation period is spent not moving. 2. Hypoactive/Not alert – animal sits in one place during the observation period; animal appears to be unaware of its surroundings or in a stupor. 3. Hyperactive/Hyperalert – animal appears excited; animal may dart and freeze during the observation period or animal may sit in one place and jump at any sound or movement.
Convulsions	0. None 1. Clonic – alternating periods of contraction and relaxation of muscles 2. Tonic – prolonged period of muscle contractions
Defecation	0. None/Normal 1. Soft (partially formed) 2. Diarrhea (watery feces usually of increased volume)
Gait	0. Normal 1. Ataxic Gait – inability of truncal, pelvic and limb muscles to move in unison so animal is not able to move in straight line (lurch). 2. Hypotonic gait – impaired gait (limp) due to limb weakness or paralysis in which the animal is unable to support is weight but can move forward in a straight line without lurching. 3. Impaired Gait – includes steppage (due to dorsiflexion of foot or toe the animal drags its forelimbs, walks on its knuckles or lifts its forelimbs unusually high to avoid dragging its toes over the ground); spastic (shuffling gait with legs rigidly extended and not lifted during movement; waddling (lateral wobbling of the pelvis); dysmetric (incoordinating movement with a coarse tremor due to overshooting goal). 4. Total gait incapacity – applies when these are severe gait abnormalities or combinations of gait abnormality.
Locomotion (speed and vigor of movement)	0. Normal 1. Somewhat impaired 2. Totally impaired
Other	0. Absent 1. Present NOTE: When present, a comment will identify finding
Posture	0. Normal (awake) – e.g., alert, sitting, standing, or rearing or Normal (sleeping) – e.g. curled up, usually with head down 1. Hunched – e.g., abnormal posture 2. Flattened (prone) –e.g., limbs spread out lying flat or on one side
Tremors	0. None 1. Slight – e.g., localized involuntary oscillatory movement 2. Severe – e.g., more to more than one area or involving whole body
Twitches	0. None 1. Slight – brief coarse involuntary muscle contraction 2. Moderate – increased frequency and severity 3. Fasciculation – wave-like ripples of a muscle or group of muscles
Unusual Behaviors	0. Absent 1. Present – Stereotypies/Bizarre behavior/Aggression be specific in describing all unusual behaviors on data sheet
Urination	0. None/Normal 1. Excessive
Vocalizations	0. Absent 1. Present

APPENDIX F: INDIVIDUAL ANIMAL DETAILED CLINICAL OBSERVATIONS

PRODUCT IDENTIFICATION

Silk Fibroin

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Removal from Cage)													
	Handling Reactivity	Handling Reactivity	Handling Reactivity	Handling Reactivity	Handling Reactivity	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Palpebral Closure	Palpebral Closure	Palpebral Closure	Palpebral Closure
	1	8	15	22	29	1	8	15	22	29	1	8	15	22
7001	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7002	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7003	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7004	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7005	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7006	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7007	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7008	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7009	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7010	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Removal from Cage)													
	Palpebral Closure	Lacrimation	Lacrimation	Lacrimation	Lacrimation	Lacrimation	Eyes	Eyes	Eyes	Eyes	Eyes	Mucous Membranes	Mucous Membranes	Mucous Membranes
	29	1	8	15	22	29	1	8	15	22	29	1	8	15
7001	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7002	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7003	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7004	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7005	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7006	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7007	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7008	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7009	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7010	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Removal from Cage)													
	Mucous Membranes	Mucous Membranes	Salivation	Salivation	Salivation	Salivation	Salivation	Emaciation	Emaciation	Emaciation	Emaciation	Emaciation	Piloerection	Piloerection
	22	29	1	8	15	22	29	1	8	15	22	29	1	8
7001	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7002	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7003	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7004	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7005	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7006	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7007	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7008	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7009	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7010	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Removal from Cage)													
	Piloerection	Piloerection	Piloerection	Fur/Skin	Fur/Skin	Fur/Skin	Fur/Skin	Fur/Skin	Muscle Tone	Muscle Tone	Muscle Tone	Muscle Tone	Muscle Tone	Respiratory Pattern
	15	22	29	1	8	15	22	29	1	8	15	22	29	1
7001	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7002	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7003	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7004	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7005	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7006	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7007	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7008	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7009	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7010	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Removal from Cage)									DetClinObs (Open Field Obs)				
	Respiratory Pattern	Respiratory Pattern	Respiratory Pattern	Respiratory Pattern	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal
	8	15	22	29	1	8	15	22	29	1	8	15	22	29
7001	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7002	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7003	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7004	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7005	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7006	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7007	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7008	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7009	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7010	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Open Field Obs)													
	Convulsions	Convulsions	Convulsions	Convulsions	Convulsions	Tremors	Tremors	Tremors	Tremors	Tremors	Posture	Posture	Posture	Posture
	1	8	15	22	29	1	8	15	22	29	1	8	15	22
7001	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7002	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7003	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7004	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7005	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7006	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7007	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7008	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7009	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7010	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Open Field Obs)													
	Posture	Gait	Gait	Gait	Gait	Gait	Locomotion	Locomotion	Locomotion	Locomotion	Locomotion	Defecation	Defecation	Defecation
	29	1	8	15	22	29	1	8	15	22	29	1	8	15
7001	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7002	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7003	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7004	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7005	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7006	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7007	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7008	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7009	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7010	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Open Field Obs)													
	Defecation	Defecation	Urination	Urination	Urination	Urination	Urination	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Vocalization (OF)	Vocalization (OF)
	22	29	1	8	15	22	29	1	8	15	22	29	1	8
7001	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7002	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7003	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7004	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7005	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7006	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7007	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7008	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7009	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7010	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Open Field Obs)												
	Vocalization (OF)	Vocalization (OF)	Vocalization (OF)	Other	Other	Other	Other	Other	Twitches	Twitches	Twitches	Twitches	Twitches
	15	22	29	1	8	15	22	29	1	8	15	22	29
7001	0	0	0	0	0	0	0	0	0	0	0	0	0
7002	0	0	0	0	0	0	0	0	0	0	0	0	0
7003	0	0	0	0	0	0	0	0	0	0	0	0	0
7004	0	0	0	0	0	0	0	0	0	0	0	0	0
7005	0	0	0	0	0	0	0	0	0	0	0	0	0
7006	0	0	0	0	0	0	0	0	0	0	0	0	0
7007	0	0	0	0	0	0	0	0	0	0	0	0	0
7008	0	0	0	0	0	0	0	0	0	0	0	0	0
7009	0	0	0	0	0	0	0	0	0	0	0	0	0
7010	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Removal from Cage)													
	Handling Reactivity	Handling Reactivity	Handling Reactivity	Handling Reactivity	Handling Reactivity	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Palpebral Closure	Palpebral Closure	Palpebral Closure	Palpebral Closure
	1	8	15	22	29	1	8	15	22	29	1	8	15	22
7021	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7022	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7023	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7024	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7025	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7026	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7027	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7028	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7029	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7030	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Removal from Cage)													
	Palpebral Closure	Lacrimation	Lacrimation	Lacrimation	Lacrimation	Lacrimation	Eyes	Eyes	Eyes	Eyes	Eyes	Mucous Membranes	Mucous Membranes	Mucous Membranes
	29	1	8	15	22	29	1	8	15	22	29	1	8	15
7021	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7022	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7023	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7024	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7025	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7026	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7027	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7028	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7029	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7030	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Removal from Cage)													
	Mucous Membranes	Mucous Membranes	Salivation	Salivation	Salivation	Salivation	Salivation	Emaciation	Emaciation	Emaciation	Emaciation	Emaciation	Piloerection	Piloerection
	22	29	1	8	15	22	29	1	8	15	22	29	1	8
7021	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7022	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7023	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7024	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7025	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7026	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7027	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7028	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7029	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7030	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Removal from Cage)													
	Piloerection	Piloerection	Piloerection	Fur/Skin	Fur/Skin	Fur/Skin	Fur/Skin	Fur/Skin	Muscle Tone	Muscle Tone	Muscle Tone	Muscle Tone	Muscle Tone	Respiratory Pattern
	15	22	29	1	8	15	22	29	1	8	15	22	29	1
7021	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7022	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7023	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7024	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7025	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7026	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7027	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7028	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7029	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7030	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Removal from Cage)									DetClinObs (Open Field Obs)				
	Respiratory Pattern	Respiratory Pattern	Respiratory Pattern	Respiratory Pattern	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal
	8	15	22	29	1	8	15	22	29	1	8	15	22	29
7021	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7022	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7023	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7024	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7025	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7026	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7027	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7028	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7029	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7030	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Open Field Obs)													
	Convulsions	Convulsions	Convulsions	Convulsions	Convulsions	Tremors	Tremors	Tremors	Tremors	Tremors	Posture	Posture	Posture	Posture
	1	8	15	22	29	1	8	15	22	29	1	8	15	22
7021	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7022	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7023	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7024	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7025	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7026	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7027	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7028	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7029	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7030	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Open Field Obs)													
	Posture	Gait	Gait	Gait	Gait	Gait	Locomotion	Locomotion	Locomotion	Locomotion	Locomotion	Defecation	Defecation	Defecation
	29	1	8	15	22	29	1	8	15	22	29	1	8	15
7021	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7022	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7023	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7024	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7025	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7026	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7027	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7028	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7029	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7030	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Open Field Obs)													
	Defecation	Defecation	Urination	Urination	Urination	Urination	Urination	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Vocalization (OF)	Vocalization (OF)
	22	29	1	8	15	22	29	1	8	15	22	29	1	8
7021	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7022	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7023	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7024	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7025	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7026	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7027	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7028	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7029	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7030	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Open Field Obs)												
	Vocalization (OF)	Vocalization (OF)	Vocalization (OF)	Other	Other	Other	Other	Other	Twitches	Twitches	Twitches	Twitches	Twitches
	15	22	29	1	8	15	22	29	1	8	15	22	29
7021	0	0	0	0	0	0	0	0	0	0	0	0	0
7022	0	0	0	0	0	0	0	0	0	0	0	0	0
7023	0	0	0	0	0	0	0	0	0	0	0	0	0
7024	0	0	0	0	0	0	0	0	0	0	0	0	0
7025	0	0	0	0	0	0	0	0	0	0	0	0	0
7026	0	0	0	0	0	0	0	0	0	0	0	0	0
7027	0	0	0	0	0	0	0	0	0	0	0	0	0
7028	0	0	0	0	0	0	0	0	0	0	0	0	0
7029	0	0	0	0	0	0	0	0	0	0	0	0	0
7030	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Removal from Cage)													
	Handling Reactivity	Handling Reactivity	Handling Reactivity	Handling Reactivity	Handling Reactivity	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Palpebral Closure	Palpebral Closure	Palpebral Closure	Palpebral Closure
	1	8	15	22	29	1	8	15	22	29	1	8	15	22
7041	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7042	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7043	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7044	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7045	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7046	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7047	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7048	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7049	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7050	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Removal from Cage)													
	Palpebral Closure	Lacrimation	Lacrimation	Lacrimation	Lacrimation	Lacrimation	Eyes	Eyes	Eyes	Eyes	Eyes	Mucous Membranes	Mucous Membranes	Mucous Membranes
	29	1	8	15	22	29	1	8	15	22	29	1	8	15
7041	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7042	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7043	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7044	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7045	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7046	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7047	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7048	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7049	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7050	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Removal from Cage)													
	Mucous Membranes	Mucous Membranes	Salivation	Salivation	Salivation	Salivation	Salivation	Emaciation	Emaciation	Emaciation	Emaciation	Emaciation	Piloerection	Piloerection
	22	29	1	8	15	22	29	1	8	15	22	29	1	8
7041	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7042	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7043	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7044	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7045	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7046	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7047	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7048	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7049	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7050	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Removal from Cage)													
	Piloerection	Piloerection	Piloerection	Fur/Skin	Fur/Skin	Fur/Skin	Fur/Skin	Fur/Skin	Muscle Tone	Muscle Tone	Muscle Tone	Muscle Tone	Muscle Tone	Respiratory Pattern
	15	22	29	1	8	15	22	29	1	8	15	22	29	1
7041	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7042	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7043	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7044	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7045	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7046	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7047	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7048	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7049	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7050	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Removal from Cage)									DetClinObs (Open Field Obs)				
	Respiratory Pattern	Respiratory Pattern	Respiratory Pattern	Respiratory Pattern	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal
	8	15	22	29	1	8	15	22	29	1	8	15	22	29
7041	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7042	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7043	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7044	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7045	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7046	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7047	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7048	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7049	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7050	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Open Field Obs)													
	Convulsions	Convulsions	Convulsions	Convulsions	Convulsions	Tremors	Tremors	Tremors	Tremors	Tremors	Posture	Posture	Posture	Posture
	1	8	15	22	29	1	8	15	22	29	1	8	15	22
7041	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7042	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7043	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7044	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7045	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7046	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7047	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7048	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7049	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7050	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Open Field Obs)													
	Posture	Gait	Gait	Gait	Gait	Gait	Locomotion	Locomotion	Locomotion	Locomotion	Locomotion	Defecation	Defecation	Defecation
	29	1	8	15	22	29	1	8	15	22	29	1	8	15
7041	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7042	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7043	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7044	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7045	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7046	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7047	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7048	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7049	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7050	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male   Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Open Field Obs)													
	Defecation	Defecation	Urination	Urination	Urination	Urination	Urination	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Vocalization (OF)	Vocalization (OF)
	22	29	1	8	15	22	29	1	8	15	22	29	1	8
7041	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7042	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7043	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7044	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7045	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7046	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7047	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7048	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7049	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7050	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Open Field Obs)												
	Vocalization (OF)	Vocalization (OF)	Vocalization (OF)	Other	Other	Other	Other	Other	Twitches	Twitches	Twitches	Twitches	Twitches
	15	22	29	1	8	15	22	29	1	8	15	22	29
7041	0	0	0	0	0	0	0	0	0	0	0	0	0
7042	0	0	0	0	0	0	0	0	0	0	0	0	0
7043	0	0	0	0	0	0	0	0	0	0	0	0	0
7044	0	0	0	0	0	0	0	0	0	0	0	0	0
7045	0	0	0	0	0	0	0	0	0	0	0	0	0
7046	0	0	0	0	0	0	0	0	0	0	0	0	0
7047	0	0	0	0	0	0	0	0	0	0	0	0	0
7048	0	0	0	0	0	0	0	0	0	0	0	0	0
7049	0	0	0	0	0	0	0	0	0	0	0	0	0
7050	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

500 mg/kg/day Group 4	DetClinObs (Removal from Cage)													
	Handling Reactivity	Handling Reactivity	Handling Reactivity	Handling Reactivity	Handling Reactivity	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Palpebral Closure	Palpebral Closure	Palpebral Closure	Palpebral Closure
	1	8	15	22	29	1	8	15	22	29	1	8	15	22
7061	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7062	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7063	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7064	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7065	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7066	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7067	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7068	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7069	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7070	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

500 mg/kg/day Group 4	DetClinObs (Removal from Cage)													
	Palpebral Closure	Lacrimation	Lacrimation	Lacrimation	Lacrimation	Lacrimation	Eyes	Eyes	Eyes	Eyes	Eyes	Mucous Membranes	Mucous Membranes	Mucous Membranes
	29	1	8	15	22	29	1	8	15	22	29	1	8	15
7061	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7062	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7063	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7064	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7065	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7066	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7067	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7068	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7069	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7070	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

500 mg/kg/day Group 4	DetClinObs (Removal from Cage)													
	Mucous Membranes	Mucous Membranes	Salivation	Salivation	Salivation	Salivation	Salivation	Emaciation	Emaciation	Emaciation	Emaciation	Emaciation	Piloerection	Piloerection
	22	29	1	8	15	22	29	1	8	15	22	29	1	8
7061	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7062	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7063	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7064	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7065	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7066	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7067	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7068	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7069	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7070	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

500 mg/kg/day Group 4	DetClinObs (Removal from Cage)													
	Piloerection	Piloerection	Piloerection	Fur/Skin	Fur/Skin	Fur/Skin	Fur/Skin	Fur/Skin	Muscle Tone	Muscle Tone	Muscle Tone	Muscle Tone	Muscle Tone	Respiratory Pattern
	15	22	29	1	8	15	22	29	1	8	15	22	29	1
7061	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7062	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7063	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7064	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7065	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7066	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7067	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7068	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7069	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7070	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

500 mg/kg/day Group 4	DetClinObs (Removal from Cage)									DetClinObs (Open Field Obs)				
	Respiratory Pattern	Respiratory Pattern	Respiratory Pattern	Respiratory Pattern	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal
	8	15	22	29	1	8	15	22	29	1	8	15	22	29
7061	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7062	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7063	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7064	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7065	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7066	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7067	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7068	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7069	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7070	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

500 mg/kg/day Group 4	DetClinObs (Open Field Obs)													
	Convulsions	Convulsions	Convulsions	Convulsions	Convulsions	Tremors	Tremors	Tremors	Tremors	Tremors	Posture	Posture	Posture	Posture
	1	8	15	22	29	1	8	15	22	29	1	8	15	22
7061	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7062	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7063	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7064	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7065	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7066	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7067	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7068	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7069	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7070	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

500 mg/kg/day Group 4	DetClinObs (Open Field Obs)													
	Posture	Gait	Gait	Gait	Gait	Gait	Locomotion	Locomotion	Locomotion	Locomotion	Locomotion	Defecation	Defecation	Defecation
	29	1	8	15	22	29	1	8	15	22	29	1	8	15
7061	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7062	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7063	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7064	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7065	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7066	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7067	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7068	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7069	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7070	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

500 mg/kg/day Group 4	DetClinObs (Open Field Obs)													
	Defecation	Defecation	Urination	Urination	Urination	Urination	Urination	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Vocalization (OF)	Vocalization (OF)
	22	29	1	8	15	22	29	1	8	15	22	29	1	8
7061	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7062	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7063	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7064	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7065	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7066	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7067	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7068	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7069	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7070	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Day(s) Relative to Start Date

500 mg/kg/day Group 4	DetClinObs (Open Field Obs)												
	Vocalization (OF)	Vocalization (OF)	Vocalization (OF)	Other	Other	Other	Other	Other	Twitches	Twitches	Twitches	Twitches	Twitches
	15	22	29	1	8	15	22	29	1	8	15	22	29
7061	0	0	0	0	0	0	0	0	0	0	0	0	0
7062	0	0	0	0	0	0	0	0	0	0	0	0	0
7063	0	0	0	0	0	0	0	0	0	0	0	0	0
7064	0	0	0	0	0	0	0	0	0	0	0	0	0
7065	0	0	0	0	0	0	0	0	0	0	0	0	0
7066	0	0	0	0	0	0	0	0	0	0	0	0	0
7067	0	0	0	0	0	0	0	0	0	0	0	0	0
7068	0	0	0	0	0	0	0	0	0	0	0	0	0
7069	0	0	0	0	0	0	0	0	0	0	0	0	0
7070	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Removal from Cage)													
	Handling Reactivity	Handling Reactivity	Handling Reactivity	Handling Reactivity	Handling Reactivity	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Palpebral Closure	Palpebral Closure	Palpebral Closure	Palpebral Closure
	1	8	15	22	29	1	8	15	22	29	1	8	15	22
7011	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7012	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7013	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7014	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7015	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7016	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7017	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7018	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7019	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7020	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Removal from Cage)													
	Palpebral Closure	Lacrimation	Lacrimation	Lacrimation	Lacrimation	Lacrimation	Eyes	Eyes	Eyes	Eyes	Eyes	Mucous Membranes	Mucous Membranes	Mucous Membranes
	29	1	8	15	22	29	1	8	15	22	29	1	8	15
7011	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7012	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7013	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7014	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7015	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7016	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7017	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7018	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7019	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7020	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Removal from Cage)													
	Mucous Membranes	Mucous Membranes	Salivation	Salivation	Salivation	Salivation	Salivation	Emaciation	Emaciation	Emaciation	Emaciation	Emaciation	Piloerection	Piloerection
	22	29	1	8	15	22	29	1	8	15	22	29	1	8
7011	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7012	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7013	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7014	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7015	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7016	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7017	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7018	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7019	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7020	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Removal from Cage)													
	Piloerection	Piloerection	Piloerection	Fur/Skin	Fur/Skin	Fur/Skin	Fur/Skin	Fur/Skin	Muscle Tone	Muscle Tone	Muscle Tone	Muscle Tone	Muscle Tone	Respiratory Pattern
	15	22	29	1	8	15	22	29	1	8	15	22	29	1
7011	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7012	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7013	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7014	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7015	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7016	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7017	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7018	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7019	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7020	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Removal from Cage)									DetClinObs (Open Field Obs)				
	Respiratory Pattern	Respiratory Pattern	Respiratory Pattern	Respiratory Pattern	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal
	8	15	22	29	1	8	15	22	29	1	8	15	22	29
7011	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7012	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7013	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7014	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7015	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7016	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7017	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7018	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7019	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7020	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Open Field Obs)													
	Convulsions	Convulsions	Convulsions	Convulsions	Convulsions	Tremors	Tremors	Tremors	Tremors	Tremors	Posture	Posture	Posture	Posture
	1	8	15	22	29	1	8	15	22	29	1	8	15	22
7011	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7012	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7013	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7014	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7015	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7016	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7017	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7018	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7019	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7020	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Open Field Obs)													
	Posture	Gait	Gait	Gait	Gait	Gait	Locomotion	Locomotion	Locomotion	Locomotion	Locomotion	Defecation	Defecation	Defecation
	29	1	8	15	22	29	1	8	15	22	29	1	8	15
7011	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7012	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7013	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7014	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7015	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7016	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7017	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7018	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7019	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7020	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Open Field Obs)													
	Defecation	Defecation	Urination	Urination	Urination	Urination	Urination	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Vocalization (OF)	Vocalization (OF)
	22	29	1	8	15	22	29	1	8	15	22	29	1	8
7011	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7012	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7013	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7014	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7015	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7016	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7017	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7018	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7019	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7020	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

0 mg/kg/day Group 1	DetClinObs (Open Field Obs)												
	Vocalization (OF)	Vocalization (OF)	Vocalization (OF)	Other	Other	Other	Other	Other	Twitches	Twitches	Twitches	Twitches	Twitches
	15	22	29	1	8	15	22	29	1	8	15	22	29
7011	0	0	0	0	0	0	0	0	0	0	0	0	0
7012	0	0	0	0	0	0	0	0	0	0	0	0	0
7013	0	0	0	0	0	0	0	0	0	0	0	0	0
7014	0	0	0	0	0	0	0	0	0	0	0	0	0
7015	0	0	0	0	0	0	0	0	0	0	0	0	0
7016	0	0	0	0	0	0	0	0	0	0	0	0	0
7017	0	0	0	0	0	0	0	0	0	0	0	0	0
7018	0	0	0	0	0	0	0	0	0	0	0	0	0
7019	0	0	0	0	0	0	0	0	0	0	0	0	0
7020	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Removal from Cage)													
	Handling Reactivity	Handling Reactivity	Handling Reactivity	Handling Reactivity	Handling Reactivity	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Palpebral Closure	Palpebral Closure	Palpebral Closure	Palpebral Closure
	1	8	15	22	29	1	8	15	22	29	1	8	15	22
7031	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7032	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7033	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7034	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7035	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7036	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7037	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7038	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7039	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7040	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Removal from Cage)													
	Palpebral Closure	Lacrimation	Lacrimation	Lacrimation	Lacrimation	Lacrimation	Eyes	Eyes	Eyes	Eyes	Eyes	Mucous Membranes	Mucous Membranes	Mucous Membranes
	29	1	8	15	22	29	1	8	15	22	29	1	8	15
7031	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7032	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7033	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7034	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7035	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7036	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7037	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7038	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7039	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7040	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Removal from Cage)													
	Mucous Membranes	Mucous Membranes	Salivation	Salivation	Salivation	Salivation	Salivation	Emaciation	Emaciation	Emaciation	Emaciation	Emaciation	Piloerection	Piloerection
	22	29	1	8	15	22	29	1	8	15	22	29	1	8
7031	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7032	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7033	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7034	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7035	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7036	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7037	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7038	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7039	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7040	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Removal from Cage)													
	Piloerection	Piloerection	Piloerection	Fur/Skin	Fur/Skin	Fur/Skin	Fur/Skin	Fur/Skin	Muscle Tone	Muscle Tone	Muscle Tone	Muscle Tone	Muscle Tone	Respiratory Pattern
	15	22	29	1	8	15	22	29	1	8	15	22	29	1
7031	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7032	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7033	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7034	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7035	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7036	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7037	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7038	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7039	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7040	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Removal from Cage)									DetClinObs (Open Field Obs)				
	Respiratory Pattern	Respiratory Pattern	Respiratory Pattern	Respiratory Pattern	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal
	8	15	22	29	1	8	15	22	29	1	8	15	22	29
7031	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7032	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7033	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7034	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7035	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7036	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7037	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7038	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7039	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7040	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Open Field Obs)													
	Convulsions	Convulsions	Convulsions	Convulsions	Convulsions	Tremors	Tremors	Tremors	Tremors	Tremors	Posture	Posture	Posture	Posture
	1	8	15	22	29	1	8	15	22	29	1	8	15	22
7031	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7032	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7033	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7034	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7035	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7036	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7037	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7038	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7039	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7040	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Open Field Obs)													
	Posture	Gait	Gait	Gait	Gait	Gait	Locomotion	Locomotion	Locomotion	Locomotion	Locomotion	Defecation	Defecation	Defecation
	29	1	8	15	22	29	1	8	15	22	29	1	8	15
7031	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7032	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7033	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7034	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7035	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7036	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7037	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7038	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7039	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7040	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Open Field Obs)													
	Defecation	Defecation	Urination	Urination	Urination	Urination	Urination	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Vocalization (OF)	Vocalization (OF)
	22	29	1	8	15	22	29	1	8	15	22	29	1	8
7031	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7032	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7033	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7034	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7035	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7036	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7037	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7038	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7039	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7040	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

125 mg/kg/day Group 2	DetClinObs (Open Field Obs)												
	Vocalization (OF)	Vocalization (OF)	Vocalization (OF)	Other	Other	Other	Other	Other	Twitches	Twitches	Twitches	Twitches	Twitches
	15	22	29	1	8	15	22	29	1	8	15	22	29
7031	0	0	0	0	0	0	0	0	0	0	0	0	0
7032	0	0	0	0	0	0	0	0	0	0	0	0	0
7033	0	0	0	0	0	0	0	0	0	0	0	0	0
7034	0	0	0	0	0	0	0	0	0	0	0	0	0
7035	0	0	0	0	0	0	0	0	0	0	0	0	0
7036	0	0	0	0	0	0	0	0	0	0	0	0	0
7037	0	0	0	0	0	0	0	0	0	0	0	0	0
7038	0	0	0	0	0	0	0	0	0	0	0	0	0
7039	0	0	0	0	0	0	0	0	0	0	0	0	0
7040	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Removal from Cage)													
	Handling Reactivity	Handling Reactivity	Handling Reactivity	Handling Reactivity	Handling Reactivity	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Palpebral Closure	Palpebral Closure	Palpebral Closure	Palpebral Closure
	1	8	15	22	29	1	8	15	22	29	1	8	15	22
7051	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7052	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7053	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7054	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7055	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7056	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7057	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7058	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7059	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7060	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
FSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Removal from Cage)													
	Palpebral Closure	Lacrimation	Lacrimation	Lacrimation	Lacrimation	Lacrimation	Eyes	Eyes	Eyes	Eyes	Eyes	Mucous Membranes	Mucous Membranes	Mucous Membranes
	29	1	8	15	22	29	1	8	15	22	29	1	8	15
7051	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7052	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7053	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7054	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7055	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7056	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7057	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7058	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7059	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7060	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Removal from Cage)													
	Mucous Membranes	Mucous Membranes	Salivation	Salivation	Salivation	Salivation	Salivation	Emaciation	Emaciation	Emaciation	Emaciation	Emaciation	Piloerection	Piloerection
	22	29	1	8	15	22	29	1	8	15	22	29	1	8
7051	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7052	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7053	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7054	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7055	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7056	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7057	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7058	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7059	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7060	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Removal from Cage)													
	Piloerection	Piloerection	Piloerection	Fur/Skin	Fur/Skin	Fur/Skin	Fur/Skin	Fur/Skin	Muscle Tone	Muscle Tone	Muscle Tone	Muscle Tone	Muscle Tone	Respiratory Pattern
	15	22	29	1	8	15	22	29	1	8	15	22	29	1
7051	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7052	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7053	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7054	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7055	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7056	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7057	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7058	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7059	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7060	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Removal from Cage)									DetClinObs (Open Field Obs)				
	Respiratory Pattern	Respiratory Pattern	Respiratory Pattern	Respiratory Pattern	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal
	8	15	22	29	1	8	15	22	29	1	8	15	22	29
7051	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7052	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7053	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7054	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7055	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7056	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7057	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7058	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7059	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7060	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Open Field Obs)													
	Convulsions	Convulsions	Convulsions	Convulsions	Convulsions	Tremors	Tremors	Tremors	Tremors	Tremors	Posture	Posture	Posture	Posture
	1	8	15	22	29	1	8	15	22	29	1	8	15	22
7051	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7052	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7053	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7054	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7055	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7056	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7057	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7058	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7059	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7060	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Open Field Obs)													
	Posture	Gait	Gait	Gait	Gait	Gait	Locomotion	Locomotion	Locomotion	Locomotion	Locomotion	Defecation	Defecation	Defecation
	29	1	8	15	22	29	1	8	15	22	29	1	8	15
7051	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7052	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7053	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7054	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7055	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7056	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7057	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7058	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7059	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7060	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Open Field Obs)													
	Defecation	Defecation	Urination	Urination	Urination	Urination	Urination	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Vocalization (OF)	Vocalization (OF)
	22	29	1	8	15	22	29	1	8	15	22	29	1	8
7051	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7052	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7053	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7054	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7055	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7056	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7057	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7058	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7059	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7060	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

250 mg/kg/day Group 3	DetClinObs (Open Field Obs)												
	Vocalization (OF)	Vocalization (OF)	Vocalization (OF)	Other	Other	Other	Other	Other	Twitches	Twitches	Twitches	Twitches	Twitches
	15	22	29	1	8	15	22	29	1	8	15	22	29
7051	0	0	0	0	0	0	0	0	0	0	0	0	0
7052	0	0	0	0	0	0	0	0	0	0	0	0	0
7053	0	0	0	0	0	0	0	0	0	0	0	0	0
7054	0	0	0	0	0	0	0	0	0	0	0	0	0
7055	0	0	0	0	0	0	0	0	0	0	0	0	0
7056	0	0	0	0	0	0	0	0	0	0	0	0	0
7057	0	0	0	0	0	0	0	0	0	0	0	0	0
7058	0	0	0	0	0	0	0	0	0	0	0	0	0
7059	0	0	0	0	0	0	0	0	0	0	0	0	0
7060	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

500 mg/kg/day Group 4	DetClinObs (Removal from Cage)													
	Handling Reactivity	Handling Reactivity	Handling Reactivity	Handling Reactivity	Handling Reactivity	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Vocalization (RC)	Palpebral Closure	Palpebral Closure	Palpebral Closure	Palpebral Closure
	1	8	15	22	29	1	8	15	22	29	1	8	15	22
7071	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7072	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7073	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7074	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7075	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7076	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7077	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7078	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7079	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7080	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

500 mg/kg/day Group 4	DetClinObs (Removal from Cage)													
	Palpebral Closure	Lacrimation	Lacrimation	Lacrimation	Lacrimation	Lacrimation	Eyes	Eyes	Eyes	Eyes	Eyes	Mucous Membranes	Mucous Membranes	Mucous Membranes
	29	1	8	15	22	29	1	8	15	22	29	1	8	15
7071	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7072	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7073	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7074	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7075	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7076	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7077	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7078	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7079	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7080	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

500 mg/kg/day Group 4	DetClinObs (Removal from Cage)													
	Mucous Membranes	Mucous Membranes	Salivation	Salivation	Salivation	Salivation	Salivation	Emaciation	Emaciation	Emaciation	Emaciation	Emaciation	Piloerection	Piloerection
	22	29	1	8	15	22	29	1	8	15	22	29	1	8
7071	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7072	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7073	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7074	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7075	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7076	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7077	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7078	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7079	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7080	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

500 mg/kg/day Group 4	DetClinObs (Removal from Cage)													
	Piloerection	Piloerection	Piloerection	Fur/Skin	Fur/Skin	Fur/Skin	Fur/Skin	Fur/Skin	Muscle Tone	Muscle Tone	Muscle Tone	Muscle Tone	Muscle Tone	Respiratory Pattern
	15	22	29	1	8	15	22	29	1	8	15	22	29	1
7071	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7072	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7073	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7074	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7075	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7076	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7077	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7078	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7079	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7080	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

500 mg/kg/day Group 4	DetClinObs (Removal from Cage)									DetClinObs (Open Field Obs)				
	Respiratory Pattern	Respiratory Pattern	Respiratory Pattern	Respiratory Pattern	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Pupillary Reflex	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal	Activity/ Arousal
	8	15	22	29	1	8	15	22	29	1	8	15	22	29
7071	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7072	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7073	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7074	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7075	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7076	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7077	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7078	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7079	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7080	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

500 mg/kg/day Group 4	DetClinObs (Open Field Obs)													
	Convulsions	Convulsions	Convulsions	Convulsions	Convulsions	Tremors	Tremors	Tremors	Tremors	Tremors	Posture	Posture	Posture	Posture
	1	8	15	22	29	1	8	15	22	29	1	8	15	22
7071	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7072	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7073	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7074	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7075	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7076	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7077	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7078	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7079	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7080	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
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	Posture	Gait	Gait	Gait	Gait	Gait	Locomotion	Locomotion	Locomotion	Locomotion	Locomotion	Defecation	Defecation	Defecation
	29	1	8	15	22	29	1	8	15	22	29	1	8	15
7071	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7072	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7073	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7074	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7075	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7076	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7077	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7078	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7079	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7080	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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	Defecation	Defecation	Urination	Urination	Urination	Urination	Urination	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Unusual Behaviors	Vocalization (OF)	Vocalization (OF)
	22	29	1	8	15	22	29	1	8	15	22	29	1	8
7071	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7072	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7073	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7074	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7075	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7076	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7077	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7078	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7079	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7080	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Individual Animal Detailed Clinical Observations
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500 mg/kg/day Group 4	DetClinObs (Open Field Obs)												
	Vocalization (OF)	Vocalization (OF)	Vocalization (OF)	Other	Other	Other	Other	Other	Twitches	Twitches	Twitches	Twitches	Twitches
	15	22	29	1	8	15	22	29	1	8	15	22	29
7071	0	0	0	0	0	0	0	0	0	0	0	0	0
7072	0	0	0	0	0	0	0	0	0	0	0	0	0
7073	0	0	0	0	0	0	0	0	0	0	0	0	0
7074	0	0	0	0	0	0	0	0	0	0	0	0	0
7075	0	0	0	0	0	0	0	0	0	0	0	0	0
7076	0	0	0	0	0	0	0	0	0	0	0	0	0
7077	0	0	0	0	0	0	0	0	0	0	0	0	0
7078	0	0	0	0	0	0	0	0	0	0	0	0	0
7079	0	0	0	0	0	0	0	0	0	0	0	0	0
7080	0	0	0	0	0	0	0	0	0	0	0	0	0