Final Report

A Repeat-Dose Toxicity Study in Rats Given Compound 2463608 by Intravenous Injection for 2 Weeks

Study:
Covance 7608-544

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17 September 2007

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Quality Assurance Statement

A Repeat-Dose Toxicity Study in Rats Given Compound 2463608 by Intravenous Injection for 2 Weeks

This report has been reviewed by the Quality Assurance Unit of Covance Laboratories Inc. and accurately reflects the raw data. The following inspections were conducted and findings reported to the principal investigator (PI), study director (SD), and associated management.

Inspection Dates		Phase	Date Reported to PI and PI Management	Date Reported to SD and SD Management
Start Date	End Date			
01 Jun 2007	01 Jun 2007	Protocol Review		01 Jun 2007
01 Jun 2007	01 Jun 2007	Protocol Amendment Review		01 Jun 2007
06 Jun 2007	06 Jun 2007	Test Article Administration		06 Jun 2007
20 Jun 2007	20 Jun 2007	Protocol Amendment Review		20 Jun 2007
11 Jul 2007	11 Jul 2007	Protocol Amendment Review		11 Jul 2007
30 Jul 2007	30 Jul 2007	Protocol Amendment Review		30 Jul 2007
15 Aug 2007	17 Aug 2007	Data Review	22 Aug 2007	22 Aug 2007
20 Aug 2007	22 Aug 2007	Draft Report Review	22 Aug 2007	22 Aug 2007
31 Aug 2007	04 Sep 2007	Revised Draft Report Review		04 Sep 2007
11 Sep 2007	11 Sep 2007	Revised Draft Report Review		11 Sep 2007

Jennifer Brandt 17 Sept 2007

Representative Date
Quality Assurance Unit
Covance Laboratories Inc.

Compliance Statement

Compound: Compound 2463608 Study: Covance 7608-544

This study, with the exception of dose analysis, formulation stability, and test article potency reassay, conformed to the following Good Laboratory Practice standards in place at the time of study initiation.

United States Food and Drug Administration (CFR 21 - Part 58)
Organisation for Economic Co-operation and Development (OECD)

Meeting the above requirements satisfies the Bilateral Agreement with Japan.

Dose analysis and test article potency reassay by the sponsor were not conducted in accordance with United States Food and Drug Administration or OECD Good Laboratory Practice standards. Test article formulation stability was established for a concentration of 0.176 mg/mL; a concentration of 0.5 mg/mL was used on this study.

Matthew D. Schroeder, PhD
Study Director
Covance Laboratories Inc.

17 Sep 07
Date

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Summary

A Repeat-Dose Toxicity Study in Rats Given Compound 2463608 by Intravenous Injection for 2 Weeks

Study: Covance 7608-544

The purpose of this study was to evaluate the toxicity of Compound 2463608 when administered daily by intravenous injection to rats for at least 2 weeks.

The toxicity of Compound 2463608 was evaluated in male and female Crl:CD(SD) rats (five/sex/group) given saline control [0.9% Sodium Chloride for Injection, USP (sterile saline)], vehicle control [20% (w/v) Captisol in 25mM acetate buffer prepared in Sterile Water for Injection, USP, pH 3.8 to 4.4], or 1.0 mg of Compound 2463608/kg of body weight (mg/kg) via slow bolus intravenous injection daily for 15 days.

All animals survived to scheduled sacrifice.

The only compound-related clinical sign seen during the dosing phase was excessive grooming. No compound-related changes in ophthalmic examination findings, body weight, or food consumption were noted.

No compound-related effects were seen on clinical pathology test results, organ weights, or microscopic morphology. All findings were attributed to vehicle or injection procedure.

Males given the vehicle control or 1.0 mg/kg had statistically significantly decreased mean absolute thymus weight, mean thymus-to-body weight percentage, and mean thymus-to-brain weight percentage when compared with the saline control group, and females given 1.0 mg/kg had statistically significant increases in these same thymus weight parameters when compared with females given the vehicle control. No correlative macroscopic or microscopic thymus findings were seen in either sex. Decreased thymus weight in males in the groups given vehicle only or Compound 2463608 and in females given vehicle only were attributed to the vehicle. Increases in thymus weight in females given Compound 2463608 were considered spurious since 4/5 animals had thymus weights within the range of concurrent saline controls. Minimal to moderate vacuolation of tubule cells in the kidney was a microscopic finding seen in all animals given either the vehicle control or the test compound. No animals given the saline control were similarly affected, indicating that the tubular vacuolation was associated with the vehicle control article.

The incidence and severity of microscopic findings at injection sites were similar across all groups, suggesting that they were due to the injection procedure and not to the vehicle or Compound 2463608.

In summary, daily intravenous administration of 1.0 mg Compound 2463608/kg to Crl:CD(SD) rats for 15 days resulted in the compound-related clinical sign of excessive grooming but no adverse findings. The no observed adverse effect level is, therefore, 1.0 mg/kg under the conditions of this study.

Introduction

The purpose of this study was to evaluate the toxicity of Compound 2463608 when administered daily by intravenous injection to rats for at least 2 weeks.

Rats historically have been used in safety evaluation studies and are recommended by appropriate regulatory agencies; the intended route of administration in humans is intravenous. Compound 2463608 has been identified as having acceptable characteristics to aid in localizing CB-1 receptors in the brain. The compound will be used in a competition trial in human subjects, first using rimonabant and subsequently with LY2562403. A single-dose expanded acute rat study has been completed, but higher exposure margins and repeat dosing are required for use of the ligand in Europe. The dose of 1.0 mg/kg used on this study represents slightly more than 1000-fold (on a mg/m^3 basis) greater than the dose to be used in human subjects. The saline group was included to control for possible adverse effects of the vehicle, 20% Captisol in 25mM acetate buffer pH 4.0.

The study initiation date was 29 May 2007, the experimental start date was 29 May 2007, animals were first dosed on 05 June 2007, the final necropsy occurred on 20 June 2007, the experimental end date is scheduled for 17 September 2007, and the study completion date is scheduled for 17 September 2007.

Procedures

Protocol Information

(Appendix A and Appendix B)

Appendix A contains the protocol and protocol amendments for this study; Appendix B contains the study deviations.

Regulatory Guidelines

The study design was based on the principles of the Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER)/International Conference on Harmonisation (ICH) Harmonised Tripartite Guidelines ICH-M3; Nonclinical Safety Studies for the Conduct of Human Clinical Trials for Pharmaceuticals (CDER, July 1997).

Test Article, Vehicle Control Article and Saline Control Article

(Appendix C)

The test article was supplied by the sponsor as follows.

Test Article	Lot No.	Storage	Potency[a]	Reserve (Archive) Sample
Compound 2463608	KD0-E01100-039-C	At room temperature	100% (theoretical)	None Required

a The actual purity of >99% and the potency reassay (see Appendix B for deviation) result of 99% demonstrated that the test article was stable for use on study.

The vehicle control article was 20% (w/v) Captisol in 25mM acetate buffer prepared in Sterile Water for Injection (SWFI), USP, pH 3.8 to 4.4. The saline control article was 0.9% Sodium Chloride for Injection, USP (sterile saline). The vehicle control article components and saline control article were stored at room temperature and supplied as follows.

Vehicle Control Article	Supplier	Lot No.	Purity	Expiration Date	Reserve (Archive) Sample
Captisol	Eli Lilly and Company	NC-04A-05025	MS	27 Mar 2012	None Required
Sodium acetate	Sigma Aldrich	066K0043	MS	30 Jun 2011	None Required
Glacial acetic acid	Sigma Aldrich	016K0667	USP	13 Feb 2012	None Required
0.9% Sodium Chloride for Injection, USP	Fisher Scientific	50036JT	USP	01 Feb 2009	None Required
SWFI, USP	Fisher Scientific	46-208-JT	USP	01 Oct 2008	None Required
SWFI, USP	Fisher Scientific	43-933-FW	USP	01 Jul 2008	None Required

MS = Meets specifications.
USP = United States Pharmacopoeia.

The prepared vehicle control article was stored in a refrigerator, set to maintain 2 to 8 degrees Celsius, until used for test article preparation or dispensing for dose administration.

Information on synthesis methods, stability, purity, composition, or other characteristics that define the test article and control article components is on file with the sponsor or the respective manufacturer. Appendix C contains the Certificates of Analysis.

Test System and Study Design

Male and female Crl:CD(SD) rats were obtained from Charles River Laboratories, Raleigh, North Carolina. Animals were randomly assigned to the following groups based on weight.

Group	No. of Animals Male	No. of Animals Female	Dose Level (mg 2463608/kg/day)[a]	Dose Concentration (mg 2463608/mL)[a]
Toxicity Animals				
1 (Saline Control)	5	5	0	0
2 (Vehicle Control)	5	5	0	0
3 (Compound 2463608)	5	5	1.0	0.5

a The dose volume was 2.0 mL/kg.

At initiation of treatment, the animals were 9.6 to 10.4 weeks of age; the males weighed from 293 to 327 g, and females weighed from 207 to 236 g. Animals were identified using an implantable microchip identification device and cage card.

Procedures

Procedure	Frequency/Comment
Dose Preparation	
Vehicle Control Article[a]	Vehicle control article, including that used for dosing, was prepared approximately weekly, sterile-filtered prior to dispensing for dose preparation or dosing, and stored in a refrigerator, set to maintain 2 to 8 degrees Celsius.
Saline Control Article	The saline control article was stored at room temperature and dosed as supplied.
Dosing Formulations	Test article for dose preparation was weighed in a laminar flow hood; dose preparation was conducted aseptically, as applicable, using autoclaved equipment and glassware according to the mixing procedure supplied by the sponsor and modified by Covance. Test article formulations were filtered through a 0.22-micron filter, aliquotted for daily use, stored at room temperature, and used within 4 days of preparation. Test article dose formulations were, as necessary, sonicated and/or allowed to stir overnight, using a stir bar and stir plate, at room temperature in a sterile hood. Dose concentrations were based on the test article as supplied.
Dose Administration[a]	Administered by slow bolus injection in a tail vein once daily for 15 days (dosing phase) at a dose volume of 2.0 mL/kg over approximately 30 to 60 seconds. Dose administration was followed by a saline flush of approximately 0.5 mL. The dose site was marked with indelible ink on each toxicity animal following the final dose administration.
Dose Analysis	
Homogeneity	For the concentration of the test article dose preparation, the mixture was a solution; therefore, no homogeneity analysis was necessary.
Stability	Stability of the test article formulation was determined separately from this study by the sponsor; stability was established for a concentration of 0.176 mg/mL while a concentration of 0.5 mg/mL was used on this study. A concentration of 0.176 mg/mL in vehicle control article was found to be stable for 5 days at room temperature.
Concentration Verification	Duplicate samples (1.0 mL each) were taken at the time of mixing from the test article, saline, and vehicle control article formulations prepared for use on Day 1 of the dosing phase. All samples were stored at room temperature until shipped on Day 2 for analysis. Two 1-mL samples were taken from the remaining Group 3 dose preparation used for dosing on Day 15. Each sample was weighed, stored at room temperature, and shipped on Day 15 for analysis.

Procedure	Frequency/Comment
Inlife Procedures	
Husbandry	Male and female rats were housed individually in stainless steel cages and offered water and Certified Rodent Diet #2014C (Harlan Teklad) ad libitum unless otherwise specified. Environmental controls for the animal room were set to maintain 18 to 26 degrees Celsius, a relative humidity of 30 to 70%, a minimum of 10 room air changes/hour, and a 12-hour light/12-hour dark cycle. The light/dark cycle was interrupted for study-related activities. Any variations to these conditions are maintained in the raw data and had no effect on the outcome of the study.
Clinical Signs	Animals were checked twice daily (a.m. and p.m.) for mortality, abnormalities, and signs of pain or distress. Additional findings were recorded as observed. Detailed observations were conducted for each animal at least once during the predose phase, on the first day of dosing (Day 1) and weekly thereafter (prior to dosing), and on the day of scheduled sacrifice; abnormal findings or an indication of normal was recorded. Once daily during the dosing phase, cageside observations were made for each animal, except on days when detailed observations were conducted.
Ophthalmic Examinations	Conducted once during the predose phase and on Day 11 of the dosing phase by a veterinarian using an indirect ophthalmoscope
Body Weights	Measured once during the predose phase, on Day 1 of the dosing phase, and weekly thereafter
Food Consumption	Quantitatively assessed weekly during the doing phase
Clinical Pathology	Samples were taken for hematology, coagulation, clinical chemistry, and urinalysis on the day of scheduled sacrifice.
Disposition of Animals	
Dosing Phase - Final Phase Sacrifice	After 15 days of treatment, all surviving animals were fasted overnight, then anesthetized with sodium pentobarbital, exsanguinated, and necropsied. Terminal body weights were recorded.
Organ Weights	Protocol-specified organ weights were recorded at the scheduled sacrifice.
Bone Marrow Smears	Bone marrow smears were prepared from the femur of each animal at scheduled sacrifices and held for possible future examination. Microscopic examination of these smears is not planned. In the event that such examination does occur, a copy of the resulting report will be included in an amendment to this study report.
Tissue Preservation	Protocol-specified tissues (when present) from each animal were preserved in 10% neutral-buffered formalin, with the exception of the epididymis, eye, optic nerve, and testis, which were preserved in modified Davidson's fixative.

Procedure	Frequency/Comment
Histopathology[a]	Preserved tissues from each animal were embedded in paraffin, sectioned, and stained with hematoxylin and eosin. All tissues from all animals in the vehicle and compound-treated groups (Groups 2 and 3) were examined microscopically by a board-certified veterinary pathologist. The kidneys, injection site, and thymus, identified potential target tissues, from all animals in the saline-treated group (Group 1) were also examined microscopically. All other prepared slides from these animals were held for possible future examination. Microscopic examination of these remaining slides is not planned. In the event that such examination does occur, a copy of the resulting report will be included in an amendment to this study report.
Miscellaneous Procedures	
Record Retention	The raw data, documentation, records, specimens, protocol, and final report generated as a result of this study will be archived in the Covance archives for at least 3 years as detailed in the protocol. The raw data, documentation, records, specimens, and contributor reports generated by Eli Lilly and Company as a result of this study will be archived in the storage facilities of Eli Lilly and Company.
Statistical Evaluation[b]	The following statistical methods were used to analyze the body weight, body weight change, food consumption, continuous clinical pathology, and organ weight data. Levene's test (Levene, 1960; Draper and Hunter, 1969) was done to test for variance homogeneity. In the case of heterogeneity of variance at $p \leq 0.05$, rank transformation was used to stabilize the variance. Comparison tests took variance heterogeneity into consideration. One-way analysis of variance [ANOVA (Winer, 1971)] was used to analyze data. If the ANOVA was significant ($p \leq 0.05$), Fisher's LSD t-test (Miller, 1980) was used for pairwise comparisons between treated and control groups. For data that exhibited heterogeneous variances after the series of transformations, Fisher's LSD t-test for unequal variances with Welch's degrees of freedom (Welch, 1947) was employed. Group comparisons (Groups 2 and 3 versus Group 1 and Group 3 versus Group 2) were evaluated at the 5.0%, two-tailed probability level. Unless otherwise specified in the protocol, only data collected on or after the first day of treatment were analyzed statistically. Statistical significance is designated throughout the text of this report by the term *significant*. Statistical analysis programs are referenced accordingly in the appropriate section of this report.
Major Computer Systems[c]	*Application Function*
Metasys	Monitors and controls environmental conditions and water flow within the facility (e.g., animal rooms)

Procedure	Frequency/Comment
REES Environmental Monitoring	Monitors and documents facility storage conditions (e.g., refrigerators, freezers, and constant room temperatures)
VPTS	Captures direct online inlife toxicology and clinical and anatomic pathology data and randomizes animals
AFLGS	Produces labels and forms
eNotes	Documents study-specific communications
TALISMAN	Documents test and control article and dose preparation information
COSTAR	Transfers data from VPTS for reporting purposes
SAS[b]	Performs statistical analysis

Note: The table contains all protocol procedures as amended (see Appendix A for the protocol and amendments).
a See Appendix B for deviations.
b References for the specific procedures performed for this study can be found in the References section.
c All version numbers of the applications are maintained by Covance. Appendix D contains definitions for the acronyms.

Sponsor, Key Personnel, and Test Sites

(Appendix D)

This study was sponsored by Eli Lilly and Company, Lilly Corporate Center, Indianapolis, Indiana, 46285. Individuals and test sites involved in planning, conducting, and reporting Covance 7608-544 are listed on the signature pages and/or in the appendices.

Peer Review

Following completion of the primary microscopic evaluation, an independent peer review evaluation was performed by the sponsor. The purpose of this peer review was a pathology data review and quality assessment of the pathology findings. Attention was directed to the completeness, accuracy, and consistency of the original evaluation. The body weight data, clinical pathology data, organ weight data, necropsy findings, and histopathology findings with interpretation of the primary pathologist were available and referred to during the review process. Histologic sections of all tissues from three animals/sex/group from the vehicle control and compound-dosed groups (Groups 2 and 3, respectively) were examined microscopically. Animals evaluated were Animal Nos. B96006, B96008, and B96010 (Group 2 males); B96011, B96013, and B96015 (Group 3 males); B96021, B90623, and B96025 (Group 2 females); and B96026, B96028, and B96030 (Group 3 females). Additionally, sections of the kidney, thymus, and intravenous site from all animals in the study were examined. The pathologic evaluation of individual animals represents the consensus of primary and reviewing pathologists.

Results

Test Article

(Table 1)

The test article was stable throughout the dosing phase. The potency was >99 and 99% Compound 2463608 at the beginning and following the end of dosing, respectively.

The Compound 2463608 concentration of each sampled dosing solution did not deviate substantially from its theoretical value. Mean assayed concentrations of Compound 2463608 ranged from 95 to 99% of theoretical values, indicating that the dose preparations were properly prepared and acceptable for use on study.

Survival and Clinical Signs

(Table 2)

All animals survived to scheduled necropsy. The only compound-related clinical sign seen during the dosing phase was excessive grooming; this was generally seen within the first hour after dosing but had resolved by the time of p.m. observations, generally done 2 to 4 hours after dosing. Excessive grooming was observed in one female given saline and in three females given vehicle control article only but was seen in all animals given compound and occurred with much higher frequency in compound-treated animals. Skin problems did not result from the excessive grooming, and, therefore, this compound-related clinical sign was not considered adverse.

Ophthalmic Evaluations

(Table 3)

No compound-related ophthalmic observations were noted; there were no visible lesions or other abnormalities in any animal.

Body Weights and Food Consumption

(Table 4 through Table 6)

No compound-related effects on body weights or food consumption were noted.

Clinical Pathology

(Table 7 through Table 9)

Administration of Compound 2463608 had no effect on clinical pathology test results. Overall, only three statistically significant differences were observed for clinical pathology test results. Two of these changes (minimal increases in monocyte count, and globulin concentration) were considered incidental as they were of very small magnitude or occurred in the vehicle group only (Group 2). The third statistically significant finding was a mild decrease in urine pH in females receiving vehicle (Group 2) and compound

(Group 3). This change was of similar magnitude in both groups and considered vehicle-related.

Anatomic Pathology

(Table 10 through Table 13)

Males given the vehicle control or 1.0 mg/kg had statistically significantly decreased mean absolute thymus weight, mean thymus-to-body weight percentage, and mean thymus-to-brain weight percentage when compared with the saline control group, and females given 1.0 mg/kg had statistically significant increases in these same thymus weight parameters when compared with females given the vehicle control. No correlative macroscopic or microscopic thymus findings were seen in either sex. Decreased thymus weight in males given vehicle only and Compound 2463608 and in females given vehicle only were attributed to the vehicle. Increases in thymus weight in females given Compound 2463608 were considered spurious since 4/5 animals had thymus weights within the range of concurrent saline controls. In females only, mean absolute spleen weight and spleen-to-brain weight percentage were statistically significantly decreased in the group given the test compound when compared with the vehicle control group. The spleen weight decreases were attributed to normal biologic variation because of a lack of microscopic or macroscopic correlates and because males were not similarly affected. No other statistically significant or compound-related organ weight changes were noted.

Vacuolation of tubule cells in the kidney was a microscopic finding seen in all animals given either the vehicle control or the test compound. No animals given the saline control were similarly affected, indicating that the tubular vacuolation was associated with the vehicle. The vacuolation tended to be more severe in males than in females, varying from slight to moderate in males and minimal to moderate in females. The vacuolation appeared to primarily affect proximal tubule cells in the outer cortex and was not accompanied by compound-related degenerative or regenerative tubular changes.

At the intravenous injection site, microscopic findings included epidermal crusts, vascular degeneration and necrosis, perivascular hemorrhage, acute to subacute vascular and perivascular inflammation, and thrombus formation. The incidence and severity of the findings varied somewhat within and between groups, but the relatively common occurrence of most findings in nearly all groups suggested that they were due to the injection procedure itself and not to the vehicle or Compound 2463608. All remaining microscopic findings and all macroscopic finding were considered incidental.

Conclusion

In conclusion, daily intravenous administration of 1.0 mg Compound 2463608/kg to Crl:CD(SD) rats for 15 days resulted in the compound-related clinical sign of excessive grooming but no adverse findings. The no observed adverse effect level is, therefore, 1.0 mg/kg under the conditions of this study.

References

Study-Specific References

Draper, N. R., and Hunter, W. G., "Transformations: Some Examples Revisited," Technometrics, 11:23-40 (1969).

Levene, H., "Robust Tests for Equality of Variances," Contributions to Probability and Statistics, (eds.) I. Olkin et al., Ch. 25, pp. 278-292, Stanford University Press: Stanford, California (1960).

Miller, R. G., Jr., Simultaneous Statistical Inference, Second Ed., Ch. 7, pp. 90-94, Springer-Verlag: New York (1980).

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Table 1: Results of Concentration Verification Analyses

	Compound 2463608 (mg/mL)		
Theoretical Concentrations	0[a]	0[b]	0.5
Day 1 Preparation			
Mean	ND	ND	.475
Percent of Theoretical	-	-	95%
Day 14/15 Preparation			
Mean	-	-	.493
Percent of Theoretical	-	-	99%

ND = None detected.

- = Not applicable.

a Saline Control.

b Vehicle Control.

Table 2: Summary of Clinical Signs

Category / Sign	Sex:	Males		
	Group:	1	2	3
	Dose Level:	0	0	1
	Dose Units:	mg 2463608/kg/day	mg 2463608/kg/day	mg 2463608/kg/day
	Number in Group:	5	5	5
		N	N	N
Behavior				
Excessive Grooming		0	0	5
Eye(s)				
Squinted-Eyes		0	0	0
Skin & Pelage				
Blue Skin, Mid Tail		0	0	0
Scaly Skin, Tail		1	0	0
Sore/Scab, Front Paws		0	0	0
Sore/Scab, Right Front Paw		0	0	0

N = Number of animals with observed sign

Table 2
Summary of Clinical Signs

Category / Sign	Sex:	F e m a l e s		
	Group:	1	2	3
	Dose Level:	0	0	1
	Dose Units:	mg 2463608/kg/day	mg 2463608/kg/day	mg 2463608/kg/day
	Number in Group:	5	5	5
		N	N	N
Behavior				
Excessive Grooming		1	3	5
Eye(s)				
Squinted-Eyes		0	0	1
Skin & Pelage				
Blue Skin, Mid Tail		0	0	1
Scaly Skin, Tail		0	0	1
Sore/Scab, Front Paws		0	1	0
Sore/Scab, Right Front Paw		0	1	0

N = Number of animals with observed sign

Table 3: Summary of Ophthalmic Observations

Category / Sign	Sex:	Males		
	Group:	1	2	3
	Dose Level:	0	0	1
	Dose Units:	mg 2463608/kg/day	mg 2463608/kg/day	mg 2463608/kg/day
	Number in Group:	5	5	5
		N	N	N
No Visible Lesions				
No Visible Lesions, Eyes		5	5	5

N = Number of animals with observed sign

Table 3
Summary of Ophthalmic Observations

Category / Sign	Sex:	F e m a l e s		
	Group:	1	2	3
	Dose Level:	0	0	1
	Dose Units:	mg 2463608/kg/day	mg 2463608/kg/day	mg 2463608/kg/day
	Number in Group:	5	5	5
		N	N	N
No Visible Lesions				
No Visible Lesions, Eyes		5	5	5

N = Number of animals with observed sign

Table 4: Mean Body Weight Data

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

		Mean body weights (g) for Group:		
Week		1M	2M	3M
DSNG 1	Mean	311	309	309
	SD	10.2	12.4	12.5
	N	5	5	5
DSNG 2	Mean	343	342	339
	SD	12.6	17.4	19.6
	N	5	5	5
DSNG 3	Mean	371	361	362
	SD	15.5	18.8	29.4
	N	5	5	5

Table 4
Mean Body Weight Data

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Week		Mean body weights (g) for Group: 1F	2F	3F
DSNG 1	Mean	220	219	215
	SD	10.6	9.1	7.1
	N	5	5	5
DSNG 2	Mean	236	233	230
	SD	11.0	7.1	7.5
	N	5	5	5
DSNG 3	Mean	249	243	236
	SD	7.9	7.2	11.1
	N	5	5	5

Table 5: Mean Body Weight Change Data

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Week		Mean body weight gain (g) for Group: 1M	2M	3M
DSNG 1	Mean	32	33	30
	SD	8.8	5.7	11.8
	N	5	5	5
DSNG 2	Mean	28	19	23
	SD	7.1	5.6	10.3
	N	5	5	5
DSNG 1- DSNG 3	Mean	60	52	53
	SD	13.7	8.6	21.7
	N	5	5	5

Table 5
Mean Body Weight Change Data

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Week		Mean body weight gain (g) for Group: 1F	2F	3F
DSNG 1	Mean	16	15	15
	SD	3.4	4.0	6.8
	N	5	5	5
DSNG 2	Mean	13	10	6
	SD	4.2	5.2	4.4
	N	5	5	5
DSNG 1- DSNG 3	Mean	29	24	22
	SD	5.4	8.2	10.6
	N	5	5	5

Table 6: Mean Food Consumption Data

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

		Mean food consumption (g/animal/period) for Group:		
Week		1M	2M	3M
DSNG 1	Mean	218	211	205
	SD	13.1	14.4	17.4
	N	5	5	5
DSNG 2	Mean	220	215	199
	SD	21.6	18.8	16.5
	N	5	5	5

Table 6
Mean Food Consumption Data

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Week		Mean food consumption (g/animal/period) for Group: 1F	2F	3F
DSNG 1	Mean	160	157	151
	SD	10.2	9.8	7.4
	N	5	5	5
DSNG 2	Mean	166	167	165
	SD	12.1	11.9	11.0
	N	5	5	5

Table 7: Mean Hematology Data

Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex		RBC E6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETI E3/uL	PRET %
1M	Mean	8.46	16.5	49.9	59.0	19.4	33.0	274.6	3.2
	SD	0.345	0.55	2.13	0.43	0.30	0.67	42.30	0.43
	N	5	5	5	5	5	5	5	5
2M	Mean	8.36	16.2	48.9	58.5	19.4	33.2	236.1	2.8
	SD	0.352	0.48	1.67	0.75	0.48	0.53	35.98	0.36
	N	5	5	5	5	5	5	5	5
3M	Mean	8.20	15.9	48.2	58.8	19.4	33.0	287.0	3.5
	SD	0.294	0.67	0.90	2.27	0.77	1.00	68.58	0.94
	N	5	5	5	5	5	5	5	5

Table 7
Mean Hematology Data
Occasion: DSNG 16

Test Article		Saline Control	Vehicle Control	2463608
Group		1	2	3
Level(mg 2463608/kg/day)		0	0	1.0

Group/ Sex		RBC E6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETI E3/uL	PRET %
1F	Mean	7.65	15.2	44.2	57.9	19.9	34.4	216.4	2.9
	SD	0.330	0.37	1.07	1.75	0.48	0.30	24.18	0.40
	N	5	5	5	5	5	5	5	5
2F	Mean	7.78	15.3	44.6	57.2	19.6	34.3	248.9	3.2
	SD	0.251	0.51	1.43	0.84	0.30	0.32	18.76	0.23
	N	5	5	5	5	5	5	5	5
3F	Mean	7.95	15.5	45.4	57.2	19.5	34.1	246.5	3.1
	SD	0.340	0.34	0.91	1.51	0.48	0.35	58.95	0.88
	N	5	5	5	5	5	5	5	5

Table 7
Mean Hematology Data
Occasion: DSNG 16

Test Article		Saline Control	Vehicle Control	2463608
Group		1	2	3
Level(mg 2463608/kg/day)		0	0	1.0

Group/ Sex		PLT E3/uL	WBC E3/uL	NEUT E3/uL	LYM E3/uL	MONO E3/uL	EOS E3/uL	BASO E3/uL	LUC E3/uL
1M	Mean	1159	7.96	1.10	6.50	0.13	0.13	0.05	0.04
	SD	151.9	2.385	0.634	1.775	0.083	0.072	0.033	0.015
	N	5	5	5	5	5	5	5	5
2M	Mean	1112	11.56	1.56	9.41	0.32 A	0.14	0.07	0.07
	SD	113.5	1.754	0.454	1.416	0.121	0.114	0.026	0.036
	N	5	5	5	5	5	5	5	5
3M	Mean	1029	8.85	1.09	7.38	0.19	0.09	0.04	0.06
	SD	114.7	2.390	0.310	2.195	0.082	0.015	0.023	0.040
	N	5	5	5	5	5	5	5	5

A Statistically significant from Group 1 at $p \leq 0.05$.

Table 7
Mean Hematology Data
Occasion: DSNG 16

Test Article		Saline Control	Vehicle Control	2463608
Group		1	2	3
Level(mg 2463608/kg/day)		0	0	1.0

Group/ Sex		PLT E3/uL	WBC E3/uL	NEUT E3/uL	LYM E3/uL	MONO E3/uL	EOS E3/uL	BASO E3/uL	LUC E3/uL
1F	Mean	1229	7.93	0.85	6.73	0.18	0.07	0.04	0.06
	SD	125.8	2.951	0.383	2.785	0.044	0.011	0.008	0.030
	N	5	5	5	5	5	5	5	5
2F	Mean	1204	7.12	1.15	5.70	0.12	0.07	0.04	0.04
	SD	107.4	3.265	0.516	2.716	0.060	0.038	0.017	0.028
	N	5	5	5	5	5	5	5	5
3F	Mean	1091	5.97	0.72	4.95	0.14	0.09	0.03	0.04
	SD	92.2	1.105	0.199	0.940	0.049	0.037	0.019	0.015
	N	5	5	5	5	5	5	5	5

Table 7
Mean Hematology Data
Occasion: DSNG 16

Test Article		Saline Control	Vehicle Control	2463608
Group		1	2	3
Level(mg 2463608/kg/day)		0	0	1.0

Group/ Sex		PNEU %	PLYM %	PMON %	PEOS %	PBAS %	PLUC %	PT seconds	APTT seconds
1M	Mean	13.3	82.2	1.5	1.8	0.6	0.6	16.8	22.2
	SD	4.75	5.93	0.55	1.18	0.30	0.05	0.65	1.80
	N	5	5	5	5	5	5	5	5
2M	Mean	13.4	81.4	2.7 A	1.3	0.6	0.6	17.2	23.0
	SD	2.82	2.37	0.78	1.14	0.18	0.30	1.85	2.34
	N	5	5	5	5	5	5	5	5
3M	Mean	12.9	82.8	2.1	1.1	0.5	0.6	16.6	22.7
	SD	3.87	4.16	0.63	0.39	0.19	0.26	0.98	1.31
	N	5	5	5	5	5	5	5	5

A Statistically significant from Group 1 at $p \leq 0.05$.

Table 7
Mean Hematology Data
Occasion: DSNG 16

Test Article		Saline Control	Vehicle Control	2463608					
Group		1	2	3					
Level(mg 2463608/kg/day)		0	0	1.0					
Group/ Sex		PNEU %	PLYM %	PMON %	PEOS %	PBAS %	PLUC %	PT seconds	APTT seconds
1F	Mean	11.5	83.9	2.4	1.0	0.5	0.7	14.8	20.5
	SD	4.83	5.33	0.67	0.37	0.17	0.22	0.63	1.25
	N	5	5	5	5	5	5	5	5
2F	Mean	16.2	79.9	1.7	1.0	0.6	0.5	14.9	22.1
	SD	4.25	4.02	0.39	0.31	0.14	0.11	0.54	1.63
	N	5	5	5	5	5	5	5	5
3F	Mean	12.2	82.9	2.3	1.5	0.5	0.6	14.3	19.9
	SD	2.36	2.71	0.65	0.58	0.26	0.11	0.57	1.98
	N	5	5	5	5	5	5	5	5

Table 8: Mean Clinical Chemistry Data

Occasion: DSNG 16

Test Article		Saline Control	Vehicle Control	2463608
Group		1	2	3
Level(mg 2463608/kg/day)		0	0	1.0

Group/ Sex		GLU mg/dL	UN mg/dL	CREA mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	AGR	CHOL mg/dL
1M	Mean	95	16	0.7	6.7	4.6	2.2	2.1	85
	SD	5.6	2.6	0.05	0.11	0.21	0.15	0.26	19.2
	N	5	5	5	5	5	5	5	5
2M	Mean	104	15	0.6	6.5	4.6	2.0	2.4	84
	SD	13.2	1.9	0.04	0.34	0.23	0.29	0.40	8.9
	N	5	5	5	5	5	5	5	5
3M	Mean	97	16	0.6	6.5	4.6	1.9	2.4	77
	SD	7.1	1.9	0.04	0.17	0.12	0.07	0.07	12.0
	N	5	5	5	5	5	5	5	5

Table 8
Mean Clinical Chemistry Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex		GLU mg/dL	UN mg/dL	CREA mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	AGR	CHOL mg/dL
1F	Mean	108	17	0.6	7.2	5.3	1.9	2.8	82
	SD	3.3	2.1	0.05	0.23	0.24	0.11	0.24	18.2
	N	5	5	5	5	5	5	5	5
2F	Mean	111	15	0.7	7.5	5.6	1.9	2.9	85
	SD	8.8	0.8	0.08	0.45	0.43	0.05	0.22	20.8
	N	5	5	5	5	5	5	5	5
3F	Mean	109	16	0.7	7.6	5.5	2.1 AB	2.7	103
	SD	11.8	2.5	0.05	0.12	0.16	0.08	0.17	10.9
	N	5	5	5	5	5	5	5	5

A Statistically significant from Group 1 at $p \leq 0.05$.
B Statistically significant from Group 2 at $p \leq 0.05$.

Table 8
Mean Clinical Chemistry Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex		TRIG mg/dL	TBIL mg/dL	AST U/L	ALT U/L	ALP U/L	GGT U/L	CK U/L	Ca mg/dL
1M	Mean	35	0.1	137	37	156	.	888	10.9
	SD	11.1	0.04	48.8	7.8	31.8	.	723.1	0.17
	N	5	5	5	5	5	0	5	5
2M	Mean	53	0.1	116	34	161	.	771	10.9
	SD	12.3	0.00	29.5	3.8	34.1	.	455.5	0.19
	N	5	5	5	5	5	0	5	5
3M	Mean	39	0.1	124	39	128	.	689	11.0
	SD	17.6	0.05	26.9	4.9	6.5	.	425.2	0.47
	N	5	5	5	5	5	0	5	5

Table 8
Mean Clinical Chemistry Data
Occasion: DSNG 16

Test Article		Saline Control	Vehicle Control	2463608
Group		1	2	3
Level(mg 2463608/kg/day)		0	0	1.0

Group/ Sex		TRIG mg/dL	TBIL mg/dL	AST U/L	ALT U/L	ALP U/L	GGT U/L	CK U/L	Ca mg/dL
1F	Mean	40	0.2	131	33	77	.	1058	11.2
	SD	8.2	0.04	46.6	3.3	20.8	.	690.4	0.19
	N	5	5	5	5	5	0	5	5
2F	Mean	37	0.2	115	30	82	.	823	11.3
	SD	6.5	0.04	16.9	3.6	23.7	.	94.2	0.28
	N	5	5	5	5	5	0	5	5
3F	Mean	40	0.2	135	31	89	.	1034	11.2
	SD	10.4	0.05	24.6	7.3	29.6	.	389.5	0.15
	N	5	5	5	5	5	0	5	5

Table 8
Mean Clinical Chemistry Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex		PHOS mg/dL	Na mmol/L	K mmol/L	Cl mmol/L
1M	Mean	8.3	146	5.8	105
	SD	1.02	0.7	0.53	1.1
	N	5	5	5	5
2M	Mean	8.2	146	5.7	103
	SD	0.33	1.8	0.35	1.1
	N	5	5	5	5
3M	Mean	8.0	145	5.6	102
	SD	0.65	1.9	0.50	1.7
	N	5	5	5	5

Table 8
Mean Clinical Chemistry Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex		PHOS mg/dL	Na mmol/L	K mmol/L	Cl mmol/L
1F	Mean	6.9	143	5.6	102
	SD	0.23	1.9	0.14	1.3
	N	5	5	5	5
2F	Mean	6.2	143	5.3	103
	SD	0.68	0.9	0.36	1.4
	N	5	5	5	5
3F	Mean	6.6	143	5.4	102
	SD	0.44	2.0	0.40	1.4
	N	5	5	5	5

Table 9: Mean Urinalysis Data

Occasion: DSNG 16

Test Article		Saline Control	Vehicle Control	2463608
Group		1	2	3
Level(mg 2463608/kg/day)		0	0	1.0
Group/ Sex		UVOL mL	SPGR	UpH
1M	Mean	33.0	1.009	6.8
	SD	17.64	0.0054	0.27
	N	5	5	5
2M	Mean	16.5	1.014	6.6
	SD	7.53	0.0049	0.22
	N	5	5	5
3M	Mean	25.1	1.012	6.6
	SD	12.36	0.0053	0.22
	N	5	5	5

Table 9
Mean Urinalysis Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex		UVOL mL	SPGR	UpH
1F	Mean	15.9	1.014	6.9
	SD	9.10	0.0060	0.22
	N	5	5	5
2F	Mean	9.6	1.020	6.3 A
	SD	8.77	0.0108	0.27
	N	5	5	5
3F	Mean	23.2	1.011	6.4 A
	SD	15.97	0.0074	0.22
	N	5	5	5

A Statistically significant from Group 1 at $p \leq 0.05$.

Table 10: Summary of Macroscopic Observations

Dosing Phase - Final Phase Sacrifice

	-- Males --			-- Females --		
Group:	1	2	3	1	2	3
Number in group:	5	5	5	5	5	5
Examined/No remarkable findings ...	4	5	5	5	5	3
Lung						
Discolored	0	0	0	0	0	1
Total:	0	0	0	0	0	1
LN, Mandibular						
Discolored	1	0	0	0	0	0
Total:	1	0	0	0	0	0
Intravenous Site						
Crusted	0	0	0	0	0	1
Total:	0	0	0	0	0	1

Table 11: Mean Organ Weight and Organ/Terminal Body Weight Data

Dosing Phase - Final Phase Sacrifice

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex		Terminal Body weight (g)	Brain		Heart		Liver	
			Unadjusted (g)	Ratio (%)	Unadjusted (g)	Ratio (%)	Unadjusted (g)	Ratio (%)
1M	Mean	338.2800	2.0416	0.6038	1.2328	0.3642	8.9068	2.6316
	SD	13.38215	0.07117	0.01641	0.08750	0.01380	0.65822	0.13314
	N	5	5	5	5	5	5	5
2M	Mean	337.9400	1.9888	0.5904	1.3653	0.4053	9.0647	2.6860
	SD	17.06423	0.09035	0.05168	0.24681	0.08141	0.69190	0.21683
	N	5	5	5	5	5	5	5
3M	Mean	333.5800	2.0789	0.6253	1.2068	0.3625	8.7538	2.6218
	SD	25.44017	0.07923	0.04082	0.07898	0.02132	0.85623	0.09540
	N	5	5	5	5	5	5	5

Table 11
Mean Organ Weight and Organ/Terminal Body Weight Data
Dosing Phase - Final Phase Sacrifice

Test Article		Saline Control	Vehicle Control	2463608
Group		1	2	3
Level(mg 2463608/kg/day)		0	0	1.0

Group/ Sex		Terminal Body weight (g)	Kidney Unadjusted (g)	Kidney Ratio (%)	Spleen Unadjusted (g)	Spleen Ratio (%)	Adrenal Unadjusted (g)	Adrenal Ratio (%)
1M	Mean	338.2800	2.3206	0.6867	0.7208	0.2137	0.0664	0.0196
	SD	13.38215	0.13091	0.04337	0.06624	0.02608	0.01136	0.00327
	N	5	5	5	5	5	5	5
2M	Mean	337.9400	2.2127	0.6564	0.7473	0.2206	0.0577	0.0170
	SD	17.06423	0.19795	0.07310	0.09215	0.01790	0.00828	0.00197
	N	5	5	5	5	5	5	5
3M	Mean	333.5800	2.2587	0.6795	0.7989	0.2390	0.0632	0.0191
	SD	25.44017	0.09478	0.04677	0.11028	0.02051	0.00566	0.00310
	N	5	5	5	5	5	5	5

Table 11
Mean Organ Weight and Organ/Terminal Body Weight Data
Dosing Phase - Final Phase Sacrifice

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex		Terminal Body weight (g)	Epididymis Unadjusted (g)	Epididymis Ratio (%)	Pituitary Unadjusted (g)	Pituitary Ratio (%)	Thymus Unadjusted (g)	Thymus Ratio (%)
1M	Mean	338.2800	1.1270	0.3339	0.0125	0.0037	0.5622	0.1661
	SD	13.38215	0.06644	0.02947	0.00194	0.00070	0.08647	0.02439
	N	5	5	5	5	5	5	5
2M	Mean	337.9400	1.2052	0.3574	0.0120	0.0036	0.4013 A	0.1182 A
	SD	17.06423	0.07195	0.02859	0.00228	0.00064	0.07041	0.01597
	N	5	5	5	5	5	5	5
3M	Mean	333.5800	1.1943	0.3598	0.0112	0.0034	0.3714 A	0.1129 A
	SD	25.44017	0.06863	0.03495	0.00150	0.00068	0.09196	0.03419
	N	5	5	5	5	5	5	5

A Statistically significant from Group 1 at $p \leq 0.05$.

Table 11
Mean Organ Weight and Organ/Terminal Body Weight Data
Dosing Phase - Final Phase Sacrifice

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex		Terminal Body weight (g)	Prostate Unadjusted (g)	Prostate Ratio (%)	Testis Unadjusted (g)	Testis Ratio (%)	Thyroid/ Parathyr Unadjusted (g)	Thyroid/ Parathyr Ratio (%)
1M	Mean	338.2800	1.0753	0.3171	3.2429	0.9592	0.0242	0.0072
	SD	13.38215	0.13984	0.02939	0.22639	0.06576	0.00800	0.00235
	N	5	5	5	5	5	5	5
2M	Mean	337.9400	1.0199	0.3036	3.2795	0.9734	0.0200	0.0059
	SD	17.06423	0.17136	0.06142	0.12711	0.07840	0.00432	0.00146
	N	5	5	5	5	5	5	5
3M	Mean	333.5800	0.9434	0.2840	3.3113	0.9959	0.0236	0.0071
	SD	25.44017	0.13838	0.04658	0.22195	0.08426	0.00308	0.00096
	N	5	5	5	5	5	5	5

Table 11
Mean Organ Weight and Organ/Terminal Body Weight Data
Dosing Phase - Final Phase Sacrifice

Test Article		Saline Control	Vehicle Control	2463608
Group		1	2	3
Level(mg 2463608/kg/day)		0	0	1.0

Group/ Sex		Terminal Body weight (g)	Brain Unadjusted (g)	Brain Ratio (%)	Heart Unadjusted (g)	Heart Ratio (%)	Liver Unadjusted (g)	Liver Ratio (%)
1F	Mean	229.1800	1.9581	0.8550	0.9221	0.4014	6.6784	2.9126
	SD	8.16315	0.06015	0.03438	0.11331	0.03561	0.45798	0.13213
	N	5	5	5	5	5	5	5
2F	Mean	228.3000	1.9031	0.8337	0.9052	0.3965	6.6945	2.9325
	SD	6.06012	0.06607	0.02460	0.06943	0.02909	0.49832	0.20732
	N	5	5	5	5	5	5	5
3F	Mean	219.2600	1.9352	0.8836	0.9332	0.4256	6.5529	2.9904
	SD	9.75233	0.04776	0.03365	0.04574	0.00972	0.31557	0.12349
	N	5	5	5	5	5	5	5

Table 11
Mean Organ Weight and Organ/Terminal Body Weight Data
Dosing Phase - Final Phase Sacrifice

Test Article		Saline Control	Vehicle Control	2463608
Group		1	2	3
Level(mg 2463608/kg/day)		0	0	1.0

Group/ Sex		Terminal Body weight (g)	Kidney Unadjusted (g)	Kidney Ratio (%)	Spleen Unadjusted (g)	Spleen Ratio (%)	Adrenal Unadjusted (g)	Adrenal Ratio (%)
1F	Mean	229.1800	1.6143	0.7033	0.5303	0.2310	0.0620	0.0270
	SD	8.16315	0.17406	0.05606	0.08656	0.03213	0.00672	0.00270
	N	5	5	5	5	5	5	5
2F	Mean	228.3000	1.5661	0.6854	0.6180	0.2708	0.0732	0.0320
	SD	6.06012	0.12110	0.03964	0.05136	0.02276	0.01022	0.00399
	N	5	5	5	5	5	5	5
3F	Mean	219.2600	1.6136	0.7364	0.4911 B	0.2245	0.0685	0.0313
	SD	9.75233	0.04784	0.01543	0.07806	0.03768	0.00915	0.00399
	N	5	5	5	5	5	5	5

B Statistically significant from Group 2 at $p \leq 0.05$.

Table 11
Mean Organ Weight and Organ/Terminal Body Weight Data
Dosing Phase - Final Phase Sacrifice

Test Article		Saline Control	Vehicle Control	2463608
Group		1	2	3
Level(mg 2463608/kg/day)		0	0	1.0

Group/ Sex		Terminal Body weight (g)	Pituitary Unadjusted (g)	Pituitary Ratio (%)	Thymus Unadjusted (g)	Thymus Ratio (%)	Uterus Unadjusted (g)	Uterus Ratio (%)
1F	Mean	229.1800	0.0134	0.0058	0.4019	0.1758	0.7154	0.3123
	SD	8.16315	0.00174	0.00063	0.05177	0.02652	0.11571	0.05034
	N	5	5	5	5	5	5	5
2F	Mean	228.3000	0.0136	0.0060	0.3327	0.1457	0.7071	0.3104
	SD	6.06012	0.00217	0.00095	0.05930	0.02601	0.22900	0.10282
	N	5	5	5	5	5	5	5
3F	Mean	219.2600	0.0164	0.0075	0.4355 B	0.1989 B	0.6921	0.3128
	SD	9.75233	0.00594	0.00254	0.05152	0.02464	0.22172	0.09053
	N	5	5	5	5	5	5	5

B Statistically significant from Group 2 at $p \leq 0.05$.

Table 11
Mean Organ Weight and Organ/Terminal Body Weight Data
Dosing Phase - Final Phase Sacrifice

Test Article		Saline Control	Vehicle Control	2463608
Group		1	2	3
Level(mg 2463608/kg/day)		0	0	1.0

Group/ Sex		Terminal Body weight (g)	Ovary Unadjusted (g)	Ovary Ratio (%)	Thyroid/ Parathyr Unadjusted (g)	Thyroid/ Parathyr Ratio (%)
1F	Mean	229.1800	0.1383	0.0602	0.0184	0.0081
	SD	8.16315	0.01833	0.00655	0.00330	0.00164
	N	5	5	5	5	5
2F	Mean	228.3000	0.1400	0.0612	0.0180	0.0079
	SD	6.06012	0.02343	0.00877	0.00301	0.00139
	N	5	5	5	5	5
3F	Mean	219.2600	0.1343	0.0614	0.0223	0.0103
	SD	9.75233	0.01099	0.00588	0.00804	0.00402
	N	5	5	5	5	5

Table 12: Mean Organ Weight and Organ/Brain Weight Data

Dosing Phase - Final Phase Sacrifice

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex		Brain weight (g)	Brain weight (g) Unadjusted (g)	Brain weight (g) Ratio (%)	Heart Unadjusted (g)	Heart Ratio (%)	Liver Unadjusted (g)	Liver Ratio (%)
1M	Mean	2.0416	2.0416	100.0000	1.2328	60.3337	8.9068	436.3624
	SD	0.07117	0.07117	0.00000	0.08750	2.38915	0.65822	29.66925
	N	5	5	5	5	5	5	5
2M	Mean	1.9888	1.9888	100.0000	1.3653	68.5038	9.0647	456.3477
	SD	0.09035	0.09035	0.00000	0.24681	10.79141	0.69190	37.07168
	N	5	5	5	5	5	5	5
3M	Mean	2.0789	2.0789	100.0000	1.2068	58.0736	8.7538	421.2012
	SD	0.07923	0.07923	0.00000	0.07898	3.59005	0.85623	39.60372
	N	5	5	5	5	5	5	5

Table 12
Mean Organ Weight and Organ/Brain Weight Data
Dosing Phase - Final Phase Sacrifice

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex		Brain weight (g)	Kidney Unadjusted (g)	Kidney Ratio (%)	Spleen Unadjusted (g)	Spleen Ratio (%)	Adrenal Unadjusted (g)	Adrenal Ratio (%)
1M	Mean	2.0416	2.3206	113.7133	0.7208	35.3612	0.0664	3.2524
	SD	0.07117	0.13091	6.16078	0.06624	3.79296	0.01136	0.53980
	N	5	5	5	5	5	5	5
2M	Mean	1.9888	2.2127	111.2008	0.7473	37.7060	0.0577	2.9019
	SD	0.09035	0.19795	7.59446	0.09215	5.43364	0.00828	0.41041
	N	5	5	5	5	5	5	5
3M	Mean	2.0789	2.2587	108.8032	0.7989	38.4808	0.0632	3.0490
	SD	0.07923	0.09478	6.74462	0.11028	5.55891	0.00566	0.34138
	N	5	5	5	5	5	5	5

Table 12
Mean Organ Weight and Organ/Brain Weight Data
Dosing Phase - Final Phase Sacrifice

Test Article		Saline Control	Vehicle Control	2463608
Group		1	2	3
Level(mg 2463608/kg/day)		0	0	1.0

Group/ Sex		Brain weight (g)	Epididymis Unadjusted (g)	Epididymis Ratio (%)	Pituitary Unadjusted (g)	Pituitary Ratio (%)	Thymus Unadjusted (g)	Thymus Ratio (%)
1M	Mean	2.0416	1.1270	55.2598	0.0125	0.6134	0.5622	27.5963
	SD	0.07117	0.06644	3.81011	0.00194	0.10993	0.08647	4.70122
	N	5	5	5	5	5	5	5
2M	Mean	1.9888	1.2052	60.7203	0.0120	0.6032	0.4013 A	20.3187 A
	SD	0.09035	0.07195	4.81643	0.00228	0.10408	0.07041	4.30106
	N	5	5	5	5	5	5	5
3M	Mean	2.0789	1.1943	57.4960	0.0112	0.5419	0.3714 A	17.9279 A
	SD	0.07923	0.06863	3.67845	0.00150	0.07969	0.09196	4.66918
	N	5	5	5	5	5	5	5

A Statistically significant from Group 1 at $p \leq 0.05$.

Table 12
Mean Organ Weight and Organ/Brain Weight Data
Dosing Phase - Final Phase Sacrifice

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex		Brain weight (g)	Prostate Unadjusted (g)	Prostate Ratio (%)	Testis Unadjusted (g)	Testis Ratio (%)	Thyroid/ Parathyr Unadjusted (g)	Thyroid/ Parathyr Ratio (%)
1M	Mean	2.0416	1.0753	52.5767	3.2429	158.8895	0.0242	1.1914
	SD	0.07117	0.13984	5.36233	0.22639	10.58630	0.00800	0.40131
	N	5	5	5	5	5	5	5
2M	Mean	1.9888	1.0199	51.2089	3.2795	164.9820	0.0200	1.0018
	SD	0.09035	0.17136	7.61984	0.12711	4.22011	0.00432	0.19219
	N	5	5	5	5	5	5	5
3M	Mean	2.0789	0.9434	45.5352	3.3113	159.2109	0.0236	1.1376
	SD	0.07923	0.13838	7.83804	0.22195	7.35351	0.00308	0.15923
	N	5	5	5	5	5	5	5

Table 12
Mean Organ Weight and Organ/Brain Weight Data
Dosing Phase - Final Phase Sacrifice

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex		Brain weight (g)	Brain weight (g) Unadjusted (g)	Brain weight (g) Ratio (%)	Heart Unadjusted (g)	Heart Ratio (%)	Liver Unadjusted (g)	Liver Ratio (%)
1F	Mean	1.9581	1.9581	100.0000	0.9221	47.1202	6.6784	341.1423
	SD	0.06015	0.06015	0.00000	0.11331	5.87717	0.45798	22.19711
	N	5	5	5	5	5	5	5
2F	Mean	1.9031	1.9031	100.0000	0.9052	47.5681	6.6945	351.6598
	SD	0.06607	0.06607	0.00000	0.06943	3.23861	0.49832	20.67396
	N	5	5	5	5	5	5	5
3F	Mean	1.9352	1.9352	100.0000	0.9332	48.2152	6.5529	338.6724
	SD	0.04776	0.04776	0.00000	0.04574	1.83379	0.31557	15.81496
	N	5	5	5	5	5	5	5

Table 12
Mean Organ Weight and Organ/Brain Weight Data
Dosing Phase - Final Phase Sacrifice

Test Article		Saline Control	Vehicle Control	2463608
Group		1	2	3
Level(mg 2463608/kg/day)		0	0	1.0

Group/ Sex		Brain weight (g)	Kidney Unadjusted (g)	Kidney Ratio (%)	Spleen Unadjusted (g)	Spleen Ratio (%)	Adrenal Unadjusted (g)	Adrenal Ratio (%)
1F	Mean	1.9581	1.6143	82.4376	0.5303	27.0984	0.0620	3.1640
	SD	0.06015	0.17406	8.31572	0.08656	4.43026	0.00672	0.32110
	N	5	5	5	5	5	5	5
2F	Mean	1.9031	1.5661	82.2213	0.6180	32.5614	0.0732	3.8518
	SD	0.06607	0.12110	4.21994	0.05136	3.58125	0.01022	0.57757
	N	5	5	5	5	5	5	5
3F	Mean	1.9352	1.6136	83.3857	0.4911 B	25.4100 B	0.0685	3.5447
	SD	0.04776	0.04784	1.55090	0.07806	4.19286	0.00915	0.49420
	N	5	5	5	5	5	5	5

B Statistically significant from Group 2 at $p \leq 0.05$.

Table 12
Mean Organ Weight and Organ/Brain Weight Data
Dosing Phase - Final Phase Sacrifice

Test Article		Saline Control	Vehicle Control	2463608
Group		1	2	3
Level(mg 2463608/kg/day)		0	0	1.0

Group/ Sex		Brain weight (g)	Pituitary Unadjusted (g)	Pituitary Ratio (%)	Thymus Unadjusted (g)	Thymus Ratio (%)	Uterus Unadjusted (g)	Uterus Ratio (%)
1F	Mean	1.9581	0.0134	0.6855	0.4019	20.5483	0.7154	36.4568
	SD	0.06015	0.00174	0.09630	0.05177	2.78592	0.11571	5.10837
	N	5	5	5	5	5	5	5
2F	Mean	1.9031	0.0136	0.7138	0.3327	17.4817	0.7071	37.4567
	SD	0.06607	0.00217	0.10349	0.05930	3.06326	0.22900	12.97132
	N	5	5	5	5	5	5	5
3F	Mean	1.9352	0.0164	0.8517	0.4355 B	22.5077 B	0.6921	35.6787
	SD	0.04776	0.00594	0.31650	0.05152	2.68145	0.22172	11.12385
	N	5	5	5	5	5	5	5

B Statistically significant from Group 2 at $p \leq 0.05$.

Table 12
Mean Organ Weight and Organ/Brain Weight Data
Dosing Phase - Final Phase Sacrifice

Test Article		Saline Control	Vehicle Control	2463608
Group		1	2	3
Level(mg 2463608/kg/day)		0	0	1.0

Group/ Sex		Brain weight (g)	Ovary Unadjusted (g)	Ovary Ratio (%)	Thyroid/ Parathyr Unadjusted (g)	Thyroid/ Parathyr Ratio (%)
1F	Mean	1.9581	0.1383	7.0780	0.0184	0.9389
	SD	0.06015	0.01833	1.04815	0.00330	0.16075
	N	5	5	5	5	5
2F	Mean	1.9031	0.1400	7.3502	0.0180	0.9462
	SD	0.06607	0.02343	1.17819	0.00301	0.16809
	N	5	5	5	5	5
3F	Mean	1.9352	0.1343	6.9441	0.0223	1.1577
	SD	0.04776	0.01099	0.58835	0.00804	0.43091
	N	5	5	5	5	5

Table 13: Summary of Microscopic Observations

Dosing Phase - Final Phase Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --			-- Animals Affected -- Females --		
Tissues With Diagnoses	Dosage group:	Ctls	2	3	Ctls	2	3
	No. in group:	5	5	5	5	5	5
Brain	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Spinal Cord	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Adrenal, Cortex	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Adrenal, Medulla	Number examined:	0	5	4	0	5	5
	Unremarkable:	0	5	4	0	5	5
Pituitary	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Nerve, Sciatic	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Trachea	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Esophagus	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Thyroid	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	3	5	0	4	4
Thymus, Ectopic		0	2	0	0	1	1
Parathyroid	Number examined:	0	5	5	0	4	5
	Unremarkable:	0	5	5	0	4	5
Heart	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	4	0	5	4
Infiltrate, Lymphocytes/Macrophages		0	0	1	0	0	0
Inflammation, Chronic, Proliferative, -Endocardial/Subendocardial, Atrium		0	0	0	0	0	1
Aorta	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 20.Jun.07 To 20.Jun.07

Table 13
Summary of Microscopic Observations
Dosing Phase - Final Phase Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males			-- Animals Affected -- Females		
Tissues With Diagnoses	Dosage group: / No. in group:	Ctls 5	2 5	3 5	Ctls 5	2 5	3 5
Tongue	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Muscle, Bi Fem	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Liver	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	0	0	0	0	0
Infiltrate, Lymphocytes/Macrophages		0	5	5	0	5	5
Necrosis, Coagulative, Focal		0	0	0	0	1	0
Vacuolation, Hepatocyte, Periportal		0	2	2	0	3	4
Spleen	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Lung	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	2	0	5	3
Inflammation, Granulomatous, with Foreign Material		0	0	1	0	0	1
Mineralization, Vessel		0	0	1	0	0	0
Crystals, Hemoglobin, with Associated Subacute Inflammation		0	0	1	0	0	1
Thymus	Number examined:	5	5	5	5	5	5
	Unremarkable:	5	5	4	5	5	5
Necrosis, Lymphocytes		0	0	1	0	0	0
Kidney	Number examined:	5	5	5	5	5	5
	Unremarkable:	1	0	0	1	0	0
Vacuolation, Tubule Cell		0	5	5	0	5	5
Basophilic Tubule		1	0	0	1	0	0
Dilatation, Tubule(s), Focal		0	0	2	1	0	0
Infiltrate, Lymphocytes/Macrophages		2	1	3	3	1	0
Inflammation, Chronic-Active, Pelvis		1	0	0	0	0	0
Mineralization, Tubule		0	0	0	4	2	3
Urinary Bladder	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Stomach, Gl	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 20.Jun.07 To 20.Jun.07

Table 13
Summary of Microscopic Observations
Dosing Phase - Final Phase Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --			-- Animals Affected -- Females --		
	Dosage group:	Ctls	2	3	Ctls	2	3
Tissues With Diagnoses	No. in group:	5	5	5	5	5	5
Stomach, Nongl	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Duodenum	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Ileum	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Colon	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Cecum	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Jejunum	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
LN, Mesenteric	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
LN, Mandibular	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Gl, Mandib Saliv	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Pancreas	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	4	5
Infiltrate, Lymphocytes/Macrophages		0	0	0	0	1	0
Nerve, Optic	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Eye	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	4	5	0	5	4
Rosette, Retina		0	1	0	0	0	1
Skin/Subcutis	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	3	5
Crust, Epidermal		0	0	0	0	2	0

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 20.Jun.07 To 20.Jun.07

Table 13
Summary of Microscopic Observations
Dosing Phase - Final Phase Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males			-- Animals Affected -- Females		
	Dosage group:	Ctls	2	3	Ctls	2	3
Tissues With Diagnoses	No. in group:	5	5	5	5	5	5
Mammary, Male	Number examined:	0	5	5			
	Unremarkable:	0	5	5			
Seminal Vesicle	Number examined:	0	5	5			
	Unremarkable:	0	5	5			
Prostate	Number examined:	0	5	5			
	Unremarkable:	0	2	4			
Infiltrate, Lymphocytes/Macrophages		0	2	1			
Inflammation, Acute		0	1	0			
Testis	Number examined:	0	5	5			
	Unremarkable:	0	4	4			
Hypoplasia, Seminiferous Tubules, Focal, Unilateral		0	1	0			
Mineralization, Seminiferous Tubules, Unilateral		0	0	1			
Epididymis	Number examined:	0	5	5			
	Unremarkable:	0	5	5			
Mammary, Female	Number examined:				0	5	5
	Unremarkable:				0	5	5
Ovary	Number examined:				0	5	5
	Unremarkable:				0	5	5
Uterus	Number examined:				0	5	5
	Unremarkable:				0	5	5
Cervix	Number examined:				0	5	5
	Unremarkable:				0	5	5
Vagina	Number examined:				0	5	5
	Unremarkable:				0	5	5
Bone, Femur	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Marrow, Femur	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 20.Jun.07 To 20.Jun.07

Table 13
Summary of Microscopic Observations
Dosing Phase - Final Phase Sacrifice

Controls from group(s): 1		-- Animals Affected --					
	Animal sex:	-- Males --			-- Females --		
	Dosage group:	Ctls	2	3	Ctls	2	3
Tissues With Diagnoses	No. in group:	5	5	5	5	5	5
Bone, Sternum	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Marrow, Sternum	Number examined:	0	5	5	0	5	5
	Unremarkable:	0	5	5	0	5	5
Intravenous Site	Number examined:	5	5	5	5	5	5
	Unremarkable:	0	0	0	0	0	0
Crust, Epidermal		1	2	1	1	0	1
Degeneration/Necrosis, Vascular		1	3	4	5	4	2
Hemorrhage, Perivascular		5	4	5	5	5	4
Inflammation, Vascular/Perivascular, Acute to Subacute		4	4	5	5	5	5
Thrombus		1	1	2	4	2	1
Death Comment	Number examined:	5	5	5	5	5	5
	Unremarkable:	0	0	0	0	0	0
Scheduled Sacrifice		5	5	5	5	5	5

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 20.Jun.07 To 20.Jun.07

Appendix A: Protocol and Protocol Amendments

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COVANCE
THE DEVELOPMENT SERVICES COMPANY

Protocol

Sponsor:

Eli Lilly and Company
Indianapolis, IN
United States of America

Study Title:

A Repeat-Dose Toxicity Study in Rats Given Compound 2463608 by Intravenous Injection for 2 Weeks

Date:

29 May 2007

Testing Facility:

Covance Laboratories Inc.
3301 Kinsman Boulevard
Madison, WI 53704-2595
United States of America

Laboratory Study Identification:

Proposal 12215A
Covance 7608-544

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Study
A Repeat-Dose Toxicity Study in Rats Given Compound 2463608 by Intravenous Injection for 2 Weeks

Purpose
To evaluate the toxicity of Compound 2463608 when administered daily by intravenous injection to rats for at least 2 weeks.

Sponsor
Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285

Study Monitor
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Study Location
Covance Laboratories Inc.
3301 Kinsman Boulevard
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Study Director
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Study Toxicologist

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Proposed Study Timetable

Experimental Start Date: 29 May 2007
Inlife Start Date: 05 June 2007
Inlife End Date: 20 June 2007
Audited Draft Report Date: To be determined
Experimental Termination Date: To be determined
Final Report Date: To be determined

Statement of Compliance

This study (with the listed exception) will conform to the following Good Laboratory Practice Standards in place at the time of study initiation:

US Food and Drug Administration (CFR 21 - Part 58)
Organisation for Economic Co-operation and Development

Dose analysis and test article potency reassay by the sponsor will not be conducted in accordance with Food and Drug Administration (FDA) Good Laboratory Practice Regulations, 21 CFR 58, or with any applicable amendments.

Regulatory Guidelines

The study design is based on the principles of the FDA Center for Drug Evaluation and Research (CDER)/ICH Harmonised Tripartite Guidelines ICH-M3; Nonclinical Safety Studies for the conduct of Human Clinical Trials for Pharmaceuticals (CDER, July 1997).

Animal Care and Use Statement

All procedures in this protocol are in compliance with the Animal Welfare Act, the Guide for the Care and Use of Laboratory Animals, and the Office of Laboratory Animal Welfare. In the opinion of the sponsor and study director, the study does not unnecessarily duplicate any previous work.

Veterinary Care/Treatment

In accordance with the Animal Welfare Act, the Guide for the Care and Use of Laboratory Animals, and the Office of Laboratory Animal Welfare, medical treatment necessary to prevent unacceptable pain and suffering, including euthanasia, is the sole responsibility of the attending Laboratory Animal Veterinarian. Discretionary medical treatment may be carried out based upon consensus agreement between the study director and the attending Laboratory Animal Veterinarian. The sponsor will be notified of any veterinary treatment.

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Major Computer Systems

The major computer systems to be used on this study may include, but not be limited to, the following systems. Metasys, a facility management system, will be used to monitor and control environmental conditions and water flow within the facility (e.g., animal rooms), and the Metasys system or the REES environmental monitoring system will be used to monitor and document facility storage conditions (e.g., refrigerators, freezers, constant temperature rooms). The Path/Tox System for OpenVMS (VPTS) application, supplied by Xybion Medical Systems Corporation, will be used for the direct online capture of inlife toxicology, clinical pathology, and anatomic pathology data. Electronic Notes will be used by study personnel to document study-specific communications. The Automated Form and Label Generation System application will be used in conjunction with the VPTS system to produce labels and forms. The TALISMAN application will be used for the dose preparation information. For reporting purposes, data will be transferred into Word directly and/or by use of the Converged Statistical Analysis and Reporting application. All version numbers of the applications are maintained by Covance.

Quality Assurance

The protocol, study conduct (least 1 study conduct inspection), and final report will be audited by the Covance Quality Assurance Unit.

Test Article

Identification

Compound 2463608

Lot Number

KD0-E01100-039-C

Potency

100% (theoretical potency)

Stability
Samples of the test article (at least 200 mg) will be reassayed after the inlife portion of the study is completed. Samples will be shipped under ambient conditions to:

John Masters, PhD
Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285
Telephone No.: 317.277.7969
Facsimile No.: 317.277.6778
E-Mail: jjm@lilly.com

Toxicology Test Chemical Assays forms, supplied by the sponsor, will be included with each shipment. The study monitor and recipient will be notified by facsimile as to the date and method of the shipment. The potency reassay results will be provided to the study director.

Storage Conditions
Ambient temperature

Characteristics
Information on synthesis methods, composition, or other characteristics that define the test article is on file with the sponsor.

Safety
The sponsor will provide relevant occupational safety information known about the test article [e.g., Material Safety Data Sheet (MSDS), safety instructions, test article identity].

Control Article

Identification
20% Captisol in 25mM acetate buffer, pH 4.0

Lot Numbers
The lot numbers of the control article components will be maintained in the raw data.

Purity
Limited to the information listed on the label of these commercially available materials or on file with the respective manufacturers, unless assigned by standard operating procedure.

Page 7

Stability
As indicated by information provided by the manufacturers.

Storage Conditions
The control article components will be stored at room temperature. The prepared control article will be stored in a refrigerator set to maintain 2 to 8 degrees Celsius for use for up to one week prior to use for test article preparation or dispensing for control article.

Characteristics
Information on synthesis methods, composition, or other characteristics that define the control article components is on file with the respective manufacturer.

Reserve (Archive) Samples

None required.

Disposition of Test Article

Any remaining test article will be returned to:

Toxicology Formulation Area
Eli Lilly and Company
Building 241, GL45
2001 West Main Street
Greenfield, IN 46140
Telephone No.: 317.276.5682
Facsimile No.: 317.651.9205

Animals

Species
Rat

Strain
Crl:CD(SD)

Source
Charles River Laboratories, Raleigh, North Carolina

Age at Initiation of Treatment
9 to 11 weeks

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Weight at Initiation of Treatment
150 to 350 g

Number and Sex
15 males and 15 females

Identification
An implantable microchip identification device and/or cage card.

Justification
Rats historically have been used in safety evaluation studies and are recommended by appropriate regulatory agencies. Compound 2463608 has been identified as having acceptable characteristics to aid in localizing CB-1 receptors in the brain. The compound will be used in a competition trial in human subjects, first using rimonabant and subsequently with LY2562403. A single-dose expanded acute rat study has been completed, but higher exposure margins and repeat dosing are required for use of the ligand in Europe. The dose proposed is slightly more than 1000-fold greater on a mg/m^3 basis than the dose to be used in human subjects. A saline group is proposed to control for possible adverse effects of the vehicle, 20% Captisol in 25mM acetate buffer pH 4.0.

Husbandry

Housing
Animals will be individually housed in stainless steel cages. Individual animals may be housed in polycarbonate cages with bedding when indicated by health conditions.

Diet
Certified Rodent Diet #2014C (Harlan Teklad) ad libitum unless otherwise specified; animals may be fed the meal-form of this diet if indicated by health conditions. The diet is routinely analyzed by the manufacturer for nutritional components and environmental contaminants. Results of specified nutrient and contaminant analyses are on file at Covance-Madison.

Water
Ad libitum. Water samples are routinely analyzed for specified microorganisms and environmental contaminants. The results are on file at Covance-Madison.

Page 9

Contaminants

No known contaminants are present in the diet or water at levels that might interfere with this study.

Environment

Environmental controls for the animal room will be set to maintain 18 to 26 degrees Celsius, a relative humidity of 30 to 70%, a minimum of 10 air changes/hour, and a 12-hour light/12-hour dark cycle. The light/dark cycle may be interrupted for study-related activities.

Acclimation (Predose Phase)

For at least 1 week

Environmental Enrichment and Dietary Supplements

The animals may be given dietary supplements (that do not require analyses) as a form of environmental enrichment. The animals may be given nylabones or gauze as enrichment devices.

Randomization

Animals may be eliminated from consideration for study selection based on data collected during acclimation (predose phase). Animals will be assigned to the study using a computerized procedure designed to achieve body weight balance with respect to groups. Prior to group assignment, animals may be excluded from the selection pool/sex to produce minimal variation. After group assignment, the mean body weight for each group/sex will not be statistically different at the 5.0% probability level, as indicated by analysis of variance F probability.

Group Designations and Dose Levels

Group	No. of Animals		Dose Level (mg 2463608/kg/day)[a]	Dose Concentration (mg 2463608/mL)[a]
	Male	Female		
Toxicity Animals				
1 (Saline Control)	5	5	0	0
2 (Vehicle Control)	5	5	0	0
3 (Compound 2463608)	5	5	1.0	0.8

a The dose volume will be 1.25 mL/kg.

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Dosing Procedures

Dose Preparation

Vehicle control article, including that used for dosing, will be prepared approximately weekly, stored at room temperature, and sterile-filtered prior to use for dose preparation or dosing. Test article dose preparations will be prepared aseptically according to the mixing procedure supplied by the sponsor and modified by Covance, aliquoted for daily use, and used within 3 days of preparation. Dose concentrations will be based on the test article as supplied. Test article dose preparations will be stored at room temperature until used for dosing.

Dose Administration

Slow bolus intravenous injection in a tail vein once daily for at least 14 days (dosing phase). Doses will be based on the most recently recorded body weight. Animals will be dosed at the volume of 1.25 mL/kg over approximately 30 to 60 seconds. Dose sites will be marked with indelible ink following dose administration. Treatment will continue through the day prior to terminal sacrifice.

Reason for Dosing Route

The intended route of administration in humans is intravenous.

Retention Samples

Retention samples will not be collected.

Dose Analysis

Homogeneity

For the concentration of the test article dose preparation, the mixtures will be a solution; therefore, no homogeneity analysis will be necessary.

Stability

Stability information on the test article formulations will be provided by the sponsor for inclusion in the final report.

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Concentration Verification

Duplicate samples (approximately 1.0 mL each) will be taken at the time of mixing from the test article, saline, and vehicle control article formulations prepared for use on Day 1. All samples will be stored at room temperature until shipped on Day 2 for analysis. Additional samples may be collected at the discretion of the study director.

One set of samples will be sent to the sponsor for analysis. The other set will be maintained at Covance. Upon notification of successful completion of the analysis, the set of samples retained by Covance will be discarded.

Sample Shipping

All samples will be identified with Lilly Toxicology TX labels and shipped by Federal Express priority overnight delivery under ambient conditions to the following:

Jeffrey A. Peterson, MS
Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285
Telephone No.: 317.276.8203
Facsimile No.: 317.655.1902
E-Mail: pete@lilly.com

Toxicology Test Chemical Assays forms, supplied by the sponsor, will be included with each shipment. The study monitor and recipient will be notified by facsimile as to the date and method of shipment.

Sample Analysis

Samples will be analyzed for Compound 2463608 content as described above. Results will be provided to the study director for inclusion in the final report.

Observation of Animals

Clinical Signs

Each animal will be observed twice daily (a.m. and p.m.) for mortality, abnormalities, and signs of pain or distress; findings will be recorded as they are observed.

Once daily during the dosing phase, cageside observations will be made for each animal (except on the days when detailed observations are conducted); abnormal findings will be recorded.

Page 12

At least once during the predose phase, on the first day of dosing (Day 1) and weekly thereafter (prior to dosing), and on the day of scheduled sacrifice, detailed observations will be made for each animal; abnormal findings or an indication of normal will be recorded.

Unscheduled observations will be recorded.

Ophthalmic Examinations

Once during the predose phase and once on Day 11 of the dosing phase. All animals will be examined by a veterinarian using an indirect ophthalmoscope. The eyes will be dilated with a mydriatic agent prior to examination.

Body Weights

At least once during the predose phase, on Day 1 of the dosing phase, and weekly thereafter.

Food Consumption

Quantitatively assessed weekly during the dosing phase.

Clinical Pathology - Toxicity Animals

Frequency and Number of Animals

Blood and urine will be collected from all animals on the day of scheduled sacrifice. Blood will also be collected for hematology and clinical chemistry tests (if possible) from animals sacrificed at an unscheduled interval.

Method of Collection

Animals will be fasted overnight for scheduled collections. Blood will be collected via a jugular vein. Urine will be collected overnight on wet ice before blood collection.

The anticoagulants will be sodium citrate for coagulation tests and potassium EDTA for the hematology tests. Samples for clinical chemistry will be collected without anticoagulant.

Tests

Hematology

red blood cell (erythrocyte) count
hemoglobin
hematocrit
mean corpuscular volume
mean corpuscular hemoglobin
mean corpuscular hemoglobin concentration
platelet count
white blood cell (leukocyte) count
differential blood cell count
blood cell morphology
reticulocyte count

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Coagulation (scheduled collections only)

prothrombin time
activated partial thromboplastin time

Clinical Chemistry

glucose
urea nitrogen
creatinine
total protein
albumin
globulin
albumin/globulin ratio
cholesterol
triglycerides
total bilirubin
alanine aminotransferase
alkaline phosphatase
gamma glutamyltransferase
aspartate aminotransferase
creatine kinase
calcium
inorganic phosphorus
sodium
potassium
chloride

Urinalysis

appearance/color
volume
specific gravity
pH
protein
glucose
ketones
bilirubin
blood
microscopic examination of sediment
urobilinogen

Termination - Toxicity Animals

Unscheduled Sacrifices and Deaths

Necropsies will be done on all animals that die or are sacrificed at an unscheduled interval. Animals to be sacrificed will be anesthetized with sodium pentobarbital and exsanguinated. Terminal body weights will be recorded for sacrificed animals.

Scheduled Sacrifice

Terminal Sacrifice (Dosing Phase - Final Phase Sacrifice)

After at least 2 weeks of treatment, all surviving animals will be fasted overnight, then anesthetized with sodium pentobarbital, exsanguinated, and necropsied. Terminal body weights will be recorded.

Page 14

Postmortem Procedures

Necropsy

The necropsy will include an examination of the external features of the carcass; external body orifices; the abdominal, thoracic, and cranial cavities; organs; and tissues.

Organ Weights

At scheduled sacrifices, the following organs (when present) will be weighed; paired organs will be weighed together.

adrenal (2)
brain
epididymis (2)
heart
kidney (2)
liver
ovary (2)
pituitary gland
prostate
spleen
testis (2)
thymus
thyroid (2 lobes) with parathyroid
uterus

Organ-to-body and organ-to-brain weight ratios will be reported as percentages.

Bone Marrow Smears

Bone marrow smears will be made from the femur of each animal at the scheduled sacrifice and held for possible future examination (added by amendment).

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Tissue Preservation

The following tissues (when present) from each animal will be preserved in 10% neutral-buffered formalin, unless otherwise indicated below.

adrenal (2)
aorta
brain
cecum
cervix
colon
duodenum
epididymis (2)[a]
esophagus
eye (2)[a]
femur with bone marrow (articular surface of the distal end)
heart
ileum
injection site(s)
jejunum
kidney (2)
lesions
liver
lung with large bronchi
lymph node (mandibular)
lymph node (mesenteric)
mammary gland (males and females)
ovary (2)
optic nerve (2)[a]
pancreas
pituitary gland
prostate
salivary gland [mandibular (2)]
sciatic nerve
seminal vesicle
skeletal muscle (thigh)
skin/subcutis
spinal cord (cervical, thoracic and lumbar)
spleen
sternum with bone marrow
stomach
testis (2)[a]
thymus
thyroid (2 lobes) with parathyroid
tongue
trachea
urinary bladder
uterus
vagina

a Preserved in modified Davidson's fixative.

Histopathology

Preserved tissues listed above (as appropriate) from each animal will be embedded in paraffin, sectioned, and stained with hematoxylin and eosin. All tissues from all animals in the vehicle and compound-treated groups (Groups 2 and 3) and from animals that die or are sacrificed at an unscheduled interval will be examined microscopically by a board-certified veterinary pathologist. If target organs are identified in Group 2 animals, those tissues from all animals in the saline-treated group (Group 1) will also be examined microscopically. All other prepared slides from these animals will be held for possible future examination (added by amendment).

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Peer Review

A pathology peer review will be performed by the sponsor and documentation of the animals and tissues examined will be retained with the raw data. Slides for the pathology peer review will be shipped to:

Monty Hyten
Eli Lilly and Company
2001 West Main Street
Building 240, GL44
Greenfield, IN 46140
Telephone No.: 317.655.9542
Facsimile No.: 317.277.4954
E-Mail: hyten_monty_j@lilly.com

After completion of the pathology peer review, all tissue slides will be returned to Covance-Madison.

Reports

One copy of the draft final report will be sent to the sponsor. At the end of 1 year after issuance of the draft report, if no requested revisions or instructions to finalize have been communicated by the sponsor, the draft report will be considered final and issued as the final report, signed by the study director, and submitted to the sponsor.

Any modifications or changes to the draft report requested 1 year after issuance will be performed at additional cost to the sponsor.

One unbound, three-hole punched copy of the signed final report will be sent to the sponsor. An electronic version of the report will also be provided in Portable Document Format.

The report will include the following information.

Page 17

Experimental Design and Methods

Results

dose analysis (provided by the sponsor)
test article potency results (provided by the sponsor)
mortality
clinical signs
ophthalmic findings
body weights
body weight changes
food consumption
clinical pathology results
organ weight data
macroscopic observations
microscopic observations

Statistical Evaluation

Levene's test will be done to test for variance homogeneity. In the case of heterogeneity of variance at $p \leq 0.05$, rank transformation will be used to stabilize the variance. Comparison tests will take variance heterogeneity into consideration.

One-way analysis of variance (ANOVA) will be used (if applicable) to analyze organ weights, continuous clinical pathology values, food consumption, and body weight data. If the ANOVA is significant, Dunnett's t-test will be used for pairwise comparisons between treated and control groups.

If the ANOVA shows significance for body weights at Week 1 of the dosing phase, one-way analysis of covariance (ANCOVA) will be used to analyze body weights, with initial body weights as the covariate. If the ANCOVA is significant, covariate-adjusted means will be used for control versus treated group comparisons.

Group comparisons (Groups 2 and 3 versus Group 1) will be evaluated at the 5.0%, two-tailed probability level. Data collected on or after the first day of treatment will be analyzed statistically.

Page 18

Record Retention

The raw data, documentation, specimens, the protocol, and final report for this study will be stored in the Covance archives for at least 3 years after report finalization. The Covance archives staff will contact the sponsor after 3 years following report finalization to determine disposition of the archived materials (except for the raw data on durable media, study correspondence, the protocol, and final report which will be kept by Covance). The sponsor will then authorize the transport of the materials to their site (or that of their designee).

The sponsor will be responsible for the maintenance of the test and control article reserve samples, and the raw data, documentation, records, specimens, and contributor reports generated by Eli Lilly and Company as a result of this study will be archived in the storage facilities of Eli Lilly and Company.

Protocol Approval

The final version of the protocol was approved by the study monitor for study director signature on 29 May 2007.

Matthew D. Schroeder, PhD
Study Director
Covance Laboratories Inc.

29 May 07
Date

Page 1

COVANCE
THE DEVELOPMENT SERVICES COMPANY

Protocol Amendment No. 1

Covance 7608-544

A Repeat-Dose Toxicity Study in Rats Given Compound 2463608 by Intravenous Injection for 2 Weeks

Sponsor:	Eli Lilly and Company, Indianapolis, Indiana
Study Monitor:	Lewis L. Truex, MS, DABT
Testing Facility:	Covance Laboratories Inc., Madison, Wisconsin
Study Director:	Matthew Schroeder, PhD

This amendment modifies the following portions of the protocol.

Effective 30 May 2007

Test Article, Storage Conditions.

To correctly reflect the storage conditions for the test article, replace the text in this section with the following.

Room temperature

Page 2

Disposition of Test Article.

To include disposition of sponsor-supplied Captisol and add timing for disposition, replace this section with the following.

Disposition of Test Article and Control Article Component

Within 30 days of the completion of dosing, any remaining test article and/or Captisol will be returned to:

Toxicology Formulation Area
Eli Lilly and Company
Building 241, GL45
2001 West Main Street
Greenfield, IN 46140
Telephone No.: 317.276.5682
Facsimile No.: 317.651.9205

Control Article.

To correctly reflect the two control articles, replace this section with the following.

Vehicle Control Article

Identification

20% (w/v) Captisol in 25mM acetate buffer prepared in Sterile Water for Injection, pH 3.8 to 4.0

Lot Numbers

The lot numbers of the vehicle control article components will be maintained in the raw data.

Purity

Limited to the information listed on the label of these commercially available materials or on file with the respective manufacturers, unless assigned by standard operating procedure.

Stability

As indicated by information provided by the manufacturers.

Page 3

Storage Conditions

The vehicle control article components will be stored at room temperature. The prepared vehicle control article will be stored in a refrigerator set to maintain 2 to 8 degrees Celsius until used for test article preparation or dispensing for dose administration.

Characteristics

Information on synthesis methods, composition, or other characteristics that define the vehicle control article components is on file with the respective manufacturer.

Saline Control Article

Identification

0.9% Sodium Chloride for Injection, USP (sterile saline)

Lot Numbers

The lot number of the saline control article will be maintained in the raw data.

Purity

Limited to the information listed on the label of this commercially available material or on file with the manufacturer, unless assigned by standard operating procedure.

Stability

As indicated by information provided by the manufacturers.

Storage Conditions

The saline control article will be stored at room temperature.

Characteristics

Information on synthesis methods, composition, or other characteristics that define the saline control article is on file with the respective manufacturer.

Page 4

Group Designations and Dose Levels.

To change the dose volume and Compound 2463608 dose concentration, replace the table in this section with the following.

Group	No. of Animals		Dose Level (mg 2463608/kg/day)[a]	Dose Concentration (mg 2463608/mL)[a]
	Male	Female		
Toxicity Animals				
1 (Saline Control)	5	5	0	0
2 (Vehicle Control)	5	5	0	0
3 (Compound 2463608)	5	5	1.0	0.5

a The dose volume will be 2.0 mL/kg.

Dosing Procedures, Dose Preparation.

To clarify dose preparation and include instructions for saline control article, replace the text in this section with the following.

Vehicle control article, including that used for dosing, will be prepared approximately weekly, sterile-filtered prior to use for dose preparation or dosing, and stored in a refrigerator set to maintain 2 to 8 degrees Celsius. Vehicle control article used for dosing will be removed from the refrigerator and allowed to equilibrate to approximately room temperature prior to administration. Test article for dose preparation will be weighed in a Laminar flow hood using autoclaved equipment and glassware; the remainder of test article dose preparation will be conducted aseptically, as applicable, according to the mixing procedure supplied by the sponsor and modified by Covance. Test article formulations will be not be sterile filtered; test article formulations will be aliquoted for daily use, stored at room temperature, and used within 3 days of preparation. Saline control article will be stored at room temperature and dosed as supplied. Dose concentrations will be based on the test article as supplied.

Dosing Procedures, Dose Administration, Sentences 3 and 4.

To change the dose volume and clarify dose site marking, replace the text in these sentences with the following.

Animals will be dosed at the volume of 2.0 mL/kg over approximately 30 to 60 seconds. The dose site will be marked with indelible ink on each toxicity animal following the final dose administration.

Page 5

Dose Analysis, Concentration Verification.

To clarify the sample size and include remove the requirement to retain one set of samples at Covance, replace the text in this section with the following.

Duplicate samples (1.0 mL each) will be taken at the time of mixing from the test article, saline, and vehicle control article formulations prepared for use on Day 1. All samples will be stored at room temperature until shipped on Day 2 for analysis. Additional samples may be collected at the discretion of the study director.

Effective 01 June 2007

Proposed Study Timetable.

To include report and experimental termination dates, replace the text in this section with the following.

Experimental Start Date: 29 May 2007
Inlife Start Date: 05 June 2007
Inlife End Date: 20 June 2007
Audited Draft Report Date: 30 August 2007
Experimental Termination Date: 17 September 2007
Final Report Date: 17 September 2007

Amendment Approval

The final version of this amendment was approved by the study monitor for study director signature on 31 May 2007.

Matthew D. Schroeder — 01 Jun 07

Matthew D. Schroeder, PhD
Study Director
Covance Laboratories Inc.

Date

Page 1

COVANCE
THE DEVELOPMENT SERVICES COMPANY

Protocol Amendment No. 2

Covance 7608-544

A Repeat-Dose Toxicity Study in Rats Given Compound 2463608 by Intravenous Injection for 2 Weeks

Sponsor:	Eli Lilly and Company, Indianapolis, Indiana
Study Monitor:	Lewis L. Truex, MS, DABT
Testing Facility:	Covance Laboratories Inc., Madison, Wisconsin
Study Director:	Matthew Schroeder, PhD

This amendment modifies the following portions of the protocol.

Effective 30 May, 04 June, and 05 June 2007

Dosing Procedures, Dose Preparation.

To clarify test article dose preparation (effective 30 May 2007), allow for sonication or overnight stirring (effective 04 June 2007), if necessary, and include a filtration step for test article formulations (effective 05 June 2007), replace the text in this section with the following.

Vehicle control article, including that used for dosing, will be prepared approximately weekly, sterile-filtered prior to use for dose preparation or dosing, and stored in a refrigerator set to maintain 2 to 8 degrees Celsius. Vehicle control article used for dosing will be removed from the refrigerator and allowed to equilibrate to approximately room temperature prior to administration. Test article for dose preparation will be weighed in a Laminar flow hood; dose preparation will be conducted aseptically, as applicable, using autoclaved equipment and glassware according to the mixing procedure supplied by the sponsor and modified by Covance. Test article formulations will be filtered through a 0.22 micron filter, aliquoted for daily use, stored at room temperature, and used within 3 days of preparation. Test article dose formulations may be sonicated and/or allowed to stir overnight, using a stir bar and stir plate, at room temperature in a sterile hood as necessary. Dose concentrations will be based on the test article as supplied. Saline control article will be stored at room temperature and dosed as supplied.

Page 2

Effective 12 June 2007

Dosing Procedures, Dose Administration, Sentence 3.

To include a saline flush after dose administration, add the following after this sentence.

Dose administration will be followed by a saline flush of approximately 0.5 mL.

Effective 19 June 2007

Dose Analysis, Concentration Verification.

To include an additional sample collection, add the following after the text in this section.

Two 1 mL samples will be taken, if possible, from the remaining Group 3 dose preparation used for dosing on Day 15. Each sample will be weighed, stored at room temperature, and shipped on Day 15 for analysis.

Amendment Approval

The final version of this amendment was approved by the study monitor for study director signature on 19 June 2007.

Matthew D. Schroeder, PhD
Study Director
Covance Laboratories Inc.

19 Jun 07
Date

Page 1

COVANCE
THE DEVELOPMENT SERVICES COMPANY

Protocol Amendment No. 3

Covance 7608-544

A Repeat-Dose Toxicity Study in Rats Given Compound 2463608 by Intravenous Injection for 2 Weeks

Sponsor:	Eli Lilly and Company, Indianapolis, Indiana
Study Monitor:	Lewis L. Truex, MS, DABT
Testing Facility:	Covance Laboratories Inc., Madison, Wisconsin
Study Director:	Matthew Schroeder, PhD

This amendment modifies the following portions of the protocol.

Effective 08 June 2007

Vehicle Control Article, Identification

To reflect an increase in the upper pH limit of the vehicle control article, replace the text in this section with the following.

20% (w/v) Captisol in 25mM acetate buffer prepared in Sterile Water for Injection, pH 3.8 to 4.4

Page 2

Amendment Approval

The final version of this amendment was approved by the study monitor for study director signature on 10 July 2007.

Matthew D. Schroeder, PhD
Study Director
Covance Laboratories Inc.

10 Jul 07
Date

Page 1

COVANCE
THE DEVELOPMENT SERVICES COMPANY

Protocol Amendment No. 4

Covance 7608-544

A Repeat-Dose Toxicity Study in Rats Given Compound 2463608 by Intravenous Injection for 2 Weeks

Sponsor:	Eli Lilly and Company, Indianapolis, Indiana
Study Monitor:	Lewis L. Truex, MS, DABT
Testing Facility:	Covance Laboratories Inc., Madison, Wisconsin
Study Director:	Matthew Schroeder, PhD

This amendment modifies the following portions of the protocol.

Effective 23 July 2007

Postmortem Procedures, Histopathology, Sentence 3.

To include identified target tissues, replace this sentence with the following.

The kidneys, injection site, and thymus, identified potential target, from all animals in the saline-treated group (Group 1) will also be examined microscopically.

Page 2

Reports, Statistical Evaluation.

To include comparison of Group 3 versus Group 2 and change the type of t-test to be used, replace the text in this section with the following.

Levene's test will be done to test for variance homogeneity. In the case of heterogeneity of variance at $p \leq 0.05$, rank transformation will be used to stabilize the variance. Comparison tests will take variance heterogeneity into consideration.

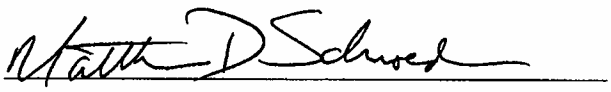
One-way analysis of variance (ANOVA) will be used (if applicable) to analyze organ weights, continuous clinical pathology values, food consumption, and body weight data. If the ANOVA is significant, Fisher's LSD t-test will be used for pairwise comparisons between treated and control groups.

If the ANOVA shows significance for body weights at Week 1 of the dosing phase, one-way analysis of covariance (ANCOVA) will be used to analyze body weights, with initial body weights as the covariate. If the ANCOVA is significant, covariate-adjusted means will be used for control versus treated group comparisons.

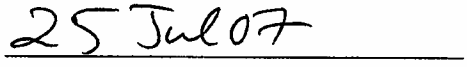
Group comparisons (Groups 2 and 3 versus Group 1 and Group 3 versus Group 2) will be evaluated at the 5.0%, two-tailed probability level. Data collected on or after the first day of treatment will be analyzed statistically.

Amendment Approval

The final version of this amendment was approved by the study monitor for study director signature on 24 July 2007.



Matthew D. Schroeder, PhD
Study Director
Covance Laboratories Inc.



Date

Appendix B: Study Deviations

Procedure	Deviations
Test Article	
Potency Reassay	The sample of test article for end-of-study potency reassay was not collected prior to shipping remaining test article to the sponsor. Instead, the sponsor transferred a sample of the remaining test article to the Principal Investigator for Test Article Potency.
Dose Preparation	
Vehicle Control Article	The vehicle control article used in dose preparations for Days 1 through 7 was outside the protocol-specified pH range of 3.8 to 4.0.
Dose Administration	The test article formulation used for dosing Group 3 on Day 15 of the dosing phase was prepared 4 days prior to use rather than within the protocol-specified maximum of 3 days. There is no positive documentation that final dose sites were marked with indelible ink. Markings were visually verified on wet tissue samples.
Disposition of Animals	
Histopathology	One of the pair of adrenal medullas was noted as missing and, therefore, not examined microscopically for Animal Nos. B96008 (Group 2 male), B96012 and B96013 (Group 3 males), and B96027 (Group 3 female).

These deviations have not affected the overall interpretation of study findings nor compromised the integrity of the study.

Appendix C: Test Article Characterization and Control Article Certificates of Analysis

www.lilly.com

Lilly Research Laboratories
A Division of Eli Lilly and Company
Lilly Corporate Center
Indianapolis, Indiana 46285 U.S.A.

Phone 317 276 2000

CHEMICAL PROCESS RESEARCH AND DEVELOPMENT

CERTIFICATE OF ANALYSIS

TITLE: Lilly CB-1 Antagonist

COMPOUND NUMBER: 2463608
LOT NUMBER: KD0-E01100-039-C
DOCUMENT PREPARATION DATE: August 6, 2007
DATE OF MANUFACTURE March 30, 2007
ITEM CODE N/A
RETEST DATE N/A
STORAGE CONDITIONS: Ambient Temperature

TEST AND METHOD	METHOD	SPECIFICATIONS	RESULT
Purity	HPLC at 215 nm	NLT 95 (area %)	>99%
Identity	^{1}H NMR (DMSO-d_6)	Conforms to structure	Conforms to structure
Appearance	Visual	White to off- white solid No Visible contaminants	White solid No visible contaminants

NLT=Not Less Than

Lot KD0-E01100-039-C was manufactured under Non-GMP conditions

The following signatures indicate that the results listed above have been generated in accordance with local Standard Operating Procedures (SOP) and local Operating Procedures (OP).

Prepared By: _____ Quality Assurance Representative 06 Aug 07 Date

Verified By: Robert A. Jagner Quality Assurance Representative 06-Aug-07 Date

CAPTISOL® - Research Grade

(β-Cyclodextrin Sulfobutyl Ethers, Sodium Salts)

Certificate of Analysis (rev. 0)

Batch Number: NC-04A-05025

Test	Specification	Result
Appearance	White to off-white solid essentially free from foreign matter	Pass
Identification (IR)	Spectrum is consistent with the SBECD standard	Pass
Average Degree of Substitution (CE)	6.0 - 7.1	6.6
β-Cyclodextrin	Maximum 0.5%	0.1%
Water (by KF)	Maximum 15.0%	4.4%[a]
Assay (anhydrous basis)	Minimum 95%	100%

Date of Manufacture: Aug 2005

References: 17CX01.HQ00025

QA APPROVED

[a] Water content shown is as delivered. Captisol® is hygroscopic and water content can be affected by handling and storage conditions.

Released By: Vincent Antle
Vincent Antle, PhD
Director of Technical Operations
and Quality Assurance

Date: 27 Mar 07

QA APPROVED

STORAGE: Store at ambient temperature in sealed containers. Protect from moisture.

CAPTISOL®-Research Grade is not for human use and may not be used in animal studies without written authorization from CyDex.

CyDex®

CyDex, Inc. • 10513 W. 84th Terr. • Lenexa, KS 66214-1643 • P: 913.685.8850 • F: 913.685.8856 • www.cydexinc.com • www.captisol.com

SIGMA-ALDRICH

3050 Spruce Street
Saint Louis, Missouri 63103 USA
Telephone (800)-521-8956 • (314) 771-5765
Fax (800)-325-5052 • (314) 771-5757
sigma-aldrich.com

COVANCE LABORATORIES (D)
3301 KINSMAN BLVD
MADISON WI 53704

PO#: D6046

CERTIFICATE OF ANALYSIS

SODIUM ACETATE, ANHYDROUS
MOLECULAR BIOLOGY REAGENT

PRODUCT NO: S2889 CAS NO: 127-09-3
LOT NO: 066K0043 FORMULA: $C_2H_3O_2Na$
FORMULA WEIGHT: 82.03 STORE AT ROOM TEMPERATURE

TEST	SPECIFICATION	RESULTS
APPEARANCE	WHITE TO OFF-WHITE POWDER	WHITE POWDER
SOLUBILITY	CLEAR COLORLESS TO VERY FAINT YELLOW SOLUTION AT 100 MG/ML IN WATER	CLEAR COLORLESS
WATER BY KARL FISCHER	NMT 1.0%	0.4%
CHLORIDE	NMT 20 PPM	CONFORMS *
SULFATE	NMT 30 PPM	CONFORMS *
HEAVY METALS	NMT 10 PPM	CONFORMS *
PURITY BY PERCHLORIC ACID TITRATION	NLT 99%	>99% *
DNASE, RNASE AND PROTEASE	NONE DETECTED	CONFORMS
		* SUPPLIER INFORMATION
RECOMMENDED RETEST	5 YEARS	JUNE 2011

QC ACCEPTANCE DATE JUNE 2006
CONTINUED ON NEXT PAGE-----

SIGMA-ALDRICH

3050 Spruce Street
Saint Louis, Missouri 63103 USA
Telephone (800)-521-8956 • (314) 771-5765
Fax (800)-325-5052 • (314) 771-5757
sigma-aldrich.com

CONTINUATION OF ------
SODIUM ACETATE, ANHYDROUS
PRODUCT NO: S2889 LOT NO: 066K0043 CAS NO: 127-09-3

RODNEY BURBACH
SUPERVISOR, ANALYTICAL SERVICES
789/20070531#1/SML1
DOCUMENT DATE: 05/31/07

SIGMA-ALDRICH

Certificate of Analysis

Product Name	Glacial acetic acid, meets USP testing specifications
Product Number	A9967
Product Brand	Sigma-Aldrich
CAS Number	64-19-7
Molecular Formula	CH_3CO_2H
Molecular Weight	60.05

TEST	SPECIFICATION	LOT 016K0667 RESULTS
IDENTITY	PASS	PASS
CONGEALING TEMPERATURE	NLT 15.6 DEG C	16.9 DEG C
LIMIT OF NONVOLATILE RESIDUE	NMT 1.0 MG	<0.1 MG
CHLORIDE	PASS	PASS
SULFATE	PASS	PASS
HEAVY METALS	NMT 5 PPM	<5 PPM
READILY OXIDIZABLE SUBSTANCES	PASS	PASS
ASSAY	99.5% TO 100.5%	100.4%
		ALL SUPPLIER DATA MEETS USP TESTING SPECIFICATIONS
QC ACCEPTANCE DATE		JANUARY 2006

Rodney Burbach, Supervisor
Analytical Services
St. Louis, Missouri USA

Hospira, Inc.
3900 Howard Lane
Austin, TX. 78728-6599

Certificate of Analysis

Product Name: 1000 ML 0.9% NACL INJ USP
Lot Number: 50036JT **List Number:** 79830449
Date of Manufacture: 02/09/2007 **Expiration Date:** 02/01/2009

STM	Test Description	Final Limits Lower	Upper	Result	Pass/Fail
75145	Meets the requirements of Drug Code 75145.				Pass
B-0813	BET: Less than 0.50 EU/mL			0.25	Pass
C-0003	Chloride Identification				Pass
C-0021	pH Determination	4.5	7.0	5.9	Pass
C-0042	Sodium Chloride Assay (%)	95.0	105.0	98.2	Pass
C-0869	Iron Determination: NMT 2 ppm (0.0002%)				Pass
C-1221	Heavy Metals Determination: NMT 10 ppm				Pass
C-1648	Sodium Identification				Pass
M-0051	Sterility: Must meet product bioburden testing requirements.				Pass
M-0476	Must meet chemical indicator testing requirements.				Pass
M-0477	Must meet chemical indicator testing requirements.				Pass
P-0416	Solution must be clear.				Pass
P-0416	Solution must not contain one or more particles which are visible upon attentive examination.				Pass
P-0452	10.0 micron Sub-Visual Particulate	0	25	2,2,2,2,3,2,3,3,4,4	Pass
P-0452	25.0 micron Sub-Visual Particulate	0	3	0,0,0,0,0,0,0,0,0,0	Pass
P-0759	Volume: 1000 mL 1090 mL				Pass

This product has been manufactured and tested in current Good Manufacturing Practices (cGMP) facilities in accordance with appropriate regulations. This product meets applicable specifications, applicable Regulatory Submissions or Marketing Authorizations and, where appropriate, Compendial requirements. The undersigned certifies this to be a true representation of the results.

Quality Certified By: _____ Date: 2.20.07

Page 1 of 1 Document ID: 935

Certificate of Analysis

PRODUCT:	STERILE WATER FOR INJECTION, USP
LIST No.:	7990-04-49 1-NDC 0409-7990-09 L/N 7990-09 LC 04 IC 49
LOT No.:	46-208-JT
SIZE:	1000 ML
MFG. DATE:	OCTOBER 4, 2006
EXP. DATE:	OCTOBER 1, 2008

TEST DESCRIPTION	TEST METHOD	SPECIFICATION	TEST RESULTS
Clarity	P-0416	Solution must be clear. Solution must not contain one or more particles which are visible upon attentive examination	PASS PASS
Volume	P-0759	1000 to 1090 mL	Meets requirement.
Particulate Matter	P-0452	Must meet test requirements. Not more than 25 particles/mL GT or equal to 10.0 um Not more than 3 particles/mL GT or equal to 25.0 um	 2, 2, 2, 2, 2 2, 2, 2, 3, 1 0, 0, 0, 0, 0 0, 0, 0, 0, 0
Sterility	G-0051	Must meet product bioburden test requirements.	Meets requirements.
Batch Continuous	M-0477 M-0476	Must meet requirements of parametric release. Must meet key and critical parameters as ~~defined in the applicable S-Specification.~~ Must meet cycle minimum and maximum parameters as applicable. Must meet chemical indicator test requirements.	Meets requirements.
Bacterial Endotoxin	B-0610	Less than 0.25 EU / mL	<0.06 EU/mL
Water	75145	The water used in solution must be drawn from a source of water which meets the requirements of Drug Code 75145.	Meets requirements.
Chloride	C-0193	Not more than 0.5 part per million	NMT 0.5 ppm

Hospira, Inc. 3900 Howard Lane Austin, Texas 78728

Certificate of Analysis

PRODUCT:	STERILE WATER FOR INJECTION, USP
LIST No.:	7990-04-49 1-NDC 0409-7990-09 L/N 7990-09 LC 04 IC 49
LOT No.:	46-208-JT
SIZE:	1000 ML
MFG. DATE:	OCTOBER 4, 2006
EXP. DATE:	OCTOBER 1, 2008

TEST DESCRIPTION	TEST METHOD	SPECIFICATION	TEST RESULTS
Sulfate	C-0057	None detected.	None detected.
Ammonia	C-0058	Not more than 0.3 part per million.	NMT 0.3 ppm
Calcium	C-0059	None detected.	None detected.
Carbon Dioxide	C-0060	None detected.	None detected.
Oxidizable substances	C-0062	Passes USP test.	Passes USP test.
pH	C-0056	Between 5.0 and 7.0	5.5
Aluminum	C-1971	Not more than 25 micrograms/liter.	<3 ppb

This product has been manufactured and tested in current Good Manufacturing Practices (cGMP) facilities in accordance with appropriate regulations. This product meets applicable specifications, applicable Regulatory Submissions or Marketing Authorizations and, where appropriate, Compendial requirements. The undersigned certifies this to be a true representation of the results.

CERTIFIED BY: _____ Date: 1.4.07

Hospira, Inc. 3900 Howard Lane Austin, Texas 78728

HOSPIRA, INC. - ROCKY MOUNT, NC

...ED: 05-10-31 WCQA7990 PAGE 1

KEYW *05-02-21* EFFC *05-10-31* SUBTYPE-7 AREA-T
DESC: *CERTIFICATE OF ANALYSIS HOSPIRA, INC. *
(ROCKY MOUNT N.C.) CQ
WRITTEN BY: B. WHITEHEAD 2-21-05
APPROVED BY: C. RITCHELL 3-24-05

SPECIFICATION: GN.11-06

THIS PRODUCT HAS BEEN MANUFACTURED AND TESTED IN CURRENT GOOD MANUFACTURING PRACTICES (CGMP) FACILTITES IN ACCORDANCE WITH APPROPRIATE REGULATIONS. THIS PRODUCT MEETS APPLICABLE SPECIFICATIONS, APPLICABLE REGULATORY SUBMISSIONS OR MARKETING AUTHORIZATIONS, AND WHERE APPROPRIATE, COMPENDIAL REQUIREMENTS. THE UNDERSIGNED CERTIFIES THIS TO BE A TRUE REPRESENTATION OF THE RESULTS.

PRODUCT MANUFACTURING INFORMATION

I. DATE OF MANUFACTURE: 7/30/06

BATCH SIZE: 950001

NDC/DIN NO.: NDC0409-7990-09

		SELECT APPLICABLE SPECIFICATION	CURRENT DATE:
MANUFACTURING FORMULA:	DOCUMENT: 92.D-7990	(✓)	7/6/04
COMMODITY AND PROCESS SUMMARY:	DOCUMENT: 35.07990049	(✓)	8/6/04
PRINTED MATERIAL SUMMARY:	DOCUMENT: 40.07990049C	(✓)	6/5/06
SAMPLING AND TESTING REQUIREMENTS:	DOCUMENT: 60.07990ALLCODE	(✓)	01/13/06

PRODUCT TEST RESULTS

J. Hardison 08/04/06

I. PHYSICAL REQUIREMENTS:

TEST	SPECIFICATION	REQUIREMENTS	RESULTS	PASS / FAIL
A. CLARITY	90.P-0416	1. SOLUTION MUST BE CLEAR.	Clear	✓ / ____
		2. SOLUTION MUST NOT CONTAIN ONE OR MORE PARTICLE WHICH ARE VISIBLE UPON ATTENTIVE EXAMINATION.		

7990-04-49 2 43-933-FW EXP. DATE 1JUL2008 JD08183
STERILE WATER FOR INJ., USP

COMMENTS:

ISSUER: RICHARDAVA 07/21/06

HOSPIRA, INC. - ROCKY MOUNT, NC
DATED: 05-10-31 WCQA7990 PAGE 2

TEST	SPECIFICATION	REQUIREMENTS	RESULTS	PASS / FAIL
I. PHYSICAL REQUIREMENTS CONT'D				
B. VOLUME	90.P-0759	1000-1090 ML	1040ml	✓ /
II. A. CHEMICAL REQUIREMENTS:				
1. CHLORIDE	90.C-0193	FINAL PRODUCT LIMITS= NMT 0.5 PPM NONE DETECTED	NmT 0.5PPm	✓ /
2. SULFATE	90.C-0057	FINAL PRODUCT LIMITS= NONE DETECTED	Passes	✓ /
3. AMMONIA	90.C-0058	FINAL PRODUCT LIMITS= NMT 0.3 PPM	NmT 0.3 PPm	✓ /
4. CALCIUM	90.C-0059	FINAL PRODUCT LIMITS= NONE DETECTED	Passes	✓ /
5. CARBON DIOXIDE	90.C-0060	FINAL PRODUCT LIMITS= NONE DETECTED	Passes	✓ /
6. OXIDIZABLE SUBSTANCE	90.C-0062	FINAL PRODUCT LIMITS= PASSES USP TEST	Passes	✓ /
7. ALUMINUM	90.C-1971	FINAL PRODUCT LIMIT= NMT 25 MCG/L	<3mcg/L	✓ /
B. PH	90.C-0056	FINAL PRODUCT LIMITS: MUST BE BETWEEN 5.0 AND 7.0	6.6	✓ /

NCMR YES ( ) NO (✓) CHECK APPLICABLE BOX

NCMR NO. _____

CQ REVIEWED BY/DATE: J.Hardison 08/04/06

FCF MQ REVIEWED BY/DATE: 8/11/06

**********END OF DOCUMENT**********

7990-04-49 2 43-933-FW EXP. DATE 1JUL2008 JD08183
STERILE WATER FOR INJ., USP

COMMENTS:

ISSUER: RICHARDAVA 07/21/06

HOSPIRA, INC. - ROCKY MOUNT, NC

DATED: 05-10-31 WBQA7990 PAGE 1

REVW *05-06-03* EFFC *05-10-31* SUBTYPE- AREA-
DESC: *CERTIFICATE OF ANALYSIS HOSPIRA, INC. *
(ROCKY MOUNT N.C.) BQ
WRITTEN BY: D. COOPER 6-07-05
APPROVED BY: C. HARRIS 6-10-05

SPECIFICATION NO.: GN.11-06

THIS PRODUCT HAS BEEN MANUFACTURED AND TESTED IN CURRENT GOOD MANUFACTURING PRACTICES (CGMP) FACILITIES IN ACCORDANCE WITH APPROPRIATE REGULATIONS. THIS PRODUCT MEETS APPLICABLE SPECIFICATIONS, APPLICABLE REGULATORY SUBMISSIONS OR MARKETING AUTHORIZATIONS AND, WHERE APPROPRIATE, COMPENDIAL REQUIREMENTS. THE UNDERSIGNED CERTIFIES THIS TO BE A TRUE REPRESENTATION OF THE RESULTS.

REFERENCE 60.07990ALLCODE SPECIFICATION FOR TESTING INFORMATION

PRODUCT TEST RESULTS

I. PHYSICAL REQUIREMENTS:

TEST	SPECIFICATION	REQUIREMENTS	RESULTS	PASS / FAIL
A. PARTICULATE MATTER	90.P-0452	MUST MEET TEST REQUIREMENTS	pass	✓ / ___

II. BIOLOGICAL REQUIREMENTS:

A. STERILITY	93.G-0051	1. MUST MEET TEST REQUIREMENTS	pass	✓ / ___
		2. MUST MEET REQUIREMENTS OF PARAMETRIC RELEASE	pass	✓ / ___
	90.M-0477	3. MUST MEET CHEMICAL INDICATOR TESTING REQUIREMENT	pass	✓ / ___
B. BACTERIAL ENDOTOXIN	90.B-0610	LESS THAN 0.25 EU/ML	<0.06EU/mL	✓ / ___

BQ REVIEWED BY/DATE: D. Vick 08-07-06

FCF MQ REVIEWED BY/DATE: [signature] 8/11/06

**********END OF DOCUMENT**********

7990-04-49 2 43-933-FW EXP. DATE 1JUL2008 JD08183
STERILE WATER FOR INJ., USP

COMMENTS:

ISSUER: RICHARDAVA 07/21/06

Appendix D: Key Personnel, Codes and Abbreviations, and Comments on the Data

The following lists of comments on the data, codes, abbreviations, and units are used by Covance. Some, but not necessarily all, of this information may be needed for this report.

Key Personnel

Study Monitor	Lewis L. Truex, MS Diplomate, ABT Eli Lilly and Company
Study Director	Matthew Schroeder, PhD
Study Toxicologist	Anne M. Brooks, MS
Report Coordinator	Betsy Nabbefeld
Manager, Animal Operations	Dan Weiser, BS, BA, ALAT
Manager, Dose Formulation	Damon R. Martinson, BS
Director, Veterinary Medicine	Donna J. Clemons, DVM, MS Diplomate, ACLAM
Anatomic Pathologist	Johnnie J. Eighmy, DVM, MS Diplomate, ACVP Diplomate, ABT
Senior Manager, Laboratory Operations	Carmen L. Wilbourn
Lead Quality Assurance	Timothy Valley, BS
Principal Investigator for Dose Analysis	Jeffrey A. Peterson, MS Eli Lilly and Company Lilly Corporate Center Indianapolis, Indiana 46285
Principal Investigator for Test Article Potency	John Masters, PhD Eli Lilly and Company Lilly Corporate Center Indianapolis, Indiana 46285
Principal Investigator for Clinical Pathology	Niraj K. Tripathi, BVSc, MVSc, PhD Diplomate, ACVP (Clinical Pathology)

General Codes and Abbreviations

N	Number of measurements in a group
Mean; MEAN	Arithmetic mean
CAM	Covariate-adjusted mean
SD; S.D.; STAND DEV; STANDARD DEV; sd; STD.DEV	Standard deviation
SE; STDERR	Standard error
SEM, S.E.M	Standard error mean
% RSD	Relative standard deviation
-	Dead animal
NA	No value; not applicable; not present
WT	Weight
NVL	No visible lesions
P	Present
C	Comment found at the end of each group for each sex
UNSCHED or SCHED	Unscheduled or scheduled
TBW	Terminal body weight
#; N; No.	Number
CV	Coefficient of variation
DT TY	Data type
Physical Exam	
Temp	Body temperature (Celsius)
HR	Heart rate
RESP	Respiration rate
CO	Clinical observation
BID, b.i.d.	Twice a day
DSNG	Dosing phase
PRED	Predose phase
RECO	Recovery phase
WK	Week
DSNG X.X	Dosing Phase Week X.Day X
RECO X.X	Recovery Phase Week X. Day X
Obs	Observations
IPD	Immediate postdose
PD	Postdose
a.m.	Ante meridian
p.m.	Post meridian
M	Male
F	Female
ND	None detected
CTLS	Controls
ID	Identification
Blood Pressure	
SYS	Systolic Pressure
DIAS	Diastolic pressure
MAP	Mean arterial pressure
WDTH	Cuff width
LOCA	Cuff location

General Codes and Abbreviations (Continued)

Elicited Behaviors

FGS1	Forelimb grip strength 1
FGS2	Forelimb grip strength 2
FGS3	Forelimb grip strength 3
HGS1	Hindlimb grip strength 1
HGS2	Hindlimb grip strength 2
HGS3	Hindlimb grip strength 3
NCRF	Nociceptive reflex
FTS1	Foot splay 1
FTS2	Foot splay 2
FTS3	Foot splay 3
BDTM	Body temperature (Celsius)
LATN	Latency
GRMS	Number of grooms
REAR	Number of rears
UNPL	Number of urine pools
FCBL	Number of fecal boli

Intraocular Pressure Measurement

ODMS	Right eye measurement
ODCN	Right eye confidence interval
OSMS	Left eye measurement
OSCN	Left eye confidence interval

Major Computer Systems

Acronym	**Definition**
AFLGS	Automated Form and Label Generation System
TALISMAN	Test Article Logging In, Storage, and Management computer system
VPTS	Xybion Path/Tox System for OpenVMS
COSTAR	Converged Statistical Analysis and Reporting application
SAS	Statistical Analysis Software
eNotes	Electronic Notes

General Codes and Abbreviations (Continued)

Units of Measure

G, g	Gram
KG, kg	Kilogram
MG, mg	Milligram
PG, pg	Picogram
L	Liter
DL, dl, dL	Deciliter
fL, fl	Femtoliter
ML, mL	Milliliter
MI	Million
TH	Thousand
MEQ	Milliequivalents
EU	Ehrlich units
PPM, ppm	Parts per million
UL, µL, uL	Microliter
U	Units
MN, min	Minute
S, s	Seconds
msec	Milliseconds
H, h	Hours
UMOL, µmol	Micromoles
MMOL, mmol	Millimoles
MOS	Milliosmoles
BPM	Beats per minute
MCG, UG, µg, ug	Microgram
pmoll	Picomoles
ng	Nanogram
IU	International units
mU	Milliunits
amol	Attomol
fmol	Femtomol
mm HG	Millimeter of Mercury
Cm	Centimeter

Codes for Clinical Pathology

Abbreviation	Definition
HEMQ	Hematology sample quality
COAQ	Coagulation sample quality
CHEQ	Chemistry sample quality
URIQ	Urine sample Quality
H	Hemolyzed
SH	Slightly Hemolyzed
L	Lipemic
I	Icteric

Codes for Blood Cell Morphology

Morphology	Abbreviation	Grading	Definition
Anisocytosis	ANIS	Normal/Nrml	Normal for species
Poikilocytosis	POIK	Slt/Rare	Slight
Polychromasia	POLY	Moderate	Moderate
Hypochromasia	HYPO	Many/Mkd	Marked

Toxic Neutrophils (toxn)

Abbreviation	Definition
Normal	Normal for species
Slt/Rare	Rare
Moderate	Moderate
Many/Mkd	Many

Codes for Clinical Pathology (Continued)

Urine Appearance

Abbreviation	Definition
Urine Color (UCOL)	
STRAW	Straw
YELLOW	Yellow
DK YELLO	Dark yellow
AMBER	Amber
RED	Red
ORANGE	Orange
GREEN	Green
BROWN	Brown
BLUE	Blue
CO	Colorless
O	Other
Urine Clarity (UCLA)	
CLEAR	Clear
SL CLOUDY	Slightly Cloudy
CLOUDY	Cloudy
TURBID	Turbid

Microscopic Examination of Urine

Grading	Definition
Casts (CAST), Red Blood Cells (URBC), White Blood Cells (UWBC), and Epithelial Cells (EPI)	
0	None seen
1	1-5 cells per field
2	6-10 cells per field
3	11-20 cells per field
4	>20 cells per field
Crystals (CRYS) and Bacteria (BACT)	
0	Not present
1	Occasional, not seen in every field
2	Few in all fields
3	Moderate in all fields
4	Many in all fields, may obscure other elements

Codes for Clinical Pathology (Continued)

Codes for Casts (CAST), Abnormal Crystals (CRYS), and Other (OTHR)

Abbreviation	Definition
H	Hyaline casts
G	Granular casts
C	Cellular casts
B	Bilirubin crystals
L	Leucine crystals
AB	Ammonium biurate crystals
T	Tyrosine crystals
CO	Calcium oxalate monohydrate crystals
H	Hippuric acid crystals
CY	Cystine crystals
U	Unknown
Y	Yeast
SP	Sperm
H	Hemolyzed
SH	Slightly hemolyzed
CHEQ	Chemistry quality
COAQ	Coagulation quality

Codes for Clinical Pathology (Continued)

Urine and Fecal Analysis

Clinitek® 200+ Analyzer, Multistix® Strip, Clinitek Atlas

Urine Glucose (UGLU)	
NEGATIVE	Negative
TRACE	100 mg/dL
1+	250 mg/dL
2+	500 mg/dL
3+	≥1000 mg/dL

Urine Ketones (UKET)	
NEGATIVE	Negative
TRACE	5 mg/dL
1+	15 mg/dL
2+	40 mg/dL
3+	≥80 mg/dL

Urine Blood (UOBL)	
NEGATIVE	Negative
TRACE	Trace
1+	Small
2+	Moderate
3+	Large

Urine Nitrite (UNIT)	
NEGATIVE	Negative
POSITIVE	Positive

Urine Protein (UPRO)	
NEGATIVE	Negative
TRACE	Trace
1+	30 mg/dL
2+	100 mg/dL
3+	≥300 mg/dL

Urine Bilirubin (UBIL)	
NEGATIVE	Negative
1+	Small
2+	Moderate
3+	Large

Leukocyte Esterase (ULEU)	
NEGATIVE	Negative
TRACE	Trace
1+	Small
2+	Moderate
3+	Large

Ictotest® Urine Bilirubin (ICTO)	
-	Negative
+	Positive

Clinitest® Urine Reducing Substances (REDS)	
NEGATIVE	Negative
TRACE	1/4 %
1+	1/2 %
2+	3/4 %
3+	1 %
4+	2 %

Hemoccult® Fecal Occult Blood (FOBL)	
NEGATIVE	Negative
POSITIVE	Positive

Abbreviation	Definition
SPGR	Urine specific gravity
UpH	Urine pH
UUBG (Eu/dL)	Urine urobilinogen
PROT	Protozoa
UVOL (mL)	Urine volume
CFWB (cells/µL)	Cerebrospinal fluid white blood cell count
UOSM (mOsm/kg)	Urine osmolality

Abbreviations and Units for Hematology

Abbreviation (Units)	Definition
Advia 120	
WBC (E3/µL)	White blood cell count
RBC (E6/µL)	Red blood cell count
HGB (g/dL)	Hemoglobin
HCT (%)	Hematocrit
MCV (fL)	Mean corpuscular volume
MCHC (g/dL)	Mean corpuscular hemoglobin concentration
MCH (pg)	Mean corpuscular hemoglobin
PLT (E3/µL or $X10^3$/mcL)	Platelet count
PNEU (%)	Percent neutrophils
PLYM (%)	Percent lymphocytes
PMON (%)	Percent monocytes
PEOS (%)	Percent eosinophils
PBAS (%)	Percent basophils
PLUC (%)	Percent large unstained cells
NEUT (E3/µL)	Absolute segmented neutrophils
LYM (E3/µL)	Absolute lymphocytes
MONO (E3/µL)	Absolute monocytes
EOS (E3/µL)	Absolute eosinophils
BASO (E3/µL)	Absolute basophils
LUC (E3/µL)	Absolute large unstained cells
PRET (%)	Percent reticulocyte
RETI (E3/µL)	Absolute reticulocyte
RDW (%)	RBC distribution width
MPV (fL)	Mean platelet volume
HDW (g/dL)	Hemoglobin distribution width
PDW (%)	Platelet distribution width
PCT (%)	Platelet crit
CWBC (E)	Corrected white blood cell count
Aggregometer	
PAGA (%)	Platelet aggregation adenosine diphosphate
PAGC (%)	Platelet aggregation collagen
PAGR (%)	Platelet aggregation ristocetin
MLA 1600C/1800 or AMAX Destiny	
APTT (seconds)	Activated partial thromboplastin time
AT3 (%)	Antithrombin III
FIB (mg/dL)	Fibrinogen
PLMG (%)	Plasminogen
PT (seconds)	Prothrombin time
TT (seconds)	Thrombin time
RVVT (seconds)	Russell's viper venom test

Abbreviations and Units for Hematology (Continued)

Abbreviation (Units)	Test
Manual	
DDIM	D-dimer
ESR (mm/hour)	Erythrocyte sedimentation rate
EMER	Estimated myeloid/erythroid ratio
FDP (µg/mL)	Fibrin/fibrinogen degradation products
MHGB (%)	Methemoglobin
LEYE (WBC/µL)	Fluid White Blood Cell Count - left eye
REYE (WBC/µL)	Fluid White Blood Cell Count - right eye
FWBC (cells/µL)	Cell-poor fluid white blood cell count
FRBC (cells/µL)	Cell-poor fluid red blood cell count
NRBC (#/100WB)	Nucleated red blood cell count
PAI1 (ng/mL)	PAI - 1
Count - Heinz Bodies	
PHZB (%)	Percent Heinz bodies
AHZB (E3/µL)	Absolute Heinz bodies
Count - Reticulocytes	
PRET (%)	Percent reticulocyte
ARET (E3/µL)	Absolute reticulocyte
Count - Differential 100 cells	
ANEU (E3/µL)	Absolute neutrophils
ALYM (E3/µL)	Absolute lymphocytes
AMON (E3/µL)	Absolute monocytes
AEOS (E3/µL)	Absolute eosinophils
ABAS (E3/µL)	Absolute basophils
PNET (%)	Percent neutrophils
PLYP (%)	Percent lymphocytes
PMNC (%)	Percent monocytes
PESP (%)	Percent eosinophils
PBSP (%)	Percent basophils
Count - M/E Ratios	
TMER	Total myeloid/erythroid
MER	Myeloid/erythroid ratio
Count - BM Differential 500 Cell	
RUBR	Rubriblast
PROR	Prorubricyte
NORM	Normochromic rubricyte
META	Metarubricyte
HEMA	Hematogone
MYEL	Myeloblast
PROG	Progranulocyte
NEMY	Neutrophilic myelocyte
EOMY	Eosinophilic myelocyte
BAMY	Basophilic myelocyte
NEUM	Neutrophilic metamyelocyte
EOSM	Eosinophilic metamyelocyte

Abbreviations and Units for Hematology (Continued)

Abbreviation (Units)	Test
BASM	Basophilic metamyelocyte
NEUB	Neutrophilic band
EOSB	Eosinophilic band
BASB	Basophilic band
BMNT	Neutrophil
BMES	Eosinophil
BMBS	Basophil
BMMN	Monocytes
BMLY	Lymphocytes
PLSM	Plasma cell
MEGA	Megakaryocyte
MACR	Macrophage
MAST	Mast cells
OTHR	Other
TBMD	Total bone marrow differential
Count - BM Differential 200 Cell	
PRLF	Proliferating erythroid
DIFF	Differentiating erythroid
PROM	Proliferating myeloid
DIFM	Differentiating myeloid
TBMD	Total bone marrow differential
Count - Erythroid Differential	
PROE	Proliferating erythroid
DIFE	Differentiating erythroid
TERD	Total erythroid differential
ABL77/Nova	
CHLR (mmol/L)	Chloride
Hct (%)	Hematocrit
ICa (mmol/L)	Ionized calcium
PCO2 (mmHg)	Partial pressure carbon dioxide
PO2 (mmHg)	Partial pressure oxygen
pH	pH
POT (mmol/L)	Potassium
SODI (mmol/L)	Sodium
cHCO (mmol/L)	Derived Bicarbonate

Abbreviations and Units for Serum Chemistry Functions

Abbreviation (Units)	Test
DPC Immulite	
ACTH (pg/mL)	Adrenocorticotropic hormone
ALDS (pg/mL)	Aldosterone
B2MI (ng/mL)	B2-microglobulin
CORT (µg/dL)	Cortisol
CRPR (mg/dL)	C-reactive protein
ESTR (pg/mL)	Estradiol
FT3 (pg/mL)	Free T3
FT4 (ng/mL)	Free T4
INSU (µIU/mL)	Insulin
PTH (pg/mL)	Parathyroid hormone
PROG (ng/mL)	Progesterone
PROL (ng/mL)	Prolactin
TEST (ng/dL)	Testosterone
TSH (µIU/mL)	Thyroid stimulating hormone
TSHD (µIU/mL)	Thyroid stimulating hormone canine
T4 (µg/dL)	Thyroxine
T4K9 (µg/dL)	Thyroxine canine
T3 (ng/dL)	Triiodothyronine
PYRD (nM)	Pyrilinks-D
FER (ng/mL)	Ferritin
FSH (mIU/mL)	Follicle stimulating hormone
LH (ng/mL)	Luteinizing hormone
GAS (pg/mL)	Gastrin
TPI (ng/mL)	Troponin I
Elise	
USOD (mmol/L)	Urine sodium
UPOT (mmol/L)	Urine potassium
UCHL (mmol/L)	Urine chloride
Hitachi 911/Analytics Modular	
GLU (mg/dL)	Glucose
UN (mg/dL)	Urea nitrogen
CREA (mg/dL)	Creatinine
CHOL (mg/dL)	Total cholesterol
AST (U/L)	Aspartate aminotransferase
ALT (U/L)	Alanine aminotransferase
ALP (U/L)	Alkaline phosphatase
TP (g/dL)	Total protein
ALB (g/dL)	Albumin
Ca (mg/dL)	Calcium
TBIL (mg/dL)	Total bilirubin
PHOS (mg/dL)	Inorganic phosphorus
TRIG (mg/dL)	Triglyceride
GGT (U/L)	Gamma glutamyltransferase
Na (mmol/L)	Sodium
K (mmol/L)	Potassium

Abbreviations and Units for Serum Chemistry Functions (Continued)

Abbreviation (Units)	Test
Cl (mmol/L)	Chloride
CK (U/L)	Creatine kinase
LDH (U/L)	Lactate dehydrogenase
DBIL (mg/dL)	Direct bilirubin
UA (mg/dL)	Uric acid
AMY (U/L)	Amylase
Mg (mg/dL)	Magnesium
HDL (mg/dL)	High density lipoprotein cholesterol
LDL (mg/dL)	Low density lipoprotein cholesterol
Fe (ug/dL)	Iron
UIBC (µg/dL)	Unsaturated Fe binding capacity
HCO3 (mmol/L)	Bicarbonate
LIP (U/L)	Lipase
SDH (U/L)	Sorbitol dehydrogenase
TBA (µmol/L)	Total bile acids
PLIP (mg/dL)	Phospholipids
GLDH (U/L)	Glutamyl dehydrogenase
LACT (mg/dL)	Lactate
FFA (µmol/L)	Free fatty acids
C3 (mg/dL)	Complement 3
C4 (mg/dL)	Complement 4
ACP (U/L)	Acid phosphatase
IGE (U/mL)	Immunoglobulin E
IGA (mg/dL)	Immunoglobulin A
IGM (mg/dL)	Immunoglobulin M
IGG (mg/dL)	Immunoglobulin G
ALD (U/L)	Aldolase
MYO (ng/dL)	Myoglobin
CFCl (mmol/L)	Cerebrospinal fluid-chloride
CFCK (U/L)	Cerebrospinal fluid-creatine kinase
CFGL (mg/dL)	Cerebrospinal fluid-glucose
CFK (mmol/L)	Cerebrospinal fluid-potassium
CFNa (mmol/L)	Cerebrospinal fluid-sodium
CSTP (mg/dL)	Cerebrospinal fluid-total protein
CRP (mg/dL)	C-reactive protein
DDIM (µg/mL)	D-dimer
GLYC (mg/dL)	Glycerol
HAPT (mg/dL)	Haptoglobin
PCHE (µmol/L)	Plasma/serum cholinesterase
AGR	Albumin/globulin ratio
VLDL (mmol/L)	Cholesterol (VLDL)
GLOB (g/dL)	Globulin
IBIL (mg/dL)	Indirect bilirubin
PFeS (%)	Percent iron saturation
UNCR	Serum bun creatinine ratio
TIBC (µg/dL)	Total iron binding capacity

Abbreviations and Units for Serum Chemistry Functions (Continued)

Abbreviation (Units)	Test
PAMY (U/L)	P-amylase
ANON (mmol/L)	Anion gap
Hitachi 911 - Urine	
UNa (mmol/L)	Urine sodium
UK (mmol/L)	Urine potassium
UCl (mmol/L)	Urine chloride
UCRE (mg/dL)	Urine creatinine
UTP (mg/dL)	Urine quantitative total protein
UCa (mg/dL)	Urine calcium
UPHO (mg/dL)	Urine phosphorus
UNAG (U/L)	Urine N-acetyl-β-D-glucosaminidase
UGGT (U/L)	Urine gamma glutamyltransferase
UALB (mg/dL)	Urine albumin
UMg (mg/dL)	Urine magnesium
UGL (mg/dL)	Urine quantitative glucose
UUN (mg/dL)	Urine urea nitrogen
RCHE (µmol/L)	Red blood cell cholinesterase
CaCL (%)	Calcium fractional clearance
ClCL (%)	Chloride fractional clearance
PCL (%)	Phosphorus fractional clearance
KCL (%)	Potassium fractional clearance
NaCL (%)	Sodium fractional clearance
CRCL (mL/min)	Creatinine clearance
NGCR	N-acetyl-β-D-glucosaminidase/urine creatinine ratio
GTCR	Urine gamma glutamyltransferase/urine creatinine ratio
CaCR	Urine calcium-creatinine ratio
UPCR	Urine protein-urine creatinine ratio
NaKR	Urine sodium/potassium ratio
MgX (mg)	Magnesium excretion
ALBX (mg)	Urine albumin excretion
CaX (mg)	Urine calcium excretion
ClX (mmol)	Urine chloride excretion
CRX (mg)	Urine creatinine excretion
GLUX (mg)	Urine glucose excretion
PX (mg)	Urine phosphorus excretion
KX (mmol)	Urine potassium excretion
NaX (mmol)	Urine sodium excretion
TPX (mg)	Urine total protein excretion
UNX (mg)	Urine urea nitrogen excretion
Osmometer	
SOSM (mOsm/kg)	Serum osmolality
Sebia	
PCBB (%)	Percent creatine kinase BB
PCMB (%)	Percent creatine kinase MB
PCMM (%)	Percent creatine kinase MM

Abbreviations and Units for Serum Chemistry Functions (Continued)

Abbreviation (Units)	Test
PHDL (%)	Percent high density lipoprotein
ELD1 (%)	Percent lactate dehydrogenase 1
ELD2 (%)	Percent lactate dehydrogenase 2
ELD3 (%)	Percent lactate dehydrogenase 3
ELD4 (%)	Percent lactate dehydrogenase 4
ELD5 (%)	Percent lactate dehydrogenase 5
PLDL (%)	Percent low density lipoprotein
PVLD (%)	Percent very low density lipoprotein
CKBB (U/L)	Absolute CK-BB
CKMB (U/L)	Absolute CK-MB
CKMM (U/L)	Absolute CK-MM
PALB (%)	Percent albumin
PEA1 (%)	Percent alpha-1 globulin
PEA2 (%)	Percent alpha-2 globulin
PBET (%)	Percent beta globulin
PGAM (%)	Percent gamma globulin
EALB (g/dL)	Absolute albumin
EA1 (g/dL)	Absolute alpha-1 globulin
EA2 (g/dL)	Absolute alpha-2 globulin
EBET (g/dL)	Absolute beta globulin
EGAM (g/dL)	Absolute gamma globulin
EHDL (mg/dL)	Absolute high density lipoprotein
ELDL (mg/dL)	Absolute low density lipoprotein
EVLD (mg/dL)	Absolute very low density lipoprotein
Manual	
CAT (nmol/L)	Catalase
LAM (U/L)	Leucine aminopeptidase
BALP (U/L)	Absolute bone alkaline phosphatase isoenzyme
LALP (U/L)	Absolute liver alkaline phosphatase isoenzyme
OALP (U/L)	Non-bone, nonliver alkaline phosphatase isoenzyme
SKET	Serum ketone
TROI (ng/mL)	Troponin I
TROT (ng/mL)	Troponin T
UCOR (ng/mL)	Urine cortisol
PKBB (%)	Percent creatine kinase BB
PKMB (%)	Percent creatine kinase MB
PKMM (%)	Percent creatine kinase MM
AKBB (U/L)	Absolute CK-BB
AKMB (U/L)	Absolute CK-MB
AKMM (U/L)	Absolute CK-MM
EHDL (U/L)	Absolute high density lipoprotein
LDLP (mg/dL)	Absolute low density lipoprotein
EVLD (µg/mL)	Absolute very low density lipoprotein

Codes for Anatomic Pathology

Code	Definition
MACROSCOPIC CODES	
EX	Indicates that organ weight is excluded from calculations
NOT TAKEN	Organ weight not taken; explanation given in necropsy notes
MISSING	Organ missing or lost
UNSUITABLE	Organ technically unsuitable for weighing
AUTOLYTIC	Organ autolyzed and could not be weighed
EXCLUDE	Weight was taken, but was excluded from all calculations
MICROSCOPIC CODES	
Codes Prefacing Neoplastic Findings	
B	Primary, benign neoplasm
M	Primary, malignant neoplasm
N	Metastatic neoplasm
I	Locally invasive neoplasm
X	Other neoplasm

Distribution of Findings

Focal
Diffuse
Multifocal

Grades for Severity or Amount

1 Minimal - describes an inconspicuous change
2 Slight - referring to a noticeable but not prominent feature
3 Moderate - a prominent feature
4 Marked - a dominant but not overwhelming feature
5 Severe - implies an overwhelming condition

Codes for Anatomic Pathology (Continued)

General Microscopic Codes

TL	Total
P	Finding present
-	Finding not present
MN	Mean
Mean; MEAN	Average
SD; S.D.; STAND DEV; STANDARD DEV; sd; STD.DEV	Standard deviation
SE; S.E.	Standard error
-; NA	No value; not applicable
#; N; No	Number
Obs	Observations
IPD	Immediate postdose
PD	Postdose
a.m.	Ante meridian
p.m.	Post meridian
M	Male
F	Female
ID	Identification

TISSUE ABBREVIATIONS

BR	Brain
LN	Lymph node
GL	Gland
SEM VES; SEMINAL VE	Seminal vesicle
STOMACH, GL	Glandular stomach
STOMACH, NONGL	Nonglandular stomach
GL, MANDIB SALIV	Mandibular salivary gland
MUSCLE, BI FEM	Biceps femoris muscle
PARATHYR	Parathyroid
LN, ANT MES/PANC	Anterior mesenteric/pancreatic lymph node
AUDITORY SEB GL	Auditory sebaceous gland
LACRIMAL GLAND, EX	Exorbital lacrimal gland
HEMATO NEOPLASIA	Hematopoietic neoplasia
LACRIMAL GL, INT	Internal lacrimal gland
CAVITY, ABDOM	Abdominal cavity
SALIV GL, PAROTID	Parotid salivary gland
LN, TRACHEOBRON	Tracheobronchial lymph node
CATHETER EXIT	Catheterization site: exit site from the body
CATHETER ENTRANC	Catheterization site: entrance site into the vessel
CATHETER TIP	Catheterization site: tissues (vascular or extravascular) associated with the catheter near its tip

Comments on the Data

Various models of calculators, computers, and computer programs were used to analyze data in this study. Because different models round off or truncate numbers differently, values in some tables (e.g., means, standard deviations, or individual values) may differ slightly from those in other tables, from individually calculated data, or from statistical analysis data. Neither the integrity nor the interpretation of the data was affected by these differences.

The unit of "mg 2463608/kg/day" in tables refers to mg of Compound 2463608/kg/day.

The number of animals listed in the heading of the summary table for observations reflects the number of animals assigned to each group at the start of the study. The summary table for observations indicates the number of animals for which a condition was observed without regard to the specific nature, severity, reversibility, number of incidences/animal, or the length of time the condition persisted.

In the mean organ weight tables, terminal body weight values reflect the accuracy of the absolute organ weight values; however, they were recorded to the tenth.

In the Individual Anatomic Pathology Data/Animal Data appendix, the day/week for organ weight and clinical signs confirmation data is reported as day/week of study.

Individual Animal Data

A Repeat-Dose Toxicity Study in Rats Given Compound 2463608 by Intravenous Injection for 2 Weeks

Study:
Covance 7608-544

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17 September 2007

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Table 14: Individual Animal Death Status

Animal Number	Group/ Subgroup	Sex	Description	Date of Death	Phase of Death	Day of Death	Terminal body Weight (g)
B96001	1/	M	Final phase sacrifice	20.Jun.07	Dosing phase	16	346.7
B96002	1/	M	Final phase sacrifice	20.Jun.07	Dosing phase	16	332.7
B96003	1/	M	Final phase sacrifice	20.Jun.07	Dosing phase	16	322.7
B96004	1/	M	Final phase sacrifice	20.Jun.07	Dosing phase	16	332.6
B96005	1/	M	Final phase sacrifice	20.Jun.07	Dosing phase	16	356.7
B96006	2/	M	Final phase sacrifice	20.Jun.07	Dosing phase	16	315.1
B96007	2/	M	Final phase sacrifice	20.Jun.07	Dosing phase	16	353.7
B96008	2/	M	Final phase sacrifice	20.Jun.07	Dosing phase	16	337.3
B96009	2/	M	Final phase sacrifice	20.Jun.07	Dosing phase	16	328.3
B96010	2/	M	Final phase sacrifice	20.Jun.07	Dosing phase	16	355.3
B96011	3/	M	Final phase sacrifice	20.Jun.07	Dosing phase	16	359.5
B96012	3/	M	Final phase sacrifice	20.Jun.07	Dosing phase	16	361.0
B96013	3/	M	Final phase sacrifice	20.Jun.07	Dosing phase	16	327.2
B96014	3/	M	Final phase sacrifice	20.Jun.07	Dosing phase	16	306.8
B96015	3/	M	Final phase sacrifice	20.Jun.07	Dosing phase	16	313.4
B96016	1/	F	Final phase sacrifice	20.Jun.07	Dosing phase	16	225.2
B96017	1/	F	Final phase sacrifice	20.Jun.07	Dosing phase	16	219.1
B96018	1/	F	Final phase sacrifice	20.Jun.07	Dosing phase	16	233.9
B96019	1/	F	Final phase sacrifice	20.Jun.07	Dosing phase	16	227.4
B96020	1/	F	Final phase sacrifice	20.Jun.07	Dosing phase	16	240.3
B96021	2/	F	Final phase sacrifice	20.Jun.07	Dosing phase	16	220.8
B96022	2/	F	Final phase sacrifice	20.Jun.07	Dosing phase	16	228.9
B96023	2/	F	Final phase sacrifice	20.Jun.07	Dosing phase	16	236.7
B96024	2/	F	Final phase sacrifice	20.Jun.07	Dosing phase	16	230.6
B96025	2/	F	Final phase sacrifice	20.Jun.07	Dosing phase	16	224.5
B96026	3/	F	Final phase sacrifice	20.Jun.07	Dosing phase	16	202.9
B96027	3/	F	Final phase sacrifice	20.Jun.07	Dosing phase	16	218.6
B96028	3/	F	Final phase sacrifice	20.Jun.07	Dosing phase	16	222.0
B96029	3/	F	Final phase sacrifice	20.Jun.07	Dosing phase	16	227.6
B96030	3/	F	Final phase sacrifice	20.Jun.07	Dosing phase	16	225.2

Table 15: Individual Clinical Signs

Animal Number	Group	Category	Signs	Days
			M a l e s	
B96001	1	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
B96002	1	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
B96003	1	Normal	Normal/No Remarkable Obs	Dosing phase 1
		Skin & Pelage	Scaly Skin, Tail	Dosing phase 7-8,15-16
B96004	1	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
B96005	1	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
B96006	2	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
B96007	2	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
B96008	2	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
B96009	2	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
B96010	2	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
B96011	3	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
		Behavior	Excessive Grooming	Dosing phase 1-2,4-6,8-9 12-13,15
B96012	3	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
		Behavior	Excessive Grooming	Dosing phase 1-2,6-9,15
B96013	3	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
		Behavior	Excessive Grooming	Dosing phase 1-5,7-13,15
B96014	3	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16

Table 15
Individual Clinical Signs

Animal Number	Group	Category	Signs	Days
			M a l e s	
B96014	3	Behavior	Excessive Grooming	Dosing phase 1-4,7-9,12 13,15
B96015	3	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
		Behavior	Excessive Grooming	Dosing phase 1-4,7-10,12 13,15

Table 15
Individual Clinical Signs

Animal Number	Group	Category	Signs	Days
			F e m a l e s	
B96016	1	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
B96017	1	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
		Behavior	Excessive Grooming	Dosing phase 6
B96018	1	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
B96019	1	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
B96020	1	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
B96021	2	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
		Behavior	Excessive Grooming	Dosing phase 6,12
B96022	2	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
B96023	2	Normal	Normal/No Remarkable Obs	Dosing phase 1,8
		Behavior	Excessive Grooming	Dosing phase 6,8,13
		Skin & Pelage	Sore/Scab, Front Paws	Dosing phase 13,15
			Sore/Scab, Right Front Paw	Dosing phase 16
B96024	2	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
		Behavior	Excessive Grooming	Dosing phase 6
B96025	2	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
B96026	3	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
		Behavior	Excessive Grooming	Dosing phase 1-4,6-13,15
		Eye(s)	Squinted-Eyes	Dosing phase 3-4,6-7,12
B96027	3	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16

Table 15
Individual Clinical Signs

Animal Number	Group	Category	Signs	Days
			F e m a l e s	
B96027	3	Behavior	Excessive Grooming	Dosing phase 1-4,6-13,15
B96028	3	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
		Behavior	Excessive Grooming	Dosing phase 1-4,7-13,15
B96029	3	Normal	Normal/No Remarkable Obs	Dosing phase 1
		Behavior	Excessive Grooming	Dosing phase 1-4,6-13,15
		Skin & Pelage	Scaly Skin, Tail	Dosing phase 7-13,15-16
B96030	3	Normal	Normal/No Remarkable Obs	Dosing phase 1,8,15-16
		Behavior	Excessive Grooming	Dosing phase 1-4,7-13,15
		Skin & Pelage	Blue Skin, Mid Tail	Dosing phase 13

Table 16: Individual Ophthalmic Observations

Animal Number	Group	Category	Signs	Days
			M a l e s	
B96001	1	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96002	1	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96003	1	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96004	1	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96005	1	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96006	2	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96007	2	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96008	2	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96009	2	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96010	2	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96011	3	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96012	3	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96013	3	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96014	3	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96015	3	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11

Table 16
Individual Ophthalmic Observations

Animal Number	Group	Category	Signs	Days
			F e m a l e s	
B96016	1	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96017	1	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96018	1	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96019	1	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96020	1	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96021	2	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96022	2	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96023	2	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96024	2	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96025	2	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96026	3	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96027	3	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96028	3	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96029	3	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11
B96030	3	No Visible Lesions	No Visible Lesions, Eyes	Dosing phase 11

Table 17: Individual Body Weight Data

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	Individual body weights (g) for Day: DSNG 1	DSNG 8	DSNG 15
1M	B96001	310	346	384
1M	B96002	303	339	361
1M	B96003	301	324	353
1M	B96004	326	348	369
1M	B96005	316	358	390
2M	B96006	299	324	337
2M	B96007	317	354	377
2M	B96008	309	346	359
2M	B96009	295	324	349
2M	B96010	325	362	382
3M	B96011	327	361	390
3M	B96012	314	359	396
3M	B96013	305	328	348
3M	B96014	306	320	330
3M	B96015	293	326	345

Table 17
Individual Body Weight Data

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	Individual body weights (g) for Day: DSNG 1	DSNG 8	DSNG 15
1F	B96016	211	229	245
1F	B96017	211	224	238
1F	B96018	216	236	252
1F	B96019	224	236	251
1F	B96020	236	253	259
2F	B96021	207	224	235
2F	B96022	231	241	242
2F	B96023	221	240	254
2F	B96024	221	232	245
2F	B96025	213	230	239
3F	B96026	213	218	218
3F	B96027	210	229	234
3F	B96028	207	230	240
3F	B96029	218	234	245
3F	B96030	225	238	244

Table 18: Individual Food Consumption Data

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	Individual food consumption (g/animal/period) at Day: DSNG 1- DSNG 7	DSNG 8- DSNG 14
1M	B96001	217	218
1M	B96002	214	196
1M	B96003	203	213
1M	B96004	218	217
1M	B96005	239	255
2M	B96006	203	204
2M	B96007	221	233
2M	B96008	207	206
2M	B96009	194	194
2M	B96010	230	236
3M	B96011	207	197
3M	B96012	231	225
3M	B96013	202	197
3M	B96014	182	179
3M	B96015	205	198

Table 18
Individual Food Consumption Data

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	Individual food consumption (g/animal/period) at Day: DSNG 1- DSNG 7	DSNG 8- DSNG 14
1F	B96016	150	180
1F	B96017	152	148
1F	B96018	175	169
1F	B96019	165	172
1F	B96020	158	161
2F	B96021	149	159
2F	B96022	162	158
2F	B96023	160	174
2F	B96024	144	160
2F	B96025	168	185
3F	B96026	142	183
3F	B96027	145	169
3F	B96028	159	157
3F	B96029	156	161
3F	B96030	155	157

Table 19: Individual Hematology Data

Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	RBC E6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETI E3/uL	PRET %
1M	B96001	8.23	16.2	48.3	58.7	19.7	33.6	240.4	2.9
1M	B96002	8.79	17.2	51.5	58.6	19.5	33.3	346.0	3.9
1M	B96003	8.29	16.0	48.8	58.8	19.3	32.8	272.2	3.3
1M	B96004	8.88	16.9	52.9	59.6	19.0	31.9	245.4	2.8
1M	B96005	8.13	16.0	48.2	59.3	19.7	33.3	269.0	3.3
	Mean	8.46	16.5	49.9	59.0	19.4	33.0	274.6	3.2
	SD	0.345	0.55	2.13	0.43	0.30	0.67	42.30	0.43
	N	5	5	5	5	5	5	5	5
2M	B96006	8.10	15.8	47.9	59.2	19.5	33.0	195.7	2.4
2M	B96007	8.85	16.5	50.7	57.3	18.6	32.5	273.5	3.1
2M	B96008	8.50	16.6	50.2	59.0	19.5	33.1	271.2	3.2
2M	B96009	7.95	15.6	46.6	58.7	19.7	33.5	234.1	2.9
2M	B96010	8.38	16.6	48.9	58.4	19.8	33.9	205.9	2.5
	Mean	8.36	16.2	48.9	58.5	19.4	33.2	236.1	2.8
	SD	0.352	0.48	1.67	0.75	0.48	0.53	35.98	0.36
	N	5	5	5	5	5	5	5	5
3M	B96011	8.49	16.4	48.5	57.1	19.3	33.9	274.9	3.2
3M	B96012	7.97	16.2	49.4	62.0	20.4	32.9	298.2	3.7
3M	B96013	8.06	14.8	47.0	58.3	18.3	31.5	229.2	2.8
3M	B96014	7.93	15.6	47.7	60.2	19.7	32.7	398.4	5.0
3M	B96015	8.54	16.3	48.2	56.5	19.1	33.9	234.2	2.7
	Mean	8.20	15.9	48.2	58.8	19.4	33.0	287.0	3.5
	SD	0.294	0.67	0.90	2.27	0.77	1.00	68.58	0.94
	N	5	5	5	5	5	5	5	5

Table 19
Individual Hematology Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	RBC E6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETI E3/uL	PRET %
1F	B96016	7.56	14.9	43.4	57.4	19.7	34.4	241.0	3.2
1F	B96017	7.42	14.8	42.9	57.8	20.0	34.6	226.4	3.1
1F	B96018	7.82	15.4	45.3	58.0	19.7	34.0	230.6	3.0
1F	B96019	8.13	15.7	45.2	55.6	19.3	34.7	181.0	2.2
1F	B96020	7.31	15.1	44.2	60.5	20.6	34.1	203.0	2.8
	Mean	7.65	15.2	44.2	57.9	19.9	34.4	216.4	2.9
	SD	0.330	0.37	1.07	1.75	0.48	0.30	24.18	0.40
	N	5	5	5	5	5	5	5	5
2F	B96021	7.83	15.7	45.4	57.9	20.1	34.7	276.4	3.5
2F	B96022	7.64	15.0	44.5	58.2	19.7	33.8	224.5	2.9
2F	B96023	7.78	15.0	43.6	56.1	19.3	34.4	252.9	3.2
2F	B96024	8.17	15.9	46.5	56.8	19.5	34.3	247.8	3.0
2F	B96025	7.50	14.7	42.9	57.2	19.6	34.3	242.7	3.2
	Mean	7.78	15.3	44.6	57.2	19.6	34.3	248.9	3.2
	SD	0.251	0.51	1.43	0.84	0.30	0.32	18.76	0.23
	N	5	5	5	5	5	5	5	5
3F	B96026	8.15	15.8	45.7	56.1	19.4	34.5	213.9	2.6
3F	B96027	8.17	15.6	46.1	56.4	19.1	33.9	178.1	2.2
3F	B96028	8.05	15.5	46.1	57.2	19.2	33.6	228.9	2.8
3F	B96029	8.02	15.5	45.3	56.5	19.4	34.3	285.2	3.6
3F	B96030	7.35	14.9	43.9	59.8	20.3	34.0	326.2	4.4
	Mean	7.95	15.5	45.4	57.2	19.5	34.1	246.5	3.1
	SD	0.340	0.34	0.91	1.51	0.48	0.35	58.95	0.88
	N	5	5	5	5	5	5	5	5

Table 19
Individual Hematology Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	PLT E3/uL	WBC E3/uL	NEUT E3/uL	LYM E3/uL	MONO E3/uL	EOS E3/uL	BASO E3/uL	LUC E3/uL
1M	B96001	1022	7.41	0.95	6.06	0.12	0.17	0.05	0.05
1M	B96002	1018	11.28	2.15	8.51	0.26	0.20	0.10	0.06
1M	B96003	1344	9.38	1.07	8.01	0.16	0.07	0.03	0.05
1M	B96004	1293	6.43	0.44	5.81	0.06	0.04	0.05	0.04
1M	B96005	1120	5.30	0.89	4.13	0.06	0.18	0.01	0.02
	Mean	1159	7.96	1.10	6.50	0.13	0.13	0.05	0.04
	SD	151.9	2.385	0.634	1.775	0.083	0.072	0.033	0.015
	N	5	5	5	5	5	5	5	5
2M	B96006	1057	10.21	1.14	8.42	0.24	0.33	0.05	0.03
2M	B96007	1031	9.78	1.39	8.02	0.20	0.06	0.07	0.05
2M	B96008	1273	13.93	1.61	11.60	0.49	0.05	0.11	0.07
2M	B96009	1187	11.10	1.33	9.11	0.40	0.11	0.05	0.11
2M	B96010	1010	12.78	2.31	9.88	0.27	0.17	0.05	0.11
	Mean	1112	11.56	1.56	9.41	0.32	0.14	0.07	0.07
	SD	113.5	1.754	0.454	1.416	0.121	0.114	0.026	0.036
	N	5	5	5	5	5	5	5	5
3M	B96011	984	9.55	1.37	7.68	0.30	0.11	0.04	0.03
3M	B96012	864	7.24	0.95	5.98	0.15	0.08	0.03	0.04
3M	B96013	1054	11.50	1.44	9.58	0.25	0.07	0.05	0.11
3M	B96014	1174	5.61	0.98	4.40	0.10	0.09	0.02	0.02
3M	B96015	1070	10.35	0.70	9.25	0.15	0.08	0.08	0.09
	Mean	1029	8.85	1.09	7.38	0.19	0.09	0.04	0.06
	SD	114.7	2.390	0.310	2.195	0.082	0.015	0.023	0.040
	N	5	5	5	5	5	5	5	5

Table 19
Individual Hematology Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	PLT E3/uL	WBC E3/uL	NEUT E3/uL	LYM E3/uL	MONO E3/uL	EOS E3/uL	BASO E3/uL	LUC E3/uL
1F	B96016	1347	10.16	1.52	8.23	0.23	0.08	0.05	0.06
1F	B96017	1169	7.55	0.60	6.58	0.22	0.06	0.03	0.07
1F	B96018	1370	4.62	0.82	3.56	0.13	0.06	0.03	0.02
1F	B96019	1182	5.68	0.63	4.72	0.16	0.08	0.04	0.04
1F	B96020	1075	11.63	0.69	10.56	0.15	0.08	0.04	0.10
	Mean	1229	7.93	0.85	6.73	0.18	0.07	0.04	0.06
	SD	125.8	2.951	0.383	2.785	0.044	0.011	0.008	0.030
	N	5	5	5	5	5	5	5	5
2F	B96021	1024	3.78	0.56	3.07	0.06	0.04	0.03	0.02
2F	B96022	1273	7.21	1.05	5.82	0.17	0.11	0.03	0.03
2F	B96023	1226	6.50	1.55	4.73	0.09	0.06	0.04	0.03
2F	B96024	1199	12.49	1.79	10.23	0.20	0.12	0.07	0.09
2F	B96025	1296	5.62	0.78	4.64	0.09	0.04	0.03	0.03
	Mean	1204	7.12	1.15	5.70	0.12	0.07	0.04	0.04
	SD	107.4	3.265	0.516	2.716	0.060	0.038	0.017	0.028
	N	5	5	5	5	5	5	5	5
3F	B96026	1127	6.18	0.70	5.07	0.20	0.12	0.06	0.04
3F	B96027	997	6.26	0.73	5.18	0.13	0.14	0.04	0.04
3F	B96028	999	7.11	1.05	5.77	0.17	0.06	0.01	0.06
3F	B96029	1123	6.16	0.55	5.40	0.08	0.07	0.03	0.03
3F	B96030	1211	4.12	0.58	3.34	0.10	0.06	0.02	0.02
	Mean	1091	5.97	0.72	4.95	0.14	0.09	0.03	0.04
	SD	92.2	1.105	0.199	0.940	0.049	0.037	0.019	0.015
	N	5	5	5	5	5	5	5	5

Table 19
Individual Hematology Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	PNEU %	PLYM %	PMON %	PEOS %	PBAS %	PLUC %	PT seconds	APTT seconds
1M	B96001	12.8	81.9	1.6	2.3	0.7	0.6	17.4	25.1
1M	B96002	19.0	75.4	2.3	1.7	0.9	0.6	15.7	20.4
1M	B96003	11.4	85.3	1.7	0.7	0.3	0.5	16.9	22.5
1M	B96004	6.8	90.4	0.9	0.7	0.7	0.6	17.0	21.2
1M	B96005	16.7	78.0	1.1	3.5	0.2	0.5	17.1	21.7
	Mean	13.3	82.2	1.5	1.8	0.6	0.6	16.8	22.2
	SD	4.75	5.93	0.55	1.18	0.30	0.05	0.65	1.80
	N	5	5	5	5	5	5	5	5
2M	B96006	11.2	82.5	2.3	3.2	0.5	0.3	16.3	21.9
2M	B96007	14.2	82.0	2.0	0.6	0.7	0.5	15.7	21.4
2M	B96008	11.6	83.3	3.5	0.3	0.8	0.5	16.6	22.8
2M	B96009	12.0	82.1	3.6	1.0	0.4	1.0	16.9	21.9
2M	B96010	18.0	77.3	2.1	1.3	0.4	0.9	20.4	27.1
	Mean	13.4	81.4	2.7	1.3	0.6	0.6	17.2	23.0
	SD	2.82	2.37	0.78	1.14	0.18	0.30	1.85	2.34
	N	5	5	5	5	5	5	5	5
3M	B96011	14.4	80.5	3.1	1.2	0.5	0.3	17.5	22.9
3M	B96012	13.2	82.6	2.0	1.2	0.5	0.5	16.8	21.4
3M	B96013	12.5	83.3	2.2	0.6	0.4	0.9	17.4	22.2
3M	B96014	17.4	78.3	1.8	1.6	0.3	0.4	15.2	24.8
3M	B96015	6.8	89.4	1.4	0.8	0.8	0.8	16.0	22.0
	Mean	12.9	82.8	2.1	1.1	0.5	0.6	16.6	22.7
	SD	3.87	4.16	0.63	0.39	0.19	0.26	0.98	1.31
	N	5	5	5	5	5	5	5	5

Table 19
Individual Hematology Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	PNEU %	PLYM %	PMON %	PEOS %	PBAS %	PLUC %	PT seconds	APTT seconds
1F	B96016	14.9	81.0	2.2	0.8	0.5	0.6	14.7	19.8
1F	B96017	7.9	87.2	2.9	0.7	0.4	0.9	14.5	20.1
1F	B96018	17.7	77.1	2.8	1.3	0.6	0.4	15.5	22.1
1F	B96019	11.1	83.2	2.8	1.5	0.8	0.6	15.4	19.0
1F	B96020	6.0	90.8	1.3	0.7	0.4	0.9	14.0	21.4
	Mean	11.5	83.9	2.4	1.0	0.5	0.7	14.8	20.5
	SD	4.83	5.33	0.67	0.37	0.17	0.22	0.63	1.25
	N	5	5	5	5	5	5	5	5
2F	B96021	14.7	81.3	1.6	1.2	0.8	0.5	15.6	20.6
2F	B96022	14.5	80.8	2.4	1.5	0.4	0.4	14.7	20.5
2F	B96023	23.8	72.8	1.4	0.9	0.6	0.5	15.3	24.1
2F	B96024	14.3	81.8	1.6	0.9	0.6	0.7	14.8	21.8
2F	B96025	13.8	82.7	1.6	0.7	0.6	0.5	14.2	23.4
	Mean	16.2	79.9	1.7	1.0	0.6	0.5	14.9	22.1
	SD	4.25	4.02	0.39	0.31	0.14	0.11	0.54	1.63
	N	5	5	5	5	5	5	5	5
3F	B96026	11.3	82.0	3.2	2.0	0.9	0.6	15.0	20.1
3F	B96027	11.7	82.8	2.1	2.2	0.6	0.6	14.1	19.8
3F	B96028	14.7	81.2	2.4	0.8	0.2	0.8	13.5	16.7
3F	B96029	8.9	87.6	1.4	1.2	0.4	0.5	14.1	20.6
3F	B96030	14.2	81.0	2.5	1.4	0.5	0.6	14.6	22.1
	Mean	12.2	82.9	2.3	1.5	0.5	0.6	14.3	19.9
	SD	2.36	2.71	0.65	0.58	0.26	0.11	0.57	1.98
	N	5	5	5	5	5	5	5	5

Table 19
Individual Hematology Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	NRML	ANIS	POLY	POIK	HYPO	TOXN
1M	B96001	YES	Normal	Normal	Normal	Normal	Normal
1M	B96002	YES	Normal	Normal	Normal	Normal	Normal
1M	B96003	YES	Normal	Normal	Normal	Normal	Normal
1M	B96004	YES	Normal	Normal	Normal	Normal	Normal
1M	B96005	YES	Normal	Normal	Normal	Normal	Normal
2M	B96006	YES	Normal	Normal	Normal	Normal	Normal
2M	B96007	YES	Normal	Normal	Normal	Normal	Normal
2M	B96008	YES	Normal	Normal	Normal	Normal	Normal
2M	B96009	YES	Normal	Normal	Normal	Normal	Normal
2M	B96010	YES	Normal	Normal	Normal	Normal	Normal
3M	B96011	YES	Normal	Normal	Normal	Normal	Normal
3M	B96012	YES	Normal	Normal	Normal	Normal	Normal
3M	B96013	YES	Normal	Normal	Normal	Normal	Normal
3M	B96014	YES	Normal	Normal	Normal	Normal	Normal
3M	B96015	YES	Normal	Normal	Normal	Normal	Normal

Table 19
Individual Hematology Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	NRML	ANIS	POLY	POIK	HYPO	TOXN
1F	B96016	YES	Normal	Normal	Normal	Normal	Normal
1F	B96017	YES	Normal	Normal	Normal	Normal	Normal
1F	B96018	YES	Normal	Normal	Normal	Normal	Normal
1F	B96019	YES	Normal	Normal	Normal	Normal	Normal
1F	B96020	YES	Normal	Normal	Normal	Normal	Normal
2F	B96021	YES	Normal	Normal	Normal	Normal	Normal
2F	B96022	YES	Normal	Normal	Normal	Normal	Normal
2F	B96023	YES	Normal	Normal	Normal	Normal	Normal
2F	B96024	YES	Normal	Normal	Normal	Normal	Normal
2F	B96025	YES	Normal	Normal	Normal	Normal	Normal
3F	B96026	YES	Normal	Normal	Normal	Normal	Normal
3F	B96027	YES	Normal	Normal	Normal	Normal	Normal
3F	B96028	YES	Normal	Normal	Normal	Normal	Normal
3F	B96029	YES	Normal	Normal	Normal	Normal	Normal
3F	B96030	YES	Normal	Normal	Normal	Normal	Normal

Table 20: Individual Clinical Chemistry Data

Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	GLU mg/dL	UN mg/dL	CREA mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	AGR	CHOL mg/dL
1M	B96001	104	17	0.7	6.8	4.6	2.2	2.1	86
1M	B96002	90	16	0.6	6.6	4.4	2.2	2.0	113
1M	B96003	92	13	0.6	6.6	4.4	2.2	2.0	81
1M	B96004	93	19	0.7	6.8	4.9	1.9	2.6	59
1M	B96005	98	13	0.7	6.8	4.5	2.3	2.0	85
	Mean	95	16	0.7	6.7	4.6	2.2	2.1	85
	SD	5.6	2.6	0.05	0.11	0.21	0.15	0.26	19.2
	N	5	5	5	5	5	5	5	5
2M	B96006	111	16	0.6	6.4	4.5	1.9	2.4	73
2M	B96007	106	13	0.6	6.7	4.7	2.0	2.4	89
2M	B96008	93	13	0.6	6.4	4.8	1.6	3.0	83
2M	B96009	90	17	0.6	6.1	4.2	1.9	2.2	96
2M	B96010	122	16	0.7	7.0	4.6	2.4	1.9	79
	Mean	104	15	0.6	6.5	4.6	2.0	2.4	84
	SD	13.2	1.9	0.04	0.34	0.23	0.29	0.40	8.9
	N	5	5	5	5	5	5	5	5
3M	B96011	98	15	0.6	6.5	4.6	1.9	2.4	66
3M	B96012	104	13	0.7	6.6	4.7	1.9	2.5	97
3M	B96013	85	15	0.6	6.6	4.6	2.0	2.3	71
3M	B96014	98	17	0.6	6.2	4.4	1.8	2.4	76
3M	B96015	100	18	0.6	6.6	4.7	1.9	2.5	73
	Mean	97	16	0.6	6.5	4.6	1.9	2.4	77
	SD	7.1	1.9	0.04	0.17	0.12	0.07	0.07	12.0
	N	5	5	5	5	5	5	5	5

Table 20
Individual Clinical Chemistry Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	GLU mg/dL	UN mg/dL	CREA mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	AGR	CHOL mg/dL
1F	B96016	108	19	0.7	7.3	5.3	2.0	2.7	90
1F	B96017	106	17	0.6	7.3	5.3	2.0	2.7	72
1F	B96018	108	18	0.7	7.1	5.1	2.0	2.6	64
1F	B96019	106	15	0.6	7.5	5.7	1.8	3.2	75
1F	B96020	114	14	0.6	6.9	5.1	1.8	2.8	110
	Mean	108	17	0.6	7.2	5.3	1.9	2.8	82
	SD	3.3	2.1	0.05	0.23	0.24	0.11	0.24	18.2
	N	5	5	5	5	5	5	5	5
2F	B96021	118	15	0.7	7.5	5.5	2.0	2.8	102
2F	B96022	102	14	0.6	7.0	5.1	1.9	2.7	77
2F	B96023	108	16	0.7	7.1	5.2	1.9	2.7	62
2F	B96024	106	15	0.6	8.0	6.1	1.9	3.2	112
2F	B96025	123	16	0.8	7.9	5.9	2.0	3.0	74
	Mean	111	15	0.7	7.5	5.6	1.9	2.9	85
	SD	8.8	0.8	0.08	0.45	0.43	0.05	0.22	20.8
	N	5	5	5	5	5	5	5	5
3F	B96026	93	16	0.7	7.5	5.4	2.1	2.6	110
3F	B96027	104	16	0.6	7.6	5.5	2.1	2.6	103
3F	B96028	108	12	0.6	7.6	5.4	2.2	2.5	105
3F	B96029	113	19	0.7	7.8	5.8	2.0	2.9	113
3F	B96030	125	16	0.7	7.5	5.5	2.0	2.8	85
	Mean	109	16	0.7	7.6	5.5	2.1	2.7	103
	SD	11.8	2.5	0.05	0.12	0.16	0.08	0.17	10.9
	N	5	5	5	5	5	5	5	5

Table 20
Individual Clinical Chemistry Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	TRIG mg/dL	TBIL mg/dL	AST U/L	ALT U/L	ALP U/L	GGT U/L	CK U/L	Ca mg/dL
1M	B96001	47	0.1	105	32	121	BDL	310	11.2
1M	B96002	45	0.1	167	34	180	BDL	1694	11.0
1M	B96003	30	0.1	117	39	128	BDL	501	10.9
1M	B96004	20	0.2	207	50	194	BDL	1655	10.8
1M	B96005	35	0.1	89	31	159	BDL	280	10.8
	Mean	35	0.1	137	37	156	.	888	10.9
	SD	11.1	0.04	48.8	7.8	31.8	.	723.1	0.17
	N	5	5	5	5	5	0	5	5
2M	B96006	50	0.1	165	34	185	BDL	1471	10.9
2M	B96007	71	0.1	110	38	114	BDL	592	10.9
2M	B96008	48	0.1	97	33	162	BDL	564	11.2
2M	B96009	38	0.1	117	28	145	BDL	941	10.7
2M	B96010	58	0.1	90	36	201	BDL	285	10.8
	Mean	53	0.1	116	34	161	.	771	10.9
	SD	12.3	0.00	29.5	3.8	34.1	.	455.5	0.19
	N	5	5	5	5	5	0	5	5
3M	B96011	57	0.2	102	32	122	BDL	423	11.3
3M	B96012	55	0.1	94	37	136	BDL	272	11.6
3M	B96013	41	0.1	156	37	122	BDL	1303	10.6
3M	B96014	20	0.1	146	43	125	BDL	947	10.5
3M	B96015	22	0.2	123	44	133	BDL	502	10.8
	Mean	39	0.1	124	39	128	.	689	11.0
	SD	17.6	0.05	26.9	4.9	6.5	.	425.2	0.47
	N	5	5	5	5	5	0	5	5

BDL = Below Detectable Limit

Table 20
Individual Clinical Chemistry Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	TRIG mg/dL	TBIL mg/dL	AST U/L	ALT U/L	ALP U/L	GGT U/L	CK U/L	Ca mg/dL
1F	B96016	49	0.2	163	34	53	BDL	1770	11.2
1F	B96017	39	0.2	158	32	105	BDL	1447	11.1
1F	B96018	27	0.1	173	28	86	BDL	1432	10.9
1F	B96019	43	0.2	93	37	80	BDL	418	11.4
1F	B96020	43	0.2	70	33	60	BDL	222	11.3
	Mean	40	0.2	131	33	77	.	1058	11.2
	SD	8.2	0.04	46.6	3.3	20.8	.	690.4	0.19
	N	5	5	5	5	5	0	5	5
2F	B96021	38	0.2	131	33	80	BDL	789	11.2
2F	B96022	38	0.2	122	32	56	BDL	921	11.0
2F	B96023	26	0.1	127	24	65	BDL	926	11.2
2F	B96024	37	0.2	107	31	116	BDL	725	11.7
2F	B96025	44	0.2	90	32	93	BDL	756	11.5
	Mean	37	0.2	115	30	82	.	823	11.3
	SD	6.5	0.04	16.9	3.6	23.7	.	94.2	0.28
	N	5	5	5	5	5	0	5	5
3F	B96026	34	0.2	171	30	78	BDL	1643	11.1
3F	B96027	30	0.2	138	30	79	BDL	880	11.1
3F	B96028	53	0.1	135	27	140	BDL	1009	11.2
3F	B96029	49	0.1	129	26	63	BDL	1065	11.4
3F	B96030	33	0.2	102	44	85	BDL	575	11.4
	Mean	40	0.2	135	31	89	.	1034	11.2
	SD	10.4	0.05	24.6	7.3	29.6	.	389.5	0.15
	N	5	5	5	5	5	0	5	5

BDL = Below Detectable Limit

Table 20
Individual Clinical Chemistry Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	PHOS mg/dL	Na mmol/L	K mmol/L	Cl mmol/L
1M	B96001	8.2	145	5.4	103
1M	B96002	9.5	147	5.9	105
1M	B96003	8.6	146	6.3	104
1M	B96004	8.6	146	6.4	106
1M	B96005	6.7	146	5.2	105
	Mean	8.3	146	5.8	105
	SD	1.02	0.7	0.53	1.1
	N	5	5	5	5
2M	B96006	8.5	148	6.2	105
2M	B96007	7.9	147	5.5	104
2M	B96008	8.1	144	5.9	103
2M	B96009	8.6	145	5.3	103
2M	B96010	7.9	144	5.6	102
	Mean	8.2	146	5.7	103
	SD	0.33	1.8	0.35	1.1
	N	5	5	5	5
3M	B96011	8.1	143	5.3	100
3M	B96012	9.0	148	6.3	104
3M	B96013	7.6	144	5.5	102
3M	B96014	8.2	145	5.8	104
3M	B96015	7.3	144	5.0	102
	Mean	8.0	145	5.6	102
	SD	0.65	1.9	0.50	1.7
	N	5	5	5	5

Table 20
Individual Clinical Chemistry Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	PHOS mg/dL	Na mmol/L	K mmol/L	Cl mmol/L
1F	B96016	7.1	143	5.6	101
1F	B96017	6.5	145	5.6	104
1F	B96018	6.9	144	5.8	103
1F	B96019	7.0	143	5.6	103
1F	B96020	7.0	140	5.4	101
	Mean	6.9	143	5.6	102
	SD	0.23	1.9	0.14	1.3
	N	5	5	5	5
2F	B96021	5.1	144	4.7	104
2F	B96022	6.5	143	5.5	102
2F	B96023	6.5	144	5.4	104
2F	B96024	6.8	142	5.6	101
2F	B96025	5.9	144	5.1	104
	Mean	6.2	143	5.3	103
	SD	0.68	0.9	0.36	1.4
	N	5	5	5	5
3F	B96026	7.1	141	5.4	101
3F	B96027	6.7	142	5.3	101
3F	B96028	6.7	144	4.9	104
3F	B96029	5.9	142	5.6	101
3F	B96030	6.5	146	6.0	103
	Mean	6.6	143	5.4	102
	SD	0.44	2.0	0.40	1.4
	N	5	5	5	5

Table 21: Individual Urinalysis Data

Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	UVOL mL	SPGR	UpH
1M	B96001	13.0	1.017	6.5
1M	B96002	14.8	1.013	7.0
1M	B96003	48.0	1.004	7.0
1M	B96004	41.0	1.007	7.0
1M	B96005	48.0	1.006	6.5
	Mean	33.0	1.009	6.8
	SD	17.64	0.0054	0.27
	N	5	5	5
2M	B96006	26.0	1.009	6.5
2M	B96007	16.0	1.011	7.0
2M	B96008	22.0	1.011	6.5
2M	B96009	10.0	1.018	6.5
2M	B96010	8.5	1.020	6.5
	Mean	16.5	1.014	6.6
	SD	7.53	0.0049	0.22
	N	5	5	5
3M	B96011	15.0	1.017	6.5
3M	B96012	28.0	1.008	6.5
3M	B96013	31.0	1.009	6.5
3M	B96014	10.5	1.018	7.0
3M	B96015	41.0	1.007	6.5
	Mean	25.1	1.012	6.6
	SD	12.36	0.0053	0.22
	N	5	5	5

Table 21
Individual Urinalysis Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	UVOL mL	SPGR	UpH
1F	B96016	8.0	1.021	6.5
1F	B96017	9.1	1.018	7.0
1F	B96018	19.0	1.010	7.0
1F	B96019	13.0	1.013	7.0
1F	B96020	30.2	1.006	7.0
	Mean	15.9	1.014	6.9
	SD	9.10	0.0060	0.22
	N	5	5	5
2F	B96021	5.6	1.019	6.5
2F	B96022	3.5	1.038	6.0
2F	B96023	8.5	1.016	6.5
2F	B96024	5.6	1.019	6.0
2F	B96025	25.0	1.009	6.5
	Mean	9.6	1.020	6.3
	SD	8.77	0.0108	0.27
	N	5	5	5
3F	B96026	19.0	1.008	6.5
3F	B96027	30.0	1.007	6.5
3F	B96028	47.0	1.004	6.5
3F	B96029	5.3	1.023	6.5
3F	B96030	14.9	1.012	6.0
	Mean	23.2	1.011	6.4
	SD	15.97	0.0074	0.22
	N	5	5	5

Table 21
Individual Urinalysis Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	UPRO	UOBL	UGLU	UKET	UBIL	UUBG Eu/dL	URBC	UWBC
1M	B96001	TRACE	1+	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
1M	B96002	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	0.2	0	0
1M	B96003	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	1
1M	B96004	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
1M	B96005	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
2M	B96006	TRACE	1+	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
2M	B96007	TRACE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
2M	B96008	TRACE	TRACE	NEGATIVE	TRACE	NEGATIVE	0.2	0	0
2M	B96009	TRACE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
2M	B96010	TRACE	TRACE	NEGATIVE	TRACE	NEGATIVE	0.2	0	0
3M	B96011	1+	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	0.2	0	0
3M	B96012	NEGATIVE	2+	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
3M	B96013	NEGATIVE	TRACE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
3M	B96014	TRACE	TRACE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
3M	B96015	NEGATIVE	1+	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0

Table 21
Individual Urinalysis Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	UPRO	UOBL	UGLU	UKET	UBIL	UUBG Eu/dL	URBC	UWBC
1F	B96016	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	1
1F	B96017	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
1F	B96018	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
1F	B96019	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
1F	B96020	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
2F	B96021	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
2F	B96022	TRACE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
2F	B96023	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
2F	B96024	NEGATIVE	TRACE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
2F	B96025	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
3F	B96026	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
3F	B96027	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
3F	B96028	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0
3F	B96029	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	1
3F	B96030	NEGATIVE	3+	NEGATIVE	NEGATIVE	NEGATIVE	0.2	0	0

Table 21
Individual Urinalysis Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	EPI	BACT	CAST	CRYS	UCOL	UCLA	OTHR
1M	B96001	1	1	0	0	YELLOW	CLEAR	0
1M	B96002	1	1	0	0	YELLOW	CLEAR	SP
1M	B96003	1	1	0	0	YELLOW	CLEAR	SP
1M	B96004	1	1	0	0	YELLOW	CLEAR	SP
1M	B96005	1	1	0	0	YELLOW	CLOUDY	SP
2M	B96006	1	1	0	0	YELLOW	CLOUDY	SP
2M	B96007	1	1	0	0	YELLOW	CLEAR	SP
2M	B96008	1	1	0	0	YELLOW	CLOUDY	SP
2M	B96009	1	1	0	0	YELLOW	CLOUDY	SP
2M	B96010	1	1	0	0	YELLOW	CLEAR	SP
3M	B96011	1	1	0	0	YELLOW	CLOUDY	SP
3M	B96012	1	1	0	0	YELLOW	CLEAR	SP
3M	B96013	1	1	0	0	YELLOW	CLOUDY	SP
3M	B96014	0	1	0	0	YELLOW	CLEAR	SP
3M	B96015	1	1	0	0	YELLOW	CLEAR	SP

Table 21
Individual Urinalysis Data
Occasion: DSNG 16

Test Article	Saline Control	Vehicle Control	2463608
Group	1	2	3
Level(mg 2463608/kg/day)	0	0	1.0

Group/ Sex	Animal Number	EPI	BACT	CAST	CRYS	UCOL	UCLA	OTHR
1F	B96016	1	1	0	0	YELLOW	CLEAR	0
1F	B96017	0	1	0	0	YELLOW	CLEAR	0
1F	B96018	1	1	0	0	YELLOW	CLEAR	0
1F	B96019	1	1	0	0	YELLOW	CLEAR	0
1F	B96020	1	1	0	0	YELLOW	CLEAR	0
2F	B96021	1	1	0	0	YELLOW	CLEAR	0
2F	B96022	0	1	0	0	YELLOW	CLEAR	0
2F	B96023	1	1	0	0	YELLOW	CLEAR	0
2F	B96024	1	1	0	0	YELLOW	CLOUDY	0
2F	B96025	1	1	0	0	YELLOW	CLEAR	0
3F	B96026	1	1	0	0	YELLOW	CLEAR	0
3F	B96027	1	1	0	0	YELLOW	CLEAR	0
3F	B96028	1	1	0	0	YELLOW	CLEAR	0
3F	B96029	1	1	0	0	YELLOW	CLEAR	0
3F	B96030	1	1	0	0	YELLOW	CLEAR	0

Table 22: Individual Animal Data

Animal: B96001 Sex: Male Group: 1 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 346.7

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0791	0.02282	3.8744	
20.Jun.07	16/3	Brain	2.0416	0.58887	100.0000	
20.Jun.07	16/3	Epididymis	1.1306	0.32610	55.3781	
20.Jun.07	16/3	Heart	1.2519	0.36109	61.3196	
20.Jun.07	16/3	Kidney	2.1158	0.61027	103.6344	
20.Jun.07	16/3	Liver	9.5577	2.75676	468.1476	
20.Jun.07	16/3	Pituitary	0.0102	0.00294	0.4996	
20.Jun.07	16/3	Prostate	1.0619	0.30629	52.0131	
20.Jun.07	16/3	Spleen	0.6941	0.20020	33.9979	
20.Jun.07	16/3	Testis	3.5803	1.03268	175.3674	
20.Jun.07	16/3	Thymus	0.6311	0.18203	30.9120	
20.Jun.07	16/3	Thyroid/Parathyr	0.0367	0.01059	1.7976	

<< Gross Observations >>

Tissue	Gross Observations / Comments
LN, Mandibular	Discolored, Bilateral, Entire, Red

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Kidney	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal.
Intravenous Site	Required tissue. Hemorrhage, Perivascular, Slight. Inflammation, Vascular/Perivascular, Acute to Subacute, Minimal.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

Table 22
Individual Animal Data

Animal: B96001	Sex: Male	Group: 1	Dose level: 0 mg/kg
Day/Week of death:16/3	Status: Final phase sacrifice	Terminal body weight (g): 346.7	

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
The following tissues are unremarkable:	
Thymus	

Table 22
Individual Animal Data

Animal: B96002 Sex: Male Group: 1 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 332.7

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0512	0.01539	2.6179	
20.Jun.07	16/3	Brain	1.9558	0.58786	100.0000	
20.Jun.07	16/3	Epididymis	1.0483	0.31509	53.5996	
20.Jun.07	16/3	Heart	1.1523	0.34635	58.9171	
20.Jun.07	16/3	Kidney	2.3561	0.70818	120.4673	
20.Jun.07	16/3	Liver	8.6555	2.60159	442.5555	
20.Jun.07	16/3	Pituitary	0.0136	0.00409	0.6954	
20.Jun.07	16/3	Prostate	1.0306	0.30977	52.6945	
20.Jun.07	16/3	Spleen	0.6828	0.20523	34.9115	
20.Jun.07	16/3	Testis	2.9686	0.89228	151.7845	
20.Jun.07	16/3	Thymus	0.6648	0.19982	33.9912	
20.Jun.07	16/3	Thyroid/Parathyr	0.0201	0.00604	1.0277	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Intravenous Site	Required tissue. Degeneration/Necrosis, Vascular, Slight. Hemorrhage, Perivascular, Slight. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight. Thrombus, Moderate.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

Table 22
Individual Animal Data

Animal: B96002	Sex: Male	Group: 1	Dose level: 0	mg/kg
Day/Week of death:16/3	Status: Final phase sacrifice		Terminal body weight (g): 332.7	

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
The following tissues are unremarkable:	
Thymus	
Kidney	

Table 22
Individual Animal Data

Animal: B96003 Sex: Male Group: 1 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 322.7

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0739	0.02290	3.7002	
20.Jun.07	16/3	Brain	1.9972	0.61890	100.0000	
20.Jun.07	16/3	Epididymis	1.2096	0.37484	60.5648	
20.Jun.07	16/3	Heart	1.1712	0.36294	58.6421	
20.Jun.07	16/3	Kidney	2.2961	0.71153	114.9660	
20.Jun.07	16/3	Liver	8.7141	2.70037	436.3159	
20.Jun.07	16/3	Pituitary	0.0152	0.00471	0.7611	
20.Jun.07	16/3	Prostate	0.9589	0.29715	48.0122	
20.Jun.07	16/3	Spleen	0.8385	0.25984	41.9838	
20.Jun.07	16/3	Testis	3.1810	0.98575	159.2730	
20.Jun.07	16/3	Thymus	0.4498	0.13939	22.5215	
20.Jun.07	16/3	Thyroid/Parathyr	0.0276	0.00855	1.3819	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	N	Scaly Skin, Tail

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Kidney	Required tissue. Inflammation, Chronic-Active, Pelvis, Slight.
Intravenous Site	Required tissue. Crust, Epidermal, Minimal. Hemorrhage, Perivascular, Minimal. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

Table 22
Individual Animal Data

Animal: B96003	Sex: Male	Group: 1	Dose level: 0 mg/kg
Day/Week of death:16/3	Status: Final phase sacrifice	Terminal body weight (g): 322.7	

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
The following tissues are unremarkable:	
Thymus	

Table 22
Individual Animal Data

Animal: B96004 Sex: Male Group: 1 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 332.6

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0587	0.01765	2.8338	
20.Jun.07	16/3	Brain	2.0714	0.62279	100.0000	
20.Jun.07	16/3	Epididymis	1.1713	0.35216	56.5463	
20.Jun.07	16/3	Heart	1.2155	0.36545	58.6801	
20.Jun.07	16/3	Kidney	2.3630	0.71046	114.0774	
20.Jun.07	16/3	Liver	8.0327	2.41512	387.7909	
20.Jun.07	16/3	Pituitary	0.0117	0.00352	0.5648	
20.Jun.07	16/3	Prostate	1.0089	0.30334	48.7062	
20.Jun.07	16/3	Spleen	0.6863	0.20634	33.1322	
20.Jun.07	16/3	Testis	3.3200	0.99820	160.2781	
20.Jun.07	16/3	Thymus	0.5216	0.15683	25.1810	
20.Jun.07	16/3	Thyroid/Parathyr	0.0198	0.00595	0.9559	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Kidney	Required tissue. Basophilic Tubule, Minimal.
Intravenous Site	Required tissue. Hemorrhage, Perivascular, Moderate. Inflammation, Vascular/Perivascular, Acute to Subacute, Minimal.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

Table 22
Individual Animal Data

Animal: B96004	Sex: Male	Group: 1	Dose level: 0 mg/kg
Day/Week of death:16/3	Status: Final phase sacrifice	Terminal body weight (g): 332.6	

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
The following tissues are unremarkable:	
Thymus	

Table 22
Individual Animal Data

Animal: B96005 Sex: Male Group: 1 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 356.7

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0693	0.01943	3.2356	
20.Jun.07	16/3	Brain	2.1418	0.60045	100.0000	
20.Jun.07	16/3	Epididymis	1.0754	0.30149	50.2101	
20.Jun.07	16/3	Heart	1.3731	0.38495	64.1096	
20.Jun.07	16/3	Kidney	2.4721	0.69305	115.4216	
20.Jun.07	16/3	Liver	9.5739	2.68402	447.0026	
20.Jun.07	16/3	Pituitary	0.0117	0.00328	0.5463	
20.Jun.07	16/3	Prostate	1.3163	0.36902	61.4577	
20.Jun.07	16/3	Spleen	0.7021	0.19683	32.7808	
20.Jun.07	16/3	Testis	3.1644	0.88713	147.7449	
20.Jun.07	16/3	Thymus	0.5435	0.15237	25.3759	
20.Jun.07	16/3	Thyroid/Parathyr	0.0170	0.00477	0.7937	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Kidney	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal.
Intravenous Site	Required tissue. Hemorrhage, Perivascular, Slight.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:
Thymus

Table 22
Individual Animal Data

Animal: B96006 Sex: Male Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 315.1

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0499	0.01584	2.3865	
20.Jun.07	16/3	Brain	2.0909	0.66357	100.0000	
20.Jun.07	16/3	Epididymis	1.1281	0.35801	53.9529	
20.Jun.07	16/3	Heart	1.6644	0.52821	79.6021	
20.Jun.07	16/3	Kidney	2.4235	0.76912	115.9070	
20.Jun.07	16/3	Liver	9.2348	2.93075	441.6663	
20.Jun.07	16/3	Pituitary	0.0124	0.00394	0.5930	
20.Jun.07	16/3	Prostate	1.2108	0.38426	57.9081	
20.Jun.07	16/3	Spleen	0.6116	0.19410	29.2506	
20.Jun.07	16/3	Testis	3.3366	1.05890	159.5772	
20.Jun.07	16/3	Thymus	0.2926	0.09286	13.9940	
20.Jun.07	16/3	Thyroid/Parathyr	0.0262	0.00831	1.2530	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Thyroid	Required tissue. Thymus, Ectopic, Present.
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal.
Kidney	Required tissue. Vacuolation, Tubule Cell, Slight.
Intravenous Site	Required tissue. Crust, Epidermal, Minimal. Hemorrhage, Perivascular, Slight.

Table 22
Individual Animal Data

Animal: B96006 Sex: Male Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 315.1

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Adrenal, Medulla	Pituitary
Nerve, Sciatic	Trachea	Esophagus	Parathyroid	Heart
Aorta	Tongue	Muscle, Bi Fem	Spleen	Lung
Thymus	Urinary Bladder	Stomach, Gl	Stomach, Nongl	Duodenum
Ileum	Colon	Cecum	Jejunum	LN, Mesenteric
LN, Mandibular	Gl, Mandib Saliv	Pancreas	Nerve, Optic	Eye
Skin/Subcutis	Mammary, Male	Seminal Vesicle	Prostate	Testis
Epididymis	Bone, Femur	Marrow, Femur	Bone, Sternum	Marrow, Sternum

Table 22
Individual Animal Data

Animal: B96007 Sex: Male Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 353.7

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0700	0.01979	3.4902	
20.Jun.07	16/3	Brain	2.0056	0.56703	100.0000	
20.Jun.07	16/3	Epididymis	1.1940	0.33757	59.5333	
20.Jun.07	16/3	Heart	1.5616	0.44150	77.8620	
20.Jun.07	16/3	Kidney	2.3285	0.65833	116.0999	
20.Jun.07	16/3	Liver	10.1530	2.87051	506.2326	
20.Jun.07	16/3	Pituitary	0.0150	0.00424	0.7479	
20.Jun.07	16/3	Prostate	1.1205	0.31679	55.8686	
20.Jun.07	16/3	Spleen	0.8590	0.24286	42.8301	
20.Jun.07	16/3	Testis	3.2566	0.92072	162.3754	
20.Jun.07	16/3	Thymus	0.4518	0.12774	22.5269	
20.Jun.07	16/3	Thyroid/Parathyr	0.0211	0.00597	1.0521	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal.
Kidney	Required tissue. Vacuolation, Tubule Cell, Slight.
Eye	Required tissue. Rosette, Retina, Present. /Rosette is unilateral.
Prostate	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal.

Table 22
Individual Animal Data

Animal: B96007 Sex: Male Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 353.7

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Intravenous Site	Required tissue. Crust, Epidermal, Minimal. Degeneration/Necrosis, Vascular, Minimal. Inflammation, Vascular/Perivascular, Acute to Subacute, Minimal.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Adrenal, Medulla	Pituitary
Nerve, Sciatic	Trachea	Esophagus	Thyroid	Parathyroid
Heart	Aorta	Tongue	Muscle, Bi Fem	Spleen
Lung	Thymus	Urinary Bladder	Stomach, Gl	Stomach, Nongl
Duodenum	Ileum	Colon	Cecum	Jejunum
LN, Mesenteric	LN, Mandibular	Gl, Mandib Saliv	Pancreas	Nerve, Optic
Skin/Subcutis	Mammary, Male	Seminal Vesicle	Testis	Epididymis
Bone, Femur	Marrow, Femur	Bone, Sternum	Marrow, Sternum	

Table 22
Individual Animal Data

Animal: B96008 Sex: Male Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 337.3

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0621	0.01841	3.0385	
20.Jun.07	16/3	Brain	2.0438	0.60593	100.0000	
20.Jun.07	16/3	Epididymis	1.2397	0.36754	60.6566	
20.Jun.07	16/3	Heart	1.2643	0.37483	61.8603	
20.Jun.07	16/3	Kidney	2.2610	0.67032	110.6273	
20.Jun.07	16/3	Liver	8.3056	2.46238	406.3803	
20.Jun.07	16/3	Pituitary	0.0129	0.00382	0.6312	
20.Jun.07	16/3	Prostate	0.8355	0.24770	40.8797	
20.Jun.07	16/3	Spleen	0.7722	0.22894	37.7826	
20.Jun.07	16/3	Testis	3.4116	1.01144	166.9244	
20.Jun.07	16/3	Thymus	0.3801	0.11269	18.5977	
20.Jun.07	16/3	Thyroid/Parathyr	0.0189	0.00560	0.9247	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Adrenal, Medulla	Required tissue; one of pair is missing; other is normal.
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal. Vacuolation, Hepatocyte, Periportal, Minimal.
Kidney	Required tissue. Vacuolation, Tubule Cell, Moderate.
Testis	Required tissue. Hypoplasia, Seminiferous Tubules, Focal, Unilateral, Minimal.

Table 22
Individual Animal Data

Animal: B96008 Sex: Male Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 337.3

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Intravenous Site	Required tissue. Hemorrhage, Perivascular, Slight. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Pituitary	Nerve, Sciatic
Trachea	Esophagus	Thyroid	Parathyroid	Heart
Aorta	Tongue	Muscle, Bi Fem	Spleen	Lung
Thymus	Urinary Bladder	Stomach, Gl	Stomach, Nongl	Duodenum
Ileum	Colon	Cecum	Jejunum	LN, Mesenteric
LN, Mandibular	Gl, Mandib Saliv	Pancreas	Nerve, Optic	Eye
Skin/Subcutis	Mammary, Male	Seminal Vesicle	Prostate	Epididymis
Bone, Femur	Marrow, Femur	Bone, Sternum	Marrow, Sternum	

Table 22
Individual Animal Data

Animal: B96009 Sex: Male Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 328.3

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0524	0.01596	2.6937	
20.Jun.07	16/3	Brain	1.9453	0.59254	100.0000	
20.Jun.07	16/3	Epididymis	1.3096	0.39890	67.3213	
20.Jun.07	16/3	Heart	1.0504	0.31995	53.9968	
20.Jun.07	16/3	Kidney	1.9106	0.58197	98.2162	
20.Jun.07	16/3	Liver	8.8326	2.69041	454.0482	
20.Jun.07	16/3	Pituitary	0.0089	0.00271	0.4575	
20.Jun.07	16/3	Prostate	1.0913	0.33241	56.0993	
20.Jun.07	16/3	Spleen	0.7118	0.21681	36.5908	
20.Jun.07	16/3	Testis	3.3181	1.01069	170.5701	
20.Jun.07	16/3	Thymus	0.4105	0.12504	21.1021	
20.Jun.07	16/3	Thyroid/Parathyr	0.0142	0.00433	0.7300	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Thyroid	Required tissue. Thymus, Ectopic, Present.
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal.
Kidney	Required tissue. Vacuolation, Tubule Cell, Slight. Infiltrate, Lymphocytes/Macrophages, Minimal.
Prostate	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal.

Table 22
Individual Animal Data

Animal: B96009 Sex: Male Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 328.3

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Intravenous Site	Required tissue. Degeneration/Necrosis, Vascular, Slight. Hemorrhage, Perivascular, Minimal. Inflammation, Vascular/Perivascular, Acute to Subacute, Minimal. Thrombus, Minimal.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Adrenal, Medulla	Pituitary
Nerve, Sciatic	Trachea	Esophagus	Parathyroid	Heart
Aorta	Tongue	Muscle, Bi Fem	Spleen	Lung
Thymus	Urinary Bladder	Stomach, Gl	Stomach, Nongl	Duodenum
Ileum	Colon	Cecum	Jejunum	LN, Mesenteric
LN, Mandibular	Gl, Mandib Saliv	Pancreas	Nerve, Optic	Eye
Skin/Subcutis	Mammary, Male	Seminal Vesicle	Testis	Epididymis
Bone, Femur	Marrow, Femur	Bone, Sternum	Marrow, Sternum	

Table 22
Individual Animal Data

Animal: B96010 Sex: Male Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 355.3

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0539	0.01517	2.9005	
20.Jun.07	16/3	Brain	1.8583	0.52302	100.0000	
20.Jun.07	16/3	Epididymis	1.1547	0.32499	62.1374	
20.Jun.07	16/3	Heart	1.2859	0.36192	69.1977	
20.Jun.07	16/3	Kidney	2.1399	0.60228	115.1536	
20.Jun.07	16/3	Liver	8.7974	2.47605	473.4113	
20.Jun.07	16/3	Pituitary	0.0109	0.00307	0.5866	
20.Jun.07	16/3	Prostate	0.8416	0.23687	45.2887	
20.Jun.07	16/3	Spleen	0.7819	0.22007	42.0761	
20.Jun.07	16/3	Testis	3.0748	0.86541	165.4631	
20.Jun.07	16/3	Thymus	0.4715	0.13270	25.3727	
20.Jun.07	16/3	Thyroid/Parathyr	0.0195	0.00549	1.0493	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal. Vacuolation, Hepatocyte, Periportal, Minimal.
Kidney	Required tissue. Vacuolation, Tubule Cell, Moderate.
Prostate	Required tissue. Inflammation, Acute, Minimal.
Intravenous Site	Required tissue. Degeneration/Necrosis, Vascular, Minimal.

Table 22
Individual Animal Data

Animal: B96010 Sex: Male Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 355.3

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Intravenous Site	Required tissue. Hemorrhage, Perivascular, Slight. Inflammation, Vascular/Perivascular, Acute to Subacute, Minimal.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Adrenal, Medulla	Pituitary
Nerve, Sciatic	Trachea	Esophagus	Thyroid	Parathyroid
Heart	Aorta	Tongue	Muscle, Bi Fem	Spleen
Lung	Thymus	Urinary Bladder	Stomach, Gl	Stomach, Nongl
Duodenum	Ileum	Colon	Cecum	Jejunum
LN, Mesenteric	LN, Mandibular	Gl, Mandib Saliv	Pancreas	Nerve, Optic
Eye	Skin/Subcutis	Mammary, Male	Seminal Vesicle	Testis
Epididymis	Bone, Femur	Marrow, Femur	Bone, Sternum	Marrow, Sternum

Table 22
Individual Animal Data

Animal: B96011 Sex: Male Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 359.5

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0563	0.01566	2.5567	
20.Jun.07	16/3	Brain	2.2021	0.61255	100.0000	
20.Jun.07	16/3	Epididymis	1.2536	0.34871	56.9275	
20.Jun.07	16/3	Heart	1.3160	0.36606	59.7611	
20.Jun.07	16/3	Kidney	2.2306	0.62047	101.2942	
20.Jun.07	16/3	Liver	9.1324	2.54031	414.7132	
20.Jun.07	16/3	Pituitary	0.0103	0.00287	0.4677	
20.Jun.07	16/3	Prostate	0.8778	0.24417	39.8620	
20.Jun.07	16/3	Spleen	0.7944	0.22097	36.0747	
20.Jun.07	16/3	Testis	3.4711	0.96554	157.6268	
20.Jun.07	16/3	Thymus	0.3000	0.08345	13.6234	
20.Jun.07	16/3	Thyroid/Parathyr	0.0261	0.00726	1.1852	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal. Vacuolation, Hepatocyte, Periportal, Slight.
Kidney	Required tissue. Vacuolation, Tubule Cell, Moderate. Dilatation, Tubule(s), Focal, Slight. Infiltrate, Lymphocytes/Macrophages, Minimal.

Table 22
Individual Animal Data

Animal: B96011	Sex: Male	Group: 3	Dose level: 1 mg/kg
Day/Week of death:16/3	Status: Final phase sacrifice	Terminal body weight (g): 359.5	

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Intravenous Site	Required tissue. Degeneration/Necrosis, Vascular, Slight. Hemorrhage, Perivascular, Slight. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Adrenal, Medulla	Pituitary
Nerve, Sciatic	Trachea	Esophagus	Thyroid	Parathyroid
Heart	Aorta	Tongue	Muscle, Bi Fem	Spleen
Lung	Thymus	Urinary Bladder	Stomach, Gl	Stomach, Nongl
Duodenum	Ileum	Colon	Cecum	Jejunum
LN, Mesenteric	LN, Mandibular	Gl, Mandib Saliv	Pancreas	Nerve, Optic
Eye	Skin/Subcutis	Mammary, Male	Seminal Vesicle	Prostate
Testis	Epididymis	Bone, Femur	Marrow, Femur	Bone, Sternum
Marrow, Sternum				

Table 22
Individual Animal Data

Animal: B96012 Sex: Male Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 361.0

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0592	0.01640	2.8500	
20.Jun.07	16/3	Brain	2.0772	0.57540	100.0000	
20.Jun.07	16/3	Epididymis	1.1165	0.30928	53.7502	
20.Jun.07	16/3	Heart	1.1851	0.32828	57.0528	
20.Jun.07	16/3	Kidney	2.3489	0.65066	113.0801	
20.Jun.07	16/3	Liver	10.0338	2.77945	483.0445	
20.Jun.07	16/3	Pituitary	0.0100	0.00277	0.4814	
20.Jun.07	16/3	Prostate	0.9695	0.26856	46.6734	
20.Jun.07	16/3	Spleen	0.9701	0.26873	46.7023	
20.Jun.07	16/3	Testis	3.4384	0.95247	165.5305	
20.Jun.07	16/3	Thymus	0.3290	0.09114	15.8386	
20.Jun.07	16/3	Thyroid/Parathyr	0.0212	0.00587	1.0206	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Adrenal, Medulla	Required tissue; one of pair is missing; other is normal.
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal. Vacuolation, Hepatocyte, Periportal, Minimal.
Lung	Required tissue. Inflammation, Granulomatous, with Foreign Material, Minimal.
Thymus	Required tissue. Necrosis, Lymphocytes, Minimal.

Table 22
Individual Animal Data

Animal: B96012 Sex: Male Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 361.0

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Kidney	Required tissue. Vacuolation, Tubule Cell, Moderate. Infiltrate, Lymphocytes/Macrophages, Minimal.
Intravenous Site	Required tissue. Hemorrhage, Perivascular, Minimal. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Pituitary	Nerve, Sciatic
Trachea	Esophagus	Thyroid	Parathyroid	Heart
Aorta	Tongue	Muscle, Bi Fem	Spleen	Urinary Bladder
Stomach, Gl	Stomach, Nongl	Duodenum	Ileum	Colon
Cecum	Jejunum	LN, Mesenteric	LN, Mandibular	Gl, Mandib Saliv
Pancreas	Nerve, Optic	Eye	Skin/Subcutis	Mammary, Male
Seminal Vesicle	Prostate	Testis	Epididymis	Bone, Femur
Marrow, Femur	Bone, Sternum	Marrow, Sternum		

Table 22
Individual Animal Data

Animal: B96013 Sex: Male Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 327.2

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0642	0.01962	3.2383	
20.Jun.07	16/3	Brain	1.9825	0.60590	100.0000	
20.Jun.07	16/3	Epididymis	1.2456	0.38068	62.8298	
20.Jun.07	16/3	Heart	1.2584	0.38460	63.4754	
20.Jun.07	16/3	Kidney	2.2707	0.69398	114.5372	
20.Jun.07	16/3	Liver	8.5178	2.60324	429.6495	
20.Jun.07	16/3	Pituitary	0.0116	0.00355	0.5851	
20.Jun.07	16/3	Prostate	1.1344	0.34670	57.2207	
20.Jun.07	16/3	Spleen	0.8201	0.25064	41.3670	
20.Jun.07	16/3	Testis	2.9273	0.89465	147.6570	
20.Jun.07	16/3	Thymus	0.3354	0.10251	16.9180	
20.Jun.07	16/3	Thyroid/Parathyr	0.0276	0.00844	1.3922	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Adrenal, Medulla	Required tissue; one of pair is missing; other is normal.
Heart	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal.
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Slight.
Kidney	Required tissue. Vacuolation, Tubule Cell, Slight. Dilatation, Tubule(s), Focal, Minimal.

Table 22
Individual Animal Data

Animal: B96013 Sex: Male Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 327.2

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Kidney	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal.
Testis	Required tissue. Mineralization, Seminiferous Tubules, Unilateral, Minimal.
Intravenous Site	Required tissue. Degeneration/Necrosis, Vascular, Slight. Hemorrhage, Perivascular, Minimal. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Pituitary	Nerve, Sciatic
Trachea	Esophagus	Thyroid	Parathyroid	Aorta
Tongue	Muscle, Bi Fem	Spleen	Lung	Thymus
Urinary Bladder	Stomach, Gl	Stomach, Nongl	Duodenum	Ileum
Colon	Cecum	Jejunum	LN, Mesenteric	LN, Mandibular
Gl, Mandib Saliv	Pancreas	Nerve, Optic	Eye	Skin/Subcutis
Mammary, Male	Seminal Vesicle	Prostate	Epididymis	Bone, Femur
Marrow, Femur	Bone, Sternum	Marrow, Sternum		

Table 22
Individual Animal Data

Animal: B96014 Sex: Male Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 306.8

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0708	0.02308	3.4056	
20.Jun.07	16/3	Brain	2.0789	0.67761	100.0000	
20.Jun.07	16/3	Epididymis	1.2330	0.40189	59.3102	
20.Jun.07	16/3	Heart	1.1481	0.37422	55.2263	
20.Jun.07	16/3	Kidney	2.1118	0.68833	101.5826	
20.Jun.07	16/3	Liver	7.8384	2.55489	377.0456	
20.Jun.07	16/3	Pituitary	0.0137	0.00447	0.6590	
20.Jun.07	16/3	Prostate	0.9764	0.31825	46.9671	
20.Jun.07	16/3	Spleen	0.6800	0.22164	32.7096	
20.Jun.07	16/3	Testis	3.3199	1.08211	159.6950	
20.Jun.07	16/3	Thymus	0.3616	0.11786	17.3938	
20.Jun.07	16/3	Thyroid/Parathyr	0.0226	0.00737	1.0871	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Adrenal, Medulla	Required tissue is not examined; inadequate and unreadable.
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal.
Lung	Required tissue. Mineralization, Vessel, Minimal.
Kidney	Required tissue. Vacuolation, Tubule Cell, Slight.
Prostate	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal.

Table 22
Individual Animal Data

Animal: B96014 Sex: Male Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 306.8

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Intravenous Site	Required tissue. Crust, Epidermal, Minimal. Degeneration/Necrosis, Vascular, Slight. Hemorrhage, Perivascular, Slight. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight. Thrombus, Minimal.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Pituitary	Nerve, Sciatic
Trachea	Esophagus	Thyroid	Parathyroid	Heart
Aorta	Tongue	Muscle, Bi Fem	Spleen	Thymus
Urinary Bladder	Stomach, Gl	Stomach, Nongl	Duodenum	Ileum
Colon	Cecum	Jejunum	LN, Mesenteric	LN, Mandibular
Gl, Mandib Saliv	Pancreas	Nerve, Optic	Eye	Skin/Subcutis
Mammary, Male	Seminal Vesicle	Testis	Epididymis	Bone, Femur
Marrow, Femur	Bone, Sternum	Marrow, Sternum		

Table 22
Individual Animal Data

Animal: B96015 Sex: Male Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 313.4

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0656	0.02093	3.1942	
20.Jun.07	16/3	Brain	2.0537	0.65530	100.0000	
20.Jun.07	16/3	Epididymis	1.1226	0.35820	54.6623	
20.Jun.07	16/3	Heart	1.1265	0.35944	54.8522	
20.Jun.07	16/3	Kidney	2.3314	0.74391	113.5219	
20.Jun.07	16/3	Liver	8.2467	2.63137	401.5533	
20.Jun.07	16/3	Pituitary	0.0106	0.00338	0.5161	
20.Jun.07	16/3	Prostate	0.7589	0.24215	36.9528	
20.Jun.07	16/3	Spleen	0.7301	0.23296	35.5505	
20.Jun.07	16/3	Testis	3.3998	1.08481	165.5451	
20.Jun.07	16/3	Thymus	0.5312	0.16950	25.8655	
20.Jun.07	16/3	Thyroid/Parathyr	0.0206	0.00657	1.0031	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal.
Lung	Required tissue. Crystals, Hemoglobin, with Associated Subacute Inflammation, Minimal.
Kidney	Required tissue. Vacuolation, Tubule Cell, Slight.
Intravenous Site	Required tissue. Degeneration/Necrosis, Vascular, Slight. Hemorrhage, Perivascular, Slight.

Table 22
Individual Animal Data

Animal: B96015 Sex: Male Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 313.4

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Intravenous Site	Required tissue. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight. Thrombus, Minimal. /A hair shaft is embedded in an area of inflammation.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Adrenal, Medulla	Pituitary
Nerve, Sciatic	Trachea	Esophagus	Thyroid	Parathyroid
Heart	Aorta	Tongue	Muscle, Bi Fem	Spleen
Thymus	Urinary Bladder	Stomach, Gl	Stomach, Nongl	Duodenum
Ileum	Colon	Cecum	Jejunum	LN, Mesenteric
LN, Mandibular	Gl, Mandib Saliv	Pancreas	Nerve, Optic	Eye
Skin/Subcutis	Mammary, Male	Seminal Vesicle	Prostate	Testis
Epididymis	Bone, Femur	Marrow, Femur	Bone, Sternum	Marrow, Sternum

Table 22
Individual Animal Data

Animal: B96016 Sex: Female Group: 1 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 225.2

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0609	0.02704	3.0484	
20.Jun.07	16/3	Brain	1.9978	0.88712	100.0000	
20.Jun.07	16/3	Heart	0.8170	0.36279	40.8950	
20.Jun.07	16/3	Kidney	1.4172	0.62931	70.9380	
20.Jun.07	16/3	Liver	6.7529	2.99862	338.0169	
20.Jun.07	16/3	Ovary	0.1289	0.05724	6.4521	
20.Jun.07	16/3	Pituitary	0.0120	0.00533	0.6007	
20.Jun.07	16/3	Spleen	0.5199	0.23086	26.0236	
20.Jun.07	16/3	Thymus	0.3786	0.16812	18.9508	
20.Jun.07	16/3	Thyroid/Parathyr	0.0184	0.00817	0.9210	
20.Jun.07	16/3	Uterus	0.6681	0.29667	33.4418	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Kidney	Required tissue. Basophilic Tubule, Minimal. Dilatation, Tubule(s), Focal, Minimal. Infiltrate, Lymphocytes/Macrophages, Minimal. Mineralization, Tubule, Minimal.
Intravenous Site	Required tissue. Degeneration/Necrosis, Vascular, Slight. Hemorrhage, Perivascular, Slight.

Table 22
Individual Animal Data

Animal: B96016	Sex: Female	Group: 1	Dose level: 0	mg/kg
Day/Week of death:16/3	Status: Final phase sacrifice	Terminal body weight (g): 225.2		

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Intravenous Site	Required tissue. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight. Thrombus, Minimal.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:
Thymus

Table 22
Individual Animal Data

Animal: B96017 Sex: Female Group: 1 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 219.1

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0550	0.02510	2.8318	
20.Jun.07	16/3	Brain	1.9422	0.88644	100.0000	
20.Jun.07	16/3	Heart	0.8156	0.37225	41.9936	
20.Jun.07	16/3	Kidney	1.5318	0.69913	78.8693	
20.Jun.07	16/3	Liver	6.3183	2.88375	325.3167	
20.Jun.07	16/3	Ovary	0.1206	0.05504	6.2095	
20.Jun.07	16/3	Pituitary	0.0129	0.00589	0.6642	
20.Jun.07	16/3	Spleen	0.5023	0.22926	25.8624	
20.Jun.07	16/3	Thymus	0.4844	0.22109	24.9408	
20.Jun.07	16/3	Thyroid/Parathyr	0.0224	0.01022	1.1533	
20.Jun.07	16/3	Uterus	0.7608	0.34724	39.1721	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Kidney	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal. Mineralization, Tubule, Minimal.
Intravenous Site	Required tissue. Degeneration/Necrosis, Vascular, Moderate. Hemorrhage, Perivascular, Slight. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight. Thrombus, Minimal.

Table 22
Individual Animal Data

Animal: B96017	Sex: Female	Group: 1	Dose level: 0 mg/kg
Day/Week of death:16/3	Status: Final phase sacrifice	Terminal body weight (g): 219.1	

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:
Thymus

Table 22
Individual Animal Data

Animal: B96018 Sex: Female Group: 1 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 233.9

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0725	0.03100	3.5873	
20.Jun.07	16/3	Brain	2.0210	0.86404	100.0000	
20.Jun.07	16/3	Heart	0.9680	0.41385	47.8971	
20.Jun.07	16/3	Kidney	1.7809	0.76139	88.1198	
20.Jun.07	16/3	Liver	6.5393	2.79577	323.5676	
20.Jun.07	16/3	Ovary	0.1272	0.05438	6.2939	
20.Jun.07	16/3	Pituitary	0.0122	0.00522	0.6037	
20.Jun.07	16/3	Spleen	0.4620	0.19752	22.8600	
20.Jun.07	16/3	Thymus	0.3590	0.15348	17.7635	
20.Jun.07	16/3	Thyroid/Parathyr	0.0208	0.00889	1.0292	
20.Jun.07	16/3	Uterus	0.8886	0.37991	43.9683	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Kidney	Required tissue. Mineralization, Tubule, Minimal.
Intravenous Site	Required tissue. Degeneration/Necrosis, Vascular, Slight. Hemorrhage, Perivascular, Slight. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight. Thrombus, Minimal.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

Table 22
Individual Animal Data

Animal: B96018	Sex: Female	Group: 1	Dose level: 0 mg/kg
Day/Week of death:16/3	Status: Final phase sacrifice	Terminal body weight (g): 233.9	

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
The following tissues are unremarkable:	
Thymus	

Table 22
Individual Animal Data

Animal: B96019 Sex: Female Group: 1 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 227.4

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0636	0.02797	3.4100	
20.Jun.07	16/3	Brain	1.8651	0.82018	100.0000	
20.Jun.07	16/3	Heart	0.9237	0.40620	49.5255	
20.Jun.07	16/3	Kidney	1.5270	0.67150	81.8723	
20.Jun.07	16/3	Liver	6.3458	2.79059	340.2392	
20.Jun.07	16/3	Ovary	0.1507	0.06627	8.0800	
20.Jun.07	16/3	Pituitary	0.0136	0.00598	0.7292	
20.Jun.07	16/3	Spleen	0.4869	0.21412	26.1058	
20.Jun.07	16/3	Thymus	0.3673	0.16152	19.6933	
20.Jun.07	16/3	Thyroid/Parathyr	0.0160	0.00704	0.8579	
20.Jun.07	16/3	Uterus	0.5818	0.25585	31.1940	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Intravenous Site	Required tissue. Crust, Epidermal, Minimal. Degeneration/Necrosis, Vascular, Moderate. Hemorrhage, Perivascular, Slight. Inflammation, Vascular/Perivascular, Acute to Subacute, Moderate. Thrombus, Minimal.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

Table 22
Individual Animal Data

Animal: B96019	Sex: Female	Group: 1	Dose level: 0 mg/kg
Day/Week of death:16/3	Status: Final phase sacrifice	Terminal body weight (g): 227.4	

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
The following tissues are unremarkable:	
Thymus	
Kidney	

Table 22
Individual Animal Data

Animal: B96020 Sex: Female Group: 1 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 240.3

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0578	0.02405	2.9427	
20.Jun.07	16/3	Brain	1.9642	0.81739	100.0000	
20.Jun.07	16/3	Heart	1.0860	0.45194	55.2897	
20.Jun.07	16/3	Kidney	1.8147	0.75518	92.3888	
20.Jun.07	16/3	Liver	7.4359	3.09442	378.5715	
20.Jun.07	16/3	Ovary	0.1641	0.06829	8.3545	
20.Jun.07	16/3	Pituitary	0.0163	0.00678	0.8299	
20.Jun.07	16/3	Spleen	0.6804	0.28315	34.6401	
20.Jun.07	16/3	Thymus	0.4202	0.17486	21.3929	
20.Jun.07	16/3	Thyroid/Parathyr	0.0144	0.00599	0.7331	
20.Jun.07	16/3	Uterus	0.6778	0.28206	34.5077	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Kidney	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal. Mineralization, Tubule, Minimal.
Intravenous Site	Required tissue. Degeneration/Necrosis, Vascular, Slight. Hemorrhage, Perivascular, Minimal. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

Table 22
Individual Animal Data

Animal: B96020	Sex: Female	Group: 1	Dose level: 0 mg/kg
Day/Week of death:16/3	Status: Final phase sacrifice	Terminal body weight (g): 240.3	

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
The following tissues are unremarkable:	
Thymus	

Table 22
Individual Animal Data

Animal: B96021 Sex: Female Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 220.8

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0645	0.02921	3.5438	
20.Jun.07	16/3	Brain	1.8201	0.82432	100.0000	
20.Jun.07	16/3	Heart	0.8298	0.37582	45.5909	
20.Jun.07	16/3	Kidney	1.4099	0.63854	77.4628	
20.Jun.07	16/3	Liver	6.1251	2.77405	336.5255	
20.Jun.07	16/3	Ovary	0.1281	0.05802	7.0381	
20.Jun.07	16/3	Pituitary	0.0117	0.00530	0.6428	
20.Jun.07	16/3	Spleen	0.6369	0.28845	34.9926	
20.Jun.07	16/3	Thymus	0.3720	0.16848	20.4384	
20.Jun.07	16/3	Thyroid/Parathyr	0.0213	0.00965	1.1703	
20.Jun.07	16/3	Uterus	0.7710	0.34918	42.3603	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal.
Kidney	Required tissue. Vacuolation, Tubule Cell, Slight. Mineralization, Tubule, Minimal.
Pancreas	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal.
Intravenous Site	Required tissue. Degeneration/Necrosis, Vascular, Minimal.

Table 22
Individual Animal Data

Animal: B96021 Sex: Female Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 220.8

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Intravenous Site	Required tissue. Hemorrhage, Perivascular, Slight. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Adrenal, Medulla	Pituitary
Nerve, Sciatic	Trachea	Esophagus	Thyroid	Parathyroid
Heart	Aorta	Tongue	Muscle, Bi Fem	Spleen
Lung	Thymus	Urinary Bladder	Stomach, Gl	Stomach, Nongl
Duodenum	Ileum	Colon	Cecum	Jejunum
LN, Mesenteric	LN, Mandibular	Gl, Mandib Saliv	Nerve, Optic	Eye
Skin/Subcutis	Mammary, Female	Ovary	Uterus	Cervix
Vagina	Bone, Femur	Marrow, Femur	Bone, Sternum	Marrow, Sternum

Table 22
Individual Animal Data

Animal: B96022 Sex: Female Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 228.9

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0670	0.02927	3.4224	
20.Jun.07	16/3	Brain	1.9577	0.85526	100.0000	
20.Jun.07	16/3	Heart	0.8475	0.37025	43.2906	
20.Jun.07	16/3	Kidney	1.6755	0.73198	85.5851	
20.Jun.07	16/3	Liver	6.4337	2.81070	328.6357	
20.Jun.07	16/3	Ovary	0.1399	0.06112	7.1461	
20.Jun.07	16/3	Pituitary	0.0122	0.00533	0.6232	
20.Jun.07	16/3	Spleen	0.5792	0.25304	29.5857	
20.Jun.07	16/3	Thymus	0.2978	0.13010	15.2117	
20.Jun.07	16/3	Thyroid/Parathyr	0.0203	0.00887	1.0369	
20.Jun.07	16/3	Uterus	0.4915	0.21472	25.1060	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Parathyroid	Required tissue is not examined; inadequate and unreadable.
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal. Vacuolation, Hepatocyte, Periportal, Minimal.
Kidney	Required tissue. Vacuolation, Tubule Cell, Minimal.
Intravenous Site	Required tissue. Hemorrhage, Perivascular, Slight. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight.

Table 22
Individual Animal Data

Animal: B96022 Sex: Female Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 228.9

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Adrenal, Medulla	Pituitary
Nerve, Sciatic	Trachea	Esophagus	Thyroid	Heart
Aorta	Tongue	Muscle, Bi Fem	Spleen	Lung
Thymus	Urinary Bladder	Stomach, Gl	Stomach, Nongl	Duodenum
Ileum	Colon	Cecum	Jejunum	LN, Mesenteric
LN, Mandibular	Gl, Mandib Saliv	Pancreas	Nerve, Optic	Eye
Skin/Subcutis	Mammary, Female	Ovary	Uterus	Cervix
Vagina	Bone, Femur	Marrow, Femur	Bone, Sternum	Marrow, Sternum

Table 22
Individual Animal Data

Animal: B96023 Sex: Female Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 236.7

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0880	0.03718	4.6544	
20.Jun.07	16/3	Brain	1.8907	0.79877	100.0000	
20.Jun.07	16/3	Heart	0.9005	0.38044	47.6279	
20.Jun.07	16/3	Kidney	1.6431	0.69417	86.9043	
20.Jun.07	16/3	Liver	6.5576	2.77043	346.8345	
20.Jun.07	16/3	Ovary	0.1739	0.07347	9.1977	
20.Jun.07	16/3	Pituitary	0.0123	0.00520	0.6506	
20.Jun.07	16/3	Spleen	0.6814	0.28787	36.0396	
20.Jun.07	16/3	Thymus	0.3368	0.14229	17.8135	
20.Jun.07	16/3	Thyroid/Parathyr	0.0178	0.00752	0.9415	
20.Jun.07	16/3	Uterus	0.8261	0.34901	43.6928	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	N	Sore/Scab, Right Front Paw

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Thyroid	Required tissue. Thymus, Ectopic, Present.
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal. Vacuolation, Hepatocyte, Periportal, Minimal.
Kidney	Required tissue. Vacuolation, Tubule Cell, Slight. Mineralization, Tubule, Minimal.

Table 22
Individual Animal Data

Animal: B96023 Sex: Female Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 236.7

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Skin/Subcutis	Required tissue. Crust, Epidermal, Minimal.
Intravenous Site	Required tissue. Degeneration/Necrosis, Vascular, Slight. Hemorrhage, Perivascular, Slight. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Adrenal, Medulla	Pituitary
Nerve, Sciatic	Trachea	Esophagus	Parathyroid	Heart
Aorta	Tongue	Muscle, Bi Fem	Spleen	Lung
Thymus	Urinary Bladder	Stomach, Gl	Stomach, Nongl	Duodenum
Ileum	Colon	Cecum	Jejunum	LN, Mesenteric
LN, Mandibular	Gl, Mandib Saliv	Pancreas	Nerve, Optic	Eye
Mammary, Female	Ovary	Uterus	Cervix	Vagina
Bone, Femur	Marrow, Femur	Bone, Sternum	Marrow, Sternum	

Table 22
Individual Animal Data

Animal: B96024 Sex: Female Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 230.6

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0667	0.02892	3.3672	
20.Jun.07	16/3	Brain	1.9809	0.85902	100.0000	
20.Jun.07	16/3	Heart	0.9932	0.43070	50.1388	
20.Jun.07	16/3	Kidney	1.6403	0.71132	82.8058	
20.Jun.07	16/3	Liver	7.4176	3.21665	374.4561	
20.Jun.07	16/3	Ovary	0.1472	0.06383	7.4310	
20.Jun.07	16/3	Pituitary	0.0166	0.00720	0.8380	
20.Jun.07	16/3	Spleen	0.5531	0.23985	27.9217	
20.Jun.07	16/3	Thymus	0.4034	0.17493	20.3645	
20.Jun.07	16/3	Thyroid/Parathyr	0.0168	0.00729	0.8481	
20.Jun.07	16/3	Uterus	0.4546	0.19714	22.9492	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal.
Kidney	Required tissue. Vacuolation, Tubule Cell, Slight. Infiltrate, Lymphocytes/Macrophages, Minimal.
Skin/Subcutis	Required tissue. Crust, Epidermal, Minimal.
Intravenous Site	Required tissue. Degeneration/Necrosis, Vascular, Moderate.

Table 22
Individual Animal Data

Animal: B96024 Sex: Female Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 230.6

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Intravenous Site	Required tissue. Hemorrhage, Perivascular, Slight. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight. Thrombus, Minimal.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Adrenal, Medulla	Pituitary
Nerve, Sciatic	Trachea	Esophagus	Thyroid	Parathyroid
Heart	Aorta	Tongue	Muscle, Bi Fem	Spleen
Lung	Thymus	Urinary Bladder	Stomach, Gl	Stomach, Nongl
Duodenum	Ileum	Colon	Cecum	Jejunum
LN, Mesenteric	LN, Mandibular	Gl, Mandib Saliv	Pancreas	Nerve, Optic
Eye	Mammary, Female	Ovary	Uterus	Cervix
Vagina	Bone, Femur	Marrow, Femur	Bone, Sternum	Marrow, Sternum

Table 22
Individual Animal Data

Animal: B96025 Sex: Female Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 224.5

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0797	0.03550	4.2714	
20.Jun.07	16/3	Brain	1.8659	0.83114	100.0000	
20.Jun.07	16/3	Heart	0.9552	0.42548	51.1925	
20.Jun.07	16/3	Kidney	1.4619	0.65118	78.3483	
20.Jun.07	16/3	Liver	6.9383	3.09056	371.8474	
20.Jun.07	16/3	Ovary	0.1108	0.04935	5.9382	
20.Jun.07	16/3	Pituitary	0.0152	0.00677	0.8146	
20.Jun.07	16/3	Spleen	0.6394	0.28481	34.2677	
20.Jun.07	16/3	Thymus	0.2534	0.11287	13.5806	
20.Jun.07	16/3	Thyroid/Parathyr	0.0137	0.00610	0.7342	
20.Jun.07	16/3	Uterus	0.9922	0.44196	53.1754	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal. Necrosis, Coagulative, Focal, Minimal. Vacuolation, Hepatocyte, Periportal, Minimal.
Kidney	Required tissue. Vacuolation, Tubule Cell, Moderate.
Intravenous Site	Required tissue. Degeneration/Necrosis, Vascular, Minimal. Hemorrhage, Perivascular, Slight.

Table 22
Individual Animal Data

Animal: B96025 Sex: Female Group: 2 Dose level: 0 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 224.5

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Intravenous Site	Required tissue. Inflammation, Vascular/Perivascular, Acute to Subacute, Minimal. Thrombus, Minimal.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Adrenal, Medulla	Pituitary
Nerve, Sciatic	Trachea	Esophagus	Thyroid	Parathyroid
Heart	Aorta	Tongue	Muscle, Bi Fem	Spleen
Lung	Thymus	Urinary Bladder	Stomach, Gl	Stomach, Nongl
Duodenum	Ileum	Colon	Cecum	Jejunum
LN, Mesenteric	LN, Mandibular	Gl, Mandib Saliv	Pancreas	Nerve, Optic
Eye	Skin/Subcutis	Mammary, Female	Ovary	Uterus
Cervix	Vagina	Bone, Femur	Marrow, Femur	Bone, Sternum
Marrow, Sternum				

Table 22
Individual Animal Data

Animal: B96026 Sex: Female Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 202.9

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0606	0.02987	3.1920	
20.Jun.07	16/3	Brain	1.8985	0.93568	100.0000	
20.Jun.07	16/3	Heart	0.8695	0.42854	45.7993	
20.Jun.07	16/3	Kidney	1.5453	0.76161	81.3958	
20.Jun.07	16/3	Liver	6.1527	3.03238	324.0822	
20.Jun.07	16/3	Ovary	0.1308	0.06447	6.8896	
20.Jun.07	16/3	Pituitary	0.0113	0.00557	0.5952	
20.Jun.07	16/3	Spleen	0.4617	0.22755	24.3192	
20.Jun.07	16/3	Thymus	0.4395	0.21661	23.1499	
20.Jun.07	16/3	Thyroid/Parathyr	0.0300	0.01479	1.5802	
20.Jun.07	16/3	Uterus	0.3897	0.19207	20.5267	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Lung	Discolored, Lobe, All, Multiple, up to 2 mm2, White

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Heart	Required tissue. Inflammation, Chronic, Proliferative, Endocardial/Subendocardial, Atrium, Marked.
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal. Vacuolation, Hepatocyte, Periportal, Minimal.
Lung	Required tissue. Crystals, Hemoglobin, with Associated Subacute Inflammation, Minimal.
Kidney	Required tissue. Vacuolation, Tubule Cell, Slight.

Table 22
Individual Animal Data

Animal: B96026 Sex: Female Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 202.9

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Kidney	Required tissue. Mineralization, Tubule, Minimal.
Intravenous Site	Required tissue. Degeneration/Necrosis, Vascular, Slight. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Adrenal, Medulla	Pituitary
Nerve, Sciatic	Trachea	Esophagus	Thyroid	Parathyroid
Aorta	Tongue	Muscle, Bi Fem	Spleen	Thymus
Urinary Bladder	Stomach, Gl	Stomach, Nongl	Duodenum	Ileum
Colon	Cecum	Jejunum	LN, Mesenteric	LN, Mandibular
Gl, Mandib Saliv	Pancreas	Nerve, Optic	Eye	Skin/Subcutis
Mammary, Female	Ovary	Uterus	Cervix	Vagina
Bone, Femur	Marrow, Femur	Bone, Sternum	Marrow, Sternum	

Table 22
Individual Animal Data

Animal: B96027 Sex: Female Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 218.6

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0731	0.03344	3.7688	
20.Jun.07	16/3	Brain	1.9396	0.88728	100.0000	
20.Jun.07	16/3	Heart	0.9123	0.41734	47.0355	
20.Jun.07	16/3	Kidney	1.5994	0.73166	82.4603	
20.Jun.07	16/3	Liver	6.6332	3.03440	341.9881	
20.Jun.07	16/3	Ovary	0.1535	0.07022	7.9140	
20.Jun.07	16/3	Pituitary	0.0176	0.00805	0.9074	
20.Jun.07	16/3	Spleen	0.6029	0.27580	31.0837	
20.Jun.07	16/3	Thymus	0.3784	0.17310	19.5092	
20.Jun.07	16/3	Thyroid/Parathyr	0.0259	0.01185	1.3353	
20.Jun.07	16/3	Uterus	0.5238	0.23962	27.0056	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Adrenal, Medulla	Required tissue; one of pair is missing; other is normal.
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal. Vacuolation, Hepatocyte, Periportal, Minimal.
Kidney	Required tissue. Vacuolation, Tubule Cell, Slight. Mineralization, Tubule, Minimal.
Eye	Required tissue. Rosette, Retina, Present.

Table 22
Individual Animal Data

Animal: B96027 Sex: Female Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 218.6

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Eye	Required tissue. /Rosettes are bilateral.
Intravenous Site	Required tissue. Hemorrhage, Perivascular, Moderate. Inflammation, Vascular/Perivascular, Acute to Subacute, Minimal.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Pituitary	Nerve, Sciatic
Trachea	Esophagus	Thyroid	Parathyroid	Heart
Aorta	Tongue	Muscle, Bi Fem	Spleen	Lung
Thymus	Urinary Bladder	Stomach, Gl	Stomach, Nongl	Duodenum
Ileum	Colon	Cecum	Jejunum	LN, Mesenteric
LN, Mandibular	Gl, Mandib Saliv	Pancreas	Nerve, Optic	Skin/Subcutis
Mammary, Female	Ovary	Uterus	Cervix	Vagina
Bone, Femur	Marrow, Femur	Bone, Sternum	Marrow, Sternum	

Table 22
Individual Animal Data

Animal: B96028 Sex: Female Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 222.0

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0825	0.03716	4.3085	
20.Jun.07	16/3	Brain	1.9148	0.86252	100.0000	
20.Jun.07	16/3	Heart	0.9678	0.43595	50.5431	
20.Jun.07	16/3	Kidney	1.6246	0.73180	84.8444	
20.Jun.07	16/3	Liver	6.9790	3.14369	364.4767	
20.Jun.07	16/3	Ovary	0.1260	0.05676	6.5803	
20.Jun.07	16/3	Pituitary	0.0144	0.00649	0.7520	
20.Jun.07	16/3	Spleen	0.5391	0.24284	28.1544	
20.Jun.07	16/3	Thymus	0.5077	0.22869	26.5145	
20.Jun.07	16/3	Thyroid/Parathyr	0.0259	0.01167	1.3526	
20.Jun.07	16/3	Uterus	0.8219	0.37023	42.9235	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Thyroid	Required tissue. Thymus, Ectopic, Present.
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal. Vacuolation, Hepatocyte, Periportal, Slight.
Lung	Required tissue. Inflammation, Granulomatous, with Foreign Material, Minimal.
Kidney	Required tissue. Vacuolation, Tubule Cell, Minimal.

Table 22
Individual Animal Data

Animal: B96028 Sex: Female Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 222.0

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Kidney	Required tissue. Mineralization, Tubule, Minimal.
Intravenous Site	Required tissue. Degeneration/Necrosis, Vascular, Moderate. Hemorrhage, Perivascular, Slight. Inflammation, Vascular/Perivascular, Acute to Subacute, Moderate. Thrombus, Slight.
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Adrenal, Medulla	Pituitary
Nerve, Sciatic	Trachea	Esophagus	Parathyroid	Heart
Aorta	Tongue	Muscle, Bi Fem	Spleen	Thymus
Urinary Bladder	Stomach, Gl	Stomach, Nongl	Duodenum	Ileum
Colon	Cecum	Jejunum	LN, Mesenteric	LN, Mandibular
Gl, Mandib Saliv	Pancreas	Nerve, Optic	Eye	Skin/Subcutis
Mammary, Female	Ovary	Uterus	Cervix	Vagina
Bone, Femur	Marrow, Femur	Bone, Sternum	Marrow, Sternum	

Table 22
Individual Animal Data

Animal: B96029 Sex: Female Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 227.6

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0632	0.02777	3.1348	
20.Jun.07	16/3	Brain	2.0161	0.88581	100.0000	
20.Jun.07	16/3	Heart	0.9849	0.43273	48.8517	
20.Jun.07	16/3	Kidney	1.6777	0.73713	83.2151	
20.Jun.07	16/3	Liver	6.6491	2.92140	329.8001	
20.Jun.07	16/3	Ovary	0.1288	0.05659	6.3886	
20.Jun.07	16/3	Pituitary	0.0127	0.00558	0.6299	
20.Jun.07	16/3	Spleen	0.4156	0.18260	20.6141	
20.Jun.07	16/3	Thymus	0.4570	0.20079	22.6675	
20.Jun.07	16/3	Thyroid/Parathyr	0.0093	0.00409	0.4613	
20.Jun.07	16/3	Uterus	0.8930	0.39236	44.2934	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Intravenous Site	Crusted, mid tail, Single, up to 5 mm2, Red, Dark

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Scaly Skin, Tail

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal.
Kidney	Required tissue. Vacuolation, Tubule Cell, Slight.
Intravenous Site	Required tissue. Crust, Epidermal, Minimal. Hemorrhage, Perivascular, Slight. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight.

Table 22
Individual Animal Data

Animal: B96029 Sex: Female Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 227.6

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Adrenal, Medulla	Pituitary
Nerve, Sciatic	Trachea	Esophagus	Thyroid	Parathyroid
Heart	Aorta	Tongue	Muscle, Bi Fem	Spleen
Lung	Thymus	Urinary Bladder	Stomach, Gl	Stomach, Nongl
Duodenum	Ileum	Colon	Cecum	Jejunum
LN, Mesenteric	LN, Mandibular	Gl, Mandib Saliv	Pancreas	Nerve, Optic
Eye	Skin/Subcutis	Mammary, Female	Ovary	Uterus
Cervix	Vagina	Bone, Femur	Marrow, Femur	Bone, Sternum
Marrow, Sternum				

Table 22
Individual Animal Data

Animal: B96030 Sex: Female Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 225.2

<< Organ Weights >>

Date	Day/week of Phase	Organ Name	Absolute Organ Weight (g)	Relative % of Body Weight	Relative % of Brain Weight	Organ Status
20.Jun.07	16/3	Adrenal	0.0633	0.02811	3.3194	
20.Jun.07	16/3	Brain	1.9070	0.84680	100.0000	
20.Jun.07	16/3	Heart	0.9315	0.41363	48.8464	
20.Jun.07	16/3	Kidney	1.6212	0.71989	85.0131	
20.Jun.07	16/3	Liver	6.3506	2.81998	333.0153	
20.Jun.07	16/3	Ovary	0.1325	0.05884	6.9481	
20.Jun.07	16/3	Pituitary	0.0262	0.01163	1.3739	
20.Jun.07	16/3	Spleen	0.4363	0.19374	22.8789	
20.Jun.07	16/3	Thymus	0.3947	0.17527	20.6974	
20.Jun.07	16/3	Thyroid/Parathyr	0.0202	0.00897	1.0593	
20.Jun.07	16/3	Uterus	0.8323	0.36958	43.6445	

<< Gross Observations >>

Tissue	Gross Observations / Comments
Observed/No remarkable findings	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Clinical Signs Confirmation >>

Date	Day/week of Phase	Verify	Confirm	Observations
20.Jun.07	16/3	Y	Y	Normal/No Remarkable Obs

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
Liver	Required tissue. Infiltrate, Lymphocytes/Macrophages, Minimal. Vacuolation, Hepatocyte, Periportal, Minimal.
Kidney	Required tissue. Vacuolation, Tubule Cell, Slight.
Intravenous Site	Required tissue. Hemorrhage, Perivascular, Slight. Inflammation, Vascular/Perivascular, Acute to Subacute, Slight.

Table 22
Individual Animal Data

Animal: B96030 Sex: Female Group: 3 Dose level: 1 mg/kg
Day/Week of death:16/3 Status: Final phase sacrifice Terminal body weight (g): 225.2

<< P a t h o l o g y O b s e r v a t i o n s >>

Tissue	Histopathologic diagnoses / Special histological comments
Death Comment	Required tissue. Scheduled Sacrifice, Present.

The following tissues are unremarkable:

Brain	Spinal Cord	Adrenal, Cortex	Adrenal, Medulla	Pituitary
Nerve, Sciatic	Trachea	Esophagus	Thyroid	Parathyroid
Heart	Aorta	Tongue	Muscle, Bi Fem	Spleen
Lung	Thymus	Urinary Bladder	Stomach, Gl	Stomach, Nongl
Duodenum	Ileum	Colon	Cecum	Jejunum
LN, Mesenteric	LN, Mandibular	Gl, Mandib Saliv	Pancreas	Nerve, Optic
Eye	Skin/Subcutis	Mammary, Female	Ovary	Uterus
Cervix	Vagina	Bone, Femur	Marrow, Femur	Bone, Sternum
Marrow, Sternum				