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SEHSC®
SILICONES ENVIRONMENTAL, HEALTH AND SAFETY COUNCIL NORTH AMERICA

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Via Certified Mail

February 02, 2011

8EHQ-10-17952

TSCA Confidential Business Information Center (7407M)
EPA East – Room 6428 Attn: Section 8(e)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

Re: Supplemental TSCA Section 8(e) Notification (8EHQ-0510-17952): Final Report – 28-Day Oral (Gavage) Toxicity Study in the Sprague-Dawley Rat with Octamethyltrisiloxane (L3)

Dear TSCA Section 8(e) Coordinator:

In accordance with the provisions of Section 8(e) of the Toxic Substances and Control Act (TSCA), as interpreted in the TSCA Section 8(e) Policy Statement and Guidance, Fed. Reg. 33129 (June 3, 2003) and other Agency guidance, the Silicones Environmental, Health and Safety Council (SEHSC)[1] submits, on behalf of its member companies, a final study report as a supplemental submission to our May 14, 2010 TSCA 8(e) notification.

Chemical Substances

107-51-7 Octamethyltrisiloxane

89110000096

Completed Study

28-Day Oral (Gavage) Toxicity Study in the Sprague-Dawley Rat with Octamethyltrisiloxane (L3)

Summary

Preliminary results from a 28-day oral (gavage) toxicity study in the Sprague-Dawley rat with Octamethyltrisiloxane (L3) were reported to EPA on May 14, 2010. The enclosed final study report for the aforementioned study is provided for the Agency's reference. Neither SEHSC, nor any member company, has made a determination at this time that any significant risk of injury to human health or the environment is presented by these findings.

[1] SEHSC is a not-for-profit trade association whose mission is to promote the safe use of silicones through product stewardship and environmental, health, and safety research. The Council is comprised of North American silicone chemical producers and importers.

CONTAINS NO CBI

If you have any questions concerning this submission, please contact me at (703) 788-6570, kthomas@sehsc.com, or at the address provided herein.

Sincerely,

Karluss V. Thomas

Karluss Thomas
Executive Director

SEHSC
2325 Dulles Corner Blvd
Suite 500
Herndon, VA 20171-3418

3°

CERTIFIED MAIL™

7010 1060 0000 0102 0521

REPORT (PART I OF II)

harlan™

28-Day Oral Toxicity (Gavage) Study in the Sprague-Dawley Rat with OCTAMETHYLTRISILOXANE (L3)

Study Director: W. H. Braun

Test Facility: **Harlan Laboratories Ltd.**
Zelgliweg 1
4452 Itingen / Switzerland

Sponsor: **SEHSC**
Silicones Environmental, Health and Safety Council
2325 Dulles Corner Blvd., Suite 500
Herndon, VA 20171 / USA

Study Identification: Harlan Laboratories Study **C53655**

Version: Final

Study Completion Date: 06-Aug-2010

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GOOD LABORATORY PRACTICE

STATEMENT OF COMPLIANCE

Harlan Laboratories Study:	C53655
Test Item:	Octamethyltrisiloxane (L3)
Study Director:	W. H. Braun
Study Title:	28-Day Oral Toxicity (Gavage) Study in the Sprague-Dawley Rat with Octamethyltrisiloxane (L3)

This study has been performed in compliance with the:

Swiss Ordinance relating to Good Laboratory Practice adopted May 18th, 2005 [SR 813.112.1]. This Ordinance is based on the OECD Principles of Good Laboratory Practice, as revised in 1997 and adopted on November 26th, 1997 by decision of the OECD Council [C (97)186/Final].

There were no circumstances that may have affected the quality or integrity of the data.

Study Director: W. H. Braun

Date: 6 August 2010

Sponsor Representative : M. L. Jovanovic

Marina Jovanovic

Date: 6 August 2010

QUALITY ASSURANCE STATEMENT

Harlan Laboratories Ltd., Zelgliweg 1, 4452 Itingen / Switzerland

Harlan Laboratories Study:	C53655
Test Item:	Octamethyltrisiloxane (L3)
Study Director:	W. H. Braun
Study Title:	28-Day Oral Toxicity (Gavage) Study in the Sprague-Dawley Rat with Octamethyltrisiloxane (L3)

The general facilities and activities are inspected at least once a year and the results are reported to the responsible person and the management.

Study procedures were periodically inspected. The study plan and this report were audited by the quality assurance. The dates are given below.

Dates and Types of QA Inspections		Dates of Reports to the Study Director and Test Facility Management
30-Nov-2009	Study plan	30-Nov-2009
23-Dec-2009	Study based (dose preparation, treatment, test item, test system, body weight)	23-Dec-2009
08-Jan-2010	Process based (sample preparation analytic)	08-Jan-2010
13-Jan-2010	Study based (vaginal smear)	13-Jan-2010
20-Jan-2010	Study based (necropsy)	20-Jan-2010
27-Jan-2010	Process based (diagnostic)	27-Jan-2010
23-Feb-2010	Process based (histotechnique)	23-Feb-2010
15-Apr-2010	Appendix formulation analysis	15-Apr-2010
01 to 06-Jul-2010	Report	06-Jul-2010

This statement also confirms that this final report reflects the raw data.

In addition this final report includes all QA-statements issued by the test site quality assurances.

Quality Assurance: (for) N. Häuselmann

6/8/2010
Date:

SIGNATURE(S) OF ADDITIONAL SCIENTIST(S)

Formulation Analysis: Dr. D. Wetzel

Doris Wetzel
Date: 06. August 2010

Histopathology: Dr. H. Iwata

Hyin Iwata
Date: 06. 08. 2010

The signature of the principal investigators (PI) is included in the phase report which is attached as an appendix to this report.

SPONSOR REPRESENTATIVE APPROVAL

Sponsor Representative: M. L. Jovanovic

Marina Jovanovic

Date: 6 August 2010

PREFACE

General Information

Test Item:	Octamethyltrisiloxane (L3)
Study Title:	28-Day Oral Toxicity (Gavage) Study in the Sprague-Dawley Rat with Octamethyltrisiloxane (L3)
Sponsor:	SEHSC Silicones Environmental, Health and Safety Council 2325 Dulles Corner Blvd., Suite 500 Herndon, VA 20171 / USA
Sponsor Representative:	M. L. Jovanovic Dow Corning Corporation Health and Environmental Sciences 2200 W. Salzburg Road, Mail# CO3101 Auburn, MI 48611 / USA
Test Facility:	Harlan Laboratories Ltd. Zelgliweg 1 4452 Itingen / Switzerland
Lead QA:	Harlan Laboratories Ltd. Quality Assurance GLP Zelgliweg 1 4452 Itingen / Switzerland

Responsibilities

Test Facility:

Study Director:	W. H. Braun
Deputy Study Director:	Dr. B. Damme
Planning Coordinator:	A. Suter
Laboratory Coordinator:	P. Althaus Ravenstijn
Necropsy / Histotechnology:	Dr. K. Weber
Clinical Laboratory Investigations:	R. Draheim
Analytical Chemistry:	Dr. D. Wetzel
Pathology:	Dr. H. Iwata

Quality Assurance:

Head of Lead QA:	T. Fink QAContact_crs.ch@harlan.com

Test Site(s):

Principal Investigator(s):

Study Phase Immunohistochemistry:	G.A. Parker, DVM, PhD, DACVP, DABT
Test Site:	WIL Biotechnics, LLC 310 Millstone Drive Hillsborough, NC 27278 / USA
Test Site QA:	WIL-Biotechnics, LLC 310 Millstone Drive Hillsborough, NC 27278 / USA Contact person: Jaimie West (Responsible for test site WIL-Biotechnics, LLC)

Schedule

Experimental Starting Date:	17-Dec-2009
Delivery of Animals:	17-Dec-2009
Acclimatization:	17 to 22-Dec-2009
Administration / Treatment:	23-Dec-2009 to 19-Jan-2010
Recovery:	20-Jan to 02 Feb-2010
Termination (Necropsy):	20-Jan-2010 and 03-Feb-2010
Experimental Completion Date:	20-Jul-2010

Accreditation

"Harlan Laboratories Ltd." is accredited as a test laboratory for analysis in the fields of clinical chemistry, hematology, blood-coagulation and urine diagnostics in accordance with the Standard ISO/IEC 17025 under accreditation number STS 085 by the Swiss Accreditation Service.

Data Requirements / Test Guidelines

The study procedures indicated in this report meet or exceed the requirements of the following guidelines:

- Commission Regulation (EC) No 440/2008 of 30 May 2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH), B. 7. "Repeated Dose (28 Days) Toxicity (Oral)", May 30, 2008.

- "Repeated Dose 28-Day Oral Toxicity Study in Rodents", OECD Guidelines for the Testing of Chemicals, Section 4, Health Effects, Number 407, October 3, 2008.

- Japanese Guidelines for Screening Toxicity Testing of Chemicals: Testing Methods for New Substances, enacted July 13, 1974, amended December 5, 1986

Animal Welfare

This study was performed in an AAALAC-accredited laboratory in accordance with the Swiss Animal Protection Law under license no. 35.

Archiving

Harlan Laboratories Ltd. (4452 Itingen / Switzerland) will retain the study plan, raw data, sample of test item(s), specimens (as long as the quality permits evaluation), and the final report of the present study for at least ten years.

All raw data generated by the Principal Investigators will be archived at their own facilities for the duration specified above (ten years). Insofar as the test site is recognized as GLP-compliant, the test site management is responsible for archiving the raw data, although Harlan Laboratories reserves the right to conduct GLP inspections of archived data pertaining to this study.

However, the pathology raw data and the final pathology phase report will be archived at Harlan Laboratories Ltd. for at least ten years.

No data will be discarded without the Sponsor's written consent.

If taken, frozen samples stored at Harlan Laboratories will be discarded after the final report has been issued.

1 SUMMARY

General

In this subacute toxicity study, Octamethyltrisiloxane (L3) was administered daily by oral gavage to SPF-bred Sprague Dawley rats of both sexes at dose levels of 5, 25, 250 and 1000 mg/kg body weight/day for a period of 28 days. A control group was treated similarly with the vehicle, dried and deacidified corn oil, only.

The groups comprised 5 animals per sex which were terminated after 28 days of treatment. Additional 5 rats per sex and group were used at 0 and 1000 mg/kg. These animals were treated for 28 days and then allowed a 14-day treatment-free recovery period after which they were terminated.

Clinical signs, outside cage observation, food consumption and body weights were recorded periodically during the acclimatization, treatment and recovery periods. Functional observational battery, locomotor activity and grip strength were assessed during week 4.

At the end of the dosing and the treatment-free recovery period, blood samples were withdrawn for hematology and plasma chemistry analyses. Urine samples were collected for urinalyses. All animals were killed, necropsied and examined post mortem. Histological examinations were performed on organs and tissues from all control and high dose animals, and all gross lesions from all animals.

From the animals of the low and middle dose groups, liver and thyroids of both sexes and the kidney and adrenal glands of males were examined to establish a no-effect level.

Mortality / Viability

All animals survived until scheduled necropsy.

Clinical Signs (Daily and Weekly)

No test item-related findings were noted at the daily observation and no abnormalities were recorded at the weekly behavioral observations in all animals at any dose level.

Functional Observational Battery

No findings were evident during the functional observation battery performed during week 4 of treatment.

Grip Strength

No test item-related differences compared to the control group were recorded in the grip strength of male and female animals at any dose level.

Locomotor Activity

There were no test item-related effects on the locomotor activity observed in male and female animals of all groups.

Food Consumption

No test item-related difference in the mean daily food consumption was noted at any dose level.

Body Weights

A test item related reduction in the body weight / body weight gain compared to the control animals was recorded in males at 1000 mg/kg/day at the end of the treatment period. This finding was not accompanied by any change in food consumption. During recovery, a significant compensatory increase in the body weight gain was noted in males at 1000 mg/kg/day.

Females had similar body weights and body weight gain during treatment, and a slight increase in body weight development during the recovery period.

Vaginal Smear for Estrus Stage

No special findings were noted concerning the estrous stage of the female animals.

Clinical Laboratory Investigations

Hematology

After the four-week treatment phase, test item related findings were noted in males at 1000 mg/kg/day. These included increased number of red blood cells and decreased mean corpuscular volume and mean corpuscular hemoglobin (with normal mean corpuscular hemoglobin concentration). Although the differences in mean corpuscular volume and mean corpuscular hemoglobin persisted at the end of the recovery period, the red blood cell count did not attain statistical significance, but was still considered to be relevant. However, the lack of statistical significance was due to a single outlier and the smaller sample size.

Additionally, the mean corpuscular hemoglobin was also below the control levels in female animals at 1000 mg/kg/day. The reticulocyte maturity index showed a higher fraction of mature cells (low fluorescence reticulocytes) and a reduced fraction of immature (middle and high fluorescence reticulocytes) only in males. In the differential white blood cell count, the relative and absolute number of eosinophils was below the control level. Significant changes of these parameters were no longer evident after the recovery period.

Further significant changes noted in the hematology parameters in male and female animals were within the historical control data for animals of this strain, sex and age, based on outliers or due to statistical method and, therefore, considered not to be treatment-related.

Clinical Biochemistry

After four weeks of treatment, several statistically significant test item-related effects which existed outside the historical data range were noted in the clinical biochemistry parameters.

Changes in liver-associated enzymes noted in males at 1000 mg/kg/day included increased mean activities for aspartate aminotransferase, alanine aminotransferase and gamma glutamyltransferase. Females of the same dose level were unaffected.

Total cholesterol and phospholipid levels were elevated in males at 250 mg/kg/day and in males and females at 1000 mg/kg/day. Triglyceride level was increased only in the females at 1000 mg/kg/day and persisted decreasing in severity up to end of the recovery period. The mean total bilirubin level was increased in males at 250 and 1000 mg/kg/day.

Significantly elevated sodium and chloride serum levels were evident in males at 1000 mg/kg/day after four weeks of treatment. An increase in serum potassium was noted in males at 25, 250 and 1000 mg/kg/day and persisted with slightly decreased severity up to the end of the 2 week recovery period. In females at 1000 mg/kg/day, the mean serum potassium level was also increased after four weeks of treatment; this did not persist until the end of the two-week recovery.

Phosphorous level was lower than the control level in males at 250 mg/kg/day and in males and females at 1000 mg/kg/day. However, the values of the females were still within the historical data.

Urinalysis

Mean urine volume was significantly increased in males at 1000 mg/kg/day and relative density was decreased in the same animals when compared to the control group. However, these values were within the range of historical data and did not appear in the females of the same dose group. Nevertheless, this effect is considered to be relevant due to the combination with changes in serum electrolyte levels (see Clinical Biochemistry) and microscopic changes.

Thyroid Hormone Determination

No analysis of the thyroid hormone levels was performed, as there were neither alterations in the organ weights nor macroscopic or microscopic changes in the thyroid.

Organ Weights

Test item-related increased mean liver weights and/or mean liver/body weight and liver/brain weight ratios were recorded in male animals at 25 mg/kg/day, in both sexes at 250 mg/kg/day and in both sexes at 1000 mg/kg/day after four weeks of treatment.

After the additional two-week recovery, elevated mean liver/body weight and liver/brain weight ratios persisted with decreased severity in males treated previously with 1000 mg/kg/day. In the

corresponding females, a higher mean liver/body weight ratio was also noted (severity also decreased).

Macroscopic / Microscopic Findings

Macroscopic findings included test item related enlargement and dark or black brown discoloration of the liver in males at 250 mg/kg/day and in males/females at 1000 mg/kg/day at necropsy after four weeks of treatment. Discoloration of the liver persisted in all males at 1000 mg/kg/day (same incidence) until the end of the recovery period.

Microscopically, the following test item-related findings were recorded:

1. Protoporphyrin accumulation in the intra-hepatic bile ducts was recorded at minimal to moderate severity in animals of both sexes at 1000 mg/kg/day and in males at 250 mg/kg/day after the treatment period. Protoporphyrin accumulation in Kupffer cells and in hepatocytes was also recorded in males at 250 mg/kg/day and 1000 mg/kg/day after the end of treatment. This pigment was characterized by birefringent, bright red appearance with dark Maltese cross in each deposit affected under polarized light.

2. Periportal chronic inflammation and bile duct proliferation at minimal to slight severity were recorded in both sexes at 1000 mg/kg/day and males at 250 mg/kg/day at the end of the four week treatment period. These lesions were associated with the above mentioned protoporphyrin accumulation and were considered to be a secondary reaction.

3. Centrilobular hepatocellular hypertrophy was recorded at minimal severity in both sexes at 1000 mg/kg/day and in males at 250 mg/kg/day at the end of the treatment period. This lesion was considered to be of a metabolic nature and of adaptive character.

4. Follicular cell hypertrophy of the thyroid gland at minimal severity was recorded in two males and in one female at 1000 mg/kg/day at the end of treatment. Centrilobular hepatocellular hypertrophy was also recorded in this case and a possible relationship between the liver enzyme-induction and the follicular cell hypertrophy was considered.

5. Hyaline droplets of the kidney were recorded at minimal severity in males at 25 mg/kg/day and at minimal to slight severity in males at 250 mg/kg/day and 1000 mg/kg/day at the end of the treatment period. The increased incidence and severity of this lesion in groups 4 and 5 was considered to be induced by test item. By contrast, minimal degrees of hyaline droplets recorded at 25 mg/kg/day were considered to be most likely incidental since they may occur also spontaneously (see also Pathology Report).

The liver findings correlated with significantly increased absolute weight of the liver and with gross lesions consisting of enlargement and discoloration. The exact pathogenesis of the protoporphyrin accumulation was not clear.

After a 14-day recovery period, protoporphyrin accumulation was still present with same incidence and severity in males and increased incidence but decreased severity in females compared to the end of the treatment phase. Periportal chronic inflammation in both sexes and bile duct proliferation in males showed the same incidence and severity after the recovery period. The hepatocellular hypertrophy, follicular cell hypertrophy of the thyroid gland and hyaline deposits of the male kidneys showed complete regression after the 14-day treatment-free recovery period.

Immunohistochemistry

Although higher mean levels of α-2μ globulin of the globular staining pattern in the kidneys of test item-treated male rats are generally indicative of a test article-related effect, the highest level of α-2μ globulin staining was noted at 250 mg/kg/day group rather than at 1000 mg/kg/day group). The globular staining pattern may be interpreted as a pathologic accumulation of alpha-2μ-globulin in the kidney, which was seen as hyaline droplet accumulation/degeneration in routinely stained kidney sections. Slight staining of the globular pattern in control male rats from the recovery group was interpreted as an early manifestation of spontaneous nephropathy of laboratory rats, which is known to include an element of hyaline droplet accumulation.

The punctate staining pattern was interpreted as the normal physiologic processing of alpha-2μ-globulin in the kidney.

Conclusion

Based on the findings in the liver (protoporphyrin accumulation accompanied by periportal chronic inflammation and bile duct proliferation), it can be concluded that males were more affected than the females by treatment with Octamethyltrisiloxane (L3). In the absence of clear reversibility of microscopic liver findings, the NOAEL of the test item was considered to be 25 mg/kg/day in the males and 250 mg/kg/day in the females.

2 PURPOSE

The purpose of this oral toxicity study was to assess the cumulative toxicity of Octamethyltrisiloxane (L3) when administered daily to rats by gavage for a period of 28 days.

The reversibility of treatment-related changes was assessed after a treatment-free 14-day recovery period.

3 MATERIALS AND METHODS

General Remark

Details of the materials and methods that are not specified in the subsequent sections of this report are contained in the appropriate standard operating procedures.

3.1 Test System

Animals:	Rat, Hsd:Sprague Dawley®™SD®™ (outbred rats)
Rationale:	Recognized by international guidelines as a recommended test system.
Breeder:	Harlan Laboratories, B.V. PO Box 553 5800 AN VENRAY / Netherlands
Number of Animals:	Group 1: 10 males and 10 females Group 2: 5 males and 5 females Group 3: 5 males and 5 females Group 4: 5 males and 5 females Group 5: 10 males and 10 females Reserve animals: Group 10: 1 male and 1 female
Age (at Delivery):	Approximately 7 weeks
Body Weight Range (at Acclimatization):	Males: 196 to 220 g (mean 207 g) Females: 152 to 183 g (mean 165 g)
Identification:	Acclimatization: Cage card and tail mark (later ear tattoo) Treatment: Cage card and individual ear tattoo
Randomization:	Randomly allocated to groups by body weight.
Acclimatization:	Under test conditions after health examination. Only animals without any visible signs of illness were used for the study.

3.2 Allocation

The group identification and animal numbers assigned to treatment are stated in the following table:

Allocation and Dose Levels in mg/kg/day		Group 1 Control* 0	Group 2 5	Group 3 25	Group 4 250	Group 5 1000	Group 10 Reserve Animals**
Males	**A**	01 - 05	11 - 15	16 - 20	21 - 25	26 - 30	100
	B	06 - 10				31 - 35	
Females	**A**	36 - 40	46 - 50	51 - 55	56 - 60	61 - 65	101
	B	41 - 45				66 - 70	

* Control animals were treated with the vehicle only

** Reserve animals were not needed and, therefore, removed from the study. Any raw data collected during the acclimatization period on reserve animals are not reported but retained in the raw data.

A Toxicity testing (termination after 28 treatment days)

B Recovery testing (termination after an additional 14-day recovery period)

3.3 Husbandry

Room Numbers, Itingen: Room no. 136

Conditions: Standard laboratory conditions. Air-conditioned with 10 - 15 air changes per hour, continuously monitored environmental conditions (temp. range: 22 ± 3 °C; relative humidity range: 30 - 70%). Values outside of these ranges occasionally occurred, usually following room cleaning, and are considered not to have any influence on the study. Therefore, these data are not reported but are retained at Harlan Laboratories Ltd. There was 12-hour fluorescent light/12-hour dark cycle with music during the light period.

Accommodation: In groups of five in Makrolon type-4 cages with wire mesh tops and standard softwood bedding ('Lignocel' J. Rettenmaier & Söhne GmbH & Co. KG, 73494 Rosenberg / Germany, imported by Provimi Kliba AG, 4303 Kaiseraugst / Switzerland).

Diet:	Pelleted standard (batch nos. 58/09 and 82/09) rat / mouse maintenance diet (Provimi Kliba AG, 4303 Kaiseraugst / Switzerland) was available *ad libitum*. The feed batches were analyzed for contaminants. Results of respective analyses for contaminants are included in Appendix I on p. 401 .
Water:	Community tap-water from Itingen was available *ad libitum* in water bottles. Results of bacteriological assay, chemical and contaminant analyses of respective samples are included in Appendix II on p. 407 .

3.4 Test Item / Vehicle

3.4.1 Test Item

Data as supplied by the Supplier (certificate of analysis see in Appendix III on p. 411).

Identification:	Octamethyltrisiloxane (L3)
Description:	Colorless liquid
Source:	Sigma-Aldrich Gmbh Industriestrasse 25 9479 Buchs / Switzerland
CAS Number:	107-51-7
Batch/Lot Number:	14110CD
Purity:	99.9% (GC)
Stability:	Stable under storage conditions.
Expiry Date:	11-Jun-2010
Storage Conditions:	At room temperature (15 - 25 °C) away from direct sunlight
Safety Precautions:	Routine hygienic procedures (gloves, goggles, face mask).
Analytical Standard:	Octamethyltrisiloxane (L3) (the test item served as its own analytical standard)

3.4.2 Vehicle and Control Item

Identification:	Corn oil (original)
Source:	Roth GmbH
Description:	Yellowish liquid
Batch Number:	049103168
Expiry Date::	28-Jan-2014
Storage Conditions:	At room temperature (15 - 25 °C) away from direct sunlight
Safety Precautions:	Routine hygienic procedures (gloves, goggles, face mask).

The corn oil was dried and deacidified as described in Section 3.5.1 (below). The following additional information refers to these vehicle preparations:

Identification:	Corn oil (dried and deacidified)
Expiry Date:	Six weeks after receipt 1) First preparation: receipt 07-Dec-2009 2) Second preparation: receipt 09-Dec-2009
Storage Conditions:	At room temperature (15 - 25 °C) away from direct sunlight

3.5 Dose Formulations

The test item was used as supplied by the Supplier. The purity was not corrected.

The dose formulations were prepared daily. Based upon the results of dose formulation analyses performed during a non-GLP dose range finding study (Harlan Laboratories study C53644), the stability of the test item formulations was considered to require daily preparation. These analyses were repeated under GLP for this study.

Octamethyltrisiloxane (L3) was weighed into a glass beaker on a tared Mettler balance and the vehicle was added to give the appropriate final concentration of the test item in the dose formulation. Each dose level was prepared individually. The mixtures were stirred using a magnetic stirrer and used at room temperature (20 ± 5 °C).

Homogeneity of the test item in the vehicle was maintained during the daily administration period using a magnetic stirrer.

3.5.1 Preparation of the Vehicle

For preparation of the dried, deacidified vehicle, corn oil was filtered through a mixture of activated silica gel and alumina (1:1, volume/volume), filled into a glass chromatography column (2.5 x 30 cm) to three quarters of its height. For filtering, a vacuum of 100 mbar was applied using a filtering bottle. The dried and deacidified vehicle was kept in a tightly sealed bottle in a desiccator under dry conditions until use.

3.5.2 Analysis of Dose Formulations

The analysis was performed by Harlan Laboratories Ltd. using a GC method provided by the Sponsor and previously adapted at Harlan Laboratories Ltd. (non-GLP range finding study, Harlan Laboratories study C53644).

After experimental start and during week 3, duplicate samples of the control group and three samples (top, middle and bottom) of about 2 g of each concentration were taken prior to dosing for analysis of homogeneity and concentration. Duplicate samples of about 2 g of each concentration were taken to confirm stability (4 hour; due to organizational reasons the samples were transferred to the analytical department approximately 4 ¼ hours after preparation).

The samples were delivered to the analytical department (Harlan Laboratories Ltd., Analytics, Itingen / Switzerland) and stored there at -20 ± 5 °C until analysis.

The test item was used as analytical standard.

Dose formulation samples (primary samples or duplicates) were discarded upon written confirmation by the study director after acceptance of the draft report.

The results of analysis were summarized in an appendix and attached to the report (see Appendix IV on p. 415).

3.6 Treatment

Method:	Oral, by gavage	
Rationale for Method:	Administration by gavage is a common and accepted route of exposure for studies of this type.	
Frequency of Administration:	Daily	
Daily Dose Levels:	Group 1:	0 mg/kg/day
	Group 2:	5 mg/kg/day
	Group 3:	25 mg/kg/day
	Group 4:	250 mg/kg/day
	Group 5:	1000 mg/kg/day

Rationale for Dose Level Selection:	The dose levels were selected based on a previous range finding toxicity study, Harlan Laboratories study C53644.	
Dose Volume:	5 mL/kg body weight	
Dose Concentrations:	Group 1:	0 mg/mL/day
	Group 2:	1 mg/mL/day
	Group 3:	5 mg/mL/day
	Group 4:	50 mg/mL/day
	Group 5:	200 mg/mL/day
Duration of Pre-Randomization Acclimatization Phase:	1 day	
Duration of Post-Randomization Acclimatization Phase:	5 days	
Duration of Treatment Phase:	28 days	
Duration of Recovery Phase:	14 days	

3.7 Phase Designation

Phase 1:	Acclimatization phase (pre-randomization)
Phase 2:	Acclimatization phase (post-randomization)
Phase 3:	Treatment phase
Phase 4	Recovery phase

3.8 Activities and Observations

3.8.1 Viability / Mortality

Observations for viability / mortality were recorded twice daily.

3.8.2 Daily Observations

The animals were observed for clinical signs once before initial dosing and daily on days 1 - 28 (twice daily during days 1 - 3) during the treatment period and once daily during days 1 to 14 of the recovery period.

3.8.3 Weekly Behavioral Observations

The animals were observed in their home cages, outside their home cages in a standard arena and in the hand. These observations were performed once before initial dosing and once weekly (weeks 1 to 3) during the treatment period.

SUMMARY OF PARAMETERS (MINIMUM REQUIREMENT FOR EACH ANIMAL)
OBSERVATIONS: DAILY (D), PRETEST (P), WEEKLY (W) AND FOB (F)

	SCORE	PARAMETER	D	P	W 1	W 2	W 3	F 4
APPEARANCE	1 - 3	Piloerection	X	X	X	X	X	X
	1 - 3	Salivation	X	X	X	X	X	X
	1	Hunched posture	X	X	X	X	X	X
MOTOR	1 - 3	Ataxia	X	X	X	X	X	X
	1 - 3	Tremor/twitching	X	X	X	X	X	X
	1	Prostration	X	X	X	X	X	X
	1	Circling		X	X	X	X	X
	1 - 3	Spasm		X	X	X	X	X
BEHAVIOR	1 - 3	Hyperactivity	X	X	X	X	X	X
	1 - 3	Somnolence	X	X	X	X	X	X
	1 - 3	Increased exploration		X	X	X	X	X
	1 - 3	Reduced grooming		X	X	X	X	X
	1 - 3	Vocalisation		X	X	X	X	X
RESPIRATION	1	Dyspnea	X	X	X	X	X	X
	1	Tachypnea	X	X	X	X	X	X
	1	Bradypnea	X	X	X	X	X	X
REFLEXES	1	Blink		X	X	X	X	X
	1	Pinna		X	X	X	X	X
	1	Iridic light reflex		X	X	X	X	X
	1	Push-off (hind leg)		X	X	X	X	X
	1	Pain response		X	X	X	X	X
	1	Startle/hearing		X	X	X	X	X
	1	Righting reflex		X	X	X	X	X
MISCELLANEOUS	1 - 3	Lacrimation		X	X	X	X	X
	1	Limbs cyanotic		X	X	X	X	X
	1	Mydriasis		X	X	X	X	X
	1	Miosis		X	X	X	X	X
	1	Exophthalmos		X	X	X	X	X
	1 - 3	Reduced muscle tone		X	X	X	X	X

NB: Findings that were detected during daily observation of the standard parameters were tracked throughout the study and progression/regression in the afflicted animal, and are listed in the tables. Parameters marked with 'X' were specifically observed for presence or absence.

3.8.4 Functional Observational Battery (Screen)

During week 4, relevant parameters (presented in Section 3.8.3) from a modified Irwin screen test were evaluated in all animals. The results are present in the summary and individual tables of the weekly detailed behavioral observations under week 4.

Grip Strength

Forelimb and hindlimb grip strength measurements were performed using a push-pull strain gauge (Mecmesin, AFG 25N). The animals were placed with the forepaws inside a triangular grasping ring and with the hind paws outside a triangular grasping ring. Using one hand, the animals were held towards the base of the tail and steadily pulled away or towards the ring until the grip was broken. Each measurement was repeated three times; the means were calculated and recorded.

Locomotor Activity

Locomotor (decreased or increased) activity was measured quantitatively with AMS Föhr Medical Instruments GmbH (FMI) and DeMeTec GmbH Activity Monitor System. Animals were monitored during the fourth treatment week for a 60-minute period and the total activity of this time period was recorded.

Low beams count was reported in 10-minute intervals and the total activity of the measuring period.

3.8.5 Food Consumption

The food consumption was recorded once during the acclimatization period and weekly thereafter, using an on-line electronic recording system consisting of a Mettler balance connected to the Harlan Laboratories computer.

3.8.6 Body Weights

Body weights were recorded weekly during acclimatization, treatment and recovery periods and before necropsy, using an on-line electronic recording system consisting of a Mettler balance connected to the Harlan Laboratories computer.

3.9 Vaginal Smear for Estrus Stage

Vaginal smears were taken over four days from all females, and the stage of estrus was evaluated.

During Week 4: 12-Jan-2010 to 15-Jan-2010

3.10 Clinical Laboratory Investigations

Blood and Urine Sampling:

After 4 Weeks:	20-Jan-2010 (satellite A and B)
After 6 Weeks (Recovery):	03-Feb-2010 (satellite B)

Blood samples were drawn from the retro-orbital plexus from all animals under light isoflurane anesthesia. The animals were fasted in metabolism cages for approximately 18 hours before blood sampling but allowed access to water *ad libitum*. The samples were collected early in the working day to reduce biological variation caused by circadian rhythms. Blood samples were drawn from the retro-orbital plexus using a micro-hematocrit glass capillary tube.

Urine was collected during the 18 hours fasting period into a specimen vial, using a metabolism cage.

In the summary and individual tables the names of some parameters have been abbreviated.

Detailed methodology, abbreviations and general remarks are described in Appendix V on p. 426 .

Clinical laboratory data are expressed, with a few exceptions, in general accordance with the International System of Units (SI).

3.10.1 Hematology

The following hematology parameters were determined:

Complete Blood Cell Count

Erythrocyte count
Hemoglobin
Hematocrit
Mean corpuscular volume
Red cell volume distribution width
Mean corpuscular hemoglobin
Mean corpuscular hemoglobin concentration
Hemoglobin concentration distribution width
Reticulocyte count
Reticulocyte maturity index (low, medium, high fluorescence)

Leukocyte count, total
Differential leukocyte count:
Neutrophils
Eosinophils
Basophils
Lymphocytes
Monocytes
Large unstained cells
Platelet count

Hemoglobin Derivatives

Methemoglobin
Heinz bodies

Coagulation

Prothrombin time (= Thromboplastin time)
Activated partial Thromboplastin time

3.10.2 Clinical Biochemistry

The following clinical biochemistry parameters were determined:

Glucose
Urea
Creatinine
Bilirubin, total
Cholesterol, total
Triglycerides
Phospholipids
Aspartate aminotransferase
Alanine aminotransferase
Lactate dehydrogenase
Alkaline phosphatase
Bile acids
Gamma-glutamyl-transferase
Creatine kinase
Sodium
Potassium
Chloride
Calcium
Phosphorus, inorganic
Protein, total
Albumin
Globulin
Albumin/Globulin ratio

3.10.3 Urinalysis

The following urine parameters were determined:

Physical Examination

Urine volume (18 hour)
Specific gravity (relative density)
Color
Appearance

Chemical Examination

pH value
Nitrite
Protein
Glucose
Ketones
Urobilinogen
Bilirubin
Erythrocytes
Leukocytes

3.11 Thyroid Hormone Determination

No analysis of the thyroid hormones (T3, T4 and TSH) was performed.

3.12 Pathology

3.12.1 Necropsy

Sacrifice:

After 4 Weeks: 20-Jan-2010 (satellite A)
After 6 Weeks (Recovery): 03-Feb-2010 (satellite B)

All satellite A and B animals were weighed and necropsied. Descriptions of all macroscopic abnormalities were recorded. All animals were anesthetized by intraperitoneal injection of pentobarbitone and killed by exsanguination.

Blood samples were taken by heart puncture for possible determination of thyroid hormones but no analysis was performed (see Section 3.11).

Samples of the following tissues and organs were collected from all animals at necropsy and fixed in neutral phosphate buffered 4% formaldehyde solution unless indicated otherwise.

Tissues / Organs	Weight	Collect	Examine
Adrenal glands	X	X	X
Aorta		X	
Bone (sternum, femur including joint)		X	
Bone marrow (femur)		X	X
Brain - including section of medulla/pons, cerebral and cerebellar cortex	X	X	X
Cecum		X	X
Colon		X	X
Duodenum		X	X
Epididymides (fixed in Bouin's solution)	X	X	X
Esophagus		X	
Eyes w/optic nerve (fixed in Davidson's solution)		X	
Harderian gland (fixed in Davidson's solution)		X	
Heart including auricles	X	X	X
Ileum, with Peyer's patches		X	X
Jejunum with Peyer's patches		X	X

Tissues / Organs	Weight	Collect	Examine
Kidneys	X	X	X
Larynx		X	
Lacrimal gland, exorbital		X	
Liver	X	X	X
Lungs, filled w/formalin at necropsy		X	X
Lymph nodes – mesenteric and mandibular		X	X
Mammary gland area		X	
Nasal cavity		X	
Ovaries	X	X	X
Pancreas		X	
Pharynx		X	
Pituitary gland	X	X	X
Seminal vesicles and Prostate gland (incl. coagulating glands)	X	X	X
Rectum		X	X
Salivary glands - mandibular, sublingual		X	
Sciatic nerve		X	X
Skeletal muscle		X	
Skin		X	
Spinal cord - cervical, midthoracic, lumbar		X	X
Spleen	X	X	X
Stomach		X	X
Testes (fixed in Bouin's solution)	X	X	X
Thymus	X	X	X
Thyroid (incl. parathyroid gland)	X	X	X
Tongue		X	
Trachea		X	X
Urinary bladder, filled w/formalin at necropsy		X	X
Uterus, with cervix	X	X	X
Vagina		X	X
All gross lesions		X	X

Samples of the kidneys (100 - 300 mg) were transferred to 70% ethanol within 48 hours, after initial fixation.

3.12.2 Organ Weights

The organs from satellite A and B animals listed in the table in Section 3.12.1 were weighed before fixation and recorded on the scheduled dates of necropsy. Relative organ weights were calculated on the basis of the body weight and brain weight.

The terminal body weight was recorded immediately prior to necropsy and the organ to terminal body weight ratios and organ to brain weight ratios were determined.

3.12.3 Histotechnique

All organ and tissue samples, as defined under Histopathology (see Section 3.12.4), were processed, embedded and cut at an approximate thickness of 2 to 4 micrometers and stained with hematoxylin and eosin.

Kidney samples (from both sexes) in 70% ethanol were histologically processed without further aldehyde fixative exposure and embedded in paraffin. Paraffin blocks were sent to the Principal Investigator of the Immunohistochemistry Study Phase for the determination of possible alpha-2u globulin accumulation in the kidney. Immunohistochemical evaluation was conducted at:

WIL-Biotechnics, LLC,
310 Millstone Drive,
Hillsborough, NC 27278 / USA

3.12.4 Histopathology

Slides of all organs and tissues listed in the table in Section 3.12.1 collected at scheduled sacrifices from all animals of the control and high-dose groups and all gross lesions from all animals were examined by the study pathologist.

Because of possible test item-related findings noted in the high dose group, the liver and thyroid of both sexes, the kidneys and adrenal gland glands of males were examined also in the animals of groups 2, 3 and 4.

A description of all abnormalities is included (see Appendix VI on p. 445). Attempts were made to correlate gross observations with microscopic findings.

A peer review was performed by Dr. T. Razinger. The findings of the study pathologist and the peer-reviewing pathologist compared favorably. The peer review report is retained in the raw data.

3.13 Data Compilation

The ToxControl computer was used to sort and present data for inclusion in the report. All electronically recorded data are conserved on a magnetic medium.

Individual values were rounded before printing. All derived values that appear in the tables represent the rounded results of calculations that used the exact raw data value.

Locomotor activity was recorded on-line, and the results were printed and transcribed into the computer system for compilation and analysis. Grip strength values were recorded on data sheets and then transcribed into the computer system for compilation and analysis.

Estrus stage and urinalysis parameters were also recorded on data sheets and transcribed into the computer system.

Severity grades for clinical symptoms were generally assigned as follows: 0 = not present, 1 = present / slight, 2 = moderate, 3 = marked.

3.14 Statistical Analysis

The following statistical methods were used to analyze body weight, grip strength, locomotor activity, clinical laboratory data, organ weights and ratios and macroscopic findings:

- The Dunnett-test [see References (1)] (many to one t-test) based on a pooled variance estimate was applied if the variables could be assumed to follow a normal distribution for the comparison of the treated groups and the control groups for each sex.

- The Steel-test [see References (2)] (many-one rank test) was applied instead of the Dunnett-test when the data could not be assumed to follow a normal distribution.

- Fisher's exact-test [see References (3)].

4 RESULTS

4.1 Analysis of Dose Formulations

(See Appendix IV on p. 415)

The linearity of the analytical system used for sample analyses was demonstrated with a good relationship between peak areas measured and working standard concentrations. All calibration points used met the acceptance limit of ±20% variation from the calibration curve derived by linear regression analysis. The regression coefficients calculated were found to exceed 0.99.

The Octamethyltrisiloxane (L3) peak was assigned in sample chromatograms by comparison to that of working standards. In blank sample chromatograms, no peak appeared at the retention time of Octamethyltrisiloxane (L3) and, therefore, it was confirmed that only dried, deacidified corn oil was administered in the control part of the experiment.

The application formulations investigated during the study were found to consist of Octamethyltrisiloxane (L3) in the range of 80.2% to 106.9%, meeting the required content limit of ±20% with reference to the nominal concentration.

As single results did not deviate more than 14.5% (<15%) from the corresponding mean, the test item solutions were considered to be homogeneous.

In addition, the test item was found to be stable in application formulations when kept 4 hours at room temperature, as demonstrated by recoveries which met the variation limit of 10% from the time-zero (homogeneity) mean.

In conclusion, the results indicate the accurate use of the test item Octamethyltrisiloxane (L3) and dried, deacidified corn oil as vehicle during this study. Application formulations were found to be homogeneously prepared and sufficiently stability under storage conditions.

4.2 Observations

4.2.1 Viability / Mortality

(See Individual Tables on p. 199)

All animals survived until scheduled necropsy.

4.2.2 Daily Observations

(See Summary Tables on p. 62 , Individual Tables on p. 210)

No test item related findings were noted in males and females at any dose level.

There were no clinical signs noted in any female animals at any dose level.

In three male animals at 1000 mg/kg/day, clinical signs were noted during the treatment phase. In animal no. 28, hunched posture and slight visible body weight loss from day 20 onwards as well as slightly ruffled fur at day 14 and again from day 22 to the end of observation time were observed. Slight dyspnea was recorded at days 13 and 14 and again from day 19 to 25. Furthermore, slight salivation was observed from day 19 to 22.

Slight salivation was also noted in animal no. 30 from day 18 to 20.

In animal no. 35, slight to moderate hair loss was observed in the right axillary region from day 10 to the end of observation.

These findings are considered to be typical background findings.

4.2.3 Weekly Behavioral Observations

(See Summary Tables on p. 69 , Individual Tables on p. 218)

There were no abnormalities recorded in any animal at any dose level.

4.2.4 Functional Observational Battery (Screen)

No findings were evident during the functional observation battery performed during week 4 of treatment.

Grip Strength

(See Summary Tables on p. 74 , Individual Tables on p. 223)

No test item-related differences compared to the control group were recorded in the mean forelimb or hindlimb grip strength values of male and female animals at any dose level.

The mean grip strength was significantly reduced ($p<0.05$) in females at 5 mg/kg/day. As there were no significant differences in the higher dose groups compared to the control, this finding is considered to be incidental.

Locomotor Activity

(See Summary Tables on p. 79 , Individual Tables on p. 234)

No test item-related effects on the locomotor activity were observed.

When compared to the control group, significantly reduced locomotor activity was recorded in males at 1000 mg/kg/day at 20 - 30 minutes ($p<0.05$), 30 - 40 minutes ($p<0.01$) and 40 - 50 minutes ($p<0.05$). In females of this dose level, significantly increased locomotor activity was noted at 0-10 minutes ($p<0.05$) and 40-50 minutes ($p<0.05$). These differences are considered to be within the normal range of variability.

4.2.5 Food Consumption

(See Figures on p. 49 , Summary Tables on p. 88 , Individual Tables on p. 245)

No test item-related difference in the mean daily food consumption was noted at any dose level.

Changes in mean food consumption were noted in male and female animals at 1000 mg/kg/day. The food consumption was increased in these animals during treatment days 22 - 28 and during the recovery period when compared to the control groups.

4.2.6 Body Weights

(See Figures on p. 55 , Summary Tables on p. 98 , Individual Tables on p. 267)

A test item-related reduction in the body weight was recorded in males at 1000 mg/kg/day when compared to the control animals.

The mean body weight in these males was significantly lower on day 8 (-9%), day 15 (-11%), day 22 (-14%) and day 28 (-11%) of the treatment phase (all $p<0.01$) as well as day 1 (-15%), day 8 (-11%; both $p<0.01$) and day 14 (-9%; $p<0.05$) of the recovery period compared to the control group. In addition, the mean body weight gain was significantly reduced in the same animals on days 8, 15, 22 and 28 of treatment ($p<0.01$), but was increased compared to the control animals during recovery (day 8; $p<0.05$). This was considered to be a compensatory reaction.

Increased mean body weight gain compared to control was noted during recovery in females at 1000 mg/kg/day (day 14; $p<0.01$).

4.2.7 Vaginal Smear for Estrous Stage

(See Individual Tables on p. 289)

No abnormal findings were noted in the estrous stage evaluation of the female animals at any dose level.

4.3 Clinical Laboratory Investigations

4.3.1 Hematology

(See Summary Tables on p. 112 , Individual Tables on p. 294)

After the four-week treatment phase, test item related and statistically significant changes were noted in males at 1000 mg/kg/day. These included increased number of red blood cells as well as decreased mean corpuscular volume and mean cell hemoglobin (with normal mean cell hemoglobin concentration).

The decrease in MCV and MCH persisted at the end of the recovery period.

Although the red blood cell count was not significantly different from control at the end of the recovery, it was still much higher at this time point compared to the control animals and even to the data at the end of the treatment phase. Therefore, it is considered to be relevant although not statistically significant. However, the lack of statistical significance was due to a single outlier and the smaller sample size.

Mean corpuscular hemoglobin level was below the control levels in the female animals at 1000 mg/kg/day.

The reticulocyte maturity index showed a higher fraction of mature (low fluorescence reticulocytes) and reduced fraction of immature (middle fluorescence and high fluorescence reticulocytes) cells only in males. In the differential white blood cell count, the relative and absolute number of eosinophils was below the control level. Significant changes of these parameters were no longer evident after the 2-week recovery period.

Other significant changes (see below) noted in the hematology parameters in male and female animals are within the historical control data for animals of this strain, sex and age, based on outliers or due to statistical method and, therefore, considered not to be test item-related.

Within the normal range of variability were reduced relative lymphocyte count ($p<0.05$), increased number of neutrophils ($p<0.05$) and platelets ($p<0.01$), increased hemoglobin distribution width ($p<0.01$) in male animals at 1000 mg/kg/day as well as decreased hemoglobin and hematocrit (both $p<0.05$) in males at 250 mg/kg/day. In females, red blood cells ($p<0.05$) and hematocrit ($p<0.01$) were reduced at 5 mg/kg/day and reduced red cell distribution width

($p<0.05$) and mean corpuscular hemoglobin concentration ($p<0.05$) were noted at 1000 mg/kg/day, but also within the range of historical data.

The mean relative methemoglobin level was the same in males at 250 mg/kg/day and 1000 mg/kg/day, but is mentioned significantly different the latter group due to the rounding difference during calculation. This parameter was also within the historical data range.

The mean thromboplastin time was significantly lower in males at 250 mg/kg/day and at 1000 mg/kg/day and in females at 25 mg/kg/day and 1000 mg/kg/day (but not at 250 mg/kg/day) when compared with the control animals. As the control values exceed the range of historical data, the statistical differences were considered to be artifacts.

4.3.2 Clinical Biochemistry

(See Summary Tables on p. 126 , Individual Tables on p. 324)

After four weeks of treatment, several test item-related effects were noted in the clinical biochemistry parameters.

Test item-related changes in liver-associated enzymes noted in males at 1000 mg/kg/day included significantly increased mean activities of aspartate aminotransferase ($p<0.05$), alanine aminotransferase ($p<0.05$) and gamma glutamyltransferase ($p<0.01$). Females of the same dose level were unaffected.

Total cholesterol and phospholipid levels were significantly elevated ($p<0.01$) in males at 250 mg/kg/day and in both sexes at 1000 mg/kg/day. Triglyceride level was increased ($p<0.01$) only in females at 1000 mg/kg/day and this difference persisted until the end of the recovery period ($p<0.05$).

Mean total bilirubin level was increased ($p<0.01$) in males at 250 mg/kg/day and 1000 mg/kg/day. In females, a significant increase was noted only at 250 mg/kg/day ($p<0.01$). As no effect was noted in females at 1000 mg/kg/day, this was considered to be not test item-related.

An increase in glucose level was noted in males and females at 5 mg/kg/day, males at 25 mg/kg/day and females at 250 and 1000 mg/kg/day when compared to the controls but was within the range of historical data for animals of this strain, sex and age and considered to be not related to treatment.

Significant changes in protein parameters noted in males and females at 250 mg/kg/day and/or 1000 mg/kg/day included increased total protein and globulin, and decreased albumin and albumin/globulin ratio. However, with exception of higher globulin and lower albumin/globulin ratio in males at 1000 mg/kg/day, all changes were within the historical data range and considered not to be test item-related.

Significantly elevated sodium and chloride serum levels were evident in males at 1000 mg/kg/day ($p<0.01$) after four weeks of treatment. An increase in serum potassium was noted in males at 25 mg/kg/day ($p<0.05$), 250 mg/kg/day ($p<0.05$) and 1000 mg/kg/day ($p<0.01$). In females at 1000 mg/kg/day, mean serum potassium level was also significantly increased after four weeks of treatment but did not persist after the recovery period. Phosphorous level was lower than control level in males at 250 mg/kg/day ($p<0.05$) as well as males and females at 1000 mg/kg/day ($p<0.05$ and $p<0.01$, resp.). However, the values in females were still within the historical data.

Further significant changes in females included increased sodium and chloride at 25 mg/kg/day and decreased calcium at 5 mg/kg/day, all within the range of the historical data and considered not to be test item-related.

After two weeks of recovery, several significant differences were noted: significantly higher potassium persisted in males ($p<0.05$) when compared with the control values. Although the triglyceride level remained significantly higher in females ($p<0.05$) when compared with the control value, it was markedly lower than at the end of the treatment period and most likely caused by a low control value. Decreased bile acid ($p<0.01$), decreased mean activity of alanine aminotransferase ($p<0.01$) and decreased mean activity of alkaline phosphatase ($p<0.05$) in males as well as decreased albumin levels in females ($p<0.05$) were noted. These differences were either within the range of the historical control data, or considered to be of no toxicological relevance.

4.3.3 Urinalysis

(See Summary Tables on p. 136 , Individual Tables on p. 344)

Mean urine volume was significantly increased in males at 1000 mg/kg/day ($p<0.01$) and the relative density was decreased in the same animals after four weeks of treatment when compared to the control group. However, these values are within the range of historical data and do not appear in females of the same dose group. Nevertheless, this effect was considered to be toxicologically relevant (but not adverse) due to the combination with changes in serum electrolyte levels (see Clinical Biochemistry) and microscopic changes.

The significant decrease in protein noted in males at 1000 mg/kg/day ($p<0.05$) was in the range of historical data. The ketones were also significantly decreased at 1000 mg/kg/day ($p<0.01$) with control levels above the historical data range. The urine pH in females at 1000 mg/kg/day was significantly different from control. Although the pH values appear identical in females at 25 and 1000 mg/kg/day, the statistical significance resulted from a rounding difference and different numbers of animals ($n = 5$ in group 2 versus $n = 10$ in group 4). In all cases, the exact raw data values were used for statistical analysis, but are rounded for printing. Therefore, the statistical significance of this parameter was considered to be an artifact.

4.4 Thyroid Hormone Analysis

No analysis of the thyroid hormone levels was performed, as there were neither alterations in the organ weights nor macroscopic or microscopic changes indicating such investigation.

4.5 Pathology

4.5.1 Organ Weights

(See Summary Tables on p. 141 , Individual Tables on p. 359)

Test item-related increases in mean absolute and relative liver weights were recorded in male animals at 25 mg/kg/day, 250 mg/kg/day and/or 1000 mg/kg/day and in females at 250 mg/kg/day and 1000 mg/kg/day after four weeks of treatment.

Mean absolute liver weights were significantly elevated in males at 250 and 1000 mg/kg/day (+56% for both groups) and in females at 1000 mg/kg/day (+37%; all $p<0.01$). The mean liver/body weight ratio was significantly increased in males at 25 mg/kg/day (+12%; $p<0.05$), 250 mg/kg/day (+52%; $p<0.01$) and 1000 mg/kg/day (+78%; $p<0.01$) and in females at 250 mg/kg/day (+12%; $p<0.05$) and 1000 mg/kg/day (+45%; $p<0.01$). Furthermore, the mean liver/brain weight ratio was significantly higher in males at 250 mg/kg/day (+57%; $p<0.01$) and 1000 mg/kg/day (+62%; $p<0.01$), and in females at 1000 mg/kg/day (44%; $p<0.01$).

Reduced mean absolute weights of the heart (-16%) and pituitary gland (-18%) were noted in males at 1000 mg/kg/day ($p<0.05$).

Elevated mean kidney/body weight ratio ($p<0.01$) was recorded in male animals at 1000 mg/kg/day. Significantly reduced mean heart/brain weight ratio ($p<0.05$) was noted in males at 1000 mg/kg/day.

Significantly decreased mean absolute brain weights were recorded in female animals at 250 mg/kg/day (-4%; $p<0.05$) and at 1000 mg/kg/day (-4%; $p<0.01$).

After two weeks of recovery, significantly lower mean absolute brain weights (-5%; $p<0.01$), lower combined absolute mean weights of the seminal vesicles/prostate glands (-15%; $p<0.01$) and lower weight of epididymides (-8%; $p<0.05$) were noted in males at 1000 mg/kg/day. Elevated mean testes/body weight ratios ($p<0.05$) and mean testes/brain weight ratios were recorded ($p<0.05$) in these animals compared to controls and mean seminal vesicles and prostate/brain weight ratio were decreased ($p<0.05$). Elevated mean liver/body weight and liver/brain weight ratios (+23%; $p<0.01$ and +15%; $p<0.05$, respectively) were recorded in males at 1000 mg/kg/day. In the corresponding females, a significantly higher mean liver/body weight ratio (+12%; $p<0.01$) was also noted.

4.5.2 Macroscopic Findings

(See Summary Tables on p. 190 , Individual Tables on p. 384)

Test item-related enlargement and dark or black brown discoloration of the liver were noted in males at 250 mg/kg/day (100% of treated animals, both $p<0.01$) and at 1000 mg/kg/day (80 - 100%, $p<0.01$ or $p<0.05$, respectively) and in females at 1000 mg/kg/day (40%) at necropsy after four weeks of treatment.

Additional findings noted in individual males or females were considered to be not related to treatment: dark red foci in the mucosa of the stomach (one control male), unilateral renal pelvis dilation (one male at 5 mg/kg), red foci or reddish discoloration of the thymus (one control male and one control female, one male at 250 mg/kg/day, one male at 1000 mg/kg/day, one female at 5 mg/kg/day), dark red nodules in epididymal adipose tissue (one male at 250 mg/kg/day), dilation of the uterus (one female at 25 mg/kg/day and one female at 250 mg/kg/day).

After two weeks of recovery, black brown discoloration of the liver was still present in all males at 1000 mg/kg/day ($p<0.01$), and enlarged / discolored lymph nodes were recorded in one of these males.

No findings were noted in the females at necropsy after the 2-week recovery period.

4.5.3 Microscopic Findings

(See Appendix VI on p. 445)

Test item-related effects were noted in the following organs:

Liver

Protoporphyrin accumulation in the intra-hepatic bile ducts was recorded at minimal to moderate severity in animals of both sexes at 1000 mg/kg/day and in males at 250 mg/kg/day after the treatment period. Protoporphyrin accumulation was recorded in Kupffer cell as well as in hepatocytes in males at 250 mg/kg/day and 1000 mg/kg/day at the end of the four week treatment period. This accumulation was characterized by birefringent, bright red appearance with dark Maltese cross in each deposit affected under polarized light.

Periportal chronic inflammation and bile duct proliferation at minimal to slight severity was recorded in both sexes at 1000 mg/kg/day and in males at 250 mg/kg/day at the end of the treatment period. Hepatocellular hypertrophy (centrilobular) was recorded at minimal severity in both sexes at 1000 mg/kg/day and in males at 250 mg/kg/day after four weeks of treatment.

With the exception of hepatocellular hypertrophy in both sexes and bile duct proliferation in females, these findings persisted in animals at 1000 mg/kg/day after the 14 day recovery period (see Table 1).

Table 1 Incidence and Mean Severity of Main Microscopic Findings in Liver

Findings/Incidence/Mean Severity Grade	Group 1		Group 2		Group 3		Group 4		Group 5	
Terminal Sacrifice	**5 M**	**5 F**	**5 M**	**5 M**	**5 F**	**5 M**	**5 M**	**5 F**	**5 M**	**5 F**
Protoporphyrin accumulation, intrahepatic bile duct #, ##	-	-	-	-	-	-	5/2.8*	-	5/3.0*	2/2.0
Protoporphyrin accumulation, Kupffer cell #	-	-	-	-	-	-	1/1.0	-	5/2.0*	-
Protoporphyrin accumulation, hepatocyte #	-	-	-	-	-	-	3/1.0	-	5/1.0*	-
Periportal chronic inflammation #, ##	-	-	-	-	-	-	5/1.2*	-	5/1.0*	2/1.0
Bile duct proliferation #	-	-	-	-	-	-	4/1.8	-	5/1.8*	1/1.0
Hepatocellular hypertrophy ##	-	-	-	-	-	-	2/1.0	-	3/1.0	3/1.0
Recovery	**5 M**	**5 F**							**5 M**	**5 F**
Protoporphyrin accumulation, intrahepatic bile duct	-	-							5/3.0*	4/1.5
Protoporphyrin accumulation, Kupffer cell	-	-							5/1.8*	-
Protoporphyrin accumulation, hepatocyte	-	-							5/1.0*	-
Periportal chronic inflammation	-	-							5/1.0*	2/1.0
Bile duct proliferation	-	-							5/2.0*	-

*: p<0.01 by One-sided Exact Fischer Test
#: p<0.01 by Armitage / Cochran Trend Test for Males
##: p<0.01 by Armitage / Cochran Trend Test for Females

Kidney

Hyaline droplets at minimal to slight severity were recorded in males at 25 mg/kg/day, 250 mg/kg/day and 1000 mg/kg/day at the end of the treatment period.

The hyaline droplets were not evident in animals after 14 day recovery period.

Table 2 Incidence and Mean Severity of Main Microscopic Findings in Kidney

Findings/Incidence/Mean Severity Grade	Group 1		Group 2		Group 3		Group 4		Group 5	
Terminal Sacrifice	**5 M**	**5 F**	**5 M**	**5 F**	**5 M**	**5 F**	**5 M**	**5 F**	**5 M**	**5 F**
Hyaline droplets	-	-	-	-	2/1.0	-	5/1.6*	-	5/1.8*	-

*: p<0.01 by One-sided Exact Fischer Test

Thyroid Glands

Follicular cell hypertrophy at minimal severity was recorded in two males and one female at 1000 mg/kg/day at the end of 28-day treatment period.

The follicular cell hypertrophy was not evident in animals after the 14-day recovery period.

Table 3 Incidence and Mean Severity of Main Microscopic Findings in Thyroid Gland

Findings/Incidence/Mean Severity Grade	Group 1		Group 2		Group 3		Group 4		Group 5	
Terminal Sacrifice	**5 M**	**5 F**	**5 M**	**5 F**	**5 M**	**5 F**	**5 M**	**5 F**	**5 M**	**5 F**
Follicular cell hypertrophy	-	-	-		-		-	-	2/1.0	1/1.0

The remaining microscopic findings recorded were within the range of normal background lesions which may be recorded in animals of this strain and age and were not considered to be test item-related.

4.5.4 Immunohistochemistry

(See Appendix VII on p. 580)

4.5.4.1 Main Study

Summaries of alpha-2μ-globulin staining in male rats sacrificed after four weeks' treatment are presented in Table 4 and Table 5.

The mean levels of punctate staining in test article-treated groups and the control group and the absence of a dose response suggests there was no biological difference based on the occurrence of α-2μ globulin of the punctate staining pattern.

There was a higher level of α-2μ globulin of the globular staining pattern in all test article-treated males. However, the highest mean staining level was noted in the 250 mg/kg/day males. Absence of a dose response raises suspicion as to the toxicologic significance of the α-2μ globulin immunohistochemical staining results. Hyaline droplets were detected at 25, 250 and 1000 mg/kg/day.

Table 4 Summary of Punctate Staining Pattern

Main Study Males					
L3 Dosage Level (mg/kg/day)	**0**	**5**	**25**	**250**	**1000**
Kidney[a]	5	5	5	5	5
Mean Stain Score	4.0	4.0	3.4	3.4	4.0

[a] = Number of tissues examined.

Table 5 Summary of Globular Staining Pattern

Main Study Males					
L3 Dosage Level (mg/kg/day)	**0**	**5**	**25**	**250**	**1000**
Kidney[a]	5	5	5	5	5
Mean Stain Score	0.4	1.2	2.2	3.2	3.0

[a] = Number of tissues examined.

4.5.4.2 Recovery

Summaries of alpha-2μ-globulin staining in male rats terminated after four weeks' treatment and two weeks' recovery are presented in Table 6 and Table 7.

Staining for alpha-2μ-globulin of the punctate pattern was present equally in male rats from the 0 and 1000 mg/kg/day recovery groups. Mean alpha-2μ-globulin staining of the punctate pattern was the same in males from the control group and 1000 mg/kg/day recovery group as compared to males from the same dosage groups in the Main Study.

Alpha-2μ-globulin staining of the globular pattern was only rarely present in male rats from the 0 mg/kg/day group, but was present to a more substantial degree in male rats from the 1000 mg/kg/day group. A decrease in the mean stain score for alpha-2μ-globulin of the globular pattern in recovery males from the 1000 mg/kg/day group as compared to the mean stain at the main necropsy suggests some recovery in the accumulation of alpha-2μ-globulin in the kidneys.

Table 6 Summary of Punctate Staining Pattern

Recovery Males					
L3 Dosage Level (mg/kg/day):	**0**	**5**	**25**	**250**	**1000**
Kidney[a]	5	N/A	N/A	N/A	5
Mean Stain Score	4.0	N/A	N/A	N/A	4.0

[a] = Number of animals examined.

Table 7 Summary of Globular Staining Pattern

Recovery Males					
L3 Dosage Level (mg/kg/day):	**0**	**5**	**25**	**250**	**1000**
Kidney[a]	5	N/A	N/A	N/A	5
Mean Stain Score	0.4	N/A	N/A	N/A	1.6

[a] = Number of animals examined.

5 DISCUSSION AND CONCLUSION

Oral administration (gavage) of Octamethyltrisiloxane (L3) to Sprague Dawley rats at doses of 5, 25, 250 and 1000 mg/kg/day, for 28 days resulted in no deaths and no test item related changes in daily or weekly observations or the functional observational battery (performed during week 4) including grip strength and locomotor activity. No findings were noted concerning the estrous stage of the female animals.

The following test item related findings were noted:

- Reduced body weight in males at 1000 mg/kg/day during the treatment and recovery period compared to the control animals. Increased body weight gain was recorded in these males and females during recovery and was considered to be a compensatory effect;

- Differences in hematological parameters, indicating either increased red cell production or decreased red cell destruction (retention) compared to control animals in males and/or females at 1000 mg/kg/day at the end of the treatment phase and recovery period (males);

- Differences in several clinical biochemistry parameters, most of which were indicative of metabolic adaptation, at 25, 250 and 1000 mg/kg/day; changes in liver associated enzymes (males of the high dose group) consistent with changes in cholesterol, phospholipid and triglyceride levels and further findings indicating test item related effects to the liver such as organ weights, macroscopic and microscopic findings (see below);

- Differences in urine parameters, generally considered to indicate a reduced ability to concentrate urine, after four weeks of treatment in males at 1000 mg/kg/day in correlation with changes in serum electrolyte concentrations (sodium, chloride) and microscopic findings in the kidney;

- Increased (adaptive) mean absolute and relative liver weights in males at 25 mg/kg/day, and in both sexes at 250 mg/kg/day and/or 1000 mg/kg/day.

- Macroscopic findings in the liver (enlargement and dark or black brown discoloration of the liver) of males at 250 mg/kg/day and 1000 mg/kg/day and females at 1000 mg/kg/day at necropsy after treatment consistent with microscopic findings. Black brown discoloration of the liver persisted in all males at 1000 mg/kg/day after recovery.

- Microscopic findings in the liver, kidney and thyroid gland (protoporphyrin accumulation in the intra-hepatic bile ducts in both sexes at 1000 mg/kg/day and in males at 250 mg/kg/day, in Kupffer and hepatocytes in males at 250 and 1000 mg/kg/day; periportal chronic inflammation and bile duct proliferation in both sexes at 1000 mg/kg/day and in males at 250 mg/kg/day; hepatocellular hypertrophy (centrilobular) in both sexes at 1000 mg/kg/day and in males at 250 mg/kg/day after

four weeks of treatment; hyaline droplet formation in the kidneys of males at 25 mg/kg/day, 250 mg/kg/day and 1000 mg/kg/day at the end of treatment; follicular cell hypertrophy in the thyroid of two males and one female at 1000 mg/kg/day at the end of the treatment period). After recovery, protoporphyrin accumulation and periportal chronic inflammation (in both sexes) and bile duct proliferation (in males only) were still present in the livers. The hepatocellular hypertrophy, follicular cell hypertrophy of the thyroid gland and hyaline deposits of the male kidneys showed complete regression after the 14-day recovery period.

- Although a higher mean level of α-2μ globulin of the globular staining pattern in the kidneys of test item-treated male rats is generally indicative of a test article-related effect, the lack of a dose–response relationship (the highest level of α-2μ globulin staining in the 250 mg/kg/day group rather than the 1000 mg/kg/day group) undermined any toxicological relevance of the difference in immunohistochemical staining intensity. The punctate staining pattern was interpreted as the normal physiologic processing of alpha-2μ-globulin in the kidney. The globular staining pattern may be interpreted as a pathologic accumulation of alpha-2μ-globulin in the kidney, which may be seen as hyaline droplet accumulation/degeneration in routinely stained kidney sections. Slight staining of the globular pattern in control male rats from the recovery group was interpreted as an early manifestation of spontaneous nephropathy of laboratory rats, which is known to include an element of hyaline droplet accumulation. The immunohistochemical staining results should be viewed in conjunction with results of routine histopathological evaluation in arriving at a final conclusion regarding a test article-related effect on α-2μ globulin accumulation in the kidneys. The presence of α-2μ globulin in the male rat kidney is a species- and gender-specific effect, and in the absence of α-2μ globulin in humans, is considered to be of no toxicological relevance to man.

Occurrence of protoporphyrin accumulation in the liver, seen microscopically after four weeks of treatment in males at 250 mg/kg/day and in both sexes at 1000 mg/kg/day, was present in all males and a portion of females at 1000 mg/kg/day until the end of recovery, was considered to be an adverse finding. Periportal chronic inflammation and bile duct proliferation in males at 250 mg/kg/day and in both sexes at 1000 mg/kg/day, were considered to be secondary to this finding. Liver findings including elevated absolute and relative liver weights which also persisted in males and females up to the end of the recovery period and the previously described macroscopic findings (discoloration) are, in correlation with the microscopic findings, also considered to be of adverse nature. Findings in the kidney (hyaline droplets, alpha-2μ-globulin) and changes in urine parameters were considered to be test item-related but not adverse. Changes in the red blood cell parameters were considered not to be adverse although not reversible in males at 1000 mg/kg/day as there were no other findings noted indicating dysfunction in blood cell production/destruction.

Based on the findings in the liver (protoporphyrin accumulation accompanied by periportal chronic inflammation and bile duct proliferation), it can be concluded that males were more affected than the females by treatment with Octamethyltrisiloxane (L3). In the absence of clear reversibility of microscopic liver findings, the NOAEL of the test item was considered to be 25 mg/kg/day in the males and 250 mg/kg/day in the females.

6 REFERENCES

1. C.W. Dunnett:
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2. R.G. Miller:
Simultaneous Statistical Inference, Springer Verlag, New York (1981).

3. R.A. Fisher:
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7 FIGURES

FOOD CONSUMPTION (G/ANIMAL/DAY) - GRAPHICS

Data excluded from Summary Report

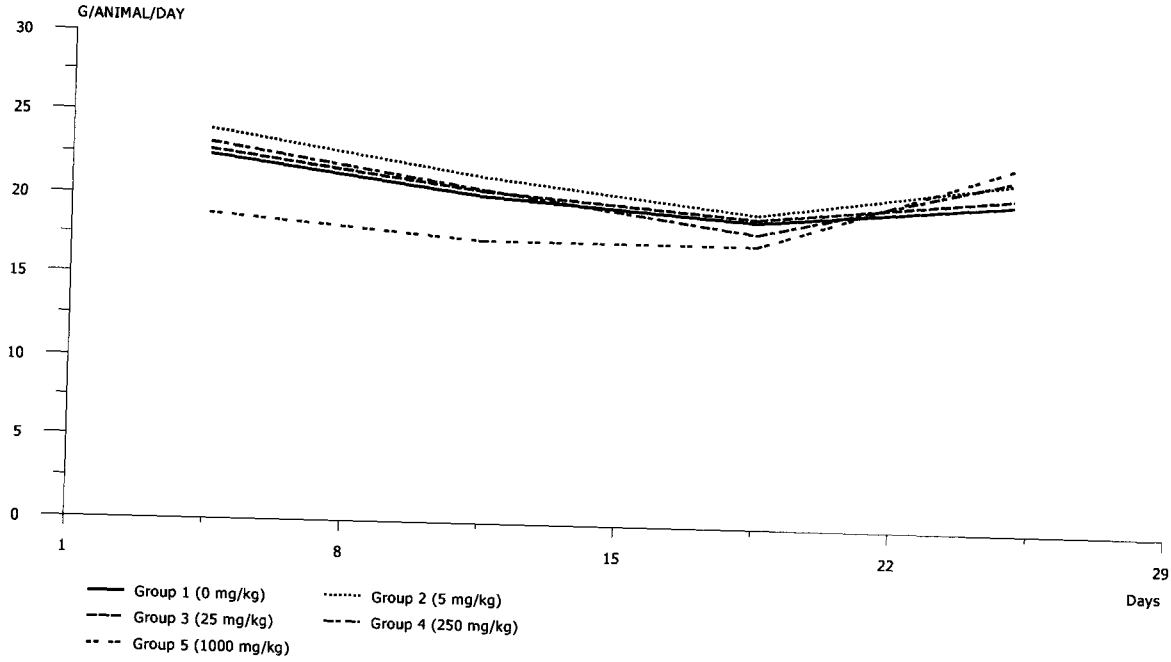
Not Reported

All Study Phases

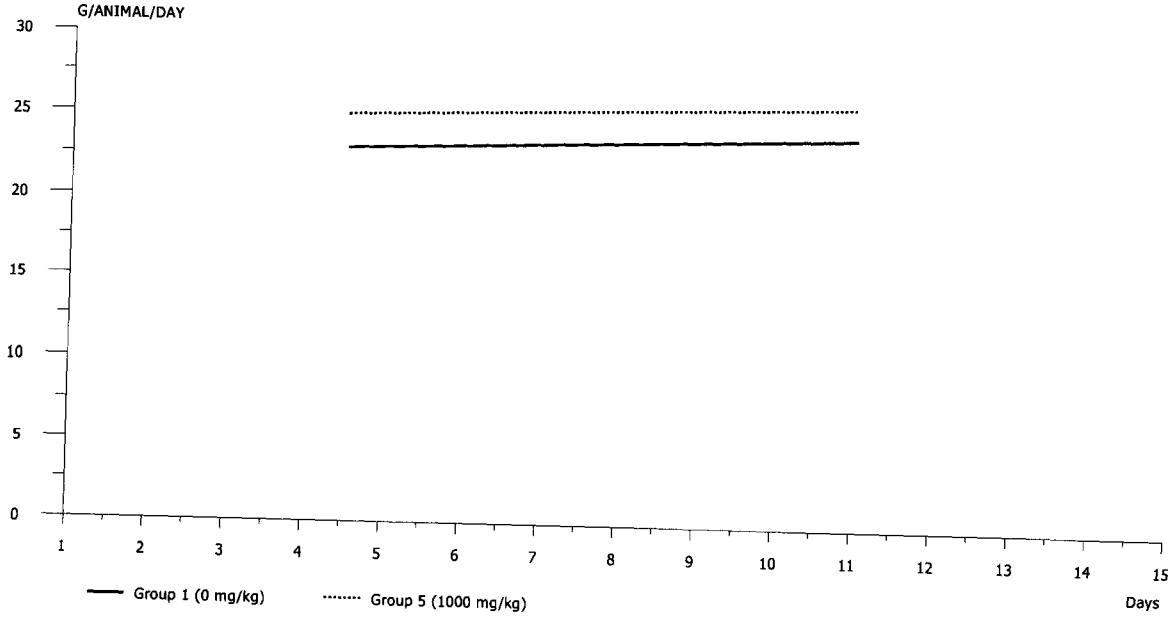
Cage 15	Male	Group 10	Reserve Removed
Cage 16	Female	Group 10	Reserve Removed

FOOD CONSUMPTION (G/ANIMAL/DAY) - GRAPHICS
MALES

TREATMENT

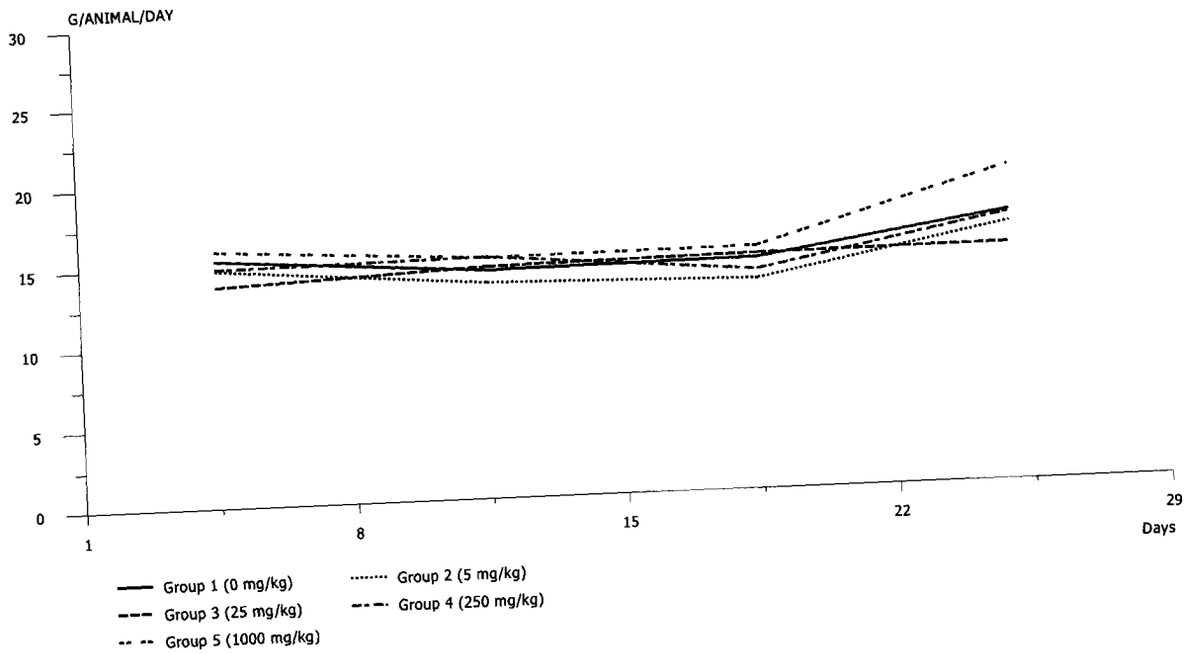


RECOVERY



FOOD CONSUMPTION (G/ANIMAL/DAY) - GRAPHICS
FEMALES

TREATMENT



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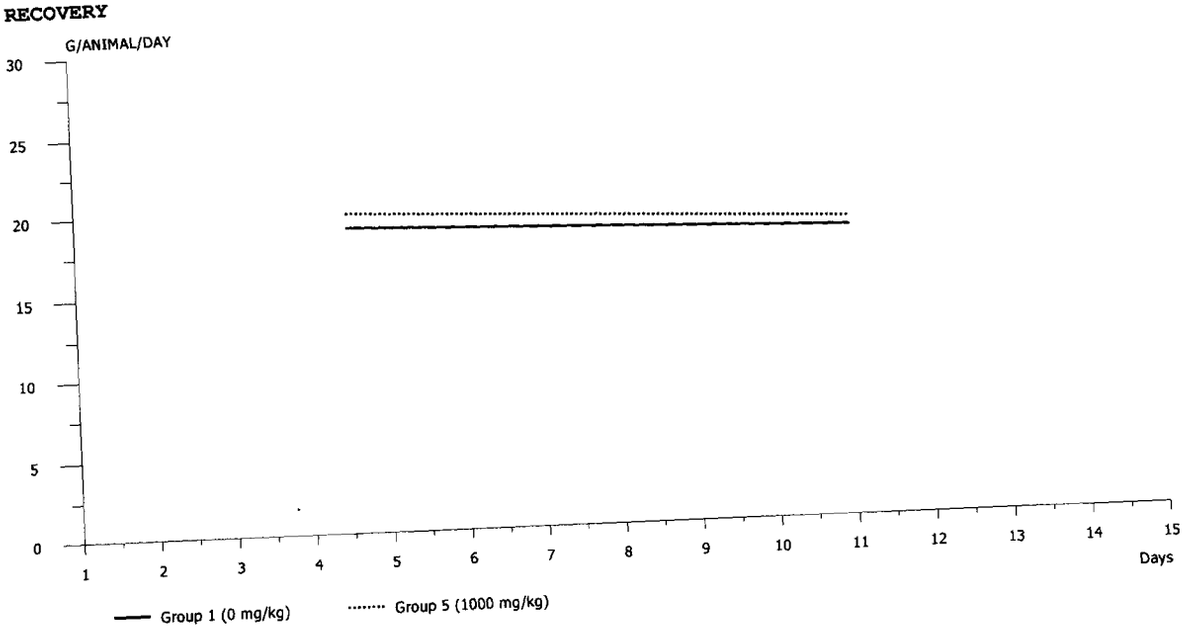

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RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY) - GRAPHICS

Data excluded from Summary Report

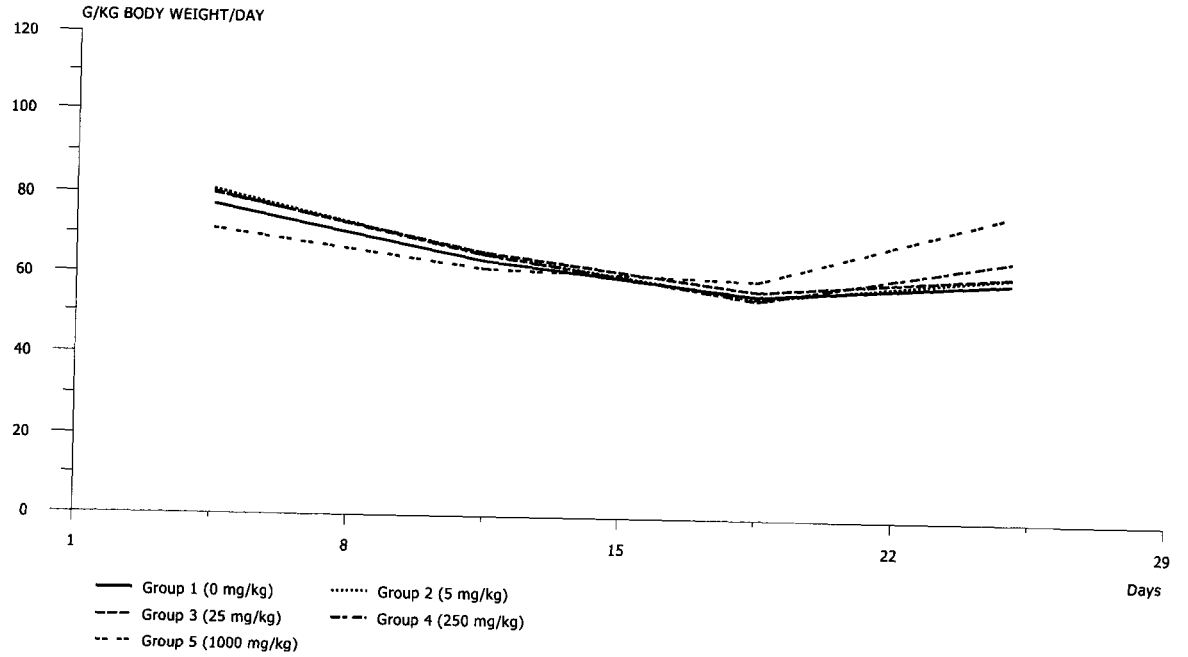
Not Reported

All Study Phases

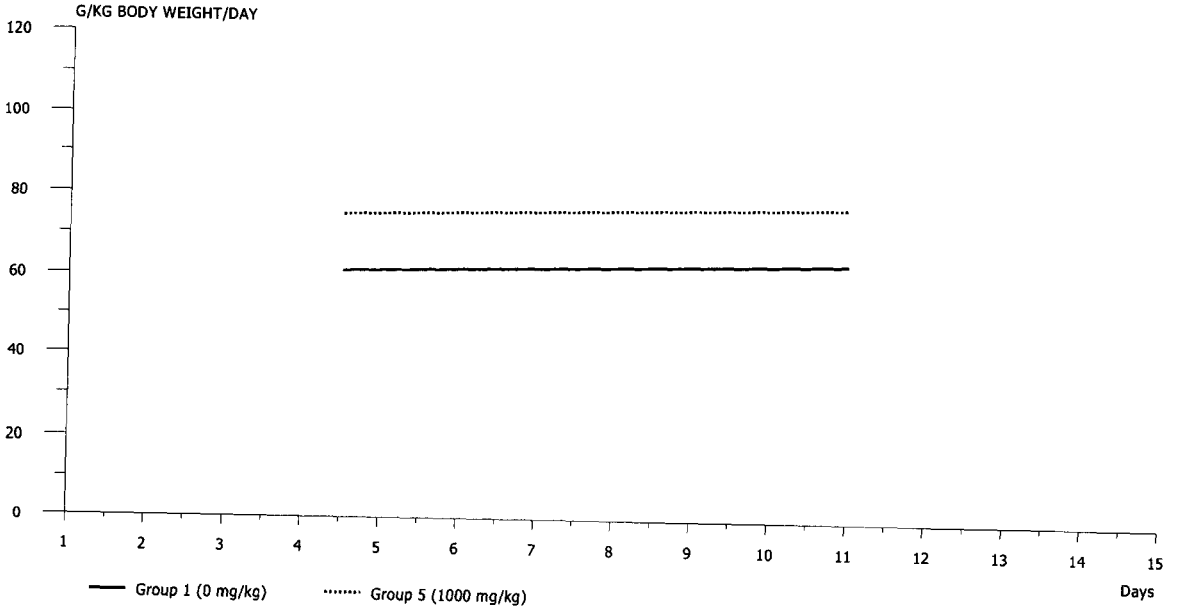
Cage 15	Male	Group 10	Reserve Removed
Cage 16	Female	Group 10	Reserve Removed

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY) - GRAPHICS
MALES

TREATMENT

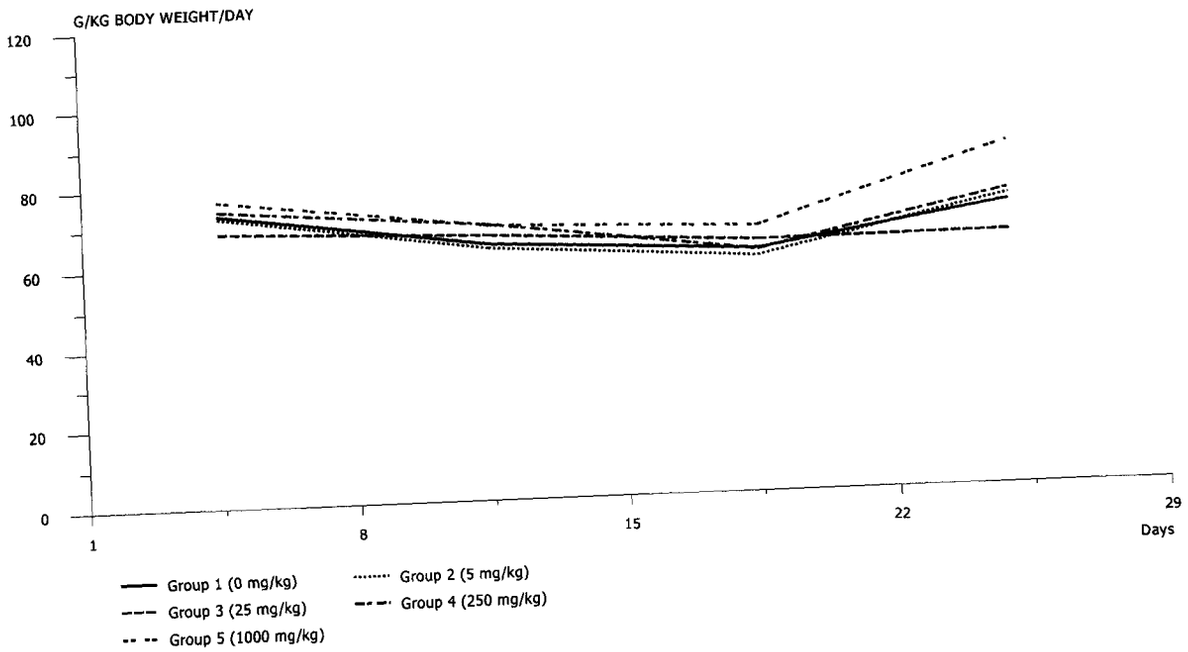


RECOVERY



RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY) - GRAPHICS
FEMALES

TREATMENT



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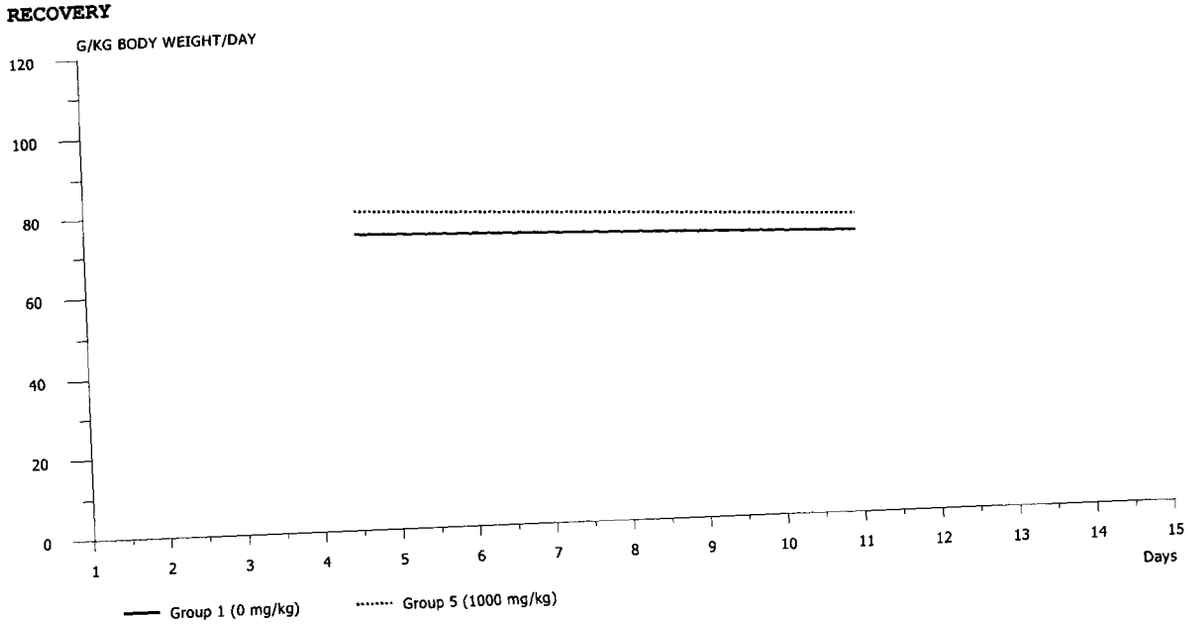

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BODY WEIGHTS (G) - GRAPHICS

Data excluded from Summary Report

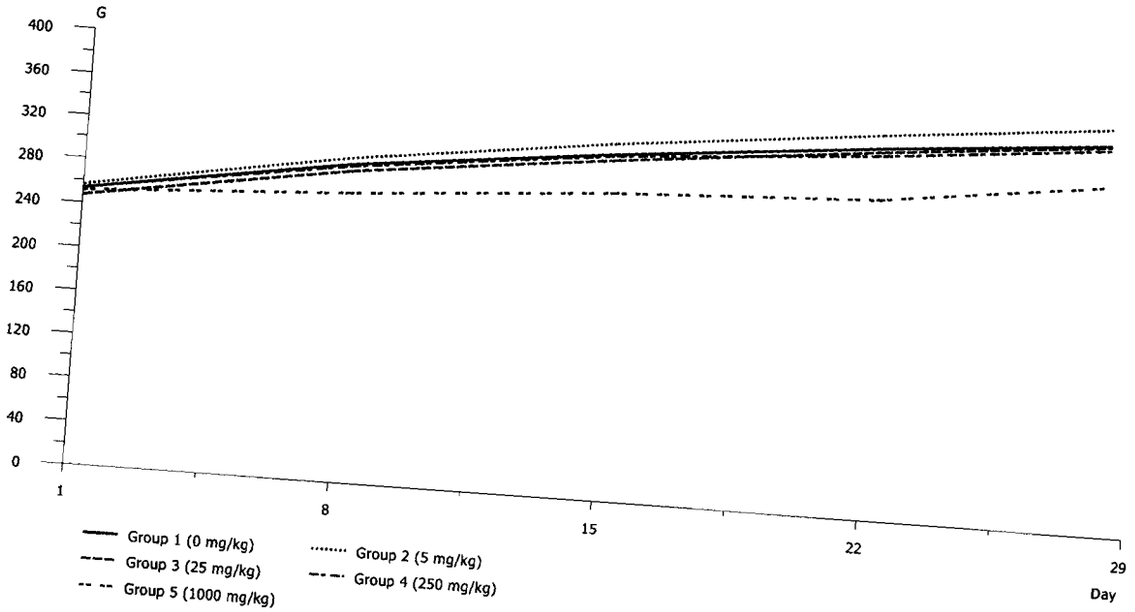
Not Reported

All Study Phases

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

BODY WEIGHTS (G) - GRAPHICS
MALES

TREATMENT



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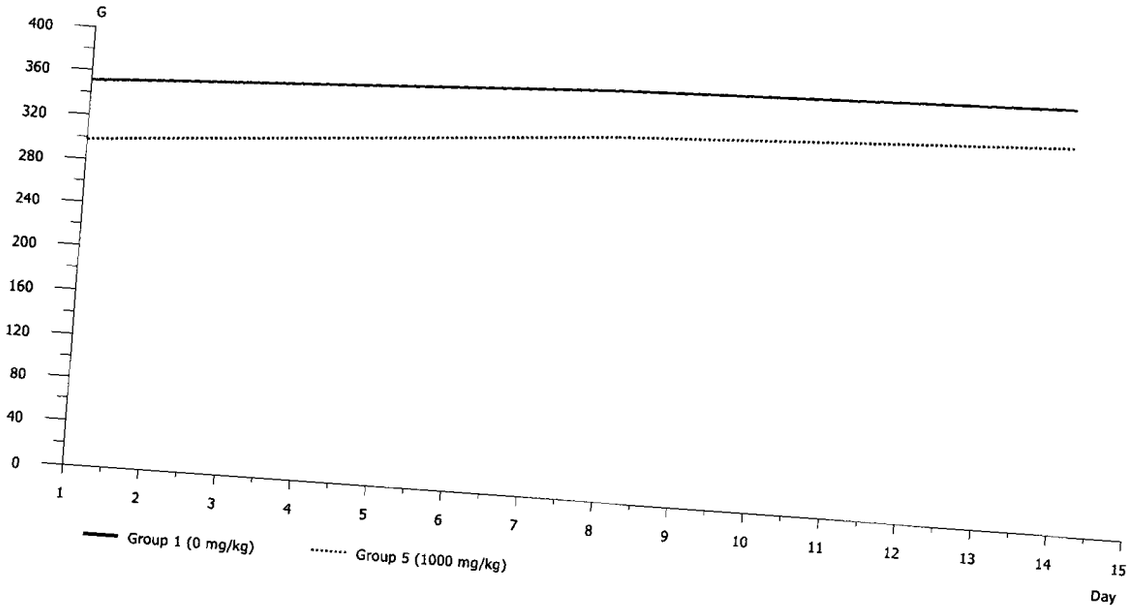
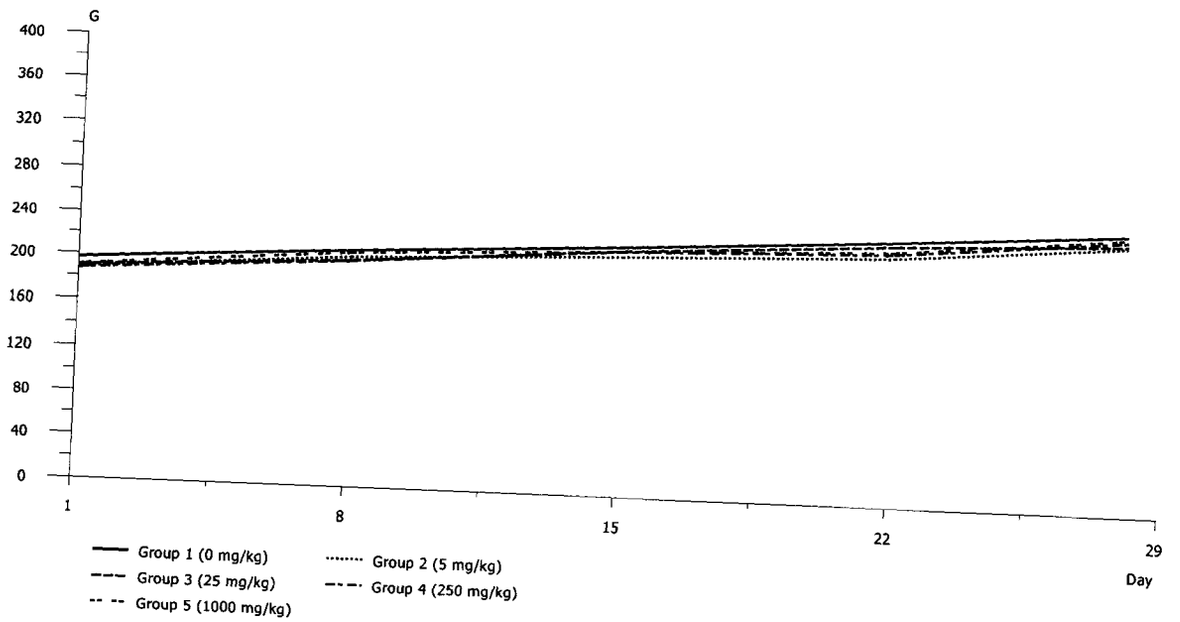


BODY WEIGHTS (G) - GRAPHICS
FEMALES

TREATMENT



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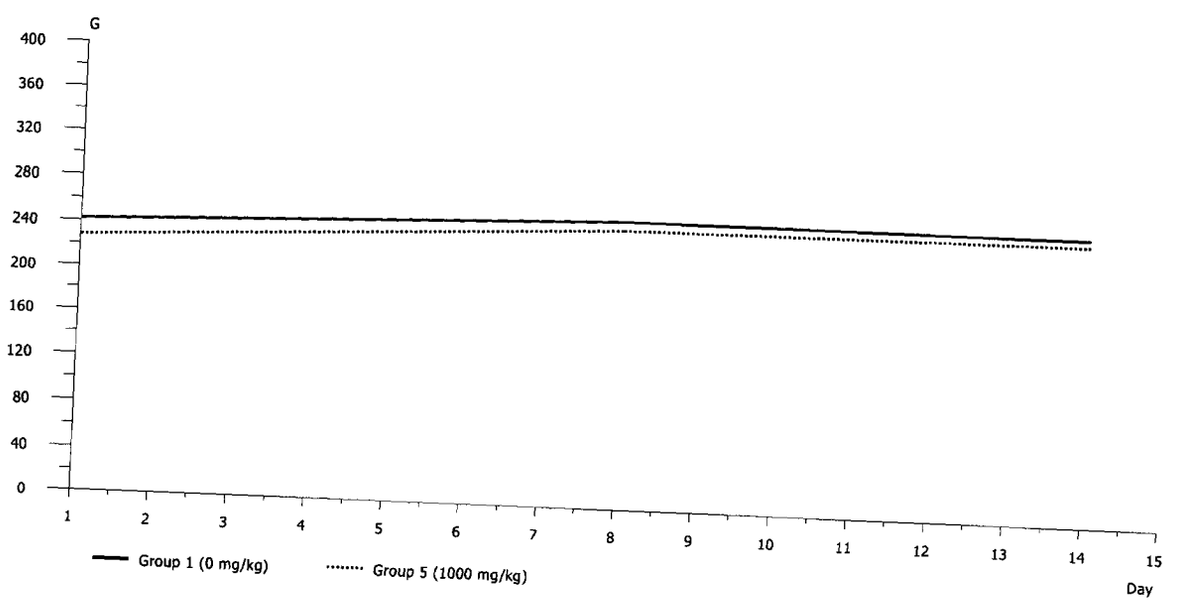


BODY WEIGHT GAIN (%) - GRAPHICS

Data excluded from Summary Report

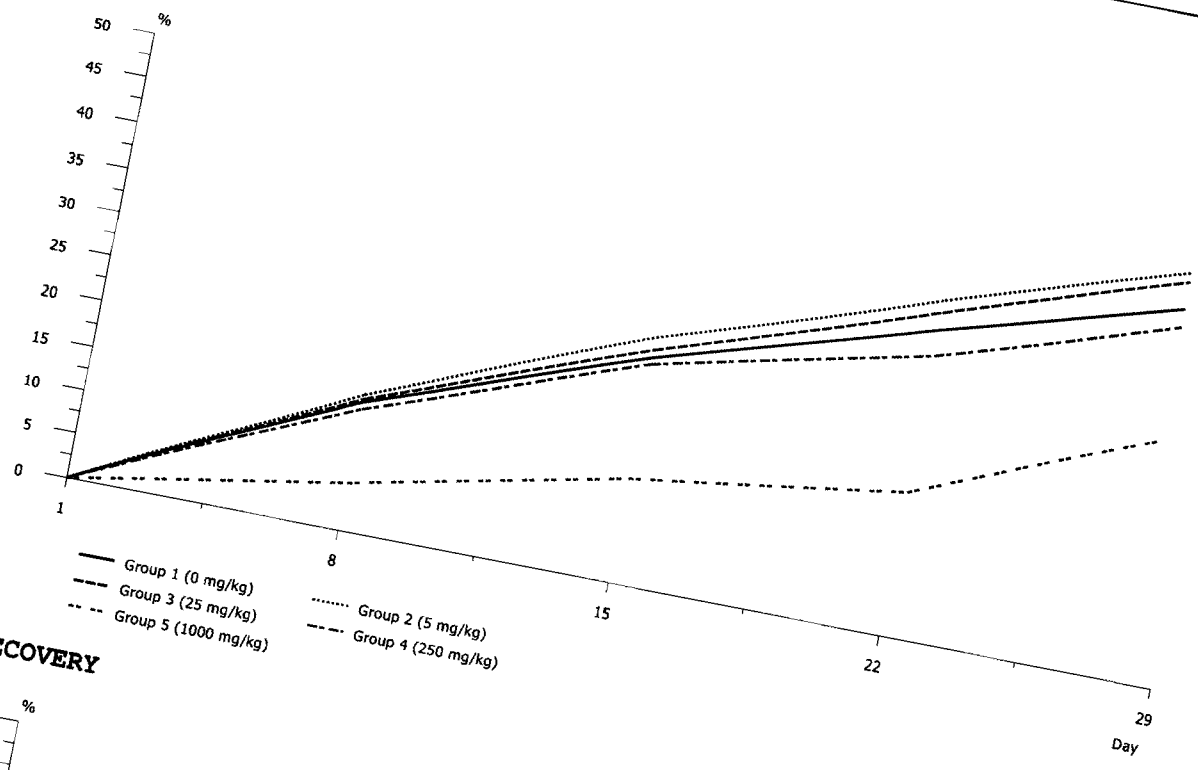
Not Reported

All Study Phases

Animal 100 Male Group 10 Reserve Removed
Animal 101 Female Group 10 Reserve Removed

BODY WEIGHT GAIN (%) - GRAPHICS
MALES

TREATMENT



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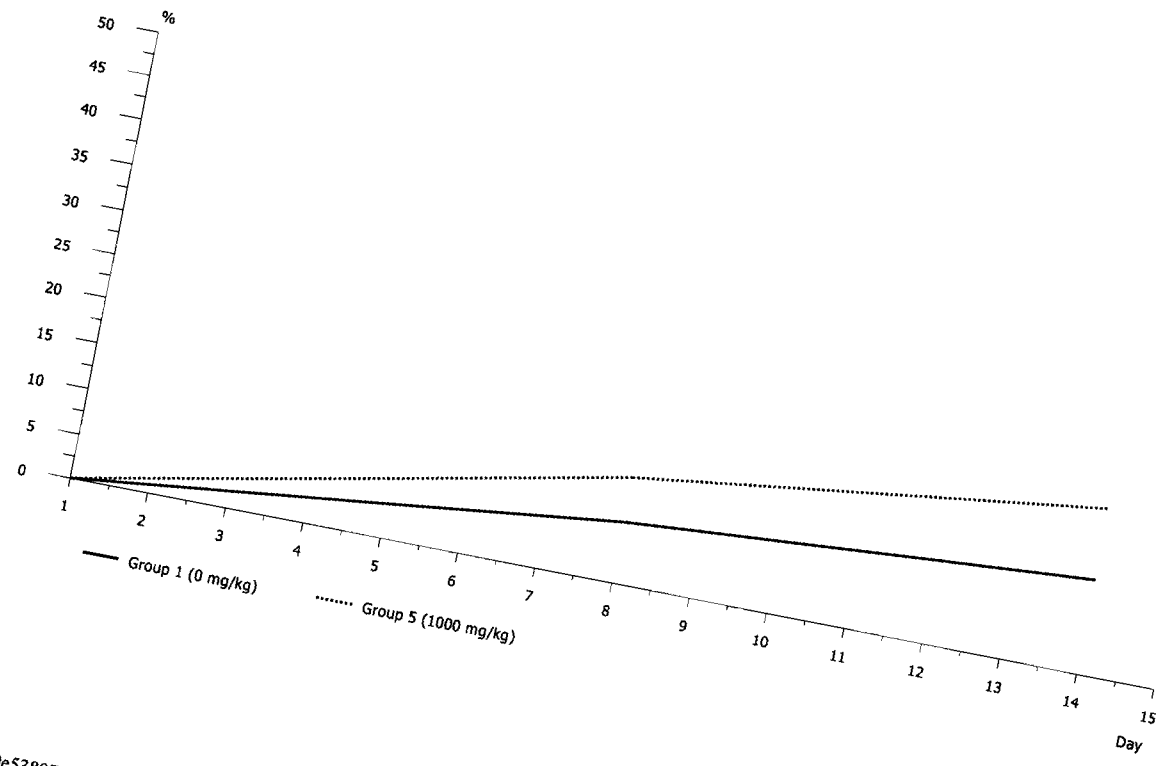

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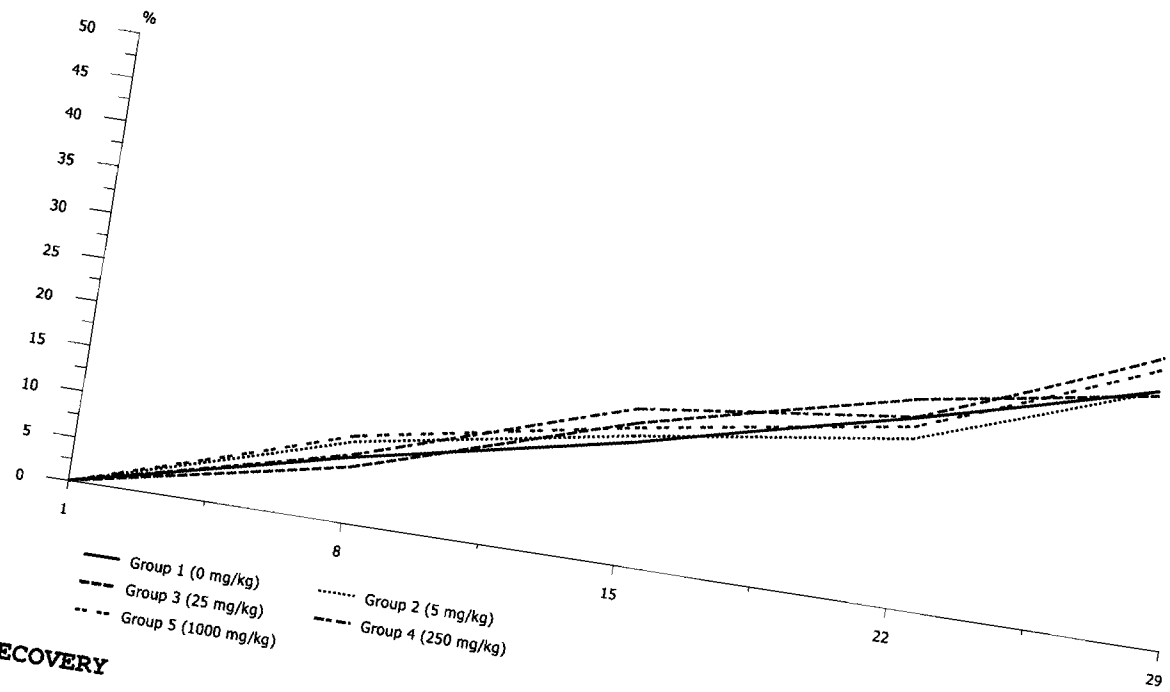
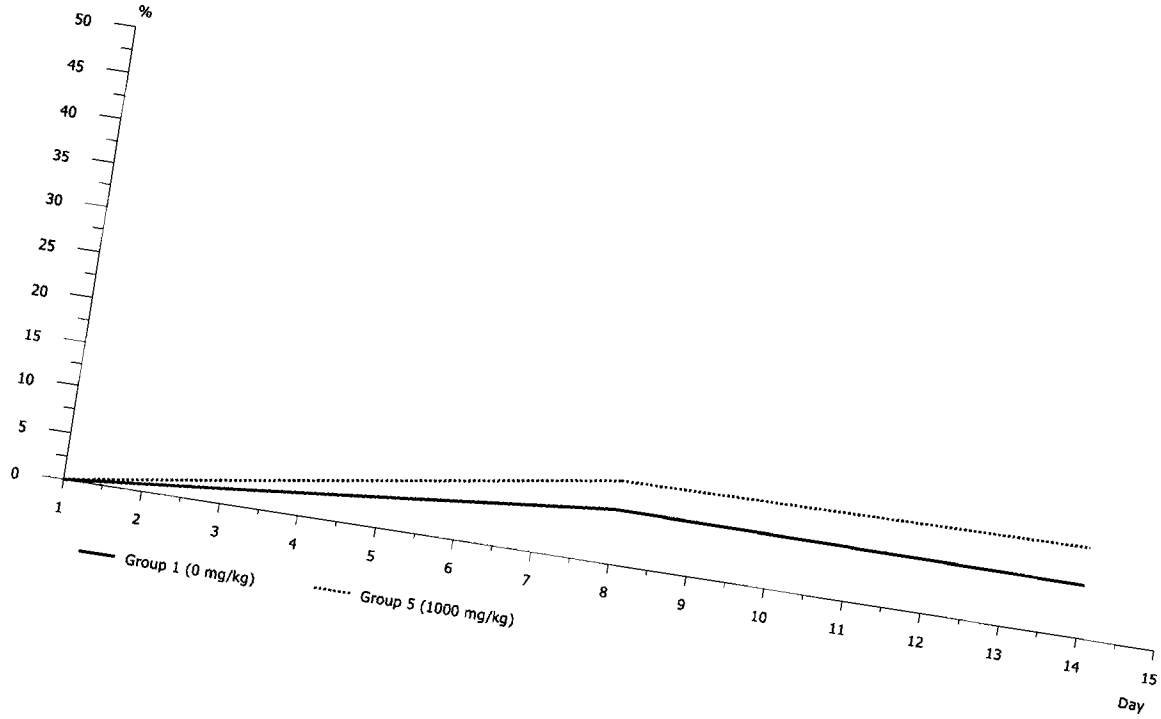
BODY WEIGHT GAIN (%) - GRAPHICS
FEMALES

TREATMENT



RECOVERY



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8 SUMMARY TABLES

CLINICAL SIGNS - SUMMARY

Affected animals as percentage to observed animals

```
0     0%
<     between 1% and 9%
1     between 10% and 19%
2     between 20% and 29%
...   ...
9     between 90% and 99%
A     100%
```

Data excluded from Summary Report

Not Reported

All Study Phases

```
Animal 100  Male   Group 10   Reserve Removed
Animal 101  Female Group 10   Reserve Removed
```

Incomplete Recordings

Selection of Findings

All findings reported

CLINICAL SIGNS - SUMMARY
MALES

POST-RANDOMIZATION

Weeks / Days
1
1 2 3 4 5

Group 1 (0 mg/kg)

No abnormality recorded.

Group 2 (5 mg/kg)

No abnormality recorded.

Group 3 (25 mg/kg)

No abnormality recorded.

Group 4 (250 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

G : Rounded group means of grades of affected animals
% : Affected animals as percentage to observed animals (See explanation on cover page)

CLINICAL SIGNS - SUMMARY
MALES

TREATMENT

```
                                  Weeks / Days
                                  1         2         3         4         5
                                  1234567123456712345671234567-
```

Group 1 (0 mg/kg)

No abnormality recorded.

Group 2 (5 mg/kg)

No abnormality recorded.

Group 3 (25 mg/kg)

No abnormality recorded.

Group 4 (250 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

```
APPEARANCE
- HUNCHED POSTURE (1)          G ....................111111111
                               % ....................111111111
- VISIBLE WEIGHT LOSS (3)      G ....................111111111
                               % ....................111111111
- RUFFLED FUR (3)              G ..............1........1111111
                               % ..............1........1111111
- HAIR LOSS (3)
  RIGHT AXILLARY REGION        G ..........122222222222211111
                               % ..........111111111111111111
BREATHING
- DYSPNEA (3)                  G .............11....1111111...
                               % .............11....1111111...
SECRETION/EXCRETION
- SALIVATION (3)               G ...................11111......
                               % ...................12211......
No further abnormality recorded.
```

G : Rounded group means of grades of affected animals
% : Affected animals as percentage to observed animals (See explanation on cover page)

CLINICAL SIGNS - SUMMARY
MALES

RECOVERY

```
                                Weeks / Days
                                1         2         3
                                1 2 3 4 5 6 7 1 2 3 4 5 6 7 -
```

Group 1 (0 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

G : Rounded group means of grades of affected animals
% : Affected animals as percentage to observed animals (See explanation on cover page)

CLINICAL SIGNS - SUMMARY
FEMALES

POST-RANDOMIZATION

Weeks / Days
1
1 2 3 4 5

Group 1 (0 mg/kg)

No abnormality recorded.

Group 2 (5 mg/kg)

No abnormality recorded.

Group 3 (25 mg/kg)

No abnormality recorded.

Group 4 (250 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

G : Rounded group means of grades of affected animals
% : Affected animals as percentage to observed animals (See explanation on cover page)

CLINICAL SIGNS - SUMMARY
FEMALES

TREATMENT

```
                                Weeks / Days
                                1         2         3         4         5
                                1234567123456712345671234567-
```

Group 1 (0 mg/kg)

No abnormality recorded.

Group 2 (5 mg/kg)

No abnormality recorded.

Group 3 (25 mg/kg)

No abnormality recorded.

Group 4 (250 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

G : Rounded group means of grades of affected animals
% : Affected animals as percentage to observed animals (See explanation on cover page)

CLINICAL SIGNS - SUMMARY
FEMALES

RECOVERY

```
                          Weeks / Days
                          1         2         3
                          1234567123456 7-
```

Group 1 (0 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

G : Rounded group means of grades of affected animals
% : Affected animals as percentage to observed animals (See explanation on cover page)

DETAILED BEHAVIORAL OBSERVATIONS - SUMMARY

Affected animals as percentage to observed animals

```
0     0%
<     between 1% and 9%
1     between 10% and 19%
2     between 20% and 29%
...   ...
9     between 90% and 99%
A     100%
```

Data excluded from Summary Report

Not Reported

All Study Phases

```
Animal 100  Male   Group 10   Reserve Removed
Animal 101  Female Group 10   Reserve Removed
```

Incomplete Recordings

Selection of Findings

All findings reported

DETAILED BEHAVIORAL OBSERVATIONS - SUMMARY
MALES

POST-RANDOMIZATION

Weeks
0
1

Group 1 (0 mg/kg)

No abnormality recorded.

Group 2 (5 mg/kg)

No abnormality recorded.

Group 3 (25 mg/kg)

No abnormality recorded.

Group 4 (250 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

G : Rounded group means of grades of affected animals
% : Affected animals as percentage to observed animals (See explanation on cover page)

DETAILED BEHAVIORAL OBSERVATIONS - SUMMARY
MALES

TREATMENT

Weeks
0
1 2 3 4 -

Group 1 (0 mg/kg)

No abnormality recorded.

Group 2 (5 mg/kg)

No abnormality recorded.

Group 3 (25 mg/kg)

No abnormality recorded.

Group 4 (250 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

G : Rounded group means of grades of affected animals
% : Affected animals as percentage to observed animals (See explanation on cover page)

DETAILED BEHAVIORAL OBSERVATIONS - SUMMARY
FEMALES

POST-RANDOMIZATION

	Weeks
	0
	1

Group 1 (0 mg/kg)

No abnormality recorded.

Group 2 (5 mg/kg)

No abnormality recorded.

Group 3 (25 mg/kg)

No abnormality recorded.

Group 4 (250 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

G : Rounded group means of grades of affected animals
% : Affected animals as percentage to observed animals (See explanation on cover page)

DETAILED BEHAVIORAL OBSERVATIONS - SUMMARY
FEMALES

TREATMENT

Weeks
0
1 2 3 4 -

Group 1 (0 mg/kg)

No abnormality recorded.

Group 2 (5 mg/kg)

No abnormality recorded.

Group 3 (25 mg/kg)

No abnormality recorded.

Group 4 (250 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

G : Rounded group means of grades of affected animals
% : Affected animals as percentage to observed animals (See explanation on cover page)

GRIP STRENGTH - SUMMARY

Data excluded from Summary Report

Not Reported

All Measurements

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

Reported Parameter

Parameter		Statistical Testing
AT WEEK 4		
Grip Fore	GRIP FORELIMB	DUNNETT, MEAN
Grip Hind	GRIP HINDLIMB	DUNNETT, MEAN

Statistical Methods

DUNNETT DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not significant (-)

GRIP STRENGTH - SUMMARY
AT WEEK 4
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
GRIP STRENGTH					
Grip Fore KILOGRAM	MEAN	1.42	1.45 -	1.44 -	1.43 -
	ST.DEV.	0.06	0.05	0.05	0.06
	MINIMUM	1.36	1.41	1.37	1.33
	MAXIMUM	1.49	1.53	1.50	1.49
	N	10	5	5	5
Grip Hind KILOGRAM	MEAN	1.03	1.04 -	1.03 -	1.03 -
	ST.DEV.	0.03	0.02	0.02	0.03
	MINIMUM	0.96	1.01	1.00	0.98
	MAXIMUM	1.06	1.07	1.05	1.05
	N	10	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

GRIP STRENGTH - SUMMARY
AT WEEK 4
MALES

		Group 5 1000 mg/kg
GRIP STRENGTH		
Grip Fore KILOGRAM	MEAN	1.43 -
	ST.DEV.	0.06
	MINIMUM	1.35
	MAXIMUM	1.52
	N	10
Grip Hind KILOGRAM	MEAN	1.01 -
	ST.DEV.	0.04
	MINIMUM	0.95
	MAXIMUM	1.09
	N	10

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

GRIP STRENGTH - SUMMARY
AT WEEK 4
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
GRIP STRENGTH					
Grip Fore KILOGRAM	MEAN	1.30	1.26 -	1.30 -	1.29 -
	ST.DEV.	0.04	0.03	0.05	0.04
	MINIMUM	1.24	1.22	1.23	1.25
	MAXIMUM	1.35	1.30	1.34	1.35
	N	10	5	5	5
Grip Hind KILOGRAM	MEAN	0.79	0.74 *	0.75 -	0.79 -
	ST.DEV.	0.03	0.03	0.02	0.04
	MINIMUM	0.75	0.71	0.73	0.73
	MAXIMUM	0.85	0.79	0.77	0.83
	N	10	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

GRIP STRENGTH - SUMMARY
AT WEEK 4
FEMALES

		Group 5 1000 mg/kg
GRIP STRENGTH		
Grip Fore KILOGRAM	MEAN	1.29 -
	ST.DEV.	0.04
	MINIMUM	1.24
	MAXIMUM	1.35
	N	10
Grip Hind KILOGRAM	MEAN	0.79 -
	ST.DEV.	0.03
	MINIMUM	0.76
	MAXIMUM	0.86
	N	10

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

LOCOMOTOR ACTIVITY - SUMMARY

Data excluded from Summary Report

Not Reported

All Measurements

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

Reported Parameter

Parameter		Statistical Testing
AT WEEK 4		
0-10 MIN	LOCOMOTOR ACTIVITY	DUNNETT, MEAN
10-20 MIN	LOCOMOTOR ACTIVITY	DUNNETT, MEAN
20-30 MIN	LOCOMOTOR ACTIVITY	DUNNETT, MEAN
30-40 MIN	LOCOMOTOR ACTIVITY	DUNNETT, MEAN
40-50 MIN	LOCOMOTOR ACTIVITY	DUNNETT, MEAN
50-60 MIN	LOCOMOTOR ACTIVITY	DUNNETT, MEAN
Total	LOCOMOTOR ACTIVITY	DUNNETT, MEAN

Statistical Methods

DUNNETT DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not significant (-)

LOCOMOTOR ACTIVITY - SUMMARY
AT WEEK 4
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
LOCOMOTOR ACTIVITY					
0-10 MIN	MEAN	462	473 -	590 -	529 -
	ST.DEV.	181	54	138	77
	MINIMUM	250	413	461	394
	MAXIMUM	720	534	824	593
	N	10	5	5	5
10-20 MIN	MEAN	274	327 -	347 -	302 -
	ST.DEV.	109	103	98	123
	MINIMUM	136	193	209	219
	MAXIMUM	481	460	448	516
	N	10	5	5	5
20-30 MIN	MEAN	300	251 -	275 -	270 -
	ST.DEV.	163	72	95	129
	MINIMUM	142	169	169	101
	MAXIMUM	738	331	350	419
	N	10	5	5	5
30-40 MIN	MEAN	284	207 -	251 -	205 -
	ST.DEV.	194	52	70	97
	MINIMUM	116	127	165	63
	MAXIMUM	773	266	324	310
	N	10	5	5	5
40-50 MIN	MEAN	191	160 -	280 -	156 -
	ST.DEV.	108	72	72	88
	MINIMUM	81	45	215	0
	MAXIMUM	460	236	404	219
	N	10	5	5	5
50-60 MIN	MEAN	148	155 -	229 -	120 -
	ST.DEV.	89	60	128	95
	MINIMUM	19	89	39	0
	MAXIMUM	269	250	376	248
	N	10	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

LOCOMOTOR ACTIVITY - SUMMARY
AT WEEK 4
MALES

		Group 5 1000 mg/kg	
LOCOMOTOR ACTIVITY			
0-10 MIN	MEAN	541	-
	ST.DEV.	149	
	MINIMUM	281	
	MAXIMUM	765	
	N	10	
10-20 MIN	MEAN	319	-
	ST.DEV.	130	
	MINIMUM	155	
	MAXIMUM	512	
	N	10	
20-30 MIN	MEAN	142	*
	ST.DEV.	117	
	MINIMUM	2	
	MAXIMUM	315	
	N	10	
30-40 MIN	MEAN	92	**
	ST.DEV.	92	
	MINIMUM	10	
	MAXIMUM	246	
	N	10	
40-50 MIN	MEAN	63	*
	ST.DEV.	82	
	MINIMUM	4	
	MAXIMUM	287	
	N	10	
50-60 MIN	MEAN	129	-
	ST.DEV.	151	
	MINIMUM	0	
	MAXIMUM	351	
	N	10	

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

LOCOMOTOR ACTIVITY - SUMMARY
AT WEEK 4
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
LOCOMOTOR ACTIVITY					
Total	MEAN	1659	1573 -	1973 -	1582 -
	ST.DEV.	627	174	396	413
	MINIMUM	924	1408	1493	967
	MAXIMUM	3221	1845	2543	2086
	N	10	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

LOCOMOTOR ACTIVITY - SUMMARY
AT WEEK 4
MALES

		Group 5 1000 mg/kg
LOCOMOTOR ACTIVITY		
Total	MEAN	1285 -
	ST.DEV.	566
	MINIMUM	478
	MAXIMUM	2296
	N	10

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

LOCOMOTOR ACTIVITY - SUMMARY
AT WEEK 4
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
LOCOMOTOR ACTIVITY					
0-10 MIN	MEAN	570	728 -	560 -	645 -
	ST.DEV.	88	163	95	176
	MINIMUM	462	556	423	343
	MAXIMUM	709	993	659	782
	N	10	5	5	5
10-20 MIN	MEAN	284	450 -	247 -	216 -
	ST.DEV.	127	199	98	144
	MINIMUM	136	227	151	60
	MAXIMUM	579	742	398	401
	N	10	5	5	5
20-30 MIN	MEAN	170	236 -	122 -	165 -
	ST.DEV.	69	142	130	106
	MINIMUM	42	66	8	18
	MAXIMUM	273	377	305	269
	N	10	5	5	5
30-40 MIN	MEAN	93	158 -	26 -	33 -
	ST.DEV.	61	101	32	29
	MINIMUM	21	19	6	0
	MAXIMUM	185	290	82	74
	N	10	5	5	5
40-50 MIN	MEAN	81	80 -	171 -	160 -
	ST.DEV.	59	87	99	51
	MINIMUM	2	6	80	73
	MAXIMUM	169	186	338	203
	N	10	5	5	5
50-60 MIN	MEAN	189	149 -	164 -	233 -
	ST.DEV.	115	118	64	105
	MINIMUM	16	26	91	107
	MAXIMUM	441	301	228	361
	N	10	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

LOCOMOTOR ACTIVITY - SUMMARY
AT WEEK 4
FEMALES

		Group 5 1000 mg/kg	
LOCOMOTOR ACTIVITY			
0-10 MIN	MEAN	725	*
	ST.DEV.	81	
	MINIMUM	619	
	MAXIMUM	851	
	N	10	
10-20 MIN	MEAN	380	-
	ST.DEV.	154	
	MINIMUM	173	
	MAXIMUM	616	
	N	10	
20-30 MIN	MEAN	209	-
	ST.DEV.	97	
	MINIMUM	85	
	MAXIMUM	352	
	N	10	
30-40 MIN	MEAN	74	-
	ST.DEV.	61	
	MINIMUM	0	
	MAXIMUM	163	
	N	10	
40-50 MIN	MEAN	187	*
	ST.DEV.	89	
	MINIMUM	7	
	MAXIMUM	363	
	N	10	
50-60 MIN	MEAN	216	-
	ST.DEV.	140	
	MINIMUM	0	
	MAXIMUM	390	
	N	10	

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

LOCOMOTOR ACTIVITY - SUMMARY
AT WEEK 4
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
LOCOMOTOR ACTIVITY					
Total	MEAN	1387	1872 -	1290 -	1452 -
	ST.DEV.	349	634	289	461
	MINIMUM	1012	1234	853	681
	MAXIMUM	2044	2775	1647	1825
	N	10	6	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

LOCOMOTOR ACTIVITY - SUMMARY
AT WEEK 4
FEMALES

		Group 5 1000 mg/kg	
LOCOMOTOR ACTIVITY			
Total	MEAN	1792	-
	ST.DEV.	353	
	MINIMUM	1343	
	MAXIMUM	2460	
	N	10	

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

FOOD CONSUMPTION (G/ANIMAL/DAY) - SUMMARY

Data excluded from Summary Report

Not Reported

All Study Phases

Cage 15	Male	Group 10	Reserve Removed
Cage 16	Female	Group 10	Reserve Removed

FOOD CONSUMPTION (G/ANIMAL/DAY) - SUMMARY
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
POST-RANDOMIZATION					
Days 1-6	MEAN	24.2	24.9	23.3	24.4
	ST.DEV.	0.4	---	---	---
	N	2	1	1	1
TREATMENT					
Days 1-8	MEAN	22.4	23.9	22.7	23.2
	ST.DEV.	0.4	---	---	---
	N	2	1	1	1
Days 8-15	MEAN	20.2	21.3	20.5	20.6
	ST.DEV.	0.4	---	---	---
	N	2	1	1	1
Days 15-22	MEAN	18.9	19.4	19.1	18.1
	ST.DEV.	0.1	---	---	---
	N	2	1	1	1
Days 22-28	MEAN	20.2	21.6	20.6	21.7
	ST.DEV.	0.7	---	---	---
	N	2	1	1	1
MEAN OF MEANS Over TREATMENT		20.4	21.6	20.7	20.9
RECOVERY					
Days 1-8	MEAN	23.0	---	---	---
	ST.DEV.	---	---	---	---
	N	1	0	0	0
Days 8-14	MEAN	24.0	---	---	---
	ST.DEV.	---	---	---	---
	N	1	0	0	0
MEAN OF MEANS Over RECOVERY		23.5	---	---	---

FOOD CONSUMPTION (G/ANIMAL/DAY) - SUMMARY
MALES

		Group 5 1000 mg/kg
POST-RANDOMIZATION		
Days 1-6	MEAN	24.1
	ST.DEV.	0.1
	N	2
TREATMENT		
Days 1-8	MEAN	18.8
	ST.DEV.	0.0
	N	2
Days 8-15	MEAN	17.3
	ST.DEV.	0.9
	N	2
Days 15-22	MEAN	17.4
	ST.DEV.	0.3
	N	2
Days 22-28	MEAN	22.5
	ST.DEV.	0.4
	N	2
MEAN OF MEANS Over TREATMENT		19.0
RECOVERY		
Days 1-8	MEAN	25.0
	ST.DEV.	---
	N	1
Days 8-14	MEAN	25.9
	ST.DEV.	---
	N	1
MEAN OF MEANS Over RECOVERY		25.4

FOOD CONSUMPTION (G/ANIMAL/DAY) - SUMMARY
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
POST-RANDOMIZATION					
Days 1-6	MEAN	18.3	17.5	17.1	16.6
	ST.DEV.	0.6	---	---	---
	N	2	1	1	1
TREATMENT					
Days 1-8	MEAN	15.4	14.8	13.8	14.9
	ST.DEV.	0.9	---	---	---
	N	2	1	1	1
Days 8-15	MEAN	14.3	13.5	14.5	15.1
	ST.DEV.	0.4	---	---	---
	N	2	1	1	1
Days 15-22	MEAN	14.4	13.1	14.7	13.7
	ST.DEV.	0.1	---	---	---
	N	2	1	1	1
Days 22-28	MEAN	16.8	16.1	14.8	16.7
	ST.DEV.	1.5	---	---	---
	N	2	1	1	1
MEAN OF MEANS Over TREATMENT		15.2	14.4	14.4	15.1
RECOVERY					
Days 1-8	MEAN	18.9	---	---	---
	ST.DEV.	---	---	---	---
	N	1	0	0	0
Days 8-14	MEAN	17.9	---	---	---
	ST.DEV.	---	---	---	---
	N	1	0	0	0
MEAN OF MEANS Over RECOVERY		18.4	---	---	---

FOOD CONSUMPTION (G/ANIMAL/DAY) - SUMMARY
FEMALES

		Group 5 1000 mg/kg
POST-RANDOMIZATION		
Days 1-6	MEAN	17.4
	ST.DEV.	0.6
	N	2
TREATMENT		
Days 1-8	MEAN	16.0
	ST.DEV.	1.3
	N	2
Days 8-15	MEAN	15.0
	ST.DEV.	0.3
	N	2
Days 15-22	MEAN	15.1
	ST.DEV.	0.2
	N	2
Days 22-28	MEAN	19.6
	ST.DEV.	1.1
	N	2
MEAN OF MEANS Over TREATMENT		16.4
RECOVERY		
Days 1-8	MEAN	19.8
	ST.DEV.	---
	N	1
Days 8-14	MEAN	18.5
	ST.DEV.	---
	N	1
MEAN OF MEANS Over RECOVERY		19.1

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY) - SUMMARY

Data excluded from Summary Report

Not Reported

All Study Phases

Cage 15	Male	Group 10	Reserve Removed
Cage 16	Female	Group 10	Reserve Removed

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY) - SUMMARY
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
POST-RANDOMIZATION					
Days 1-6	MEAN	111.0	113.9	108.1	112.1
	ST.DEV.	2.5	---	---	---
	N	2	1	1	1
TREATMENT					
Days 1-8	MEAN	77.4	80.9	80.1	80.3
	ST.DEV.	0.2	---	---	---
	N	2	1	1	1
Days 8-15	MEAN	63.7	65.3	65.8	65.2
	ST.DEV.	1.8	---	---	---
	N	2	1	1	1
Days 15-22	MEAN	55.5	54.8	56.7	54.4
	ST.DEV.	1.1	---	---	---
	N	2	1	1	1
Days 22-28	MEAN	59.4	61.1	61.2	65.2
	ST.DEV.	1.3	---	---	---
	N	2	1	1	1
MEAN OF MEANS Over TREATMENT		64.0	65.5	65.9	66.3
RECOVERY					
Days 1-8	MEAN	61.3	---	---	---
	ST.DEV.	---	---	---	---
	N	1	0	0	0
Days 8-14	MEAN	63.9	---	---	---
	ST.DEV.	---	---	---	---
	N	1	0	0	0
MEAN OF MEANS Over RECOVERY		62.6	---	---	---

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY) - SUMMARY
MALES

		Group 5 1000 mg/kg
POST-RANDOMIZATION		
Days 1-6	MEAN	110.0
	ST.DEV.	1.5
	N	2
TREATMENT		
Days 1-8	MEAN	71.3
	ST.DEV.	0.5
	N	2
Days 8-15	MEAN	61.6
	ST.DEV.	3.2
	N	2
Days 15-22	MEAN	59.4
	ST.DEV.	0.2
	N	2
Days 22-28	MEAN	76.9
	ST.DEV.	0.2
	N	2
MEAN OF MEANS Over TREATMENT		67.3
RECOVERY		
Days 1-8	MEAN	75.1
	ST.DEV.	---
	N	1
Days 8-14	MEAN	77.7
	ST.DEV.	---
	N	1
MEAN OF MEANS Over RECOVERY		76.4

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY) - SUMMARY
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
POST-RANDOMIZATION					
Days 1-6	MEAN	105.7	102.0	98.4	97.5
	ST.DEV.	3.8	---	---	---
	N	2	1	1	1
TREATMENT					
Days 1-8	MEAN	73.0	72.3	68.5	74.1
	ST.DEV.	4.1	---	---	---
	N	2	1	1	1
Days 8-15	MEAN	63.9	62.9	66.0	68.7
	ST.DEV.	1.8	---	---	---
	N	2	1	1	1
Days 15-22	MEAN	60.6	58.9	62.7	60.4
	ST.DEV.	0.3	---	---	---
	N	2	1	1	1
Days 22-28	MEAN	70.6	72.2	63.1	73.5
	ST.DEV.	6.6	---	---	---
	N	2	1	1	1
MEAN OF MEANS Over TREATMENT		67.0	66.6	65.1	69.2
RECOVERY					
Days 1-8	MEAN	73.8	---	---	---
	ST.DEV.	---	---	---	---
	N	1	0	0	0
Days 8-14	MEAN	70.1	---	---	---
	ST.DEV.	---	---	---	---
	N	1	0	0	0
MEAN OF MEANS Over RECOVERY		71.9	---	---	---

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY) - SUMMARY
FEMALES

		Group 5 1000 mg/kg
POST-RANDOMIZATION		
Days 1-6	MEAN	101.1
	ST.DEV.	2.9
	N	2
TREATMENT		
Days 1-8	MEAN	76.5
	ST.DEV.	3.2
	N	2
Days 8-15	MEAN	68.5
	ST.DEV.	0.0
	N	2
Days 15-22	MEAN	66.2
	ST.DEV.	2.1
	N	2
Days 22-28	MEAN	85.5
	ST.DEV.	3.2
	N	2
MEAN OF MEANS Over TREATMENT		74.2
RECOVERY		
Days 1-8	MEAN	79.6
	ST.DEV.	---
	N	1
Days 8-14	MEAN	74.4
	ST.DEV.	---
	N	1
MEAN OF MEANS Over RECOVERY		77.0

BODY WEIGHTS (G) - SUMMARY

Data excluded from Summary Report

Not Reported

All Study Phases

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

BODY WEIGHTS (G) - SUMMARY
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
PRE-RANDOMIZATION					
Day 1	MEAN	207	207 -	206 -	207 -
	ST.DEV.	5	5	5	5
	MINIMUM	200	201	200	201
	MAXIMUM	216	215	213	213
	N	10	5	5	5
POST-RANDOMIZATION					
Day 1	MEAN	218	219 -	216 -	218 -
	ST.DEV.	6	6	8	4
	MINIMUM	210	213	206	212
	MAXIMUM	227	229	226	224
	N	10	5	5	5
TREATMENT					
Day 1	MEAN	253	256 -	247 -	253 -
	ST.DEV.	5	8	4	2
	MINIMUM	245	251	241	251
	MAXIMUM	259	270	252	256
	N	10	5	5	5
Day 8	MEAN	290	296 -	284 -	288 -
	ST.DEV.	8	13	2	15
	MINIMUM	277	287	280	269
	MAXIMUM	300	319	285	310
	N	10	5	5	5
Day 15	MEAN	317	327 -	311 -	315 -
	ST.DEV.	9	16	5	23
	MINIMUM	302	314	306	286
	MAXIMUM	328	354	317	351
	N	10	5	5	5
Day 22	MEAN	340	353 -	337 -	333 -
	ST.DEV.	13	19	8	34
	MINIMUM	321	338	326	285
	MAXIMUM	357	386	347	380
	N	10	5	5	5
Day 28	MEAN	359	374 -	357 -	354 -
	ST.DEV.	16	21	9	30
	MINIMUM	334	354	345	314
	MAXIMUM	375	408	367	398
	N	10	5	5	5

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

BODY WEIGHTS (G) - SUMMARY
MALES

		Group 5 1000 mg/kg
PRE-RANDOMIZATION		
Day 1	MEAN	207 -
	ST.DEV.	7
	MINIMUM	196
	MAXIMUM	220
	N	10
POST-RANDOMIZATION		
Day 1	MEAN	219 -
	ST.DEV.	6
	MINIMUM	211
	MAXIMUM	230
	N	10
TREATMENT		
Day 1	MEAN	251 -
	ST.DEV.	9
	MINIMUM	240
	MAXIMUM	262
	N	10
Day 8	MEAN	264 **
	ST.DEV.	12
	MINIMUM	250
	MAXIMUM	281
	N	10
Day 15	MEAN	281 **
	ST.DEV.	14
	MINIMUM	258
	MAXIMUM	303
	N	10
Day 22	MEAN	292 **
	ST.DEV.	32
	MINIMUM	214
	MAXIMUM	332
	N	10
Day 28	MEAN	319 **
	ST.DEV.	27
	MINIMUM	259
	MAXIMUM	355
	N	10

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

BODY WEIGHTS (G) - SUMMARY
MALES

		Group 1 **0 mg/kg**	Group 5 1000 mg/kg
RECOVERY			
Day 1	MEAN	351	298 **
	ST.DEV.	13	17
	MINIMUM	329	288
	MAXIMUM	362	328
	N	5	5
Day 8	MEAN	375	333 **
	ST.DEV.	15	20
	MINIMUM	351	312
	MAXIMUM	391	362
	N	5	5
Day 14	MEAN	388	352 *
	ST.DEV.	16	24
	MINIMUM	363	326
	MAXIMUM	407	378
	N	5	5

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

BODY WEIGHTS (G) - SUMMARY
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
PRE-RANDOMIZATION					
Day 1	MEAN	167	162 -	164 -	164 -
	ST.DEV.	7	6	4	4
	MINIMUM	159	152	157	158
	MAXIMUM	183	168	168	169
	N	10	5	5	5
POST-RANDOMIZATION					
Day 1	MEAN	173	172 -	173 -	170 -
	ST.DEV.	9	3	7	3
	MINIMUM	163	169	163	167
	MAXIMUM	189	175	182	174
	N	10	5	5	5
TREATMENT					
Day 1	MEAN	197	188 -	190 -	187 -
	ST.DEV.	12	9	6	4
	MINIMUM	183	181	180	183
	MAXIMUM	218	204	196	192
	N	10	5	5	5
Day 8	MEAN	211	205 -	202 -	201 -
	ST.DEV.	12	13	7	8
	MINIMUM	196	190	190	192
	MAXIMUM	229	223	209	212
	N	10	5	5	5
Day 15	MEAN	223	214 -	220 -	219 -
	ST.DEV.	17	6	10	10
	MINIMUM	208	206	206	205
	MAXIMUM	260	220	232	229
	N	10	5	5	5
Day 22	MEAN	238	223 -	234 -	227 -
	ST.DEV.	16	10	13	7
	MINIMUM	220	207	215	221
	MAXIMUM	269	234	247	238
	N	10	5	5	5
Day 28	MEAN	252	241 -	243 -	247 -
	ST.DEV.	19	10	16	12
	MINIMUM	231	229	216	229
	MAXIMUM	288	252	259	262
	N	10	5	5	5

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

BODY WEIGHTS (G) - SUMMARY
FEMALES

		Group 5 1000 mg/kg
PRE-RANDOMIZATION		
Day 1	MEAN	165 -
	ST.DEV.	4
	MINIMUM	159
	MAXIMUM	172
	N	10
POST-RANDOMIZATION		
Day 1	MEAN	172 -
	ST.DEV.	4
	MINIMUM	166
	MAXIMUM	178
	N	10
TREATMENT		
Day 1	MEAN	190 -
	ST.DEV.	5
	MINIMUM	184
	MAXIMUM	199
	N	10
Day 8	MEAN	209 -
	ST.DEV.	12
	MINIMUM	195
	MAXIMUM	230
	N	10
Day 15	MEAN	219 -
	ST.DEV.	13
	MINIMUM	210
	MAXIMUM	252
	N	10
Day 22	MEAN	229 -
	ST.DEV.	10
	MINIMUM	216
	MAXIMUM	251
	N	10
Day 28	MEAN	249 -
	ST.DEV.	11
	MINIMUM	230
	MAXIMUM	268
	N	10

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

BODY WEIGHTS (G) - SUMMARY
FEMALES

		Group 1 **0 mg/kg**	Group 5 1000 mg/kg
RECOVERY			
Day 1	MEAN	242	228 -
	ST.DEV.	18	8
	MINIMUM	221	219
	MAXIMUM	266	238
	N	5	5
Day 8	MEAN	256	248 -
	ST.DEV.	17	16
	MINIMUM	234	230
	MAXIMUM	279	262
	N	5	5
Day 14	MEAN	256	250 -
	ST.DEV.	17	10
	MINIMUM	237	239
	MAXIMUM	279	259
	N	5	5

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

BODY WEIGHT GAIN (%) - SUMMARY

Data excluded from Summary Report

Not Reported

All Study Phases

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

BODY WEIGHT GAIN (%) - SUMMARY
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
POST-RANDOMIZATION					
Day 1	MEAN	0.0	0.0	0.0	0.0
	ST.DEV.	0.0	0.0	0.0	0.0
	MINIMUM	0.0	0.0	0.0	0.0
	MAXIMUM	0.0	0.0	0.0	0.0
	N	10	5	5	5
TREATMENT					
Day 1	MEAN	0.0	0.0	0.0	0.0
	ST.DEV.	0.0	0.0	0.0	0.0
	MINIMUM	0.0	0.0	0.0	0.0
	MAXIMUM	0.0	0.0	0.0	0.0
	N	10	5	5	5
Day 8	MEAN	14.7	15.5 -	15.0 -	13.9 -
	ST.DEV.	1.9	2.4	1.5	5.8
	MINIMUM	12.3	12.7	13.2	6.3
	MAXIMUM	17.1	18.3	16.5	22.4
	N	10	5	5	5
Day 15	MEAN	25.2	27.5 -	26.1 -	24.5 -
	ST.DEV.	2.5	2.5	2.8	8.9
	MINIMUM	20.5	24.8	22.7	13.2
	MAXIMUM	28.5	31.4	29.2	38.2
	N	10	5	5	5
Day 22	MEAN	34.5	37.7 -	36.4 -	31.6 -
	ST.DEV.	4.0	3.6	4.1	13.1
	MINIMUM	26.9	34.4	30.8	12.9
	MAXIMUM	39.7	43.2	41.8	49.8
	N	10	5	5	5
Day 28	MEAN	41.7	45.8 -	44.7 -	39.7 -
	ST.DEV.	5.0	4.7	5.3	11.7
	MINIMUM	32.8	41.1	38.1	24.4
	MAXIMUM	47.5	51.2	50.3	57.0
	N	10	5	5	5
RECOVERY					
Day 1	MEAN	0.0			
	ST.DEV.	0.0			
	MINIMUM	0.0			
	MAXIMUM	0.0			
	N	5			

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

BODY WEIGHT GAIN (%) - SUMMARY
MALES

		Group 5 1000 mg/kg
POST-RANDOMIZATION		
Day 1	MEAN	0.0
	ST.DEV.	0.0
	MINIMUM	0.0
	MAXIMUM	0.0
	N	10
TREATMENT		
Day 1	MEAN	0.0
	ST.DEV.	0.0
	MINIMUM	0.0
	MAXIMUM	0.0
	N	10
Day 8	MEAN	5.2**
	ST.DEV.	3.3
	MINIMUM	-1.0
	MAXIMUM	11.4
	N	10
Day 15	MEAN	11.9**
	ST.DEV.	3.6
	MINIMUM	6.0
	MAXIMUM	20.1
	N	10
Day 22	MEAN	16.3**
	ST.DEV.	11.5
	MINIMUM	-12.3
	MAXIMUM	31.6
	N	10
Day 28	MEAN	26.9**
	ST.DEV.	8.8
	MINIMUM	6.2
	MAXIMUM	39.6
	N	10
RECOVERY		
Day 1	MEAN	0.0
	ST.DEV.	0.0
	MINIMUM	0.0
	MAXIMUM	0.0
	N	5

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

BODY WEIGHT GAIN (%) - SUMMARY
MALES

		Group 1 **0 mg/kg**	Group 5 1000 mg/kg
RECOVERY			
Day 8	MEAN	6.9	11.8 *
	ST.DEV.	0.7	4.4
	MINIMUM	6.0	7.9
	MAXIMUM	8.0	19.1
	N	5	5
Day 14	MEAN	10.6	18.3 -
	ST.DEV.	1.4	7.4
	MINIMUM	9.0	12.7
	MAXIMUM	12.6	31.2
	N	5	5

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

BODY WEIGHT GAIN (%) - SUMMARY
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
POST-RANDOMIZATION					
Day 1	MEAN	0.0	0.0	0.0	0.0
	ST.DEV.	0.0	0.0	0.0	0.0
	MINIMUM	0.0	0.0	0.0	0.0
	MAXIMUM	0.0	0.0	0.0	0.0
	N	10	5	5	5
TREATMENT					
Day 1	MEAN	0.0	0.0	0.0	0.0
	ST.DEV.	0.0	0.0	0.0	0.0
	MINIMUM	0.0	0.0	0.0	0.0
	MAXIMUM	0.0	0.0	0.0	0.0
	N	10	5	5	5
Day 8	MEAN	7.4	9.1 -	6.3 -	7.7 -
	ST.DEV.	3.9	3.9	2.9	5.3
	MINIMUM	2.0	3.7	2.0	1.7
	MAXIMUM	12.7	14.6	9.6	16.3
	N	10	5	5	5
Day 15	MEAN	13.6	14.3 -	15.7 -	17.3 -
	ST.DEV.	5.0	4.2	3.4	5.2
	MINIMUM	4.0	7.8	10.4	11.6
	MAXIMUM	21.5	18.3	18.7	25.3
	N	10	5	5	5
Day 22	MEAN	21.2	18.8 -	23.4 -	21.3 -
	ST.DEV.	7.0	4.7	5.4	5.5
	MINIMUM	12.1	13.1	18.9	17.1
	MAXIMUM	38.3	23.4	32.0	30.6
	N	10	5	5	5
Day 28	MEAN	28.5	28.5 -	27.9 -	32.0 -
	ST.DEV.	9.7	5.8	5.5	7.5
	MINIMUM	15.6	20.5	20.1	24.8
	MAXIMUM	47.4	34.6	35.0	43.4
	N	10	5	5	5
RECOVERY					
Day 1	MEAN	0.0			
	ST.DEV.	0.0			
	MINIMUM	0.0			
	MAXIMUM	0.0			
	N	5			

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

BODY WEIGHT GAIN (%) - SUMMARY
FEMALES

		Group 5 1000 mg/kg
POST-RANDOMIZATION		
Day 1	MEAN	0.0
	ST.DEV.	0.0
	MINIMUM	0.0
	MAXIMUM	0.0
	N	10
TREATMENT		
Day 1	MEAN	0.0
	ST.DEV.	0.0
	MINIMUM	0.0
	MAXIMUM	0.0
	N	10
Day 8	MEAN	9.7 -
	ST.DEV.	4.4
	MINIMUM	2.0
	MAXIMUM	17.5
	N	10
Day 15	MEAN	15.2 -
	ST.DEV.	5.2
	MINIMUM	7.2
	MAXIMUM	26.6
	N	10
Day 22	MEAN	20.2 -
	ST.DEV.	3.1
	MINIMUM	16.1
	MAXIMUM	26.0
	N	10
Day 28	MEAN	30.8 -
	ST.DEV.	3.9
	MINIMUM	22.8
	MAXIMUM	36.0
	N	10
RECOVERY		
Day 1	MEAN	0.0
	ST.DEV.	0.0
	MINIMUM	0.0
	MAXIMUM	0.0
	N	5

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

BODY WEIGHT GAIN (%) - SUMMARY
FEMALES

		Group 1 **0 mg/kg**	Group 5 1000 mg/kg
RECOVERY			
Day 8	MEAN	5.9	8.9 -
	ST.DEV.	5.4	4.2
	MINIMUM	-3.1	3.4
	MAXIMUM	10.2	13.5
	N	5	5
Day 14	MEAN	5.7	9.6**
	ST.DEV.	1.3	1.7
	MINIMUM	4.1	7.4
	MAXIMUM	7.5	11.7
	N	5	5

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

Hematology - SUMMARY

Data excluded from Summary Report

Not Reported

All Measurements

Animal 100 Male Group 10 Reserve Removed
Animal 101 Female Group 10 Reserve Removed

Reported Parameter

Parameter		Statistical Testing
After 4 Weeks		
RBC	ERYTHROCYTES (RBC)	DUNNETT
HB	HEMOGLOBIN (HB)	DUNNETT
HCT	HEMATOCRIT (HCT)	DUNNETT
MCV	MEAN CORPUSCULAR VOLUME (MCV)	DUNNETT
RDW	RED CELL VOL. DISTR. WIDTH (RDW)	DUNNETT
MCH	MEAN CORPUSCULAR HEMOGLOBIN (MCH)	DUNNETT
MCHC	MEAN CORPUSCULAR HEMOGLOBIN CONC. (MCHC)	DUNNETT
HDW	HEMOGLOBIN CONC. DISTR. WIDTH	DUNNETT
RETI	RETICULOCYTE (REL)	STEEL
RETI	RETICULOCYTE (ABS)	DUNNETT
L RETI	MATURITY INDEX (L-RETI)	STEEL
M RETI	MATURITY INDEX (M-RETI)	STEEL
H RETI	MATURITY INDEX (H-RETI)	STEEL
WBC	LEUKOCYTES, TOTAL (WBC)	DUNNETT
NEUT	NEUTROPHILS (NEUT)	STEEL
EOS	EOSINOPHILS (EOS)	STEEL
BASO	BASOPHILS (BASO)	STEEL
LYMPH	LYMPHOCYTES (LYMPH)	STEEL
MONO	MONOCYTES (MONO)	STEEL
LUC	LARGE UNSTAINED CELLS (LUC)	STEEL
NEUT	NEUTROPHILS (NEUT)	DUNNETT
EOS	EOSINOPHILS (EOS)	DUNNETT
BASO	BASOPHILS (BASO)	DUNNETT
LYMPH	LYMPHOCYTES (LYMPH)	DUNNETT
MONO	MONOCYTES (MONO)	DUNNETT
LUC	LARGE UNSTAINED CELLS (LUC)	DUNNETT
PLATELETS	THROMBOCYTES (PLATELETS)	DUNNETT
MET-HB	METHEMOGLOBIN (MET-HB)	STEEL
HEINZ BOD	HEINZ BODIES	STEEL
PT	PROTHROMBIN TIME (PT)	STEEL
PTT	PARTIAL THROMBOPLASTIN TIME (PTT)	STEEL
After 6 Weeks (Recovery)		
RBC	ERYTHROCYTES (RBC)	DUNNETT

Hematology - SUMMARY

Reported Parameter

Parameter		Statistical Testing
After 6 Weeks (Recovery)		
HB	HEMOGLOBIN (HB)	DUNNETT
HCT	HEMATOCRIT (HCT)	DUNNETT
MCV	MEAN CORPUSCULAR VOLUME (MCV)	DUNNETT
RDW	RED CELL VOL. DISTR. WIDTH (RDW)	DUNNETT
MCH	MEAN CORPUSCULAR HEMOGLOBIN (MCH)	DUNNETT
MCHC	MEAN CORPUSCULAR HEMOGLOBIN CONC. (MCHC)	DUNNETT
HDW	HEMOGLOBIN CONC. DISTR. WIDTH	DUNNETT
RETI	RETICULOCYTE (REL)	STEEL
RETI	RETICULOCYTE (ABS)	DUNNETT
L RETI	MATURITY INDEX (L-RETI)	STEEL
M RETI	MATURITY INDEX (M-RETI)	STEEL
H RETI	MATURITY INDEX (H-RETI)	STEEL
WBC	LEUKOCYTES, TOTAL (WBC)	DUNNETT
NEUT	NEUTROPHILS (NEUT)	STEEL
EOS	EOSINOPHILS (EOS)	STEEL
BASO	BASOPHILS (BASO)	STEEL
LYMPH	LYMPHOCYTES (LYMPH)	STEEL
MONO	MONOCYTES (MONO)	STEEL
LUC	LARGE UNSTAINED CELLS (LUC)	STEEL
NEUT	NEUTROPHILS (NEUT)	DUNNETT
EOS	EOSINOPHILS (EOS)	DUNNETT
BASO	BASOPHILS (BASO)	DUNNETT
LYMPH	LYMPHOCYTES (LYMPH)	DUNNETT
MONO	MONOCYTES (MONO)	DUNNETT
LUC	LARGE UNSTAINED CELLS (LUC)	DUNNETT
PLATELETS	THROMBOCYTES (PLATELETS)	DUNNETT
MET-HB	METHEMOGLOBIN (MET-HB)	STEEL
HEINZ BOD	HEINZ BODIES	STEEL
PT	PROTHROMBIN TIME (PT)	STEEL
PTT	PARTIAL THROMBOPLASTIN TIME (PTT)	STEEL

Statistical Methods

DUNNETT	DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not significant (-)
STEEL	STEEL-Test sig. at 5% (*), 1% (**) or not significant (-)

Hematology - SUMMARY
MALES

		GENERAL					
		RBC	HB	HCT	MCV	RDW	MCH
		T/l	mmol/l	rel. 1	fl	rel. 1	fmol
After 4 Weeks							
Group 1	MEAN/MEDIAN	8.62	9.6	0.46	53.1	0.118	1.11
	ST.DEV.	0.29	0.2	0.01	1.1	0.002	0.03
	N	10	10	10	10	10	10
Group 2	MEAN/MEDIAN	8.47-	9.5-	0.45-	53.1-	0.118-	1.13-
	ST.DEV.	0.25	0.3	0.01	1.2	0.001	0.03
	N	5	5	5	5	5	5
Group 3	MEAN/MEDIAN	8.67-	9.7-	0.46-	52.7-	0.119-	1.12-
	ST.DEV.	0.18	0.3	0.01	1.0	0.005	0.04
	N	5	5	5	5	5	5
Group 4	MEAN/MEDIAN	8.39-	9.2*	0.43*	51.7-	0.114-	1.09-
	ST.DEV.	0.39	0.4	0.01	1.5	0.002	0.04
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	9.05**	9.6-	0.46-	50.5**	0.117-	1.06**
	ST.DEV.	0.28	0.2	0.02	1.2	0.004	0.02
	N	10	10	10	10	10	10
After 6 Weeks (Recovery)							
Group 1	MEAN/MEDIAN	8.76	9.9	0.46	52.6	0.127	1.12
	ST.DEV.	0.36	0.6	0.01	0.9	0.001	0.04
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	9.21-	9.6-	0.45-	49.4**	0.128-	1.04**
	ST.DEV.	0.30	0.2	0.01	0.7	0.004	0.02
	N	5	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Hematology - SUMMARY
MALES

		GENERAL		RETICULOCYTE COUNT			
		MCHC mmol/l	HDW mmol/l	RETI rel. 1	RETI G/l	L RETI rel. 1	M RETI rel. 1
After 4 Weeks							
Group 1	MEAN/MEDIAN	21.00	1.68	0.027	232	0.638	0.298
	ST.DEV.	0.22	0.03	0.003	22	0.034	0.021
	N	10	10	10	10	10	10
Group 2	MEAN/MEDIAN	21.16-	1.68-	0.028-	233-	0.644-	0.291-
	ST.DEV.	0.10	0.06	0.002	9	0.040	0.027
	N	5	5	5	5	5	5
Group 3	MEAN/MEDIAN	21.17-	1.65-	0.026-	232-	0.646-	0.301-
	ST.DEV.	0.34	0.04	0.004	36	0.029	0.018
	N	5	5	5	5	5	5
Group 4	MEAN/MEDIAN	21.13-	1.72-	0.028-	239-	0.649-	0.301-
	ST.DEV.	0.42	0.13	0.004	27	0.049	0.035
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	20.92-	1.83**	0.028-	258-	0.712**	0.257**
	ST.DEV.	0.25	0.06	0.005	48	0.032	0.024
	N	10	10	10	10	10	10
After 6 Weeks (Recovery)							
Group 1	MEAN/MEDIAN	21.38	1.74	0.029	238	0.574	0.333
	ST.DEV.	0.85	0.06	0.003	28	0.076	0.054
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	21.11-	1.80-	0.024-	221-	0.670-	0.281-
	ST.DEV.	0.27	0.06	0.002	16	0.039	0.033
	N	5	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Hematology - SUMMARY
MALES

		RETICULOCYTE COUNT	GENERAL	DIFF.WBC COUNT (REL)		
		H RETI	WBC	NEUT	EOS	BASO
		rel. 1	G/l	rel. 1	rel. 1	rel. 1
After 4 Weeks						
Group 1	MEAN/MEDIAN	0.060	14.02	0.118	0.005	0.006
	ST.DEV.	0.016	1.37	0.033	0.001	0.001
	N	10	10	10	10	10
Group 2	MEAN/MEDIAN	0.059-	11.67-	0.103-	0.005-	0.005-
	ST.DEV.	0.019	0.86	0.022	0.001	0.001
	N	5	5	5	5	5
Group 3	MEAN/MEDIAN	0.050-	13.06-	0.102-	0.006-	0.006-
	ST.DEV.	0.013	2.21	0.009	0.001	0.001
	N	5	5	5	5	5
Group 4	MEAN/MEDIAN	0.061-	13.56-	0.124-	0.004-	0.006-
	ST.DEV.	0.016	2.32	0.033	0.001	0.001
	N	5	5	5	5	5
Group 5	MEAN/MEDIAN	0.034**	14.40-	0.166-	0.003*	0.005-
	ST.DEV.	0.010	2.88	0.041	0.001	0.001
	N	10	10	10	10	10
After 6 Weeks (Recovery)						
Group 1	MEAN/MEDIAN	0.074	13.17	0.099	0.007	0.005
	ST.DEV.	0.023	3.68	0.026	0.001	0.001
	N	5	5	5	5	5
Group 5	MEAN/MEDIAN	0.046-	12.54-	0.092-	0.008-	0.004-
	ST.DEV.	0.010	1.10	0.034	0.036	0.000
	N	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Hematology - SUMMARY
MALES

		DIFF.WBC COUNT (REL)			DIFF.WBC COUNT (ABS)		
		LYMPH	MONO	LUC	NEUT	EOS	BASO
		rel. 1	rel. 1	rel. 1	G/l	G/l	G/l
After 4 Weeks							
Group 1	MEAN/MEDIAN	0.832	0.031	0.012	1.66	0.07	0.08
	ST.DEV.	0.035	0.006	0.004	0.48	0.02	0.02
	N	10	10	10	10	10	10
Group 2	MEAN/MEDIAN	0.849-	0.024-	0.012-	1.13-	0.06-	0.06-
	ST.DEV.	0.024	0.006	0.003	0.22	0.01	0.01
	N	5	5	5	5	5	5
Group 3	MEAN/MEDIAN	0.850-	0.031-	0.011-	1.37-	0.07-	0.07-
	ST.DEV.	0.018	0.008	0.004	0.30	0.02	0.02
	N	5	5	5	5	5	5
Group 4	MEAN/MEDIAN	0.828-	0.029-	0.009-	1.82-	0.06-	0.07-
	ST.DEV.	0.035	0.003	0.003	0.63	0.01	0.02
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	0.780*	0.034-	0.013-	2.39*	0.04**	0.08-
	ST.DEV.	0.046	0.007	0.004	0.78	0.02	0.03
	N	10	10	10	10	10	10
After 6 Weeks (Recovery)							
Group 1	MEAN/MEDIAN	0.847	0.034	0.009	1.27	0.09	0.07
	ST.DEV.	0.022	0.002	0.003	0.23	0.03	0.03
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	0.847-	0.035-	0.009-	1.38-	0.32-	0.05-
	ST.DEV.	0.066	0.006	0.003	0.57	0.52	0.00
	N	5	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Hematology - SUMMARY
MALES

		DIFF.WBC COUNT (ABS)			GENERAL		
		LYMPH G/l	MONO G/l	LUC G/l	PLATELETS G/l	MET-HB rel. 1	HEINZ BOD rel. 1
After 4 Weeks							
Group 1	MEAN/MEDIAN	11.61	0.41	0.18	1055	0.010	0.000
	ST.DEV.	1.28	0.10	0.07	147	0.001	0.000
	N	10	10	10	10	10	10
Group 2	MEAN/MEDIAN	9.97-	0.31-	0.14-	1022-	0.010-	0.000-
	ST.DEV.	0.92	0.06	0.03	111	0.001	0.000
	N	5	5	5	5	5	5
Group 3	MEAN/MEDIAN	10.98-	0.40-	0.16-	1023-	0.010-	0.000-
	ST.DEV.	1.77	0.14	0.06	87	0.001	0.000
	N	5	5	5	5	5	5
Group 4	MEAN/MEDIAN	11.09-	0.39-	0.13-	1171-	0.009-	0.000-
	ST.DEV.	1.89	0.09	0.02	93	0.001	0.000
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	11.21-	0.50-	0.18-	1281**	0.009*	0.000-
	ST.DEV.	2.47	0.14	0.07	170	0.001	0.000
	N	10	10	10	10	10	10
After 6 Weeks (Recovery)							
Group 1	MEAN/MEDIAN	11.18	0.45	0.13	1009	0.011	0.000
	ST.DEV.	3.33	0.15	0.05	113	0.000	0.000
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	10.24-	0.42-	0.12-	1078-	0.011-	0.000-
	ST.DEV.	0.57	0.06	0.03	120	0.001	0.000
	N	5	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Hematology - SUMMARY
MALES

		COAGULATION	
		PT	PTT
		rel. 1	sec
After 4 Weeks			
Group 1	MEAN/MEDIAN	0.87	25.4
	ST.DEV.	0.08	1.6
	N	10	10
Group 2	MEAN/MEDIAN	0.86-	25.1-
	ST.DEV.	0.14	0.7
	N	5	5
Group 3	MEAN/MEDIAN	0.87-	24.6-
	ST.DEV.	0.02	1.9
	N	5	5
Group 4	MEAN/MEDIAN	0.92-	19.1**
	ST.DEV.	0.04	0.9
	N	5	5
Group 5	MEAN/MEDIAN	0.88-	17.6**
	ST.DEV.	0.10	1.3
	N	10	10
After 6 Weeks (Recovery)			
Group 1	MEAN/MEDIAN	0.82	24.7
	ST.DEV.	0.09	1.2
	N	5	5
Group 5	MEAN/MEDIAN	0.84-	23.5-
	ST.DEV.	0.10	1.5
	N	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Hematology - SUMMARY
FEMALES

		GENERAL					
		RBC	HB	HCT	MCV	RDW	MCH
		T/l	mmol/l	rel. 1	fl	rel. 1	fmol
After 4 Weeks							
Group 1	MEAN/MEDIAN	8.02	9.4	0.43	53.7	0.112	1.17
	ST.DEV.	0.19	0.3	0.01	0.8	0.004	0.02
	N	10	10	10	10	10	10
Group 2	MEAN/MEDIAN	7.72*	9.0-	0.41**	53.3-	0.116-	1.17-
	ST.DEV.	0.26	0.3	0.01	1.3	0.004	0.02
	N	5	5	5	5	5	5
Group 3	MEAN/MEDIAN	7.93-	9.2-	0.42-	53.5-	0.113-	1.16-
	ST.DEV.	0.20	0.2	0.01	0.8	0.002	0.03
	N	5	5	5	5	5	5
Group 4	MEAN/MEDIAN	7.78-	9.0-	0.42-	53.7-	0.114-	1.15-
	ST.DEV.	0.19	0.4	0.02	1.8	0.004	0.04
	N	4	4	4	4	4	4
Group 5	MEAN/MEDIAN	8.08-	9.2-	0.43-	53.3-	0.107*	1.14*
	ST.DEV.	0.20	0.3	0.01	0.9	0.003	0.02
	N	10	10	10	10	10	10
After 6 Weeks (Recovery)							
Group 1	MEAN/MEDIAN	8.49	10.0	0.46	54.1	0.127	1.18
	ST.DEV.	0.22	0.2	0.01	1.0	0.004	0.03
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	8.38-	9.8-	0.45-	52.8*	0.123-	1.17-
	ST.DEV.	0.18	0.2	0.01	0.4	0.003	0.01
	N	5	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Hematology - SUMMARY
FEMALES

		GENERAL		RETICULOCYTE COUNT			
		MCHC mmol/l	HDW mmol/l	RETI rel. 1	RETI G/l	L RETI rel. 1	M RETI rel. 1
After 4 Weeks							
Group 1	MEAN/MEDIAN	21.76	1.59	0.035	273	0.621	0.321
	ST.DEV.	0.36	0.06	0.008	64	0.069	0.053
	N	10	10	10	10	10	10
Group 2	MEAN/MEDIAN	21.97-	1.64-	0.038-	290-	0.609-	0.335-
	ST.DEV.	0.22	0.06	0.005	33	0.042	0.024
	N	5	5	5	5	5	5
Group 3	MEAN/MEDIAN	21.70-	1.60-	0.027-	241-	0.641-	0.305-
	ST.DEV.	0.36	0.05	0.010	71	0.085	0.052
	N	5	5	5	5	5	5
Group 4	MEAN/MEDIAN	21.48-	1.55-	0.037-	294-	0.586-	0.334-
	ST.DEV.	0.27	0.07	0.004	29	0.063	0.027
	N	4	4	4	4	4	4
Group 5	MEAN/MEDIAN	21.28*	1.53-	0.032-	248-	0.626-	0.310-
	ST.DEV.	0.34	0.05	0.006	50	0.045	0.030
	N	10	10	10	10	10	10
After 6 Weeks (Recovery)							
Group 1	MEAN/MEDIAN	21.86	1.67	0.025	246	0.646	0.305
	ST.DEV.	0.30	0.08	0.011	95	0.067	0.047
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	22.07-	1.60-	0.020-	176-	0.682-	0.277-
	ST.DEV.	0.23	0.05	0.003	26	0.066	0.056
	N	5	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Hematology - SUMMARY
FEMALES

		RETICULOCYTE COUNT	GENERAL	DIFF.WBC COUNT (REL)		
		H RETI	WBC	NEUT	EOS	BASO
		rel. 1	G/l	rel. 1	rel. 1	rel. 1
After 4 Weeks						
Group 1	MEAN/MEDIAN	0.060	9.20	0.110	0.011	0.004
	ST.DEV.	0.019	1.61	0.029	0.004	0.001
	N	10	10	10	10	10
Group 2	MEAN/MEDIAN	0.056-	8.09-	0.126-	0.012-	0.003-
	ST.DEV.	0.020	1.47	0.042	0.003	0.000
	N	5	5	5	5	5
Group 3	MEAN/MEDIAN	0.054-	8.06-	0.101-	0.011-	0.003-
	ST.DEV.	0.034	0.85	0.027	0.012	0.000
	N	5	5	5	5	5
Group 4	MEAN/MEDIAN	0.078-	6.69*	0.127-	0.011-	0.004-
	ST.DEV.	0.042	1.09	0.010	0.002	0.001
	N	4	4	4	4	4
Group 5	MEAN/MEDIAN	0.061-	7.62-	0.110-	0.013-	0.004-
	ST.DEV.	0.017	1.74	0.033	0.003	0.001
	N	10	10	10	10	10
After 6 Weeks (Recovery)						
Group 1	MEAN/MEDIAN	0.049	10.05	0.099	0.012	0.004
	ST.DEV.	0.021	1.46	0.032	0.001	0.001
	N	5	5	5	5	5
Group 5	MEAN/MEDIAN	0.030*	9.09-	0.114-	0.012-	0.005-
	ST.DEV.	0.011	1.42	0.055	0.004	0.002
	N	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Hematology - SUMMARY
FEMALES

		DIFF.WBC COUNT (REL)			DIFF.WBC COUNT (ABS)		
		LYMPH	MONO	LUC	NEUT	EOS	BASO
		rel. 1	rel. 1	rel. 1	G/l	G/l	G/l
After 4 Weeks							
Group 1	MEAN/MEDIAN	0.835	0.027	0.012	1.00	0.10	0.04
	ST.DEV.	0.035	0.005	0.004	0.26	0.03	0.02
	N	10	10	10	10	10	10
Group 2	MEAN/MEDIAN	0.816-	0.022-	0.012-	1.09-	0.09-	0.03-
	ST.DEV.	0.044	0.004	0.003	0.30	0.01	0.01
	N	5	5	5	5	5	5
Group 3	MEAN/MEDIAN	0.857-	0.022-	0.009-	0.87-	0.13-	0.03-
	ST.DEV.	0.038	0.003	0.002	0.22	0.09	0.01
	N	5	5	5	5	5	5
Group 4	MEAN/MEDIAN	0.825-	0.022-	0.012-	0.84-	0.08-	0.03-
	ST.DEV.	0.009	0.003	0.002	0.11	0.03	0.01
	N	4	4	4	4	4	4
Group 5	MEAN/MEDIAN	0.825-	0.040-	0.012-	0.85-	0.10-	0.03-
	ST.DEV.	0.040	0.010	0.005	0.20	0.03	0.01
	N	10	10	10	10	10	10
After 6 Weeks (Recovery)							
Group 1	MEAN/MEDIAN	0.846	0.031	0.008	1.10	0.12	0.04
	ST.DEV.	0.032	0.004	0.001	0.19	0.02	0.01
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	0.822-	0.026-	0.008-	1.18-	0.12-	0.04-
	ST.DEV.	0.050	0.006	0.002	0.56	0.03	0.02
	N	5	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Hematology - SUMMARY
FEMALES

		DIFF.WBC COUNT (ABS)			GENERAL		
		LYMPH	MONO	LUC	PLATELETS	MET-HB	HEINZ BOD
		G/l	G/l	G/l	G/l	rel. 1	rel. 1
After 4 Weeks							
Group 1	MEAN/MEDIAN	7.70	0.24	0.12	1151	0.010	0.000
	ST.DEV.	1.46	0.06	0.05	150	0.000	0.000
	N	10	10	10	10	10	10
Group 2	MEAN/MEDIAN	6.61 -	0.17 -	0.10 -	1121 -	0.010 -	0.000 -
	ST.DEV.	1.41	0.03	0.03	79	0.000	0.000
	N	5	5	5	5	5	5
Group 3	MEAN/MEDIAN	6.79 -	0.16 -	0.08 -	1066 -	0.010 -	0.000 -
	ST.DEV.	0.85	0.02	0.02	63	0.001	0.000
	N	5	5	5	5	5	5
Group 4	MEAN/MEDIAN	5.51 *	0.15 *	0.08 -	1127 -	0.010 -	0.000 -
	ST.DEV.	0.89	0.05	0.03	87	0.001	0.000
	N	4	4	4	4	5	5
Group 5	MEAN/MEDIAN	6.27 -	0.27 -	0.10 -	1179 -	0.010 -	0.000 -
	ST.DEV.	1.63	0.08	0.03	149	0.001	0.000
	N	10	10	10	10	10	10
After 6 Weeks (Recovery)							
Group 1	MEAN/MEDIAN	8.39	0.31	0.09	1023	0.012	0.000
	ST.DEV.	1.44	0.07	0.01	90	0.000	0.000
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	7.41 -	0.26 -	0.08 -	1117 -	0.012 -	0.000 -
	ST.DEV.	1.17	0.07	0.03	169	0.001	0.000
	N	5	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Hematology - SUMMARY
FEMALES

		COAGULATION	
		PT	PTT
		rel. 1	sec
After 4 Weeks			
Group 1	MEAN/MEDIAN	0.86	26.3
	ST.DEV.	0.09	1.6
	N	9	9
Group 2	MEAN/MEDIAN	0.87-	25.6-
	ST.DEV.	0.07	1.7
	N	5	5
Group 3	MEAN/MEDIAN	0.91-	23.2*
	ST.DEV.	0.04	1.3
	N	5	5
Group 4	MEAN/MEDIAN	0.88-	23.9-
	ST.DEV.	0.04	9.4
	N	5	5
Group 5	MEAN/MEDIAN	0.90-	21.5**
	ST.DEV.	0.06	2.1
	N	10	10
After 6 Weeks (Recovery)			
Group 1	MEAN/MEDIAN	0.80	25.5
	ST.DEV.	0.08	1.1
	N	5	5
Group 5	MEAN/MEDIAN	0.79-	24.4-
	ST.DEV.	0.04	2.4
	N	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Biochemistry - SUMMARY

Data excluded from Summary Report

Not Reported

All Measurements

Animal 100 Male Group 10 Reserve Removed
Animal 101 Female Group 10 Reserve Removed

Reported Parameter

Parameter		Statistical Testing
After 4 Weeks		
GLUCOSE	GLUCOSE	DUNNETT
UREA	UREA	DUNNETT
CREAT	CREATININE	DUNNETT
BILI-T	BILIRUBIN, TOTAL	STEEL
BILE AC	BILE ACIDS	DUNNETT
CHOLEST	CHOLESTEROL, TOTAL	DUNNETT
TRIGLY	TRIGLYCERIDES	DUNNETT
PHOS-LIP	PHOSPHOLIPIDS	DUNNETT
ASAT	ASPARTATE AMINOTRANSFERASE (ASAT)	DUNNETT
ALAT	ALANINE AMINOTRANSFERASE (ALAT)	DUNNETT
LDH	LACTATE DEHYDROGENASE (LDH)	DUNNETT
ALP	ALKALINE PHOSPHATASE (ALP)	DUNNETT
GGT	GAMMA-GLUTAMYLTRANSFERASE (GGT)	STEEL
CK	CREATINE KINASE (CK)	DUNNETT
SODIUM	SODIUM	DUNNETT
POTASSIUM	POTASSIUM	DUNNETT
CHLORIDE	CHLORIDE	DUNNETT
CALCIUM	CALCIUM	DUNNETT
PHOSPHORUS	PHOSPHORUS	DUNNETT
PROTEIN	PROTEIN, TOTAL	DUNNETT
ALBUMIN	ALBUMIN	DUNNETT
GLOBULIN	GLOBULIN	DUNNETT
A/G RATIO	A/G RATIO	STEEL
After 6 Weeks (Recovery)		
GLUCOSE	GLUCOSE	DUNNETT
UREA	UREA	DUNNETT
CREAT	CREATININE	DUNNETT
BILI-T	BILIRUBIN, TOTAL	STEEL
BILE AC	BILE ACIDS	DUNNETT
CHOLEST	CHOLESTEROL, TOTAL	DUNNETT
TRIGLY	TRIGLYCERIDES	DUNNETT
PHOS-LIP	PHOSPHOLIPIDS	DUNNETT
ASAT	ASPARTATE AMINOTRANSFERASE (ASAT)	DUNNETT

Biochemistry - SUMMARY

Reported Parameter

Parameter		Statistical Testing
After 6 Weeks (Recovery)		
ALAT	ALANINE AMINOTRANSFERASE (ALAT)	DUNNETT
LDH	LACTATE DEHYDROGENASE (LDH)	DUNNETT
ALP	ALKALINE PHOSPHATASE (ALP)	DUNNETT
GGT	GAMMA-GLUTAMYLTRANSFERASE (GGT)	STEEL
CK	CREATINE KINASE (CK)	DUNNETT
SODIUM	SODIUM	DUNNETT
POTASSIUM	POTASSIUM	DUNNETT
CHLORIDE	CHLORIDE	DUNNETT
CALCIUM	CALCIUM	DUNNETT
PHOSPHORUS	PHOSPHORUS	DUNNETT
PROTEIN	PROTEIN, TOTAL	DUNNETT
ALBUMIN	ALBUMIN	DUNNETT
GLOBULIN	GLOBULIN	DUNNETT
A/G RATIO	A/G RATIO	STEEL

Statistical Methods

DUNNETT	DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not significant (-)
STEEL	STEEL-Test sig. at 5% (*), 1% (**) or not significant (-)

Biochemistry - SUMMARY
MALES

		GENERAL					
		GLUCOSE mmol/l	UREA mmol/l	CREAT µmol/l	BILI-T µmol/l	BILE AC µmol/l	CHOLEST mmol/l
After 4 Weeks							
Group 1	MEAN/MEDIAN	5.00	4.91	26.3	2.05	32.65	2.62
	ST.DEV.	0.48	0.42	1.6	0.15	12.81	0.22
	N	10	10	10	10	10	10
Group 2	MEAN/MEDIAN	6.24**	5.07-	25.8-	1.80-	41.62-	2.65-
	ST.DEV.	0.91	0.76	1.3	0.22	41.58	0.26
	N	5	5	5	5	5	5
Group 3	MEAN/MEDIAN	6.36**	4.77-	24.9-	2.00-	25.26-	2.59-
	ST.DEV.	0.80	0.77	2.1	0.34	8.38	0.18
	N	5	5	5	5	5	5
Group 4	MEAN/MEDIAN	5.83-	5.09-	28.6-	3.10**	31.84-	4.21**
	ST.DEV.	0.83	0.38	2.2	0.67	6.65	0.43
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	5.59-	5.48-	27.6-	2.90**	46.02-	4.72**
	ST.DEV.	0.52	0.89	2.3	0.92	26.18	0.77
	N	10	10	10	10	10	10
After 6 Weeks (Recovery)							
Group 1	MEAN/MEDIAN	4.30	5.94	26.3	2.00	24.16	2.86
	ST.DEV.	0.23	0.39	0.8	0.23	3.28	0.39
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	4.72-	5.55-	25.1-	1.90-	12.62**	3.24-
	ST.DEV.	0.83	0.53	2.1	0.11	2.51	0.44
	N	5	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Biochemistry - SUMMARY
MALES

		GENERAL					
		TRIGLY	PHOS-LIP	ASAT	ALAT	LDH	ALP
		mmol/l	mmol/l	U/l	U/l	U/l	U/l
After 4 Weeks							
Group 1	MEAN/MEDIAN	0.43	1.94	67.6	38.3	124.2	107.7
	ST.DEV.	0.12	0.15	4.4	4.8	36.9	12.1
	N	10	10	10	10	10	10
Group 2	MEAN/MEDIAN	0.50-	1.99-	69.4-	37.2-	147.9-	95.4-
	ST.DEV.	0.19	0.13	6.3	6.5	79.0	21.5
	N	5	5	5	5	5	5
Group 3	MEAN/MEDIAN	0.40-	1.97-	67.9-	34.2-	98.8-	88.0-
	ST.DEV.	0.22	0.13	2.1	4.0	20.1	15.0
	N	5	5	5	5	5	5
Group 4	MEAN/MEDIAN	0.53-	2.76**	102.7-	66.3-	164.3-	112.9-
	ST.DEV.	0.16	0.15	33.9	24.7	57.9	38.1
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	0.30-	2.98**	161.1*	134.0*	259.2*	93.4-
	ST.DEV.	0.15	0.43	115.6	120.2	151.6	15.4
	N	10	10	10	10	10	10
After 6 Weeks (Recovery)							
Group 1	MEAN/MEDIAN	0.47	2.21	69.9	44.1	167.0	89.5
	ST.DEV.	0.19	0.25	3.7	3.3	63.2	9.2
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	0.38-	2.45-	69.0-	33.9**	193.9-	71.5*
	ST.DEV.	0.10	0.24	6.6	3.9	34.6	13.8
	N	5	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Biochemistry - SUMMARY
MALES

		GENERAL					
		GGT U/l	CK U/l	SODIUM mmol/l	POTASSIUM mmol/l	CHLORIDE mmol/l	CALCIUM mmol/l
After 4 Weeks							
Group 1	MEAN/MEDIAN	0.0	150.3	144.9	3.85	104.2	2.68
	ST.DEV.	0.0	28.4	0.4	0.17	0.9	0.05
	N	10	10	10	10	10	10
Group 2	MEAN/MEDIAN	0.0-	170.9-	145.0-	3.90-	104.3-	2.64-
	ST.DEV.	0.0	37.3	1.0	0.15	1.3	0.06
	N	5	5	5	5	5	5
Group 3	MEAN/MEDIAN	0.0-	156.9-	145.5-	4.11*	105.0-	2.70-
	ST.DEV.	0.0	28.6	0.2	0.15	0.6	0.05
	N	5	5	5	5	5	5
Group 4	MEAN/MEDIAN	0.0-	159.5-	144.9-	4.12*	104.6-	2.71-
	ST.DEV.	3.0	26.5	1.4	0.26	1.3	0.04
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	2.7**	153.4-	146.3**	4.36**	106.9**	2.74-
	ST.DEV.	3.8	39.5	0.8	0.15	1.4	0.08
	N	10	10	10	10	10	10
After 6 Weeks (Recovery)							
Group 1	MEAN/MEDIAN	0.0	168.2	143.4	3.86	102.1	2.67
	ST.DEV.	0.0	31.0	1.6	0.15	1.3	0.04
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	0.0-	170.3-	143.0-	4.16*	102.4-	2.62-
	ST.DEV.	0.0	33.4	0.8	0.18	1.0	0.06
	N	5	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Biochemistry - SUMMARY
MALES

		GENERAL				
		PHOSPHORUS mmol/l	PROTEIN g/l	ALBUMIN g/l	GLOBULIN g/l	A/G RATIO
After 4 Weeks						
Group 1	MEAN/MEDIAN	2.30	61.28	41.67	19.61	2.15
	ST.DEV.	0.08	1.87	1.05	1.44	0.16
	N	10	10	10	10	10
Group 2	MEAN/MEDIAN	2.21-	61.33-	41.60-	19.73-	2.07-
	ST.DEV.	0.13	1.90	0.80	1.30	0.13
	N	5	5	5	5	5
Group 3	MEAN/MEDIAN	2.27-	61.53-	41.62-	19.91-	2.13-
	ST.DEV.	0.14	1.97	0.96	1.08	0.07
	N	5	5	5	5	5
Group 4	MEAN/MEDIAN	2.11*	64.39*	38.56**	25.83**	1.50*
	ST.DEV.	0.04	2.08	1.83	1.32	0.11
	N	5	5	5	5	5
Group 5	MEAN/MEDIAN	2.18*	66.10**	38.81**	27.30**	1.39**
	ST.DEV.	0.13	1.94	1.22	1.73	0.12
	N	10	10	10	10	10
After 6 Weeks (Recovery)						
Group 1	MEAN/MEDIAN	2.38	64.78	41.93	22.85	1.83
	ST.DEV.	0.06	1.48	1.09	0.49	0.03
	N	5	5	5	5	5
Group 5	MEAN/MEDIAN	2.25-	62.61-	40.89-	21.72-	1.93-
	ST.DEV.	0.18	1.83	0.68	1.26	0.08
	N	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Biochemistry - SUMMARY
FEMALES

		GENERAL					
		GLUCOSE mmol/l	UREA mmol/l	CREAT µmol/l	BILI-T µmol/l	BILE AC µmol/l	CHOLEST mmol/l
After 4 Weeks							
Group 1	MEAN/MEDIAN	4.68	5.17	28.5	2.20	15.02	2.76
	ST.DEV.	0.33	0.65	2.5	0.30	6.16	0.33
	N	10	10	10	10	10	10
Group 2	MEAN/MEDIAN	5.31*	5.87-	29.5-	1.90-	15.76-	2.68-
	ST.DEV.	0.50	0.59	3.2	0.26	3.79	0.27
	N	5	5	5	5	5	5
Group 3	MEAN/MEDIAN	5.18-	5.99-	28.3-	2.70-	18.84-	2.74-
	ST.DEV.	0.51	0.63	2.2	0.49	8.99	0.31
	N	5	5	5	5	5	5
Group 4	MEAN/MEDIAN	5.59**	5.71-	28.4-	3.40**	15.46-	3.06-
	ST.DEV.	0.48	0.62	3.2	0.91	5.81	0.22
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	5.29*	5.88-	28.5-	2.60-	16.31-	4.64**
	ST.DEV.	0.46	1.07	2.1	0.57	2.37	0.64
	N	10	10	10	10	10	10
After 6 Weeks (Recovery)							
Group 1	MEAN/MEDIAN	4.27	6.21	30.0	2.30	10.02	2.63
	ST.DEV.	0.59	1.20	1.2	0.35	5.27	0.67
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	4.28-	6.60-	30.4-	1.90-	13.40-	3.00-
	ST.DEV.	0.47	0.50	2.3	0.28	5.56	0.49
	N	5	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Biochemistry - SUMMARY
FEMALES

		GENERAL					
		TRIGLY	PHOS-LIP	ASAT	ALAT	LDH	ALP
		mmol/l	mmol/l	U/l	U/l	U/l	U/l
After 4 Weeks							
Group 1	MEAN/MEDIAN	0.32	2.20	65.6	31.1	171.9	57.7
	ST.DEV.	0.13	0.29	6.7	4.1	62.3	7.0
	N	10	10	10	10	10	10
Group 2	MEAN/MEDIAN	0.30-	2.26-	66.6-	26.8-	112.0-	54.1-
	ST.DEV.	0.07	0.28	1.8	2.8	15.2	7.3
	N	5	5	5	5	5	5
Group 3	MEAN/MEDIAN	0.25-	2.26-	71.5-	29.4-	169.7-	63.4-
	ST.DEV.	0.05	0.25	2.5	4.6	48.1	8.3
	N	5	5	5	5	5	5
Group 4	MEAN/MEDIAN	0.31-	2.33-	69.8-	26.4-	220.3-	57.3-
	ST.DEV.	0.09	0.13	6.7	2.9	177.5	7.0
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	0.63**	3.39**	61.6-	27.4-	171.4-	44.9**
	ST.DEV.	0.23	0.42	7.1	2.7	93.6	3.0
	N	10	10	10	10	10	10
After 6 Weeks (Recovery)							
Group 1	MEAN/MEDIAN	0.26	2.29	72.7	34.8	192.6	42.2
	ST.DEV.	0.06	0.45	5.9	10.5	58.9	5.7
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	0.34*	2.53-	66.4-	28.7-	142.8-	41.7-
	ST.DEV.	0.03	0.23	4.0	4.8	46.9	3.1
	N	5	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Biochemistry - SUMMARY
FEMALES

		GENERAL					
		GGT	CK	SODIUM	POTASSIUM	CHLORIDE	CALCIUM
		U/l	U/l	mmol/l	mmol/l	mmol/l	mmol/l
After 4 Weeks							
Group 1	MEAN/MEDIAN	0.0	151.0	147.1	3.83	106.9	2.71
	ST.DEV.	0.0	34.9	1.3	0.21	1.4	0.05
	N	10	10	10	10	10	10
Group 2	MEAN/MEDIAN	0.0-	124.0-	146.4-	3.79-	107.4-	2.62*
	ST.DEV.	0.0	25.8	0.6	0.21	1.7	0.07
	N	5	5	5	5	5	5
Group 3	MEAN/MEDIAN	0.0-	156.0-	148.9*	3.94-	109.3**	2.77-
	ST.DEV.	0.0	22.9	2.2	0.13	1.6	0.09
	N	5	5	5	5	5	5
Group 4	MEAN/MEDIAN	0.0-	157.0-	147.5-	3.92-	107.8-	2.68-
	ST.DEV.	0.0	44.0	1.0	0.27	0.9	0.08
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	0.0-	148.0-	147.1-	4.11*	107.7-	2.73-
	ST.DEV.	1.1	37.3	0.8	0.19	0.9	0.04
	N	10	10	10	10	10	10
After 6 Weeks (Recovery)							
Group 1	MEAN/MEDIAN	0.0	181.4	142.1	3.48	102.2	2.62
	ST.DEV.	0.0	33.2	0.5	0.10	1.0	0.03
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	0.0-	165.2-	142.0-	3.73-	102.8-	2.56-
	ST.DEV.	0.0	94.9	1.0	0.31	0.5	0.05
	N	5	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Biochemistry - SUMMARY
FEMALES

		GENERAL				
		PHOSPHORUS mmol/l	PROTEIN g/l	ALBUMIN g/l	GLOBULIN g/l	A/G RATIO
After 4 Weeks						
Group 1	MEAN/MEDIAN	2.13	60.79	43.17	17.63	2.34
	ST.DEV.	0.09	2.13	2.10	1.71	0.32
	N	10	10	10	10	10
Group 2	MEAN/MEDIAN	2.08-	60.90-	43.49-	17.41-	2.52-
	ST.DEV.	0.13	1.70	0.87	1.11	0.14
	N	5	5	5	5	5
Group 3	MEAN/MEDIAN	2.12-	62.92-	44.90-	18.01-	2.52-
	ST.DEV.	0.13	1.92	2.25	1.23	0.26
	N	5	5	5	5	5
Group 4	MEAN/MEDIAN	2.04-	62.17-	42.85-	19.32-	2.17-
	ST.DEV.	0.10	0.52	0.88	0.70	0.12
	N	5	5	5	5	5
Group 5	MEAN/MEDIAN	1.92**	65.88**	42.94-	22.95**	1.87**
	ST.DEV.	0.12	1.64	1.28	2.04	0.21
	N	10	10	10	10	10
After 6 Weeks (Recovery)						
Group 1	MEAN/MEDIAN	2.02	62.21	42.87	19.34	2.17
	ST.DEV.	0.12	0.99	1.19	1.01	0.17
	N	5	5	5	5	5
Group 5	MEAN/MEDIAN	2.02-	62.32-	41.08*	21.24-	1.95-
	ST.DEV.	0.12	2.07	0.50	2.30	0.21
	N	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Urinalysis - SUMMARY

Data excluded from Summary Report

Not Reported

All Measurements

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

Reported Parameter

Parameter		Statistical Testing
After 4 Weeks		
VOLUME/18h	VOLUME/18h	STEEL
REL DENS	RELATIVE DENSITY	STEEL
pH	pH	STEEL
NITRITE	NITRITE	
PROTEIN	PROTEIN	STEEL
GLUCOSE	GLUCOSE	STEEL
KETONES	KETONES	STEEL
UROBILI	UROBILINOGEN	STEEL
BILIRUBIN	BILIRUBIN	STEEL
ERY	ERYTHROCYES	STEEL
LEU	LEUCOCYTES	STEEL
After 6 Weeks (Recovery)		
VOLUME/18h	VOLUME/18h	STEEL
REL DENS	RELATIVE DENSITY	STEEL
pH	pH	STEEL
NITRITE	NITRITE	
PROTEIN	PROTEIN	STEEL
GLUCOSE	GLUCOSE	STEEL
KETONES	KETONES	STEEL
UROBILI	UROBILINOGEN	STEEL
BILIRUBIN	BILIRUBIN	STEEL
ERY	ERYTHROCYES	STEEL
LEU	LEUCOCYTES	STEEL

Statistical Methods

STEEL STEEL-Test sig. at 5% (*), 1% (**) or not significant (-)

Urinalysis - SUMMARY
MALES

		GENERAL					
		VOLUME/18h	REL DENS	pH	NITRITE	PROTEIN	GLUCOSE
		ml	rel. 1		SCORE 0/1	g/l	mmol/l
After 4 Weeks							
Group 1	MEAN/MEDIAN	3.3	1.073	5.5	0	0.75	0
	ST.DEV.	2.7	0.046	0.8	---	0.24	0
	N	10	10	10	10	10	10
Group 2	MEAN/MEDIAN	3.1-	1.073-	5.0-	0	0.75-	0-
	ST.DEV.	2.6	0.023	0.5	---	0.22	0
	N	5	5	5	5	5	5
Group 3	MEAN/MEDIAN	4.7-	1.043-	6.0-	0	0.75-	0-
	ST.DEV.	3.8	0.020	0.9	---	0.27	0
	N	5	5	5	5	5	5
Group 4	MEAN/MEDIAN	7.5-	1.034-	6.0-	0	0.75-	0-
	ST.DEV.	1.2	0.009	0.5	---	0.27	0
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	11.5**	1.028*	6.8-	1	0.25*	0-
	ST.DEV.	4.5	0.014	0.8	---	0.16	0
	N	10	10	10	10	10	10
After 6 Weeks (Recovery)							
Group 1	MEAN/MEDIAN	7.8	1.031	7.0	0	0.25	0
	ST.DEV.	2.1	0.007	0.3	---	0.00	0
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	6.5-	1.033-	7.0-	1	0.25-	0-
	ST.DEV.	4.4	0.011	0.3	---	0.11	0
	N	5	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Urinalysis - SUMMARY
MALES

		GENERAL				
		KETONES	UROBILI	BILIRUBIN	ERY	LEU
		mmol/l	µmol/l	µmol/l	per µl	per µl
After 4 Weeks						
Group 1	MEAN/MEDIAN	1.5	0	0	10	25
	ST.DEV.	1.2	5	0	5	32
	N	10	10	10	10	10
Group 2	MEAN/MEDIAN	1.5-	0-	0-	10-	100-
	ST.DEV.	1.7	8	0	19	199
	N	5	5	5	5	5
Group 3	MEAN/MEDIAN	1.5-	0-	0-	0-	25-
	ST.DEV.	1.7	0	0	5	34
	N	5	5	5	5	5
Group 4	MEAN/MEDIAN	0.5-	0-	0-	10-	25-
	ST.DEV.	0.5	0	0	7	0
	N	5	5	5	5	5
Group 5	MEAN/MEDIAN	0.0**	9-	0-	18-	25-
	ST.DEV.	0.3	41	7	9	32
	N	10	10	10	10	10
After 6 Weeks (Recovery)						
Group 1	MEAN/MEDIAN	0.5	0	0	10	25
	ST.DEV.	0.4	0	0	5	34
	N	5	5	5	5	5
Group 5	MEAN/MEDIAN	0.5-	0-	0-	10-	100-
	ST.DEV.	0.2	0	0	5	190
	N	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Urinalysis - SUMMARY
FEMALES

		GENERAL					
		VOLUME/18h	REL DENS	pH	NITRITE	PROTEIN	GLUCOSE
		ml	rel. 1		SCORE 0/1	g/l	mmol/l
After 4 Weeks							
Group 1	MEAN/MEDIAN	5.5	1.040	6.0	0	0.25	0
	ST.DEV.	2.8	0.021	0.6	---	0.29	0
	N	10	10	10	10	10	10
Group 2	MEAN/MEDIAN	5.4-	1.029-	6.0-	0	0.25-	0-
	ST.DEV.	2.2	0.013	0.5	---	0.00	0
	N	5	5	5	5	5	5
Group 3	MEAN/MEDIAN	2.5-	1.069-	5.0-	0	0.75-	0-
	ST.DEV.	1.6	0.032	0.5	---	0.27	0
	N	5	5	5	5	5	5
Group 4	MEAN/MEDIAN	5.5-	1.041-	6.0-	0	0.25-	0-
	ST.DEV.	0.9	0.011	0.0	---	0.00	0
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	5.8-	1.043-	5.0**	0	0.25-	0-
	ST.DEV.	3.4	0.015	0.0	---	0.24	0
	N	10	10	10	10	10	10
After 6 Weeks (Recovery)							
Group 1	MEAN/MEDIAN	4.3	1.042	6.5	0	0.25	0
	ST.DEV.	7.6	0.027	0.8	---	0.11	0
	N	5	5	5	5	5	5
Group 5	MEAN/MEDIAN	8.8-	1.021-	6.5-	0	0.00-	0-
	ST.DEV.	4.9	0.015	0.0	---	0.14	0
	N	5	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

Urinalysis - SUMMARY
FEMALES

		GENERAL				
		KETONES mmol/l	UROBILI µmol/l	BILIRUBIN µmol/l	ERY per µl	LEU per µl
After 4 Weeks						
Group 1	MEAN/MEDIAN	0.5	0	0	0	13
	ST.DEV.	0.5	0	5	0	155
	N	10	10	10	10	10
Group 2	MEAN/MEDIAN	0.5 -	0 -	0 -	0 -	25 -
	ST.DEV.	0.0	0	0	4	14
	N	5	5	5	5	5
Group 3	MEAN/MEDIAN	0.5 -	0 -	0 -	0 -	0 -
	ST.DEV.	0.5	0	0	0	14
	N	5	5	5	5	5
Group 4	MEAN/MEDIAN	0.5 -	0 -	0 -	0 -	0 -
	ST.DEV.	0.3	0	0	0	11
	N	5	5	5	5	5
Group 5	MEAN/MEDIAN	0.0 -	0 -	0 -	0 -	0 -
	ST.DEV.	0.3	0	0	3	32
	N	10	10	10	10	10
After 6 Weeks (Recovery)						
Group 1	MEAN/MEDIAN	0.5	0	0	0	0
	ST.DEV.	0.6	0	8	4	43
	N	5	5	5	5	5
Group 5	MEAN/MEDIAN	0.0 -	0 -	0 -	0 -	0 -
	ST.DEV.	0.3	0	0	0	14
	N	5	5	5	5	5

*/**/- : Significant at 5% (*), 1% (**) or not significant (-)

ORGAN WEIGHTS (GRAM) - SUMMARY

Exclusions from Summary

Not Reported

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

Selection of Organs

All organs reported

ORGAN WEIGHTS (GRAM) - SUMMARY
AFTER 4 WEEKS
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg		Group 3 25 mg/kg		Group 4 250 mg/kg	
BODY W.	MEAN	332.4	356.0	-	342.9	-	341.8	-
	ST.DEV.	22.2	21.2		9.5		31.3	
	MINIMUM	306.9	334.9		332.4		300.2	
	MAXIMUM	357.5	391.0		351.3		386.9	
	N	5	5		5		5	
BRAIN	MEAN	1.85	1.88	-	1.81	-	1.84	-
	ST.DEV.	0.06	0.05		0.07		0.08	
	MINIMUM	1.81	1.80		1.72		1.74	
	MAXIMUM	1.95	1.92		1.91		1.97	
	N	5	5		5		5	
PITUITARY	MEAN	0.011	0.012	-	0.011	-	0.012	-
	ST.DEV.	0.001	0.001		0.001		0.002	
	MINIMUM	0.010	0.011		0.009		0.009	
	MAXIMUM	0.012	0.013		0.013		0.013	
	N	5	5		5		5	
HEART	MEAN	1.26	1.29	-	1.19	-	1.21	-
	ST.DEV.	0.07	0.11		0.06		0.14	
	MINIMUM	1.17	1.16		1.13		1.06	
	MAXIMUM	1.32	1.45		1.25		1.43	
	N	5	5		5		5	
THYROIDS	MEAN	0.018	0.018	-	0.018	-	0.016	-
	ST.DEV.	0.003	0.005		0.006		0.002	
	MINIMUM	0.014	0.014		0.013		0.014	
	MAXIMUM	0.022	0.025		0.028		0.019	
	N	5	5		5		5	
LIVER	MEAN	9.67	10.89	-	11.13	-	15.05	**
	ST.DEV.	0.61	1.08		0.35		1.41	
	MINIMUM	8.99	9.53		10.76		13.55	
	MAXIMUM	10.33	12.37		11.71		17.15	
	N	5	5		5		5	
THYMUS	MEAN	0.456	0.459	-	0.458	-	0.448	-
	ST.DEV.	0.029	0.067		0.053		0.092	
	MINIMUM	0.415	0.378		0.405		0.352	
	MAXIMUM	0.495	0.530		0.521		0.571	
	N	5	5		5		5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN WEIGHTS (GRAM) - SUMMARY
AFTER 4 WEEKS
MALES

		Group 5 1000 mg/kg	
BODY W.	MEAN	291.3	-
	ST.DEV.	36.9	
	MINIMUM	228.5	
	MAXIMUM	323.3	
	N	5	
BRAIN	MEAN	1.78	-
	ST.DEV.	0.04	
	MINIMUM	1.71	
	MAXIMUM	1.81	
	N	5	
PITUITARY	MEAN	0.009	*
	ST.DEV.	0.001	
	MINIMUM	0.008	
	MAXIMUM	0.010	
	N	5	
HEART	MEAN	1.06	*
	ST.DEV.	0.07	
	MINIMUM	0.95	
	MAXIMUM	1.15	
	N	5	
THYROIDS	MEAN	0.017	-
	ST.DEV.	0.003	
	MINIMUM	0.013	
	MAXIMUM	0.022	
	N	5	
LIVER	MEAN	15.08	**
	ST.DEV.	2.03	
	MINIMUM	11.96	
	MAXIMUM	17.09	
	N	5	
THYMUS	MEAN	0.341	-
	ST.DEV.	0.095	
	MINIMUM	0.190	
	MAXIMUM	0.423	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN WEIGHTS (GRAM) - SUMMARY
AFTER 4 WEEKS
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg		Group 3 25 mg/kg		Group 4 250 mg/kg	
KIDNEYS	MEAN	2.02	2.13	-	2.06	-	2.16	-
	ST.DEV.	0.11	0.10		0.13		0.16	
	MINIMUM	1.87	2.04		1.91		2.00	
	MAXIMUM	2.17	2.28		2.26		2.34	
	N	5	5		5		5	
ADRENALS	MEAN	0.055	0.052	-	0.052	-	0.050	-
	ST.DEV.	0.007	0.004		0.002		0.003	
	MINIMUM	0.045	0.048		0.050		0.047	
	MAXIMUM	0.064	0.056		0.055		0.054	
	N	5	5		5		5	
SPLEEN	MEAN	0.86	0.86	-	0.83	-	1.03	-
	ST.DEV.	0.12	0.14		0.06		0.10	
	MINIMUM	0.70	0.70		0.78		0.92	
	MAXIMUM	0.99	1.01		0.93		1.19	
	N	5	5		5		5	
TESTES	MEAN	3.60	3.66	-	3.64	-	3.73	-
	ST.DEV.	0.25	0.18		0.26		0.28	
	MINIMUM	3.29	3.44		3.42		3.34	
	MAXIMUM	3.96	3.92		4.02		4.11	
	N	5	5		5		5	
PROST/SEMI	MEAN	1.922	1.678	-	1.874	-	1.678	-
	ST.DEV.	0.246	0.228		0.127		0.347	
	MINIMUM	1.600	1.485		1.737		1.417	
	MAXIMUM	2.177	2.057		2.049		2.249	
	N	5	5		5		5	
EPIDIDYMID	MEAN	1.113	1.047	-	1.098	-	1.046	-
	ST.DEV.	0.039	0.038		0.050		0.074	
	MINIMUM	1.052	1.014		1.035		0.978	
	MAXIMUM	1.155	1.106		1.167		1.158	
	N	5	5		5		5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN WEIGHTS (GRAM) - SUMMARY
AFTER 4 WEEKS
MALES

		Group 5 1000 mg/kg	
KIDNEYS	MEAN	2.15	-
	ST.DEV.	0.29	
	MINIMUM	1.69	
	MAXIMUM	2.44	
	N	5	
ADRENALS	MEAN	0.051	-
	ST.DEV.	0.007	
	MINIMUM	0.045	
	MAXIMUM	0.063	
	N	5	
SPLEEN	MEAN	0.87	-
	ST.DEV.	0.15	
	MINIMUM	0.62	
	MAXIMUM	0.99	
	N	5	
TESTES	MEAN	3.52	-
	ST.DEV.	0.23	
	MINIMUM	3.18	
	MAXIMUM	3.80	
	N	5	
PROST/SEMI	MEAN	1.603	-
	ST.DEV.	0.400	
	MINIMUM	1.021	
	MAXIMUM	2.150	
	N	5	
EPIDIDYMID	MEAN	1.006	-
	ST.DEV.	0.129	
	MINIMUM	0.777	
	MAXIMUM	1.077	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BODY WEIGHT RATIOS (%) - SUMMARY
AFTER 4 WEEKS
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg		Group 3 25 mg/kg		Group 4 250 mg/kg	
BODY W.	MEAN	332.4	356.0	-	342.9	-	341.8	-
	ST.DEV.	22.2	21.2		9.5		31.3	
	MINIMUM	306.9	334.9		332.4		300.2	
	MAXIMUM	357.5	391.0		351.3		386.9	
	N	5	5		5		5	
BRAIN	MEAN	0.56	0.53	-	0.53	-	0.54	-
	ST.DEV.	0.04	0.03		0.03		0.03	
	MINIMUM	0.51	0.48		0.49		0.51	
	MAXIMUM	0.60	0.57		0.57		0.58	
	N	5	5		5		5	
PITUITARY	MEAN	0.003	0.003	-	0.003	-	0.003	-
	ST.DEV.	0.001	0.001		0.000		0.001	
	MINIMUM	0.003	0.003		0.003		0.003	
	MAXIMUM	0.004	0.004		0.004		0.004	
	N	5	5		5		5	
HEART	MEAN	0.38	0.36	-	0.35	-	0.35	-
	ST.DEV.	0.04	0.01		0.02		0.01	
	MINIMUM	0.34	0.35		0.32		0.34	
	MAXIMUM	0.42	0.38		0.36		0.37	
	N	5	5		5		5	
THYROIDS	MEAN	0.006	0.005	-	0.005	-	0.005	-
	ST.DEV.	0.001	0.001		0.002		0.001	
	MINIMUM	0.005	0.004		0.004		0.004	
	MAXIMUM	0.006	0.006		0.008		0.005	
	N	5	5		5		5	
LIVER	MEAN	2.91	3.05	-	3.25	*	4.41	**
	ST.DEV.	0.05	0.14		0.09		0.30	
	MINIMUM	2.85	2.85		3.13		3.92	
	MAXIMUM	2.96	3.20		3.35		4.65	
	N	5	5		5		5	
THYMUS	MEAN	0.137	0.129	-	0.133	-	0.130	-
	ST.DEV.	0.009	0.015		0.014		0.021	
	MINIMUM	0.125	0.108		0.116		0.116	
	MAXIMUM	0.148	0.148		0.150		0.165	
	N	5	5		5		5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BODY WEIGHT RATIOS (%) - SUMMARY
AFTER 4 WEEKS
MALES

		Group 5 1000 mg/kg	
BODY W.	MEAN	291.3	-
	ST.DEV.	36.9	
	MINIMUM	228.5	
	MAXIMUM	323.3	
	N	5	
BRAIN	MEAN	0.62	-
	ST.DEV.	0.08	
	MINIMUM	0.55	
	MAXIMUM	0.75	
	N	5	
PITUITARY	MEAN	0.003	-
	ST.DEV.	0.000	
	MINIMUM	0.003	
	MAXIMUM	0.004	
	N	5	
HEART	MEAN	0.37	-
	ST.DEV.	0.03	
	MINIMUM	0.35	
	MAXIMUM	0.42	
	N	5	
THYROIDS	MEAN	0.006	-
	ST.DEV.	0.000	
	MINIMUM	0.006	
	MAXIMUM	0.007	
	N	5	
LIVER	MEAN	5.18	**
	ST.DEV.	0.24	
	MINIMUM	4.93	
	MAXIMUM	5.56	
	N	5	
THYMUS	MEAN	0.115	-
	ST.DEV.	0.024	
	MINIMUM	0.083	
	MAXIMUM	0.145	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BODY WEIGHT RATIOS (%) - SUMMARY
AFTER 4 WEEKS
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
KIDNEYS	MEAN	0.61	0.60 -	0.60 -	0.63 -
	ST.DEV.	0.03	0.02	0.03	0.05
	MINIMUM	0.57	0.58	0.57	0.59
	MAXIMUM	0.64	0.62	0.64	0.70
	N	5	5	5	5
ADRENALS	MEAN	0.017	0.014 -	0.015 -	0.015 -
	ST.DEV.	0.002	0.001	0.001	0.002
	MINIMUM	0.014	0.013	0.014	0.012
	MAXIMUM	0.018	0.016	0.017	0.018
	N	5	5	5	5
SPLEEN	MEAN	0.26	0.24 -	0.24 -	0.30 -
	ST.DEV.	0.03	0.03	0.01	0.03
	MINIMUM	0.23	0.20	0.23	0.27
	MAXIMUM	0.31	0.28	0.26	0.33
	N	5	5	5	5
TESTES	MEAN	1.09	1.03 -	1.06 -	1.10 -
	ST.DEV.	0.12	0.08	0.06	0.13
	MINIMUM	0.92	0.94	0.99	0.97
	MAXIMUM	1.19	1.12	1.14	1.26
	N	5	5	5	5
PROST/SEMI	MEAN	0.581	0.472 -	0.548 -	0.493 -
	ST.DEV.	0.088	0.070	0.051	0.101
	MINIMUM	0.463	0.424	0.501	0.388
	MAXIMUM	0.693	0.594	0.616	0.651
	N	5	5	5	5
EPIDIDYMID	MEAN	0.336	0.295 -	0.320 -	0.309 -
	ST.DEV.	0.020	0.024	0.013	0.041
	MINIMUM	0.312	0.264	0.299	0.253
	MAXIMUM	0.365	0.330	0.332	0.359
	N	5	5	5	5

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BODY WEIGHT RATIOS (%) - SUMMARY
AFTER 4 WEEKS
MALES

		Group 5 1000 mg/kg	
KIDNEYS	MEAN	0.74	**
	ST.DEV.	0.06	
	MINIMUM	0.67	
	MAXIMUM	0.84	
	N	5	
ADRENALS	MEAN	0.018	-
	ST.DEV.	0.004	
	MINIMUM	0.014	
	MAXIMUM	0.023	
	N	5	
SPLEEN	MEAN	0.30	-
	ST.DEV.	0.02	
	MINIMUM	0.27	
	MAXIMUM	0.31	
	N	5	
TESTES	MEAN	1.22	-
	ST.DEV.	0.11	
	MINIMUM	1.07	
	MAXIMUM	1.39	
	N	5	
PROST/SEMI	MEAN	0.544	-
	ST.DEV.	0.080	
	MINIMUM	0.447	
	MAXIMUM	0.665	
	N	5	
EPIDIDYMID	MEAN	0.345	-
	ST.DEV.	0.010	
	MINIMUM	0.333	
	MAXIMUM	0.361	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BRAIN WEIGHT RATIOS (%) - SUMMARY
AFTER 4 WEEKS
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg		Group 3 25 mg/kg		Group 4 250 mg/kg	
BRAIN	MEAN	1.85	1.88	-	1.81	-	1.84	-
	ST.DEV.	0.06	0.05		0.07		0.08	
	MINIMUM	1.81	1.80		1.72		1.74	
	MAXIMUM	1.95	1.92		1.91		1.97	
	N	5	5		5		5	
PITUITARY	MEAN	0.605	0.628	-	0.612	-	0.632	-
	ST.DEV.	0.042	0.051		0.101		0.109	
	MINIMUM	0.538	0.582		0.471		0.492	
	MAXIMUM	0.656	0.688		0.756		0.747	
	N	5	5		5		5	
HEART	MEAN	68.33	68.66	-	66.07	-	65.64	-
	ST.DEV.	4.75	6.42		3.51		4.70	
	MINIMUM	62.56	60.42		60.21		60.92	
	MAXIMUM	72.93	76.72		69.06		72.59	
	N	5	5		5		5	
THYROIDS	MEAN	0.991	0.947	-	0.985	-	0.859	-
	ST.DEV.	0.153	0.244		0.337		0.090	
	MINIMUM	0.773	0.729		0.710		0.769	
	MAXIMUM	1.148	1.323		1.547		0.964	
	N	5	5		5		5	
LIVER	MEAN	522.32	580.42	-	617.13	-	818.48	**
	ST.DEV.	36.94	60.23		32.53		47.95	
	MINIMUM	483.33	496.35		563.35		744.51	
	MAXIMUM	570.72	654.50		639.89		870.56	
	N	5	5		5		5	
THYMUS	MEAN	24.631	24.402	-	25.441	-	24.316	-
	ST.DEV.	1.572	3.314		3.632		4.524	
	MINIMUM	22.928	21.000		21.204		20.230	
	MAXIMUM	27.049	28.042		29.186		31.374	
	N	5	5		5		5	
KIDNEYS	MEAN	108.85	113.62	-	114.35	-	117.59	-
	ST.DEV.	5.05	6.84		6.72		5.50	
	MINIMUM	100.54	106.25		107.33		111.54	
	MAXIMUM	113.11	121.11		123.50		126.23	
	N	5	5		5		5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BRAIN WEIGHT RATIOS (%) - SUMMARY
AFTER 4 WEEKS
MALES

		Group 5 1000 mg/kg	
BRAIN	MEAN	1.78	-
	ST.DEV.	0.04	
	MINIMUM	1.71	
	MAXIMUM	1.81	
	N	5	
PITUITARY	MEAN	0.505	-
	ST.DEV.	0.032	
	MINIMUM	0.468	
	MAXIMUM	0.556	
	N	5	
HEART	MEAN	59.74	*
	ST.DEV.	3.10	
	MINIMUM	55.56	
	MAXIMUM	64.25	
	N	5	
THYROIDS	MEAN	0.964	-
	ST.DEV.	0.168	
	MINIMUM	0.760	
	MAXIMUM	1.229	
	N	5	
LIVER	MEAN	845.83	**
	ST.DEV.	101.95	
	MINIMUM	699.42	
	MAXIMUM	954.75	
	N	5	
THYMUS	MEAN	19.084	-
	ST.DEV.	5.083	
	MINIMUM	11.111	
	MAXIMUM	23.500	
	N	5	
KIDNEYS	MEAN	120.46	-
	ST.DEV.	14.09	
	MINIMUM	98.83	
	MAXIMUM	135.56	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BRAIN WEIGHT RATIOS (%) - SUMMARY
AFTER 4 WEEKS
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
ADRENALS	MEAN	2.997	2.762 -	2.904 -	2.710 -
	ST.DEV.	0.421	0.241	0.139	0.267
	MINIMUM	2.419	2.540	2.762	2.386
	MAXIMUM	3.536	3.111	3.081	3.103
	N	5	5	5	5
SPLEEN	MEAN	46.69	45.72 -	46.18 -	55.93 -
	ST.DEV.	6.65	7.49	2.74	3.95
	MINIMUM	38.67	37.04	43.98	50.55
	MAXIMUM	54.70	53.44	50.82	60.41
	N	5	5	5	5
TESTES	MEAN	194.46	195.11 -	201.62 -	203.56 -
	ST.DEV.	8.99	13.62	16.70	17.35
	MINIMUM	181.77	182.01	184.82	183.52
	MAXIMUM	203.08	217.78	219.67	225.82
	N	5	5	5	5
PROST/SEMI	MEAN	104.071	89.318 -	103.817 -	91.615 -
	ST.DEV.	15.201	11.628	6.264	19.703
	MINIMUM	82.051	78.906	95.967	76.193
	MAXIMUM	120.276	108.836	111.477	123.571
	N	5	5	5	5
EPIDIDYMID	MEAN	60.127	55.766 -	60.871 -	57.160 -
	ST.DEV.	1.442	2.426	3.817	5.717
	MINIMUM	58.122	53.651	56.806	49.645
	MAXIMUM	61.713	59.056	65.291	63.626
	N	5	5	5	5

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BRAIN WEIGHT RATIOS (%) - SUMMARY
AFTER 4 WEEKS
MALES

		Group 5 1000 mg/kg	
ADRENALS	MEAN	2.879	-
	ST.DEV.	0.423	
	MINIMUM	2.514	
	MAXIMUM	3.520	
	N	5	
SPLEEN	MEAN	48.76	-
	ST.DEV.	7.57	
	MINIMUM	36.26	
	MAXIMUM	55.31	
	N	5	
TESTES	MEAN	197.62	-
	ST.DEV.	9.69	
	MINIMUM	185.96	
	MAXIMUM	209.94	
	N	5	
PROST/SEMI	MEAN	89.773	-
	ST.DEV.	21.385	
	MINIMUM	59.708	
	MAXIMUM	120.112	
	N	5	
EPIDIDYMID	MEAN	56.422	-
	ST.DEV.	6.176	
	MINIMUM	45.439	
	MAXIMUM	60.168	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN WEIGHTS (GRAM) - SUMMARY
AFTER 4 WEEKS
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg		Group 3 25 mg/kg		Group 4 250 mg/kg	
BODY W.	MEAN	251.1	233.4	-	233.2	-	238.3	-
	ST.DEV.	20.6	11.4		15.0		13.1	
	MINIMUM	234.5	222.3		210.8		220.6	
	MAXIMUM	284.1	250.1		252.4		256.5	
	N	5	5		5		5	
BRAIN	MEAN	1.77	1.72	-	1.75	-	1.70	*
	ST.DEV.	0.03	0.02		0.04		0.03	
	MINIMUM	1.73	1.69		1.71		1.67	
	MAXIMUM	1.80	1.74		1.80		1.74	
	N	5	5		5		5	
PITUITARY	MEAN	0.013	0.013	-	0.012	-	0.011	-
	ST.DEV.	0.002	0.001		0.001		0.001	
	MINIMUM	0.012	0.012		0.011		0.009	
	MAXIMUM	0.016	0.014		0.014		0.013	
	N	5	5		5		5	
HEART	MEAN	0.97	0.90	-	0.93	-	0.92	-
	ST.DEV.	0.07	0.06		0.07		0.03	
	MINIMUM	0.90	0.81		0.81		0.87	
	MAXIMUM	1.08	0.98		1.01		0.96	
	N	5	5		5		5	
THYROIDS	MEAN	0.019	0.020	-	0.017	-	0.016	-
	ST.DEV.	0.003	0.003		0.003		0.003	
	MINIMUM	0.016	0.015		0.012		0.012	
	MAXIMUM	0.023	0.023		0.020		0.020	
	N	5	5		5		5	
LIVER	MEAN	8.48	7.88	-	7.79	-	9.00	-
	ST.DEV.	1.17	0.46		0.80		0.54	
	MINIMUM	7.02	7.32		6.60		8.48	
	MAXIMUM	10.27	8.44		8.63		9.76	
	N	5	5		5		5	
THYMUS	MEAN	0.401	0.397	-	0.335	-	0.350	-
	ST.DEV.	0.068	0.067		0.041		0.064	
	MINIMUM	0.330	0.289		0.275		0.293	
	MAXIMUM	0.500	0.457		0.376		0.451	
	N	5	5		5		5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN WEIGHTS (GRAM) - SUMMARY
AFTER 4 WEEKS
FEMALES

		Group 5 1000 mg/kg	
BODY W.	MEAN	238.2	-
	ST.DEV.	12.2	
	MINIMUM	223.2	
	MAXIMUM	256.8	
	N	5	
BRAIN	MEAN	1.69	**
	ST.DEV.	0.04	
	MINIMUM	1.64	
	MAXIMUM	1.74	
	N	5	
PITUITARY	MEAN	0.012	-
	ST.DEV.	0.001	
	MINIMUM	0.010	
	MAXIMUM	0.013	
	N	5	
HEART	MEAN	0.90	-
	ST.DEV.	0.05	
	MINIMUM	0.84	
	MAXIMUM	0.96	
	N	5	
THYROIDS	MEAN	0.016	-
	ST.DEV.	0.003	
	MINIMUM	0.013	
	MAXIMUM	0.020	
	N	5	
LIVER	MEAN	11.65	**
	ST.DEV.	1.30	
	MINIMUM	10.51	
	MAXIMUM	13.59	
	N	5	
THYMUS	MEAN	0.306	-
	ST.DEV.	0.056	
	MINIMUM	0.219	
	MAXIMUM	0.365	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN WEIGHTS (GRAM) - SUMMARY
AFTER 4 WEEKS
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
KIDNEYS	MEAN	1.46	1.47 -	1.45 -	1.40 -
	ST.DEV.	0.05	0.11	0.15	0.05
	MINIMUM	1.41	1.32	1.25	1.34
	MAXIMUM	1.55	1.59	1.63	1.45
	N	5	5	5	5
ADRENALS	MEAN	0.063	0.063 -	0.065 -	0.064 -
	ST.DEV.	0.004	0.004	0.006	0.007
	MINIMUM	0.057	0.058	0.058	0.056
	MAXIMUM	0.067	0.069	0.072	0.073
	N	5	5	5	5
SPLEEN	MEAN	0.79	0.71 -	0.69 -	0.74 -
	ST.DEV.	0.08	0.06	0.04	0.04
	MINIMUM	0.70	0.65	0.62	0.70
	MAXIMUM	0.90	0.79	0.72	0.79
	N	5	5	5	5
OVARIES	MEAN	0.088	0.087 -	0.095 -	0.095 -
	ST.DEV.	0.011	0.019	0.011	0.006
	MINIMUM	0.075	0.058	0.083	0.088
	MAXIMUM	0.098	0.110	0.109	0.101
	N	5	5	5	5
UTERUS	MEAN	0.65	0.75 -	0.88 -	0.74 -
	ST.DEV.	0.15	0.10	0.46	0.22
	MINIMUM	0.49	0.59	0.57	0.61
	MAXIMUM	0.86	0.85	1.69	1.13
	N	5	5	5	5

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN WEIGHTS (GRAM) - SUMMARY
AFTER 4 WEEKS
FEMALES

		Group 5 1000 mg/kg	
KIDNEYS	MEAN	1.45	-
	ST.DEV.	0.08	
	MINIMUM	1.32	
	MAXIMUM	1.52	
	N	5	
ADRENALS	MEAN	0.063	-
	ST.DEV.	0.003	
	MINIMUM	0.059	
	MAXIMUM	0.067	
	N	5	
SPLEEN	MEAN	0.76	-
	ST.DEV.	0.10	
	MINIMUM	0.65	
	MAXIMUM	0.89	
	N	5	
OVARIES	MEAN	0.087	-
	ST.DEV.	0.021	
	MINIMUM	0.066	
	MAXIMUM	0.123	
	N	5	
UTERUS	MEAN	0.63	-
	ST.DEV.	0.16	
	MINIMUM	0.51	
	MAXIMUM	0.88	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BODY WEIGHT RATIOS (%) - SUMMARY
AFTER 4 WEEKS
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg		Group 3 25 mg/kg		Group 4 250 mg/kg	
BODY W.	MEAN	251.1	233.4	-	233.2	-	238.3	-
	ST.DEV.	20.6	11.4		15.0		13.1	
	MINIMUM	234.5	222.3		210.8		220.6	
	MAXIMUM	284.1	250.1		252.4		256.5	
	N	5	5		5		5	
BRAIN	MEAN	0.71	0.74	-	0.76	-	0.72	-
	ST.DEV.	0.05	0.03		0.05		0.03	
	MINIMUM	0.63	0.69		0.70		0.68	
	MAXIMUM	0.75	0.77		0.82		0.76	
	N	5	5		5		5	
PITUITARY	MEAN	0.005	0.006	-	0.005	-	0.005	-
	ST.DEV.	0.001	0.001		0.001		0.000	
	MINIMUM	0.005	0.005		0.004		0.004	
	MAXIMUM	0.006	0.006		0.006		0.005	
	N	5	5		5		5	
HEART	MEAN	0.39	0.38	-	0.40	-	0.39	-
	ST.DEV.	0.01	0.03		0.01		0.02	
	MINIMUM	0.38	0.36		0.38		0.37	
	MAXIMUM	0.39	0.44		0.40		0.41	
	N	5	5		5		5	
THYROIDS	MEAN	0.008	0.008	-	0.008	-	0.006	-
	ST.DEV.	0.001	0.001		0.002		0.001	
	MINIMUM	0.007	0.006		0.005		0.005	
	MAXIMUM	0.009	0.010		0.009		0.008	
	N	5	5		5		5	
LIVER	MEAN	3.37	3.38	-	3.34	-	3.78	*
	ST.DEV.	0.27	0.12		0.18		0.16	
	MINIMUM	2.95	3.24		3.13		3.59	
	MAXIMUM	3.61	3.55		3.59		4.00	
	N	5	5		5		5	
THYMUS	MEAN	0.160	0.169	-	0.144	-	0.147	-
	ST.DEV.	0.025	0.024		0.021		0.028	
	MINIMUM	0.139	0.129		0.109		0.121	
	MAXIMUM	0.194	0.189		0.159		0.189	
	N	5	5		5		5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BODY WEIGHT RATIOS (%) - SUMMARY
AFTER 4 WEEKS
FEMALES

		Group 5 1000 mg/kg	
BODY W.	MEAN	238.2	-
	ST.DEV.	12.2	
	MINIMUM	223.2	
	MAXIMUM	256.8	
	N	5	
BRAIN	MEAN	0.71	-
	ST.DEV.	0.04	
	MINIMUM	0.66	
	MAXIMUM	0.77	
	N	5	
PITUITARY	MEAN	0.005	-
	ST.DEV.	0.000	
	MINIMUM	0.004	
	MAXIMUM	0.005	
	N	5	
HEART	MEAN	0.38	-
	ST.DEV.	0.01	
	MINIMUM	0.36	
	MAXIMUM	0.39	
	N	5	
THYROIDS	MEAN	0.007	-
	ST.DEV.	0.001	
	MINIMUM	0.005	
	MAXIMUM	0.008	
	N	5	
LIVER	MEAN	4.88	**
	ST.DEV.	0.31	
	MINIMUM	4.58	
	MAXIMUM	5.29	
	N	5	
THYMUS	MEAN	0.129	-
	ST.DEV.	0.027	
	MINIMUM	0.085	
	MAXIMUM	0.154	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BODY WEIGHT RATIOS (%) - SUMMARY
AFTER 4 WEEKS
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
KIDNEYS	MEAN	0.58	0.63 -	0.62 -	0.59 -
	ST.DEV.	0.03	0.04	0.04	0.02
	MINIMUM	0.55	0.57	0.59	0.57
	MAXIMUM	0.62	0.68	0.69	0.61
	N	5	5	5	5
ADRENALS	MEAN	0.025	0.027 -	0.028 -	0.027 -
	ST.DEV.	0.001	0.002	0.001	0.002
	MINIMUM	0.024	0.025	0.027	0.024
	MAXIMUM	0.027	0.030	0.030	0.030
	N	5	5	5	5
SPLEEN	MEAN	0.31	0.30 -	0.30 -	0.31 -
	ST.DEV.	0.02	0.02	0.03	0.01
	MINIMUM	0.29	0.29	0.26	0.29
	MAXIMUM	0.34	0.33	0.33	0.32
	N	5	5	5	5
OVARIES	MEAN	0.035	0.037 -	0.041 -	0.040 -
	ST.DEV.	0.003	0.007	0.004	0.002
	MINIMUM	0.032	0.026	0.037	0.038
	MAXIMUM	0.039	0.044	0.047	0.042
	N	5	5	5	5
UTERUS	MEAN	0.26	0.32 -	0.38 -	0.31 -
	ST.DEV.	0.05	0.05	0.19	0.11
	MINIMUM	0.21	0.25	0.23	0.24
	MAXIMUM	0.31	0.38	0.71	0.51
	N	5	5	5	5

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BODY WEIGHT RATIOS (%) - SUMMARY
AFTER 4 WEEKS
FEMALES

		Group 5 1000 mg/kg	
KIDNEYS	MEAN	0.61	-
	ST.DEV.	0.05	
	MINIMUM	0.56	
	MAXIMUM	0.67	
	N	5	
ADRENALS	MEAN	0.027	-
	ST.DEV.	0.002	
	MINIMUM	0.025	
	MAXIMUM	0.029	
	N	5	
SPLEEN	MEAN	0.32	-
	ST.DEV.	0.04	
	MINIMUM	0.28	
	MAXIMUM	0.37	
	N	5	
OVARIES	MEAN	0.036	-
	ST.DEV.	0.007	
	MINIMUM	0.028	
	MAXIMUM	0.048	
	N	5	
UTERUS	MEAN	0.26	-
	ST.DEV.	0.05	
	MINIMUM	0.22	
	MAXIMUM	0.34	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BRAIN WEIGHT RATIOS (%) - SUMMARY
AFTER 4 WEEKS
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
BRAIN	MEAN	1.77	1.72 -	1.75 -	1.70 *
	ST.DEV.	0.03	0.02	0.04	0.03
	MINIMUM	1.73	1.69	1.71	1.67
	MAXIMUM	1.80	1.74	1.80	1.74
	N	5	5	5	5
PITUITARY	MEAN	0.747	0.767 -	0.696 -	0.659 -
	ST.DEV.	0.086	0.056	0.073	0.098
	MINIMUM	0.674	0.702	0.625	0.517
	MAXIMUM	0.889	0.809	0.791	0.778
	N	5	5	5	5
HEART	MEAN	54.68	52.19 -	53.08 -	54.19 -
	ST.DEV.	3.66	3.17	4.06	2.39
	MINIMUM	51.14	47.93	47.09	50.29
	MAXIMUM	60.00	56.65	57.39	56.47
	N	5	5	5	5
THYROIDS	MEAN	1.087	1.150 -	0.995 -	0.940 -
	ST.DEV.	0.180	0.191	0.193	0.198
	MINIMUM	0.909	0.877	0.682	0.719
	MAXIMUM	1.307	1.329	1.170	1.198
	N	5	5	5	5
LIVER	MEAN	479.79	458.02 -	444.61 -	528.38 -
	ST.DEV.	59.62	23.24	46.61	22.14
	MINIMUM	405.78	433.14	383.72	507.78
	MAXIMUM	570.56	485.06	492.98	560.92
	N	5	5	5	5
THYMUS	MEAN	22.678	23.079 -	19.126 -	20.623 -
	ST.DEV.	3.826	3.859	2.459	4.010
	MINIMUM	19.075	16.705	15.625	17.168
	MAXIMUM	28.409	26.416	21.637	27.006
	N	5	5	5	5
KIDNEYS	MEAN	82.54	85.32 -	82.98 -	82.16 -
	ST.DEV.	2.20	5.62	8.07	3.43
	MINIMUM	80.34	77.19	72.67	77.46
	MAXIMUM	86.11	91.91	92.09	86.83
	N	5	5	5	5

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BRAIN WEIGHT RATIOS (%) - SUMMARY
AFTER 4 WEEKS
FEMALES

		Group 5 1000 mg/kg	
BRAIN	MEAN	1.69	**
	ST.DEV.	0.04	
	MINIMUM	1.64	
	MAXIMUM	1.74	
	N	5	
PITUITARY	MEAN	0.687	-
	ST.DEV.	0.060	
	MINIMUM	0.606	
	MAXIMUM	0.747	
	N	5	
HEART	MEAN	53.11	-
	ST.DEV.	3.51	
	MINIMUM	49.71	
	MAXIMUM	57.32	
	N	5	
THYROIDS	MEAN	0.937	-
	ST.DEV.	0.173	
	MINIMUM	0.788	
	MAXIMUM	1.220	
	N	5	
LIVER	MEAN	690.70	**
	ST.DEV.	80.52	
	MINIMUM	614.62	
	MAXIMUM	799.41	
	N	5	
THYMUS	MEAN	18.152	-
	ST.DEV.	3.361	
	MINIMUM	12.882	
	MAXIMUM	20.977	
	N	5	
KIDNEYS	MEAN	86.04	-
	ST.DEV.	4.65	
	MINIMUM	80.00	
	MAXIMUM	92.68	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BRAIN WEIGHT RATIOS (%) - SUMMARY
AFTER 4 WEEKS
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
ADRENALS	MEAN	3.579	3.686 -	3.731 -	3.770 -
	ST.DEV.	0.221	0.244	0.280	0.371
	MINIMUM	3.202	3.432	3.372	3.353
	MAXIMUM	3.750	4.035	4.091	4.294
	N	5	5	5	5
SPLEEN	MEAN	44.61	41.50 -	39.40 -	43.35 -
	ST.DEV.	4.58	3.00	2.54	1.83
	MINIMUM	39.77	37.57	35.03	41.18
	MAXIMUM	50.00	45.40	41.52	45.40
	N	5	5	5	5
OVARIES	MEAN	5.002	5.061 -	5.429 -	5.572 -
	ST.DEV.	0.576	1.064	0.559	0.375
	MINIMUM	4.335	3.432	4.826	5.087
	MAXIMUM	5.568	6.358	6.056	6.048
	N	5	5	5	5
UTERUS	MEAN	37.01	43.60 -	50.22 -	43.70 -
	ST.DEV.	8.08	5.80	25.60	13.61
	MINIMUM	27.84	34.50	32.39	35.63
	MAXIMUM	47.78	49.13	95.48	67.66
	N	5	5	5	5

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BRAIN WEIGHT RATIOS (%) - SUMMARY
AFTER 4 WEEKS
FEMALES

		Group 5 1000 mg/kg	
ADRENALS	MEAN	3.758	-
	ST.DEV.	0.214	
	MINIMUM	3.563	
	MAXIMUM	4.085	
	N	5	
SPLEEN	MEAN	45.09	-
	ST.DEV.	6.43	
	MINIMUM	38.51	
	MAXIMUM	54.27	
	N	5	
OVARIES	MEAN	5.161	-
	ST.DEV.	1.228	
	MINIMUM	4.000	
	MAXIMUM	7.235	
	N	5	
UTERUS	MEAN	37.62	-
	ST.DEV.	9.35	
	MINIMUM	29.82	
	MAXIMUM	51.76	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN WEIGHTS (GRAM) - SUMMARY
AFTER 6 WEEKS
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
BODY W.	MEAN	372.2			
	ST.DEV.	15.7			
	MINIMUM	346.6			
	MAXIMUM	385.9			
	N	5			
BRAIN	MEAN	1.89			
	ST.DEV.	0.04			
	MINIMUM	1.85			
	MAXIMUM	1.93			
	N	5			
PITUITARY	MEAN	0.011			
	ST.DEV.	0.001			
	MINIMUM	0.010			
	MAXIMUM	0.012			
	N	5			
HEART	MEAN	1.24			
	ST.DEV.	0.10			
	MINIMUM	1.14			
	MAXIMUM	1.41			
	N	5			
THYROIDS	MEAN	0.017			
	ST.DEV.	0.003			
	MINIMUM	0.012			
	MAXIMUM	0.021			
	N	5			
LIVER	MEAN	11.01			
	ST.DEV.	0.59			
	MINIMUM	10.09			
	MAXIMUM	11.72			
	N	5			
THYMUS	MEAN	0.405			
	ST.DEV.	0.053			
	MINIMUM	0.327			
	MAXIMUM	0.459			
	N	5			

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN WEIGHTS (GRAM) - SUMMARY
AFTER 6 WEEKS
MALES

		Group 5 1000 mg/kg	
BODY W.	MEAN	329.9	**
	ST.DEV.	22.2	
	MINIMUM	305.9	
	MAXIMUM	355.7	
	N	5	
BRAIN	MEAN	1.79	**
	ST.DEV.	0.04	
	MINIMUM	1.76	
	MAXIMUM	1.85	
	N	5	
PITUITARY	MEAN	0.011	-
	ST.DEV.	0.001	
	MINIMUM	0.010	
	MAXIMUM	0.012	
	N	5	
HEART	MEAN	1.10	-
	ST.DEV.	0.09	
	MINIMUM	0.98	
	MAXIMUM	1.22	
	N	5	
THYROIDS	MEAN	0.019	-
	ST.DEV.	0.007	
	MINIMUM	0.013	
	MAXIMUM	0.030	
	N	5	
LIVER	MEAN	11.97	-
	ST.DEV.	0.82	
	MINIMUM	11.02	
	MAXIMUM	12.99	
	N	5	
THYMUS	MEAN	0.365	-
	ST.DEV.	0.032	
	MINIMUM	0.313	
	MAXIMUM	0.391	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN WEIGHTS (GRAM) - SUMMARY
AFTER 6 WEEKS
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
KIDNEYS	MEAN	2.23			
	ST.DEV.	0.16			
	MINIMUM	2.05			
	MAXIMUM	2.46			
	N	5			
ADRENALS	MEAN	0.052			
	ST.DEV.	0.003			
	MINIMUM	0.048			
	MAXIMUM	0.056			
	N	5			
SPLEEN	MEAN	0.90			
	ST.DEV.	0.14			
	MINIMUM	0.74			
	MAXIMUM	1.11			
	N	5			
TESTES	MEAN	3.65			
	ST.DEV.	0.23			
	MINIMUM	3.44			
	MAXIMUM	3.99			
	N	5			
PROST/SEMI	MEAN	2.306			
	ST.DEV.	0.093			
	MINIMUM	2.211			
	MAXIMUM	2.408			
	N	5			
EPIDIDYMID	MEAN	1.166			
	ST.DEV.	0.054			
	MINIMUM	1.103			
	MAXIMUM	1.231			
	N	5			

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN WEIGHTS (GRAM) - SUMMARY
AFTER 6 WEEKS
MALES

		Group 5 1000 mg/kg	
KIDNEYS	MEAN	2.04	-
	ST.DEV.	0.11	
	MINIMUM	1.92	
	MAXIMUM	2.21	
	N	5	
ADRENALS	MEAN	0.049	-
	ST.DEV.	0.004	
	MINIMUM	0.045	
	MAXIMUM	0.055	
	N	5	
SPLEEN	MEAN	0.84	-
	ST.DEV.	0.12	
	MINIMUM	0.70	
	MAXIMUM	1.01	
	N	5	
TESTES	MEAN	3.78	-
	ST.DEV.	0.11	
	MINIMUM	3.62	
	MAXIMUM	3.89	
	N	5	
PROST/SEMI	MEAN	1.969	**
	ST.DEV.	0.181	
	MINIMUM	1.745	
	MAXIMUM	2.232	
	N	5	
EPIDIDYMID	MEAN	1.071	*
	ST.DEV.	0.072	
	MINIMUM	0.987	
	MAXIMUM	1.182	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BODY WEIGHT RATIOS (%) - SUMMARY
AFTER 6 WEEKS
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
BODY W.	MEAN	372.2			
	ST.DEV.	15.7			
	MINIMUM	346.6			
	MAXIMUM	385.9			
	N	5			
BRAIN	MEAN	0.51			
	ST.DEV.	0.03			
	MINIMUM	0.48			
	MAXIMUM	0.55			
	N	5			
PITUITARY	MEAN	0.003			
	ST.DEV.	0.000			
	MINIMUM	0.003			
	MAXIMUM	0.003			
	N	5			
HEART	MEAN	0.33			
	ST.DEV.	0.02			
	MINIMUM	0.31			
	MAXIMUM	0.37			
	N	5			
THYROIDS	MEAN	0.004			
	ST.DEV.	0.001			
	MINIMUM	0.003			
	MAXIMUM	0.005			
	N	5			
LIVER	MEAN	2.96			
	ST.DEV.	0.06			
	MINIMUM	2.90			
	MAXIMUM	3.04			
	N	5			
THYMUS	MEAN	0.108			
	ST.DEV.	0.010			
	MINIMUM	0.094			
	MAXIMUM	0.120			
	N	5			

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (~)

ORGAN/BODY WEIGHT RATIOS (%) - SUMMARY
AFTER 6 WEEKS
MALES

		Group 5 1000 mg/kg	
BODY W.	MEAN	329.9	**
	ST.DEV.	22.2	
	MINIMUM	305.9	
	MAXIMUM	355.7	
	N	5	
BRAIN	MEAN	0.54	-
	ST.DEV.	0.04	
	MINIMUM	0.50	
	MAXIMUM	0.59	
	N	5	
PITUITARY	MEAN	0.003	-
	ST.DEV.	0.000	
	MINIMUM	0.003	
	MAXIMUM	0.004	
	N	5	
HEART	MEAN	0.33	-
	ST.DEV.	0.02	
	MINIMUM	0.30	
	MAXIMUM	0.36	
	N	5	
THYROIDS	MEAN	0.006	-
	ST.DEV.	0.002	
	MINIMUM	0.004	
	MAXIMUM	0.009	
	N	5	
LIVER	MEAN	3.63	**
	ST.DEV.	0.18	
	MINIMUM	3.37	
	MAXIMUM	3.87	
	N	5	
THYMUS	MEAN	0.111	-
	ST.DEV.	0.014	
	MINIMUM	0.088	
	MAXIMUM	0.127	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BODY WEIGHT RATIOS (%) - SUMMARY
AFTER 6 WEEKS
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
KIDNEYS	MEAN	0.60			
	ST.DEV.	0.03			
	MINIMUM	0.57			
	MAXIMUM	0.64			
	N	5			
ADRENALS	MEAN	0.014			
	ST.DEV.	0.001			
	MINIMUM	0.013			
	MAXIMUM	0.015			
	N	5			
SPLEEN	MEAN	0.24			
	ST.DEV.	0.03			
	MINIMUM	0.21			
	MAXIMUM	0.29			
	N	5			
TESTES	MEAN	0.98			
	ST.DEV.	0.10			
	MINIMUM	0.89			
	MAXIMUM	1.15			
	N	5			
PROST/SEMI	MEAN	0.621			
	ST.DEV.	0.047			
	MINIMUM	0.578			
	MAXIMUM	0.693			
	N	5			
EPIDIDYMID	MEAN	0.314			
	ST.DEV.	0.023			
	MINIMUM	0.292			
	MAXIMUM	0.349			
	N	5			

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BODY WEIGHT RATIOS (%) - SUMMARY
AFTER 6 WEEKS
MALES

		Group 5 1000 mg/kg	
KIDNEYS	MEAN	0.62	-
	ST.DEV.	0.02	
	MINIMUM	0.59	
	MAXIMUM	0.64	
	N	5	
ADRENALS	MEAN	0.015	-
	ST.DEV.	0.001	
	MINIMUM	0.013	
	MAXIMUM	0.016	
	N	5	
SPLEEN	MEAN	0.25	-
	ST.DEV.	0.02	
	MINIMUM	0.23	
	MAXIMUM	0.28	
	N	5	
TESTES	MEAN	1.15	*
	ST.DEV.	0.07	
	MINIMUM	1.09	
	MAXIMUM	1.23	
	N	5	
PROST/SEMI	MEAN	0.598	-
	ST.DEV.	0.055	
	MINIMUM	0.533	
	MAXIMUM	0.667	
	N	5	
EPIDIDYMID	MEAN	0.325	-
	ST.DEV.	0.021	
	MINIMUM	0.295	
	MAXIMUM	0.350	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BRAIN WEIGHT RATIOS (%) - SUMMARY
AFTER 6 WEEKS
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
BRAIN	MEAN	1.89			
	ST.DEV.	0.04			
	MINIMUM	1.85			
	MAXIMUM	1.93			
	N	5			
PITUITARY	MEAN	0.583			
	ST.DEV.	0.041			
	MINIMUM	0.532			
	MAXIMUM	0.645			
	N	5			
HEART	MEAN	65.76			
	ST.DEV.	6.39			
	MINIMUM	59.38			
	MAXIMUM	76.22			
	N	5			
THYROIDS	MEAN	0.903			
	ST.DEV.	0.192			
	MINIMUM	0.625			
	MAXIMUM	1.129			
	N	5			
LIVER	MEAN	583.62			
	ST.DEV.	38.92			
	MINIMUM	525.52			
	MAXIMUM	630.11			
	N	5			
THYMUS	MEAN	21.475			
	ST.DEV.	3.091			
	MINIMUM	17.031			
	MAXIMUM	24.811			
	N	5			
KIDNEYS	MEAN	118.05			
	ST.DEV.	10.40			
	MINIMUM	106.77			
	MAXIMUM	132.97			
	N	5			

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BRAIN WEIGHT RATIOS (%) - SUMMARY
AFTER 6 WEEKS
MALES

		Group 5 1000 mg/kg	
BRAIN	MEAN	1.79	**
	ST.DEV.	0.04	
	MINIMUM	1.76	
	MAXIMUM	1.85	
	N	5	
PITUITARY	MEAN	0.625	-
	ST.DEV.	0.062	
	MINIMUM	0.556	
	MAXIMUM	0.682	
	N	5	
HEART	MEAN	61.46	-
	ST.DEV.	4.36	
	MINIMUM	55.37	
	MAXIMUM	65.95	
	N	5	
THYROIDS	MEAN	1.060	-
	ST.DEV.	0.377	
	MINIMUM	0.739	
	MAXIMUM	1.695	
	N	5	
LIVER	MEAN	668.06	*
	ST.DEV.	41.39	
	MINIMUM	622.60	
	MAXIMUM	711.36	
	N	5	
THYMUS	MEAN	20.398	-
	ST.DEV.	2.095	
	MINIMUM	16.919	
	MAXIMUM	22.216	
	N	5	
KIDNEYS	MEAN	113.93	-
	ST.DEV.	5.02	
	MINIMUM	107.87	
	MAXIMUM	119.46	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BRAIN WEIGHT RATIOS (%) - SUMMARY
AFTER 6 WEEKS
MALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
ADRENALS	MEAN	2.745			
	ST.DEV.	0.186			
	MINIMUM	2.553			
	MAXIMUM	3.027			
	N	5			
SPLEEN	MEAN	47.63			
	ST.DEV.	7.77			
	MINIMUM	38.54			
	MAXIMUM	59.68			
	N	5			
TESTES	MEAN	193.55			
	ST.DEV.	11.99			
	MINIMUM	183.42			
	MAXIMUM	207.81			
	N	5			
PROST/SEMI	MEAN	122.123			
	ST.DEV.	3.253			
	MINIMUM	117.606			
	MAXIMUM	125.052			
	N	5			
EPIDIDYMID	MEAN	61.754			
	ST.DEV.	3.081			
	MINIMUM	58.670			
	MAXIMUM	66.541			
	N	5			

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BRAIN WEIGHT RATIOS (%) - SUMMARY
AFTER 6 WEEKS
MALES

		Group 5 1000 mg/kg	
ADRENALS	MEAN	2.749	-
	ST.DEV.	0.295	
	MINIMUM	2.432	
	MAXIMUM	3.125	
	N	5	
SPLEEN	MEAN	47.06	-
	ST.DEV.	6.41	
	MINIMUM	38.89	
	MAXIMUM	54.59	
	N	5	
TESTES	MEAN	210.96	*
	ST.DEV.	5.43	
	MINIMUM	204.52	
	MAXIMUM	217.61	
	N	5	
PROST/SEMI	MEAN	109.760	*
	ST.DEV.	8.129	
	MINIMUM	98.588	
	MAXIMUM	120.649	
	N	5	
EPIDIDYMID	MEAN	59.828	-
	ST.DEV.	4.771	
	MINIMUM	54.833	
	MAXIMUM	67.159	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN WEIGHTS (GRAM) - SUMMARY
AFTER 6 WEEKS
FEMALES

		Group 1 **0 mg/kg**	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
BODY W.	MEAN	246.1			
	ST.DEV.	15.1			
	MINIMUM	230.7			
	MAXIMUM	268.3			
	N	5			
BRAIN	MEAN	1.76			
	ST.DEV.	0.06			
	MINIMUM	1.68			
	MAXIMUM	1.84			
	N	5			
PITUITARY	MEAN	0.013			
	ST.DEV.	0.001			
	MINIMUM	0.012			
	MAXIMUM	0.014			
	N	5			
HEART	MEAN	0.86			
	ST.DEV.	0.10			
	MINIMUM	0.76			
	MAXIMUM	1.02			
	N	5			
THYROIDS	MEAN	0.018			
	ST.DEV.	0.002			
	MINIMUM	0.015			
	MAXIMUM	0.020			
	N	5			
LIVER	MEAN	7.43			
	ST.DEV.	0.71			
	MINIMUM	6.68			
	MAXIMUM	8.18			
	N	5			
THYMUS	MEAN	0.336			
	ST.DEV.	0.065			
	MINIMUM	0.280			
	MAXIMUM	0.417			
	N	5			

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN WEIGHTS (GRAM) - SUMMARY
AFTER 6 WEEKS
FEMALES

		Group 5 1000 mg/kg	
BODY W.	MEAN	233.9	-
	ST.DEV.	13.5	
	MINIMUM	212.5	
	MAXIMUM	246.8	
	N	5	
BRAIN	MEAN	1.78	-
	ST.DEV.	0.04	
	MINIMUM	1.73	
	MAXIMUM	1.83	
	N	5	
PITUITARY	MEAN	0.012	-
	ST.DEV.	0.001	
	MINIMUM	0.010	
	MAXIMUM	0.014	
	N	5	
HEART	MEAN	0.90	-
	ST.DEV.	0.11	
	MINIMUM	0.81	
	MAXIMUM	1.10	
	N	5	
THYROIDS	MEAN	0.015	-
	ST.DEV.	0.004	
	MINIMUM	0.012	
	MAXIMUM	0.022	
	N	5	
LIVER	MEAN	7.88	-
	ST.DEV.	0.44	
	MINIMUM	7.21	
	MAXIMUM	8.40	
	N	5	
THYMUS	MEAN	0.319	-
	ST.DEV.	0.044	
	MINIMUM	0.263	
	MAXIMUM	0.380	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN WEIGHTS (GRAM) - SUMMARY
AFTER 6 WEEKS
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
KIDNEYS	MEAN	1.50			
	ST.DEV.	0.13			
	MINIMUM	1.35			
	MAXIMUM	1.65			
	N	5			
ADRENALS	MEAN	0.063			
	ST.DEV.	0.005			
	MINIMUM	0.058			
	MAXIMUM	0.071			
	N	5			
SPLEEN	MEAN	0.67			
	ST.DEV.	0.06			
	MINIMUM	0.57			
	MAXIMUM	0.72			
	N	5			
OVARIES	MEAN	0.262			
	ST.DEV.	0.366			
	MINIMUM	0.081			
	MAXIMUM	0.916			
	N	5			
UTERUS	MEAN	0.66			
	ST.DEV.	0.34			
	MINIMUM	0.12			
	MAXIMUM	0.95			
	N	5			

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN WEIGHTS (GRAM) - SUMMARY
AFTER 6 WEEKS
FEMALES

		Group 5 1000 mg/kg	
KIDNEYS	MEAN	1.48	-
	ST.DEV.	0.13	
	MINIMUM	1.29	
	MAXIMUM	1.60	
	N	5	
ADRENALS	MEAN	0.061	-
	ST.DEV.	0.008	
	MINIMUM	0.050	
	MAXIMUM	0.071	
	N	5	
SPLEEN	MEAN	0.64	-
	ST.DEV.	0.07	
	MINIMUM	0.59	
	MAXIMUM	0.74	
	N	5	
OVARIES	MEAN	0.120	-
	ST.DEV.	0.018	
	MINIMUM	0.101	
	MAXIMUM	0.141	
	N	5	
UTERUS	MEAN	0.68	-
	ST.DEV.	0.12	
	MINIMUM	0.57	
	MAXIMUM	0.85	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BODY WEIGHT RATIOS (%) - SUMMARY
AFTER 6 WEEKS
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
BODY W.	MEAN	246.1			
	ST.DEV.	15.1			
	MINIMUM	230.7			
	MAXIMUM	268.3			
	N	5			
BRAIN	MEAN	0.72			
	ST.DEV.	0.05			
	MINIMUM	0.66			
	MAXIMUM	0.76			
	N	5			
PITUITARY	MEAN	0.005			
	ST.DEV.	0.000			
	MINIMUM	0.005			
	MAXIMUM	0.006			
	N	5			
HEART	MEAN	0.35			
	ST.DEV.	0.03			
	MINIMUM	0.33			
	MAXIMUM	0.38			
	N	5			
THYROIDS	MEAN	0.007			
	ST.DEV.	0.001			
	MINIMUM	0.006			
	MAXIMUM	0.009			
	N	5			
LIVER	MEAN	3.02			
	ST.DEV.	0.16			
	MINIMUM	2.77			
	MAXIMUM	3.22			
	N	5			
THYMUS	MEAN	0.137			
	ST.DEV.	0.026			
	MINIMUM	0.110			
	MAXIMUM	0.172			
	N	5			

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BODY WEIGHT RATIOS (%) - SUMMARY
AFTER 6 WEEKS
FEMALES

		Group 5 1000 mg/kg	
BODY W.	MEAN	233.9	-
	ST.DEV.	13.5	
	MINIMUM	212.5	
	MAXIMUM	246.8	
	N	5	
BRAIN	MEAN	0.76	-
	ST.DEV.	0.04	
	MINIMUM	0.71	
	MAXIMUM	0.81	
	N	5	
PITUITARY	MEAN	0.005	-
	ST.DEV.	0.001	
	MINIMUM	0.004	
	MAXIMUM	0.006	
	N	5	
HEART	MEAN	0.38	-
	ST.DEV.	0.04	
	MINIMUM	0.34	
	MAXIMUM	0.45	
	N	5	
THYROIDS	MEAN	0.006	-
	ST.DEV.	0.002	
	MINIMUM	0.005	
	MAXIMUM	0.009	
	N	5	
LIVER	MEAN	3.37	**
	ST.DEV.	0.14	
	MINIMUM	3.20	
	MAXIMUM	3.56	
	N	5	
THYMUS	MEAN	0.137	-
	ST.DEV.	0.020	
	MINIMUM	0.114	
	MAXIMUM	0.161	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BODY WEIGHT RATIOS (%) - SUMMARY
AFTER 6 WEEKS
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
KIDNEYS	MEAN	0.61			
	ST.DEV.	0.03			
	MINIMUM	0.58			
	MAXIMUM	0.65			
	N	5			
ADRENALS	MEAN	0.025			
	ST.DEV.	0.002			
	MINIMUM	0.023			
	MAXIMUM	0.028			
	N	5			
SPLEEN	MEAN	0.27			
	ST.DEV.	0.03			
	MINIMUM	0.22			
	MAXIMUM	0.30			
	N	5			
OVARIES	MEAN	0.109			
	ST.DEV.	0.155			
	MINIMUM	0.035			
	MAXIMUM	0.387			
	N	5			
UTERUS	MEAN	0.27			
	ST.DEV.	0.14			
	MINIMUM	0.05			
	MAXIMUM	0.40			
	N	5			

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BODY WEIGHT RATIOS (%) - SUMMARY
AFTER 6 WEEKS
FEMALES

		Group 5 1000 mg/kg	
KIDNEYS	MEAN	0.63	-
	ST.DEV.	0.04	
	MINIMUM	0.60	
	MAXIMUM	0.69	
	N	5	
ADRENALS	MEAN	0.026	-
	ST.DEV.	0.003	
	MINIMUM	0.024	
	MAXIMUM	0.031	
	N	5	
SPLEEN	MEAN	0.28	-
	ST.DEV.	0.02	
	MINIMUM	0.25	
	MAXIMUM	0.30	
	N	5	
OVARIES	MEAN	0.051	-
	ST.DEV.	0.007	
	MINIMUM	0.041	
	MAXIMUM	0.060	
	N	5	
UTERUS	MEAN	0.29	-
	ST.DEV.	0.05	
	MINIMUM	0.24	
	MAXIMUM	0.36	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BRAIN WEIGHT RATIOS (%) - SUMMARY
AFTER 6 WEEKS
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
BRAIN	MEAN	1.76			
	ST.DEV.	0.06			
	MINIMUM	1.68			
	MAXIMUM	1.84			
	N	5			
PITUITARY	MEAN	0.741			
	ST.DEV.	0.052			
	MINIMUM	0.686			
	MAXIMUM	0.814			
	N	5			
HEART	MEAN	49.17			
	ST.DEV.	5.61			
	MINIMUM	43.43			
	MAXIMUM	56.67			
	N	5			
THYROIDS	MEAN	1.051			
	ST.DEV.	0.164			
	MINIMUM	0.815			
	MAXIMUM	1.190			
	N	5			
LIVER	MEAN	423.58			
	ST.DEV.	48.97			
	MINIMUM	363.04			
	MAXIMUM	486.90			
	N	5			
THYMUS	MEAN	19.086			
	ST.DEV.	3.518			
	MINIMUM	15.815			
	MAXIMUM	23.167			
	N	5			
KIDNEYS	MEAN	85.49			
	ST.DEV.	9.29			
	MINIMUM	76.09			
	MAXIMUM	98.21			
	N	5			

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BRAIN WEIGHT RATIOS (%) - SUMMARY
AFTER 6 WEEKS
FEMALES

		Group 5 1000 mg/kg	
BRAIN	MEAN	1.78	-
	ST.DEV.	0.04	
	MINIMUM	1.73	
	MAXIMUM	1.83	
	N	5	
PITUITARY	MEAN	0.687	-
	ST.DEV.	0.082	
	MINIMUM	0.556	
	MAXIMUM	0.782	
	N	5	
HEART	MEAN	50.99	-
	ST.DEV.	7.26	
	MINIMUM	45.25	
	MAXIMUM	63.58	
	N	5	
THYROIDS	MEAN	0.855	-
	ST.DEV.	0.217	
	MINIMUM	0.656	
	MAXIMUM	1.222	
	N	5	
LIVER	MEAN	443.37	-
	ST.DEV.	16.14	
	MINIMUM	416.76	
	MAXIMUM	459.02	
	N	5	
THYMUS	MEAN	17.970	-
	ST.DEV.	2.513	
	MINIMUM	14.693	
	MAXIMUM	21.111	
	N	5	
KIDNEYS	MEAN	83.29	-
	ST.DEV.	6.08	
	MINIMUM	74.57	
	MAXIMUM	89.39	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BRAIN WEIGHT RATIOS (%) - SUMMARY
AFTER 6 WEEKS
FEMALES

		Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
ADRENALS	MEAN	3.569			
	ST.DEV.	0.380			
	MINIMUM	3.314			
	MAXIMUM	4.226			
	N	5			
SPLEEN	MEAN	38.06			
	ST.DEV.	2.45			
	MINIMUM	33.93			
	MAXIMUM	40.00			
	N	5			
OVARIES	MEAN	15.095			
	ST.DEV.	21.343			
	MINIMUM	4.629			
	MAXIMUM	53.256			
	N	5			
UTERUS	MEAN	37.39			
	ST.DEV.	19.70			
	MINIMUM	6.98			
	MAXIMUM	56.55			
	N	5			

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

ORGAN/BRAIN WEIGHT RATIOS (%) - SUMMARY
AFTER 6 WEEKS
FEMALES

		Group 5 1000 mg/kg	
ADRENALS	MEAN	3.423	-
	ST.DEV.	0.433	
	MINIMUM	2.890	
	MAXIMUM	3.966	
	N	5	
SPLEEN	MEAN	36.23	-
	ST.DEV.	3.25	
	MINIMUM	32.96	
	MAXIMUM	41.11	
	N	5	
OVARIES	MEAN	6.718	-
	ST.DEV.	0.825	
	MINIMUM	5.838	
	MAXIMUM	7.705	
	N	5	
UTERUS	MEAN	38.29	-
	ST.DEV.	6.01	
	MINIMUM	32.95	
	MAXIMUM	46.45	
	N	5	

*/**/- : DUNNETT-Test based on pooled variance sig. at 5% (*), 1% (**) or not sig. (-)

MACROSCOPICAL FINDINGS - SUMMARY
AFTER 4 WEEKS
ALL NECROPSIES

Not Reported

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

MACROSCOPICAL FINDINGS - SUMMARY
AFTER 4 WEEKS
ALL NECROPSIES
MALES

	Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
ANIMALS EXAMINED	5	5	5	5
ANIMALS COMPLETED	5	5	5	5
ANIMALS WITHOUT FINDINGS	3	4	5	0
ANIMALS AFFECTED				
STOMACH				
- FOCUS/FOCI	1 (20%)	0 (0%) -	0 (0%) -	0 (0%) -
LIVER				
- ENLARGED	0 (0%)	0 (0%) -	0 (0%) -	5 (100%) **
- DISCOLORATION	0 (0%)	0 (0%) -	0 (0%) -	5 (100%) **
KIDNEYS				
- PELVIC DILATION	0 (0%)	1 (20%) -	0 (0%) -	0 (0%) -
THYMUS				
- FOCUS/FOCI	0 (0%)	0 (0%) -	0 (0%) -	1 (20%) -
- DISCOLORATION	1 (20%)	0 (0%) -	0 (0%) -	0 (0%) -
BODY CAVITIES				
- NODULE(S)	0 (0%)	0 (0%) -	0 (0%) -	1 (20%) -

*/**/- : Fisher's Exact Test significant at 5% (*), 1% (**) or not significant (-)

MACROSCOPICAL FINDINGS - SUMMARY
AFTER 4 WEEKS
ALL NECROPSIES
MALES

	Group 5 1000 mg/kg
ANIMALS EXAMINED	5
ANIMALS COMPLETED	5
ANIMALS WITHOUT FINDINGS	0
ANIMALS AFFECTED	
STOMACH	
- FOCUS/FOCI	0 (0%) -
LIVER	
- ENLARGED	4 (80%) *
- DISCOLORATION	5 (100%) **
KIDNEYS	
- PELVIC DILATION	0 (0%) -
THYMUS	
- FOCUS/FOCI	1 (20%) -
- DISCOLORATION	0 (0%) -
BODY CAVITIES	
- NODULE(S)	0 (0%) -

*/**/- : Fisher's Exact Test significant at 5% (*), 1% (**) or not significant (-)

MACROSCOPICAL FINDINGS - SUMMARY
AFTER 4 WEEKS
ALL NECROPSIES
FEMALES

	Group 1 0 mg/kg	Group 2 5 mg/kg	Group 3 25 mg/kg	Group 4 250 mg/kg
ANIMALS EXAMINED	5	5	5	5
ANIMALS COMPLETED	5	5	5	5
ANIMALS WITHOUT FINDINGS	4	4	4	4
ANIMALS AFFECTED				
LIVER				
- ENLARGED	0 (0%)	0 (0%) -	0 (0%) -	0 (0%) -
- DISCOLORATION	0 (0%)	0 (0%) -	0 (0%) -	0 (0%) -
UTERUS				
- DILATION	0 (0%)	0 (0%) -	1 (20%) -	1 (20%) -
THYMUS				
- FOCUS/FOCI	1 (20%)	1 (20%) -	0 (0%) -	0 (0%) -

*/**/- : Fisher's Exact Test significant at 5% (*), 1% (**) or not significant (-)

MACROSCOPICAL FINDINGS - SUMMARY
AFTER 4 WEEKS
ALL NECROPSIES
FEMALES

	Group 5 1000 mg/kg
ANIMALS EXAMINED	5
ANIMALS COMPLETED	5
ANIMALS WITHOUT FINDINGS	2
ANIMALS AFFECTED	
LIVER	
- ENLARGED	2 (40%) -
- DISCOLORATION	2 (40%) -
UTERUS	
- DILATION	0 (0%) -
THYMUS	
- FOCUS/FOCI	0 (0%) -

*/**/- : Fisher's Exact Test significant at 5% (*), 1% (**) or not significant (-)

MACROSCOPICAL FINDINGS - SUMMARY
AFTER 6 WEEKS
ALL NECROPSIES

Not Reported

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

MACROSCOPICAL FINDINGS - SUMMARY
AFTER 6 WEEKS
ALL NECROPSIES
MALES

	Group 1 **0 mg/kg**	Group 5 1000 mg/kg
ANIMALS EXAMINED	5	5
ANIMALS COMPLETED	5	5
ANIMALS WITHOUT FINDINGS	5	0
ANIMALS AFFECTED		
LIVER		
- DISCOLORATION	0 (0%)	5 (100%) **
LYMPH NODES		
- ENLARGED	0 (0%)	1 (20%) -
- DISCOLORATION	0 (0%)	1 (20%) -

*/**/- : Fisher's Exact Test significant at 5% (*), 1% (**) or not significant (-)

MACROSCOPICAL FINDINGS - SUMMARY
AFTER 6 WEEKS
ALL NECROPSIES
FEMALES

	Group 1 **0 mg/kg**	Group 5 1000 mg/kg
ANIMALS EXAMINED	5	5
ANIMALS COMPLETED	5	5
ANIMALS WITHOUT FINDINGS	5	5

*/**/- : Fisher's Exact Test significant at 5% (*), 1% (**) or not significant (-)

9 INDIVIDUAL TABLES

MORTALITY DATA
ALL NECROPSIES

Animal(s) without death date / death status

Not Reported

Animal 100	Male	Group 1	Reserve Removed
Animal 101	Female	Group 1	Reserve Removed

MORTALITY DATA
ALL NECROPSIES
MALES

Group 1 (0 mg/kg)

PRE-RANDOMIZATION (Days 1 to 1)

No mortality data recorded

POST-RANDOMIZATION (Days 1 to 5)

No mortality data recorded

TREATMENT (Days 1 to 29)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
1	20-JAN-10	29	X				
2	20-JAN-10	29	X				
3	20-JAN-10	29	X				
4	20-JAN-10	29	X				
5	20-JAN-10	29	X				
		Total:	5	0	0	0	

RECOVERY (Days 1 to 15)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
6	03-FEB-10	15	X				
7	03-FEB-10	15	X				
8	03-FEB-10	15	X				
9	03-FEB-10	15	X				
10	03-FEB-10	15	X				
		Total:	5	0	0	0	

P = PLANNED NECROPSY , K = KILLED IN EXTR. , S = SPONTAN. DEATH , O = OTHER

MORTALITY DATA
ALL NECROPSIES
MALES

Group 2 (5 mg/kg)

PRE-RANDOMIZATION (Days 1 to 1)

No mortality data recorded

POST-RANDOMIZATION (Days 1 to 5)

No mortality data recorded

TREATMENT (Days 1 to 29)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
11	20-JAN-10	29	X				
12	20-JAN-10	29	X				
13	20-JAN-10	29	X				
14	20-JAN-10	29	X				
15	20-JAN-10	29	X				
		Total:	5	0	0	0	

RECOVERY (Days 1 to 15)

No Animals started

P = PLANNED NECROPSY , K = KILLED IN EXTR. , S = SPONTAN. DEATH , O = OTHER

MORTALITY DATA
ALL NECROPSIES
MALES

Group 3 (25 mg/kg)

PRE-RANDOMIZATION (Days 1 to 1)

No mortality data recorded

POST-RANDOMIZATION (Days 1 to 5)

No mortality data recorded

TREATMENT (Days 1 to 29)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
16	20-JAN-10	29	X				
17	20-JAN-10	29	X				
18	20-JAN-10	29	X				
19	20-JAN-10	29	X				
20	20-JAN-10	29	X				
		Total:	5	0	0	0	

RECOVERY (Days 1 to 15)

No Animals started

P = PLANNED NECROPSY , K = KILLED IN EXTR. , S = SPONTAN. DEATH , O = OTHER

MORTALITY DATA
ALL NECROPSIES
MALES

Group 4 (250 mg/kg)

PRE-RANDOMIZATION (Days 1 to 1)

No mortality data recorded

POST-RANDOMIZATION (Days 1 to 5)

No mortality data recorded

TREATMENT (Days 1 to 29)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
21	20-JAN-10	29	X				
22	20-JAN-10	29	X				
23	20-JAN-10	29	X				
24	20-JAN-10	29	X				
25	20-JAN-10	29	X				
		Total:	5	0	0	0	

RECOVERY (Days 1 to 15)

No Animals started

P = PLANNED NECROPSY , K = KILLED IN EXTR. , S = SPONTAN. DEATH , O = OTHER

MORTALITY DATA
ALL NECROPSIES
MALES

Group 5 (1000 mg/kg)

PRE-RANDOMIZATION (Days 1 to 1)

No mortality data recorded

POST-RANDOMIZATION (Days 1 to 5)

No mortality data recorded

TREATMENT (Days 1 to 29)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
26	20-JAN-10	29	X				
27	20-JAN-10	29	X				
28	20-JAN-10	29	X				
29	20-JAN-10	29	X				
30	20-JAN-10	29	X				
		Total:	5	0	0	0	

RECOVERY (Days 1 to 15)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
31	03-FEB-10	15	X				
32	03-FEB-10	15	X				
33	03-FEB-10	15	X				
34	03-FEB-10	15	X				
35	03-FEB-10	15	X				
		Total:	5	0	0	0	

P = PLANNED NECROPSY , K = KILLED IN EXTR. , S = SPONTAN. DEATH , O = OTHER

MORTALITY DATA
ALL NECROPSIES
FEMALES

Group 1 (0 mg/kg)

PRE-RANDOMIZATION (Days 1 to 1)

No mortality data recorded

POST-RANDOMIZATION (Days 1 to 5)

No mortality data recorded

TREATMENT (Days 1 to 29)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
36	20-JAN-10	29	X				
37	20-JAN-10	29	X				
38	20-JAN-10	29	X				
39	20-JAN-10	29	X				
40	20-JAN-10	29	X				
		Total:	5	0	0	0	

RECOVERY (Days 1 to 15)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
41	03-FEB-10	15	X				
42	03-FEB-10	15	X				
43	03-FEB-10	15	X				
44	03-FEB-10	15	X				
45	03-FEB-10	15	X				
		Total:	5	0	0	0	

P = PLANNED NECROPSY , K = KILLED IN EXTR. , S = SPONTAN. DEATH , O = OTHER

MORTALITY DATA
ALL NECROPSIES
FEMALES

Group 2 (5 mg/kg)

PRE-RANDOMIZATION (Days 1 to 1)

No mortality data recorded

POST-RANDOMIZATION (Days 1 to 5)

No mortality data recorded

TREATMENT (Days 1 to 29)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
46	20-JAN-10	29	X				
47	20-JAN-10	29	X				
48	20-JAN-10	29	X				
49	20-JAN-10	29	X				
50	20-JAN-10	29	X				
		Total:	5	0	0	0	

RECOVERY (Days 1 to 15)

No Animals started

P = PLANNED NECROPSY , K = KILLED IN EXTR. , S = SPONTAN. DEATH , O = OTHER

MORTALITY DATA
ALL NECROPSIES
FEMALES

Group 3 (25 mg/kg)

PRE-RANDOMIZATION (Days 1 to 1)

No mortality data recorded

POST-RANDOMIZATION (Days 1 to 5)

No mortality data recorded

TREATMENT (Days 1 to 29)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
51	20-JAN-10	29	X				
52	20-JAN-10	29	X				
53	20-JAN-10	29	X				
54	20-JAN-10	29	X				
55	20-JAN-10	29	X				
		Total:	5	0	0	0	

RECOVERY (Days 1 to 15)

No Animals started

P = PLANNED NECROPSY , K = KILLED IN EXTR. , S = SPONTAN. DEATH , O = OTHER

MORTALITY DATA
ALL NECROPSIES
FEMALES

Group 4 (250 mg/kg)

PRE-RANDOMIZATION (Days 1 to 1)

No mortality data recorded

POST-RANDOMIZATION (Days 1 to 5)

No mortality data recorded

TREATMENT (Days 1 to 29)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
56	20-JAN-10	29	X				
57	20-JAN-10	29	X				
58	20-JAN-10	29	X				
59	20-JAN-10	29	X				
60	20-JAN-10	29	X				
		Total:	5	0	0	0	

RECOVERY (Days 1 to 15)

No Animals started

P = PLANNED NECROPSY , K = KILLED IN EXTR. , S = SPONTAN. DEATH , O = OTHER

MORTALITY DATA
ALL NECROPSIES
FEMALES

Group 5 (1000 mg/kg)

PRE-RANDOMIZATION (Days 1 to 1)

No mortality data recorded

POST-RANDOMIZATION (Days 1 to 5)

No mortality data recorded

TREATMENT (Days 1 to 29)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
61	20-JAN-10	29	X				
62	20-JAN-10	29	X				
63	20-JAN-10	29	X				
64	20-JAN-10	29	X				
65	20-JAN-10	29	X				
		Total:	5	0	0	0	

RECOVERY (Days 1 to 15)

ANIMAL	DEATH DATE	DAY	P	K	S	O	COMMENT
66	03-FEB-10	15	X				
67	03-FEB-10	15	X				
68	03-FEB-10	15	X				
69	03-FEB-10	15	X				
70	03-FEB-10	15	X				
		Total:	5	0	0	0	

P = PLANNED NECROPSY , K = KILLED IN EXTR. , S = SPONTAN. DEATH , O = OTHER

CLINICAL SIGNS

Comments

Data excluded from Summary Report

Not Reported

All Study Phases

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

Incomplete Recordings

Selection of Findings

All findings reported

CLINICAL SIGNS
MALES

POST-RANDOMIZATION

Weeks / Days
1
1 2 3 4 5

Group 1 (0 mg/kg)

No abnormality recorded.

Group 2 (5 mg/kg)

No abnormality recorded.

Group 3 (25 mg/kg)

No abnormality recorded.

Group 4 (250 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

CLINICAL SIGNS
MALES

TREATMENT

```
                                Weeks / Days
                                1         2         3         4         5
                                1234567123456712345671234567-
```

Group 1 (0 mg/kg)

No abnormality recorded.

Group 2 (5 mg/kg)

No abnormality recorded.

Group 3 (25 mg/kg)

No abnormality recorded.

Group 4 (250 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

Animal 28

```
APPEARANCE
- HUNCHED POSTURE (1)          ....................111111111
- VISIBLE WEIGHT LOSS (3)      ....................111111111
- RUFFLED FUR (3)              .............1.......1111111
BREATHING
- DYSPNEA (3)                  ............11....1111111...
SECRETION/EXCRETION
- SALIVATION (3)               ...................1111......
```

Animal 30

```
SECRETION/EXCRETION
- SALIVATION (3)               ..................111........
```

CLINICAL SIGNS
MALES

TREATMENT

```
                                Weeks / Days
                                1         2         3         4         5
                                1234567123456712345671234567-
```

Group 5 (1000 mg/kg)

Animal 35

```
APPEARANCE
-HAIR LOSS (3)
  RIGHT AXILLARY REGION         .........122222222222222211111
```

No further abnormality recorded.

CLINICAL SIGNS
MALES

RECOVERY

```
                    Weeks / Days
                    1         2         3
                    1234567123456 7-
```

Group 1 (0 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

CLINICAL SIGNS
FEMALES

POST-RANDOMIZATION

	Weeks / Days
	1
	1 2 3 4 5

Group 1 (0 mg/kg)

No abnormality recorded.

Group 2 (5 mg/kg)

No abnormality recorded.

Group 3 (25 mg/kg)

No abnormality recorded.

Group 4 (250 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

CLINICAL SIGNS
FEMALES

TREATMENT

```
                                Weeks / Days
                                1         2         3         4         5
                                1 2 3 4 5 6 7 1 2 3 4 5 6 7 1 2 3 4 5 6 7 1 2 3 4 5 6 7 -
```

Group 1 (0 mg/kg)

No abnormality recorded.

Group 2 (5 mg/kg)

No abnormality recorded.

Group 3 (25 mg/kg)

No abnormality recorded.

Group 4 (250 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

CLINICAL SIGNS
FEMALES

RECOVERY

```
                          Weeks / Days
                          1         2         3
                          1 2 3 4 5 6 7 1 2 3 4 5 6 7 -
```

Group 1 (0 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

DETAILED BEHAVIORAL OBSERVATIONS

Comments

Data excluded from Summary Report

Not Reported

All Study Phases

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

Incomplete Recordings

Selection of Findings

All findings reported

DETAILED BEHAVIORAL OBSERVATIONS
MALES

POST-RANDOMIZATION

Weeks
0
1

Group 1 (0 mg/kg)

No abnormality recorded.

Group 2 (5 mg/kg)

No abnormality recorded.

Group 3 (25 mg/kg)

No abnormality recorded.

Group 4 (250 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

DETAILED BEHAVIORAL OBSERVATIONS
MALES

TREATMENT

Weeks
0
1 2 3 4 -

Group 1 (0 mg/kg)

No abnormality recorded.

Group 2 (5 mg/kg)

No abnormality recorded.

Group 3 (25 mg/kg)

No abnormality recorded.

Group 4 (250 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

DETAILED BEHAVIORAL OBSERVATIONS
FEMALES

POST-RANDOMIZATION

Weeks
0
1

Group 1 (0 mg/kg)

No abnormality recorded.

Group 2 (5 mg/kg)

No abnormality recorded.

Group 3 (25 mg/kg)

No abnormality recorded.

Group 4 (250 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

DETAILED BEHAVIORAL OBSERVATIONS
FEMALES

TREATMENT

Weeks
0
1 2 3 4 -

Group 1 (0 mg/kg)

No abnormality recorded.

Group 2 (5 mg/kg)

No abnormality recorded.

Group 3 (25 mg/kg)

No abnormality recorded.

Group 4 (250 mg/kg)

No abnormality recorded.

Group 5 (1000 mg/kg)

No abnormality recorded.

GRIP STRENGTH

Comments

Data excluded from Summary Report

Not Reported

All Measurements

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

Reported Parameter

AT WEEK 4

Grip Fore	GRIP FORELIMB
Grip Hind	GRIP HINDLIMB

GRIP STRENGTH
AT WEEK 4
MALES

Group 1 (0 mg/kg)

	GRIP STRENGTH	
	Grip Fore KILOGRAM	Grip Hind KILOGRAM
1	1.36	1.00
2	1.37	0.96
3	1.36	1.02
4	1.37	1.02
5	1.46	1.06
6	1.48	1.06
7	1.47	1.03
8	1.49	1.05
9	1.47	1.04
10	1.39	1.05

GRIP STRENGTH
AT WEEK 4
MALES

Group 2 (5 mg/kg)

	GRIP STRENGTH	
	Grip Fore KILOGRAM	Grip Hind KILOGRAM
11	1.41	1.01
12	1.41	1.04
13	1.47	1.04
14	1.42	1.05
15	1.53	1.07

GRIP STRENGTH
AT WEEK 4
MALES

Group 3 (25 mg/kg)

	GRIP STRENGTH	
	Grip Fore KILOGRAM	Grip Hind KILOGRAM
16	1.46	1.05
17	1.37	1.00
18	1.47	1.01
19	1.41	1.03
20	1.50	1.05

GRIP STRENGTH
AT WEEK 4
MALES

Group 4 (250 mg/kg)

	GRIP STRENGTH	
	Grip Fore KILOGRAM	Grip Hind KILOGRAM
21	1.40	1.05
22	1.33	0.98
23	1.49	1.02
24	1.47	1.04
25	1.44	1.04

GRIP STRENGTH
AT WEEK 4
MALES

Group 5 (1000 mg/kg)

	GRIP STRENGTH	
	Grip Fore KILOGRAM	Grip Hind KILOGRAM
26	1.52	0.99
27	1.39	1.09
28	1.40	0.97
29	1.45	1.06
30	1.44	1.01
31	1.51	1.01
32	1.37	0.97
33	1.35	0.95
34	1.48	1.01
35	1.42	1.00

GRIP STRENGTH
AT WEEK 4
FEMALES

Group 1 (0 mg/kg)

	GRIP STRENGTH	
	Grip Fore KILOGRAM	Grip Hind KILOGRAM
36	1.33	0.83
37	1.34	0.85
38	1.35	0.81
39	1.32	0.78
40	1.29	0.80
41	1.26	0.75
42	1.29	0.78
43	1.24	0.75
44	1.26	0.79
45	1.34	0.75

GRIP STRENGTH
AT WEEK 4
FEMALES

Group 2 (5 mg/kg)

	GRIP STRENGTH	
	Grip Fore KILOGRAM	Grip Hind KILOGRAM
46	1.27	0.76
47	1.27	0.71
48	1.30	0.72
49	1.22	0.73
50	1.25	0.79

GRIP STRENGTH
AT WEEK 4
FEMALES

Group 3 (25 mg/kg)

	GRIP STRENGTH	
	Grip Fore KILOGRAM	Grip Hind KILOGRAM
51	1.34	0.77
52	1.29	0.74
53	1.33	0.75
54	1.23	0.73
55	1.34	0.76

GRIP STRENGTH
AT WEEK 4
FEMALES

Group 4 (250 mg/kg)

	GRIP STRENGTH	
	Grip Fore KILOGRAM	Grip Hind KILOGRAM
56	1.35	0.82
57	1.25	0.73
58	1.28	0.83
59	1.26	0.79
60	1.30	0.75

GRIP STRENGTH
AT WEEK 4
FEMALES

Group 5 (1000 mg/kg)

	GRIP STRENGTH	
	Grip Fore KILOGRAM	Grip Hind KILOGRAM
61	1.34	0.77
62	1.31	0.80
63	1.24	0.77
64	1.25	0.76
65	1.35	0.81
66	1.26	0.77
67	1.29	0.76
68	1.31	0.82
69	1.29	0.86
70	1.29	0.76

LOCOMOTOR ACTIVITY

Comments

Data excluded from Summary Report

Not Reported

All Measurements

Animal 100 Male Group 10 Reserve Removed
Animal 101 Female Group 10 Reserve Removed

Reported Parameter

AT WEEK 4

0-10 MIN LOCOMOTOR ACTIVITY
10-20 MIN LOCOMOTOR ACTIVITY
20-30 MIN LOCOMOTOR ACTIVITY
30-40 MIN LOCOMOTOR ACTIVITY
40-50 MIN LOCOMOTOR ACTIVITY
50-60 MIN LOCOMOTOR ACTIVITY
Total LOCOMOTOR ACTIVITY

LOCOMOTOR ACTIVITY
AT WEEK 4
MALES

Group 1 (0 mg/kg)

	LOCOMOTOR ACTIVITY						
	0-10 MIN	10-20 MIN	20-30 MIN	30-40 MIN	40-50 MIN	50-60 MIN	Total
1	412	271	191	202	88	209	1373
2	300	207	229	398	146	112	1392
3	282	173	283	231	189	120	1278
4	505	373	275	160	255	83	1651
5	250	136	280	301	161	245	1373
6	590	391	738	773	460	269	3221
7	605	237	264	183	212	234	1735
8	273	197	142	116	162	34	924
9	681	481	261	334	155	159	2071
10	720	275	338	137	81	19	1570

LOCOMOTOR ACTIVITY
AT WEEK 4
MALES

Group 2 (5 mg/kg)

	LOCOMOTOR ACTIVITY						
	0-10 MIN	10-20 MIN	20-30 MIN	30-40 MIN	40-50 MIN	50-60 MIN	Total
11	466	308	183	266	157	127	1507
12	524	193	169	227	45	250	1408
13	413	281	270	188	157	157	1466
14	430	392	331	127	203	154	1637
15	534	460	300	226	236	89	1845

LOCOMOTOR ACTIVITY
AT WEEK 4
MALES

Group 3 (25 mg/kg)

	LOCOMOTOR ACTIVITY						
	0-10 MIN	10-20 MIN	20-30 MIN	30-40 MIN	40-50 MIN	50-60 MIN	Total
16	824	417	350	305	271	376	2543
17	461	209	173	165	248	237	1493
18	559	287	169	191	404	306	1916
19	530	376	338	271	215	39	1769
20	575	448	347	324	263	185	2142

LOCOMOTOR ACTIVITY
AT WEEK 4
MALES

Group 4 (250 mg/kg)

	LOCOMOTOR ACTIVITY						
	0-10 MIN	10-20 MIN	20-30 MIN	30-40 MIN	40-50 MIN	50-60 MIN	Total
21	553	250	101	63	0	0	967
22	554	232	252	155	182	142	1517
23	549	516	375	310	183	153	2086
24	394	219	203	261	219	248	1544
25	593	294	419	235	196	59	1796

LOCOMOTOR ACTIVITY
AT WEEK 4
MALES

Group 5 (1000 mg/kg)

	LOCOMOTOR ACTIVITY						
	0-10 MIN	10-20 MIN	20-30 MIN	30-40 MIN	40-50 MIN	50-60 MIN	Total
26	589	494	162	174	20	6	1445
27	591	410	204	120	56	291	1672
28	486	274	60	25	46	339	1230
29	515	285	315	246	33	351	1745
30	696	355	131	85	65	61	1393
31	525	187	2	10	18	25	767
32	337	159	17	12	22	0	547
33	281	155	20	10	4	8	478
34	622	355	196	19	81	0	1273
35	765	512	310	216	287	206	2296

LOCOMOTOR ACTIVITY
AT WEEK 4
FEMALES

Group 1 (0 mg/kg)

	LOCOMOTOR ACTIVITY						
	0-10 MIN	10-20 MIN	20-30 MIN	30-40 MIN	40-50 MIN	50-60 MIN	Total
36	503	180	42	24	81	182	1012
37	462	269	175	89	2	16	1013
38	558	225	177	21	151	239	1371
39	709	288	134	36	24	138	1329
40	605	380	273	158	169	191	1776
41	703	579	103	80	138	441	2044
42	585	346	263	123	97	210	1624
43	482	136	174	163	57	202	1214
44	602	220	164	185	79	220	1470
45	487	219	199	48	12	53	1018

LOCOMOTOR ACTIVITY
AT WEEK 4
FEMALES

Group 2 (5 mg/kg)

	LOCOMOTOR ACTIVITY						
	0-10 MIN	10-20 MIN	20-30 MIN	30-40 MIN	40-50 MIN	50-60 MIN	Total
46	993	742	377	290	186	187	2775
47	703	548	364	153	164	301	2233
48	735	371	261	117	6	32	1522
49	556	361	66	209	16	26	1234
50	651	227	112	19	30	197	1236

LOCOMOTOR ACTIVITY
AT WEEK 4
FEMALES

Group 3 (25 mg/kg)

	LOCOMOTOR ACTIVITY						
	0-10 MIN	10-20 MIN	20-30 MIN	30-40 MIN	40-50 MIN	50-60 MIN	Total
51	659	167	12	9	338	176	1361
52	617	262	77	8	173	228	1365
53	597	398	208	82	142	220	1647
54	503	151	8	6	80	105	853
55	423	258	305	24	123	91	1224

LOCOMOTOR ACTIVITY
AT WEEK 4
FEMALES

Group 4 (250 mg/kg)

	LOCOMOTOR ACTIVITY						
	0-10 MIN	10-20 MIN	20-30 MIN	30-40 MIN	40-50 MIN	50-60 MIN	Total
56	758	241	260	47	203	316	1825
57	669	60	105	11	171	361	1377
58	343	83	18	0	73	164	681
59	672	401	172	74	163	218	1700
60	782	296	269	33	189	107	1676

LOCOMOTOR ACTIVITY
AT WEEK 4
FEMALES

Group 5 (1000 mg/kg)

	LOCOMOTOR ACTIVITY						
	0-10 MIN	10-20 MIN	20-30 MIN	30-40 MIN	40-50 MIN	50-60 MIN	Total
61	727	275	85	14	237	300	1638
62	831	552	334	0	7	14	1738
63	643	304	200	86	158	264	1655
64	851	616	277	58	143	310	2255
65	784	400	136	139	198	206	1863
66	761	574	352	30	363	380	2460
67	651	385	273	162	221	193	1885
68	619	290	206	64	162	390	1731
69	661	173	138	136	208	0	1316
70	717	232	93	23	177	107	1349

FOOD CONSUMPTION (G/ANIMAL/DAY)

Comments

Data excluded from Summary Report

Not Reported

All Study Phases

Cage 15 Male Group 10 Reserve Removed
Cage 16 Female Group 10 Reserve Removed

FOOD CONSUMPTION (G/ANIMAL/DAY)
MALES

Group 1 (0 mg/kg)

CAGE	1	2
POST-RANDOMIZATION		
Days 1-6	23.9	24.5

CAGE	1	2
TREATMENT		
Days 1-8	22.2	22.7
8-15	20.4	19.9
15-22	19.0	18.8
22-28	19.8	20.7

CAGE	1	2
RECOVERY		
Days 1-8	---	23.0
8-14	---	24.0

FOOD CONSUMPTION (G/ANIMAL/DAY)
MALES

Group 2 (5 mg/kg)

CAGE	3
POST-RANDOMIZATION	
Days 1-6	24.9

CAGE	3
TREATMENT	
Days 1-8	23.9
8-15	21.3
15-22	19.4
22-28	21.6

CAGE	3
RECOVERY	
Days 1-8	---
8-14	---

FOOD CONSUMPTION (G/ANIMAL/DAY)
MALES

Group 3 (25 mg/kg)

CAGE	4
POST-RANDOMIZATION	
Days 1-6	23.3

CAGE	4
TREATMENT	
Days 1-8	22.7
8-15	20.5
15-22	19.1
22-28	20.6

CAGE	4
RECOVERY	
Days 1-8	---
8-14	---

FOOD CONSUMPTION (G/ANIMAL/DAY)
MALES

Group 4 (250 mg/kg)

CAGE	5
POST-RANDOMIZATION	
Days 1-6	24.4

CAGE	5
TREATMENT	
Days 1-8	23.2
8-15	20.6
15-22	18.1
22-28	21.7

CAGE	5
RECOVERY	
Days 1-8	---
8-14	---

FOOD CONSUMPTION (G/ANIMAL/DAY)
MALES

Group 5 (1000 mg/kg)

CAGE	6	7
POST-RANDOMIZATION		
Days 1-6	24.1	24.0

CAGE	6	7
TREATMENT		
Days 1-8	18.8	18.8
8-15	16.7	18.0
15-22	17.1	17.6
22-28	22.2	22.8

CAGE	6	7
RECOVERY		
Days 1-8	---	25.0
8-14	---	25.9

FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES

Group 1 (0 mg/kg)

CAGE	8	9
POST-RANDOMIZATION		
Days 1-6	17.9	18.7

CAGE	8	9
TREATMENT		
Days 1-8	14.8	16.0
8-15	14.6	14.0
15-22	14.5	14.4
22-28	17.9	15.7

CAGE	8	9
RECOVERY		
Days 1-8	---	18.9
8-14	---	17.9

FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES

Group 2 (5 mg/kg)

CAGE	10
POST-RANDOMIZATION	
Days 1-6	17.5

CAGE	10
TREATMENT	
Days 1-8	14.8
8-15	13.5
15-22	13.1
22-28	16.1

CAGE	10
RECOVERY	
Days 1-8	---
8-14	---

FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES

Group 3 (25 mg/kg)

CAGE	11
POST-RANDOMIZATION	
Days 1-6	17.1

CAGE	11
TREATMENT	
Days 1-8	13.8
8-15	14.5
15-22	14.7
22-28	14.8

CAGE	11
RECOVERY	
Days 1-8	---
8-14	---

FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES

Group 4 (250 mg/kg)

CAGE	12
POST-RANDOMIZATION	
Days 1-6	16.6

CAGE	12
TREATMENT	
Days 1-8	14.9
8-15	15.1
15-22	13.7
22-28	16.7

CAGE	12
RECOVERY	
Days 1-8	---
8-14	---

FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES

Group 5 (1000 mg/kg)

CAGE	13	14
POST-RANDOMIZATION		
Days 1-6	17.8	17.0

CAGE	13	14
TREATMENT		
Days 1-8	16.9	15.0
8-15	15.2	14.8
15-22	15.0	15.3
22-28	20.3	18.8

CAGE	13	14
RECOVERY		
Days 1-8	---	19.8
8-14	---	18.5

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)

Comments

Data excluded from Summary Report

Not Reported

All Study Phases

Cage 15	Male	Group 10	Reserve Removed
Cage 16	Female	Group 10	Reserve Removed

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)
MALES

Group 1 (0 mg/kg)

CAGE	1	2
POST-RANDOMIZATION		
Days 1-6	109.3	112.8

CAGE	1	2
TREATMENT		
Days 1-8	77.2	77.5
8-15	64.9	62.4
15-22	56.2	54.7
22-28	58.5	60.3

CAGE	1	2
RECOVERY		
Days 1-8	---	61.3
8-14	---	63.9

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)
MALES

Group 2 (5 mg/kg)

CAGE		3
POST-RANDOMIZATION		
Days	1-6	113.9

CAGE		3
TREATMENT		
Days	1-8	80.9
	8-15	65.3
	15-22	54.8
	22-28	61.1

CAGE		3
RECOVERY		
Days	1-8	---
	8-14	---

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)
MALES

Group 3 (25 mg/kg)

CAGE	4
POST-RANDOMIZATION	
Days 1-6	108.1

CAGE	4
TREATMENT	
Days 1-8	80.1
8-15	65.8
15-22	56.7
22-28	61.2

CAGE	4
RECOVERY	
Days 1-8	---
8-14	---

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)
MALES

Group 4 (250 mg/kg)

CAGE	5
POST-RANDOMIZATION	
Days 1-6	112.1

CAGE	5
TREATMENT	
Days 1-8	80.3
8-15	65.2
15-22	54.4
22-28	65.2

CAGE	5
RECOVERY	
Days 1-8	---
8-14	---

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)
MALES

Group 5 (1000 mg/kg)

CAGE	6	7
POST-RANDOMIZATION		
Days 1-6	111.1	109.0

CAGE	6	7
TREATMENT		
Days 1-8	70.9	71.6
8-15	59.4	63.9
15-22	59.2	59.5
22-28	76.8	77.0

CAGE	6	7
RECOVERY		
Days 1-8	---	75.1
8-14	---	77.7

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)
FEMALES

Group 1 (0 mg/kg)

CAGE		8	9
POST-RANDOMIZATION			
Days	1-6	103.0	108.4

CAGE		8	9
TREATMENT			
Days	1-8	70.1	75.9
	8-15	65.2	62.6
	15-22	60.8	60.4
	22-28	75.3	65.9

CAGE		8	9
RECOVERY			
Days	1-8	---	73.8
	8-14	---	70.1

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)
FEMALES

Group 2 (5 mg/kg)

CAGE	10
POST-RANDOMIZATION	
Days 1-6	102.0

CAGE	10
TREATMENT	
Days 1-8	72.3
8-15	62.9
15-22	58.9
22-28	72.2

CAGE	10
RECOVERY	
Days 1-8	---
8-14	---

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)
FEMALES

Group 3 (25 mg/kg)

CAGE	11
POST-RANDOMIZATION	
Days 1-6	98.4

CAGE	11
TREATMENT	
Days 1-8	68.5
8-15	66.0
15-22	62.7
22-28	63.1

CAGE	11
RECOVERY	
Days 1-8	---
8-14	---

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)
FEMALES

Group 4 (250 mg/kg)

CAGE	12
POST-RANDOMIZATION	
Days 1-6	97.5

CAGE	12
TREATMENT	
Days 1-8	74.1
8-15	68.7
15-22	60.4
22-28	73.5

CAGE	12
RECOVERY	
Days 1-8	---
8-14	---

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)
FEMALES

Group 5 (1000 mg/kg)

CAGE	13	14
POST-RANDOMIZATION		
Days 1-6	103.1	99.0

CAGE	13	14
TREATMENT		
Days 1-8	78.8	74.3
8-15	68.5	68.5
15-22	64.7	67.7
22-28	87.8	83.2

CAGE	13	14
RECOVERY		
Days 1-8	---	79.6
8-14	---	74.4

BODY WEIGHTS (G)

Comments

Data excluded from Summary Report

Not Reported

All Study Phases

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

BODY WEIGHTS (G)
MALES

Group 1 (0 mg/kg)

Animal		1	2	3	4	5	6	7
PRE-RANDOMIZATION								
Day	1	208	205	200	205	216	212	204

Animal		1	2	3	4	5	6	7
POST-RANDOMIZATION								
Day	1	222	212	210	223	227	221	214

Animal		1	2	3	4	5	6	7
TREATMENT								
Day	1	255	245	248	254	259	256	257
	8	289	277	278	293	300	298	292
	15	317	302	303	322	328	325	324
	22	343	321	323	343	357	348	354
	28	367	334	336	361	375	367	375

Animal		1	2	3	4	5	6	7
RECOVERY								
Day	1						356	362
	8						380	391
	14						390	407

Animal		8	9	10
PRE-RANDOMIZATION				
Day	1	212	207	201

Animal		8	9	10
POST-RANDOMIZATION				
Day	1	220	217	213

Animal		8	9	10
TREATMENT				
Day	1	256	256	246
	8	288	299	288
	15	308	323	316
	22	325	347	344
	28	340	370	363

Animal		8	9	10
RECOVERY				
Day	1	329	357	351
	8	351	382	372
	14	363	396	383

BODY WEIGHTS (G)
MALES

Group 2 (5 mg/kg)

Animal		11	12	13	14	15
PRE-RANDOMIZATION						
Day	1	201	211	206	215	205

Animal		11	12	13	14	15
POST-RANDOMIZATION						
Day	1	213	217	218	229	218

Animal		11	12	13	14	15
TREATMENT						
Day	1	254	251	254	270	252
	8	287	289	289	319	296
	15	322	314	320	354	324
	22	349	338	342	386	350
	28	366	354	361	408	379

BODY WEIGHTS (G)
MALES

Group 3 (25 mg/kg)

Animal		16	17	18	19	20
PRE-RANDOMIZATION						
Day	1	213	206	208	204	200
Animal		16	17	18	19	20
POST-RANDOMIZATION						
Day	1	221	212	226	215	206
Animal		16	17	18	19	20
TREATMENT						
Day	1	252	245	250	241	247
	8	285	285	283	280	285
	15	312	317	306	307	315
	22	341	347	326	334	336
	28	360	367	345	362	351

BODY WEIGHTS (G)
MALES

Group 4 (250 mg/kg)

Animal		21	22	23	24	25
PRE-RANDOMIZATION						
Day	1	213	206	204	209	201

Animal		21	22	23	24	25
POST-RANDOMIZATION						
Day	1	218	220	215	224	212

Animal		21	22	23	24	25
TREATMENT						
Day	1	253	251	254	256	254
	8	269	290	286	287	310
	15	286	311	315	314	351
	22	285	330	334	337	380
	28	314	342	358	357	398

BODY WEIGHTS (G)
MALES

Group 5 (1000 mg/kg)

Animal		26	27	28	29	30	31	32
PRE-RANDOMIZATION								
Day	1	212	207	202	205	205	212	220
Animal		26	27	28	29	30	31	32
POST-RANDOMIZATION								
Day	1	221	222	214	211	216	226	230
Animal		26	27	28	29	30	31	32
TREATMENT								
Day	1	258	260	244	246	253	262	262
	8	274	257	256	259	281	279	275
	15	288	284	258	271	303	299	290
	22	302	307	214	290	332	324	286
	28	329	332	259	317	353	355	320
Animal		26	27	28	29	30	31	32
RECOVERY								
Day	1						328	288
	8						362	344
	14						377	378

Animal		33	34	35
PRE-RANDOMIZATION				
Day	1	196	202	207
Animal		33	34	35
POST-RANDOMIZATION				
Day	1	213	216	216
Animal		33	34	35
TREATMENT				
Day	1	240	246	242
	8	259	251	250
	15	270	277	270
	22	285	295	289
	28	308	308	310
Animal		33	34	35
RECOVERY				
Day	1	290	290	294
	8	318	312	329
	14	334	326	346

BODY WEIGHTS (G)
FEMALES

Group 1 (0 mg/kg)

Animal		36	37	38	39	40	41	42
PRE-RANDOMIZATION								
Day	1	165	163	183	159	160	165	167
Animal		36	37	38	39	40	41	42
POST-RANDOMIZATION								
Day	1	175	172	189	163	168	166	174
Animal		36	37	38	39	40	41	42
TREATMENT								
Day	1	193	201	218	183	183	196	200
	8	203	225	229	200	196	204	224
	15	216	224	260	208	212	214	208
	22	230	241	269	228	220	227	224
	28	237	264	288	251	246	240	231
Animal		36	37	38	39	40	41	42
RECOVERY								
Day	1						238	221
	8						263	234
	14						248	237

Animal		43	44	45
PRE-RANDOMIZATION				
Day	1	171	168	163
Animal		43	44	45
POST-RANDOMIZATION				
Day	1	183	177	163
Animal		43	44	45
TREATMENT				
Day	1	211	195	186
	8	220	199	209
	15	246	221	226
	22	248	234	257
	28	258	233	274
Animal		43	44	45
RECOVERY				
Day	1	253	233	266
	8	279	247	258
	14	268	247	279

BODY WEIGHTS (G)
FEMALES

Group 2 (5 mg/kg)

Animal		46	47	48	49	50
PRE-RANDOMIZATION						
Day	1	168	166	164	152	161
Animal		46	47	48	49	50
POST-RANDOMIZATION						
Day	1	175	171	174	170	169
Animal		46	47	48	49	50
TREATMENT						
Day	1	204	181	187	184	183
	8	223	196	214	202	190
	15	220	211	218	217	206
	22	234	224	230	221	207
	28	246	233	252	245	229

BODY WEIGHTS (G)
FEMALES

Group 3 (25 mg/kg)

Animal		51	52	53	54	55
PRE-RANDOMIZATION						
Day	1	166	165	168	157	162

Animal		51	52	53	54	55
POST-RANDOMIZATION						
Day	1	176	171	182	163	175

Animal		51	52	53	54	55
TREATMENT						
Day	1	193	192	196	180	187
	8	209	204	200	190	205
	15	214	225	232	206	222
	22	230	234	245	215	247
	28	243	259	251	216	244

BODY WEIGHTS (G)
FEMALES

Group 4 (250 mg/kg)

Animal		56	57	58	59	60
PRE-RANDOMIZATION						
Day	1	169	158	165	167	162
Animal		56	57	58	59	60
POST-RANDOMIZATION						
Day	1	174	167	172	170	168
Animal		56	57	58	59	60
TREATMENT						
Day	1	183	192	189	184	188
	8	212	205	192	195	201
	15	229	228	216	205	220
	22	238	225	222	221	228
	28	262	241	251	229	251

BODY WEIGHTS (G)
FEMALES

Group 5 (1000 mg/kg)

Animal		61	62	63	64	65	66	67
PRE-RANDOMIZATION								
Day	1	159	168	170	163	167	172	160
Animal		61	62	63	64	65	66	67
POST-RANDOMIZATION								
Day	1	168	176	177	170	172	178	171
Animal		61	62	63	64	65	66	67
TREATMENT								
Day	1	185	199	195	196	186	190	187
	8	203	229	211	230	201	203	202
	15	212	252	226	210	212	213	216
	22	221	251	237	227	224	229	224
	28	248	268	258	258	245	243	230
Animal		61	62	63	64	65	66	67
RECOVERY								
Day	1						232	219
	8						260	231
	14						257	240

Animal		68	69	70
PRE-RANDOMIZATION				
Day	1	165	163	165
Animal		68	69	70
POST-RANDOMIZATION				
Day	1	166	169	174
Animal		68	69	70
TREATMENT				
Day	1	184	189	191
	8	202	211	195
	15	211	227	213
	22	216	235	224
	28	237	257	245
Animal		68	69	70
RECOVERY				
Day	1	222	238	228
	8	230	262	258
	14	239	259	254

BODY WEIGHT GAIN (%)

Comments

Data excluded from Summary Report

Not Reported

All Study Phases

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

BODY WEIGHT GAIN (%)
MALES

Group 1 (0 mg/kg)

Animal		1	2	3	4	5	6	7
POST-RANDOMIZATION								
Day	1	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Animal		1	2	3	4	5	6	7
TREATMENT								
Day	1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	8	13.5	12.9	12.3	15.4	15.8	16.6	13.5
	15	24.4	23.1	22.4	26.9	26.6	27.2	26.0
	22	34.5	31.1	30.1	35.2	37.9	36.0	37.9
	28	43.9	36.2	35.4	42.2	44.9	43.4	45.9

Animal		1	2	3	4	5	6	7
RECOVERY								
Day	1						0.0	0.0
	8						6.6	8.0
	14						9.7	12.6

Animal		8	9	10
POST-RANDOMIZATION				
Day	1	0.0	0.0	0.0

Animal		8	9	10
TREATMENT				
Day	1	0.0	0.0	0.0
	8	12.7	16.9	17.1
	15	20.5	26.2	28.5
	22	26.9	35.7	39.7
	28	32.8	44.7	47.5

Animal		8	9	10
RECOVERY				
Day	1	0.0	0.0	0.0
	8	6.9	6.9	6.0
	14	10.6	11.0	9.0

BODY WEIGHT GAIN (%)
MALES

Group 2 (5 mg/kg)

Animal		11	12	13	14	15
POST-RANDOMIZATION						
Day	1	0.0	0.0	0.0	0.0	0.0

Animal		11	12	13	14	15
TREATMENT						
Day	1	0.0	0.0	0.0	0.0	0.0
	8	12.7	14.9	13.7	18.3	17.6
	15	26.8	24.8	26.1	31.4	28.6
	22	37.3	34.7	34.4	43.2	39.1
	28	44.1	41.1	42.0	51.2	50.4

BODY WEIGHT GAIN (%)
MALES

Group 3 (25 mg/kg)

Animal		16	17	18	19	20
POST-RANDOMIZATION						
Day	1	0.0	0.0	0.0	0.0	0.0

Animal		16	17	18	19	20
TREATMENT						
Day	1	0.0	0.0	0.0	0.0	0.0
	8	13.2	16.5	13.5	16.3	15.4
	15	23.7	29.2	22.7	27.2	27.5
	22	35.2	41.8	30.8	38.7	35.8
	28	43.0	50.0	38.1	50.3	42.0

BODY WEIGHT GAIN (%)
MALES

Group 4 (250 mg/kg)

Animal		21	22	23	24	25
POST-RANDOMIZATION						
Day	1	0.0	0.0	0.0	0.0	0.0

Animal		21	22	23	24	25
TREATMENT						
Day	1	0.0	0.0	0.0	0.0	0.0
	8	6.3	15.5	12.8	12.3	22.4
	15	13.2	23.8	24.2	22.9	38.2
	22	12.9	31.4	31.8	32.0	49.8
	28	24.4	36.3	41.1	39.8	57.0

BODY WEIGHT GAIN (%)
MALES

Group 5 (1000 mg/kg)

Animal		26	27	28	29	30	31	32
POST-RANDOMIZATION								
Day	1	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Animal		26	27	28	29	30	31	32
TREATMENT								
Day	1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	8	6.2	-1.0	5.3	5.6	11.4	6.3	4.8
	15	11.7	9.5	6.0	10.1	20.1	13.8	10.6
	22	17.0	18.1	-12.3	18.1	31.6	23.5	9.0
	28	27.4	27.8	6.2	29.0	39.6	35.4	22.0

Animal		26	27	28	29	30	31	32
RECOVERY								
Day	1						0.0	0.0
	8						10.2	19.1
	14						14.8	31.2

Animal		33	34	35
POST-RANDOMIZATION				
Day	1	0.0	0.0	0.0

Animal		33	34	35
TREATMENT				
Day	1	0.0	0.0	0.0
	8	8.0	2.2	3.1
	15	12.6	12.7	11.7
	22	18.7	20.0	19.5
	28	28.4	25.4	28.1

Animal		33	34	35
RECOVERY				
Day	1	0.0	0.0	0.0
	8	9.6	7.9	12.1
	14	15.2	12.7	17.7

BODY WEIGHT GAIN (%)
FEMALES

Group 1 (0 mg/kg)

Animal		36	37	38	39	40	41	42
POST-RANDOMIZATION								
Day	1	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Animal		36	37	38	39	40	41	42
TREATMENT								
Day	1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	8	5.0	12.2	5.2	9.4	7.5	4.2	12.0
	15	11.6	11.5	19.2	13.6	16.0	9.4	4.0
	22	19.3	20.3	23.3	24.6	20.4	16.0	12.1
	28	22.5	31.4	32.0	36.9	34.7	22.7	15.6

Animal		36	37	38	39	40	41	42
RECOVERY								
Day	1						0.0	0.0
	8						10.1	6.3
	14						4.1	7.5

Animal		43	44	45
POST-RANDOMIZATION				
Day	1	0.0	0.0	0.0

Animal		43	44	45
TREATMENT				
Day	1	0.0	0.0	0.0
	8	4.0	2.0	12.7
	15	16.3	13.2	21.5
	22	17.6	20.2	38.3
	28	22.2	19.4	47.4

Animal		43	44	45
RECOVERY				
Day	1	0.0	0.0	0.0
	8	10.2	5.9	-3.1
	14	5.9	6.1	4.8

BODY WEIGHT GAIN (%)
FEMALES

Group 2 (5 mg/kg)

Animal		46	47	48	49	50
POST-RANDOMIZATION						
Day	1	0.0	0.0	0.0	0.0	0.0

Animal		46	47	48	49	50
TREATMENT						
Day	1	0.0	0.0	0.0	0.0	0.0
	8	9.1	8.0	14.6	10.0	3.7
	15	7.8	16.3	16.6	18.3	12.8
	22	14.6	23.4	22.9	20.0	13.1
	28	20.5	28.4	34.6	33.5	25.3

BODY WEIGHT GAIN (%)
FEMALES

Group 3 (25 mg/kg)

Animal		51	52	53	54	55
POST-RANDOMIZATION						
Day	1	0.0	0.0	0.0	0.0	0.0

Animal		51	52	53	54	55
TREATMENT						
Day	1	0.0	0.0	0.0	0.0	0.0
	8	8.1	6.5	2.0	5.4	9.6
	15	10.4	17.0	18.2	14.3	18.7
	22	18.9	21.7	24.8	19.5	32.0
	28	25.8	35.0	28.1	20.1	30.7

BODY WEIGHT GAIN (%)
FEMALES

Group 4 (250 mg/kg)

Animal		56	57	58	59	60
POST-RANDOMIZATION						
Day	1	0.0	0.0	0.0	0.0	0.0

Animal		56	57	58	59	60
TREATMENT						
Day	1	0.0	0.0	0.0	0.0	0.0
	8	16.3	7.1	1.7	6.3	7.1
	15	25.3	18.8	14.0	11.6	17.0
	22	30.6	17.4	17.1	20.3	21.2
	28	43.4	25.8	32.6	24.8	33.6

BODY WEIGHT GAIN (%)
FEMALES

Group 5 (1000 mg/kg)

Animal		61	62	63	64	65	66	67
POST-RANDOMIZATION								
Day	1	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Animal		61	62	63	64	65	66	67
TREATMENT								
Day	1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	8	9.7	15.3	8.1	17.5	8.4	6.8	8.0
	15	14.3	26.6	16.2	7.2	14.4	12.2	15.2
	22	19.2	26.0	21.4	16.1	20.5	20.6	19.4
	28	34.0	34.6	32.4	31.6	32.0	27.9	22.8

Animal		61	62	63	64	65	66	67
RECOVERY								
Day	1						0.0	0.0
	8						11.9	5.7
	14						10.7	9.7

Animal		68	69	70
POST-RANDOMIZATION				
Day	1	0.0	0.0	0.0

Animal		68	69	70
TREATMENT				
Day	1	0.0	0.0	0.0
	8	9.6	11.8	2.0
	15	14.4	20.4	11.4
	22	17.5	24.4	17.0
	28	28.8	36.0	28.0

Animal		68	69	70
RECOVERY				
Day	1	0.0	0.0	0.0
	8	3.4	10.0	13.5
	14	7.4	8.8	11.7

ESTROUS CYCLES

Comments

Data excluded from Summary Report

Not Reported

All Study Phases

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

Incomplete Recordings

ESTROUS CYCLES
FEMALES

TREATMENT

Group 1 (0 mg/kg)

	Day of Evaluation			
Fem.	21	22	23	24
36	D	P	E	M
37	M	D	D	P
38	M	D	D	D
39	D	D	D	P
40	M	D	D	P
41	D	P	E	M
42	M	D	D	E
43	D	P	E	M
44	D	E	M	D
45	D	D	D	D

Group 2 (5 mg/kg)

	Day of Evaluation			
Fem.	21	22	23	24
46	D	D	P	E
47	D	P	E	M
48	M	D	D	D
49	E	M	D	D
50	E	M	D	D

D = DIESTROUS, M = METESTROUS, P = PROESTROUS, E = ESTROUS, N = NO SAMPLE, NC = NUMBER OF CYCLES, PL = PLUG, SP = SPERM, MDE = MEAN# OF DAYS OF CYCLE, / = START OF CYCLE

ESTROUS CYCLES
FEMALES

TREATMENT

Group 3 (25 mg/kg)

	Day of Evaluation			
Fem.	21	22	23	24
51	D	D	P	E
52	P	E	M	D
53	M	D	D	P
54	D	P	E	M
55	D	D	D	D

Group 4 (250 mg/kg)

	Day of Evaluation			
Fem.	21	22	23	24
56	P	E	M	D
57	P	E	D	D
58	D	E	M	P
59	D	D	D	E
60	P	E	M	D

D = DIESTROUS, M = METESTROUS, P = PROESTROUS, E = ESTROUS, N = NO SAMPLE, NC = NUMBER OF CYCLES, PL = PLUG, SP = SPERM, MDE = MEAN# OF DAYS OF CYCLE, / = START OF CYCLE

ESTROUS CYCLES
FEMALES

TREATMENT

Group 5 (1000 mg/kg)

	Day of Evaluation			
Fem.	21	22	23	24
61	E	M	D	D
62	D	D	D	D
63	D	D	P	E
64	D	D	D	D
65	D	D	P	E
66	D	D	D	D
67	P	E	M	D
68	D	D	D	D
69	P	E	E	M
70	D	P	E	M

D = DIESTROUS, M = METESTROUS, P = PROESTROUS, E = ESTROUS, N = NO SAMPLE, NC = NUMBER OF CYCLES, PL = PLUG, SP = SPERM, MDE = MEAN# OF DAYS OF CYCLE, / = START OF CYCLE

REPORT (PART II OF II)

harlan™

28-Day Oral Toxicity (Gavage) Study in the Sprague-Dawley Rat with OCTAMETHYLTRISILOXANE (L3)

Study Director: W. H. Braun

Test Facility: **Harlan Laboratories Ltd.**
Zelgliweg 1
4452 Itingen / Switzerland

Sponsor: **SEHSC**
Silicones Environmental, Health and Safety Council
2325 Dulles Corner Blvd., Suite 500
Herndon, VA 20171 / USA

Study Identification: Harlan Laboratories Study **C53655**

Version: Final

Study Completion Date: 06-Aug-2010

Hematology

Comments

a coagulated sample

Data excluded from Summary Report

Not Reported

All Measurements

Animal 100 Male Group 10 Reserve Removed
Animal 101 Female Group 10 Reserve Removed

Reported Parameter

After 4 Weeks

RBC	ERYTHROCYTES (RBC)
HB	HEMOGLOBIN (HB)
HCT	HEMATOCRIT (HCT)
MCV	MEAN CORPUSCULAR VOLUME (MCV)
RDW	RED CELL VOL. DISTR. WIDTH (RDW)
MCH	MEAN CORPUSCULAR HEMOGLOBIN (MCH)
MCHC	MEAN CORPUSCULAR HEMOGLOBIN CONC. (MCHC)
HDW	HEMOGLOBIN CONC. DISTR. WIDTH
RETI	RETICULOCYTE (REL)
RETI	RETICULOCYTE (ABS)
L RETI	MATURITY INDEX (L-RETI)
M RETI	MATURITY INDEX (M-RETI)
H RETI	MATURITY INDEX (H-RETI)
WBC	LEUKOCYTES, TOTAL (WBC)
NEUT	NEUTROPHILS (NEUT)
EOS	EOSINOPHILS (EOS)
BASO	BASOPHILS (BASO)
LYMPH	LYMPHOCYTES (LYMPH)
MONO	MONOCYTES (MONO)
LUC	LARGE UNSTAINED CELLS (LUC)
NEUT	NEUTROPHILS (NEUT)
EOS	EOSINOPHILS (EOS)
BASO	BASOPHILS (BASO)
LYMPH	LYMPHOCYTES (LYMPH)
MONO	MONOCYTES (MONO)
LUC	LARGE UNSTAINED CELLS (LUC)
PLATELETS	THROMBOCYTES (PLATELETS)
MET-HB	METHEMOGLOBIN (MET-HB)
HEINZ BOD	HEINZ BODIES
PT	PROTHROMBIN TIME (PT)
PTT	PARTIAL THROMBOPLASTIN TIME (PTT)

After 6 Weeks (Recovery)

Hematology

Reported Parameter

After 6 Weeks (Recovery)

RBC	ERYTHROCYTES (RBC)
HB	HEMOGLOBIN (HB)
HCT	HEMATOCRIT (HCT)
MCV	MEAN CORPUSCULAR VOLUME (MCV)
RDW	RED CELL VOL. DISTR. WIDTH (RDW)
MCH	MEAN CORPUSCULAR HEMOGLOBIN (MCH)
MCHC	MEAN CORPUSCULAR HEMOGLOBIN CONC. (MCHC)
HDW	HEMOGLOBIN CONC. DISTR. WIDTH
RETI	RETICULOCYTE (REL)
RETI	RETICULOCYTE (ABS)
L RETI	MATURITY INDEX (L-RETI)
M RETI	MATURITY INDEX (M-RETI)
H RETI	MATURITY INDEX (H-RETI)
WBC	LEUKOCYTES, TOTAL (WBC)
NEUT	NEUTROPHILS (NEUT)
EOS	EOSINOPHILS (EOS)
BASO	BASOPHILS (BASO)
LYMPH	LYMPHOCYTES (LYMPH)
MONO	MONOCYTES (MONO)
LUC	LARGE UNSTAINED CELLS (LUC)
NEUT	NEUTROPHILS (NEUT)
EOS	EOSINOPHILS (EOS)
BASO	BASOPHILS (BASO)
LYMPH	LYMPHOCYTES (LYMPH)
MONO	MONOCYTES (MONO)
LUC	LARGE UNSTAINED CELLS (LUC)
PLATELETS	THROMBOCYTES (PLATELETS)
MET-HB	METHEMOGLOBIN (MET-HB)
HEINZ BOD	HEINZ BODIES
PT	PROTHROMBIN TIME (PT)
PTT	PARTIAL THROMBOPLASTIN TIME (PTT)

Hematology
After 4 Weeks
MALES

Group 1 (0 mg/kg)

	GENERAL						
	RBC T/l	HB mmol/l	HCT rel. 1	MCV fl	RDW rel. 1	MCH fmol	MCHC mmol/l
1	8.90	9.8	0.47	52.5	0.117	1.10	20.96
2	8.31	9.7	0.45	54.3	0.116	1.17	21.50
3	8.59	9.6	0.45	52.9	0.116	1.11	21.03
4	8.63	9.6	0.46	53.8	0.117	1.11	20.72
5	9.05	9.6	0.46	50.9	0.116	1.06	20.89
6	8.37	9.5	0.45	54.3	0.116	1.13	20.80
7	8.54	9.5	0.45	53.0	0.118	1.11	20.97
8	9.06	9.9	0.47	52.3	0.119	1.09	20.91
9	8.40	9.3	0.44	52.7	0.118	1.11	21.08
10	8.35	9.6	0.45	54.3	0.122	1.15	21.16

	GENERAL	RETICULOCYTE COUNT					GENERAL
	HDW mmol/l	RETI rel. 1	RETI G/l	L RETI rel. 1	M RETI rel. 1	H RETI rel. 1	WBC G/l
1	1.67	0.027	241	0.691	0.269	0.040	14.53
2	1.66	0.023	192	0.666	0.281	0.053	12.71
3	1.71	0.025	215	0.601	0.328	0.071	13.79
4	1.64	0.025	212	0.610	0.313	0.078	15.55
5	1.66	0.027	242	0.662	0.293	0.045	13.43
6	1.71	0.027	226	0.599	0.335	0.067	13.34
7	1.73	0.029	245	0.657	0.293	0.050	17.07
8	1.64	0.025	230	0.670	0.285	0.045	12.72
9	1.73	0.030	255	0.619	0.306	0.075	13.21
10	1.68	0.032	264	0.615	0.302	0.083	13.81

	DIFF.WBC COUNT (REL)					
	NEUT rel. 1	EOS rel. 1	BASO rel. 1	LYMPH rel. 1	MONO rel. 1	LUC rel. 1
1	0.189	0.004	0.007	0.750	0.033	0.018
2	0.130	0.007	0.006	0.824	0.021	0.012
3	0.109	0.005	0.004	0.845	0.029	0.008
4	0.139	0.006	0.006	0.806	0.031	0.011
5	0.139	0.007	0.005	0.816	0.023	0.010
6	0.106	0.003	0.006	0.840	0.030	0.015
7	0.074	0.006	0.006	0.865	0.031	0.018
8	0.127	0.005	0.005	0.814	0.038	0.012
9	0.091	0.004	0.004	0.872	0.022	0.007
10	0.088	0.004	0.004	0.852	0.034	0.019

Hematology
After 4 Weeks
MALES

Group 1 (0 mg/kg)

	DIFF.WBC COUNT (ABS)						GENERAL
	NEUT G/l	EOS G/l	BASO G/l	LYMPH G/l	MONO G/l	LUC G/l	PLATELETS G/l
1	2.74	0.05	0.10	10.89	0.48	0.27	1191
2	1.65	0.09	0.08	10.47	0.27	0.15	1082
3	1.50	0.07	0.06	11.65	0.40	0.11	1296
4	2.16	0.09	0.10	12.54	0.49	0.17	1147
5	1.87	0.10	0.07	10.95	0.31	0.13	1192
6	1.41	0.05	0.08	11.21	0.41	0.20	900
7	1.26	0.10	0.11	14.76	0.54	0.30	881
8	1.61	0.06	0.06	10.35	0.48	0.15	968
9	1.20	0.05	0.05	11.52	0.28	0.10	992
10	1.22	0.05	0.05	11.77	0.46	0.26	901

	GENERAL		COAGULATION	
	MET-HB rel. 1	HEINZ BOD rel. 1	PT rel. 1	PTT sec
1	0.010	0.000	0.76	25.4
2	0.010	0.000	0.92	26.6
3	0.009	0.000	0.86	26.7
4	0.010	0.000	0.85	25.4
5	0.009	0.000	0.94	22.8
6	0.010	0.000	0.85	25.4
7	0.010	0.000	0.87	22.2
8	0.010	0.000	0.73	26.0
9	0.010	0.000	0.96	23.9
10	0.011	0.000	0.96	26.5

Hematology
After 4 Weeks
MALES

Group 2 (5 mg/kg)

	GENERAL						
	RBC	HB	HCT	MCV	RDW	MCH	MCHC
	T/l	mmol/l	rel. 1	fl	rel. 1	fmol	mmol/l
11	8.30	9.2	0.44	52.6	0.119	1.11	21.14
12	8.85	9.6	0.45	51.3	0.117	1.09	21.14
13	8.21	9.4	0.44	54.0	0.119	1.14	21.09
14	8.45	9.5	0.45	53.4	0.119	1.13	21.12
15	8.56	9.9	0.47	54.3	0.117	1.16	21.33

	GENERAL	RETICULOCYTE COUNT					GENERAL
	HDW	RETI	RETI	L RETI	M RETI	H RETI	WBC
	mmol/l	rel. 1	G/l	rel. 1	rel. 1	rel. 1	G/l
11	1.61	0.029	236	0.626	0.316	0.058	10.41
12	1.69	0.025	220	0.705	0.249	0.045	11.58
13	1.77	0.028	228	0.674	0.267	0.059	12.79
14	1.63	0.029	244	0.604	0.300	0.096	11.98
15	1.69	0.028	237	0.644	0.291	0.065	11.60

	DIFF.WBC COUNT (REL)					
	NEUT	EOS	BASO	LYMPH	MONO	LUC
	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1
11	0.116	0.005	0.004	0.834	0.029	0.012
12	0.116	0.005	0.004	0.827	0.037	0.010
13	0.085	0.003	0.006	0.872	0.024	0.009
14	0.103	0.006	0.005	0.849	0.023	0.013
15	0.066	0.006	0.005	0.884	0.024	0.016

	DIFF.WBC COUNT (ABS)						GENERAL
	NEUT	EOS	BASO	LYMPH	MONO	LUC	PLATELETS
	G/l	G/l	G/l	G/l	G/l	G/l	G/l
11	1.20	0.05	0.05	8.68	0.30	0.12	973
12	1.35	0.06	0.05	9.58	0.42	0.12	1132
13	1.09	0.04	0.08	11.16	0.31	0.11	857
14	1.24	0.08	0.06	10.17	0.27	0.16	1038
15	0.77	0.06	0.05	10.25	0.27	0.19	1108

Hematology
After 4 Weeks
MALES

Group 2 (5 mg/kg)

	GENERAL		COAGULATION	
	MET-HB rel. 1	HEINZ BOD rel. 1	PT rel. 1	PTT sec
11	0.010	0.000	0.83	25.6
12	0.009	0.000	0.74	25.4
13	0.011	0.000	1.12	25.1
14	0.010	0.000	0.86	24.2
15	0.010	0.000	0.91	24.0

Hematology
After 4 Weeks
MALES

Group 3 (25 mg/kg)

	GENERAL						
	RBC T/l	HB mmol/l	HCT rel. 1	MCV fl	RDW rel. 1	MCH fmol	MCHC mmol/l
16	8.90	9.4	0.46	51.2	0.127	1.06	20.76
17	8.63	9.6	0.46	52.9	0.119	1.12	21.11
18	8.48	9.6	0.45	52.5	0.119	1.13	21.50
19	8.52	9.5	0.46	53.4	0.117	1.12	20.94
20	8.80	10.2	0.47	53.7	0.113	1.16	21.52

	GENERAL	RETICULOCYTE COUNT					GENERAL
	HDW mmol/l	RETI rel. 1	RETI G/l	L RETI rel. 1	M RETI rel. 1	H RETI rel. 1	WBC G/l
16	1.69	0.026	232	0.631	0.318	0.050	15.79
17	1.59	0.026	226	0.646	0.301	0.053	13.36
18	1.69	0.023	199	0.663	0.299	0.038	9.84
19	1.64	0.034	293	0.605	0.325	0.070	12.26
20	1.65	0.024	211	0.681	0.279	0.040	14.05

	DIFF.WBC COUNT (REL)					
	NEUT rel. 1	EOS rel. 1	BASO rel. 1	LYMPH rel. 1	MONO rel. 1	LUC rel. 1
16	0.112	0.006	0.006	0.835	0.031	0.011
17	0.116	0.005	0.006	0.815	0.040	0.019
18	0.102	0.006	0.004	0.860	0.019	0.010
19	0.097	0.005	0.005	0.850	0.032	0.012
20	0.096	0.006	0.007	0.853	0.027	0.011

	DIFF.WBC COUNT (ABS)						GENERAL
	NEUT G/l	EOS G/l	BASO G/l	LYMPH G/l	MONO G/l	LUC G/l	PLATELETS G/l
16	1.76	0.09	0.09	13.18	0.49	0.18	987
17	1.55	0.06	0.07	10.88	0.53	0.25	939
18	1.01	0.06	0.04	8.46	0.18	0.10	1052
19	1.18	0.06	0.06	10.42	0.39	0.14	1161
20	1.35	0.09	0.09	11.98	0.39	0.15	978

Hematology
After 4 Weeks
MALES

Group 3 (25 mg/kg)

	GENERAL		COAGULATION	
	MET-HB rel. 1	HEINZ BOD rel. 1	PT rel. 1	PTT sec
16	0.011	0.000	0.88	25.8
17	0.009	0.000	0.84	24.6
18	0.009	0.000	0.87	26.3
19	0.011	0.000	0.87	21.4
20	0.010	0.000	0.89	24.0

Hematology
After 4 Weeks
MALES

Group 4 (250 mg/kg)

	GENERAL						
	RBC	HB	HCT	MCV	RDW	MCH	MCHC
	T/l	mmol/l	rel. 1	fl	rel. 1	fmol	mmol/l
21	8.30	9.6	0.44	53.0	0.116	1.16	21.73
22	8.94	9.5	0.45	50.1	0.114	1.07	21.29
23	7.86	8.6	0.42	52.9	0.115	1.09	20.65
24	8.48	9.2	0.44	52.4	0.115	1.09	20.80
25	8.39	8.9	0.42	49.9	0.110	1.06	21.18

	GENERAL	RETICULOCYTE COUNT					GENERAL
	HDW	RETI	RETI	L RETI	M RETI	H RETI	WBC
	mmol/l	rel. 1	G/l	rel. 1	rel. 1	rel. 1	G/l
21	1.83	0.028	235	0.664	0.276	0.061	13.41
22	1.86	0.025	217	0.649	0.301	0.051	15.21
23	1.55	0.030	238	0.582	0.338	0.080	9.97
24	1.68	0.034	285	0.607	0.323	0.070	13.22
25	1.66	0.026	221	0.706	0.253	0.040	15.98

	DIFF.WBC COUNT (REL)					
	NEUT	EOS	BASO	LYMPH	MONO	LUC
	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1
21	0.121	0.003	0.006	0.834	0.025	0.012
22	0.191	0.005	0.006	0.758	0.033	0.009
23	0.124	0.005	0.004	0.827	0.027	0.014
24	0.127	0.004	0.005	0.828	0.029	0.008
25	0.105	0.004	0.006	0.847	0.029	0.009

	DIFF.WBC COUNT (ABS)						GENERAL
	NEUT	EOS	BASO	LYMPH	MONO	LUC	PLATELETS
	G/l	G/l	G/l	G/l	G/l	G/l	G/l
21	1.63	0.05	0.08	11.17	0.34	0.15	1184
22	2.91	0.07	0.08	11.53	0.50	0.13	1081
23	1.24	0.05	0.04	8.24	0.27	0.14	1133
24	1.67	0.05	0.06	10.95	0.38	0.11	1133
25	1.68	0.06	0.10	13.54	0.46	0.14	1324

Hematology
After 4 Weeks
MALES

Group 4 (250 mg/kg)

	GENERAL		COAGULATION	
	MET-HB rel. 1	HEINZ BOD rel. 1	PT rel. 1	PTT sec
21	0.010	0.000	0.92	19.8
22	0.009	0.000	0.94	19.1
23	0.008	0.000	1.00	20.3
24	0.009	0.000	0.92	19.0
25	0.010	0.000	0.88	18.0

Hematology
After 4 Weeks
MALES

Group 5 (1000 mg/kg)

	GENERAL						
	RBC	HB	HCT	MCV	RDW	MCH	MCHC
	T/l	mmol/l	rel. 1	fl	rel. 1	fmol	mmol/l
26	8.93	9.5	0.45	50.6	0.116	1.07	21.06
27	8.82	9.5	0.46	51.6	0.121	1.07	20.76
28	9.12	9.8	0.47	51.0	0.125	1.08	21.15
29	9.14	9.2	0.43	47.4	0.118	1.01	21.32
30	8.50	9.3	0.44	51.5	0.117	1.09	21.18
31	9.16	9.7	0.47	50.9	0.115	1.05	20.71
32	9.56	10.0	0.49	50.9	0.116	1.05	20.52
33	9.24	9.7	0.47	50.6	0.115	1.05	20.84
34	8.96	9.4	0.45	50.3	0.113	1.05	20.97
35	9.06	9.5	0.46	50.6	0.115	1.05	20.71

	GENERAL	RETICULOCYTE COUNT					GENERAL
	HDW	RETI	RETI	L RETI	M RETI	H RETI	WBC
	mmol/l	rel. 1	G/l	rel. 1	rel. 1	rel. 1	G/l
26	1.76	0.023	205	0.739	0.236	0.025	13.23
27	1.81	0.031	273	0.712	0.252	0.036	15.29
28	1.97	0.041	371	0.711	0.264	0.025	11.27
29	1.80	0.025	226	0.738	0.230	0.032	13.39
30	1.87	0.025	213	0.657	0.298	0.045	19.99
31	1.77	0.029	265	0.703	0.261	0.036	17.23
32	1.77	0.025	240	0.757	0.219	0.024	16.97
33	1.88	0.032	295	0.677	0.272	0.051	11.96
34	1.85	0.027	239	0.720	0.253	0.027	11.48
35	1.82	0.028	253	0.673	0.281	0.046	13.22

	DIFF.WBC COUNT (REL)					
	NEUT	EOS	BASO	LYMPH	MONO	LUC
	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1
26	0.136	0.003	0.005	0.815	0.028	0.014
27	0.175	0.005	0.006	0.756	0.039	0.019
28	0.182	0.006	0.007	0.764	0.031	0.011
29	0.160	0.004	0.006	0.773	0.042	0.014
30	0.118	0.003	0.005	0.836	0.026	0.012
31	0.133	0.002	0.007	0.814	0.036	0.009
32	0.260	0.003	0.005	0.670	0.044	0.018
33	0.136	0.002	0.004	0.798	0.046	0.013
34	0.172	0.002	0.004	0.786	0.027	0.008
35	0.190	0.003	0.004	0.766	0.031	0.007

Hematology
After 4 Weeks
MALES

Group 5 (1000 mg/kg)

	DIFF.WBC COUNT (ABS)						GENERAL
	NEUT G/l	EOS G/l	BASO G/l	LYMPH G/l	MONO G/l	LUC G/l	PLATELETS G/l
26	1.80	0.04	0.06	10.79	0.37	0.18	1171
27	2.68	0.07	0.09	11.56	0.59	0.29	1213
28	2.06	0.06	0.07	8.60	0.35	0.12	1000
29	2.15	0.06	0.08	10.35	0.56	0.19	1264
30	2.36	0.05	0.11	16.72	0.51	0.24	1213
31	2.29	0.03	0.12	14.02	0.62	0.15	1591
32	4.42	0.04	0.08	11.37	0.75	0.30	1355
33	1.62	0.03	0.05	9.54	0.56	0.16	1334
34	1.98	0.03	0.04	9.02	0.31	0.10	1176
35	2.51	0.03	0.05	10.13	0.40	0.09	1490

	GENERAL		COAGULATION	
	MET-HB rel. 1	HEINZ BOD rel. 1	PT rel. 1	PTT sec
26	0.009	0.000	0.71	20.1
27	0.009	0.000	0.85	18.8
28	0.008	0.000	0.91	16.5
29	0.009	0.000	0.76	19.1
30	0.009	0.000	0.77	19.3
31	0.010	0.000	0.94	16.7
32	0.009	0.000	0.77	17.6
33	0.008	0.000	1.02	17.5
34	0.008	0.000	0.96	17.0
35	0.010	0.000	0.93	16.9

Hematology
After 4 Weeks
FEMALES

Group 1 (0 mg/kg)

	GENERAL						
	RBC T/l	HB mmol/l	HCT rel. 1	MCV fl	RDW rel. 1	MCH fmol	MCHC mmol/l
36	8.01	9.5	0.43	53.7	0.112	1.19	22.11
37	8.29	9.8	0.45	53.9	0.113	1.18	21.98
38	8.03	9.2	0.43	53.6	0.113	1.14	21.31
39	7.80	9.4	0.42	53.7	0.112	1.20	22.36
40	8.02	9.3	0.42	52.9	0.118	1.16	21.87
41	7.89	9.4	0.43	54.1	0.112	1.19	21.96
42	7.75	8.7	0.41	52.3	0.111	1.13	21.55
43	7.93	9.2	0.43	54.5	0.107	1.16	21.37
44	8.30	9.6	0.44	53.1	0.105	1.16	21.76
45	8.16	9.6	0.45	54.9	0.117	1.17	21.33

	GENERAL	RETICULOCYTE COUNT					GENERAL
	HDW mmol/l	RETI rel. 1	RETI G/l	L RETI rel. 1	M RETI rel. 1	H RETI rel. 1	WBC G/l
36	1.60	0.024	189	0.761	0.206	0.033	9.44
37	1.60	0.038	313	0.625	0.313	0.062	10.16
38	1.49	0.036	291	0.545	0.369	0.086	7.04
39	1.59	0.032	248	0.668	0.271	0.061	11.07
40	1.58	0.046	365	0.643	0.300	0.058	10.67
41	1.64	0.039	306	0.536	0.368	0.096	8.20
42	1.69	0.034	263	0.607	0.337	0.057	7.43
43	1.52	0.026	203	0.616	0.329	0.055	11.15
44	1.62	0.024	197	0.707	0.243	0.050	9.60
45	1.58	0.044	356	0.592	0.329	0.080	7.22

	DIFF.WBC COUNT (REL)					
	NEUT rel. 1	EOS rel. 1	BASO rel. 1	LYMPH rel. 1	MONO rel. 1	LUC rel. 1
36	0.061	0.011	0.005	0.893	0.021	0.009
37	0.139	0.009	0.005	0.802	0.026	0.019
38	0.142	0.019	0.003	0.799	0.027	0.009
39	0.121	0.011	0.005	0.828	0.023	0.012
40	0.100	0.010	0.005	0.837	0.031	0.017
41	0.110	0.003	0.003	0.833	0.035	0.016
42	0.090	0.009	0.002	0.866	0.022	0.011
43	0.080	0.008	0.004	0.867	0.028	0.013
44	0.110	0.012	0.004	0.846	0.021	0.009
45	0.155	0.014	0.003	0.781	0.034	0.012

Hematology
After 4 Weeks
FEMALES

Group 1 (0 mg/kg)

	DIFF.WBC COUNT (ABS)						GENERAL
	NEUT G/l	EOS G/l	BASO G/l	LYMPH G/l	MONO G/l	LUC G/l	PLATELETS G/l
36	0.58	0.11	0.04	8.43	0.20	0.08	1030
37	1.41	0.10	0.05	8.15	0.26	0.19	1225
38	1.00	0.14	0.02	5.63	0.19	0.07	1116
39	1.34	0.12	0.06	9.17	0.25	0.13	1369
40	1.07	0.10	0.05	8.93	0.33	0.19	1288
41	0.90	0.03	0.02	6.84	0.29	0.13	891
42	0.67	0.07	0.01	6.43	0.16	0.08	1102
43	0.89	0.09	0.05	9.66	0.31	0.14	1226
44	1.05	0.11	0.03	8.12	0.20	0.08	996
45	1.12	0.10	0.02	5.64	0.25	0.09	1270

	GENERAL		COAGULATION	
	MET-HB rel. 1	HEINZ BOD rel. 1	PT rel. 1	PTT sec
36	0.010	0.000	0.86	26.3
37	0.010	0.000	0.91	27.9
38	0.009	0.000	0.88	24.1
39	0.010	0.000	--- a	--- a
40	0.009	0.000	0.94	27.0
41	0.010	0.000	0.85	23.6
42	0.010	0.000	0.85	26.7
43	0.010	0.000	0.73	26.6
44	0.010	0.000	0.86	25.6
45	0.010	0.000	1.06	23.6

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Hematology
After 4 Weeks
FEMALES

Group 2 (5 mg/kg)

	GENERAL						
	RBC	HB	HCT	MCV	RDW	MCH	MCHC
	T/l	mmol/l	rel. 1	fl	rel. 1	fmol	mmol/l
46	7.86	9.3	0.42	54.0	0.112	1.19	22.02
47	7.55	8.7	0.39	52.1	0.114	1.16	22.25
48	8.02	9.1	0.41	51.6	0.115	1.14	22.01
49	7.80	9.2	0.42	54.3	0.115	1.18	21.65
50	7.37	8.8	0.40	54.4	0.123	1.19	21.91

	GENERAL	RETICULOCYTE COUNT					GENERAL
	HDW	RETI	RETI	L RETI	M RETI	H RETI	WBC
	mmol/l	rel. 1	G/l	rel. 1	rel. 1	rel. 1	G/l
46	1.69	0.038	296	0.609	0.335	0.056	9.85
47	1.57	0.031	235	0.644	0.312	0.044	6.60
48	1.71	0.036	291	0.667	0.300	0.033	8.88
49	1.60	0.040	312	0.567	0.361	0.073	8.60
50	1.65	0.043	318	0.579	0.339	0.081	6.54

	DIFF.WBC COUNT (REL)					
	NEUT	EOS	BASO	LYMPH	MONO	LUC
	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1
46	0.119	0.009	0.003	0.837	0.019	0.012
47	0.195	0.014	0.003	0.753	0.025	0.010
48	0.160	0.012	0.003	0.791	0.025	0.009
49	0.085	0.008	0.004	0.870	0.017	0.015
50	0.126	0.016	0.003	0.816	0.022	0.017

	DIFF.WBC COUNT (ABS)						GENERAL
	NEUT	EOS	BASO	LYMPH	MONO	LUC	PLATELETS
	G/l	G/l	G/l	G/l	G/l	G/l	G/l
46	1.18	0.09	0.03	8.24	0.19	0.12	1182
47	1.29	0.09	0.02	4.97	0.17	0.07	1176
48	1.42	0.11	0.03	7.03	0.22	0.08	1015
49	0.73	0.07	0.03	7.49	0.15	0.13	1175
50	0.82	0.10	0.02	5.34	0.14	0.11	1059

Hematology
After 4 Weeks
FEMALES

Group 2 (5 mg/kg)

	GENERAL		COAGULATION	
	MET-HB rel. 1	HEINZ BOD rel. 1	PT rel. 1	PTT sec
46	0.010	0.000	0.82	26.0
47	0.010	0.000	0.91	22.1
48	0.010	0.000	0.87	26.1
49	0.010	0.000	0.85	25.3
50	0.010	0.000	1.00	25.6

Hematology
After 4 Weeks
FEMALES

Group 3 (25 mg/kg)

	GENERAL						
	RBC T/l	HB mmol/l	HCT rel. 1	MCV fl	RDW rel. 1	MCH fmol	MCHC mmol/l
51	7.91	8.9	0.42	53.0	0.111	1.12	21.19
52	7.68	9.1	0.42	54.9	0.115	1.19	21.64
53	8.24	9.5	0.44	53.0	0.110	1.15	21.67
54	7.86	9.3	0.42	53.3	0.115	1.18	22.18
55	7.97	9.3	0.42	53.3	0.113	1.16	21.80

	GENERAL	RETICULOCYTE COUNT					GENERAL
	HDW mmol/l	RETI rel. 1	RETI G/l	L RETI rel. 1	M RETI rel. 1	H RETI rel. 1	WBC G/l
51	1.62	0.035	279	0.641	0.305	0.054	7.00
52	1.56	0.045	346	0.513	0.376	0.111	9.36
53	1.53	0.020	167	0.743	0.237	0.019	7.87
54	1.67	0.027	210	0.683	0.273	0.044	7.97
55	1.61	0.025	202	0.619	0.323	0.058	8.09

	DIFF.WBC COUNT (REL)					
	NEUT rel. 1	EOS rel. 1	BASO rel. 1	LYMPH rel. 1	MONO rel. 1	LUC rel. 1
51	0.116	0.011	0.003	0.839	0.022	0.009
52	0.098	0.007	0.003	0.869	0.015	0.008
53	0.101	0.010	0.003	0.857	0.019	0.010
54	0.079	0.015	0.004	0.866	0.022	0.014
55	0.151	0.036	0.003	0.778	0.023	0.008

	DIFF.WBC COUNT (ABS)						GENERAL
	NEUT G/l	EOS G/l	BASO G/l	LYMPH G/l	MONO G/l	LUC G/l	PLATELETS G/l
51	0.81	0.08	0.02	5.88	0.15	0.06	1072
52	0.91	0.07	0.03	8.13	0.14	0.08	1090
53	0.79	0.08	0.03	6.74	0.15	0.08	1006
54	0.63	0.12	0.03	6.91	0.18	0.11	1008
55	1.22	0.29	0.02	6.29	0.19	0.07	1156

Hematology
After 4 Weeks
FEMALES

Group 3 (25 mg/kg)

	GENERAL		COAGULATION	
	MET-HB rel. 1	HEINZ BOD rel. 1	PT rel. 1	PTT sec
51	0.011	0.000	0.94	23.3
52	0.010	0.000	0.91	21.6
53	0.011	0.000	0.95	23.2
54	0.009	0.000	0.89	24.5
55	0.010	0.000	0.86	21.4

Hematology
After 4 Weeks
FEMALES

Group 4 (250 mg/kg)

	GENERAL						
	RBC T/l	HB mmol/l	HCT rel. 1	MCV fl	RDW rel. 1	MCH fmol	MCHC mmol/l
56	7.71	8.7	0.40	51.7	0.120	1.12	21.72
57	8.05	9.4	0.43	53.8	0.113	1.17	21.67
58	--- a	---	---	---	---	---	---
59	7.69	9.2	0.43	56.0	0.111	1.20	21.40
60	7.65	8.6	0.41	53.1	0.113	1.12	21.14

	GENERAL	RETICULOCYTE COUNT					GENERAL
	HDW mmol/l	RETI rel. 1	RETI G/l	L RETI rel. 1	M RETI rel. 1	H RETI rel. 1	WBC G/l
56	1.53	0.044	337	0.592	0.325	0.082	6.38
57	1.62	0.035	281	0.512	0.342	0.146	6.28
58	---	---	---	---	---	---	---
59	1.46	0.036	276	0.666	0.286	0.048	5.82
60	1.59	0.037	281	0.580	0.346	0.074	8.28

	DIFF.WBC COUNT (REL)					
	NEUT rel. 1	EOS rel. 1	BASO rel. 1	LYMPH rel. 1	MONO rel. 1	LUC rel. 1
56	0.140	0.012	0.004	0.814	0.021	0.009
57	0.130	0.010	0.003	0.823	0.023	0.011
58	---	---	---	---	---	---
59	0.123	0.009	0.004	0.835	0.018	0.012
60	0.116	0.014	0.004	0.826	0.025	0.014

	DIFF.WBC COUNT (ABS)						GENERAL
	NEUT G/l	EOS G/l	BASO G/l	LYMPH G/l	MONO G/l	LUC G/l	PLATELETS G/l
56	0.89	0.08	0.03	5.19	0.13	0.06	1104
57	0.81	0.06	0.02	5.17	0.15	0.07	1216
58	---	---	---	---	---	---	---
59	0.71	0.05	0.02	4.86	0.10	0.07	1172
60	0.96	0.12	0.04	6.83	0.21	0.12	1016

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Hematology
After 4 Weeks
FEMALES

Group 4 (250 mg/kg)

	GENERAL		COAGULATION	
	MET-HB rel. 1	HEINZ BOD rel. 1	PT rel. 1	PTT sec
56	0.011	0.000	0.88	21.0
57	0.010	0.000	0.88	23.3
58	0.011	0.000	0.95	44.1
59	0.010	0.000	0.94	23.9
60	0.010	0.000	0.86	25.0

Hematology
After 4 Weeks
FEMALES

Group 5 (1000 mg/kg)

	GENERAL						
	RBC T/l	HB mmol/l	HCT rel. 1	MCV fl	RDW rel. 1	MCH fmol	MCHC mmol/l
61	7.95	9.1	0.44	54.9	0.108	1.15	20.96
62	8.30	9.3	0.44	52.7	0.102	1.12	21.23
63	7.79	8.6	0.41	52.6	0.105	1.10	20.88
64	7.86	8.9	0.42	53.7	0.111	1.13	20.97
65	8.19	9.2	0.43	52.5	0.108	1.13	21.50
66	8.17	9.4	0.43	53.0	0.105	1.15	21.62
67	8.12	9.1	0.42	51.6	0.104	1.12	21.62
68	7.83	9.2	0.42	54.0	0.114	1.17	21.70
69	8.24	9.5	0.44	53.8	0.107	1.16	21.51
70	8.34	9.3	0.45	53.7	0.108	1.12	20.84

	GENERAL	RETICULOCYTE COUNT					GENERAL
	HDW mmol/l	RETI rel. 1	RETI G/l	L RETI rel. 1	M RETI rel. 1	H RETI rel. 1	WBC G/l
61	1.52	0.037	296	0.638	0.300	0.062	6.53
62	1.47	0.025	204	0.614	0.317	0.069	6.04
63	1.50	0.032	249	0.593	0.342	0.065	7.11
64	1.51	0.031	244	0.568	0.342	0.090	8.52
65	1.48	0.027	221	0.637	0.303	0.060	7.08
66	1.50	0.023	187	0.707	0.260	0.033	8.18
67	1.63	0.024	192	0.693	0.276	0.031	5.88
68	1.55	0.036	283	0.585	0.349	0.066	7.65
69	1.53	0.032	262	0.658	0.290	0.052	11.94
70	1.58	0.041	343	0.615	0.326	0.060	7.27

	DIFF.WBC COUNT (REL)					
	NEUT rel. 1	EOS rel. 1	BASO rel. 1	LYMPH rel. 1	MONO rel. 1	LUC rel. 1
61	0.088	0.017	0.002	0.861	0.021	0.011
62	0.175	0.018	0.003	0.735	0.048	0.021
63	0.157	0.011	0.004	0.778	0.040	0.011
64	0.067	0.013	0.004	0.858	0.041	0.018
65	0.116	0.012	0.005	0.835	0.021	0.011
66	0.099	0.009	0.004	0.840	0.037	0.010
67	0.120	0.009	0.003	0.809	0.040	0.019
68	0.104	0.013	0.003	0.814	0.050	0.015
69	0.087	0.013	0.004	0.856	0.028	0.012
70	0.134	0.013	0.006	0.802	0.039	0.006

Hematology
After 4 Weeks
FEMALES

Group 5 (1000 mg/kg)

	DIFF.WBC COUNT (ABS)						GENERAL
	NEUT G/l	EOS G/l	BASO G/l	LYMPH G/l	MONO G/l	LUC G/l	PLATELETS G/l
61	0.58	0.11	0.01	5.62	0.14	0.07	1366
62	1.06	0.11	0.02	4.44	0.29	0.13	1001
63	1.12	0.08	0.03	5.54	0.28	0.07	1175
64	0.57	0.11	0.03	7.31	0.35	0.15	1275
65	0.82	0.08	0.04	5.91	0.15	0.08	900
66	0.81	0.08	0.04	6.87	0.30	0.08	1091
67	0.71	0.05	0.02	4.75	0.23	0.11	1308
68	0.80	0.10	0.03	6.22	0.38	0.12	1296
69	1.04	0.15	0.05	10.22	0.33	0.14	1131
70	0.98	0.09	0.04	5.83	0.28	0.05	1248

	GENERAL		COAGULATION	
	MET-HB rel. 1	HEINZ BOD rel. 1	PT rel. 1	PTT sec
61	0.009	0.000	0.87	22.3
62	0.009	0.000	0.91	17.3
63	0.010	0.000	0.92	20.6
64	0.009	0.000	0.88	22.4
65	0.010	0.000	0.75	23.6
66	0.010	0.000	0.91	20.6
67	0.009	0.000	0.94	18.9
68	0.011	0.000	0.82	23.1
69	0.009	0.000	0.94	19.8
70	0.011	0.000	0.85	22.9

Hematology
After 6 Weeks (Recovery)
MALES

Group 1 (0 mg/kg)

	GENERAL						
	RBC T/l	HB mmol/l	HCT rel. 1	MCV fl	RDW rel. 1	MCH fmol	MCHC mmol/l
6	8.31	8.8	0.44	53.1	0.127	1.06	19.87
7	9.09	10.4	0.48	52.4	0.128	1.14	21.76
8	9.14	10.2	0.47	51.7	0.126	1.11	21.56
9	8.78	10.0	0.46	52.1	0.126	1.13	21.78
10	8.49	10.0	0.46	53.9	0.128	1.18	21.93

	GENERAL	RETICULOCYTE COUNT					GENERAL
	HDW mmol/l	RETI rel. 1	RETI G/l	L RETI rel. 1	M RETI rel. 1	H RETI rel. 1	WBC G/l
6	1.69	0.026	219	0.737	0.230	0.033	9.66
7	1.81	0.029	262	0.573	0.353	0.074	19.21
8	1.68	0.022	200	0.668	0.271	0.061	10.88
9	1.81	0.030	267	0.567	0.350	0.082	13.01
10	1.72	0.029	242	0.574	0.333	0.093	13.10

	DIFF.WBC COUNT (REL)					
	NEUT rel. 1	EOS rel. 1	BASO rel. 1	LYMPH rel. 1	MONO rel. 1	LUC rel. 1
6	0.103	0.005	0.004	0.845	0.034	0.009
7	0.074	0.007	0.006	0.866	0.036	0.011
8	0.141	0.007	0.005	0.810	0.031	0.006
9	0.084	0.007	0.004	0.860	0.033	0.013
10	0.099	0.006	0.006	0.847	0.034	0.008

	DIFF.WBC COUNT (ABS)						GENERAL
	NEUT G/l	EOS G/l	BASO G/l	LYMPH G/l	MONO G/l	LUC G/l	PLATELETS G/l
6	0.99	0.05	0.04	8.16	0.33	0.09	873
7	1.42	0.14	0.12	16.63	0.70	0.20	904
8	1.54	0.07	0.06	8.82	0.33	0.07	1104
9	1.09	0.09	0.05	11.19	0.43	0.17	1116
10	1.30	0.08	0.07	11.10	0.45	0.11	1046

Hematology
After 6 Weeks (Recovery)
MALES

Group 1 (0 mg/kg)

	GENERAL		COAGULATION	
	MET-HB rel. 1	HEINZ BOD rel. 1	PT rel. 1	PTT sec
6	0.011	0.000	0.84	24.7
7	0.011	0.000	0.80	24.0
8	0.011	0.000	0.63	26.5
9	0.011	0.000	0.83	24.3
10	0.011	0.000	0.82	26.4

Hematology
After 6 Weeks (Recovery)
MALES

Group 5 (1000 mg/kg)

	GENERAL						
	RBC T/l	HB mmol/l	HCT rel. 1	MCV fl	RDW rel. 1	MCH fmol	MCHC mmol/l
31	9.08	9.6	0.45	49.2	0.125	1.06	21.46
32	9.18	9.6	0.46	50.6	0.135	1.05	20.77
33	9.16	9.5	0.45	49.3	0.125	1.04	21.15
34	9.71	9.9	0.47	48.8	0.126	1.02	20.92
35	8.93	9.4	0.44	49.3	0.130	1.05	21.24

	GENERAL	RETICULOCYTE COUNT					GENERAL
	HDW mmol/l	RETI rel. 1	RETI G/l	L RETI rel. 1	M RETI rel. 1	H RETI rel. 1	WBC G/l
31	1.79	0.022	200	0.747	0.224	0.029	11.38
32	1.70	0.024	219	0.663	0.281	0.056	14.19
33	1.87	0.023	214	0.694	0.257	0.049	11.79
34	1.82	0.024	235	0.647	0.311	0.042	12.94
35	1.80	0.027	238	0.670	0.284	0.046	12.40

	DIFF.WBC COUNT (REL)					
	NEUT rel. 1	EOS rel. 1	BASO rel. 1	LYMPH rel. 1	MONO rel. 1	LUC rel. 1
31	0.092	0.009	0.004	0.849	0.035	0.010
32	0.168	0.088	0.003	0.704	0.028	0.009
33	0.085	0.007	0.004	0.847	0.042	0.015
34	0.089	0.005	0.004	0.859	0.035	0.008
35	0.107	0.008	0.004	0.845	0.028	0.008

	DIFF.WBC COUNT (ABS)						GENERAL
	NEUT G/l	EOS G/l	BASO G/l	LYMPH G/l	MONO G/l	LUC G/l	PLATELETS G/l
31	1.05	0.10	0.05	9.66	0.40	0.11	1175
32	2.38	1.25	0.05	9.99	0.40	0.13	972
33	1.00	0.08	0.05	9.98	0.50	0.18	1017
34	1.15	0.07	0.05	11.12	0.45	0.10	989
35	1.33	0.10	0.05	10.47	0.35	0.10	1236

Hematology
After 6 Weeks (Recovery)
MALES

Group 5 (1000 mg/kg)

	GENERAL		COAGULATION	
	MET-HB rel. 1	HEINZ BOD rel. 1	PT rel. 1	PTT sec
31	0.012	0.000	0.90	22.0
32	0.011	0.000	0.66	23.5
33	0.011	0.000	0.84	24.4
34	0.012	0.000	0.82	25.5
35	0.011	0.000	0.91	22.3

Hematology
After 6 Weeks (Recovery)
FEMALES

Group 1 (0 mg/kg)

	GENERAL						
	RBC	HB	HCT	MCV	RDW	MCH	MCHC
	T/l	mmol/l	rel. 1	fl	rel. 1	fmol	mmol/l
41	8.36	10.1	0.46	55.0	0.133	1.21	22.04
42	8.85	10.1	0.47	52.6	0.131	1.14	21.61
43	8.55	10.3	0.47	54.9	0.125	1.20	21.88
44	8.30	9.9	0.45	53.6	0.125	1.20	22.24
45	8.39	9.8	0.46	54.5	0.123	1.17	21.51

	GENERAL	RETICULOCYTE COUNT					GENERAL
	HDW	RETI	RETI	L RETI	M RETI	H RETI	WBC
	mmol/l	rel. 1	G/l	rel. 1	rel. 1	rel. 1	G/l
41	1.74	0.025	213	0.646	0.305	0.049	9.16
42	1.70	0.030	269	0.549	0.363	0.087	12.20
43	1.58	0.019	166	0.646	0.304	0.049	10.26
44	1.59	0.022	182	0.734	0.236	0.030	10.32
45	1.74	0.048	400	0.608	0.336	0.056	8.33

	DIFF.WBC COUNT (REL)					
	NEUT	EOS	BASO	LYMPH	MONO	LUC
	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1
41	0.113	0.010	0.003	0.835	0.031	0.008
42	0.099	0.011	0.005	0.846	0.032	0.007
43	0.087	0.014	0.004	0.851	0.035	0.010
44	0.098	0.012	0.004	0.854	0.024	0.008
45	0.167	0.012	0.004	0.777	0.031	0.010

	DIFF.WBC COUNT (ABS)						GENERAL
	NEUT	EOS	BASO	LYMPH	MONO	LUC	PLATELETS
	G/l	G/l	G/l	G/l	G/l	G/l	G/l
41	1.03	0.09	0.03	7.64	0.28	0.08	914
42	1.20	0.14	0.06	10.32	0.39	0.09	1037
43	0.89	0.14	0.04	8.72	0.36	0.10	1124
44	1.01	0.13	0.04	8.82	0.25	0.08	948
45	1.39	0.10	0.03	6.47	0.25	0.08	1090

Hematology
After 6 Weeks (Recovery)
FEMALES

Group 1 (0 mg/kg)

	GENERAL		COAGULATION	
	MET-HB rel. 1	HEINZ BOD rel. 1	PT rel. 1	PTT sec
41	0.012	0.000	0.77	25.5
42	0.012	0.000	0.86	23.5
43	0.011	0.000	0.66	26.1
44	0.012	0.000	0.80	25.8
45	0.012	0.000	0.83	24.4

Hematology
After 6 Weeks (Recovery)
FEMALES

Group 5 (1000 mg/kg)

	GENERAL						
	RBC	HB	HCT	MCV	RDW	MCH	MCHC
	T/l	mmol/l	rel. 1	fl	rel. 1	fmol	mmol/l
66	8.46	9.8	0.45	52.8	0.123	1.16	21.94
67	8.21	9.6	0.43	52.2	0.127	1.17	22.40
68	8.39	9.7	0.45	53.2	0.125	1.16	21.81
69	8.64	10.1	0.46	52.9	0.118	1.17	22.17
70	8.20	9.6	0.44	53.1	0.124	1.17	22.02

	GENERAL	RETICULOCYTE COUNT					GENERAL
	HDW	RETI	RETI	L RETI	M RETI	H RETI	WBC
	mmol/l	rel. 1	G/l	rel. 1	rel. 1	rel. 1	G/l
66	1.56	0.020	172	0.781	0.206	0.013	7.54
67	1.61	0.025	207	0.682	0.277	0.041	8.33
68	1.62	0.019	159	0.620	0.339	0.040	8.74
69	1.65	0.017	143	0.750	0.221	0.029	11.26
70	1.54	0.024	197	0.662	0.307	0.030	9.59

	DIFF.WBC COUNT (REL)					
	NEUT	EOS	BASO	LYMPH	MONO	LUC
	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1
66	0.105	0.012	0.005	0.832	0.036	0.010
67	0.149	0.020	0.003	0.794	0.026	0.008
68	0.062	0.012	0.006	0.884	0.026	0.008
69	0.114	0.012	0.006	0.822	0.034	0.011
70	0.210	0.011	0.003	0.747	0.023	0.007

	DIFF.WBC COUNT (ABS)						GENERAL
	NEUT	EOS	BASO	LYMPH	MONO	LUC	PLATELETS
	G/l	G/l	G/l	G/l	G/l	G/l	G/l
66	0.79	0.09	0.04	6.27	0.27	0.08	1123
67	1.25	0.16	0.02	6.62	0.21	0.07	1272
68	0.55	0.11	0.05	7.73	0.23	0.07	1271
69	1.29	0.14	0.07	9.26	0.38	0.13	1051
70	2.01	0.10	0.03	7.16	0.22	0.07	869

Hematology
After 6 Weeks (Recovery)
FEMALES

Group 5 (1000 mg/kg)

	GENERAL		COAGULATION	
	MET-HB rel. 1	HEINZ BOD rel. 1	PT rel. 1	PTT sec
66	0.011	0.000	0.80	24.0
67	0.011	0.000	0.85	21.4
68	0.012	0.000	0.73	28.0
69	0.012	0.000	0.79	24.4
70	0.012	0.000	0.79	25.9

Biochemistry

Comments

Data excluded from Summary Report

Not Reported

All Measurements

Animal 100 Male Group 10 Reserve Removed
Animal 101 Female Group 10 Reserve Removed

Reported Parameter

After 4 Weeks

GLUCOSE	GLUCOSE
UREA	UREA
CREAT	CREATININE
BILI-T	BILIRUBIN, TOTAL
BILE AC	BILE ACIDS
CHOLEST	CHOLESTEROL, TOTAL
TRIGLY	TRIGLYCERIDES
PHOS-LIP	PHOSPHOLIPIDS
ASAT	ASPARTATE AMINOTRANSFERASE (ASAT)
ALAT	ALANINE AMINOTRANSFERASE (ALAT)
LDH	LACTATE DEHYDROGENASE (LDH)
ALP	ALKALINE PHOSPHATASE (ALP)
GGT	GAMMA-GLUTAMYLTRANSFERASE (GGT)
CK	CREATINE KINASE (CK)
SODIUM	SODIUM
POTASSIUM	POTASSIUM
CHLORIDE	CHLORIDE
CALCIUM	CALCIUM
PHOSPHORUS	PHOSPHORUS
PROTEIN	PROTEIN, TOTAL
ALBUMIN	ALBUMIN
GLOBULIN	GLOBULIN
A/G RATIO	A/G RATIO

After 6 Weeks (Recovery)

GLUCOSE	GLUCOSE
UREA	UREA
CREAT	CREATININE
BILI-T	BILIRUBIN, TOTAL
BILE AC	BILE ACIDS
CHOLEST	CHOLESTEROL, TOTAL
TRIGLY	TRIGLYCERIDES
PHOS-LIP	PHOSPHOLIPIDS

Biochemistry

Reported Parameter

After 6 Weeks (Recovery)

ASAT	ASPARTATE AMINOTRANSFERASE (ASAT)
ALAT	ALANINE AMINOTRANSFERASE (ALAT)
LDH	LACTATE DEHYDROGENASE (LDH)
ALP	ALKALINE PHOSPHATASE (ALP)
GGT	GAMMA-GLUTAMYLTRANSFERASE (GGT)
CK	CREATINE KINASE (CK)
SODIUM	SODIUM
POTASSIUM	POTASSIUM
CHLORIDE	CHLORIDE
CALCIUM	CALCIUM
PHOSPHORUS	PHOSPHORUS
PROTEIN	PROTEIN, TOTAL
ALBUMIN	ALBUMIN
GLOBULIN	GLOBULIN
A/G RATIO	A/G RATIO

Biochemistry
After 4 Weeks
MALES

Group 1 (0 mg/kg)

	GENERAL						
	GLUCOSE mmol/l	UREA mmol/l	CREAT µmol/l	BILI-T µmol/l	BILE AC µmol/l	CHOLEST mmol/l	TRIGLY mmol/l
1	4.26	4.72	25.6	2.10	20.40	2.64	0.69
2	4.88	5.38	26.9	2.00	34.40	2.18	0.28
3	4.69	5.60	28.2	2.00	22.10	2.78	0.39
4	5.24	5.32	25.2	2.10	42.50	2.72	0.41
5	4.84	4.43	27.9	1.70	26.80	2.32	0.42
6	4.93	4.95	26.1	2.20	20.90	2.53	0.42
7	4.71	4.37	25.0	1.90	44.40	2.78	0.56
8	5.19	5.03	28.9	2.20	60.00	2.67	0.33
9	5.22	4.75	24.5	2.10	26.30	2.62	0.36
10	6.06	4.57	24.7	2.00	28.70	2.91	0.46

	GENERAL						
	PHOS-LIP mmol/l	ASAT U/l	ALAT U/l	LDH U/l	ALP U/l	GGT U/l	CK U/l
1	2.03	64.1	34.4	113.0	101.5	0.0	131.8
2	1.69	68.0	39.8	168.0	95.4	0.0	150.2
3	1.99	70.2	41.9	126.6	95.6	0.0	156.4
4	2.06	75.7	38.3	115.9	116.5	0.0	140.1
5	1.75	64.4	32.7	82.7	107.2	0.0	138.5
6	1.89	68.4	36.6	109.9	104.6	0.0	153.6
7	2.02	68.9	38.8	167.5	136.6	0.0	218.4
8	1.90	71.6	49.6	82.1	111.4	0.0	114.8
9	1.89	62.7	35.5	183.8	108.2	0.0	168.7
10	2.17	61.7	35.6	92.8	100.4	0.0	130.4

	GENERAL						
	SODIUM mmol/l	POTASSIUM mmol/l	CHLORIDE mmol/l	CALCIUM mmol/l	PHOSPHORUS mmol/l	PROTEIN g/l	ALBUMIN g/l
1	144.8	3.54	102.6	2.76	2.26	62.80	41.00
2	144.4	4.06	105.4	2.65	2.44	59.55	41.30
3	144.9	3.97	105.0	2.67	2.32	61.35	42.67
4	145.0	3.94	103.2	2.76	2.27	61.42	41.69
5	145.0	3.73	103.7	2.70	2.26	58.84	41.38
6	145.1	3.65	105.4	2.64	2.23	58.58	40.40
7	144.4	3.88	104.5	2.68	2.21	62.65	41.30
8	145.9	3.76	104.5	2.64	2.41	64.48	44.19
9	144.8	3.97	103.8	2.64	2.34	62.08	41.53
10	144.6	4.02	103.6	2.69	2.30	61.00	41.23

Biochemistry
After 4 Weeks
MALES

Group 1 (0 mg/kg)

	GENERAL	
	GLOBULIN g/l	A/G RATIO
1	21.80	1.88
2	18.25	2.26
3	18.68	2.28
4	19.73	2.11
5	17.46	2.37
6	18.18	2.22
7	21.35	1.93
8	20.29	2.18
9	20.55	2.02
10	19.77	2.09

Biochemistry
After 4 Weeks
MALES

Group 2 (5 mg/kg)

	GENERAL						
	GLUCOSE mmol/l	UREA mmol/l	CREAT µmol/l	BILI-T µmol/l	BILE AC µmol/l	CHOLEST mmol/l	TRIGLY mmol/l
11	7.28	4.66	25.9	1.70	28.20	2.63	0.53
12	5.22	4.30	23.8	2.10	22.70	2.40	0.49
13	6.59	6.32	25.4	1.80	20.20	2.50	0.20
14	6.75	4.98	27.2	2.20	115.80	2.63	0.70
15	5.35	5.08	26.5	1.80	21.20	3.07	0.58

	GENERAL						
	PHOS-LIP mmol/l	ASAT U/l	ALAT U/l	LDH U/l	ALP U/l	GGT U/l	CK U/l
11	2.02	74.4	34.8	127.4	83.7	0.0	180.4
12	1.89	60.2	28.9	78.7	81.2	0.0	117.1
13	1.82	69.7	34.9	179.9	89.3	0.0	215.3
14	2.04	75.9	44.1	84.3	133.3	0.0	153.3
15	2.16	66.6	43.5	269.0	89.3	0.0	188.6

	GENERAL						
	SODIUM mmol/l	POTASSIUM mmol/l	CHLORIDE mmol/l	CALCIUM mmol/l	PHOSPHORUS mmol/l	PROTEIN g/l	ALBUMIN g/l
11	143.6	3.88	104.4	2.57	2.30	58.20	40.63
12	144.7	3.70	103.6	2.67	2.20	61.48	41.44
13	145.6	4.09	105.7	2.60	2.09	61.32	41.16
14	146.2	4.02	105.2	2.65	2.37	62.45	42.67
15	144.7	3.83	102.5	2.73	2.08	63.18	42.09

	GENERAL	
	GLOBULIN g/l	A/G RATIO
11	17.57	2.31
12	20.04	2.07
13	20.16	2.04
14	19.78	2.16
15	21.09	2.00

Biochemistry
After 4 Weeks
MALES

Group 3 (25 mg/kg)

	GENERAL						
	GLUCOSE mmol/l	UREA mmol/l	CREAT µmol/l	BILI-T µmol/l	BILE AC µmol/l	CHOLEST mmol/l	TRIGLY mmol/l
16	6.28	4.94	27.2	1.70	32.80	2.72	0.64
17	6.22	4.12	24.5	2.00	20.60	2.43	0.21
18	6.60	4.00	22.9	1.50	17.80	2.82	0.40
19	7.47	4.85	22.9	2.00	19.30	2.39	0.17
20	5.25	5.92	26.8	2.40	35.80	2.57	0.60

	GENERAL						
	PHOS-LIP mmol/l	ASAT U/l	ALAT U/l	LDH U/l	ALP U/l	GGT U/l	CK U/l
16	2.08	65.7	36.0	83.1	79.7	0.0	170.1
17	1.94	68.6	27.7	127.5	82.7	0.0	191.2
18	2.09	65.9	33.2	90.3	75.2	0.0	144.0
19	1.78	68.4	37.0	111.7	89.2	0.0	163.6
20	1.97	70.7	37.3	81.5	113.3	0.0	115.6

	GENERAL						
	SODIUM mmol/l	POTASSIUM mmol/l	CHLORIDE mmol/l	CALCIUM mmol/l	PHOSPHORUS mmol/l	PROTEIN g/l	ALBUMIN g/l
16	145.3	4.11	104.4	2.67	2.29	59.16	40.25
17	145.7	4.05	105.2	2.69	2.46	63.29	42.68
18	145.5	4.05	105.7	2.69	2.07	60.55	41.43
19	145.4	4.36	105.5	2.66	2.22	60.82	41.36
20	145.8	3.98	104.4	2.78	2.33	63.83	42.39

	GENERAL	
	GLOBULIN g/l	A/G RATIO
16	18.91	2.13
17	20.61	2.07
18	19.12	2.17
19	19.46	2.13
20	21.44	1.98

Biochemistry
After 4 Weeks
MALES

Group 4 (250 mg/kg)

	GENERAL						
	GLUCOSE mmol/l	UREA mmol/l	CREAT µmol/l	BILI-T µmol/l	BILE AC µmol/l	CHOLEST mmol/l	TRIGLY mmol/l
21	5.08	5.19	26.0	4.50	39.40	4.59	0.53
22	5.30	5.03	29.3	2.80	27.20	4.27	0.61
23	5.32	5.69	27.7	3.10	28.20	3.47	0.45
24	6.90	4.75	28.3	3.30	25.70	4.41	0.32
25	6.53	4.77	31.9	3.00	38.70	4.32	0.73

	GENERAL						
	PHOS-LIP mmol/l	ASAT U/l	ALAT U/l	LDH U/l	ALP U/l	GGT U/l	CK U/l
21	2.90	150.9	97.6	140.4	83.5	2.3	128.5
22	2.79	92.7	69.8	251.1	83.8	0.0	140.4
23	2.51	71.8	42.8	118.2	115.0	0.0	173.5
24	2.79	74.7	40.2	116.9	105.6	0.0	159.6
25	2.80	123.4	81.1	194.8	176.4	7.0	195.3

	GENERAL						
	SODIUM mmol/l	POTASSIUM mmol/l	CHLORIDE mmol/l	CALCIUM mmol/l	PHOSPHORUS mmol/l	PROTEIN g/l	ALBUMIN g/l
21	145.9	4.00	104.2	2.72	2.16	66.47	41.16
22	146.5	3.93	106.1	2.74	2.11	66.19	39.70
23	144.4	3.96	104.9	2.65	2.06	61.48	37.20
24	144.4	4.16	105.1	2.74	2.09	64.52	36.78
25	143.1	4.57	102.6	2.71	2.15	63.30	37.96

	GENERAL	
	GLOBULIN g/l	A/G RATIO
21	25.31	1.63
22	26.49	1.50
23	24.28	1.53
24	27.74	1.33
25	25.34	1.50

Biochemistry
After 4 Weeks
MALES

Group 5 (1000 mg/kg)

	GENERAL						
	GLUCOSE mmol/l	UREA mmol/l	CREAT µmol/l	BILI-T µmol/l	BILE AC µmol/l	CHOLEST mmol/l	TRIGLY mmol/l
26	5.96	4.60	27.0	3.20	46.20	4.20	0.29
27	6.18	5.22	28.4	3.20	50.80	4.85	0.35
28	4.98	5.92	26.2	2.90	42.90	5.01	0.62
29	5.08	4.58	25.3	2.90	38.80	4.68	0.34
30	5.74	4.16	28.9	2.20	20.60	3.42	0.16
31	5.70	6.38	24.9	2.70	36.90	4.83	0.28
32	5.28	7.14	32.8	5.30	116.45	6.36	0.45
33	4.89	5.63	28.6	2.50	37.90	4.03	0.18
34	5.62	5.54	26.5	2.10	28.70	4.89	0.22
35	6.43	5.63	27.6	3.70	40.90	4.89	0.15

	GENERAL						
	PHOS-LIP mmol/l	ASAT U/l	ALAT U/l	LDH U/l	ALP U/l	GGT U/l	CK U/l
26	2.76	158.9	100.6	231.5	97.6	2.8	152.2
27	3.08	216.7	180.9	207.1	98.6	6.7	139.8
28	3.40	227.5	225.9	177.2	87.3	5.8	145.2
29	2.83	87.7	55.4	144.9	108.3	2.6	138.4
30	2.21	67.7	42.1	98.1	94.5	0.0	116.3
31	3.04	112.4	75.7	192.0	78.1	0.0	149.5
32	3.81	448.1	429.0	587.3	122.1	12.2	243.6
33	2.63	89.3	60.6	391.8	78.6	0.0	200.9
34	3.03	73.3	45.6	397.1	70.4	2.6	127.5
35	2.97	129.8	123.8	165.4	98.7	3.6	120.2

	GENERAL						
	SODIUM mmol/l	POTASSIUM mmol/l	CHLORIDE mmol/l	CALCIUM mmol/l	PHOSPHORUS mmol/l	PROTEIN g/l	ALBUMIN g/l
26	146.7	4.42	108.6	2.63	2.07	64.09	37.67
27	144.8	4.57	107.2	2.74	2.00	67.29	38.37
28	144.9	4.31	104.3	2.73	2.18	64.46	40.72
29	146.0	4.09	106.6	2.73	2.32	66.52	39.84
30	146.7	4.26	106.8	2.68	2.16	65.28	37.55
31	146.7	4.18	105.7	2.84	2.41	66.57	39.65
32	146.8	4.46	109.3	2.89	2.28	69.21	39.93
33	147.2	4.36	106.4	2.74	2.19	68.12	39.14
34	146.8	4.51	106.6	2.68	2.04	62.86	37.03
35	146.6	4.41	107.8	2.75	2.12	66.63	38.16

Biochemistry
After 4 Weeks
MALES

Group 5 (1000 mg/kg)

	GENERAL	
	GLOBULIN g/l	A/G RATIO
26	26.42	1.43
27	28.92	1.33
28	23.74	1.72
29	26.68	1.49
30	27.73	1.35
31	26.92	1.47
32	29.28	1.36
33	28.98	1.35
34	25.83	1.43
35	28.47	1.34

Biochemistry
After 4 Weeks
FEMALES

Group 1 (0 mg/kg)

	GENERAL						
	GLUCOSE mmol/l	UREA mmol/l	CREAT µmol/l	BILI-T µmol/l	BILE AC µmol/l	CHOLEST mmol/l	TRIGLY mmol/l
36	4.73	5.15	27.2	2.60	10.80	2.76	0.21
37	4.14	4.84	30.4	2.30	13.40	2.90	0.51
38	4.78	5.05	29.1	1.70	10.30	2.54	0.21
39	4.23	5.02	24.3	1.70	23.90	3.00	0.39
40	4.57	5.22	26.5	2.20	14.90	3.38	0.54
41	4.85	4.60	27.9	2.20	13.00	2.38	0.24
42	4.93	6.41	33.3	1.80	28.30	2.46	0.22
43	5.29	4.27	27.9	2.20	11.90	2.34	0.38
44	4.54	5.00	30.3	2.40	9.60	2.90	0.20
45	4.69	6.15	28.5	2.00	14.10	2.94	0.31

	GENERAL						
	PHOS-LIP mmol/l	ASAT U/l	ALAT U/l	LDH U/l	ALP U/l	GGT U/l	CK U/l
36	2.24	61.9	26.7	125.0	50.8	0.0	138.4
37	2.32	71.0	31.1	189.1	49.8	0.0	232.5
38	1.86	52.9	28.7	259.2	65.5	0.0	143.1
39	2.45	63.6	31.0	111.5	59.0	0.0	144.5
40	2.61	71.2	38.0	145.4	67.8	0.0	172.1
41	1.93	65.7	31.9	177.1	66.8	0.0	130.3
42	1.83	76.4	37.7	193.1	53.9	0.0	140.8
43	2.00	59.5	26.0	58.4	53.1	0.0	96.6
44	2.56	69.1	28.4	242.5	50.6	0.0	150.7
45	2.23	64.5	31.2	218.1	59.5	0.0	161.1

	GENERAL						
	SODIUM mmol/l	POTASSIUM mmol/l	CHLORIDE mmol/l	CALCIUM mmol/l	PHOSPHORUS mmol/l	PROTEIN g/l	ALBUMIN g/l
36	146.8	3.88	107.1	2.70	2.20	60.30	44.40
37	146.2	3.73	104.9	2.72	2.21	61.53	42.84
38	145.7	4.08	105.1	2.79	2.13	63.16	42.69
39	145.9	3.61	105.0	2.77	1.97	62.50	44.04
40	150.0	4.18	108.6	2.79	2.22	63.42	46.35
41	146.4	3.79	107.2	2.69	2.10	58.47	40.46
42	147.4	4.01	108.2	2.63	2.04	56.98	39.45
43	147.0	3.71	107.8	2.66	2.24	59.27	42.95
44	147.2	3.81	107.6	2.68	2.06	60.17	45.53
45	148.2	3.51	107.0	2.71	2.15	62.14	42.95

Biochemistry
After 4 Weeks
FEMALES

Group 1 (0 mg/kg)

	GENERAL	
	GLOBULIN g/l	A/G RATIO
36	15.90	2.79
37	18.69	2.29
38	20.47	2.09
39	18.46	2.39
40	17.07	2.72
41	18.01	2.25
42	17.53	2.25
43	16.32	2.63
44	14.64	3.11
45	19.19	2.24

Biochemistry
After 4 Weeks
FEMALES

Group 2 (5 mg/kg)

	GENERAL						
	GLUCOSE mmol/l	UREA mmol/l	CREAT µmol/l	BILI-T µmol/l	BILE AC µmol/l	CHOLEST mmol/l	TRIGLY mmol/l
46	4.57	6.34	32.3	2.30	20.10	2.24	0.20
47	5.40	5.73	25.5	1.80	13.80	2.81	0.26
48	5.07	5.15	30.6	1.90	10.60	2.74	0.34
49	5.69	5.52	26.9	1.70	18.60	2.97	0.36
50	5.82	6.59	32.4	2.20	15.70	2.65	0.34

	GENERAL						
	PHOS-LIP mmol/l	ASAT U/l	ALAT U/l	LDH U/l	ALP U/l	GGT U/l	CK U/l
46	1.80	65.5	27.3	123.7	47.8	0.0	116.9
47	2.54	64.3	24.4	115.1	65.6	0.0	98.5
48	2.39	69.0	29.8	95.0	54.5	0.0	105.0
49	2.33	67.7	29.1	97.6	54.9	0.0	138.4
50	2.25	66.4	23.4	128.6	47.7	0.0	161.2

	GENERAL						
	SODIUM mmol/l	POTASSIUM mmol/l	CHLORIDE mmol/l	CALCIUM mmol/l	PHOSPHORUS mmol/l	PROTEIN g/l	ALBUMIN g/l
46	145.7	3.62	105.8	2.65	2.05	62.17	43.27
47	147.0	3.89	109.9	2.56	1.98	62.03	44.23
48	146.0	3.72	108.1	2.60	1.96	61.98	44.53
49	147.0	4.11	107.1	2.72	2.28	60.00	42.96
50	146.3	3.62	105.9	2.57	2.15	58.31	42.46

	GENERAL	
	GLOBULIN g/l	A/G RATIO
46	18.90	2.29
47	17.80	2.48
48	17.45	2.55
49	17.04	2.52
50	15.85	2.68

Biochemistry
After 4 Weeks
FEMALES

Group 3 (25 mg/kg)

	GENERAL						
	GLUCOSE mmol/l	UREA mmol/l	CREAT µmol/l	BILI-T µmol/l	BILE AC µmol/l	CHOLEST mmol/l	TRIGLY mmol/l
51	5.53	5.37	28.8	1.90	12.10	2.70	0.22
52	4.78	6.07	27.4	2.70	33.20	3.04	0.35
53	5.51	5.44	27.0	2.70	22.10	2.50	0.22
54	4.48	6.93	32.0	3.10	14.30	3.08	0.24
55	5.58	6.12	26.5	2.10	12.50	2.38	0.24

	GENERAL						
	PHOS-LIP mmol/l	ASAT U/l	ALAT U/l	LDH U/l	ALP U/l	GGT U/l	CK U/l
51	2.18	67.3	30.1	125.9	63.4	0.0	126.9
52	2.64	72.7	36.4	113.8	75.2	0.0	170.9
53	2.13	71.4	27.1	201.3	62.8	0.0	176.2
54	2.37	73.6	29.5	182.6	51.7	0.0	170.3
55	2.00	72.4	24.0	225.0	64.0	0.0	135.7

	GENERAL						
	SODIUM mmol/l	POTASSIUM mmol/l	CHLORIDE mmol/l	CALCIUM mmol/l	PHOSPHORUS mmol/l	PROTEIN g/l	ALBUMIN g/l
51	147.5	3.77	108.4	2.67	1.97	59.92	42.89
52	146.8	3.93	107.7	2.73	2.15	62.76	43.48
53	151.5	4.13	111.9	2.85	2.00	65.04	47.43
54	151.0	3.87	109.3	2.87	2.25	64.05	47.27
55	147.9	3.98	109.0	2.71	2.25	62.81	43.44

	GENERAL	
	GLOBULIN g/l	A/G RATIO
51	17.03	2.52
52	19.28	2.26
53	17.61	2.69
54	16.78	2.82
55	19.37	2.24

Biochemistry
After 4 Weeks
FEMALES

Group 4 (250 mg/kg)

	GENERAL						
	GLUCOSE mmol/l	UREA mmol/l	CREAT µmol/l	BILI-T µmol/l	BILE AC µmol/l	CHOLEST mmol/l	TRIGLY mmol/l
56	5.73	6.35	29.2	3.40	12.30	3.00	0.30
57	6.32	6.30	30.1	4.70	25.80	3.35	0.21
58	5.24	4.88	27.0	2.70	12.60	3.08	0.35
59	5.56	5.51	23.8	4.40	12.70	2.73	0.25
60	5.09	5.49	32.1	2.80	13.90	3.12	0.43

	GENERAL						
	PHOS-LIP mmol/l	ASAT U/l	ALAT U/l	LDH U/l	ALP U/l	GGT U/l	CK U/l
56	2.24	63.0	23.3	76.9	58.5	0.0	98.9
57	2.28	66.6	24.8	529.8	50.7	0.0	219.7
58	2.50	80.2	29.8	183.2	65.1	0.0	168.9
59	2.20	66.8	24.9	156.6	49.5	0.0	157.4
60	2.45	72.2	29.0	154.8	62.6	0.0	140.2

	GENERAL						
	SODIUM mmol/l	POTASSIUM mmol/l	CHLORIDE mmol/l	CALCIUM mmol/l	PHOSPHORUS mmol/l	PROTEIN g/l	ALBUMIN g/l
56	146.2	3.87	106.6	2.60	2.02	62.77	42.54
57	148.2	3.87	108.4	2.65	2.13	61.72	41.98
58	148.0	4.16	108.2	2.73	2.11	62.33	43.68
59	148.5	4.17	108.8	2.79	1.87	62.49	43.89
60	146.7	3.51	107.0	2.64	2.05	61.56	42.17

	GENERAL	
	GLOBULIN g/l	A/G RATIO
56	20.23	2.10
57	19.74	2.13
58	18.65	2.34
59	18.60	2.36
60	19.39	2.17

Biochemistry
After 4 Weeks
FEMALES

Group 5 (1000 mg/kg)

	GENERAL						
	GLUCOSE mmol/l	UREA mmol/l	CREAT µmol/l	BILI-T µmol/l	BILE AC µmol/l	CHOLEST mmol/l	TRIGLY mmol/l
61	5.31	5.88	28.7	2.10	17.40	4.16	0.45
62	6.07	4.96	32.6	3.10	12.00	4.35	0.35
63	5.13	4.61	26.8	3.00	18.50	5.38	0.63
64	5.06	5.96	29.4	1.40	14.10	3.71	0.54
65	6.01	5.89	29.6	2.60	17.20	4.05	0.68
66	4.90	4.91	30.3	1.90	14.40	4.42	0.42
67	5.36	8.36	26.9	2.60	16.30	5.27	0.47
68	4.60	6.68	25.5	3.10	19.40	4.39	1.10
69	5.36	5.63	26.6	2.10	18.70	5.57	0.81
70	5.11	5.96	28.4	2.80	15.10	5.10	0.81

	GENERAL						
	PHOS-LIP mmol/l	ASAT U/l	ALAT U/l	LDH U/l	ALP U/l	GGT U/l	CK U/l
61	3.17	47.3	26.1	183.9	44.7	0.0	137.5
62	3.31	55.2	24.1	123.5	43.9	2.2	121.1
63	3.73	60.2	27.6	139.2	49.6	0.0	136.7
64	2.65	66.7	29.1	410.4	40.5	0.0	229.2
65	3.14	69.4	28.7	102.1	45.9	0.0	134.1
66	3.22	61.8	23.5	112.7	43.3	0.0	112.0
67	3.51	56.6	24.8	135.8	47.9	2.8	110.5
68	3.31	63.5	31.8	102.7	43.3	0.0	150.0
69	4.24	70.9	29.2	168.7	41.7	0.0	193.1
70	3.65	64.4	29.1	234.6	48.4	0.0	155.5

	GENERAL						
	SODIUM mmol/l	POTASSIUM mmol/l	CHLORIDE mmol/l	CALCIUM mmol/l	PHOSPHORUS mmol/l	PROTEIN g/l	ALBUMIN g/l
61	147.2	4.26	108.3	2.73	1.92	65.01	42.58
62	146.0	4.13	107.7	2.71	1.79	63.47	44.26
63	146.0	3.79	106.7	2.69	1.87	65.00	41.14
64	147.4	4.30	108.2	2.76	2.10	68.45	44.39
65	146.1	3.81	106.4	2.65	1.72	64.45	42.63
66	147.8	4.06	107.5	2.71	2.05	67.11	42.38
67	147.6	4.00	108.3	2.72	1.82	67.40	41.31
68	147.3	4.29	108.1	2.75	1.99	66.63	45.02
69	147.3	4.17	106.5	2.78	2.01	67.02	42.62
70	148.1	4.30	109.2	2.80	1.95	64.27	43.02

Biochemistry
After 4 Weeks
FEMALES

Group 5 (1000 mg/kg)

	GENERAL GLOBULIN g/l	A/G RATIO
61	22.43	1.90
62	19.21	2.30
63	23.86	1.72
64	24.06	1.84
65	21.82	1.95
66	24.73	1.71
67	26.09	1.58
68	21.61	2.08
69	24.40	1.75
70	21.25	2.02

Biochemistry
After 6 Weeks (Recovery)
MALES

Group 1 (0 mg/kg)

	GENERAL						
	GLUCOSE mmol/l	UREA mmol/l	CREAT µmol/l	BILI-T µmol/l	BILE AC µmol/l	CHOLEST mmol/l	TRIGLY mmol/l
6	3.99	5.71	26.5	2.50	20.50	2.67	0.30
7	4.13	5.51	26.3	2.00	28.80	3.42	0.54
8	4.50	6.49	25.0	2.30	24.20	2.46	0.32
9	4.41	6.15	26.4	2.00	25.60	2.65	0.42
10	4.49	5.83	27.1	2.00	21.70	3.09	0.75

	GENERAL						
	PHOS-LIP mmol/l	ASAT U/l	ALAT U/l	LDH U/l	ALP U/l	GGT U/l	CK U/l
6	2.11	75.3	42.3	213.6	78.2	0.0	221.0
7	2.46	70.7	45.2	252.5	102.7	0.0	167.4
8	1.93	70.8	48.5	138.0	93.5	0.0	158.0
9	2.05	66.5	39.8	127.7	86.9	0.0	140.8
10	2.49	66.2	44.8	103.0	86.2	0.0	153.7

	GENERAL						
	SODIUM mmol/l	POTASSIUM mmol/l	CHLORIDE mmol/l	CALCIUM mmol/l	PHOSPHORUS mmol/l	PROTEIN g/l	ALBUMIN g/l
6	141.7	3.78	101.5	2.64	2.27	63.77	41.18
7	145.6	4.02	104.2	2.73	2.41	67.10	43.58
8	144.4	4.02	102.2	2.67	2.43	65.44	42.33
9	143.1	3.80	101.6	2.63	2.39	63.63	40.82
10	142.3	3.68	100.8	2.68	2.38	63.97	41.74

	GENERAL	
	GLOBULIN g/l	A/G RATIO
6	22.59	1.82
7	23.52	1.85
8	23.11	1.83
9	22.81	1.79
10	22.23	1.88

Biochemistry
After 6 Weeks (Recovery)
MALES

Group 5 (1000 mg/kg)

	GENERAL						
	GLUCOSE mmol/l	UREA mmol/l	CREAT µmol/l	BILI-T µmol/l	BILE AC µmol/l	CHOLEST mmol/l	TRIGLY mmol/l
31	4.34	6.33	24.6	1.80	16.40	3.70	0.46
32	4.05	5.59	28.5	1.90	12.90	3.09	0.50
33	5.55	5.21	25.4	2.00	13.10	2.61	0.29
34	5.67	5.69	23.2	1.90	10.70	3.21	0.29
35	3.98	4.95	23.6	2.10	10.00	3.60	0.36

	GENERAL						
	PHOS-LIP mmol/l	ASAT U/l	ALAT U/l	LDH U/l	ALP U/l	GGT U/l	CK U/l
31	2.66	61.7	28.2	210.4	60.0	0.0	213.6
32	2.37	67.7	32.3	185.7	87.3	0.0	187.7
33	2.08	79.3	37.8	141.1	65.9	0.0	123.7
34	2.53	65.9	33.8	234.6	59.0	0.0	165.8
35	2.63	70.2	37.3	197.7	85.4	0.0	160.8

	GENERAL						
	SODIUM mmol/l	POTASSIUM mmol/l	CHLORIDE mmol/l	CALCIUM mmol/l	PHOSPHORUS mmol/l	PROTEIN g/l	ALBUMIN g/l
31	144.0	3.97	101.6	2.70	2.42	64.67	41.28
32	143.5	4.02	103.4	2.64	2.47	63.77	41.26
33	143.1	4.19	101.7	2.54	2.15	60.01	39.82
34	142.0	4.44	101.7	2.59	2.14	61.63	40.62
35	142.6	4.20	103.6	2.62	2.08	62.97	41.46

	GENERAL	
	GLOBULIN g/l	A/G RATIO
31	23.39	1.76
32	22.51	1.83
33	20.19	1.97
34	21.01	1.93
35	21.51	1.93

Biochemistry
After 6 Weeks (Recovery)
FEMALES

Group 1 (0 mg/kg)

	GENERAL						
	GLUCOSE mmol/l	UREA mmol/l	CREAT µmol/l	BILI-T µmol/l	BILE AC µmol/l	CHOLEST mmol/l	TRIGLY mmol/l
41	5.15	6.61	31.0	2.10	6.70	1.79	0.19
42	3.50	7.75	31.6	2.30	16.00	2.75	0.32
43	4.13	4.46	28.8	1.90	2.90	2.11	0.24
44	4.37	5.85	29.2	2.80	10.90	3.38	0.23
45	4.21	6.38	29.4	2.50	13.60	3.14	0.32

	GENERAL						
	PHOS-LIP mmol/l	ASAT U/l	ALAT U/l	LDH U/l	ALP U/l	GGT U/l	CK U/l
41	1.70	66.2	25.7	110.5	40.6	0.0	125.1
42	2.43	81.4	49.2	243.8	38.9	0.0	186.1
43	1.93	68.4	26.5	153.9	39.4	0.0	207.6
44	2.76	72.9	30.0	210.0	39.8	0.0	204.1
45	2.62	74.4	42.4	244.6	52.4	0.0	184.2

	GENERAL						
	SODIUM mmol/l	POTASSIUM mmol/l	CHLORIDE mmol/l	CALCIUM mmol/l	PHOSPHORUS mmol/l	PROTEIN g/l	ALBUMIN g/l
41	142.0	3.46	102.9	2.57	1.88	60.57	41.33
42	141.4	3.65	100.9	2.64	2.00	62.63	43.12
43	142.4	3.49	102.6	2.63	1.96	63.18	43.27
44	142.8	3.38	103.2	2.65	2.08	62.16	44.47
45	141.8	3.42	101.6	2.63	2.20	62.50	42.16

	GENERAL	
	GLOBULIN g/l	A/G RATIO
41	19.24	2.15
42	19.51	2.21
43	19.91	2.17
44	17.69	2.51
45	20.34	2.07

Biochemistry
After 6 Weeks (Recovery)
FEMALES

Group 5 (1000 mg/kg)

	GENERAL						
	GLUCOSE mmol/l	UREA mmol/l	CREAT µmol/l	BILI-T µmol/l	BILE AC µmol/l	CHOLEST mmol/l	TRIGLY mmol/l
66	4.33	6.22	31.0	1.90	14.90	3.21	0.31
67	4.21	6.96	29.8	1.80	18.30	3.69	0.39
68	3.72	7.30	30.1	2.50	14.60	2.68	0.35
69	4.12	6.23	27.2	2.00	15.40	3.01	0.31
70	5.01	6.30	33.7	1.90	3.80	2.42	0.33

	GENERAL						
	PHOS-LIP mmol/l	ASAT U/l	ALAT U/l	LDH U/l	ALP U/l	GGT U/l	CK U/l
66	2.54	69.0	26.2	168.8	40.4	0.0	139.8
67	2.92	64.5	25.0	141.0	44.1	0.0	138.6
68	2.42	67.3	36.8	113.8	44.7	0.0	115.9
69	2.45	70.6	29.4	205.5	37.0	0.0	332.4
70	2.33	60.6	26.0	84.9	42.5	0.0	99.5

	GENERAL						
	SODIUM mmol/l	POTASSIUM mmol/l	CHLORIDE mmol/l	CALCIUM mmol/l	PHOSPHORUS mmol/l	PROTEIN g/l	ALBUMIN g/l
66	142.1	3.50	102.2	2.49	2.06	62.05	40.82
67	141.5	4.27	103.2	2.60	1.99	65.95	40.84
68	141.9	3.70	102.5	2.62	1.97	61.09	41.36
69	143.6	3.65	102.9	2.58	2.19	61.42	40.57
70	140.8	3.55	103.4	2.52	1.87	61.10	41.82

	GENERAL	
	GLOBULIN g/l	A/G RATIO
66	21.23	1.92
67	25.11	1.63
68	19.73	2.10
69	20.85	1.95
70	19.28	2.17

Urinalysis

Comments

Data excluded from Summary Report

Not Reported

All Measurements

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

Reported Parameter

After 4 Weeks

VOLUME/18h	VOLUME/18h
REL DENS	RELATIVE DENSITY
COLOR	COLOR
APPEARANCE	APPEARANCE
pH	pH
NITRITE	NITRITE
PROTEIN	PROTEIN
GLUCOSE	GLUCOSE
KETONES	KETONES
UROBILI	UROBILINOGEN
BILIRUBIN	BILIRUBIN
ERY	ERYTHROCYES
LEU	LEUCOCYTES

After 6 Weeks (Recovery)

VOLUME/18h	VOLUME/18h
REL DENS	RELATIVE DENSITY
COLOR	COLOR
APPEARANCE	APPEARANCE
pH	pH
NITRITE	NITRITE
PROTEIN	PROTEIN
GLUCOSE	GLUCOSE
KETONES	KETONES
UROBILI	UROBILINOGEN
BILIRUBIN	BILIRUBIN
ERY	ERYTHROCYES
LEU	LEUCOCYTES

Urinalysis
After 4 Weeks
MALES

Group 1 (0 mg/kg)

	GENERAL						
	VOLUME/18h ml	REL DENS rel. 1	COLOR	APPEARANCE	pH	NITRITE SCORE 0/1	PROTEIN g/l
1	2.5	1.146	yellow	clear	5.0	0	0.75
2	4.2	1.052	yellow	clear	6.5	0	0.75
3	1.2	1.082	yellow	clear	5.0	0	0.75
4	1.7	1.116	yellow	clear	5.0	0	0.75
5	8.6	1.027	yellow	cloudy	7.0	1	0.25
6	8.6	1.050	yellow	cloudy	6.5	0	0.25
7	1.9	1.112	yellow	clear	5.0	0	0.75
8	5.2	1.034	yellow	cloudy	6.5	0	0.25
9	4.4	1.063	yellow	clear	6.0	0	0.75
10	2.1	1.154	yellow	clear	5.0	0	0.75

	GENERAL					
	GLUCOSE mmol/l	KETONES mmol/l	UROBILI µmol/l	BILIRUBIN µmol/l	ERY per µl	LEU per µl
1	0	1.5	0	0	0	25
2	0	1.5	0	0	10	100
3	0	5.0	0	0	10	25
4	0	1.5	0	0	10	25
5	0	0.5	0	0	10	100
6	0	0.5	0	0	10	25
7	0	1.5	0	0	0	25
8	0	1.5	0	0	10	25
9	0	1.5	0	0	0	25
10	0	1.5	17	0	0	25

Urinalysis
After 4 Weeks
MALES

Group 2 (5 mg/kg)

	GENERAL						
	VOLUME/18h ml	REL DENS rel. 1	COLOR	APPEARANCE	pH	NITRITE SCORE 0/1	PROTEIN g/l
11	8.0	1.030	yellow	clear	6.0	0	0.25
12	3.1	1.073	yellow	clear	5.0	0	0.75
13	2.5	1.078	yellow	clear	5.0	0	0.75
14	2.1	1.079	yellow	clear	5.0	0	0.75
15	6.3	1.043	yellow	clear	6.0	0	0.75

	GENERAL					
	GLUCOSE mmol/l	KETONES mmol/l	UROBILI µmol/l	BILIRUBIN µmol/l	ERY per µl	LEU per µl
11	0	0.5	0	0	0	25
12	0	1.5	17	0	10	25
13	0	1.5	0	0	10	100
14	0	5.0	0	0	10	100
15	0	1.5	0	0	50	500

Urinalysis
After 4 Weeks
MALES

Group 3 (25 mg/kg)

	GENERAL						
	VOLUME/18h ml	REL DENS rel. 1	COLOR	APPEARANCE	pH	NITRITE SCORE 0/1	PROTEIN g/l
16	3.3	1.073	yellow	clear	5.0	0	0.75
17	12.1	1.018	light yel	cloudy	7.0	1	0.25
18	4.7	1.042	yellow	clear	6.5	0	0.75
19	5.4	1.043	yellow	clear	6.0	0	0.25
20	2.6	1.043	yellow	clear	5.0	0	0.75

	GENERAL					
	GLUCOSE mmol/l	KETONES mmol/l	UROBILI µmol/l	BILIRUBIN µmol/l	ERY per µl	LEU per µl
16	0	1.5	0	0	0	25
17	0	0.5	0	0	10	25
18	0	1.5	0	0	0	25
19	0	1.5	0	0	10	100
20	0	5.0	0	0	0	25

Urinalysis
After 4 Weeks
MALES

Group 4 (250 mg/kg)

	GENERAL						
	VOLUME/18h ml	REL DENS rel. 1	COLOR	APPEARANCE	pH	NITRITE SCORE 0/1	PROTEIN g/l
21	7.5	1.037	yellow	clear	6.5	0	0.75
22	8.4	1.033	yellow	clear	6.0	1	0.25
23	5.9	1.033	yellow	clear	6.0	0	0.75
24	7.5	1.034	yellow	clear	6.0	0	0.25
25	5.6	1.054	yellow	turbid	5.0	0	0.75

	GENERAL					
	GLUCOSE mmol/l	KETONES mmol/l	UROBILI µmol/l	BILIRUBIN µmol/l	ERY per µl	LEU per µl
21	0	0.5	0	0	10	25
22	0	0.5	0	0	10	25
23	0	1.5	0	0	10	25
24	0	0.5	0	0	10	25
25	0	1.5	0	0	25	25

Urinalysis
After 4 Weeks
MALES

Group 5 (1000 mg/kg)

	GENERAL						
	VOLUME/18h ml	REL DENS rel. 1	COLOR	APPEARANCE	pH	NITRITE SCORE 0/1	PROTEIN g/l
26	15.4	1.019	yellow	turbid	7.0	0	0.25
27	16.4	1.016	yellow	turbid	7.0	1	0.25
28	4.8	1.043	yellow br	turbid	5.0	0	0.25
29	15.5	1.015	yellow	turbid	7.0	0	0.25
30	14.4	1.022	yellow	turbid	6.5	1	0.25
31	7.1	1.047	yellow	turbid	6.5	1	0.25
32	12.7	1.024	yellow	turbid	7.0	0	0.25
33	6.0	1.045	yellow	turbid	6.5	1	0.25
34	6.2	1.054	yellow br	turbid	5.0	1	0.75
35	10.3	1.031	yellow	turbid	7.0	1	0.25

	GENERAL					
	GLUCOSE mmol/l	KETONES mmol/l	UROBILI µmol/l	BILIRUBIN µmol/l	ERY per µl	LEU per µl
26	0	0.0	0	0	25	25
27	0	0.0	0	0	25	100
28	0	0.5	17	17	10	25
29	0	0.0	0	0	25	25
30	0	0.0	0	0	10	25
31	0	0.5	17	0	10	25
32	0	0.0	17	0	25	100
33	0	0.5	17	0	10	25
34	0	0.5	135	17	25	25
35	0	0.0	0	0	0	25

Urinalysis
After 4 Weeks
FEMALES

Group 1 (0 mg/kg)

	GENERAL						
	VOLUME/18h ml	REL DENS rel. 1	COLOR	APPEARANCE	pH	NITRITE SCORE 0/1	PROTEIN g/l
36	1.7	1.080	yellow	clear	5.0	0	0.25
37	6.6	1.033	yellow	turbid	6.5	0	0.25
38	4.3	1.050	yellow	clear	6.0	0	0.75
39	7.7	1.027	yellow	clear	6.0	0	0.25
40	9.5	1.021	yellow	clear	6.5	0	0.00
41	7.6	1.028	yellow	turbid	6.0	0	0.00
42	1.6	1.077	yellow	turbid	5.0	0	0.75
43	3.6	1.046	yellow	turbid	6.0	0	0.75
44	2.7	1.055	yellow	turbid	5.0	0	0.25
45	7.8	1.032	yellow	turbid	6.0	0	0.25

	GENERAL					
	GLUCOSE mmol/l	KETONES mmol/l	UROBILI µmol/l	BILIRUBIN µmol/l	ERY per µl	LEU per µl
36	0	1.5	0	0	0	0
37	0	0.5	0	0	0	25
38	0	0.5	0	0	0	500
39	0	0.0	0	0	0	0
40	0	0.0	0	0	0	0
41	0	0.5	0	0	0	25
42	0	1.5	0	0	0	25
43	0	0.5	0	17	0	25
44	0	0.5	0	0	0	0
45	0	0.5	0	0	0	0

Urinalysis
After 4 Weeks
FEMALES

Group 2 (5 mg/kg)

	GENERAL						
	VOLUME/18h ml	REL DENS rel. 1	COLOR	APPEARANCE	pH	NITRITE SCORE 0/1	PROTEIN g/l
46	5.4	1.036	yellow	turbid	6.0	1	0.25
47	7.1	1.026	yellow	turbid	7.0	0	0.25
48	8.9	1.022	yellow	turbid	7.0	0	0.25
49	4.8	1.029	yellow	clear	6.0	1	0.25
50	3.1	1.055	yellow	turbid	6.0	0	0.25

	GENERAL					
	GLUCOSE mmol/l	KETONES mmol/l	UROBILI µmol/l	BILIRUBIN µmol/l	ERY per µl	LEU per µl
46	0	0.5	0	0	0	25
47	0	0.5	0	0	0	0
48	0	0.5	0	0	0	0
49	0	0.5	0	0	10	25
50	0	0.5	0	0	0	25

Urinalysis
After 4 Weeks
FEMALES

Group 3 (25 mg/kg)

	GENERAL						
	VOLUME/18h ml	REL DENS rel. 1	COLOR	APPEARANCE	pH	NITRITE SCORE 0/1	PROTEIN g/l
51	2.5	1.069	yellow	clear	5.0	0	0.75
52	5.8	1.033	yellow	clear	6.0	0	0.25
53	3.2	1.046	yellow	clear	6.0	1	0.25
54	1.8	1.112	yellow	clear	5.0	0	0.75
55	1.9	1.088	yellow	clear	5.0	0	0.75

	GENERAL					
	GLUCOSE mmol/l	KETONES mmol/l	UROBILI µmol/l	BILIRUBIN µmol/l	ERY per µl	LEU per µl
51	0	0.5	0	0	0	0
52	0	0.5	0	0	0	0
53	0	0.5	0	0	0	0
54	0	1.5	0	0	0	25
55	0	1.5	0	0	0	25

Urinalysis
After 4 Weeks
FEMALES

Group 4 (250 mg/kg)

	GENERAL						
	VOLUME/18h ml	REL DENS rel. 1	COLOR	APPEARANCE	pH	NITRITE SCORE 0/1	PROTEIN g/l
56	4.7	1.050	yellow	clear	6.0	1	0.25
57	6.2	1.029	yellow	turbid	6.0	1	0.25
58	5.5	1.041	yellow	clear	6.0	0	0.25
59	6.4	1.027	yellow	turbid	6.0	0	0.25
60	4.5	1.048	yellow	clear	6.0	0	0.25

	GENERAL					
	GLUCOSE mmol/l	KETONES mmol/l	UROBILI µmol/l	BILIRUBIN µmol/l	ERY per µl	LEU per µl
56	0	0.5	0	0	0	0
57	0	0.0	0	0	0	0
58	0	0.5	0	0	0	0
59	0	0.0	0	0	0	0
60	0	0.5	0	0	0	25

Urinalysis
After 4 Weeks
FEMALES

Group 5 (1000 mg/kg)

	GENERAL						
	VOLUME/18h ml	REL DENS rel. 1	COLOR	APPEARANCE	pH	NITRITE SCORE 0/1	PROTEIN g/l
61	3.8	1.059	yellow	clear	5.0	0	0.25
62	7.4	1.033	yellow	clear	5.0	1	0.75
63	8.8	1.022	yellow	clear	5.0	1	0.00
64	5.0	1.045	yellow	clear	5.0	0	0.25
65	6.6	1.041	yellow	clear	5.0	1	0.25
66	14.0	1.015	light yel	cloudy	5.0	0	0.25
67	3.7	1.050	yellow	clear	5.0	0	0.25
68	4.2	1.057	yellow	clear	5.0	0	0.25
69	10.1	1.027	yellow	cloudy	5.0	1	0.25
70	3.7	1.054	yellow	clear	5.0	0	0.75

	GENERAL					
	GLUCOSE mmol/l	KETONES mmol/l	UROBILI µmol/l	BILIRUBIN µmol/l	ERY per µl	LEU per µl
61	0	0.5	0	0	0	0
62	0	0.0	0	0	0	100
63	0	0.0	0	0	10	0
64	0	0.5	0	0	0	0
65	0	0.0	0	0	0	25
66	0	0.0	0	0	0	0
67	0	0.5	0	0	0	0
68	0	0.0	0	0	0	0
69	0	0.0	0	0	0	0
70	0	0.5	0	0	0	25

Urinalysis
After 6 Weeks (Recovery)
MALES

Group 1 (0 mg/kg)

	GENERAL						
	VOLUME/18h ml	REL DENS rel. 1	COLOR	APPEARANCE	pH	NITRITE SCORE 0/1	PROTEIN g/l
6	4.3	1.045	yellow	clear	6.5	0	0.25
7	10.1	1.029	yellow	cloudy	7.0	0	0.25
8	7.8	1.031	yellow	cloudy	7.0	1	0.25
9	7.2	1.031	yellow	cloudy	7.0	0	0.25
10	8.4	1.028	yellow	cloudy	6.5	0	0.25

	GENERAL					
	GLUCOSE mmol/l	KETONES mmol/l	UROBILI µmol/l	BILIRUBIN µmol/l	ERY per µl	LEU per µl
6	0	0.5	0	0	10	100
7	0	0.5	0	0	0	25
8	0	1.5	0	0	10	25
9	0	0.5	0	0	0	25
10	0	0.5	0	0	10	25

Urinalysis
After 6 Weeks (Recovery)
MALES

Group 5 (1000 mg/kg)

	GENERAL						
	VOLUME/18h ml	REL DENS rel. 1	COLOR	APPEARANCE	pH	NITRITE SCORE 0/1	PROTEIN g/l
31	6.0	1.038	yellow	cloudy	7.0	1	0.25
32	6.5	1.032	yellow	cloudy	7.0	0	0.25
33	7.4	1.033	yellow	cloudy	6.5	1	0.25
34	4.0	1.047	yellow	cloudy	6.5	0	0.25
35	15.3	1.017	yellow	clear	7.0	1	0.00

	GENERAL					
	GLUCOSE mmol/l	KETONES mmol/l	UROBILI µmol/l	BILIRUBIN µmol/l	ERY per µl	LEU per µl
31	0	0.5	0	0	10	100
32	0	0.5	0	0	0	500
33	0	0.5	0	0	10	100
34	0	0.5	0	0	10	100
35	0	0.0	0	0	0	25

Urinalysis
After 6 Weeks (Recovery)
FEMALES

Group 1 (0 mg/kg)

	GENERAL						
	VOLUME/18h ml	REL DENS rel. 1	COLOR	APPEARANCE	pH	NITRITE SCORE 0/1	PROTEIN g/l
41	2.5	1.063	yellow	clear	6.5	0	0.25
42	2.5	1.074	yellow	clear	5.0	0	0.25
43	7.0	1.021	yellow	clear	6.5	0	0.25
44	4.3	1.042	yellow	clear	6.0	0	0.25
45	20.5	1.011	light yel	clear	7.0	0	0.00

	GENERAL					
	GLUCOSE mmol/l	KETONES mmol/l	UROBILI µmol/l	BILIRUBIN µmol/l	ERY per µl	LEU per µl
41	0	1.5	0	0	10	100
42	0	0.5	0	17	0	0
43	0	0.0	0	0	0	25
44	0	0.5	0	0	0	0
45	0	0.0	0	0	0	0

Urinalysis
After 6 Weeks (Recovery)
FEMALES

Group 5 (1000 mg/kg)

	GENERAL						
	VOLUME/18h ml	REL DENS rel. 1	COLOR	APPEARANCE	pH	NITRITE SCORE 0/1	PROTEIN g/l
66	8.9	1.021	light yel	clear	6.5	0	0.00
67	8.8	1.019	light yel	clear	6.5	0	0.00
68	3.6	1.048	yellow	clear	6.5	0	0.25
69	15.2	1.012	light yel	clear	6.5	0	0.00
70	3.3	1.039	yellow	clear	6.5	0	0.25

	GENERAL					
	GLUCOSE mmol/l	KETONES mmol/l	UROBILI µmol/l	BILIRUBIN µmol/l	ERY per µl	LEU per µl
66	0	0.0	0	0	0	25
67	0	0.0	0	0	0	0
68	0	0.5	0	0	0	0
69	0	0.0	0	0	0	0
70	0	0.5	0	0	0	25

ORGAN WEIGHTS (GRAM)

Comments

Exclusions

Not Reported

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

Selection of Organs

All organs reported

Animals without scheduled necropsy

ORGAN WEIGHTS (GRAM)
AFTER 4 WEEKS
MALES

Group 1 (0 mg/kg)

Animal	BODY W.	BRAIN	PITUITARY	HEART	THYROIDS	LIVER	THYMUS
1	345.7	1.95	0.012	1.22	0.022	9.86	0.460
2	306.9	1.81	0.011	1.30	0.014	9.06	0.415
3	311.3	1.86	0.010	1.31	0.018	8.99	0.462
4	340.5	1.83	0.012	1.17	0.021	10.09	0.495
5	357.5	1.81	0.011	1.32	0.017	10.33	0.448

Animal	KIDNEYS	ADRENALS	SPLEEN	TESTES	PROST/SEMI	EPIDIDYMID
1	2.17	0.055	0.83	3.96	1.600	1.155
2	1.95	0.054	0.70	3.63	1.878	1.052
3	1.87	0.045	0.97	3.69	2.158	1.135
4	2.07	0.059	0.83	3.45	1.798	1.108
5	2.02	0.064	0.99	3.29	2.177	1.117

Group 2 (5 mg/kg)

Animal	BODY W.	BRAIN	PITUITARY	HEART	THYROIDS	LIVER	THYMUS
11	350.3	1.80	0.011	1.32	0.015	10.77	0.378
12	334.9	1.92	0.013	1.16	0.014	9.53	0.444
13	346.2	1.89	0.013	1.26	0.020	10.36	0.416
14	391.0	1.89	0.011	1.45	0.025	12.37	0.526
15	357.5	1.89	0.011	1.25	0.015	11.43	0.530

Animal	KIDNEYS	ADRENALS	SPLEEN	TESTES	PROST/SEMI	EPIDIDYMID
11	2.18	0.056	0.84	3.92	1.485	1.063
12	2.04	0.051	0.75	3.71	1.515	1.106
13	2.06	0.049	0.70	3.55	2.057	1.014
14	2.28	0.055	1.01	3.68	1.687	1.033
15	2.10	0.048	0.99	3.44	1.646	1.018

ORGAN WEIGHTS (GRAM)
AFTER 4 WEEKS
MALES

Group 3 (25 mg/kg)

Animal	BODY W.	BRAIN	PITUITARY	HEART	THYROIDS	LIVER	THYMUS
16	346.7	1.81	0.011	1.25	0.028	11.03	0.521
17	351.1	1.72	0.013	1.13	0.017	10.99	0.502
18	332.4	1.91	0.009	1.15	0.018	10.76	0.405
19	351.3	1.83	0.011	1.25	0.013	11.71	0.409
20	333.1	1.76	0.011	1.18	0.013	11.16	0.452

Animal	KIDNEYS	ADRENALS	SPLEEN	TESTES	PROST/SEMI	EPIDIDYMID
16	2.07	0.050	0.83	3.42	1.737	1.035
17	2.03	0.053	0.79	3.77	1.811	1.123
18	2.05	0.055	0.84	3.53	2.049	1.085
19	2.26	0.051	0.93	4.02	1.813	1.167
20	1.91	0.053	0.78	3.44	1.962	1.079

Group 4 (250 mg/kg)

Animal	BODY W.	BRAIN	PITUITARY	HEART	THYROIDS	LIVER	THYMUS
21	300.2	1.74	0.013	1.06	0.015	13.96	0.352
22	330.9	1.83	0.009	1.15	0.017	15.39	0.397
23	345.4	1.82	0.013	1.16	0.014	13.55	0.402
24	345.7	1.82	0.010	1.24	0.014	15.18	0.571
25	386.9	1.97	0.013	1.43	0.019	17.15	0.516

Animal	KIDNEYS	ADRENALS	SPLEEN	TESTES	PROST/SEMI	EPIDIDYMID
21	2.00	0.054	1.00	3.77	1.457	1.079
22	2.31	0.049	1.06	3.64	1.417	1.028
23	2.12	0.051	0.92	4.11	2.249	1.158
24	2.03	0.047	0.97	3.34	1.768	0.989
25	2.34	0.047	1.19	3.80	1.501	0.978

ORGAN WEIGHTS (GRAM)
AFTER 4 WEEKS
MALES

Group 5 (1000 mg/kg)

Animal	BODY W.	BRAIN	PITUITARY	HEART	THYROIDS	LIVER	THYMUS
26	306.8	1.81	0.009	1.09	0.017	15.12	0.320
27	307.1	1.79	0.009	1.06	0.017	17.09	0.355
28	228.5	1.71	0.008	0.95	0.013	11.96	0.190
29	290.9	1.80	0.010	1.07	0.017	14.59	0.423
30	323.3	1.79	0.009	1.15	0.022	16.63	0.417

Animal	KIDNEYS	ADRENALS	SPLEEN	TESTES	PROST/SEMI	EPIDIDYMID
26	2.24	0.048	0.95	3.80	1.622	1.069
27	2.07	0.063	0.94	3.67	1.578	1.059
28	1.69	0.053	0.62	3.18	1.021	0.777
29	2.44	0.047	0.85	3.48	1.643	1.049
30	2.30	0.045	0.99	3.47	2.150	1.077

ORGAN/BODY WEIGHT RATIOS (%)
AFTER 4 WEEKS
MALES

Group 1 (0 mg/kg)

Animal	BODY W. (GRAM)	BRAIN (%)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
1	345.7	0.56	0.003	0.35	0.006	2.85	0.133
2	306.9	0.59	0.004	0.42	0.005	2.95	0.135
3	311.3	0.60	0.003	0.42	0.006	2.89	0.148
4	340.5	0.54	0.004	0.34	0.006	2.96	0.145
5	357.5	0.51	0.003	0.37	0.005	2.89	0.125

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	PROST/SEMI (%)	EPIDIDYMID (%)
1	0.63	0.016	0.24	1.15	0.463	0.334
2	0.64	0.018	0.23	1.18	0.612	0.343
3	0.60	0.014	0.31	1.19	0.693	0.365
4	0.61	0.017	0.24	1.01	0.528	0.325
5	0.57	0.018	0.28	0.92	0.609	0.312

Group 2 (5 mg/kg)

Animal	BODY W. (GRAM)	BRAIN (%)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
11	350.3	0.51	0.003	0.38	0.004	3.07	0.108
12	334.9	0.57	0.004	0.35	0.004	2.85	0.133
13	346.2	0.55	0.004	0.36	0.006	2.99	0.120
14	391.0	0.48	0.003	0.37	0.006	3.16	0.135
15	357.5	0.53	0.003	0.35	0.004	3.20	0.148

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	PROST/SEMI (%)	EPIDIDYMID (%)
11	0.62	0.016	0.24	1.12	0.424	0.303
12	0.61	0.015	0.22	1.11	0.452	0.330
13	0.60	0.014	0.20	1.03	0.594	0.293
14	0.58	0.014	0.26	0.94	0.431	0.264
15	0.59	0.013	0.28	0.96	0.460	0.285

ORGAN/BODY WEIGHT RATIOS (%)
AFTER 4 WEEKS
MALES

Group 3 (25 mg/kg)

Animal	BODY W. (GRAM)	BRAIN (%)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
16	346.7	0.52	0.003	0.36	0.008	3.18	0.150
17	351.1	0.49	0.004	0.32	0.005	3.13	0.143
18	332.4	0.57	0.003	0.35	0.005	3.24	0.122
19	351.3	0.52	0.003	0.36	0.004	3.33	0.116
20	333.1	0.53	0.003	0.35	0.004	3.35	0.136

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	PROST/SEMI (%)	EPIDIDYMID (%)
16	0.60	0.014	0.24	0.99	0.501	0.299
17	0.58	0.015	0.23	1.07	0.516	0.320
18	0.62	0.017	0.25	1.06	0.616	0.326
19	0.64	0.015	0.26	1.14	0.516	0.332
20	0.57	0.016	0.23	1.03	0.589	0.324

Group 4 (250 mg/kg)

Animal	BODY W. (GRAM)	BRAIN (%)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
21	300.2	0.58	0.004	0.35	0.005	4.65	0.117
22	330.9	0.55	0.003	0.35	0.005	4.65	0.120
23	345.4	0.53	0.004	0.34	0.004	3.92	0.116
24	345.7	0.53	0.003	0.36	0.004	4.39	0.165
25	386.9	0.51	0.003	0.37	0.005	4.43	0.133

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	PROST/SEMI (%)	EPIDIDYMID (%)
21	0.67	0.018	0.33	1.26	0.485	0.359
22	0.70	0.015	0.32	1.10	0.428	0.311
23	0.61	0.015	0.27	1.19	0.651	0.335
24	0.59	0.014	0.28	0.97	0.511	0.286
25	0.60	0.012	0.31	0.98	0.388	0.253

ORGAN/BODY WEIGHT RATIOS (%)
AFTER 4 WEEKS
MALES

Group 5 (1000 mg/kg)

Animal	BODY W. (GRAM)	BRAIN (%)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
26	306.8	0.59	0.003	0.36	0.006	4.93	0.104
27	307.1	0.58	0.003	0.35	0.006	5.56	0.116
28	228.5	0.75	0.004	0.42	0.006	5.23	0.083
29	290.9	0.62	0.003	0.37	0.006	5.02	0.145
30	323.3	0.55	0.003	0.36	0.007	5.14	0.129

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	PROST/SEMI (%)	EPIDIDYMID (%)
26	0.73	0.016	0.31	1.24	0.529	0.348
27	0.67	0.021	0.31	1.20	0.514	0.345
28	0.74	0.023	0.27	1.39	0.447	0.340
29	0.84	0.016	0.29	1.20	0.565	0.361
30	0.71	0.014	0.31	1.07	0.665	0.333

ORGAN/BRAIN WEIGHT RATIOS (%)
AFTER 4 WEEKS
MALES

Group 1 (0 mg/kg)

Animal	BRAIN (GRAM)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
1	1.95	0.615	62.56	1.128	505.64	23.590
2	1.81	0.608	71.82	0.773	500.55	22.928
3	1.86	0.538	70.43	0.968	483.33	24.839
4	1.83	0.656	63.93	1.148	551.37	27.049
5	1.81	0.608	72.93	0.939	570.72	24.751

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	PROST/SEMI (%)	EPIDIDYMID (%)
1	111.28	2.821	42.56	203.08	82.051	59.231
2	107.73	2.983	38.67	200.55	103.757	58.122
3	100.54	2.419	52.15	198.39	116.022	61.022
4	113.11	3.224	45.36	188.52	98.251	60.546
5	111.60	3.536	54.70	181.77	120.276	61.713

Group 2 (5 mg/kg)

Animal	BRAIN (GRAM)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
11	1.80	0.611	73.33	0.833	598.33	21.000
12	1.92	0.677	60.42	0.729	496.35	23.125
13	1.89	0.688	66.67	1.058	548.15	22.011
14	1.89	0.582	76.72	1.323	654.50	27.831
15	1.89	0.582	66.14	0.794	604.76	28.042

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	PROST/SEMI (%)	EPIDIDYMID (%)
11	121.11	3.111	46.67	217.78	82.500	59.056
12	106.25	2.656	39.06	193.23	78.906	57.604
13	108.99	2.593	37.04	187.83	108.836	53.651
14	120.63	2.910	53.44	194.71	89.259	54.656
15	111.11	2.540	52.38	182.01	87.090	53.862

ORGAN/BRAIN WEIGHT RATIOS (%)
AFTER 4 WEEKS
MALES

Group 3 (25 mg/kg)

Animal	BRAIN (GRAM)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
16	1.81	0.608	69.06	1.547	609.39	28.785
17	1.72	0.756	65.70	0.988	638.95	29.186
18	1.91	0.471	60.21	0.942	563.35	21.204
19	1.83	0.601	68.31	0.710	639.89	22.350
20	1.76	0.625	67.05	0.739	634.09	25.682

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	PROST/SEMI (%)	EPIDIDYMID (%)
16	114.36	2.762	45.86	188.95	95.967	57.182
17	118.02	3.081	45.93	219.19	105.291	65.291
18	107.33	2.880	43.98	184.82	107.277	56.806
19	123.50	2.787	50.82	219.67	99.071	63.770
20	108.52	3.011	44.32	195.45	111.477	61.307

Group 4 (250 mg/kg)

Animal	BRAIN (GRAM)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
21	1.74	0.747	60.92	0.862	802.30	20.230
22	1.83	0.492	62.84	0.929	840.98	21.694
23	1.82	0.714	63.74	0.769	744.51	22.088
24	1.82	0.549	68.13	0.769	834.07	31.374
25	1.97	0.660	72.59	0.964	870.56	26.193

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	PROST/SEMI (%)	EPIDIDYMID (%)
21	114.94	3.103	57.47	216.67	83.736	62.011
22	126.23	2.678	57.92	198.91	77.432	56.175
23	116.48	2.802	50.55	225.82	123.571	63.626
24	111.54	2.582	53.30	183.52	97.143	54.341
25	118.78	2.386	60.41	192.89	76.193	49.645

ORGAN/BRAIN WEIGHT RATIOS (%)
AFTER 4 WEEKS
MALES

Group 5 (1000 mg/kg)

Animal	BRAIN (GRAM)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
26	1.81	0.497	60.22	0.939	835.36	17.680
27	1.79	0.503	59.22	0.950	954.75	19.832
28	1.71	0.468	55.56	0.760	699.42	11.111
29	1.80	0.556	59.44	0.944	810.56	23.500
30	1.79	0.503	64.25	1.229	929.05	23.296

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	PROST/SEMI (%)	EPIDIDYMID (%)
26	123.76	2.652	52.49	209.94	89.613	59.061
27	115.64	3.520	52.51	205.03	88.156	59.162
28	98.83	3.099	36.26	185.96	59.708	45.439
29	135.56	2.611	47.22	193.33	91.278	58.278
30	128.49	2.514	55.31	193.85	120.112	60.168

ORGAN WEIGHTS (GRAM)
AFTER 4 WEEKS
FEMALES

Group 1 (0 mg/kg)

Animal	BODY W.	BRAIN	PITUITARY	HEART	THYROIDS	LIVER	THYMUS
36	237.7	1.73	0.013	0.92	0.016	7.02	0.330
37	258.2	1.76	0.012	1.00	0.023	8.56	0.500
38	284.1	1.80	0.016	1.08	0.019	10.27	0.413
39	240.8	1.78	0.012	0.93	0.022	8.16	0.343
40	234.5	1.76	0.013	0.90	0.016	8.41	0.417

Animal	KIDNEYS	ADRENALS	SPLEEN	OVARIES	UTERUS
36	1.41	0.062	0.80	0.075	0.73
37	1.44	0.066	0.83	0.098	0.55
38	1.55	0.067	0.90	0.098	0.86
39	1.43	0.057	0.71	0.079	0.64
40	1.46	0.064	0.70	0.092	0.49

Group 2 (5 mg/kg)

Animal	BODY W.	BRAIN	PITUITARY	HEART	THYROIDS	LIVER	THYMUS
46	250.1	1.73	0.014	0.92	0.023	8.10	0.457
47	223.4	1.73	0.014	0.98	0.023	7.51	0.289
48	238.0	1.74	0.014	0.89	0.020	8.44	0.450
49	233.4	1.71	0.012	0.89	0.015	8.03	0.399
50	222.3	1.69	0.012	0.81	0.018	7.32	0.390

Animal	KIDNEYS	ADRENALS	SPLEEN	OVARIES	UTERUS
46	1.59	0.063	0.73	0.110	0.72
47	1.53	0.066	0.65	0.093	0.85
48	1.50	0.061	0.79	0.092	0.79
49	1.32	0.069	0.73	0.083	0.59
50	1.40	0.058	0.67	0.058	0.80

ORGAN WEIGHTS (GRAM)
AFTER 4 WEEKS
FEMALES

Group 3 (25 mg/kg)

Animal	BODY W.	BRAIN	PITUITARY	HEART	THYROIDS	LIVER	THYMUS
51	230.5	1.80	0.012	0.92	0.017	7.70	0.325
52	252.4	1.76	0.011	1.01	0.012	8.63	0.275
53	237.2	1.77	0.014	0.96	0.019	7.58	0.376
54	210.8	1.72	0.013	0.81	0.019	6.60	0.328
55	235.0	1.71	0.011	0.95	0.020	8.43	0.370

Animal	KIDNEYS	ADRENALS	SPLEEN	OVARIES	UTERUS
51	1.38	0.070	0.72	0.109	0.77
52	1.55	0.072	0.70	0.104	0.57
53	1.63	0.063	0.62	0.087	1.69
54	1.25	0.058	0.70	0.083	0.68
55	1.46	0.064	0.71	0.093	0.70

Group 4 (250 mg/kg)

Animal	BODY W.	BRAIN	PITUITARY	HEART	THYROIDS	LIVER	THYMUS
56	256.5	1.74	0.009	0.94	0.019	9.76	0.360
57	233.8	1.73	0.011	0.87	0.015	9.35	0.297
58	238.0	1.67	0.013	0.93	0.020	8.70	0.451
59	220.6	1.67	0.012	0.91	0.012	8.48	0.351
60	242.4	1.70	0.011	0.96	0.014	8.70	0.293

Animal	KIDNEYS	ADRENALS	SPLEEN	OVARIES	UTERUS
56	1.45	0.069	0.79	0.098	0.62
57	1.34	0.061	0.75	0.088	0.72
58	1.45	0.056	0.75	0.101	0.63
59	1.35	0.062	0.70	0.089	1.13
60	1.40	0.073	0.70	0.098	0.61

ORGAN WEIGHTS (GRAM)
AFTER 4 WEEKS
FEMALES

Group 5 (1000 mg/kg)

Animal	BODY W.	BRAIN	PITUITARY	HEART	THYROIDS	LIVER	THYMUS
61	236.4	1.74	0.013	0.89	0.017	11.10	0.365
62	256.8	1.70	0.012	0.96	0.014	13.59	0.219
63	240.4	1.64	0.012	0.94	0.020	12.34	0.319
64	223.2	1.71	0.011	0.85	0.015	10.51	0.288
65	234.0	1.65	0.010	0.84	0.013	10.71	0.340

Animal	KIDNEYS	ADRENALS	SPLEEN	OVARIES	UTERUS
61	1.46	0.062	0.67	0.080	0.52
62	1.47	0.065	0.80	0.123	0.88
63	1.52	0.067	0.89	0.082	0.69
64	1.49	0.064	0.79	0.085	0.51
65	1.32	0.059	0.65	0.066	0.57

ORGAN/BODY WEIGHT RATIOS (%)
AFTER 4 WEEKS
FEMALES

Group 1 (0 mg/kg)

Animal	BODY W. (GRAM)	BRAIN (%)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
36	237.7	0.73	0.005	0.39	0.007	2.95	0.139
37	258.2	0.68	0.005	0.39	0.009	3.32	0.194
38	284.1	0.63	0.006	0.38	0.007	3.61	0.145
39	240.8	0.74	0.005	0.39	0.009	3.39	0.142
40	234.5	0.75	0.006	0.38	0.007	3.59	0.178

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	OVARIES (%)	UTERUS (%)
36	0.59	0.026	0.34	0.032	0.31
37	0.56	0.026	0.32	0.038	0.21
38	0.55	0.024	0.32	0.034	0.30
39	0.59	0.024	0.29	0.033	0.27
40	0.62	0.027	0.30	0.039	0.21

Group 2 (5 mg/kg)

Animal	BODY W. (GRAM)	BRAIN (%)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
46	250.1	0.69	0.006	0.37	0.009	3.24	0.183
47	223.4	0.77	0.006	0.44	0.010	3.36	0.129
48	238.0	0.73	0.006	0.37	0.008	3.55	0.189
49	233.4	0.73	0.005	0.38	0.006	3.44	0.171
50	222.3	0.76	0.005	0.36	0.008	3.29	0.175

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	OVARIES (%)	UTERUS (%)
46	0.64	0.025	0.29	0.044	0.29
47	0.68	0.030	0.29	0.042	0.38
48	0.63	0.026	0.33	0.039	0.33
49	0.57	0.030	0.31	0.036	0.25
50	0.63	0.026	0.30	0.026	0.36

ORGAN/BODY WEIGHT RATIOS (%)
AFTER 4 WEEKS
FEMALES

Group 3 (25 mg/kg)

Animal	BODY W. (GRAM)	BRAIN (%)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
51	230.5	0.78	0.005	0.40	0.007	3.34	0.141
52	252.4	0.70	0.004	0.40	0.005	3.42	0.109
53	237.2	0.75	0.006	0.40	0.008	3.20	0.159
54	210.8	0.82	0.006	0.38	0.009	3.13	0.156
55	235.0	0.73	0.005	0.40	0.009	3.59	0.157

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	OVARIES (%)	UTERUS (%)
51	0.60	0.030	0.31	0.047	0.33
52	0.61	0.029	0.28	0.041	0.23
53	0.69	0.027	0.26	0.037	0.71
54	0.59	0.028	0.33	0.039	0.32
55	0.62	0.027	0.30	0.040	0.30

Group 4 (250 mg/kg)

Animal	BODY W. (GRAM)	BRAIN (%)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
56	256.5	0.68	0.004	0.37	0.007	3.81	0.140
57	233.8	0.74	0.005	0.37	0.006	4.00	0.127
58	238.0	0.70	0.005	0.39	0.008	3.66	0.189
59	220.6	0.76	0.005	0.41	0.005	3.84	0.159
60	242.4	0.70	0.005	0.40	0.006	3.59	0.121

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	OVARIES (%)	UTERUS (%)
56	0.57	0.027	0.31	0.038	0.24
57	0.57	0.026	0.32	0.038	0.31
58	0.61	0.024	0.32	0.042	0.26
59	0.61	0.028	0.32	0.040	0.51
60	0.58	0.030	0.29	0.040	0.25

ORGAN/BODY WEIGHT RATIOS (%)
AFTER 4 WEEKS
FEMALES

Group 5 (1000 mg/kg)

Animal	BODY W. (GRAM)	BRAIN (%)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
61	236.4	0.74	0.005	0.38	0.007	4.70	0.154
62	256.8	0.66	0.005	0.37	0.005	5.29	0.085
63	240.4	0.68	0.005	0.39	0.008	5.13	0.133
64	223.2	0.77	0.005	0.38	0.007	4.71	0.129
65	234.0	0.71	0.004	0.36	0.006	4.58	0.145

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	OVARIES (%)	UTERUS (%)
61	0.62	0.026	0.28	0.034	0.22
62	0.57	0.025	0.31	0.048	0.34
63	0.63	0.028	0.37	0.034	0.29
64	0.67	0.029	0.35	0.038	0.23
65	0.56	0.025	0.28	0.028	0.24

ORGAN/BRAIN WEIGHT RATIOS (%)
AFTER 4 WEEKS
FEMALES

Group 1 (0 mg/kg)

Animal	BRAIN (GRAM)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
36	1.73	0.751	53.18	0.925	405.78	19.075
37	1.76	0.682	56.82	1.307	486.36	28.409
38	1.80	0.889	60.00	1.056	570.56	22.944
39	1.78	0.674	52.25	1.236	458.43	19.270
40	1.76	0.739	51.14	0.909	477.84	23.693

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	OVARIES (%)	UTERUS (%)
36	81.50	3.584	46.24	4.335	42.20
37	81.82	3.750	47.16	5.568	31.25
38	86.11	3.722	50.00	5.444	47.78
39	80.34	3.202	39.89	4.438	35.96
40	82.95	3.636	39.77	5.227	27.84

Group 2 (5 mg/kg)

Animal	BRAIN (GRAM)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
46	1.73	0.809	53.18	1.329	468.21	26.416
47	1.73	0.809	56.65	1.329	434.10	16.705
48	1.74	0.805	51.15	1.149	485.06	25.862
49	1.71	0.702	52.05	0.877	469.59	23.333
50	1.69	0.710	47.93	1.065	433.14	23.077

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	OVARIES (%)	UTERUS (%)
46	91.91	3.642	42.20	6.358	41.62
47	88.44	3.815	37.57	5.376	49.13
48	86.21	3.506	45.40	5.287	45.40
49	77.19	4.035	42.69	4.854	34.50
50	82.84	3.432	39.64	3.432	47.34

ORGAN/BRAIN WEIGHT RATIOS (%)
AFTER 4 WEEKS
FEMALES

Group 3 (25 mg/kg)

Animal	BRAIN (GRAM)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
51	1.80	0.667	51.11	0.944	427.78	18.056
52	1.76	0.625	57.39	0.682	490.34	15.625
53	1.77	0.791	54.24	1.073	428.25	21.243
54	1.72	0.756	47.09	1.105	383.72	19.070
55	1.71	0.643	55.56	1.170	492.98	21.637

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	OVARIES (%)	UTERUS (%)
51	76.67	3.889	40.00	6.056	42.78
52	88.07	4.091	39.77	5.909	32.39
53	92.09	3.559	35.03	4.915	95.48
54	72.67	3.372	40.70	4.826	39.53
55	85.38	3.743	41.52	5.439	40.94

Group 4 (250 mg/kg)

Animal	BRAIN (GRAM)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
56	1.74	0.517	54.02	1.092	560.92	20.690
57	1.73	0.636	50.29	0.867	540.46	17.168
58	1.67	0.778	55.69	1.198	520.96	27.006
59	1.67	0.719	54.49	0.719	507.78	21.018
60	1.70	0.647	56.47	0.824	511.76	17.235

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	OVARIES (%)	UTERUS (%)
56	83.33	3.966	45.40	5.632	35.63
57	77.46	3.526	43.35	5.087	41.62
58	86.83	3.353	44.91	6.048	37.72
59	80.84	3.713	41.92	5.329	67.66
60	82.35	4.294	41.18	5.765	35.88

ORGAN/BRAIN WEIGHT RATIOS (%)
AFTER 4 WEEKS
FEMALES

Group 5 (1000 mg/kg)

Animal	BRAIN (GRAM)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
61	1.74	0.747	51.15	0.977	637.93	20.977
62	1.70	0.706	56.47	0.824	799.41	12.882
63	1.64	0.732	57.32	1.220	752.44	19.451
64	1.71	0.643	49.71	0.877	614.62	16.842
65	1.65	0.606	50.91	0.788	649.09	20.606

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	OVARIES (%)	UTERUS (%)
61	83.91	3.563	38.51	4.598	29.89
62	86.47	3.824	47.06	7.235	51.76
63	92.68	4.085	54.27	5.000	42.07
64	87.13	3.743	46.20	4.971	29.82
65	80.00	3.576	39.39	4.000	34.55

ORGAN WEIGHTS (GRAM)
AFTER 6 WEEKS
MALES

Group 1 (0 mg/kg)

Animal	BODY W.	BRAIN	PITUITARY	HEART	THYROIDS	LIVER	THYMUS
6	374.9	1.93	0.011	1.20	0.017	11.02	0.414
7	385.9	1.86	0.012	1.21	0.021	11.72	0.444
8	346.6	1.92	0.011	1.14	0.012	10.09	0.327
9	383.4	1.85	0.011	1.41	0.019	11.13	0.459
10	370.1	1.88	0.010	1.24	0.016	11.09	0.380

Animal	KIDNEYS	ADRENALS	SPLEEN	TESTES	PROST/SEMI	EPIDIDYMID
6	2.15	0.054	0.91	3.54	2.408	1.160
7	2.30	0.051	1.11	3.44	2.230	1.126
8	2.05	0.050	0.74	3.99	2.401	1.208
9	2.46	0.056	0.90	3.80	2.281	1.231
10	2.17	0.048	0.83	3.50	2.211	1.103

Group 5 (1000 mg/kg)

Animal	BODY W.	BRAIN	PITUITARY	HEART	THYROIDS	LIVER	THYMUS
31	355.7	1.85	0.012	1.22	0.020	12.99	0.313
32	349.3	1.76	0.012	1.15	0.013	12.52	0.391
33	305.9	1.80	0.010	1.10	0.017	11.29	0.387
34	311.3	1.78	0.010	1.06	0.015	12.05	0.357
35	327.1	1.77	0.012	0.98	0.030	11.02	0.377

Animal	KIDNEYS	ADRENALS	SPLEEN	TESTES	PROST/SEMI	EPIDIDYMID
31	2.21	0.045	1.01	3.89	2.232	1.049
32	2.06	0.055	0.92	3.83	1.926	1.182
33	1.97	0.047	0.70	3.73	2.039	0.987
34	1.92	0.046	0.82	3.83	1.902	1.091
35	2.05	0.053	0.77	3.62	1.745	1.047

ORGAN/BODY WEIGHT RATIOS (%)
AFTER 6 WEEKS
MALES

Group 1 (0 mg/kg)

Animal	BODY W. (GRAM)	BRAIN (%)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
6	374.9	0.51	0.003	0.32	0.005	2.94	0.110
7	385.9	0.48	0.003	0.31	0.005	3.04	0.115
8	346.6	0.55	0.003	0.33	0.003	2.91	0.094
9	383.4	0.48	0.003	0.37	0.005	2.90	0.120
10	370.1	0.51	0.003	0.34	0.004	3.00	0.103

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	PROST/SEMI (%)	EPIDIDYMID (%)
6	0.57	0.014	0.24	0.94	0.642	0.309
7	0.60	0.013	0.29	0.89	0.578	0.292
8	0.59	0.014	0.21	1.15	0.693	0.349
9	0.64	0.015	0.23	0.99	0.595	0.321
10	0.59	0.013	0.22	0.95	0.597	0.298

Group 5 (1000 mg/kg)

Animal	BODY W. (GRAM)	BRAIN (%)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
31	355.7	0.52	0.003	0.34	0.006	3.65	0.088
32	349.3	0.50	0.003	0.33	0.004	3.58	0.112
33	305.9	0.59	0.003	0.36	0.006	3.69	0.127
34	311.3	0.57	0.003	0.34	0.005	3.87	0.115
35	327.1	0.54	0.004	0.30	0.009	3.37	0.115

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	PROST/SEMI (%)	EPIDIDYMID (%)
31	0.62	0.013	0.28	1.09	0.627	0.295
32	0.59	0.016	0.26	1.10	0.551	0.338
33	0.64	0.015	0.23	1.22	0.667	0.323
34	0.62	0.015	0.26	1.23	0.611	0.350
35	0.63	0.016	0.24	1.11	0.533	0.320

ORGAN/BRAIN WEIGHT RATIOS (%)
AFTER 6 WEEKS
MALES

Group 1 (0 mg/kg)

Animal	BRAIN (GRAM)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
6	1.93	0.570	62.18	0.881	570.98	21.451
7	1.86	0.645	65.05	1.129	630.11	23.871
8	1.92	0.573	59.38	0.625	525.52	17.031
9	1.85	0.595	76.22	1.027	601.62	24.811
10	1.88	0.532	65.96	0.851	589.89	20.213

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	PROST/SEMI (%)	EPIDIDYMID (%)
6	111.40	2.798	47.15	183.42	124.767	60.104
7	123.66	2.742	59.68	184.95	119.892	60.538
8	106.77	2.604	38.54	207.81	125.052	62.917
9	132.97	3.027	48.65	205.41	123.297	66.541
10	115.43	2.553	44.15	186.17	117.606	58.670

Group 5 (1000 mg/kg)

Animal	BRAIN (GRAM)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
31	1.85	0.649	65.95	1.081	702.16	16.919
32	1.76	0.682	65.34	0.739	711.36	22.216
33	1.80	0.556	61.11	0.944	627.22	21.500
34	1.78	0.562	59.55	0.843	676.97	20.056
35	1.77	0.678	55.37	1.695	622.60	21.299

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	PROST/SEMI (%)	EPIDIDYMID (%)
31	119.46	2.432	54.59	210.27	120.649	56.703
32	117.05	3.125	52.27	217.61	109.432	67.159
33	109.44	2.611	38.89	207.22	113.278	54.833
34	107.87	2.584	46.07	215.17	106.854	61.292
35	115.82	2.994	43.50	204.52	98.588	59.153

ORGAN WEIGHTS (GRAM)
AFTER 6 WEEKS
FEMALES

Group 1 (0 mg/kg)

Animal	BODY W.	BRAIN	PITUITARY	HEART	THYROIDS	LIVER	THYMUS
41	236.6	1.72	0.014	0.90	0.020	7.26	0.295
42	230.7	1.75	0.012	0.76	0.020	6.86	0.396
43	254.0	1.68	0.013	0.83	0.020	8.18	0.280
44	240.9	1.84	0.013	0.81	0.015	6.68	0.291
45	268.3	1.80	0.013	1.02	0.017	8.17	0.417

Animal	KIDNEYS	ADRENALS	SPLEEN	OVARIES	UTERUS
41	1.47	0.061	0.65	0.916	0.12
42	1.35	0.058	0.69	0.081	0.93
43	1.65	0.071	0.57	0.109	0.95
44	1.40	0.061	0.72	0.098	0.67
45	1.63	0.062	0.72	0.104	0.61

Group 5 (1000 mg/kg)

Animal	BODY W.	BRAIN	PITUITARY	HEART	THYROIDS	LIVER	THYMUS
66	243.5	1.73	0.012	1.10	0.014	7.79	0.299
67	230.8	1.79	0.014	0.81	0.015	7.90	0.263
68	212.5	1.73	0.012	0.86	0.013	7.21	0.342
69	246.8	1.80	0.010	0.85	0.022	8.09	0.380
70	236.0	1.83	0.013	0.90	0.012	8.40	0.311

Animal	KIDNEYS	ADRENALS	SPLEEN	OVARIES	UTERUS
66	1.45	0.065	0.61	0.101	0.58
67	1.60	0.071	0.59	0.124	0.64
68	1.29	0.050	0.59	0.102	0.57
69	1.59	0.058	0.74	0.130	0.77
70	1.47	0.060	0.69	0.141	0.85

ORGAN/BODY WEIGHT RATIOS (%)
AFTER 6 WEEKS
FEMALES

Group 1 (0 mg/kg)

Animal	BODY W. (GRAM)	BRAIN (%)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
41	236.6	0.73	0.006	0.38	0.008	3.07	0.125
42	230.7	0.76	0.005	0.33	0.009	2.97	0.172
43	254.0	0.66	0.005	0.33	0.008	3.22	0.110
44	240.9	0.76	0.005	0.34	0.006	2.77	0.121
45	268.3	0.67	0.005	0.38	0.006	3.05	0.155

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	OVARIES (%)	UTERUS (%)
41	0.62	0.026	0.27	0.387	0.05
42	0.59	0.025	0.30	0.035	0.40
43	0.65	0.028	0.22	0.043	0.37
44	0.58	0.025	0.30	0.041	0.28
45	0.61	0.023	0.27	0.039	0.23

Group 5 (1000 mg/kg)

Animal	BODY W. (GRAM)	BRAIN (%)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
66	243.5	0.71	0.005	0.45	0.006	3.20	0.123
67	230.8	0.78	0.006	0.35	0.006	3.42	0.114
68	212.5	0.81	0.006	0.40	0.006	3.39	0.161
69	246.8	0.73	0.004	0.34	0.009	3.28	0.154
70	236.0	0.78	0.006	0.38	0.005	3.56	0.132

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	OVARIES (%)	UTERUS (%)
66	0.60	0.027	0.25	0.041	0.24
67	0.69	0.031	0.26	0.054	0.28
68	0.61	0.024	0.28	0.048	0.27
69	0.64	0.024	0.30	0.053	0.31
70	0.62	0.025	0.29	0.060	0.36

ORGAN/BRAIN WEIGHT RATIOS (%)
AFTER 6 WEEKS
FEMALES

Group 1 (0 mg/kg)

Animal	BRAIN (GRAM)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
41	1.72	0.814	52.33	1.163	422.09	17.151
42	1.75	0.686	43.43	1.143	392.00	22.629
43	1.68	0.774	49.40	1.190	486.90	16.667
44	1.84	0.707	44.02	0.815	363.04	15.815
45	1.80	0.722	56.67	0.944	453.89	23.167

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	OVARIES (%)	UTERUS (%)
41	85.47	3.547	37.79	53.256	6.98
42	77.14	3.314	39.43	4.629	53.14
43	98.21	4.226	33.93	6.488	56.55
44	76.09	3.315	39.13	5.326	36.41
45	90.56	3.444	40.00	5.778	33.89

Group 5 (1000 mg/kg)

Animal	BRAIN (GRAM)	PITUITARY (%)	HEART (%)	THYROIDS (%)	LIVER (%)	THYMUS (%)
66	1.73	0.694	63.58	0.809	450.29	17.283
67	1.79	0.782	45.25	0.838	441.34	14.693
68	1.73	0.694	49.71	0.751	416.76	19.769
69	1.80	0.556	47.22	1.222	449.44	21.111
70	1.83	0.710	49.18	0.656	459.02	16.995

Animal	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	OVARIES (%)	UTERUS (%)
66	83.82	3.757	35.26	5.838	33.53
67	89.39	3.966	32.96	6.927	35.75
68	74.57	2.890	34.10	5.896	32.95
69	88.33	3.222	41.11	7.222	42.78
70	80.33	3.279	37.70	7.705	46.45

MACROSCOPICAL FINDINGS
AFTER 4 WEEKS
ALL NECROPSIES

Animals without necropsy

Animals not recorded

Animals not completed

Animals with not translated finding

Not Reported

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

MACROSCOPICAL FINDINGS
AFTER 4 WEEKS
ALL NECROPSIES
MALES

Group 1 (0 mg/kg)

Animal 1 PLANNED NECROPSY , 20-JAN-2010

THYMUS DISCOLORATION, REDDISH.

Animal 2 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 3 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 4 PLANNED NECROPSY , 20-JAN-2010

STOMACH MUCOSA, FUNDUS: FOCUS/FOCI, D=2 MM, DARK RED.

Animal 5 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

MACROSCOPICAL FINDINGS
AFTER 4 WEEKS
ALL NECROPSIES
MALES

Group 2 (5 mg/kg)

Animal 11 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 12 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 13 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 14 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 15 PLANNED NECROPSY , 20-JAN-2010

KIDNEYS RIGHT SIDE: PELVIC DILATION.

MACROSCOPICAL FINDINGS
AFTER 4 WEEKS
ALL NECROPSIES
MALES

Group 3 (25 mg/kg)

Animal 16 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 17 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 18 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 19 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 20 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

MACROSCOPICAL FINDINGS
AFTER 4 WEEKS
ALL NECROPSIES
MALES

Group 4 (250 mg/kg)

Animal 21 PLANNED NECROPSY , 20-JAN-2010

LIVER	DISCOLORATION, BLACK BROWN. ENLARGED.
THYMUS	FOCUS/FOCI, ISOLATED, D=2 MM, DARK RED.

Animal 22 PLANNED NECROPSY , 20-JAN-2010

LIVER	DISCOLORATION, BLACK BROWN. ENLARGED.

Animal 23 PLANNED NECROPSY , 20-JAN-2010

LIVER	ENLARGED. DISCOLORATION, DARK BROWN.
BODY CAVITIES	EPIDIDYMAL ADIPOSE TISSUE, LEFT SIDE: NODULE(S), D=10 MM, DARK RED.

Animal 24 PLANNED NECROPSY , 20-JAN-2010

LIVER	DISCOLORATION, BLACK BROWN. ENLARGED.

Animal 25 PLANNED NECROPSY , 20-JAN-2010

LIVER	ENLARGED. DISCOLORATION, BLACK BROWN.

MACROSCOPICAL FINDINGS
AFTER 4 WEEKS
ALL NECROPSIES
MALES

Group 5 (1000 mg/kg)

Animal 26 PLANNED NECROPSY , 20-JAN-2010

LIVER	ENLARGED.
	DISCOLORATION, BLACK BROWN.
THYMUS	FOCUS/FOCI, ISOLATED, D=2 MM, REDDISH.

Animal 27 PLANNED NECROPSY , 20-JAN-2010

LIVER	ENLARGED.
	DISCOLORATION, BLACK BROWN.

Animal 28 PLANNED NECROPSY , 20-JAN-2010

LIVER	DISCOLORATION, BLACK BROWN.

Animal 29 PLANNED NECROPSY , 20-JAN-2010

LIVER	DISCOLORATION, BLACK BROWN.
	ENLARGED.

Animal 30 PLANNED NECROPSY , 20-JAN-2010

LIVER	ENLARGED.
	DISCOLORATION, BLACK BROWN.

MACROSCOPICAL FINDINGS
AFTER 4 WEEKS
ALL NECROPSIES
FEMALES

Group 1 (0 mg/kg)

Animal 36 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 37 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 38 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 39 PLANNED NECROPSY , 20-JAN-2010

THYMUS FOCUS/FOCI, SEVERAL, D=2 MM, DARK RED.

Animal 40 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

MACROSCOPICAL FINDINGS
AFTER 4 WEEKS
ALL NECROPSIES
FEMALES

Group 2 (5 mg/kg)

Animal 46 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 47 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 48 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 49 PLANNED NECROPSY , 20-JAN-2010

THYMUS FOCUS/FOCI, SEVERAL, D=2 MM, DARK RED.

Animal 50 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

MACROSCOPICAL FINDINGS
AFTER 4 WEEKS
ALL NECROPSIES
FEMALES

Group 3 (25 mg/kg)

Animal 51 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 52 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 53 PLANNED NECROPSY , 20-JAN-2010

UTERUS BOTH HORNS: DILATION, D=7 MM.

Animal 54 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 55 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

MACROSCOPICAL FINDINGS
AFTER 4 WEEKS
ALL NECROPSIES
FEMALES

Group 4 (250 mg/kg)

Animal 56 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 57 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 58 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 59 PLANNED NECROPSY , 20-JAN-2010

UTERUS BOTH HORNS: DILATION, D=6 MM.

Animal 60 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

MACROSCOPICAL FINDINGS
AFTER 4 WEEKS
ALL NECROPSIES
FEMALES

Group 5 (1000 mg/kg)

Animal 61 PLANNED NECROPSY , 20-JAN-2010

LIVER DISCOLORATION, DARK BROWN.

Animal 62 PLANNED NECROPSY , 20-JAN-2010

LIVER ENLARGED.

Animal 63 PLANNED NECROPSY , 20-JAN-2010

LIVER DISCOLORATION, BLACK BROWN.
ENLARGED.

Animal 64 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

Animal 65 PLANNED NECROPSY , 20-JAN-2010

NO FINDINGS NOTED

MACROSCOPICAL FINDINGS
AFTER 6 WEEKS
ALL NECROPSIES

Animals without necropsy

Animals not recorded

Animals not completed

Animals with not translated finding

Not Reported

Animal 100	Male	Group 10	Reserve Removed
Animal 101	Female	Group 10	Reserve Removed

MACROSCOPICAL FINDINGS
AFTER 6 WEEKS
ALL NECROPSIES
MALES

Group 1 (0 mg/kg)

Animal 6 PLANNED NECROPSY , 03-FEB-2010

NO FINDINGS NOTED

Animal 7 PLANNED NECROPSY , 03-FEB-2010

NO FINDINGS NOTED

Animal 8 PLANNED NECROPSY , 03-FEB-2010

NO FINDINGS NOTED

Animal 9 PLANNED NECROPSY , 03-FEB-2010

NO FINDINGS NOTED

Animal 10 PLANNED NECROPSY , 03-FEB-2010

NO FINDINGS NOTED

MACROSCOPICAL FINDINGS
AFTER 6 WEEKS
ALL NECROPSIES
MALES

Group 5 (1000 mg/kg)

Animal 31 PLANNED NECROPSY , 03-FEB-2010

LIVER	DISCOLORATION, BLACK BROWN.
LYMPH NODES	PORTALES: ENLARGED, D=6 MM.
	PORTALES: DISCOLORATION, DARK RED.

Animal 32 PLANNED NECROPSY , 03-FEB-2010

LIVER	DISCOLORATION, BLACK BROWN.

Animal 33 PLANNED NECROPSY , 03-FEB-2010

LIVER	DISCOLORATION, BLACK BROWN.

Animal 34 PLANNED NECROPSY , 03-FEB-2010

LIVER	DISCOLORATION, BLACK BROWN.

Animal 35 PLANNED NECROPSY , 03-FEB-2010

LIVER	DISCOLORATION, BLACK BROWN.

MACROSCOPICAL FINDINGS
AFTER 6 WEEKS
ALL NECROPSIES
FEMALES

Group 1 (0 mg/kg)

Animal 41 PLANNED NECROPSY , 03-FEB-2010

NO FINDINGS NOTED

Animal 42 PLANNED NECROPSY , 03-FEB-2010

NO FINDINGS NOTED

Animal 43 PLANNED NECROPSY , 03-FEB-2010

NO FINDINGS NOTED

Animal 44 PLANNED NECROPSY , 03-FEB-2010

NO FINDINGS NOTED

Animal 45 PLANNED NECROPSY , 03-FEB-2010

NO FINDINGS NOTED

MACROSCOPICAL FINDINGS
AFTER 6 WEEKS
ALL NECROPSIES
FEMALES

Group 5 (1000 mg/kg)

Animal 66 PLANNED NECROPSY , 03-FEB-2010

NO FINDINGS NOTED

Animal 67 PLANNED NECROPSY , 03-FEB-2010

NO FINDINGS NOTED

Animal 68 PLANNED NECROPSY , 03-FEB-2010

NO FINDINGS NOTED

Animal 69 PLANNED NECROPSY , 03-FEB-2010

NO FINDINGS NOTED

Animal 70 PLANNED NECROPSY , 03-FEB-2010

NO FINDINGS NOTED

APPENDIX I - CHEMICAL ANALYSIS OF FEED

LUFA-ITL GmbH

AGROLAB Laborgruppe
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LUFA - ITL Dr.-Hell-Str. 6, 24107 Kiel

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RINAUSTRASSE
4303 KAISERAUGST / SCHWEIZ
SCHWEIZ

Date 02.09.2009
Customer no. 1209835
Page 1 of 2

TEST REPORT

Order no. 633558

Sample No.	**808512**
Order No.	**GLP Schadstoffuntersuchung**
Sample Arrival	**19.08.2009**
Sample code	**TEKLAD GLOBAL REDENT 2014 PELL. 10 MM ECKIG Alleinfuttermittel für Mäuse und Ratten Rezeptur 3253 - GLP-Batch 58/09 Fabr.-Code: 0908014 (pelletiert) - Hergestellt: 17.08.09 - MHD: 17.02.10**
Sample packing	**2 x plastic bag**

	Unit	Result	limits acc. GV-SOLAS A-08-2001	Substance	Method
Trace-Elements/Heavy-Metals					
Copper	mg/kg	10,7		OM	VDLUFA VII 2.2.2.6
Selenium	mg/kg	0,22		OM	VDLUFA VII 2.2.2.5; ICPMS
Cadmium	mg/kg	0,07	0,4	OM	VDLUFA VII 2.2.2.5; ICPMS
Lead	mg/kg	0,21	1,5	OM	VDLUFA VII 2.2.2.5; ICPMS
Mercury	mg/kg	<0,02	0,1	OM	§64 LFGB L00.00-19
Arsenic	mg/kg	0,32	1	OM	VDLUFA VII 2.2.2.5; ICPMS
Mycotoxins					
Aflatoxine B1	µg/kg	<1,00	10	OM	HPLC-VDLUFA Bd. III, 16.1.4
Aflatoxine B2	µg/kg	<1,00	5	OM	HPLC-VDLUFA Bd. III 16.1.4
Aflatoxine G1	µg/kg	<1,00	5	OM	HPLC-VDLUFA Bd. III, 16.1.4
Aflatoxine G2	µg/kg	<1,00	5	OM	HPLC-VDLUFA Bd. III, 16.1.4
Sum Aflatoxines	µg/kg	n.d.		OM	calculated
PCB					
PCB 28	mg/kg	<0,0020		OM	acc. to §64 LFGB L00.00-34
PCB 52	mg/kg	<0,0020		OM	acc. to §64 LFGB L00.00-34
PCB 101	mg/kg	<0,0020		OM	acc. to §64 LFGB L00.00-34
PCB 118	mg/kg	<0,0020		OM	acc. to §64 LFGB L00.00-34
PCB 138	mg/kg	<0,0020		OM	acc. to §64 LFGB L00.00-34
PCB 153	mg/kg	<0,0020		OM	acc. to §64 LFGB L00.00-34
PCB 180	mg/kg	<0,0020		OM	acc. to §64 LFGB L00.00-34
sum PCB	mg/kg	n.d.	0,05	OM	calculated
Organochlorous-Pesticides GC-Multiresiduesanalysis					
Dieldrin	mg/kg	<0,005		OM	acc. to §64 LFGB L00.00-34
HCH-gamma (Lindan)	mg/kg	<0,005	0,1	OM	acc. to §64 LFGB L00.00-34
Heptachlor	mg/kg	<0,00500		OM	acc. to §64 LFGB L00.00-34
Heptachlorepoxide-cis	mg/kg	<0,00500		OM	acc. to §64 LFGB L00.00-34
Heptachlorepoxide-trans	mg/kg	<0,00500		OM	acc. to §64 LFGB L00.00-34
o,p-DDD	mg/kg	<0,00500		OM	acc. to §64 LFGB L00.00-34

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Date 02.09.2009
Customer no. 1209835
Page 2 of 2

Order no. 633558 Sample No. 808512

	Unit	Result	limits acc. GV-SOLAS A-06-2001	Substance	Method	
o,p-DDE	mg/kg	<0,00500		OM	acc. to §64 LFGB L00.00-34	
o,p-DDT	mg/kg	<0,005		OM	acc. to §64 LFGB L00.00-34	
p,p-DDD	mg/kg	<0,00500		OM	acc. to §64 LFGB L00.00-34	
p,p-DDE	mg/kg	<0,010		OM	acc. to §64 LFGB L00.00-34	
p,p-DDT	mg/kg	<0,00500		OM	acc. to §64 LFGB L00.00-34	
Sum DDTs	mg/kg	n.d.	0,05	OM	calculated	
Sum Heptachlor	mg/kg	n.d.	0,01	OM	calculated	
Organo-Phosphorous Pesticides GC-Multiresidueanalysis						
Malathion	mg/kg	<0,010	1	OM	acc. to §64 LFGB L00.00-34	
nitrosamines						
N-Nitrosodibutylamin	µg/kg	<5,00		OM	GC-Inhousemethod	
N-Nitrosodiethylamin	µg/kg	<5,00	10	OM	GC-Inhousemethod	
N-Nitrosodiisopropylamin	µg/kg	<5,00		OM	GC-Inhousemethod	
N-Nitrosodimethylamin	µg/kg	<5,00	10	OM	GC-Inhousemethod	
N-Nitrosodipropylamin	µg/kg	<5,00		OM	GC-Inhousemethod	
N-Nitrosomethylethylamin	µg/kg	<5,00		OM	GC-Inhousemethod	
N-Nitrosomorpholin	µg/kg	<5,00		OM	GC-Inhousemethod	
N-Nitrosopiperidin	µg/kg	<5,00		OM	GC-Inhousemethod	
N-Nitrosopyrrolidin	µg/kg	<5,00		OM	GC-Inhousemethod	
Sum Nitrosamines	µg/kg	n.d.		OM	calculated	
Estrogenes						
dienestrol	µg/kg	<10,0		OM	no object	v)
diethyl stilbestrol	µg/kg	<1,00		OM	no object	v)
hexestrol	µg/kg	<2,00		OM	no object	v)
Sum Estrogenes	µg/kg	n.d.		OM	calculated	v)

Explanation: "<", n.d.: not detected, below limit of detection.
The actual limit of detection can be different to the standard value for a particular analysis due to matrix effects or insufficient sample volume.
Remark: OM=original matter, DM=dry matter
v) Remitted to an accredited labpratory

LUFA - ITL Dr. E. Hanßen, Tel. 0431/1228-130
feeding stuffs

External laboratory

TIERGESUNDHEITSDIENST, SENATOR-GERAUER STR 23, 85586 POING
Parameter
Sum Estrogenes

Zentrale Analytik - Organische Henkel KGaA, Henkelstrasse 67 ¿ Gebäude Z43, 40589 Düsseldorf
Parameter
Sum Nitrosamines

The analytical results are valid for the delivered sample material only. The testing period is the time between the receipt of the sample and the reporting date. Validation of results is not possible for samples of unknown origin.

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SCHWEIZ

Date 09.12.2009
Customer no. 1209835
Page 1 of 3

TEST REPORT

Order no. 665888

Sample No.	**53076**
Order No.	**GLP Schadstoffuntersuchung**
Sample Arrival	**30.11.2009**
Sample code	**TEKLAD GLOBAL RODENT 2914 C - Pel. 10 mm eckig** **Alleinfuttermittel für Mäuse und Ratten** **Rezeptur 3255 - GLP-Batch 82/09** **Fabr.-Code: 0911023 - Hergestellt: 26.11.09 - MHD: 26.08.10**
Sample packing	**plastic bag**

	Unit	Result	limits acc. GV-SOLAS A-08-2001		Substance	Method
Trace-Elements/Heavy-Metals						
Copper	mg/kg	**12,2**			OM	VDLUFA VII 2.2.2 6
Selenium	mg/kg	**<0,10**			OM	VDLUFA VII 2.2.2 5, ICPMS
Cadmium	mg/kg	**0,07**	0,4		OM	VDLUFA VII 2.2.2 5, ICPMS
Lead	mg/kg	**<0,10**	1,5		OM	VDLUFA VII 2.2.2 5; ICPMS
Mercury	mg/kg	**<0,02**	0,1		OM	§64 LFGB L00 00-19
Arsenic	mg/kg	**<0,10**	1		OM	VDLUFA VII 2.2.2 5, ICPMS
Mycotoxins						
Aflatoxine B1	µg/kg	**<1,00**	10		OM	HPLC-VDLUFA Bd III, 16.1.4
Aflatoxine B2	µg/kg	**<1,00**	5		OM	HPLC-VDLUFA Bd III, 16.1.4
Aflatoxine G1	µg/kg	**<1,00**	5		OM	HPLC-VDLUFA Bd III, 16.1.4
Aflatoxine G2	µg/kg	**<1,00**	5		OM	HPLC-VDLUFA Bd III, 16.1.4
Sum Aflatoxines	µg/kg	**n.d.**			OM	calculated
PCB						
PCB 28	mg/kg	**<0,0020**			OM	acc. to §64 LFGB L00.00-34
PCB 52	mg/kg	**<0,0020**			OM	acc. to §64 LFGB L00.00-34
PCB 101	mg/kg	**<0,0020**			OM	acc. to §64 LFGB L00.00-34
PCB 118	mg/kg	**<0,0020**			OM	acc. to §64 LFGB L00.00-34
PCB 138	mg/kg	**<0,0020**			OM	acc. to §64 LFGB L00.00-34
PCB 153	mg/kg	**<0,0020**			OM	acc. to §64 LFGB L00.00-34
PCB 180	mg/kg	**<0,0020**			OM	acc. to §64 LFGB L00.00-34
sum PCB	mg/kg	**n.d.**	0,05		OM	calculated
Organochlorous-Pesticides GC-Multiresidueanalysis						
Dieldrin	mg/kg	**<0,002**			OM	acc. to §64 LFGB L00.00-34
HCH-gamma (Lindan)	mg/kg	**<0,002**	0,1		OM	acc. to §64 LFGB L00.00-34
Heptachlor	mg/kg	**<0,00200**			OM	acc. to §64 LFGB L00.00-34
Heptachlorepoxide-cis	mg/kg	**<0,00200**			OM	acc. to §64 LFGB L00.00-34
Heptachlorepoxide-trans	mg/kg	**<0,00200**			OM	acc. to §64 LFGB L00.00-34
o,p-DDD	mg/kg	**<0,00200**			OM	acc. to §64 LFGB L00.00-34

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Date 09.12.2009
Customer no. 1209835
Page 2 of 3

Order no. 665888 Sample No. 53076

	Unit	Result	limits acc GV-SOLAS A-08-2001		Substance	Method
o,p-DDE	mg/kg	**<0,00200**			OM	acc. to §64 LFGB L00.00-34
o,p-DDT	mg/kg	**<0,002**			OM	acc. to §64 LFGB L00.00-34
p,p-DDD	mg/kg	**<0,00200**			OM	acc. to §64 LFGB L00.00-34
p,p-DDE	mg/kg	**<0,00200**			OM	acc. to §64 LFGB L00.00-34
p,p-DDT	mg/kg	**<0,00200**			OM	acc. to §64 LFGB L00.00-34
Sum DDTs	mg/kg	**n.d.**	0,05		OM	calculated
Sum Heptachlor	mg/kg	**n.d.**	0,01		OM	calculated
Organo-Phosphorous Pesticides GC-Multiresidueanalysis						
Malathion	mg/kg	**<0,010**	1		OM	acc. to §64 LFGB L00.00-34
nitrosamines						
N-Nitrosodibutylamin	µg/kg	**<5,00**			OM	GC-Inhousemethod
N-Nitrosodiethylamin	µg/kg	**<5,00**	10		OM	GC-Inhousemethod
N-Nitrosodiisopropylamin	µg/kg	**<5,00**			OM	GC-Inhousemethod
N-Nitrosodimethylamin	µg/kg	**<5,00**	10		OM	GC-Inhousemethod
N-Nitrosodipropylamin	µg/kg	**<5,00**			OM	GC-Inhousemethod
N-Nitrosomethylethylamin	µg/kg	**<5,00**			OM	GC-Inhousemethod
N-Nitrosomorpholin	µg/kg	**<5,00**			OM	GC-Inhousemethod
N-Nitrosopiperidin	µg/kg	**<5,00**			OM	GC-Inhousemethod
N-Nitrosopyrrolidin	µg/kg	**<5,00**			OM	GC-Inhousemethod
Sum Nitrosamines	µg/kg	**n.d.**			OM	calculated
Estrogenes						
dienestrol	µg/kg	**<10,0**			OM	no object v)
diethyl stilbestrol	µg/kg	**<1,00**			OM	no object v)
hexestrol	µg/kg	**<2,00**			OM	no object v)
Sum Estrogenes	µg/kg	**n.d.**			OM	calculated v)

Explanation "<", n.d not detected, below limit of detection
The actual limit of detection can be different to the standard value for a particular analysis due to matrix effects or insufficient sample volume.
Remark. OM=original matter, DM=dry matter
v) Remitted to an accredited laboratory

LUFA - ITL Dr. Wehage, Tel. 0431/1228-220

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PROVIMI KLIBA AG

External laboratory

TIERGESUNDHEITSDIENST, SENATOR-GERAUER STR 23, 85586 POING
Parameter
Sum Estrogenes
Zentrale Analytik - Organische Henkel KGaA, Henkelstrasse 67 ¿ Gebäude Z43, 40589 Düsseldorf
Parameter
Sum Nitrosamines

LUFA-ITL GmbH

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Date	09.12.2009
Customer no.	1209835
Page 3 of 3	

Order no. 665888 Sample No. 53076

The analytical results are valid for the delivered sample material only The testing period is the time between the receipt of the sample and the reporting date Validation of results is not possible for samples of unknown origin

APPENDIX II - DRINKING WATER ANALYSIS

harlan™

BACTERIOLOGICAL ASSAY OF DRINKING WATER, ITINGEN

Official Laboratory	Liestal, July 28, 2009
Basel-Landschaft	Ref.no. 200076925
Sampling point:	59.99.N Net water Harlan Ltd., Itingen, Room No. 10
Sampled on:	July 13, 2009
Sample:	H_2O, Harlan Laboratories Ltd.
Time of sampling	07.30
Water temperature (°C)	---

BACTERIOLOGICAL TEST:

Aerobic mesophilic bacteria / ml	0
E.coli / 100 ml	0
Enterococci / 100 ml	0
Clostridium perfringens	0

ASSESSMENT:

At the time of sampling, the tested bacteriological parameters met the requirements for drinking water according to "Artikel 3 der Verordnung über Trink-, Quell-, und Mineralwasser (SR 817.022.102)

Official Laboratory
The Official Chemist

(signed Dr. P. Wenk)

KANTONALES LABORATORIUM BASEL-LANDSCHAFT

harlan™

CHEMICAL WATER ANALYSIS, ITINGEN

Official Laboratory Basel-Landschaft	Liestal, July 28, 2009 Ref. no. 200076926
Sampling point:	59.99.N, Net water Halan Ltd., Itingen, Room no. 10
Sampled on:	July 13, 2009
Time of sampling	07.25
Water temperature (°C)	---

CHEMICAL TEST:

Appearance			clear, colourless
Odor			not remarkable
Taste			not remarkable
UV-absorption at 254 nm/100 cm			1.19
pH value			7.25
Oxygen demand	($KMnO_4$ cons.)	mg/l	2.2
Turbidity	FNU		0.02
Chloride	Cl^-	mg/l	24.0
Nitrate	NO_3^-	mg/l	17.0
Sulphate	SO_4^{--}	mg/l	115.0
Nitrite	NO_2^-	mg/l	<0.005
Total hardness		fr.H°	39.8
Alkaline hardness		fr.H°	27.1
Non carbonate hardness		fr.H°	12.7
Calcium	Ca^{++}	mg/l	139.0
Magnesium	Mg^{++}	mg/l	12.2

ASSESSMENT:

At the time of sampling, the tested chemical parameters met the requirements for drinking water according to "Artikel 3 der Verordnung über Trink-, Quell-, und Mineralwasser (SR 817.022.102)

Official Laboratory
The Official Chemist

(signed Dr. P. Wen

KANTONALES LABORATORIUM BASEL-LANDSCHAFT

harlan™

CONTAMINANT ASSAY OF DRINKING WATER, ITINGEN

Harlan Laboratories Study.: C58021

Date of Sampling: July 13, 2009

Sample: H_2O, Harlan Laboratories Ltd., Itingen, Room No. 10

PARAMETER	ASSAY LEVEL µg/l	LIMIT * µg/l
Lindane	< 0.05	0.1
Heptachlor	< 0.05	0.1
Malathion	< 0.05	0.1
DDT, total	< 0.05	0.1
Dieldrin	< 0.05	0.1
Cadmium	< 0.5	5
Arsenic	< 3	50
Lead	< 3	50
Mercury	< 1	1
Selenium	< 3	10
Copper	< 4	1500
PCBs (28, 52, 101, 138, 153, 180)	< 0.05	0.1
Nitrosamines, total (DMN, DEN, NPIP, NMORPH)	< 0.05	----

< 0.05 = less than 0.05 microgram per liter

* Schweizer Lebensmittelbuch

Issued by for Dr. D. Flade

September 08, 2009

APPENDIX III - CERTIFICATE OF ANALYSIS

235709 Octamethyltrisiloxane 98%

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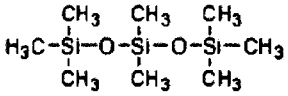
Image



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- Organometallic Reagents > Organosilicon > Siloxanes

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- 235709 (Aldrich)

235709 Octamethyltrisiloxane

Aldrich 98%

Price and Availability

Product Number	Your Price CHF	Available to Ship	Quantity	Actions
235709-5ML	43.10	12.06.2009	details ..	
235709-100ML	178.50	12.06.2009	details ..	
235709-500ML	643.00	Date not Available	details ..	

CAS Number:	107-51-7
Linear Formula:	$[(CH_3)_3SiO]_2Si(CH_3)_2$
Molecular Weight:	236.53
Beilstein Registry Number:	1753063
EC Number:	203-497-4
MDL number:	MFCD00008264
PubChem Substance ID:	24853996

Specifications Related Products References Reviews

Description

Packaging 5, 100, 500 mL in glass btl

Properties

vapor density	>1 (vs air)
assay	98%
refractive index	n20/D 1.384(lit.)
bp	153 °C(lit.)
mp	-82 °C(lit.)
density	0.82 g/mL at 25 °C(lit.)

Safety

Risk Statements	10
Safety Statements	23-24/25
RIDADR	UN 1993 3/PG 3
WGK Germany	3
Flash Point(F)	84 °F
Flash Point(C)	29 °C

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Certificate Of Analysis

Certificate of Analysis

SIGMA-ALDRICH

Product Name	Octamethyltrisiloxane, 98%
Product Number	235709
Product Brand	ALDRICH
CAS Number	107-51-7
Molecular Formula	$[(CH_3)_3SiO]_2Si(CH_3)_2$
Molecular Weight	236.53

TEST	SPECIFICATION	LOT 14110CD RESULTS
APPEARANCE	COLORLESS LIQUID	COLORLESS LIQUID
INFRARED SPECTRUM	CONFORMS TO STRUCTURE.	CONFORMS TO STRUCTURE.
GAS LIQUID CHROMATOGRAPHY	97.5% (MINIMUM)	99.9%
QUALITY CONTROL ACCEPTANCE DATE		MARCH 2005

Barbara Rajzer, Supervisor
Quality Control
Milwaukee, Wisconsin USA

Specification Sheet

SIGMA-ALDRICH

Product Name	Octamethyltrisiloxane, 98%
Product Number	235709
Product Brand	ALDRICH
CAS Number	107-51-7
Molecular Weight	236.53

TEST	**SPECIFICATION**
Appearance (Color)	Colorless
Appearance (Form)	Liquid
Infrared spectrum	Conforms to Structure
Purity (GC)	≥97.5 %

APPENDIX IV - FORMULATION ANALYSIS

Determination of Content, Homogeneity and Stability of OCTAMETHYLTRISILOXANE (L3) in Application Formulations

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1.2 Study Samples and Storage 2
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1 MATERIALS AND METHODS

1.1 Analytical Standard

The test item as described in the main report was used as analytical standard.

1.2 Study Samples and Storage

Representative samples were dispatched to the analytical laboratories internally (under ambient conditions) and stored at room temperature until analysis.

1.3 Reagents and Materials

Acetone: Baker no. 9254

1.4 Analytical Procedure

1.4.1 Preparation of Standard Solutions

Stock solutions of Octamethyltrisiloxane (L3) in acetone were prepared for external standard calibration. For example, 25.35 mg of Octamethyltrisiloxane (L3) was exactly weighed into a 50 mL volumetric flask and approximately 40 mL of acetone was added. Then, the mixture was sonicated for 5 minutes and the flask was brought to volume with acetone to yield a solution with a concentration of 507.0 µg/mL. Aliquots of this stock standard solution were used to prepare five working standard solutions in acetone with a concentration range of 10.14 to 101.4 µg/mL. Ten standard solutions derived from two stock standard solutions were used for calibration.

1.4.2 Analysis of Samples

The samples received were dissolved in acetone by sonication for 5 minutes and then diluted to volume with acetone. Where necessary, sample solutions were further diluted with acetone into the calibration range.

1.4.3 Gas Chromatographic Conditions

GC:	AGILENT 6850
Column:	DB 5, 30 m x 0.25 mm, 1.0 µm
Carrier Gas:	Helium, 1.0 mL/min, constant flow

Injection:	1 µL, split		
Detector:	FID		
Temperatures:	Injector:		250 °C
	Detector:		280 °C
	Oven:		40 °C for 3 min
		at	20 °C/min to 250 °C
			250 °C for 0 min

1.4.4 Evaluation of Results

Injected samples were quantified by comparing peak areas of Octamethyltrisiloxane (L3) with reference to the calibration curve. The latter was obtained by correlation of the peak areas of the working standards with their corresponding concentrations (µg/mL), using the linear regression model following equation 1:

$$y = a + b \cdot x \qquad (1)$$

where

y	=	Response of Octamethyltrisiloxane (L3)
a	=	Intercept derived from linear regression of calibration data
b	=	Slope derived from linear regression of calibration data
x	=	Actual concentration of Octamethyltrisiloxane (L3) in sample aliquot [µg/mL]

Sample aliquot concentrations were corrected for density of the application formulation and for dilution using equation 2:

$$c_{Actual} = \frac{x \cdot V \cdot D}{W \cdot 1000} \qquad (2)$$

where

c_{Actual}	=	Actual sample concentration [mg/mL]
x	=	Actual concentration of Octamethyltrisiloxane (L3) in sample aliquot according to equation 1 [µg/mL]
V	=	Dilution volume [mL]
D	=	Density of application formulation [0.92 g/mL; density of vehicle as provided by the supplier]
W	=	Sample weight [g]

The sample recovery was determined as follows:

$$R = \frac{c_{Actual}}{c_{Nominal}} \cdot 100 \qquad (3)$$

where

R	=	Sample recovery [%]
c_{Actual}	=	Actual sample concentration [mg/mL]
$c_{Nominal}$	=	Nominal sample concentration [mg/mL]

2 RESULTS AND CONCLUSION

The linearity of the analytical system used for sample analyses was demonstrated with a good relationship between peak areas measured and working standard concentrations. All calibration points used met the acceptance limit of ±20% variation from the calibration curve derived by linear regression analysis. The regression coefficients calculated were found to be better than 0.99. An example is presented in Figure 1.

The Octamethyltrisiloxane (L3) peak was assigned in sample chromatograms by comparison to that of working standards. In blank sample chromatograms no peak appeared at the retention time of Octamethyltrisiloxane (L3) and, therefore, it was confirmed that only corn oil was administered in the control part of the experiment. Examples of chromatograms are shown in Figure 2 and Figure 3.

The application formulations investigated during the study were found to comprise Octamethyltrisiloxane (L3) in the range of 80.2% to 106.9% and, thus, the required content limit of ±20% with reference to the nominal concentration was met. The homogeneous distribution of OCTAMETHYLTRISILOXANE (L3) in the preparations was approved because single results found did not deviate more than 14.5% (<15%) from the corresponding mean.

In addition, the test item was found to be stable in application formulations when kept 4 hours at room temperature due to recoveries which met the variation limit of 10% from the time-zero (homogeneity) mean.

In conclusion, the results indicate the accurate use of the test item Octamethyltrisiloxane (L3) and corn oil as vehicle during this study. Application formulations were found to be homogeneously prepared and sufficient formulation stability under storage conditions was approved. Detailed results are shown in Table 1.

Table 1 Detailed Results of Application Formulation Analysis
(Rounded results presented are based on calculations with exact data)

Dose Group	Sample taken from/ after	Date of Analysis	Nominal Concentration [mg/mL]	Actual Concentration [mg/mL]	Recovery	Mean Recovery	Maximum Variation from Mean
Date of Preparation: 23-Dec-2009							
1	vehicle	12-Jan-10	0.000	---	---	---	---
2	top	13-Jan-10	1.000	0.908	90.8% [1]	88.8%	2.3%
	middle	13-Jan-10	1.000	0.877	87.7% [1]		
	bottom	12-Jan-10	1.000	0.878	87.8%		
	4 hours/RT	12-Jan-10	1.000	0.856	85.6%	---	3.6%
3	top	12-Jan-10	5.000	4.545	90.9%	90.5%	---
	middle	12-Jan-10	5.000	4 509	90.2%		
	bottom	12-Jan-10	5.000	1 222	24.4% [2/3]		
	4 hours/RT	12-Jan-10	5.000	4.091	81.8%	---	9.6%
4	top	12-Jan-10	50.00	50.26	100.5%	100.1%	3.7%
	middle	12-Jan-10	50.00	51.65	103.3%		
	bottom	13-Jan-10	50.00	48 22	96.4% [1]		
	4 hours/RT	13-Jan-10	50.00	46 99	94.0% [1]	---	6.1%
5	top	12-Jan-10	200.0	171.2	85.6%	88.8%	8.2%
	middle	12-Jan-10	200.0	169.4	84.7%		
	bottom	13-Jan-10	200.0	192.0	96.0% [1]		
	4 hours/RT	13-Jan-10	200.0	189.5	94.8% [1]	---	6 8%
Date of Preparation: 06-Jan-2010							
1	vehicle	12-Jan-10	0.000	---	---	---	---
2	top	12-Jan-10	1.000	0.931	93.1%	89.3%	4.2%
	middle	12-Jan-10	1.000	0.882	88.2%		
	bottom	12-Jan-10	1.000	0.866	86.6%		
3	top	12-Jan-10	5 000	4.922	98.4%	91.4%	12.3%
	middle	12-Jan-10	5.000	4.782	95.6%		
	bottom	12-Jan-10	5.000	4.010	80.2%		
4	top	13-Jan-10	50.00	53.44	106.9% [1]	93.3%	14.5%
	middle	12-Jan-10	50.00	43.80	87.6%		
	bottom	12-Jan-10	50.00	42.78	85.6%		
5	top	13-Jan-10	200.0	198.0	99.0% [1]	97.3%	1.7%
	middle	13-Jan-10	200.0	191.6	95.8% [1]		
	bottom	13-Jan-10	200.0	194.6	97.3% [1]		

1 result of repeated analysis
2 result was regarded as an outlier and therefore not considered in the calculation of the mean
3 result was confirmed by re-analysis

Figure 1 Example of Calibration Curve

Date of analysis: 12-Jan-2010

Standard Concentration [µg/mL]	Peak Area [counts]	Variation of Peak Area
10.14	14.01	14.0%
25.35	33.97	1.2%
50.70	66.78	-4.0%
76.05	100.7	-4.5%
101.4	147.5	4.3%
11.27	14.93	8.6%
28.17	37.66	0.3%
56.34	74.49	-3.9%
84.51	119.0	1.5%
112.7	155.4	-1.1%

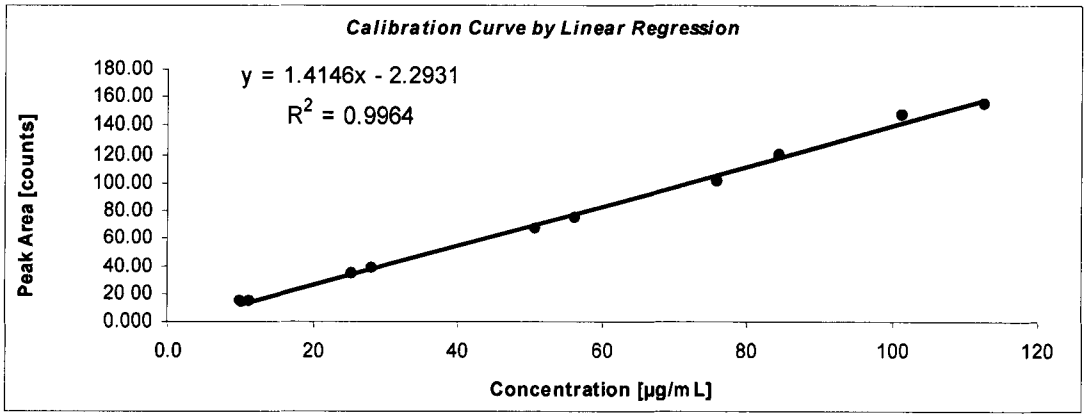
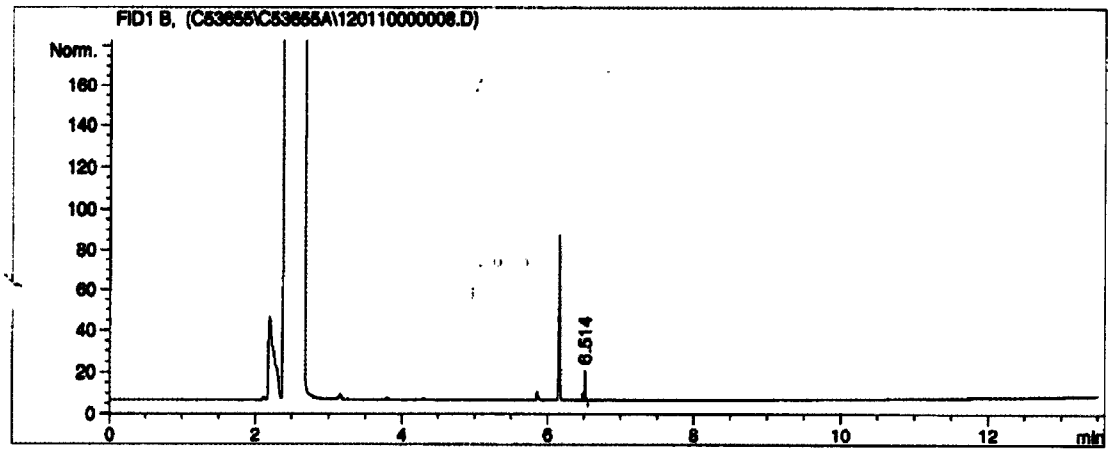


Figure 2 Typical GC-Chromatograms of Standard Solutions

(A) Standard solution: 10.14 µg/mL
(B) Standard solution: 101.4 µg/mL
Date of analysis: 12-Jan-2010

(A)



(B)

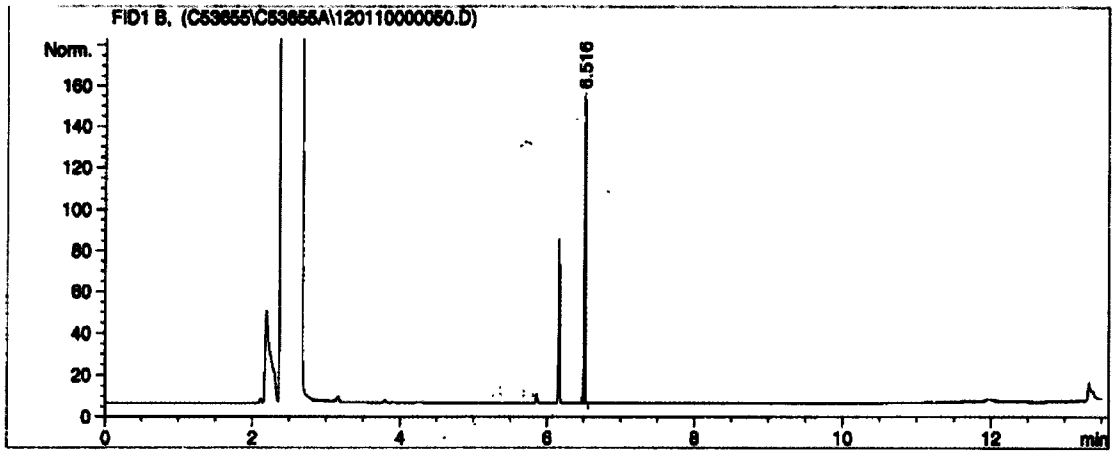
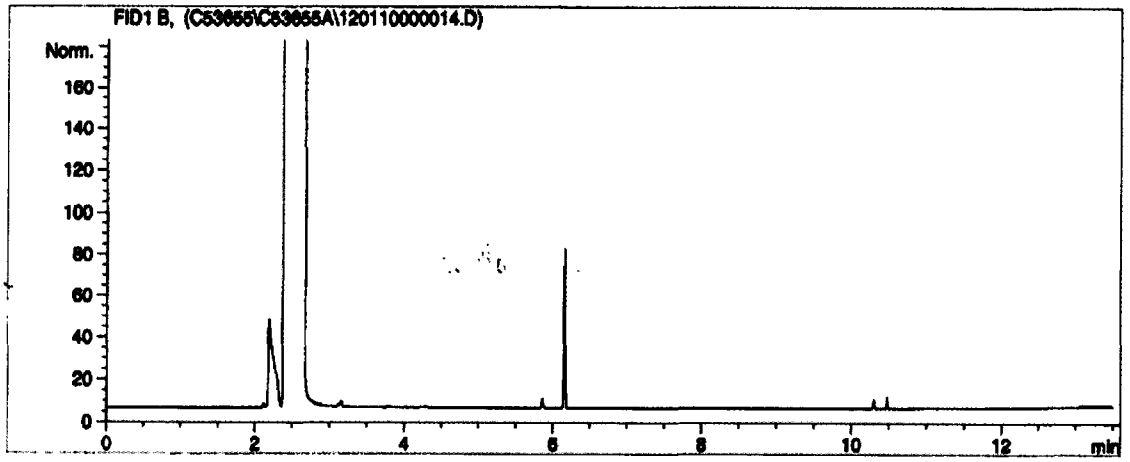


Figure 3 Typical GC-Chromatograms of Test Samples

(A) Dose group 1, control sample, 23x diluted
(B) Dose group 2 (top), nominal content: 1.000 mg/mL, 23x diluted
Date of analysis: 12-Jan-2010

(A)



(B)

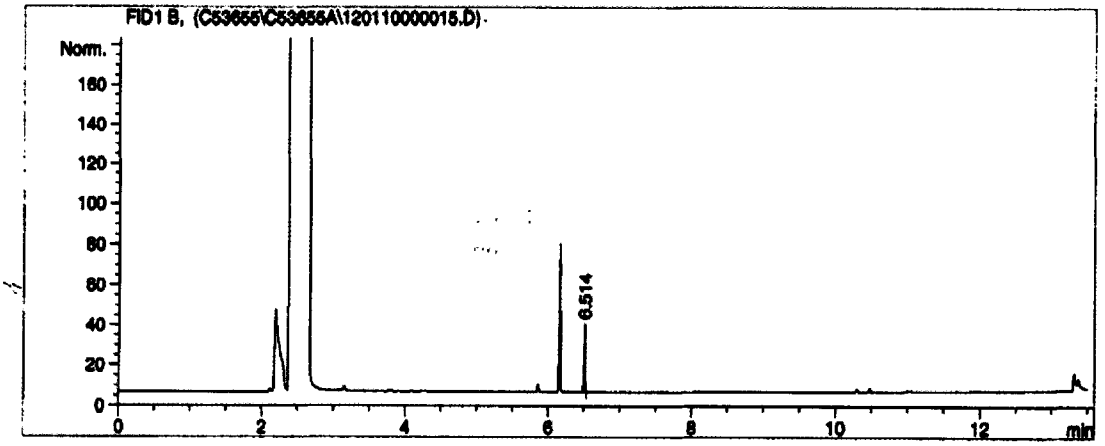
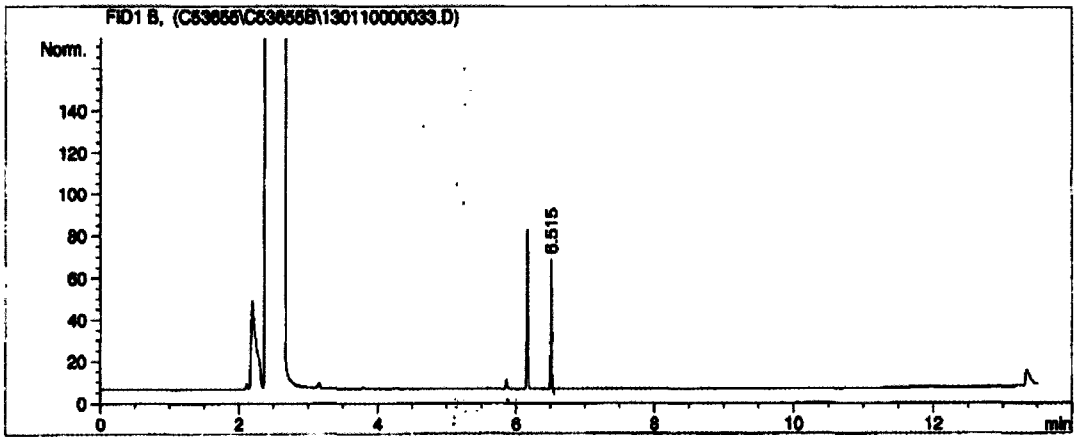


Figure 3 Cont'd

(C) Dose group 5 (top), nominal content: 200.0 mg/mL, 4550x diluted
Date of analysis: 13-Jan-2010

(C)



APPENDIX V - CLINICAL LABORATORY INVESTIGATIONS

CLINICAL LABORATORY INVESTIGATIONS

Blood and Urine Sampling:

After 4 Weeks:	20-Jan-2010 (satellite A and B)
After 6 Weeks (Recovery):	03-Feb-2010 (satellite B)

Blood samples were drawn from the retro-orbital plexus from all animals under light isoflurane anesthesia. The animals were fasted for approximately 18 hours before blood sampling but allowed access to water *ad libitum*. The samples were collected early in the working day to reduce biological variation caused by circadian rhythms. Urine samples were collected during fasting using metabolism cages.

In the summary and individual tables the names of some parameters have been abbreviated. Any abbreviation has been defined in this section. Clinical laboratory data are expressed, with a few exceptions, in general accordance with the International System of Units (SI).

Key to abbreviations of units:

L	liter	g	gram	m	milli (10^{-3})
mol	mole	G	giga (10^{9})	µ	micro (10^{-6})
sec	seconds	T	tera (10^{12})	f	femto (10^{-15})
U	Unit				

Hematology

The following anticoagulants were used during blood collection:

Complete Blood Cell Count:	Tri-potassium-EDTA
Methemoglobin:	Lithium heparin
Coagulation:	Sodium citrate, 3.2% (1 part anticoagulant to 9 parts blood)

Complete Blood Cell Count

Parameter	Abbreviation	Unit	Instrumentation
Erythrocyte count	RBC	T/L	Advia 120[1]
Hemoglobin	HB	mmol/L	Advia 120
Hematocrit	HCT	rel.1	Advia 120
Mean corpuscular volume	MCV	fL	Advia 120
Red cell volume distribution width	RDW	rel.1	Advia 120

[1] ADVIA 120 hematology system (Bayer)

Parameter	Abbreviation	Unit		Instrumentation
Mean corpuscular hemoglobin	MCH	fmol		Advia 120
Mean corpuscular hemoglobin concentration	MCHC	mmol/L		Advia 120
Hemoglobin concentration distribution width	HDW	mmol/L		Advia 120
		relative	absolute	
Reticulocyte count	RETI	rel.1	G/L	Advia 120
Reticulocyte maturity index (low, medium, high fluorescence)	L RETI M RETI H RETI	rel.1 rel.1 rel.1		Advia 120
Leukocyte count, total	WBC	G/L		Advia 120
Differential leukocyte count		relative	absolute	Advia 120
Neutrophils	NEUT	rel.1	G/L	Advia 120
Eosinophils	EOS	rel.1	G/L	Advia 120
Basophils	BASO	rel.1	G/L	Advia 120
Lymphocytes	LYMPH	rel.1	G/L	Advia 120
Monocytes	MONO	rel.1	G/L	Advia 120
Large unstained cells	LUC	rel.1	G/L	Advia 120
Platelet count	PLATELETS	G/L		Advia 120

Hemoglobin Derivatives

Parameter	Abbre-viation	Unit	Method	Instrumentation
Methemoglobin	MET-HB	rel. 1	Spectrometry, results given as ratio of total hemoglobin	OSM3[2]
Heinz bodies	HEINZ BOD	rel.1	Microscopic examination of New Methylene Blue stained films, results given as ratio of total RBC	Microscope

[2] Hemoximeter OSM3

Coagulation

Parameter	Abbre-viation	Unit	Method	Instrumentation
Prothrombin time (=Thromboplastin time)	PT	rel. 1	Clotting assay, thromboplastin from rabbit brain tissue, results as ratio of normal activity	STA[3]
Activated partial thromboplastin time	PTT	sec	Clotting assay, cephalin from rabbit cerebral tissue, silica surface activator	STA

[3] STA-compact analyzer (Roche Diagnostics)

Clinical Biochemistry

Lithium heparin was used as anticoagulant during blood collection.

Parameter	Abbre-viation	Unit	Method	Instrumentation
Glucose		mmol/L	Hexokinase/G6P-DH	Hitachi 917[4]
Urea		mmol/L	Urease/GLDH	Hitachi 917
Creatinine	CREAT	µmol/L	Enzymatic colorimetric test	Hitachi 917
Bilirubin, total	BILI-T	µmol/L	Reaction with 2,5-Dichloro-phenyl-diazonium salt	Hitachi 917
Bile acids	BILE AC	µmol/L	Colorimetric, enzymatic (3α-HSD, Diaphorase)	Hitachi 917
Cholesterol, total	CHOLEST	mmol/L	Enzymatic, CHOD/PAP	Hitachi 917
Triglycerides	TRIGLY	mmol/L	Glycerol-Kinase GPO/PAP method	Hitachi 917
Phospholipids	PHOS-LIP	mmol/L	Phospholipase-Cholinoxidase-Peroxidase-reaction	Hitachi 917
Aspartate aminotransferase EC 2.6.1.1[5]	ASAT	U/L 37 °C	MDH/NADH coupled reaction	Hitachi 917
Alanine aminotransferase EC 2.6.1.2	ALAT	U/L 37 °C	LDH/NADH coupled reaction	Hitachi 917
Lactate dehydrogenase EC 1.1.1.27	LDH	U/L 37 °C	NADH/LDH coupled reaction using pyruvate as substrate	Hitachi 917
Alkaline phosphatase EC 3.1.3.1	ALP	U/L 37 °C	p-Nitrophenyl-phosphate as substrate	Hitachi 917
Gamma-glutamyl transferase EC 2.3.2.2	GGT	U/L 37 °C	Substrate: L-gamma-glutamyl-3-carboxy-4-nitroanilide	Hitachi 917
Creatine kinase EC 2.7.3.2	CK	U/L 37 °C	HK/ATP and G6P-DH/NADPH coupled reaction method	Hitachi 917

[4] Hitachi 917 analyzer, Roche Diagnostics
[5] Identification of enzymes with EC-Number (Enzyme Commission) according to Enzyme Nomenclature, Recommendations (1972) of the IUPAC and IUB, Elsevier Scient. Publ. Comp., Amsterdam, 1973

Parameter	Abbre-viation	Unit	Method	Instrumentation
Sodium		mmol/L	Ion selective electrode	Hitachi 917
Potassium		mmol/L	Ion selective electrode	Hitachi 917
Chloride		mmol/L	Ion selective electrode	Hitachi 917
Calcium		mmol/L	o-Cresolphthalein complexone method	Hitachi 917
Phosphorus		mmol/L	Phosphomolybdate reaction	Hitachi 917
Protein, total	PROTEIN	g/L	Biuret reaction	Hitachi 917
Albumin		g/L	Bromocresol green method	Hitachi 917
Globulin		g/L	Calculated value (total protein minus albumin)	
Albumin / Globulin Ratio	A/G RATIO		Calculated value (albumin / globulin)	

Urinalysis

Physical Examination

Parameter	Abbreviation	Unit	Method / Instrumentation
Urine volume (18-hour)		mL	Volumetric[6]
Relative density (= Specific gravity)	REL DENS	rel.1	Refractometer[7]
Color			Visual inspection
Appearance			Visual inspection

The following urine components were investigated using a semi-automated test strip analyzer Miditron (Roche Diagnostics) applying reflectance spectroscopy. Results are given as discrete values representing a concentration range (semi-quantitative results).

Chemical Examination

Parameter	Abbreviation	Unit	Set Points	Instrumentation
pH-value	pH		5.0, 6.0, 6.5, 7.0, 8.0, 9.0	Miditron[8]
Nitrite		score	0 (negative), 1 (positive)	Miditron
Protein		g/L	0, 0.25, 0.75, 1.50, 5.00	Miditron
Glucose		mmol/L	0, 3, 6, 17, 56	Miditron
Ketones		mmol/L	0, 0.5, 1.5, 5.0, 15.0	Miditron
Urobilinogen	UROBILI	µmol/L	0, 17, 68, 135, 203	Miditron
Bilirubin		µmol /L	0, 17, 50, 100	Miditron
Erythrocytes	ERY	per µL	0, 10, 25, 50, 150, 250	Miditron
Leukocytes	LEU	per µL	0, 25, 100, 500	Miditron

6 Mettler balance
7 Clinical Refractometer SU-202, Kernco
8 Miditron semi-automated urine chemistry analyzer and reagent test strips, Roche Diagnostics

HISTORICAL DATA - HEMATOLOGY

STRAIN: RAT / SPRAGUE DAWLEY RAT,SPF QUALITY (MALES) AGE: FROM 8 TO 12 WEEKS
DATA COLLECTION PERIOD: 09-OCT-02 TO 01-JUN-07

PARAMETER	UNIT	N	MEAN	STAND.DEV	95% TOLERANCE LIMITS	
ERYTHROCYTES (RBC)	T/l	65	7.87	0.43	---	---
HEMOGLOBIN (HB)	mmol/l	65	9.5	0.4	---	---
HEMATOCRIT (HCT)	rel. 1	65	0.44	0.02	---	---
MEAN CORPUSCULAR VOLUME (MCV)	fl	65	56.6	3.3	---	---
RED CELL VOL. DISTR. WIDTH (RDW)	rel. 1	65	0.119	0.008	---	---
MEAN CORPUSCULAR HEMOGLOBIN (MCH)	fmol	65	1.21	0.05	---	---
MEAN CORPUSCULAR HEMOGLOBIN CONC.	mmol/l	65	21.39	0.84	---	---
HEMOGLOBIN CONC. DISTR. WIDTH	mmol/l	65	1.60	0.23	---	---
RETICULOCYTE COUNT.....						
RETICULOCYTE (REL)	rel. 1	65	0.032	0.009	---	---
RETICULOCYTE (ABS)	G/l	65	247	60	---	---
MATURITY INDEX (L-RETI)	rel. 1	65	0.485	0.101	---	---
MATURITY INDEX (M-RETI)	rel. 1	65	0.356	0.040	---	---
MATURITY INDEX (H-RETI)	rel. 1	65	0.159	0.104	---	---
LEUKOCYTES, TOTAL (WBC)	G/l	65	10.10	3.66	---	---
DIFF.WBC COUNT (REL).....						
NEUTROPHILS (NEUT)	rel. 1	11	0.189	0.078	---	---
EOSINOPHILS (EOS)	rel. 1	65	0.014	0.008	---	---
BASOPHILS (BASO)	rel. 1	65	0.003	0.002	---	---
LYMPHOCYTES (LYMPH)	rel. 1	65	0.782	0.070	---	---
MONOCYTES (MONO)	rel. 1	65	0.024	0.008	---	---
LARGE UNSTAINED CELLS (LUC)	rel. 1	65	0.009	0.003	---	---
DIFF.WBC COUNT (ABS).....						
NEUTROPHILS (NEUT)	G/l	11	2.72	1.52	---	---
EOSINOPHILS (EOS)	G/l	65	0.13	0.07	---	---
BASOPHILS (BASO)	G/l	65	0.03	0.03	---	---
LYMPHOCYTES (LYMPH)	G/l	65	7.96	3.08	---	---
MONOCYTES (MONO)	G/l	65	0.23	0.10	---	---
LARGE UNSTAINED CELLS (LUC)	G/l	65	0.09	0.05	---	---
THROMBOCYTES (PLATELETS)	G/l	65	1208	170	---	---
METHEMOGLOBIN (MET-HB)	rel. 1	10	0.008	0.003	---	---
COAGULATION.....						
PROTHROMBIN TIME (PT)	rel. 1	65	0.84	0.06	---	---
PARTIAL THROMBOPLASTIN TIME (PTT)	sec	65	18.2	2.2	---	---

HISTORICAL DATA - HEMATOLOGY

STRAIN: RAT / SPRAGUE DAWLEY RAT,SPF QUALITY (MALES) AGE: FROM 13 TO 18 WEEKS
DATA COLLECTION PERIOD: 09-OCT-02 TO 01-JUN-07

PARAMETER	UNIT	N	MEAN	STAND.DEV	95% TOLERANCE LIMITS	
ERYTHROCYTES (RBC)	T/l	50	8.59	0.44	---	---
HEMOGLOBIN (HB)	mmol/l	50	9.9	0.4	---	---
HEMATOCRIT (HCT)	rel. 1	50	0.45	0.02	---	---
MEAN CORPUSCULAR VOLUME (MCV)	fl	50	52.5	1.9	---	---
RED CELL VOL. DISTR. WIDTH (RDW)	rel. 1	50	0.132	0.009	---	---
MEAN CORPUSCULAR HEMOGLOBIN (MCH)	fmol	50	1.15	0.04	---	---
MEAN CORPUSCULAR HEMOGLOBIN CONC.	mmol/l	50	21.98	0.46	---	---
HEMOGLOBIN CONC. DISTR. WIDTH	mmol/l	50	1.86	0.14	---	---
RETICULOCYTE COUNT.....						
RETICULOCYTE (REL)	rel. 1	50	0.023	0.004	---	---
RETICULOCYTE (ABS)	G/l	50	197	30	---	---
MATURITY INDEX (L-RETI)	rel. 1	50	0.664	0.142	---	---
MATURITY INDEX (M-RETI)	rel. 1	50	0.272	0.076	---	---
MATURITY INDEX (H-RETI)	rel. 1	50	0.064	0.085	---	---
LEUKOCYTES, TOTAL (WBC)	G/l	50	10.07	2.83	---	---
DIFF.WBC COUNT (REL).....						
NEUTROPHILS (NEUT)	rel. 1	20	0.177	0.041	---	---
EOSINOPHILS (EOS)	rel. 1	50	0.014	0.005	---	---
BASOPHILS (BASO)	rel. 1	50	0.008	0.005	---	---
LYMPHOCYTES (LYMPH)	rel. 1	50	0.786	0.057	---	---
MONOCYTES (MONO)	rel. 1	50	0.023	0.008	---	---
LARGE UNSTAINED CELLS (LUC)	rel. 1	50	0.009	0.003	---	---
DIFF.WBC COUNT (ABS).....						
NEUTROPHILS (NEUT)	G/l	20	1.68	0.62	---	---
EOSINOPHILS (EOS)	G/l	50	0.13	0.05	---	---
BASOPHILS (BASO)	G/l	50	0.09	0.07	---	---
LYMPHOCYTES (LYMPH)	G/l	50	7.97	2.49	---	---
MONOCYTES (MONO)	G/l	50	0.22	0.08	---	---
LARGE UNSTAINED CELLS (LUC)	G/l	50	0.08	0.04	---	---
THROMBOCYTES (PLATELETS)	G/l	50	1055	147	---	---
COAGULATION.....						
PROTHROMBIN TIME (PT)	rel. 1	50	0.82	0.06	---	---
PARTIAL THROMBOPLASTIN TIME (PTT)	sec	50	15.9	1.9	---	---

HISTORICAL DATA - HEMATOLOGY

STRAIN: RAT / SPRAGUE DAWLEY RAT,SPF QUALITY (FEMALES) AGE: FROM 8 TO 12 WEEKS
DATA COLLECTION PERIOD: 09-OCT-02 TO 01-JUN-07

PARAMETER	UNIT	N	MEAN	STAND.DEV	95% TOLERANCE LIMITS	
ERYTHROCYTES (RBC)	T/l	65	7.61	0.46	---	---
HEMOGLOBIN (HB)	mmol/l	65	9.2	0.5	---	---
HEMATOCRIT (HCT)	rel. 1	65	0.42	0.02	---	---
MEAN CORPUSCULAR VOLUME (MCV)	fl	65	55.8	3.0	---	---
RED CELL VOL. DISTR. WIDTH (RDW)	rel. 1	65	0.114	0.009	---	---
MEAN CORPUSCULAR HEMOGLOBIN (MCH)	fmol	65	1.21	0.05	---	---
MEAN CORPUSCULAR HEMOGLOBIN CONC.	mmol/l	65	21.68	0.95	---	---
HEMOGLOBIN CONC. DISTR. WIDTH	mmol/l	65	1.50	0.19	---	---
RETICULOCYTE COUNT						
RETICULOCYTE (REL)	rel. 1	65	0.032	0.009	---	---
RETICULOCYTE (ABS)	G/l	65	240	64	---	---
MATURITY INDEX (L-RETI)	rel. 1	65	0.472	0.102	---	---
MATURITY INDEX (M-RETI)	rel. 1	65	0.343	0.050	---	---
MATURITY INDEX (H-RETI)	rel. 1	65	0.185	0.116	---	---
LEUKOCYTES, TOTAL (WBC)	G/l	65	6.33	2.66	---	---
DIFF.WBC COUNT (REL)						
NEUTROPHILS (NEUT)	rel. 1	11	0.200	0.125	---	---
EOSINOPHILS (EOS)	rel. 1	65	0.018	0.008	---	---
BASOPHILS (BASO)	rel. 1	65	0.002	0.001	---	---
LYMPHOCYTES (LYMPH)	rel. 1	65	0.759	0.087	---	---
MONOCYTES (MONO)	rel. 1	65	0.023	0.008	---	---
LARGE UNSTAINED CELLS (LUC)	rel. 1	65	0.008	0.003	---	---
DIFF.WBC COUNT (ABS)						
NEUTROPHILS (NEUT)	G/l	11	2.26	1.96	---	---
EOSINOPHILS (EOS)	G/l	65	0.10	0.05	---	---
BASOPHILS (BASO)	G/l	65	0.02	0.02	---	---
LYMPHOCYTES (LYMPH)	G/l	65	4.80	2.00	---	---
MONOCYTES (MONO)	G/l	65	0.14	0.07	---	---
LARGE UNSTAINED CELLS (LUC)	G/l	65	0.05	0.04	---	---
THROMBOCYTES (PLATELETS)	G/l	65	1249	224	---	---
METHEMOGLOBIN (MET-HB)	rel. 1	10	0.008	0.002	---	---
COAGULATION						
PROTHROMBIN TIME (PT)	rel. 1	64	0.93	0.10	---	---
PARTIAL THROMBOPLASTIN TIME (PTT)	sec	64	18.4	2.3	---	---

HISTORICAL DATA - HEMATOLOGY

STRAIN: RAT / SPRAGUE DAWLEY RAT,SPF QUALITY (FEMALES) AGE: FROM 13 TO 18 WEEKS
DATA COLLECTION PERIOD: 09-OCT-02 TO 01-JUN-07

PARAMETER	UNIT	N	MEAN	STAND.DEV	95% TOLERANCE LIMITS	
ERYTHROCYTES (RBC)	T/l	49	8.01	0.30	---	---
HEMOGLOBIN (HB)	mmol/l	49	9.7	0.3	---	---
HEMATOCRIT (HCT)	rel. 1	49	0.43	0.02	---	---
MEAN CORPUSCULAR VOLUME (MCV)	fl	49	53.5	2.0	---	---
RED CELL VOL. DISTR. WIDTH (RDW)	rel. 1	49	0.124	0.008	---	---
MEAN CORPUSCULAR HEMOGLOBIN (MCH)	fmol	49	1.21	0.03	---	---
MEAN CORPUSCULAR HEMOGLOBIN CONC.	mmol/l	49	22.70	0.76	---	---
HEMOGLOBIN CONC. DISTR. WIDTH	mmol/l	49	1.61	0.10	---	---
RETICULOCYTE COUNT.....						
RETICULOCYTE (REL)	rel. 1	49	0.023	0.006	---	---
RETICULOCYTE (ABS)	G/l	49	182	45	---	---
MATURITY INDEX (L-RETI)	rel. 1	49	0.645	0.135	---	---
MATURITY INDEX (M-RETI)	rel. 1	49	0.288	0.084	---	---
MATURITY INDEX (H-RETI)	rel. 1	49	0.067	0.077	---	---
LEUKOCYTES, TOTAL (WBC)	G/l	49	5.78	2.37	---	---
DIFF.WBC COUNT (REL).....						
NEUTROPHILS (NEUT)	rel. 1	20	0.267	0.080	---	---
EOSINOPHILS (EOS)	rel. 1	49	0.017	0.006	---	---
BASOPHILS (BASO)	rel. 1	49	0.006	0.004	---	---
LYMPHOCYTES (LYMPH)	rel. 1	49	0.754	0.094	---	---
MONOCYTES (MONO)	rel. 1	49	0.023	0.006	---	---
LARGE UNSTAINED CELLS (LUC)	rel. 1	49	0.012	0.005	---	---
DIFF.WBC COUNT (ABS).....						
NEUTROPHILS (NEUT)	G/l	20	1.02	0.36	---	---
EOSINOPHILS (EOS)	G/l	49	0.09	0.04	---	---
BASOPHILS (BASO)	G/l	49	0.04	0.04	---	---
LYMPHOCYTES (LYMPH)	G/l	49	4.50	2.21	---	---
MONOCYTES (MONO)	G/l	49	0.13	0.06	---	---
LARGE UNSTAINED CELLS (LUC)	G/l	49	0.07	0.05	---	---
THROMBOCYTES (PLATELETS)	G/l	49	1092	128	---	---
COAGULATION.....						
PROTHROMBIN TIME (PT)	rel. 1	50	0.84	0.07	---	---
PARTIAL THROMBOPLASTIN TIME (PTT)	sec	50	13.2	2.5	---	---

HISTORICAL DATA - CLINICAL BIOCHEMISTRY

STRAIN: RAT / SPRAGUE DAWLEY RAT,SPF QUALITY (MALES) AGE: FROM 8 TO 12 WEEKS
DATA COLLECTION PERIOD: 09-OCT-02 TO 01-JUN-07

PARAMETER	UNIT	N	MEAN	STAND.DEV	95% TOLERANCE LIMITS	
GLUCOSE	mmol/l	66	4.94	1.53	---	---
UREA	mmol/l	66	4.96	0.78	---	---
CREATININE	µmol/l	66	21.1	2.9	---	---
BILIRUBIN, TOTAL	µmol/l	66	1.40	0.44	---	---
CHOLESTEROL, TOTAL	mmol/l	66	1.80	0.41	---	---
TRIGLYCERIDES	mmol/l	66	0.41	0.16	---	---
PHOSPHOLIPIDS	mmol/l	66	1.47	0.25	---	---
ASPARTATE AMINOTRANSFERASE (ASAT)	U/l	66	85.6	20.0	---	---
ALANINE AMINOTRANSFERASE (ALAT)	U/l	66	35.6	10.8	---	---
LACTATE DEHYDROGENASE (LDH)	U/l	51	276.3	294.1	---	---
ALKALINE PHOSPHATASE (ALP)	U/l	66	144.0	67.2	---	---
GAMMA-GLUTAMYLTRANSFERASE (GGT)	U/l	66	0.0	0.3	---	---
CREATINE KINASE (CK)	U/l	66	344.8	745.8	---	---
SODIUM	mmol/l	66	144.5	5.0	---	---
POTASSIUM	mmol/l	66	3.54	0.35	---	---
CHLORIDE	mmol/l	66	102.4	3.4	---	---
CALCIUM	mmol/l	66	2.79	0.13	---	---
PHOSPHORUS	mmol/l	66	2.55	0.32	---	---
PROTEIN, TOTAL	g/l	66	64.31	3.77	---	---
ALBUMIN	g/l	61	40.18	2.83	---	---
GLOBULIN	g/l	61	23.75	2.69	---	---
A/G RATIO	-	61	1.72	0.25	---	---

HISTORICAL DATA - CLINICAL BIOCHEMISTRY

STRAIN: RAT / SPRAGUE DAWLEY RAT,SPF QUALITY (MALES) AGE: FROM 13 TO 18 WEEKS
DATA COLLECTION PERIOD: 09-OCT-02 TO 01-JUN-07

PARAMETER	UNIT	N	MEAN	STAND.DEV	95% TOLERANCE LIMITS	
GLUCOSE	mmol/l	50	5.45	0.71	---	---
UREA	mmol/l	50	4.78	0.67	---	---
CREATININE	µmol/l	50	22.5	3.1	---	---
BILIRUBIN, TOTAL	µmol/l	50	1.68	0.30	---	---
CHOLESTEROL, TOTAL	mmol/l	50	1.64	0.41	---	---
TRIGLYCERIDES	mmol/l	50	0.46	0.21	---	---
PHOSPHOLIPIDS	mmol/l	50	1.31	0.25	---	---
ASPARTATE AMINOTRANSFERASE (ASAT)	U/l	50	78.1	12.3	---	---
ALANINE AMINOTRANSFERASE (ALAT)	U/l	50	33.4	9.6	---	---
LACTATE DEHYDROGENASE (LDH)	U/l	25	137.7	25.1	---	---
ALKALINE PHOSPHATASE (ALP)	U/l	50	101.5	27.6	---	---
GAMMA-GLUTAMYLTRANSFERASE (GGT)	U/l	50	0.0	0.0	---	---
CREATINE KINASE (CK)	U/l	50	159.7	83.0	---	---
SODIUM	mmol/l	50	145.6	1.9	---	---
POTASSIUM	mmol/l	50	3.72	0.26	---	---
CHLORIDE	mmol/l	50	106.3	2.6	---	---
CALCIUM	mmol/l	50	2.80	0.07	---	---
PHOSPHORUS	mmol/l	50	2.30	0.26	---	---
PROTEIN, TOTAL	g/l	50	67.50	2.58	---	---
ALBUMIN	g/l	50	41.10	1.65	---	---
GLOBULIN	g/l	50	26.40	2.39	---	---
A/G RATIO	-	50	1.57	0.17	---	---

HISTORICAL DATA - CLINICAL BIOCHEMISTRY

STRAIN: RAT / SPRAGUE DAWLEY RAT,SPF QUALITY (FEMALES) AGE: FROM 8 TO 12 WEEKS
DATA COLLECTION PERIOD: 09-OCT-02 TO 01-JUN-07

PARAMETER	UNIT	N	MEAN	STAND.DEV	95% TOLERANCE LIMITS	
GLUCOSE	mmol/l	66	5.08	0.71	---	---
UREA	mmol/l	66	5.87	1.04	---	---
CREATININE	µmol/l	66	25.3	3.6	---	---
BILIRUBIN, TOTAL	µmol/l	66	1.80	0.47	---	---
CHOLESTEROL, TOTAL	mmol/l	66	2.02	0.44	---	---
TRIGLYCERIDES	mmol/l	66	0.29	0.10	---	---
PHOSPHOLIPIDS	mmol/l	66	1.76	0.35	---	---
ASPARTATE AMINOTRANSFERASE (ASAT)	U/l	66	88.4	15.0	---	---
ALANINE AMINOTRANSFERASE (ALAT)	U/l	66	32.3	7.4	---	---
LACTATE DEHYDROGENASE (LDH)	U/l	51	221.2	228.8	---	---
ALKALINE PHOSPHATASE (ALP)	U/l	66	76.4	22.2	---	---
GAMMA-GLUTAMYLTRANSFERASE (GGT)	U/l	66	0.0	0.0	---	---
CREATINE KINASE (CK)	U/l	66	177.5	74.5	---	---
SODIUM	mmol/l	66	144.5	3.3	---	---
POTASSIUM	mmol/l	66	3.32	0.37	---	---
CHLORIDE	mmol/l	65	105.4	2.4	---	---
CALCIUM	mmol/l	66	2.76	0.11	---	---
PHOSPHORUS	mmol/l	66	2.09	0.26	---	---
PROTEIN, TOTAL	g/l	66	66.40	3.35	---	---
ALBUMIN	g/l	61	44.05	2.77	---	---
GLOBULIN	g/l	61	22.26	3.13	---	---
A/G RATIO	-	61	2.01	0.28	---	---

HISTORICAL DATA - CLINICAL BIOCHEMISTRY

STRAIN: RAT / SPRAGUE DAWLEY RAT,SPF QUALITY (FEMALES) AGE: FROM 13 TO 18 WEEKS
DATA COLLECTION PERIOD: 09-OCT-02 TO 01-JUN-07

PARAMETER	UNIT	N	MEAN	STAND.DEV	95% TOLERANCE LIMITS	
GLUCOSE	mmol/l	50	5.51	0.76	---	---
UREA	mmol/l	50	6.02	1.13	---	---
CREATININE	µmol/l	50	29.1	3.9	---	---
BILIRUBIN, TOTAL	µmol/l	50	2.48	0.47	---	---
CHOLESTEROL, TOTAL	mmol/l	50	1.99	0.47	---	---
TRIGLYCERIDES	mmol/l	50	0.30	0.08	---	---
PHOSPHOLIPIDS	mmol/l	50	1.83	0.32	---	---
ASPARTATE AMINOTRANSFERASE (ASAT)	U/l	50	83.5	15.0	---	---
ALANINE AMINOTRANSFERASE (ALAT)	U/l	50	27.2	8.7	---	---
LACTATE DEHYDROGENASE (LDH)	U/l	25	129.1	28.6	---	---
ALKALINE PHOSPHATASE (ALP)	U/l	50	48.1	21.3	---	---
GAMMA-GLUTAMYLTRANSFERASE (GGT)	U/l	50	0.0	0.0	---	---
CREATINE KINASE (CK)	U/l	50	136.2	34.8	---	---
SODIUM	mmol/l	50	142.1	2.4	---	---
POTASSIUM	mmol/l	50	3.23	0.25	---	---
CHLORIDE	mmol/l	50	105.4	1.9	---	---
CALCIUM	mmol/l	50	2.75	0.07	---	---
PHOSPHORUS	mmol/l	50	1.72	0.30	---	---
PROTEIN, TOTAL	g/l	50	69.52	3.39	---	---
ALBUMIN	g/l	50	46.53	2.59	---	---
GLOBULIN	g/l	50	23.00	1.60	---	---
A/G RATIO	-	50	2.03	0.15	---	---

HISTORICAL DATA - URINALYSIS

STRAIN: RAT / SPRAGUE DAWLEY RAT,SPF QUALITY (MALES) AGE: FROM 8 TO 12 WEEKS
DATA COLLECTION PERIOD: 09-OCT-02 TO 01-JUN-07

PARAMETER	UNIT	N	MEAN	STAND.DEV	95% TOLERANCE LIMITS	
VOLUME/18h	ml	61	10.0	5.8	---	---
RELATIVE DENSITY	rel. 1	11	1.023	0.008	---	---
pH	-	61	6.9	0.6	---	---
PROTEIN	g/l	61	0.25	0.19	---	---
GLUCOSE	mmol/l	61	0	0	---	---
KETONES	mmol/l	61	0.6	0.5	---	---
UROBILINOGEN	µmol/l	61	0	0	---	---
BILIRUBIN	µmol/l	61	1	4	---	---
ERYTHROCYES	per µl	61	16	33	---	---
LEUCOCYTES	per µl	61	61	70	---	---

HISTORICAL DATA - URINALYSIS

STRAIN: RAT / SPRAGUE DAWLEY RAT,SPF QUALITY (MALES) AGE: FROM 13 TO 18 WEEKS
DATA COLLECTION PERIOD: 09-OCT-02 TO 01-JUN-07

PARAMETER	UNIT	N	MEAN	STAND.DEV	95% TOLERANCE LIMITS	
VOLUME/18h	ml	50	8.0	3.0	---	---
RELATIVE DENSITY	rel. 1	20	1.058	0.022	---	---
pH	-	50	6.9	0.6	---	---
PROTEIN	g/l	50	0.42	0.26	---	---
GLUCOSE	mmol/l	50	0	0	---	---
KETONES	mmol/l	50	0.9	0.5	---	---
UROBILINOGEN	µmol/l	50	0	2	---	---
BILIRUBIN	µmol/l	50	1	4	---	---
ERYTHROCYES	per µl	50	14	10	---	---
LEUCOCYTES	per µl	50	66	38	---	---

HISTORICAL DATA - URINALYSIS

STRAIN: RAT / SPRAGUE DAWLEY RAT,SPF QUALITY (FEMALES) AGE: FROM 8 TO 12 WEEKS
DATA COLLECTION PERIOD: 09-OCT-02 TO 01-JUN-07

PARAMETER	UNIT	N	MEAN	STAND.DEV	95% TOLERANCE LIMITS	
VOLUME/18h	ml	61	7.7	5.2	---	---
RELATIVE DENSITY	rel. 1	11	1.031	0.017	---	---
pH	-	61	6.5	0.6	---	---
PROTEIN	g/l	61	0.22	0.16	---	---
GLUCOSE	mmol/l	61	0	0	---	---
KETONES	mmol/l	61	0.2	0.2	---	---
UROBILINOGEN	µmol/l	61	1	4	---	---
BILIRUBIN	µmol/l	61	3	6	---	---
ERYTHROCYES	per µl	61	25	56	---	---
LEUCOCYTES	per µl	61	27	33	---	---

HISTORICAL DATA - URINALYSIS

STRAIN: RAT / SPRAGUE DAWLEY RAT,SPF QUALITY (FEMALES) AGE: FROM 13 TO 18 WEEKS
DATA COLLECTION PERIOD: 09-OCT-02 TO 01-JUN-07

PARAMETER	UNIT	N	MEAN	STAND.DEV	95% TOLERANCE LIMITS	
VOLUME/18h	ml	50	6.7	3.7	---	---
RELATIVE DENSITY	rel. 1	20	1.044	0.012	---	---
pH	-	50	6.4	0.7	---	---
PROTEIN	g/l	50	0.32	0.21	---	---
GLUCOSE	mmol/l	50	0	0	---	---
KETONES	mmol/l	50	0.2	0.3	---	---
UROBILINOGEN	µmol/l	50	0	1	---	---
BILIRUBIN	µmol/l	50	1	4	---	---
ERYTHROCYES	per µl	50	6	6	---	---
LEUCOCYTES	per µl	50	18	27	---	---

APPENDIX VI - HISTOPATHOLOGY

Histopathology Examination

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[1] Animal organ finding table

1 MATERIALS AND METHODS

1.1 Allocation

Allocation and Dose Levels in mg/kg/day		Group 1 Control* 0	Group 2 5	Group 3 25	Group 4 250	Group 5 1000
Males	**A**	01 - 05	11 - 15	16 - 20	21 - 25	26 - 30
	B	06 - 10				31 - 35
Females	**A**	36 - 40	46 - 50	51 - 55	56 - 60	61 - 65
	B	41 - 45				66 - 70

* Control animals were treated with the vehicle only
A Toxicity testing (termination after 28 treatment days)
B Recovery testing (termination after an additional 14-day recovery period)

1.2 Necropsy and Histopathology

Necropsies and histological preparation of the tissues were performed at Harlan Laboratories Ltd., Itingen / Switzerland.

All animals were weighed, anesthetized by intravenous injection of sodium pentobarbital, killed by exsanguination and necropsied. Descriptions of all macroscopic abnormalities were recorded. Samples of the following tissues and organs were collected from all animals at necropsy and, unless otherwise indicated, fixed in neutral phosphate buffered 4% formaldehyde solution:

Tissues / Organs	Weight	Collect	Examine
Adrenal glands	X	X	X
Aorta		X	
Bone (sternum, femur including joint)		X	
Bone marrow (femur)		X	X
Brain - including section of medulla/pons, cerebral and cerebellar cortex	X	X	X
Cecum		X	X
Colon		X	X
Duodenum		X	X

Tissues / Organs	Weight	Collect	Examine
Epididymides (fixed in Bouin's solution)	X	X	X
Esophagus		X	
Eyes w/optic nerve (fixed in Davidson's solution)		X	
Harderian gland (fixed in Davidson's solution)		X	
Heart including auricles	X	X	X
Ileum, with Peyer's patches		X	X
Jejunum with Peyer's patches		X	X
Kidneys	X	X	X
Larynx		X	
Lacrimal gland, exorbital		X	
Liver	X	X	X
Lungs, filled w/formalin at necropsy		X	X
Lymph nodes – mesenteric and mandibular		X	X
Mammary gland area		X	
Nasal cavity		X	
Ovaries	X	X	X
Pancreas		X	
Pharynx		X	
Pituitary gland	X	X	X
Seminal vesicles and Prostate gland (incl. coagulating glands)	X	X	X
Rectum		X	X
Salivary glands - mandibular, sublingual		X	
Sciatic nerve		X	X
Skeletal muscle		X	
Skin		X	
Spinal cord - cervical, midthoracic, lumbar		X	X
Spleen	X	X	X
Stomach		X	X
Testes (fixed in Bouin's solution)	X	X	X
Thymus	X	X	X
Thyroid (incl. parathyroid gland)	X	X	X

Tissues / Organs	Weight	Collect	Examine
Tongue		X	
Trachea		X	X
Urinary bladder, filled w/formalin at necropsy		X	X
Uterus, with cervix	X	X	X
Vagina		X	X
All gross lesions		X	X

Samples of the kidneys (100 - 300 mg) were transferred to 70% ethanol within 48 hours, after initial fixation.

Slides of all organs and tissues (see list above) and all gross lesions from the animals of the control and high-dose groups were processed, embedded in paraffin, cut at a nominal thickness of 2 - 4 micrometers, stained with hematoxylin & eosin (H&E) and examined by light microscope by the study pathologist.

Because of possible test item-related findings noted in the high dose group, the liver and thyroid of both sexes, the kidneys and adrenal gland glands of males were examined also in the animals of groups 2, 3 and 4. Also, all liver sections from all animals were examined using polarized light, because brown pigment as protoporphyrin-like deposit was recorded in the liver.

1.3 Data Compilation

The animal data and necropsy findings were transferred electronically via transfer file into the PathData System.

The microscopic findings were recorded during histopathologic examination by the pathologist and directly entered into the PathData System. The slides were evaluated during February and March 2010.

Histologic changes were described, wherever possible, according to distribution, severity and morphologic character. Severity scores were assigned as given under "Explanation of Codes and Symbols".

All microscopic findings are listed in the "Table of Individual Microscopic Findings", along with an explanation of the codes and symbols used. Computer-generated incidence tables derived from these data are also presented as well as the complete narrative of the macroscopic and microscopic findings.

1.4 Statistical Analysis

The following statistical methods were used to analyze histological findings:

- Fisher's exact-test [see References (1)].
- Armitage / Cochran Trend Test [see References (2)]

1.5 Peer Review

The following sections were reviewed by Dr. Tanja Razinger (Department of Pathology, Harlan Laboratories Ltd., Itingen / Switzerland): all organs of animal nos. 1, 26, 30, 36, 61 and 65, as well as liver and thyroid glands of all animals, kidneys and adrenal glands of all males.

The assessment of the study pathologist and reviewing pathologist compared favorably.

2 RESULTS

2.1 Mortality

All animals survived the scheduled study period.

2.2 Macroscopic Findings

Macroscopically, the treatment related macroscopic findings recorded were enlargement and discoloration (black brown or dark brown) of the liver in both sexes of group 5 and in males of group 4 after the 28 day treatment period. Discoloration (black brown or dark brown) of the liver was also recorded in males of group 5 after 14 day recovery period.

All other findings recorded were within the range of normal background lesions which may be recorded in animals of this strain and age.

Table 1 Incidence of Main Macroscopic Findings in Liver

Findings/Incidence	Group 1		Group 2		Group 3		Group 4		Group 5	
Terminal Sacrifice	**5 M**	**5 F**	**5 M**	**5 F**	**5 M**	**5 F**	**5 M**	**5 F**	**5 M**	**5 F**
Enlarged	-	-	-	-	-	-	5	-	4	2
Discoloration (black brown or dark brown)	-	-	-	-	-	-	5	-	5	2
Recovery	**5 M**	**5 F**							**5 M**	**5 F**
Enlarged	-	-							-	-
Discoloration (black brown or dark brown)	-	-							5	-

2.3 Microscopic Findings

2.3.1 Liver

Protoporphyrin accumulation (protoporphyrin like brownish pigment) in the intrahepatic bile ducts was recorded at minimal to moderate severity in animals of both sexes of group 5 and in males of group 4 after the 28 day treatment period. Protoporphyrin accumulation (protoporphyrin like brownish pigment) in Kupffer cell as well as in hepatocytes was also recorded in males of groups 4 and 5 at the end of 28 day treatment period. This pigment was characterized by birefringent, bright red appearance with dark Maltese cross in each deposit affected under polarized light.

Periportal chronic inflammation as well as bile duct proliferation at minimal to slight severity was recorded in both sexes in group 5 and in males of group 4 at the end of 28 day treatment period.
Hepatocellular hypertrophy (centrilobular) was recorded at minimal severity in both sexes of group 5 and in males of group 4 at the end of 28 day treatment period.

These findings except hepatocellular hypertrophy were also recorded in animals of group 5 after 14 day recovery period.

Table 2 Incidence and Mean Severity of Main Microscopic Findings in Liver

Findings/Incidence/Mean Severity Grade	**Group 1**		**Group 2**		**Group 3**		**Group 4**		**Group 5**	
Terminal Sacrifice	**5 M**	**5 F**	**5 M**	**5 M**	**5 F**	**5 M**	**5 M**	**5 F**	**5 M**	**5 F**
Protoporphyrin accumulation, intrahepatic bile duct #, ##	-	-	-	-	-	-	5/2.8*	-	5/3.0*	2/2.0
Protoporphyrin accumulation, Kupffer cell #	-	-	-	-	-	-	1/1.0	-	5/2.0*	-
Protoporphyrin accumulation, hepatocyte #	-	-	-	-	-	-	3/1.0	-	5/1.0*	-
Periportal chronic inflammation #, ##	-	-	-	-	-	-	5/1.2*	-	5/1.0*	2/1.0
Bile duct proliferation #	-	-	-	-	-	-	4/1.8	-	5/1.8*	1/1.0
Hepatocellular hypertrophy ##	-	-	-	-	-	-	2/1.0	-	3/1.0	3/1.0
Recovery	**5 M**	**5 F**							**5 M**	**5 F**
Protoporphyrin accumulation, intrahepatic bile duct	-	-							5/3.0*	4/1.5
Protoporphyrin accumulation, Kupffer cell	-	-							5/1.8*	-
Protoporphyrin accumulation, hepatocyte	-	-							5/1.0*	-
Periportal chronic inflammation	-	-							5/1.0*	2/1.0
Bile duct proliferation	-	-							5/2.0*	-

* : P<0.01 by One-sided Exact Fischer Test
# : P<0.01 by Armitage / Cochran Trend Test for Males
: P<0.01 by Armitage / Cochran Trend Test for Females

2.3.2 Kidney

Hyaline droplets at minimal to slight severity were recorded in males of groups 3, 4 and 5 at the end of 28 day treatment period.

The hyaline droplets were not recorded in animals after 14 day recovery period.

Table 3 Incidence and Mean Severity of Main Microscopic Findings in Kidney

Findings/Incidence/Mean Severity Grade	Group 1		Group 2		Group 3		Group 4		Group 5	
Terminal Sacrifice	**5 M**	**5 F**	**5 M**	**5 F**	**5 M**	**5 F**	**5 M**	**5 F**	**5 M**	**5 F**
Hyaline droplets	-	-	-	-	2/1.0	-	5/1.6*	-	5/1.8*	-

* : P<0.01 by One-sided Exact Fischer Test

2.3.3 Thyroid Glands

Follicular cell hypertrophy at minimal severity was recorded in two males and one female of group 5 at the end of 28 day treatment period.

The follicular cell hypertrophy was not recorded in animals after 14 day recovery period.

Table 4 Incidence and Mean Severity of Main Microscopic Findings in Thyroid Gland

Findings/Incidence/Mean Severity Grade	Group 1		Group 2		Group 3		Group 4		Group 5	
Terminal Sacrifice	**5 M**	**5 F**	**5 M**	**5 F**	**5 M**	**5 F**	**5 M**	**5 F**	**5 M**	**5 F**
Follicular cell hypertrophy	-	-	-		-		-	-	2/1.0	1/1.0

2.3.4 Other Findings

The remainder of findings recorded was within the range of normal background lesions which may be recorded in animals of this strain and age.

3 DISCUSSION AND CONCLUSION

Under the conditions of this experiment, there were no premature deaths. All animals survived the scheduled study period.

Macroscopically, the treatment related macroscopic findings recorded were enlargement and discoloration (black brown or dark brown) of the liver in both sexes of groups 5 and males of group 4 at the end of 28 day treatment period. Discoloration of the liver was also recorded in males of group 5 after 14 day recovery period.

Microscopically, the following treatment related findings were recorded:

1. Protoporphyrin accumulation (protoporphyrin like brownish pigment) in the intrahepatic bile ducts was recorded at minimal to moderate severity in animals of both sexes of group 5 and in males of group 4 after the 28 day treatment period. Protoporphyrin accumulation (protoporphyrin like brownish pigment) in Kupffer cell as well as in hepatocytes was also recorded in males of groups 4 and 5 at the end of 28 day treatment period. This pigment was characterized by birefringent, bright red appearance with dark Maltese cross in each deposit affected under polarized light.
2. Periportal chronic inflammation as well as bile duct proliferation at minimal to slight severity was recorded in both sexes of groups 5 and males of group 4 at the end of 28 day treatment period. These lesions were associated with the above mentioned protoporphyrin accumulation (protoporphyrin like brownish pigment) and were considered to be a secondary reaction.
3. Centrilobular hepatocellular hypertrophy was recorded at minimal severity in both sexes of group 5 and in males of group 4 at the end of 28 day treatment period. This lesion was considered to be of metabolic nature and of adaptive character like as enzyme induction
4. Follicular cell hypertrophy of the thyroid gland at minimal severity was recorded in two males and one female of group 5 at the end of 28 day treatment period. Centrilobular hepatocellular hypertrophy was also recorded in this case and a possible relationship between the liver enzyme-induction and the follicular cell hypertrophy was considered.
5. Hyaline droplets of the kidney were recorded at minimal severity in males of group 3 and at minimal to slight severity in males of group 4 and 5 at the end of 28 day treatment period. The increased incidence and severity of this lesion in groups 4 and 5 was considered to be induced by test item. By contrast, minimal degrees of hyaline droplets recorded in group 3 were considered to be most likely incidental, since they may occur also spontaneously in control males (Our historical control data shows an occurrence of 40.82% of hyaline droplets).

These liver findings correlated with significantly increased absolute weight of the liver as well as with gross lesions consisting of enlargement and discoloration. The exact pathogenesis of protoporphyrin accumulation (protoporphyrin like brownish pigment) and the sex difference of these treatment related findings were not clear. Further examination is need for diagnosis of

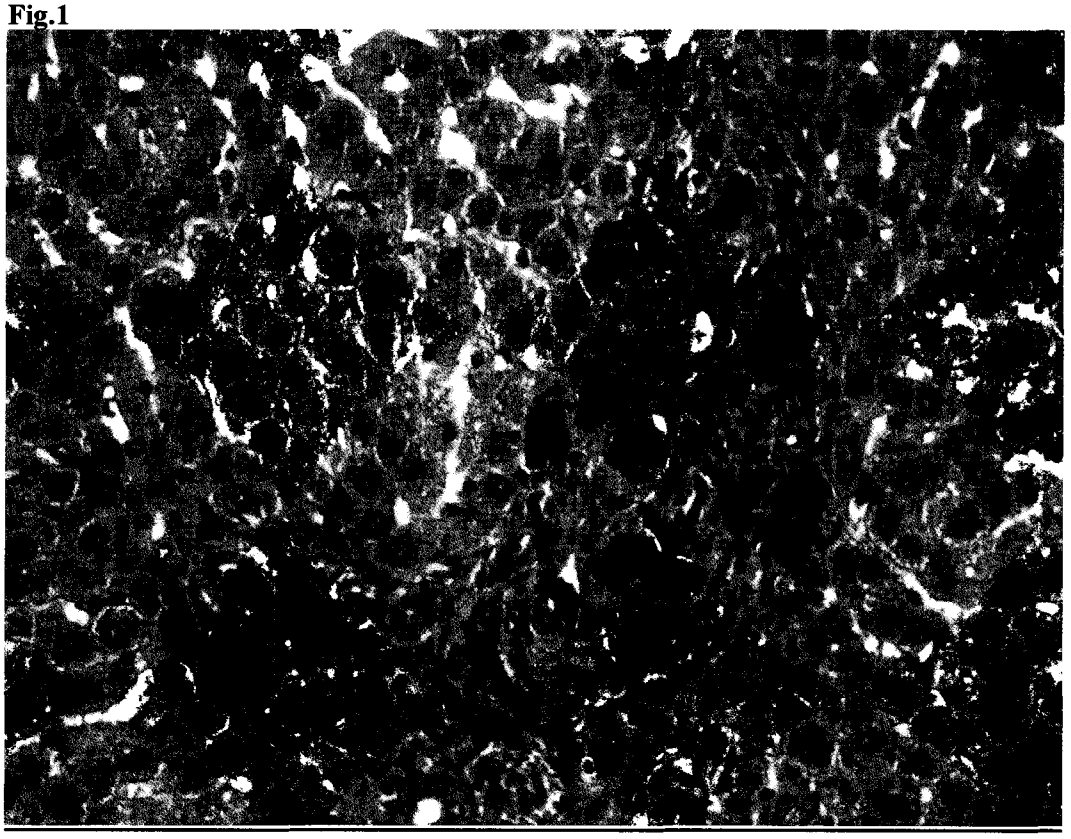
protoporphinosis / porphilinosis, because Maltese cross appearance under polarized light occurs also in cholesterol, starch, silica and other minerals deposits. After a 14-day recovery period, protoporphyrin accumulation (protoporphyrin like brownish pigment) along with bile duct proliferation and periportal chronic inflammation were still present in the livers. Therefore these lesions did not show regression after the recovery period. The hepatocellular hypertrophy, follicular cell hypertrophy of the thyroid gland and hyaline deposits of the male kidneys showed complete regression after the 14-day treatment-free recovery period.

Based on morphological findings a NOEL could be established at 25 mg/kg/day for both males and females.

4 FIGURE

Key to Illustration:
Fig.1: Animal No. 26 (group5):
Protoporphyrin accumulation (Protoporphyrin like brownish pigment) in intrahepatic bile duct characterized by birefringent, bright red appearance with dark Maltese cross under polarized light.

Fig.1



5 REFERENCES

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TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0
Selected Findings

DOSE GROUP:	01		02		03		04		05	
SEX :	M	F	M	F	M	F	M	F	M	F
NO.ANIMALS:	5	5	5	5	5	5	5	5	5	5
LIVER :	5	5	5	5	5	5	5	5	5	5
– Protoporph., bile D.										
GRADE 1 :	–	–	–	–	–	–	–	–	–	1
GRADE 2 :	–	–	–	–	–	–	1	–	–	–
GRADE 3 :	–	–	–	–	–	–	4	–	5	1
TOTAL AFFECTED :	–	–	–	–	–	–	5	–	5	2
MEAN SEVERITY :	–	–	–	–	–	–	2.8	–	3.0	2.0
– Protoporph., Kupffer										
GRADE 1 :	–	–	–	–	–	–	1	–	–	–
GRADE 2 :	–	–	–	–	–	–	–	–	5	–
TOTAL AFFECTED :	–	–	–	–	–	–	1	–	5	–
MEAN SEVERITY :	–	–	–	–	–	–	1.0	–	2.0	–
– Protoporph., hepato.										
GRADE 1 :	–	–	–	–	–	–	3	–	5	–
TOTAL AFFECTED :	–	–	–	–	–	–	3	–	5	–
MEAN SEVERITY :	–	–	–	–	–	–	1.0	–	1.0	–
– Peripor.chro.inflam.										
GRADE 1 :	–	–	–	–	–	–	4	–	5	2
GRADE 2 :	–	–	–	–	–	–	1	–	–	–
TOTAL AFFECTED :	–	–	–	–	–	–	5	–	5	2
MEAN SEVERITY :	–	–	–	–	–	–	1.2	–	1.0	1.0
– Bile duct prolifer.										
GRADE 1 :	–	–	–	–	–	–	1	–	1	1
GRADE 2 :	–	–	–	–	–	–	3	–	4	–
TOTAL AFFECTED :	–	–	–	–	–	–	4	–	5	1
MEAN SEVERITY :	–	–	–	–	–	–	1.8	–	1.8	1.0

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SPONSOR : SEHSC *PathData©System V6.2b5*

SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0
Selected Findings

DOSE GROUP:	01		02		03		04		05	
SEX :	M	F	M	F	M	F	M	F	M	F
NO.ANIMALS:	5	5	5	5	5	5	5	5	5	5
LIVER CONT'D.	5	5	5	5	5	5	5	5	5	5
- Hepatocel.hypertrop.										
GRADE 1 :	-	-	-	-	-	-	2	-	3	3
TOTAL AFFECTED :	-	-	-	-	-	-	2	-	3	3
MEAN SEVERITY :	-	-	-	-	-	-	1.0	-	1.0	1.0
KIDNEYS :	5	5	5	-	5	-	5	-	5	5
- Hyaline droplets										
GRADE 1 :	-	-	-	-	2	-	2	-	1	-
GRADE 2 :	-	-	-	-	-	-	3	-	4	-
TOTAL AFFECTED :	-	-	-	-	2	-	5	-	5	-
MEAN SEVERITY :	-	-	-	-	1.0	-	1.6	-	1.8	-
THYROID GLAND :	5	5	5	5	5	5	5	5	5	5
- Follic.C.hypertrophy										
GRADE 1 :	-	-	-	-	-	-	-	-	2	1
TOTAL AFFECTED :	-	-	-	-	-	-	-	-	2	1
MEAN SEVERITY :	-	-	-	-	-	-	-	-	1.0	1.0

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SPONSOR : SEHSC *PathData©System V6.2b5*

SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1
Selected Findings

DOSE GROUP:	01		02		03		04		05	
SEX :	M	F	M	F	M	F	M	F	M	F
NO.ANIMALS:	5	5	-	-	-	-	-	-	5	5
LIVER :	5	5	-	-	-	-	-	-	5	5
- Protoporph., bile D.										
GRADE 1 :	-	-	-	-	-	-	-	-	-	2
GRADE 2 :	-	-	-	-	-	-	-	-	-	2
GRADE 3 :	-	-	-	-	-	-	-	-	5	-
TOTAL AFFECTED :	-	-	-	-	-	-	-	-	5	4
MEAN SEVERITY :	-	-	-	-	-	-	-	-	3.0	1.5
- Protoporph., Kupffer										
GRADE 1 :	-	-	-	-	-	-	-	-	1	-
GRADE 2 :	-	-	-	-	-	-	-	-	4	-
TOTAL AFFECTED :	-	-	-	-	-	-	-	-	5	-
MEAN SEVERITY :	-	-	-	-	-	-	-	-	1.8	-
- Protoporph., hepato.										
GRADE 1 :	-	-	-	-	-	-	-	-	5	-
TOTAL AFFECTED :	-	-	-	-	-	-	-	-	5	-
MEAN SEVERITY :	-	-	-	-	-	-	-	-	1.0	-
- Peripor.chro.inflam.										
GRADE 1 :	-	-	-	-	-	-	-	-	5	2
TOTAL AFFECTED :	-	-	-	-	-	-	-	-	5	2
MEAN SEVERITY :	-	-	-	-	-	-	-	-	1.0	1.0
- Bile duct prolifer.										
GRADE 2 :	-	-	-	-	-	-	-	-	5	-
TOTAL AFFECTED :	-	-	-	-	-	-	-	-	5	-
MEAN SEVERITY :	-	-	-	-	-	-	-	-	2.0	-

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NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

DOSE GROUP:	01		02		03		04		05	
SEX :	M	F	M	F	M	F	M	F	M	F
NO.ANIMALS:	5	5	5	5	5	5	5	5	5	5
HEART WITH AURICLES :	5	5	–	–	–	–	–	–	5	5
– Mononuclear foci :	–	–	–	–	–	–	–	–	–	1
TRACHEA :	5	5	–	–	–	–	–	–	5	5
– Mononuclear foci :	1	1	–	–	–	–	–	–	1	1
LIVER :	5	5	5	5	5	5	5	5	5	5
– Protoporph., bile D.:	–	–	–	–	–	–	5	–	5	2
– Protoporph., Kupffer:	–	–	–	–	–	–	1	–	5	–
– Protoporph., hepato.:	–	–	–	–	–	–	3	–	5	–
– Malt.cross, P. light:	–	–	–	–	–	–	5	–	5	2
– Bright red, P.light :	–	–	–	–	–	–	5	–	5	2
– Peripor.chro.inflam.:	–	–	–	–	–	–	5	–	5	2
– Bile duct prolifer. :	–	–	–	–	–	–	4	–	5	1
– Hepatocel.hypertrop.:	–	–	–	–	–	–	2	–	3	3
– Fatty change :	4	2	2	2	1	1	3	1	3	3
– Inflammatory foci :	1	3	4	4	4	3	2	3	–	3
– Glycogen Increase :	–	2	–	4	1	5	1	4	–	1
– Hematopoietic foci :	1	2	1	2	–	–	1	2	–	1
– No histol. correlate:	–	–	–	–	–	–	–	–	–	1
SPLEEN :	5	5	–	–	–	–	–	–	5	5
– Extramed.hemopoiesis:	5	5	–	–	–	–	–	–	5	5
– Hemosiderin deposits:	–	5	–	–	–	–	–	–	1	5
KIDNEYS :	5	5	5	–	5	–	5	–	5	5
– Hyaline droplets :	–	–	–	–	2	–	5	–	5	–
– Tubular basophilia :	2	2	4	–	3	–	2	–	4	–
– Cortical mineraliz. :	–	–	–	–	–	–	1	–	–	–
– Mononuclear Infiltr.:	–	1	1	–	–	–	–	–	–	–
– Hyaline casts :	1	1	2	–	–	–	1	–	–	2
– Pelvic dilation :	–	–	1	–	–	–	–	–	–	–
– Tubular dilatation :	–	–	–	–	–	–	–	–	1	–

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NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: KO

DOSE GROUP:	01		02		03		04		05	
SEX :	M	F	M	F	M	F	M	F	M	F
NO.ANIMALS:	5	5	5	5	5	5	5	5	5	5
STOMACH :	5	5	–	–	–	–	–	–	5	5
– Glandular dilation :	–	1	–	–	–	–	–	–	–	–
– Gld.Stomach Erosion :	1	–	–	–	–	–	–	–	–	–
– Gld.Stomach Edema :	1	–	–	–	–	–	–	–	–	–
– Inflamm. infiltrate :	1	–	–	–	–	–	–	–	–	–
– Hemorrhage :	2	–	–	–	–	–	–	–	–	–
PEYERS PATCHES JEJ. :	5	5	–	–	–	–	–	–	5	5
– Lymphoid hyperplasia:	4	4	–	–	–	–	–	–	5	5
PEYERS PATCHES ILEUM :	5	5	–	–	–	–	–	–	5	5
– Lymphoid hyperplasia:	5	5	–	–	–	–	–	–	5	4
LUNGS :	5	5	–	–	–	–	–	–	5	5
– Alveolar macrophages:	2	3	–	–	–	–	–	–	1	–
– Alveolar hemorrhage :	1	–	–	–	–	–	–	–	2	1
– Vascular Mineraliz. :	1	2	–	–	–	–	–	–	–	3
– Osseous metaplasia :	1	–	–	–	–	–	–	–	–	–
– Microgranuloma :	–	–	–	–	–	–	–	–	1	–
THYMUS :	5	5	–	1	–	–	1	–	5	5
– Cyst (s) :	–	3	–	–	–	–	–	–	1	1
– Atrophy/involution :	–	–	–	–	–	–	–	–	1	–
– Hemorrhage :	–	1	–	1	–	–	1	–	–	1
– No histol. correlate:	1	–	–	–	–	–	–	–	1	–
OVARIES :	–	5	–	–	–	–	–	–	–	5
– Cyst, corpus luteum :	–	1	–	–	–	–	–	–	–	–
MANDIB.LYMPH NODES :	5	5	–	–	–	–	–	–	5	5
– Lymphoid Hyperplasia:	–	1	–	–	–	–	–	–	–	–
THYROID GLAND :	5	5	5	5	5	5	5	5	5	5
– Ultimobranchial Cyst:	2	1	1	1	1	1	–	2	1	2
– Follic.C.hypertrophy:	–	–	–	–	–	–	–	–	2	1
– Thymic ectopia :	–	–	–	–	1	–	–	–	–	–

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SPONSOR : SEHSC *PathData©System V6.2b5*

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

DOSE GROUP:	01		02		03		04		05	
SEX :	M	F	M	F	M	F	M	F	M	F
NO.ANIMALS:	5	5	5	5	5	5	5	5	5	5
ADRENAL CORTICES :	5	5	5	–	5	–	5	–	5	5
– Vacuolation, Z.fasc.:	2	–	1	–	3	–	2	–	3	–
– Foc.Hypertrophy/Z.F.:	1	–	–	–	–	–	–	–	–	–
CEREBELLUM :	5	5	–	–	–	–	–	–	5	5
– Hemorrhage :	–	1	–	–	–	–	–	–	–	–
UTERUS :	–	5	–	–	–	1	–	1	–	5
– Distended lumina :	–	1	–	–	–	1	–	1	–	–
VAGINA :	–	5	–	–	–	–	–	–	–	5
– Cycle:Proestrus :	–	1	–	–	–	–	–	–	–	–
– Cycle:Estrus :	–	1	–	–	–	–	–	–	–	–
– Cycle:Metestrus :	–	–	–	–	–	–	–	–	–	1
– Cycle:Diestrus :	–	3	–	–	–	–	–	–	–	4
– Mucification :	–	4	–	–	–	–	–	–	–	4
– Epidermal Cyst :	–	1	–	–	–	–	–	–	–	–
BONE MARROW, FEMUR :	5	5	–	–	–	–	–	–	5	5
– Fatty replacement :	5	4	–	–	–	–	–	–	5	5
– Incr. granulopoiesis:	–	1	–	–	–	–	–	–	–	–
BODY CAVITIES :	–	–	–	–	–	–	1	–	–	–
– Fat granuloma :	–	–	–	–	–	–	1	–	–	–

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1

DOSE GROUP:	01		02		03		04		05	
SEX :	M	F	M	F	M	F	M	F	M	F
NO.ANIMALS:	5	5	-	-	-	-	-	-	5	5
HEART WITH AURICLES :	5	5	-	-	-	-	-	-	5	5
- Mononuclear foci :	1	-	-	-	-	-	-	-	-	1
- Valvular hemocyst :	-	-	-	-	-	-	-	-	-	1
TRACHEA :	5	5	-	-	-	-	-	-	5	5
- Mononuclear foci :	1	-	-	-	-	-	-	-	-	-
- Inflamm. infiltrate :	-	1	-	-	-	-	-	-	-	-
LIVER :	5	5	-	-	-	-	-	-	5	5
- Protoporph., bile D.:	-	-	-	-	-	-	-	-	5	4
- Protoporph., Kupffer:	-	-	-	-	-	-	-	-	5	-
- Protoporph., hepato.:	-	-	-	-	-	-	-	-	5	-
- Malt.cross, P. light:	-	-	-	-	-	-	-	-	5	4
- Bright red, P.light :	-	-	-	-	-	-	-	-	5	4
- Peripor.chro.inflam.:	-	-	-	-	-	-	-	-	5	2
- Bile duct prolifer. :	-	-	-	-	-	-	-	-	5	-
- Fatty change :	2	2	-	-	-	-	-	-	2	4
- Inflammatory foci :	2	3	-	-	-	-	-	-	2	-
- Glycogen Increase :	-	2	-	-	-	-	-	-	-	4
- Hematopoietic foci :	2	-	-	-	-	-	-	-	-	-
SPLEEN :	5	5	-	-	-	-	-	-	5	5
- Extramed.hemopoiesis:	5	4	-	-	-	-	-	-	5	4
- Hemosiderin deposits:	2	5	-	-	-	-	-	-	1	5
KIDNEYS :	5	5	-	-	-	-	-	-	5	5
- Tubular basophilia :	2	2	-	-	-	-	-	-	3	2
- Hyaline casts :	-	1	-	-	-	-	-	-	-	1
- Papillary mineraliz.:	2	1	-	-	-	-	-	-	2	2
STOMACH :	5	5	-	-	-	-	-	-	5	5
- Glandular dilation :	1	-	-	-	-	-	-	-	-	-
- Gld.Stomach Edema :	-	-	-	-	-	-	-	-	1	-
- Inflamm. infiltrate :	-	-	-	-	-	-	-	-	1	-
PEYERS PATCHES JEJ. :	5	5	-	-	-	-	-	-	4	3
- Lymphoid hyperplasia:	2	3	-	-	-	-	-	-	1	2

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1

DOSE GROUP:	01		02		03		04		05	
SEX :	M	F	M	F	M	F	M	F	M	F
NO.ANIMALS:	5	5	–	–	–	–	–	–	5	5
PEYERS PATCHES ILEUM :	5	5	–	–	–	–	–	–	5	5
– Lymphoid hyperplasia:	5	5	–	–	–	–	–	–	4	4
LUNGS :	5	5	–	–	–	–	–	–	5	5
– Alveolar macrophages:	1	1	–	–	–	–	–	–	1	1
– Alveolar hemorrhage :	–	1	–	–	–	–	–	–	–	–
– Cholesterin deposits:	–	1	–	–	–	–	–	–	–	–
– Vascular Mineraliz. :	5	1	–	–	–	–	–	–	4	3
THYMUS :	5	5	–	–	–	–	–	–	5	5
– Cyst (s) :	–	3	–	–	–	–	–	–	1	2
– Atrophy/involution :	2	1	–	–	–	–	–	–	1	1
TESTES :	5	–	–	–	–	–	–	–	5	–
– Focal tubul. atrophy:	–	–	–	–	–	–	–	–	1	–
EPIDIDYMIDES :	5	–	–	–	–	–	–	–	5	–
– Mononuclear Infiltr.:	2	–	–	–	–	–	–	–	–	–
MANDIB.LYMPH NODES :	5	5	–	–	–	–	–	–	5	5
– Lymphoid Hyperplasia:	1	1	–	–	–	–	–	–	–	1
THYROID GLAND :	5	5	–	–	–	–	–	–	5	5
– Ultimobranchial Cyst:	1	2	–	–	–	–	–	–	1	2
– Thymic ectopia :	1	–	–	–	–	–	–	–	–	–
ADRENAL CORTICES :	5	5	–	–	–	–	–	–	5	5
– Vacuolation, Z.fasc.:	2	–	–	–	–	–	–	–	1	–
PROSTATE GLAND :	5	–	–	–	–	–	–	–	5	–
– Mononuclear Infiltr.:	–	–	–	–	–	–	–	–	1	–
UTERUS :	–	5	–	–	–	–	–	–	–	5
– Distended lumina :	–	2	–	–	–	–	–	–	–	–

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1

DOSE GROUP:	01		02		03		04		05	
SEX :	M	F	M	F	M	F	M	F	M	F
NO.ANIMALS:	5	5	–	–	–	–	–	–	5	5
VAGINA :	–	5	–	–	–	–	–	–	–	5
– Cycle:Proestrus :	–	1	–	–	–	–	–	–	–	–
– Cycle:Estrus :	–	1	–	–	–	–	–	–	–	1
– Cycle:Metestrus :	–	–	–	–	–	–	–	–	–	2
– Cycle:Diestrus :	–	3	–	–	–	–	–	–	–	2
– Mucification :	–	1	–	–	–	–	–	–	–	–
BONE MARROW, FEMUR :	5	5	–	–	–	–	–	–	5	5
– Fatty replacement :	5	5	–	–	–	–	–	–	5	5
PITUITARY GLAND :	5	4	–	–	–	–	–	–	5	5
– Cyst :	1	–	–	–	–	–	–	–	1	–
LYMPH NODES :	–	–	–	–	–	–	–	–	1	–
– Erythrophagocytosis :	–	–	–	–	–	–	–	–	1	–
– Congestion :	–	–	–	–	–	–	–	–	1	–
– Hemosiderin deposits:	–	–	–	–	–	–	–	–	1	–

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STATISTICAL EVALUATION Harlan Laboratories C53655

TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
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SPONSOR : SEHSC *PathData©System V6.2b5*

TREND TEST STATISTICS ON NON-NEOPLASTIC LESIONS (Armitage, 1955)

Evaluation Mode : GRADINGS 1 - 5 COMBINED SEX: MALE
DOSE GROUPS : 01,02,03,04,05
STATUS AT NECROPSY: K0,R1 INCL. DEATHS
Negative/Positive : - / +
No calculation : n<3 in either group and sex

ORGAN/TISSUE	FINDING	TREND	P-VALUE
LIVER	Protoporph., bile D.	6364.286+	< 0.0005+
LIVER	Protoporph., Kupffer	6667.143+	< 0.0005+
LIVER	Protoporph., hepato.	6515.714+	< 0.0005+
LIVER	Peripor.chro.inflam.	6364.286+	< 0.0005+
LIVER	Bile duct prolifer.	6440.000+	< 0.0005+
LIVER	Hepatocel.hypertrop.	1871.429+	0.0202+
KIDNEYS	Hyaline droplets	2391.429+	0.0268+
THYROID GLAND	Follic.C.hypertrophy	1348.571+	n<3/Grp/Sex

Evaluation Mode : GRADINGS 1 - 5 COMBINED SEX: FEMALE
DOSE GROUPS : 01,02,03,04,05
STATUS AT NECROPSY: K0,R1 INCL. DEATHS
Negative/Positive : - / +
No calculation : n<3 in either group and sex

ORGAN/TISSUE	FINDING	TREND	P-VALUE
LIVER	Protoporph., bile D.	4045.714+	< 0.0005+
LIVER	Peripor.chro.inflam.	2697.143+	0.0006+
LIVER	Bile duct prolifer.	674.286+	n<3/Grp/Sex
LIVER	Hepatocel.hypertrop.	2022.857+	0.0028+
THYROID GLAND	Follic.C.hypertrophy	674.286+	n<3/Grp/Sex

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

FISHER'S EXACT TEST (ONE-SIDED) ON NON-NEOPLASTIC LESIONS
STATUS AT NECROPSY: K0

	DOSE GROUP :	01		02		03		04		05	
	SEX :	M	F	M	F	M	F	M	F	M	F
ORGAN/FINDING	NO. ANIMALS :	5	5	5	5	5	5	5	5	5	5
HEART WITH AURICLE	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Mononuclear foci	:	-	-	-	-	-	-	-	-	-	1
	p - Value/P :	-	-	-	-	-	-	-	-	-	0.5000
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
TRACHEA	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Mononuclear foci	:	1	1	-	-	-	-	-	-	1	1
	p - Value/P :	-	-	-	-	-	-	-	-	0.7778	0.7778
	p - Value/N :	-	-	-	-	-	-	-	-	0.7778	0.7778
LIVER	No.Examin :	5	5	5	5	5	5	5	5	5	5
- Protoporph., bile D.	:	-	-	-	-	-	-	5	-	5	2
	p - Value/P :	-	-	-	-	-	-	0.0040	-	0.0040	0.2222
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Protoporph., Kupffer	:	-	-	-	-	-	-	1	-	5	-
	p - Value/P :	-	-	-	-	-	-	0.5000	-	0.0040	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Protoporph., hepato.	:	-	-	-	-	-	-	3	-	5	-
	p - Value/P :	-	-	-	-	-	-	0.0833	-	0.0040	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Malt.cross, P. light	:	-	-	-	-	-	-	5	-	5	2
	p - Value/P :	-	-	-	-	-	-	0.0040	-	0.0040	0.2222
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Bright red, P.light	:	-	-	-	-	-	-	5	-	5	2
	p - Value/P :	-	-	-	-	-	-	0.0040	-	0.0040	0.2222
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Peripor.chro.inflam.	:	-	-	-	-	-	-	5	-	5	2
	p - Value/P :	-	-	-	-	-	-	0.0040	-	0.0040	0.2222
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Bile duct prolifer.	:	-	-	-	-	-	-	4	-	5	1
	p - Value/P :	-	-	-	-	-	-	0.0238	-	0.0040	0.5000
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Hepatocel.hypertrop.	:	-	-	-	-	-	-	2	-	3	3
	p - Value/P :	-	-	-	-	-	-	0.2222	-	0.0833	0.0833
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Fatty change	:	4	2	2	2	1	1	3	1	3	3
	p - Value/P :	-	-	0.9762	0.7381	0.9960	0.9167	0.9167	0.9167	0.9167	0.5000
	p - Value/N :	-	-	0.2619	0.7381	0.1032	0.5000	0.5000	0.5000	0.5000	0.8968
- Inflammatory foci	:	1	3	4	4	4	3	2	3	-	3
	p - Value/P :	-	-	0.1032	0.5000	0.1032	0.7381	0.5000	0.7381	-	0.7381
	p - Value/N :	-	-	0.9960	0.9167	0.9960	0.7381	0.9167	0.7381	0.5000	0.7381
- Glycogen Increase	:	-	2	-	4	1	5	1	4	-	1
	p - Value/P :	-	-	-	0.2619	0.5000	0.0833	0.5000	0.2619	-	0.9167
	p - Value/N :	-	-	-	0.9762	-	-	-	0.9762	-	0.5000
- Hematopoietic foci	:	1	2	1	2	-	-	1	2	-	1
	p - Value/P :	-	-	0.7778	0.7381	-	-	0.7778	0.7381	-	0.9167
	p - Value/N :	-	-	0.7778	0.7381	0.5000	0.2222	0.7778	0.7381	0.5000	0.5000
- No histol. correlate	:	-	-	-	-	-	-	-	-	-	1
	p - Value/P :	-	-	-	-	-	-	-	-	-	0.5000
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
SPLEEN	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Extramed.hemopoiesis	:	5	5	-	-	-	-	-	-	5	5
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Hemosiderin deposits	:	-	5	-	-	-	-	-	-	1	5
	p - Value/P :	-	-	-	-	-	-	-	-	0.5000	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-

One-Sided Exact Fisher Test; Control=01, P/N = Positiv/Negativ

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

FISHER'S EXACT TEST (ONE-SIDED) ON NON-NEOPLASTIC LESIONS
STATUS AT NECROPSY: K0

	DOSE GROUP :	01		02		03		04		05	
	SEX :	M	F	M	F	M	F	M	F	M	F
ORGAN/FINDING	NO. ANIMALS :	5	5	5	5	5	5	5	5	5	5
KIDNEYS	No.Examin :	5	5	5	-	5	-	5	-	5	5
- Hyaline droplets	:	-	-	-	-	2	-	5	-	5	-
	p - Value/P :	-	-	-	-	0.2222	-	0.0040	-	0.0040	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Tubular basophilia	:	2	2	4	-	3	-	2	-	4	-
	p - Value/P :	-	-	0.2619	-	0.5000	-	0.7381	-	0.2619	-
	p - Value/N :	-	-	0.9762	-	0.8968	-	0.7381	-	0.9762	0.2222
- Cortical mineraliz.	:	-	-	-	-	-	-	1	-	-	-
	p - Value/P :	-	-	-	-	-	-	0.5000	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Mononuclear Infiltr.	:	-	1	1	-	-	-	-	-	-	-
	p - Value/P :	-	-	0.5000	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000
- Hyaline casts	:	1	1	2	-	-	-	1	-	-	2
	p - Value/P :	-	-	0.5000	-	-	-	0.7778	-	-	0.5000
	p - Value/N :	-	-	0.9167	-	0.5000	-	0.7778	-	0.5000	0.9167
- Pelvic dilation	:	-	-	1	-	-	-	-	-	-	-
	p - Value/P :	-	-	0.5000	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Tubular dilatation	:	-	-	-	-	-	-	-	-	1	-
	p - Value/P :	-	-	-	-	-	-	-	-	0.5000	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
STOMACH	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Glandular dilation	:	-	1	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000
- Gld.Stomach Erosion	:	1	-	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	0.5000	-
- Gld.Stomach Edema	:	1	-	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	0.5000	-
- Inflamm. infiltrate	:	1	-	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	0.5000	-
- Hemorrhage	:	2	-	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	0.2222	-
PEYERS PATCHES JEJ	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Lymphoid hyperplasia	:	4	4	-	-	-	-	-	-	5	5
	p - Value/P :	-	-	-	-	-	-	-	-	0.5000	0.5000
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
PEYERS PATCHES ILE	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Lymphoid hyperplasia	:	5	5	-	-	-	-	-	-	5	4
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000

One-Sided Exact Fisher Test; Control=01, P/N = Positiv/Negativ

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

FISHER'S EXACT TEST (ONE-SIDED) ON NON-NEOPLASTIC LESIONS
STATUS AT NECROPSY: K0

	DOSE GROUP :	01		02		03		04		05	
	SEX :	M	F	M	F	M	F	M	F	M	F
ORGAN/FINDING	NO. ANIMALS :	5	5	5	5	5	5	5	5	5	5
LUNGS	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Alveolar macrophages	:	2	3	-	-	-	-	-	-	1	-
	p - Value/P :	-	-	-	-	-	-	-	-	0.9167	-
	p - Value/N :	-	-	-	-	-	-	-	-	0.5000	0.0833
- Alveolar hemorrhage	:	1	-	-	-	-	-	-	-	2	1
	p - Value/P :	-	-	-	-	-	-	-	-	0.5000	0.5000
	p - Value/N :	-	-	-	-	-	-	-	-	0.9167	-
- Vascular Mineraliz.	:	1	2	-	-	-	-	-	-	-	3
	p - Value/P :	-	-	-	-	-	-	-	-	-	0.5000
	p - Value/N :	-	-	-	-	-	-	-	-	0.5000	0.8968
- Osseous metaplasia	:	1	-	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	0.5000	-
- Microgranuloma	:	-	-	-	-	-	-	-	-	1	-
	p - Value/P :	-	-	-	-	-	-	-	-	0.5000	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
THYMUS	No.Examin :	5	5	-	1	-	-	1	-	5	5
- Cyst (s)	:	-	3	-	-	-	-	-	-	1	1
	p - Value/P :	-	-	-	-	-	-	-	-	0.5000	0.9762
	p - Value/N :	-	-	-	0.5000	-	-	-	-	-	0.2619
- Atrophy/involution	:	-	-	-	-	-	-	-	-	1	-
	p - Value/P :	-	-	-	-	-	-	-	-	0.5000	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Hemorrhage	:	-	1	-	1	-	-	1	-	-	1
	p - Value/P :	-	-	-	0.3333	-	-	0.1667	-	-	0.7778
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.7778
- No histol. correlate	:	1	-	-	-	-	-	-	-	1	-
	p - Value/P :	-	-	-	-	-	-	-	-	0.7778	-
	p - Value/N :	-	-	-	-	-	-	0.8333	-	0.7778	-
OVARIES	No.Examin :	-	5	-	-	-	-	-	-	-	5
- Cyst, corpus luteum	:	-	1	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000
MANDIB.LYMPH NODES	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Lymphoid Hyperplasia	:	-	1	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000
THYROID GLAND	No.Examin :	5	5	5	5	5	5	5	5	5	5
- Ultimobranchial Cyst	:	2	1	1	1	1	1	-	2	1	2
	p - Value/P :	-	-	0.9167	0.7778	0.9167	0.7778	-	0.5000	0.9167	0.5000
	p - Value/N :	-	-	0.5000	0.7778	0.5000	0.7778	0.2222	0.9167	0.5000	0.9167
- Follic.C.hypertrophy	:	-	-	-	-	-	-	-	-	2	1
	p - Value/P :	-	-	-	-	-	-	-	-	0.2222	0.5000
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Thymic ectopia	:	-	-	-	-	1	-	-	-	-	-
	p - Value/P :	-	-	-	-	0.5000	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
ADRENAL CORTICES	No.Examin :	5	5	5	-	5	-	5	-	5	5
- Vacuolation, Z.fasc.	:	2	-	1	-	3	-	2	-	3	-
	p - Value/P :	-	-	0.9167	-	0.5000	-	0.7381	-	0.5000	-
	p - Value/N :	-	-	0.5000	-	0.8968	-	0.7381	-	0.8968	-
- Foc.Hypertrophy/Z.F.	:	1	-	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	0.5000	-	0.5000	-	0.5000	-	0.5000	-

One-Sided Exact Fisher Test; Control=01, P/N = Positiv/Negativ

PATHOLOGY REPORT PAGE : 27/ 134
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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

FISHER'S EXACT TEST (ONE-SIDED) ON NON-NEOPLASTIC LESIONS
STATUS AT NECROPSY: K0

ORGAN/FINDING	DOSE GROUP :	01		02		03		04		05	
	SEX :	M	F	M	F	M	F	M	F	M	F
	NO. ANIMALS :	5	5	5	5	5	5	5	5	5	5
CEREBELLUM	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Hemorrhage	:	-	1	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000
UTERUS	No.Examin :	-	5	-	-	-	1	-	1	-	5
- Distended lumina	:	-	1	-	-	-	1	-	1	-	-
	p - Value/P :	-	-	-	-	-	0.3333	-	0.3333	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000
VAGINA	No.Examin :	-	5	-	-	-	-	-	-	-	5
- Cycle:Proestrus	:	-	1	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000
- Cycle:Estrus	:	-	1	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000
- Cycle:Metestrus	:	-	-	-	-	-	-	-	-	-	1
	p - Value/P :	-	-	-	-	-	-	-	-	-	0.5000
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Cycle:Diestrus	:	-	3	-	-	-	-	-	-	-	4
	p - Value/P :	-	-	-	-	-	-	-	-	-	0.5000
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.9167
- Mucification	:	-	4	-	-	-	-	-	-	-	4
	p - Value/P :	-	-	-	-	-	-	-	-	-	0.7778
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.7778
- Epidermal Cyst	:	-	1	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000
BONE MARROW, FEMUR	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Fatty replacement	:	5	4	-	-	-	-	-	-	5	5
	p - Value/P :	-	-	-	-	-	-	-	-	-	0.5000
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Incr. granulopoiesis	:	-	1	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000
BODY CAVITIES	No.Examin :	-	-	-	-	-	-	1	-	-	-
- Fat granuloma	:	-	-	-	-	-	-	1	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-

One-Sided Exact Fisher Test; Control=01, P/N = Positiv/Negativ

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

FISHER'S EXACT TEST (ONE-SIDED) ON NON-NEOPLASTIC LESIONS
STATUS AT NECROPSY: R1

DOSE GROUP :	01		02		03		04		05	
SEX :	M	F	M	F	M	F	M	F	M	F
ORGAN/FINDING NO. ANIMALS :	5	5	-	-	-	-	-	-	5	5
HEART WITH AURICLENo.Examin :	5	5	-	-	-	-	-	-	5	5
- Mononuclear foci :	1	-	-	-	-	-	-	-	-	1
p - Value/P :	-	-	-	-	-	-	-	-	-	0.5000
p - Value/N :	-	-	-	-	-	-	-	-	0.5000	-
- Valvular hemocyst :	-	-	-	-	-	-	-	-	-	1
p - Value/P :	-	-	-	-	-	-	-	-	-	0.5000
p - Value/N :	-	-	-	-	-	-	-	-	-	-
TRACHEA No.Examin :	5	5	-	-	-	-	-	-	5	5
- Mononuclear foci :	1	-	-	-	-	-	-	-	-	-
p - Value/P :	-	-	-	-	-	-	-	-	-	-
p - Value/N :	-	-	-	-	-	-	-	-	0.5000	-
- Inflamm. infiltrate :	-	1	-	-	-	-	-	-	-	-
p - Value/P :	-	-	-	-	-	-	-	-	-	-
p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000
LIVER No.Examin :	5	5	-	-	-	-	-	-	5	5
- Protoporph., bile D. :	-	-	-	-	-	-	-	-	5	4
p - Value/P :	-	-	-	-	-	-	-	-	0.0040	0.0238
p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Protoporph., Kupffer :	-	-	-	-	-	-	-	-	5	-
p - Value/P :	-	-	-	-	-	-	-	-	0.0040	-
p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Protoporph., hepato. :	-	-	-	-	-	-	-	-	5	-
p - Value/P :	-	-	-	-	-	-	-	-	0.0040	-
p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Malt.cross, P. light :	-	-	-	-	-	-	-	-	5	4
p - Value/P :	-	-	-	-	-	-	-	-	0.0040	0.0238
p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Bright red, P.light :	-	-	-	-	-	-	-	-	5	4
p - Value/P :	-	-	-	-	-	-	-	-	0.0040	0.0238
p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Peripor.chro.inflam. :	-	-	-	-	-	-	-	-	5	2
p - Value/P :	-	-	-	-	-	-	-	-	0.0040	0.2222
p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Bile duct prolifer. :	-	-	-	-	-	-	-	-	5	-
p - Value/P :	-	-	-	-	-	-	-	-	0.0040	-
p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Fatty change :	2	2	-	-	-	-	-	-	2	4
p - Value/P :	-	-	-	-	-	-	-	-	0.7381	0.2619
p - Value/N :	-	-	-	-	-	-	-	-	0.7381	0.9762
- Inflammatory foci :	2	3	-	-	-	-	-	-	2	-
p - Value/P :	-	-	-	-	-	-	-	-	0.7381	-
p - Value/N :	-	-	-	-	-	-	-	-	0.7381	0.0833
- Glycogen Increase :	-	2	-	-	-	-	-	-	-	4
p - Value/P :	-	-	-	-	-	-	-	-	-	0.2619
p - Value/N :	-	-	-	-	-	-	-	-	-	0.9762
- Hematopoietic foci :	2	-	-	-	-	-	-	-	-	-
p - Value/P :	-	-	-	-	-	-	-	-	-	-
p - Value/N :	-	-	-	-	-	-	-	-	0.2222	-
SPLEEN No.Examin :	5	5	-	-	-	-	-	-	5	5
- Extramed.hemopoiesis :	5	4	-	-	-	-	-	-	5	4
p - Value/P :	-	-	-	-	-	-	-	-	-	0.7778
p - Value/N :	-	-	-	-	-	-	-	-	-	0.7778
- Hemosiderin deposits :	2	5	-	-	-	-	-	-	1	5
p - Value/P :	-	-	-	-	-	-	-	-	0.9167	-
p - Value/N :	-	-	-	-	-	-	-	-	0.5000	-

One-Sided Exact Fisher Test; Control=01, P/N = Positiv/Negativ

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

FISHER'S EXACT TEST (ONE-SIDED) ON NON-NEOPLASTIC LESIONS
STATUS AT NECROPSY: R1

	DOSE GROUP :	01		02		03		04		05	
	SEX :	M	F	M	F	M	F	M	F	M	F
ORGAN/FINDING	NO. ANIMALS :	5	5	-	-	-	-	-	-	5	5
KIDNEYS	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Tubular basophilia	:	2	2	-	-	-	-	-	-	3	2
	p - Value/P :	-	-	-	-	-	-	-	-	0.5000	0.7381
	p - Value/N :	-	-	-	-	-	-	-	-	0.8968	0.7381
- Hyaline casts	:	-	1	-	-	-	-	-	-	-	1
	p - Value/P :	-	-	-	-	-	-	-	-	-	0.7778
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.7778
- Papillary mineraliz.	:	2	1	-	-	-	-	-	-	2	2
	p - Value/P :	-	-	-	-	-	-	-	-	0.7381	0.5000
	p - Value/N :	-	-	-	-	-	-	-	-	0.7381	0.9167
STOMACH	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Glandular dilation	:	1	-	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	0.5000	-
- Gld.Stomach Edema	:	-	-	-	-	-	-	-	-	1	-
	p - Value/P :	-	-	-	-	-	-	-	-	0.5000	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Inflamm. infiltrate	:	-	-	-	-	-	-	-	-	1	-
	p - Value/P :	-	-	-	-	-	-	-	-	0.5000	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
PEYERS PATCHES JEJ	No.Examin :	5	5	-	-	-	-	-	-	4	3
- Lymphoid hyperplasia	:	2	3	-	-	-	-	-	-	1	2
	p - Value/P :	-	-	-	-	-	-	-	-	0.8810	0.7143
	p - Value/N :	-	-	-	-	-	-	-	-	0.5952	0.8214
PEYERS PATCHES ILE	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Lymphoid hyperplasia	:	5	5	-	-	-	-	-	-	4	4
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	0.5000	0.5000
LUNGS	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Alveolar macrophages	:	1	1	-	-	-	-	-	-	1	1
	p - Value/P :	-	-	-	-	-	-	-	-	0.7778	0.7778
	p - Value/N :	-	-	-	-	-	-	-	-	0.7778	0.7778
- Alveolar hemorrhage	:	-	1	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000
- Cholesterin deposits	:	-	1	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000
- Vascular Mineraliz.	:	5	1	-	-	-	-	-	-	4	3
	p - Value/P :	-	-	-	-	-	-	-	-	-	0.2619
	p - Value/N :	-	-	-	-	-	-	-	-	0.5000	0.9762
THYMUS	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Cyst (s)	:	-	3	-	-	-	-	-	-	1	2
	p - Value/P :	-	-	-	-	-	-	-	-	0.5000	0.8968
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000
- Atrophy/involution	:	2	1	-	-	-	-	-	-	1	1
	p - Value/P :	-	-	-	-	-	-	-	-	0.9167	0.7778
	p - Value/N :	-	-	-	-	-	-	-	-	0.5000	0.7778
TESTES	No.Examin :	5	-	-	-	-	-	-	-	5	-
- Focal tubul. atrophy	:	-	-	-	-	-	-	-	-	1	-
	p - Value/P :	-	-	-	-	-	-	-	-	0.5000	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-

One-Sided Exact Fisher Test; Control=01, P/N = Positiv/Negativ

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SUMMARY TABLES Harlan Laboratories C53655

TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

FISHER'S EXACT TEST (ONE-SIDED) ON NON-NEOPLASTIC LESIONS
STATUS AT NECROPSY: R1

	DOSE GROUP :	01		02		03		04		05	
	SEX :	M	F	M	F	M	F	M	F	M	F
ORGAN/FINDING	NO. ANIMALS :	5	5	-	-	-	-	-	-	5	5
EPIDIDYMIDES	No.Examin :	5	-	-	-	-	-	-	-	5	-
- Mononuclear Infiltr.	:	2	-	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	0.2222	-
MANDIB.LYMPH NODES	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Lymphoid Hyperplasia	:	1	1	-	-	-	-	-	-	-	1
	p - Value/P :	-	-	-	-	-	-	-	-	-	0.7778
	p - Value/N :	-	-	-	-	-	-	-	-	0.5000	0.7778
THYROID GLAND	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Ultimobranchial Cyst		1	2	-	-	-	-	-	-	1	2
	p - Value/P :	-	-	-	-	-	-	-	-	0.7778	0.7381
	p - Value/N :	-	-	-	-	-	-	-	-	0.7778	0.7381
- Thymic ectopia		1	-	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	0.5000	-
ADRENAL CORTICES	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Vacuolation, Z.fasc.	:	2	-	-	-	-	-	-	-	1	-
	p - Value/P :	-	-	-	-	-	-	-	-	0.9167	-
	p - Value/N :	-	-	-	-	-	-	-	-	0.5000	-
PROSTATE GLAND	No.Examin :	5	-	-	-	-	-	-	-	5	-
- Mononuclear Infiltr.	:	-	-	-	-	-	-	-	-	1	-
	p - Value/P :	-	-	-	-	-	-	-	-	0.5000	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
UTERUS	No.Examin :	-	5	-	-	-	-	-	-	-	5
- Distended lumina	:	-	2	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.2222
VAGINA	No.Examin :	-	5	-	-	-	-	-	-	-	5
- Cycle:Proestrus	:	-	1	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000
- Cycle:Estrus	:	-	1	-	-	-	-	-	-	-	1
	p - Value/P :	-	-	-	-	-	-	-	-	-	0.7778
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.7778
- Cycle:Metestrus	:	-	-	-	-	-	-	-	-	-	2
	p - Value/P :	-	-	-	-	-	-	-	-	-	0.2222
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Cycle:Diestrus	:	-	3	-	-	-	-	-	-	-	2
	p - Value/P :	-	-	-	-	-	-	-	-	-	0.8968
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000
- Mucification	:	-	1	-	-	-	-	-	-	-	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	0.5000
BONE MARROW, FEMUR	No.Examin :	5	5	-	-	-	-	-	-	5	5
- Fatty replacement	:	5	5	-	-	-	-	-	-	5	5
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	No.Examin :	5	4	-	-	-	-	-	-	5	5
- Cyst	:	1	-	-	-	-	-	-	-	1	-
	p - Value/P :	-	-	-	-	-	-	-	-	0.7778	-
	p - Value/N :	-	-	-	-	-	-	-	-	0.7778	-

One-Sided Exact Fisher Test; Control=01, P/N = Positiv/Negativ

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

FISHER'S EXACT TEST (ONE-SIDED) ON NON-NEOPLASTIC LESIONS
STATUS AT NECROPSY: R1

	DOSE GROUP :	01		02		03		04		05	
	SEX :	M	F	M	F	M	F	M	F	M	F
ORGAN/FINDING	NO. ANIMALS :	5	5	-	-	-	-	-	-	5	5
LYMPH NODES	No.Examin :	-	-	-	-	-	-	-	-	1	-
- Erythrophagocytosis	:	-	-	-	-	-	-	-	-	1	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Congestion	:	-	-	-	-	-	-	-	-	1	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-
- Hemosiderin deposits	:	-	-	-	-	-	-	-	-	1	-
	p - Value/P :	-	-	-	-	-	-	-	-	-	-
	p - Value/N :	-	-	-	-	-	-	-	-	-	-

One-Sided Exact Fisher Test; Control=01, P/N = Positiv/Negativ

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

CORRELATION TABLE: NECROPSY - MICROSCOPY DOSE GROUP 01, MALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 1
THYMUS	
- 01: DISCOLORATION, REDDISH.	- No histological correlate.
	ANIMAL NO: 4
STOMACH	
- 01: MUCOSA, FUNDUS: FOCUS/FOCI, D= 2 MM, DARK RED.	- Glandular stomach erosion, focal, grade 1.

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CORRELATION TABLE: NECROPSY - MICROSCOPY DOSE GROUP 01, FEMALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 39
THYMUS	
- 01: FOCUS/FOCI, SEVERAL, D=2 MM, DARK RED.	- Hemorrhage, multifocal, grade 1.

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SPONSOR : SEHSC

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CORRELATION TABLE: NECROPSY - MICROSCOPY DOSE GROUP 02, MALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 15
KIDNEYS	
- 01: RIGHT SIDE: PELVIC DILATION.	- Pelvic dilation, unilateral, grade 2.

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CORRELATION TABLE: NECROPSY - MICROSCOPY DOSE GROUP 02, FEMALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 49
THYMUS	
- 01: FOCUS/FOCI, SEVERAL, D=2 MM, DARK RED.	- Hemorrhage, focal, grade 1.

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TEST SYSTEM : RAT, 28-Day, Oral (Gavage)
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CORRELATION TABLE: NECROPSY - MICROSCOPY DOSE GROUP 03, FEMALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 53
UTERUS	
- 01: BOTH HORNS: DILATION, D=7 MM.	- Distended lumina of uterine horns.

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SPONSOR : SEHSC *PathData©System V6.2b5*

CORRELATION TABLE: NECROPSY - MICROSCOPY DOSE GROUP 04, MALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 21
LIVER	
- 01: DISCOLORATION, BLACK BROWN.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.
- 02: ENLARGED.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.
THYMUS	
- 01: FOCUS/FOCI, ISOLATED, D=2 MM, DARK RED.	- Hemorrhage, multifocal, grade 1.
	ANIMAL NO: 22
LIVER	
- 01: DISCOLORATION, BLACK BROWN.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.
- 02: ENLARGED.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.
	ANIMAL NO: 23
LIVER	
- 01: ENLARGED.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 2.
- 02: DISCOLORATION, DARK BROWN.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 2.
BODY CAVITIES	
- 01: EPIDIDYMAL ADIPOSE TISSUE, LEFT SIDE: NODULE(S), D=10 MM, DARK RED.	- Fat granuloma, grade 2.

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CORRELATION TABLE: NECROPSY - MICROSCOPY DOSE GROUP 04, MALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 24
LIVER	
- 01: DISCOLORATION, BLACK BROWN.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.
- 02: ENLARGED.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.
	ANIMAL NO: 25
LIVER	
- 01: ENLARGED.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.
- 02: DISCOLORATION, BLACK BROWN.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.

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CORRELATION TABLE: NECROPSY - MICROSCOPY DOSE GROUP 04, FEMALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 59
UTERUS	
- 01: BOTH HORNS: DILATION, D=6 MM.	- Distended lumina of uterine horns.

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CORRELATION TABLE: NECROPSY - MICROSCOPY DOSE GROUP 05, MALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 26
LIVER	
- 01: ENLARGED.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3. Hepatocellular hypertrophy, grade 1.
- 02: DISCOLORATION, BLACK BROWN.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.
THYMUS	
- 01: FOCUS/FOCI, ISOLATED, D=2 MM, REDDISH.	- No histological correlate.
	ANIMAL NO: 27
LIVER	
- 01: ENLARGED.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3. Hepatocellular hypertrophy, grade 1.
- 02: DISCOLORATION, BLACK BROWN.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.
	ANIMAL NO: 28
LIVER	
- 01: DISCOLORATION, BLACK BROWN.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.

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CORRELATION TABLE: NECROPSY - MICROSCOPY DOSE GROUP 05, MALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 29
LIVER	
- 01: ENLARGED.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3. Hepatocellular hypertrophy, grade 1.
- 02: DISCOLORATION, BLACK BROWN.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3. Hepatocellular hypertrophy, grade 1.
	ANIMAL NO: 30
LIVER	
- 01: ENLARGED.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.
- 02: DISCOLORATION, BLACK BROWN.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.
	ANIMAL NO: 31
LIVER	
- 01: DISCOLORATION, BLACK BROWN.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.
LYMPH NODES	
- 01: PORTALES: ENLARGED, D=6 MM.	- Congestion, bilateral.
- 02: PORTALES: DISCOLORATION, DARK RED.	- Congestion, bilateral.

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CORRELATION TABLE: NECROPSY - MICROSCOPY DOSE GROUP 05, MALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 32
LIVER	
- 01: DISCOLORATION, BLACK BROWN.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.
	ANIMAL NO: 33
LIVER	
- 01: DISCOLORATION, BLACK BROWN.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.
	ANIMAL NO: 34
LIVER	
- 01: DISCOLORATION, BLACK BROWN.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.
	ANIMAL NO: 35
LIVER	
- 01: DISCOLORATION, BLACK BROWN.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.

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CORRELATION TABLE: NECROPSY - MICROSCOPY DOSE GROUP 05, FEMALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 61
LIVER	
- 01: DISCOLORATION, DARK BROWN.	- No histological correlate.
	ANIMAL NO: 62
LIVER	
- 01: ENLARGED.	- Hepatocellular hypertrophy, grade 1.
	ANIMAL NO: 63
LIVER	
- 01: DISCOLORATION, BLACK BROWN.	- Protoporphyrin accumulation, intrahepatic bile duct, grade 3.
- 02: ENLARGED.	- Hepatocellular hypertrophy, grade 1.

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EXPLANATION OF CODES AND SYMBOLS

CODES AND SYMBOLS USED AT ANIMAL LEVEL:

M = Male animal
F = Female animal
K0 = Terminal sacrifice group
R1...R9 = Recovery / post-treatment group 1...9

CODES AND SYMBOLS USED AT ORGAN LEVEL:

G = Gross observation checked off histologically
0 = Tissue not present for histologic examination
' = Histologic examination not required
+ = Organ examined, findings present
– = Organ examined, no pathologic findings noted (AOFT only)
(= Only one of paired organs examined/present

CODES AND SYMBOLS USED AT FINDING LEVEL:

GRADE 1 = Minimal / very few / very small
GRADE 2 = Slight / few / small
GRADE 3 = Moderate / moderate number / moderate size
P = Finding present, severity not scored
(= Finding unilateral in paired organs

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TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, 0 mg/kg

ANIMAL NUMBER :

	1	2	3	4	5	6	7	8	9	10
	MK0	MK0	MK0	MK0	MK0	MR1	MR1	MR1	MR1	MR1
HEART WITH AURICLES	–	–	–	–	–	–	–	–	+	–
– Mononuclear foci	.	.	.	.	.	.	.	.	2.	.
TRACHEA	–	–	–	+	–	–	–	–	–	+
– Mononuclear foci	.	.	.	1.	.	.	.	.	.	1.
LIVER	+	+	+	+	+	+	+	–	+	+
– Fatty change	1.	1.	1.	.	1.	.	1.	.	1.	.
– Inflammatory foci	.	.	.	1.	.	.	1.	.	.	1.
– Hematopoietic foci	.	.	.	1.	.	1.	1.	.	.	.
SPLEEN	+	+	+	+	+	+	+	+	+	+
– Extramed.hemopoiesis	1.	1.	1.	1.	1.	2.	1.	1.	2.	1.
– Hemosiderin deposits	.	.	.	.	.	1.	1.	.	.	.
MESENT. LYMPH NODE	–	–	–	–	–	–	–	–	–	–
KIDNEYS	–	–	–	+	+	–	–	–	+	+
– Tubular basophilia	.	.	.	(1.	1.	.	.	.	(1.	1.
– Hyaline casts	.	.	.	(1.	.	.	.	.	.	.
– Papillary mineraliz.	.	.	.	.	.	.	.	.	1.	(1.
URINARY BLADDER	–	–	–	–	–	–	–	–	–	–
STOMACH	–	+	+	+G	+	–	–	–	+	–
– Glandular dilation	.	.	.	.	.	.	.	.	1.	.
– Gld.Stomach Erosion	.	.	.	1.	.	.	.	.	.	.
– Gld.Stomach Edema	.	.	.	.	2.	.	.	.	.	.
– Inflamm. infiltrate	.	2.	.	.	.	.	.	.	.	.
– Hemorrhage	.	.	2.	2.	.	.	.	.	.	.
DUODENUM	–	–	–	–	–	–	–	–	–	–
JEJUNUM	–	–	–	–	–	–	–	–	–	–
PEYERS PATCHES JEJ.	+	+	+	–	+	–	+	+	–	–
– Lymphoid hyperplasia	1.	1.	1.	.	1.	.	1.	1.	.	.
ILEUM	–	–	–	–	–	–	–	–	–	–

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SPONSOR : SEHSC *PathData©System V6.2b5*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, 0 mg/kg

ANIMAL NUMBER :

	1	2	3	4	5	6	7	8	9	10
	MK0	MK0	MK0	MK0	MK0	MR1	MR1	MR1	MR1	MR1
PEYERS PATCHES ILEUM	+	+	+	+	+	+	+	+	+	+
– Lymphoid hyperplasia	1.	1.	1.	1.	1.	1.	1.	1.	1.	1.
CECUM	–	–	–	–	–	–	–	–	–	–
COLON	–	–	–	–	–	–	–	–	–	–
RECTUM	–	–	–	–	–	–	–	–	–	–
LUNGS	+	+	–	–	–	+	+	+	+	+
– Alveolar macrophages	1.	1.	.	.	.	.	.	.	1.	.
– Alveolar hemorrhage	.	1.	.	.	.	.	.	.	.	.
– Vascular Mineraliz.	1.	.	.	.	.	1.	1.	1.	1.	1.
– Osseous metaplasia	1.	.	.	.	.	.	.	.	.	.
THYMUS	+G	–	–	–	–	–	+	+	–	–
– Atrophy/involution	.	.	.	.	.	.	1.	1.	.	.
– No histol. correlate	P.	.	.	.	.	.	.	.	.	.
TESTES	–	–	–	–	–	–	–	–	–	–
EPIDIDYMIDES	–	–	–	–	–	–	+	+	–	–
– Mononuclear Infiltr.	.	.	.	.	.	.	(1.	(1.	.	.
MANDIB.LYMPH NODES	(–	(–	(–	(–	(–	(–	(–	(–	(–	(+
– Lymphoid Hyperplasia	.	.	.	.	.	.	.	.	.	(1.
THYROID GLAND	+	–	+	–	–	+	–	–	(+	–
– Ultimobranchial Cyst	(P.	.	(P.	.	.	P.	.	.	.	.
– Thymic ectopia	.	.	.	.	.	.	.	.	(P.	.
PARATHYROID GLANDS	(–	(–	(–	(–	–	(–	–	(–	(–	0
ADRENAL CORTICES	+	–	–	+	–	+	+	–	–	–
– Vacuolation, Z.fasc.	1.	.	.	1.	.	(1.	(1.	.	.	.
– Foc.Hypertrophy/Z.F.	1.	.	.	.	.	.	.	.	.	.
ADRENAL MEDULLAS	(–	–	–	(–	–	–	–	–	–	–

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SPONSOR : SEHSC *PathData©System V6.2b5*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, 0 mg/kg

ANIMAL NUMBER :

	1	2	3	4	5	6	7	8	9	10
	MK0	MK0	MK0	MK0	MK0	MR1	MR1	MR1	MR1	MR1
SCIATIC NERVE	–	–	–	–	–	–	–	–	–	–
CEREBRUM	–	–	–	–	–	–	–	–	–	–
CEREBELLUM	–	–	–	–	–	–	–	–	–	–
MEDULLA OBLONGATA	–	–	–	–	–	–	–	–	–	–
PONS	–	–	–	–	–	–	–	–	–	–
PROSTATE GLAND	–	–	–	–	–	–	–	–	–	–
SEMINAL VESICLES	–	–	–	–	–	–	–	–	–	–
COAGULATING GLANDS	–	–	–	–	–	–	–	–	–	–
BONE MARROW, FEMUR	+	+	+	+	+	+	+	+	+	+
– Fatty replacement	1.	2.	2.	2.	1.	1.	2.	2.	1.	2.
PITUITARY GLAND	–	–	–	–	–	–	–	+	–	–
– Cyst	.	.	.	.	.	.	.	P.	.	.
SPINAL CORD, CERVIC.	–	–	–	–	–	–	–	–	–	–
SPINAL CORD, THORAC.	–	–	–	–	–	–	–	–	–	–
SPINAL CORD, LUMBAR	–	–	–	–	–	–	–	–	–	–

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SPONSOR : SEHSC *PathData©System V6.2b5*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, 0 mg/kg

ANIMAL NUMBER :	36	37	38	39	40	41	42	43	44	45
	FK0	FK0	FK0	FK0	FK0	FR1	FR1	FR1	FR1	FR1
HEART WITH AURICLES	–	–	–	–	–	–	–	–	–	–
TRACHEA	–	–	–	+	–	+	–	–	–	–
– Mononuclear foci	.	.	.	1.	.	.	.	.	.	.
– Inflamm. infiltrate	.	.	.	.	.	1.	.	.	.	.
LIVER	+	+	+	+	+	+	–	+	+	+
– Fatty change	1.	.	1.	.	.	1.	.	.	1.	.
– Inflammatory foci	.	1.	1.	1.	.	1.	.	1.	1.	.
– Glycogen Increase	.	.	.	1.	1.	.	.	1.	.	1.
– Hematopoietic foci	.	.	1.	.	1.	.	.	.	.	.
SPLEEN	+	+	+	+	+	+	+	+	+	+
– Extramed.hemopoiesis	1.	2.	1.	2.	2.	1.	1.	1.	.	1.
– Hemosiderin deposits	1.	1.	1.	1.	1.	1.	1.	1.	1.	1.
MESENT. LYMPH NODE	–	–	–	–	–	–	–	–	–	–
KIDNEYS	–	+	+	+	+	+	–	+	+	–
– Tubular basophilia	.	(1.	.	(1.	.	(1.	.	(1.	.	.
– Mononuclear Infiltr.	.	.	.	.	(1.	.	.	.	.	.
– Hyaline casts	.	.	(1.	.	.	.	.	(1.	.	.
– Papillary mineraliz.	.	.	.	.	.	.	.	.	(1.	.
URINARY BLADDER	–	–	–	–	–	–	–	–	–	–
STOMACH	–	–	–	–	+	–	–	–	–	–
– Glandular dilation	.	.	.	.	1.	.	.	.	.	.
DUODENUM	–	–	–	–	–	–	–	–	–	–
JEJUNUM	–	–	–	–	–	–	–	–	–	–
PEYERS PATCHES JEJ.	+	–	+	+	+	+	–	+	–	+
– Lymphoid hyperplasia	1.	.	1.	1.	1.	1.	.	1.	.	1.
ILEUM	–	–	–	–	–	–	–	–	–	–

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, 0 mg/kg

ANIMAL NUMBER :

	36	37	38	39	40	41	42	43	44	45
	FK0	FK0	FK0	FK0	FK0	FR1	FR1	FR1	FR1	FR1
PEYERS PATCHES ILEUM	+	+	+	+	+	+	+	+	+	+
– Lymphoid hyperplasia	1.	1.	1.	1.	1.	1.	2.	1.	2.	1.
CECUM	–	–	–	–	–	–	–	–	–	–
COLON	–	–	–	–	–	–	–	–	–	–
RECTUM	–	–	–	–	–	–	–	–	–	–
LUNGS	–	+	+	–	+	–	–	–	+	+
– Alveolar macrophages	.	1.	1.	.	1.	.	.	.	1.	.
– Alveolar hemorrhage	.	.	.	.	.	.	.	.	1.	.
– Cholesterin deposits	.	.	.	.	.	.	.	.	.	1.
– Vascular Mineraliz.	.	.	1.	.	1.	.	.	.	1.	.
THYMUS	–	–	+	+G	+	+	+	–	+	–
– Cyst (s)	.	.	P.	P.	P.	P.	P.	.	P.	.
– Atrophy/involution	.	.	.	.	.	.	.	.	1.	.
– Hemorrhage	.	.	.	1.	.	.	.	.	.	.
OVARIES	–	–	+	–	–	–	–	–	–	–
– Cyst, corpus luteum	.	.	(P.	.	.	.	.	.	.	.
MANDIB.LYMPH NODES	(–	(+	(–	(–	(–	(–	(–	(–	(–	(+
– Lymphoid Hyperplasia	.	(2.	.	.	.	.	.	.	.	(1.
THYROID GLAND	–	–	–	+	–	–	+	–	–	+
– Ultimobranchial Cyst	.	.	.	(P.	.	.	(P.	.	.	(P.
PARATHYROID GLANDS	(–	(–	(–	(–	0	(–	0	(–	(–	–
ADRENAL CORTICES	–	–	–	–	–	–	–	–	–	–
ADRENAL MEDULLAS	–	–	–	–	(–	0	(–	–	–	(–
SCIATIC NERVE	–	–	–	–	–	–	–	–	–	–
CEREBRUM	–	–	–	–	–	–	–	–	–	–

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, 0 mg/kg

ANIMAL NUMBER :

	36	37	38	39	40	41	42	43	44	45
	FK0	FK0	FK0	FK0	FK0	FR1	FR1	FR1	FR1	FR1
CEREBELLUM	–	–	–	–	+	–	–	–	–	–
– Hemorrhage	.	.	.	.	1.	.	.	.	.	.
MEDULLA OBLONGATA	–	–	–	–	–	–	–	–	–	–
PONS	–	–	–	–	–	–	–	–	–	–
UTERUS	–	–	+	–	–	+	–	+	–	–
– Distended lumina	.	.	P.	.	.	P.	.	P.	.	.
CERVIX	–	–	–	–	–	–	–	–	–	–
VAGINA	+	+	+	+	+	+	+	+	+	+
– Cycle:Proestrus	.	.	P.	.	.	.	.	P.	.	.
– Cycle:Estrus	P.	.	.	.	.	P.	.	.	.	.
– Cycle:Diestrus	.	P.	.	P.	P.	.	P.	.	P.	P.
– Mucification	.	2.	3.	2.	2.	.	.	.	.	2.
– Epidermal Cyst	.	P.	.	.	.	.	.	.	.	.
BONE MARROW, FEMUR	+	+	+	+	–	+	+	+	+	+
– Fatty replacement	1.	2.	2.	2.	.	1.	1.	2.	1.	2.
– Incr. granulopoiesis	.	.	1.	.	.	.	.	.	.	.
PITUITARY GLAND	–	–	–	–	–	–	0	–	–	–
SPINAL CORD, CERVIC.	–	–	–	–	–	–	–	–	–	–
SPINAL CORD, THORAC.	–	–	–	–	–	–	–	–	–	–
SPINAL CORD, LUMBAR	–	–	–	–	–	–	–	–	–	–

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SPONSOR : SEHSC *PathData©System V6.2b5*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 02, 5 mg/kg

ANIMAL NUMBER :	11	12	13	14	15	46	47	48	49	50
	MK0	MK0	MK0	MK0	MK0	FK0	FK0	FK0	FK0	FK0
LIVER	+	+	–	+	+	+	+	+	+	+
– Fatty change	1.	1.	.	.	.	.	1.	.	1.	.
– Inflammatory foci	1.	1.	.	1.	1.	1.	1.	1.	.	1.
– Glycogen Increase	.	.	.	.	.	1.	1.	1.	1.	.
– Hematopoietic foci	.	.	.	.	1.	.	.	.	1.	1.
KIDNEYS	+	–	+	+	+G	'	'	'	'	'
– Tubular basophilia	(1.	.	(1.	(1.	(1.					
– Mononuclear Infiltr.	.	.	.	(1.	.					
– Hyaline casts	.	.	(1.	.	1.					
– Pelvic dilation	.	.	.	.	(2.					
THYMUS	'	'	'	'	'	'	'	'	+G	'
– Hemorrhage									1.	
THYROID GLAND	–	–	–	+	–	–	–	–	+	–
– Ultimobranchial Cyst	.	.	.	(P.	.	.	.	.	(P.	.
ADRENAL CORTICES	–	+	–	–	–	'	'	'	'	'
– Vacuolation, Z.fasc.	.	(1.	.	.	.					
ADRENAL MEDULLAS	–	–	–	–	–	'	'	'	'	'

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SPONSOR : SEHSC *PathData©System V6.2b5*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 03, 25 mg/kg

ANIMAL NUMBER :

	16	17	18	19	20	51	52	53	54	55
	MK0	MK0	MK0	MK0	MK0	FK0	FK0	FK0	FK0	FK0
LIVER	+	+	—	+	+	+	+	+	+	+
— Fatty change	.	.	.	1.	.	.	.	.	.	1.
— Inflammatory foci	1.	1.	.	1.	1.	1.	1.	.	1.	.
— Glycogen Increase	1.	.	.	.	.	1.	1.	1.	1.	1.
KIDNEYS	+	+	+	—	—	'	'	'	'	'
— Hyaline droplets	.	1.	1.	.	.					
— Tubular basophilia	1.	(1.	(1.	.	.					
THYROID GLAND	+	—	—	—	—	—	+	—	—	—
— Ultimobranchial Cyst	(P.	.	.	.	.	.	(P.	.	.	.
— Thymic ectopia	(P.	.	.	.	.	.	.	.	.	.
ADRENAL CORTICES	+	—	+	+	—	'	'	'	'	'
— Vacuolation, Z.fasc.	1.	.	2.	1.	.					
ADRENAL MEDULLAS	—	—	—	—	—	'	'	'	'	'
UTERUS						'	'	+G	'	'
— Distended lumina								P.		

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TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 04, 250 mg/kg

ANIMAL NUMBER :	21	22	23	24	25	56	57	58	59	60
	MK0	MK0	MK0	MK0	MK0	FK0	FK0	FK0	FK0	FK0
LIVER	+G	+G	+G	+G	+G	+	+	+	+	+
– Protoporph., bile D.	3.	3.	2.	3.	3.	.	.	.	.	.
– Protoporph., Kupffer	1.	.	.	.	.	.	.	.	.	.
– Protoporph., hepato.	1.	1.	.	.	1.	.	.	.	.	.
– Malt.cross, P. light	P.	P.	P.	P.	P.	.	.	.	.	.
– Bright red, P.light	P.	P.	P.	P.	P.	.	.	.	.	.
– Peripor.chro.inflam.	1.	1.	2.	1.	1.	.	.	.	.	.
– Bile duct prolifer.	2.	2.	.	1.	2.	.	.	.	.	.
– Hepatocel.hypertrop.	1.	1.	.	.	.	.	.	.	.	.
– Fatty change	1.	.	1.	.	1.	.	.	.	1.	.
– Inflammatory foci	1.	.	.	.	1.	1.	.	1.	.	1.
– Glycogen Increase	.	.	1.	.	.	1.	1.	.	1.	1.
– Hematopoietic foci	.	.	.	.	1.	.	.	1.	1.	.
KIDNEYS	+	+	+	+	+	'	'	'	'	'
– Hyaline droplets	1.	2.	1.	2.	2.					
– Tubular basophilia	(1.	1.	.	.	.					
– Cortical mineraliz.	.	.	.	.	(1.					
– Hyaline casts	.	(1.	.	.	.					
THYMUS	+G	'	'	'	'	'	'	'	'	'
– Hemorrhage	1.									
THYROID GLAND	–	–	–	–	–	–	–	–	+	+
– Ultimobranchial Cyst	.	.	.	.	.	.	.	.	(P.	(P.
ADRENAL CORTICES	–	+	+	–	–	'	'	'	'	'
– Vacuolation, Z.fasc.	.	1.	1.	.	.					
ADRENAL MEDULLAS	–	–	–	–	–	'	'	'	'	'
UTERUS						'	'	'	+G	'
– Distended lumina									P.	
BODY CAVITIES	'	'	+G	'	'	'	'	'	'	'
– Fat granuloma			2.							

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TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 05, 1000 mg/kg

ANIMAL NUMBER :	26	27	28	29	30	31	32	33	34	35
	MK0	MK0	MK0	MK0	MK0	MR1	MR1	MR1	MR1	MR1
HEART WITH AURICLES	–	–	–	–	–	–	–	–	–	–
TRACHEA	–	+	–	–	–	–	–	–	–	–
– Mononuclear foci	.	1.	.	.	.	.	.	.	.	.
LIVER	+G	+G	+G	+G	+G	+G	+G	+G	+G	+G
– Protoporph., bile D.	3.	3.	3.	3.	3.	3.	3.	3.	3.	3.
– Protoporph., Kupffer	2.	2.	2.	2.	2.	2.	2.	2.	1.	2.
– Protoporph., hepato.	1.	1.	1.	1.	1.	1.	1.	1.	1.	1.
– Malt.cross, P. light	P.	P.	P.	P.	P.	P.	P.	P.	P.	P.
– Bright red, P.light	P.	P.	P.	P.	P.	P.	P.	P.	P.	P.
– Peripor.chro.inflam.	1.	1.	1.	1.	1.	1.	1.	1.	1.	1.
– Bile duct prolifer.	1.	2.	2.	2.	2.	2.	2.	2.	2.	2.
– Hepatocel.hypertrop.	1.	1.	.	1.	.	.	.	.	.	.
– Fatty change	1.	.	.	1.	1.	1.	.	.	1.	.
– Inflammatory foci	.	.	.	.	.	1.	.	.	.	1.
SPLEEN	+	+	+	+	+	+	+	+	+	+
– Extramed.hemopoiesis	1.	1.	1.	2.	1.	1.	1.	1.	1.	1.
– Hemosiderin deposits	.	.	.	.	1.	.	.	1.	.	.
MESENT. LYMPH NODE	–	–	–	–	–	–	–	–	–	–
KIDNEYS	+	+	+	+	+	+	+	+	–	+
– Hyaline droplets	2.	1.	2.	2.	2.	.	.	.	.	.
– Tubular basophilia	.	1.	(1.	1.	(1.	.	1.	(1.	.	1.
– Tubular dilatation	.	.	.	1.	.	.	.	.	.	.
– Papillary mineraliz.	.	.	.	.	.	(1.	.	.	.	(1.
URINARY BLADDER	–	–	–	–	–	–	–	–	–	–
STOMACH	–	–	–	–	–	+	–	–	–	–
– Gld.Stomach Edema	.	.	.	.	.	2.	.	.	.	.
– Inflamm. infiltrate	.	.	.	.	.	1.	.	.	.	.
DUODENUM	–	–	–	–	–	–	–	–	–	–
JEJUNUM	–	–	–	–	–	–	–	–	–	–

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TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 05, 1000 mg/kg

ANIMAL NUMBER :

	26	27	28	29	30	31	32	33	34	35
	MK0	MK0	MK0	MK0	MK0	MR1	MR1	MR1	MR1	MR1
PEYERS PATCHES JEJ.	+	+	+	+	+	+	—	—	—	0
— Lymphoid hyperplasia	1.	1.	1.	1.	1.	1.	.	.	.	.
ILEUM	—	—	—	—	—	—	—	—	—	—
PEYERS PATCHES ILEUM	+	+	+	+	+	+	+	—	+	+
— Lymphoid hyperplasia	1.	1.	1.	1.	1.	1.	1.	.	1.	1.
CECUM	—	—	—	—	—	—	—	—	—	—
COLON	—	—	—	—	—	—	—	—	—	—
RECTUM	—	—	—	—	—	—	—	—	—	—
LUNGS	+	+	+	—	—	+	+	+	—	+
— Alveolar macrophages	1.	.	.	.	.	.	.	1.	.	.
— Alveolar hemorrhage	.	1.	1.	.	.	.	.	.	.	.
— Vascular Mineraliz.	.	.	.	.	.	1.	1.	1.	.	1.
— Microgranuloma	.	.	2.	.	.	.	.	.	.	.
THYMUS	+G	—	—	+	—	—	—	—	+	—
— Cyst (s)	P.	.	.	.	.	.	.	.	P.	.
— Atrophy/involution	.	.	.	1.	.	.	.	.	1.	.
— No histol. correlate	P.	.	.	.	.	.	.	.	.	.
TESTES	—	—	—	—	—	+	—	—	—	—
— Focal tubul. atrophy	.	.	.	.	.	(1.	.	.	.	.
EPIDIDYMIDES	—	—	—	—	—	—	—	—	—	—
MANDIB.LYMPH NODES	(—	(—	(—	(—	(—	(—	(—	(—	(—	(—
THYROID GLAND	—	+	—	+	+	—	+	—	—	—
— Ultimobranchial Cyst	.	(P.	.	.	.	.	(P.	.	.	.
— Follic.C.hypertrophy	.	.	.	1.	1.	.	.	.	.	.
PARATHYROID GLANDS	—	0	—	—	0	—	(—	—	(—	(—

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TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 05, 1000 mg/kg

ANIMAL NUMBER :	26	27	28	29	30	31	32	33	34	35
	MK0	MK0	MK0	MK0	MK0	MR1	MR1	MR1	MR1	MR1
ADRENAL CORTICES	–	+	–	+	+	–	+	–	–	–
– Vacuolation, Z.fasc.	.	(1.	.	2.	2.	.	2.	.	.	.
ADRENAL MEDULLAS	–	–	–	(–	–	–	–	–	–	–
SCIATIC NERVE	–	–	–	–	–	–	–	–	–	–
CEREBRUM	–	–	–	–	–	–	–	–	–	–
CEREBELLUM	–	–	–	–	–	–	–	–	–	–
MEDULLA OBLONGATA	–	–	–	–	–	–	–	–	–	–
PONS	–	–	–	–	–	–	–	–	–	–
PROSTATE GLAND	–	–	–	–	–	–	–	–	+	–
– Mononuclear Infiltr.	.	.	.	.	.	.	.	.	1.	.
SEMINAL VESICLES	–	–	–	–	–	–	–	–	–	–
COAGULATING GLANDS	–	–	–	–	–	–	–	–	–	–
BONE MARROW, FEMUR	+	+	+	+	+	+	+	+	+	+
– Fatty replacement	2.	2.	2.	1.	1.	2.	2.	2.	2.	1.
PITUITARY GLAND	–	–	–	–	–	–	–	–	–	+
– Cyst	.	.	.	.	.	.	.	.	.	P.
SPINAL CORD, CERVIC.	–	–	–	–	–	–	–	–	–	–
SPINAL CORD, THORAC.	–	–	–	–	–	–	–	–	–	–
SPINAL CORD, LUMBAR	–	–	–	–	–	–	–	–	–	–
LYMPH NODES	'	'	'	'	'	+G	'	'	'	'
– Erythrophagocytosis						2.				
– Congestion						P.				
– Hemosiderin deposits						2.				

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SPONSOR : SEHSC *PathData©System V6.2b5*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 05, 1000 mg/kg

ANIMAL NUMBER :

	61	62	63	64	65	66	67	68	69	70
	FK0	FK0	FK0	FK0	FK0	FR1	FR1	FR1	FR1	FR1
HEART WITH AURICLES	–	–	–	–	+	–	–	–	+	–
– Mononuclear foci	.	.	.	.	1.	.	.	.	1.	.
– Valvular hemocyst	.	.	.	.	.	.	.	.	2.	.
TRACHEA	–	+	–	–	–	–	–	–	–	–
– Mononuclear foci	.	1.	.	.	.	.	.	.	.	.
LIVER	+G	+G	+G	+	+	+	+	+	+	+
– Protoporph., bile D.	.	.	3.	.	1.	2.	.	1.	2.	1.
– Malt.cross, P. light	.	.	P.	.	P.	P.	.	P.	P.	P.
– Bright red, P.light	.	.	P.	.	P.	P.	.	P.	P.	P.
– Peripor.chro.inflam.	.	.	1.	.	1.	1.	.	.	1.	.
– Bile duct prolifer.	.	.	1.	.	.	.	.	.	.	.
– Hepatocel.hypertrop.	.	1.	1.	.	1.	.	.	.	.	.
– Fatty change	1.	2.	.	1.	.	1.	1.	.	1.	1.
– Inflammatory foci	1.	1.	1.	.	.	.	.	.	.	.
– Glycogen Increase	.	.	.	.	1.	.	1.	1.	1.	1.
– Hematopoietic foci	1.	.	.	.	.	.	.	.	.	.
– No histol. correlate	P.	.	.	.	.	.	.	.	.	.
SPLEEN	+	+	+	+	+	+	+	+	+	+
– Extramed.hemopoiesis	1.	2.	2.	2.	1.	1.	1.	1.	1.	.
– Hemosiderin deposits	1.	1.	1.	1.	1.	1.	2.	1.	1.	1.
MESENT. LYMPH NODE	–	–	–	–	–	–	–	–	–	–
KIDNEYS	+	+	–	–	–	+	–	–	+	+
– Tubular basophilia	.	.	.	.	.	(1.	.	.	(1.	.
– Hyaline casts	(1.	1.	.	.	.	.	.	.	.	(1.
– Papillary mineraliz.	.	.	.	.	.	.	.	.	(1.	(1.
URINARY BLADDER	–	–	–	–	–	–	–	–	–	–
STOMACH	–	–	–	–	–	–	–	–	–	–
DUODENUM	–	–	–	–	–	–	–	–	–	–
JEJUNUM	–	–	–	–	–	–	–	–	–	–

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TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 05, 1000 mg/kg

ANIMAL NUMBER :

	61	62	63	64	65	66	67	68	69	70
	FK0	FK0	FK0	FK0	FK0	FR1	FR1	FR1	FR1	FR1
PEYERS PATCHES JEJ.	+	+	+	+	+	0	0	–	+	+
– Lymphoid hyperplasia	1.	1.	1.	1.	1.	.	.	.	1.	1.
ILEUM	–	–	–	–	–	–	–	–	–	–
PEYERS PATCHES ILEUM	–	+	+	+	+	+	–	+	+	+
– Lymphoid hyperplasia	.	1.	1.	1.	1.	1.	.	1.	1.	1.
CECUM	–	–	–	–	–	–	–	–	–	–
COLON	–	–	–	–	–	–	–	–	–	–
RECTUM	–	–	–	–	–	–	–	–	–	–
LUNGS	+	+	–	–	+	+	–	+	+	+
– Alveolar macrophages	.	.	.	.	.	.	.	.	.	1.
– Alveolar hemorrhage	1.	.	.	.	.	.	.	.	.	.
– Vascular Mineraliz.	1.	1.	.	.	1.	1.	.	1.	1.	.
THYMUS	–	–	–	+	+	+	+	–	+	–
– Cyst (s)	.	.	.	.	P.	.	P.	.	P.	.
– Atrophy/involution	.	.	.	.	.	1.	.	.	.	.
– Hemorrhage	.	.	.	1.	.	.	.	.	.	.
OVARIES	–	–	–	–	–	–	–	–	–	–
MANDIB.LYMPH NODES	(–	(–	(–	(–	(–	(–	(+	(–	(–	(–
– Lymphoid Hyperplasia	.	.	.	.	.	.	(1.	.	.	.
THYROID GLAND	–	–	+	+	+	–	+	+	–	(–
– Ultimobranchial Cyst	.	.	P.	.	(P.	.	(P.	(P.	.	.
– Follic.C.hypertrophy	.	.	.	(1.	.	.	.	.	.	.
PARATHYROID GLANDS	(–	0	(–	(–	0	(–	(–	(–	0	(–
ADRENAL CORTICES	–	–	–	–	–	–	–	–	–	–
ADRENAL MEDULLAS	–	–	–	–	–	–	–	–	–	–

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 05, 1000 mg/kg

ANIMAL NUMBER :	61	62	63	64	65	66	67	68	69	70
	FK0	FK0	FK0	FK0	FK0	FR1	FR1	FR1	FR1	FR1
SCIATIC NERVE	–	–	–	–	–	–	–	–	–	–
CEREBRUM	–	–	–	–	–	–	–	–	–	–
CEREBELLUM	–	–	–	–	–	–	–	–	–	–
MEDULLA OBLONGATA	–	–	–	–	–	–	–	–	–	–
PONS	–	–	–	–	–	–	–	–	–	–
UTERUS	–	–	–	–	–	–	–	–	–	–
CERVIX	–	–	–	–	–	–	–	–	–	–
VAGINA	+	+	+	+	+	+	+	+	+	+
– Cycle:Estrus	.	.	.	.	.	.	.	.	.	P.
– Cycle:Metestrus	.	P.	.	.	.	P.	.	.	P.	.
– Cycle:Diestrus	P.	.	P.	P.	P.	.	P.	P.	.	.
– Mucification	2.	.	1.	2.	1.	.	.	.	.	.
BONE MARROW, FEMUR	+	+	+	+	+	+	+	+	+	+
– Fatty replacement	1.	1.	2.	2.	2.	2.	1.	2.	1.	1.
PITUITARY GLAND	–	–	–	–	–	–	–	–	–	–
SPINAL CORD, CERVIC.	–	–	–	–	–	–	–	–	–	–
SPINAL CORD, THORAC.	–	–	–	–	–	–	–	–	–	–
SPINAL CORD, LUMBAR	–	–	–	–	–	–	–	–	–	–

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SPONSOR : SEHSC *PathData©System V6.2b5*

ANIMAL HEADING DATA
DOSE GROUP : 01, 0 mg/kg

ANIMAL NUMBER	SEX M/F	DEFINED AND FINAL STATE OF NECROPSY		TEST DAYS	FIRST AND LAST DAY UNDER TEST		DATE OF NECROPSY
1	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
2	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
3	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
4	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
5	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
6	M	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
7	M	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
8	M	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
9	M	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
10	M	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
36	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
37	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
38	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
39	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
40	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
41	F	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
42	F	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
43	F	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
44	F	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
45	F	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 1

* NECROPSY FINDINGS

THYMUS:
01: DISCOLORATION, REDDISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Alveolar macrophages, focal/multifocal, grade 1
-Vascular mineralization, focal, grade 1
-Osseous metaplasia, grade 1
THYMUS:
-No histological correlate
This finding corresponds to necropsy observation no: 01.
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, single, unilateral
PARATHYROID GLANDS:
Only one of paired organs examined/present
ADRENAL CORTICES:
-Vacuolation, Zona fasciculata, bilateral, grade 1
-Focal hypertrophy (z.fasciculata), multiple, bilateral, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg MALE

CONT./FF. ANIMAL NO. : 1

ADRENAL MEDULLAS:
Only one of paired organs examined/present
BONE MARROW (FEMUR):
-Fatty replacement, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 2

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
STOMACH:
-Inflammatory cell infiltrate, submucosa, grade 2
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Alveolar macrophages, focal/multifocal, grade 1
-Alveolar hemorrhage, focal/multifocal, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg MALE

CONT./FF. ANIMAL NO. : 2

PARATHYROID GLANDS:
Only one of paired organs examined/present
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 3

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
STOMACH:
-Hemorrhage, focal, grade 2
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, single, unilateral
PARATHYROID GLANDS:
Only one of paired organs examined/present

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg MALE

CONT./FF. ANIMAL NO. : 3

BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 4

* NECROPSY FINDINGS

STOMACH:
01: MUCOSA, FUNDUS: FOCUS/FOCI, D=2 MM, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

TRACHEA:
-Mononuclear cell foci, grade 1
LIVER:
-Inflammatory cell foci, grade 1
-Hematopoietic foci, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
-Hyaline casts, unilateral, grade 1
STOMACH:
-Glandular stomach erosion, focal, grade 1
This finding corresponds to necropsy observation no: 01.
-Hemorrhage, focal, grade 2
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg MALE

CONT./FF. ANIMAL NO. : 4

MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
PARATHYROID GLANDS:
Only one of paired organs examined/present
ADRENAL CORTICES:
-Vacuolation, Zona fasciculata, bilateral, grade 1
ADRENAL MEDULLAS:
Only one of paired organs examined/present
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 5

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
KIDNEYS:
-Tubular basophilia, bilateral, grade 1
STOMACH:
-Glandular stomach edema, submucosal, grade 2
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg MALE

CONT./FF. ANIMAL NO. : 5

PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
BONE MARROW (FEMUR):
-Fatty replacement, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 6

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Hematopoietic foci, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 2
-Hemosiderin deposits, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Vascular mineralization, focal, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, bilateral

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg MALE

CONT./FF. ANIMAL NO. : 6

PARATHYROID GLANDS:
Only one of paired organs examined/present
ADRENAL CORTICES:
-Vacuolation, Zona fasciculata, unilateral, grade 1
BONE MARROW (FEMUR):
-Fatty replacement, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 7

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
-Inflammatory cell foci, grade 1
-Hematopoietic foci, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
-Hemosiderin deposits, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Vascular mineralization, focal, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg MALE

CONT./FF. ANIMAL NO. : 7

THYMUS:
-Atrophy/involution, grade 1
EPIDIDYMIDES:
-Mononuclear infiltration, focal, unilateral, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
ADRENAL CORTICES:
-Vacuolation, Zona fasciculata, focal, unilateral, grade 1
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 8

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

SPLEEN:
-Extramedullary hemopoiesis, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Vascular mineralization, focal, grade 1
THYMUS:
-Atrophy/involution, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
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SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg MALE

CONT./FF. ANIMAL NO. : 8

EPIDIDYMIDES:
-Mononuclear infiltration, focal, unilateral, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
PARATHYROID GLANDS:
Only one of paired organs examined/present
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
PITUITARY GLAND:
-Cyst, single, pars distalis
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 9

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

HEART WITH AURICLES:
-Mononuclear cell foci, grade 2
LIVER:
-Fatty change, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 2
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
-Papillary mineralization, focal/multifocal, bilateral, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg MALE

CONT./FF. ANIMAL NO. : 9

STOMACH:
-Mucosal gland dilation, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Alveolar macrophages, focal/multifocal, grade 1
-Vascular mineralization, focal, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
-Thymic ectopia, unilateral
PARATHYROID GLANDS:
Only one of paired organs examined/present
BONE MARROW (FEMUR):
-Fatty replacement, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 10

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TRACHEA:
-Mononuclear cell foci, grade 1
LIVER:
-Inflammatory cell foci, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg MALE

CONT./FF. ANIMAL NO. : 10

SPLEEN:
-Extramedullary hemopoiesis, grade 1
KIDNEYS:
-Tubular basophilia, bilateral, grade 1
-Papillary mineralization, focal/multifocal, unilateral, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Vascular mineralization, focal, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
-Lymphoid hyperplasia, unilateral, grade 1
PARATHYROID GLANDS:
Tissue not present for histologic examination
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 36

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* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
-Hemosiderin deposits, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
PARATHYROID GLANDS:
Only one of paired organs examined/present
VAGINA:
-Estrus phase of the estrous cycle
BONE MARROW (FEMUR):
-Fatty replacement, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
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SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 37

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 2
-Hemosiderin deposits, grade 1
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Alveolar macrophages, focal/multifocal, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
-Lymphoid hyperplasia, unilateral, grade 2
PARATHYROID GLANDS:
Only one of paired organs examined/present
VAGINA:
-Diestrus phase of the estrous cycle
-Mucification, grade 2
-Epidermal cyst, single
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
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SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 38

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* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
-Inflammatory cell foci, grade 1
-Hematopoietic foci, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
-Hemosiderin deposits, grade 1
KIDNEYS:
-Hyaline casts, unilateral, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Alveolar macrophages, focal/multifocal, grade 1
-Vascular mineralization, focal, grade 1
THYMUS:
-Cyst (s)
OVARIES:
-Cyst, corpus luteum, unilateral
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
PARATHYROID GLANDS:
Only one of paired organs examined/present
UTERUS:
-Distended lumina of uterine horns
VAGINA:
-Proestrus phase of the estrous cycle
-Mucification, grade 3

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.:* 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 38

BONE MARROW (FEMUR):
-Fatty replacement, grade 2
-Increased granulopoiesis, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 39

* NECROPSY FINDINGS

THYMUS:
01: FOCUS/FOCI, SEVERAL, D=2 MM, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

TRACHEA:
-Mononuclear cell foci, grade 1
LIVER:
-Inflammatory cell foci, grade 1
-Increased hepatocytic glycogen deposits, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 2
-Hemosiderin deposits, grade 1
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 39

THYMUS:
-Cyst (s)
-Hemorrhage, multifocal, grade 1
This finding corresponds to necropsy observation no: 01.
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, single, unilateral
PARATHYROID GLANDS:
Only one of paired organs examined/present
VAGINA:
-Diestrus phase of the estrous cycle
-Mucification, grade 2
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 40

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Increased hepatocytic glycogen deposits, grade 1
-Hematopoietic foci, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 2
-Hemosiderin deposits, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 40

KIDNEYS:
-Mononuclear infiltration, focal, unilateral, grade 1
STOMACH:
-Mucosal gland dilation, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Alveolar macrophages, focal/multifocal, grade 1
-Vascular mineralization, focal, grade 1
THYMUS:
-Cyst (s)
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
PARATHYROID GLANDS:
Tissue not present for histologic examination
ADRENAL MEDULLAS:
Only one of paired organs examined/present
CEREBELLUM:
-Hemorrhage, focal, grade 1
VAGINA:
-Diestrus phase of the estrous cycle
-Mucification, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg FEMALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 41

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* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TRACHEA:
-Inflammatory cell infiltrate, submucosa, grade 1
LIVER:
-Fatty change, grade 1
-Inflammatory cell foci, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
-Hemosiderin deposits, grade 1
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
THYMUS:
-Cyst (s)
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
PARATHYROID GLANDS:
Only one of paired organs examined/present
ADRENAL MEDULLAS:
Tissue not present for histologic examination
UTERUS:
-Distended lumina of uterine horns
VAGINA:
-Estrus phase of the estrous cycle
BONE MARROW (FEMUR):
-Fatty replacement, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 41

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 42

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

SPLEEN:
-Extramedullary hemopoiesis, grade 1
-Hemosiderin deposits, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 2
THYMUS:
-Cyst (s)
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, unilateral
PARATHYROID GLANDS:
Tissue not present for histologic examination
ADRENAL MEDULLAS:
Only one of paired organs examined/present
VAGINA:
-Diestrus phase of the estrous cycle
BONE MARROW (FEMUR):
-Fatty replacement, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 42

PITUITARY GLAND:
Tissue not present for histologic examination
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 43

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Increased hepatocytic glycogen deposits, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
-Hemosiderin deposits, grade 1
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
-Hyaline casts, unilateral, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
PARATHYROID GLANDS:
Only one of paired organs examined/present

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 43

UTERUS:
-Distended lumina of uterine horns
VAGINA:
-Proestrus phase of the estrous cycle
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 44

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
-Inflammatory cell foci, grade 1
SPLEEN:
-Hemosiderin deposits, grade 1
KIDNEYS:
-Papillary mineralization, focal/multifocal, unilateral, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 2
LUNGS:
-Alveolar macrophages, focal/multifocal, grade 1
-Alveolar hemorrhage, focal/multifocal, grade 1
-Vascular mineralization, focal, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 44

THYMUS:
-Cyst (s)
-Atrophy/involution, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
PARATHYROID GLANDS:
Only one of paired organs examined/present
VAGINA:
-Diestrus phase of the estrous cycle
BONE MARROW (FEMUR):
-Fatty replacement, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 45

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Increased hepatocytic glycogen deposits, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
-Hemosiderin deposits, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, 0 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 45

LUNGS:
-Cholesterin crystal deposits, focal, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
-Lymphoid hyperplasia, unilateral, grade 1
THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, unilateral
ADRENAL MEDULLAS:
Only one of paired organs examined/present
VAGINA:
-Diestrus phase of the estrous cycle
-Mucification, grade 2
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

ANIMAL HEADING DATA
DOSE GROUP : 02, 5 mg/kg

ANIMAL NUMBER	SEX M/F	DEFINED AND FINAL STATE OF NECROPSY		TEST DAYS	FIRST AND LAST DAY UNDER TEST		DATE OF NECROPSY
11	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
12	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
13	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
14	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
15	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
46	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
47	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
48	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
49	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
50	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 5 mg/kg MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 11

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
-Inflammatory cell foci, grade 1
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 12

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
-Inflammatory cell foci, grade 1
ADRENAL CORTICES:
-Vacuolation, Zona fasciculata, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 5 mg/kg MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 13

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:
-Tubular basophilia, unilateral, grade 1
-Hyaline casts, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 14

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
-Mononuclear infiltration, focal, unilateral, grade 1
THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, single, unilateral
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 5 mg/kg MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 15

* NECROPSY FINDINGS

KIDNEYS:
01: RIGHT SIDE: PELVIC DILATION.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Hematopoietic foci, grade 1
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
-Hyaline casts, bilateral, grade 1
-Pelvic dilation, unilateral, grade 2
This finding corresponds to necropsy observation no: 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 5 mg/kg FEMALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 28 * ANIMAL NO. : 46

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Increased hepatocytic glycogen deposits, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: KO
DAYS ON TEST : 28 * ANIMAL NO. : 47

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
-Inflammatory cell foci, grade 1
-Increased hepatocytic glycogen deposits, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 5 mg/kg FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 48

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Increased hepatocytic glycogen deposits, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 49

* NECROPSY FINDINGS

THYMUS:
01: FOCUS/FOCI, SEVERAL, D=2 MM, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
-Increased hepatocytic glycogen deposits, grade 1
-Hematopoietic foci, grade 1
THYMUS:
-Hemorrhage, focal, grade 1
This finding corresponds to necropsy observation no: 01.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 5 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 49

THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, single, unilateral

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 50

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Hematopoietic foci, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

ANIMAL HEADING DATA
DOSE GROUP : 03, 25 mg/kg

ANIMAL NUMBER	SEX M/F	DEFINED AND FINAL STATE OF NECROPSY		TEST DAYS	FIRST AND LAST DAY UNDER TEST		DATE OF NECROPSY
16	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
17	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
18	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
19	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
20	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
51	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
52	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
53	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
54	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
55	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.:* 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 25 mg/kg MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 16

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Increased hepatocytic glycogen deposits, grade 1
KIDNEYS:
-Tubular basophilia, bilateral, grade 1
THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, single, unilateral
-Thymic ectopia, unilateral
ADRENAL CORTICES:
-Vacuolation, Zona fasciculata, bilateral, grade 1
ADRENAL MEDULLAS:
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 17

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 25 mg/kg MALE

CONT./FF. ANIMAL NO. : 17

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
KIDNEYS:
-Hyaline droplets, bilateral, grade 1
-Tubular basophilia, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 18

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:
-Hyaline droplets, bilateral, grade 1
-Tubular basophilia, unilateral, grade 1
ADRENAL CORTICES:
-Vacuolation, Zona fasciculata, bilateral, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 25 mg/kg MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 19

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
-Inflammatory cell foci, grade 1
ADRENAL CORTICES:
-Vacuolation, Zona fasciculata, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 20

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 25 mg/kg FEMALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 28 * ANIMAL NO. : 51

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Increased hepatocytic glycogen deposits, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: KO
DAYS ON TEST : 28 * ANIMAL NO. : 52

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Increased hepatocytic glycogen deposits, grade 1
THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, single, unilateral

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.:* 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 25 mg/kg FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 53

* NECROPSY FINDINGS

UTERUS:
01: BOTH HORNS: DILATION, D=7 MM.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Increased hepatocytic glycogen deposits, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted
UTERUS:
-Distended lumina of uterine horns
This finding corresponds to necropsy observation no: 01.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 54

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Increased hepatocytic glycogen deposits, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 25 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 54

THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 55

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
-Increased hepatocytic glycogen deposits, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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INDIVIDUAL ANIMAL DATA Harlan Laboratories C53655

TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

ANIMAL HEADING DATA
DOSE GROUP : 04, 250 mg/kg

ANIMAL NUMBER	SEX M/F	DEFINED AND FINAL STATE OF NECROPSY		TEST DAYS	FIRST AND LAST DAY UNDER TEST		DATE OF NECROPSY
21	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
22	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
23	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
24	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
25	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
56	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
57	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
58	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
59	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
60	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 250 mg/kg MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 21

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* NECROPSY FINDINGS

LIVER:
01: DISCOLORATION, BLACK BROWN.
02: ENLARGED.
THYMUS:
01: FOCUS/FOCI, ISOLATED, D=2 MM, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 3
This finding corresponds to necropsy observations nos: 01,02.
-Protoporphyrin accumulation, Kupffer cells, grade 1
-Protoporphyrin accumulation, hepatocyte, grade 1
-Maltese cross under polarized light
-Bright red (birefringent), under polarized light
-Periportal chronic inflammation, grade 1
-Bile duct proliferation, bile duct, grade 2
-Hepatocellular hypertrophy, centrilobular, grade 1
-Fatty change, grade 1
-Inflammatory cell foci, grade 1
KIDNEYS:
-Hyaline droplets, bilateral, grade 1
-Tubular basophilia, unilateral, grade 1
THYMUS:
-Hemorrhage, multifocal, grade 1
This finding corresponds to necropsy observation no: 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 250 mg/kg MALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 28 * ANIMAL NO. : 22

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* NECROPSY FINDINGS

LIVER:
01: DISCOLORATION, BLACK BROWN.
02: ENLARGED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 3
This finding corresponds to necropsy observations nos: 01,02.
-Protoporphyrin accumulation, hepatocyte, grade 1
-Maltese cross under polarized light
-Bright red (birefringent), under polarized light
-Periportal chronic inflammation, grade 1
-Bile duct proliferation, bile duct, grade 2
-Hepatocellular hypertrophy, centrilobular, grade 1
KIDNEYS:
-Hyaline droplets, bilateral, grade 2
-Tubular basophilia, bilateral, grade 1
-Hyaline casts, unilateral, grade 1
ADRENAL CORTICES:
-Vacuolation, Zona fasciculata, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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INDIVIDUAL ANIMAL DATA Harlan Laboratories C53655

TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 250 mg/kg MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 23

* NECROPSY FINDINGS

LIVER:
01: ENLARGED.
02: DISCOLORATION, DARK BROWN.
BODY CAVITIES:
01: EPIDIDYMAL ADIPOSE TISSUE, LEFT SIDE: NODULE(S), D=10 MM, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 2
This finding corresponds to necropsy observations nos: 01,02.
-Maltese cross under polarized light
-Bright red (birefringent), under polarized light
-Periportal chronic inflammation, grade 2
-Fatty change, grade 1
-Increased hepatocytic glycogen deposits, grade 1
KIDNEYS:
-Hyaline droplets, bilateral, grade 1
ADRENAL CORTICES:
-Vacuolation, Zona fasciculata, bilateral, grade 1
BODY CAVITIES:
-Fat granuloma, grade 2
This finding corresponds to necropsy observation no: 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.:* 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 250 mg/kg MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 24

* NECROPSY FINDINGS

LIVER:
01: DISCOLORATION, BLACK BROWN.
02: ENLARGED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 3
This finding corresponds to necropsy observations nos: 01,02.
-Maltese cross under polarized light
-Bright red (birefringent), under polarized light
-Periportal chronic inflammation, grade 1
-Bile duct proliferation, bile duct, grade 1
KIDNEYS:
-Hyaline droplets, bilateral, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 25

* NECROPSY FINDINGS

LIVER:
01: ENLARGED.
02: DISCOLORATION, BLACK BROWN.
NO OTHER NECROPSY OBSERVATIONS NOTED

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 250 mg/kg MALE

CONT./FF. ANIMAL NO. : 25

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* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 3
This finding corresponds to necropsy observations nos: 01,02.
-Protoporphyrin accumulation, hepatocyte, grade 1
-Maltese cross under polarized light
-Bright red (birefringent), under polarized light
-Periportal chronic inflammation, grade 1
-Bile duct proliferation, bile duct, grade 2
-Fatty change, grade 1
-Inflammatory cell foci, grade 1
-Hematopoietic foci, grade 1
KIDNEYS:
-Hyaline droplets, bilateral, grade 2
-Cortical mineralization, focal/multifocal, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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INDIVIDUAL ANIMAL DATA Harlan Laboratories C53655

TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 250 mg/kg FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 56

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Increased hepatocytic glycogen deposits, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 57

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Increased hepatocytic glycogen deposits, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 250 mg/kg FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 58

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Hematopoietic foci, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 59

* NECROPSY FINDINGS

UTERUS:
01: BOTH HORNS: DILATION, D=6 MM.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
-Increased hepatocytic glycogen deposits, grade 1
-Hematopoietic foci, grade 1
THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, single, unilateral

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 250 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 59

UTERUS:
-Distended lumina of uterine horns
This finding corresponds to necropsy observation no: 01.

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 60

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Increased hepatocytic glycogen deposits, grade 1
THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, single, unilateral

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INDIVIDUAL ANIMAL DATA Harlan Laboratories C53655

TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

ANIMAL HEADING DATA
DOSE GROUP : 05, 1000 mg/kg

ANIMAL NUMBER	SEX M/F	DEFINED AND FINAL STATE OF NECROPSY		TEST DAYS	FIRST AND LAST DAY UNDER TEST		DATE OF NECROPSY
26	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
27	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
28	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
29	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
30	M	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
31	M	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
32	M	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
33	M	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
34	M	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
35	M	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
61	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
62	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
63	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
64	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
65	F	K0	K0	28	23-DEC-09	19-JAN-10	20-JAN-10
66	F	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
67	F	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
68	F	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
69	F	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10
70	F	R1	R1	28	23-DEC-09	19-JAN-10	03-FEB-10

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg MALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 28 * ANIMAL NO. : 26

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* NECROPSY FINDINGS

LIVER:
01: ENLARGED.
02: DISCOLORATION, BLACK BROWN.
THYMUS:
01: FOCUS/FOCI, ISOLATED, D=2 MM, REDDISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 3
This finding corresponds to necropsy observations nos: 01,02.
-Protoporphyrin accumulation, Kupffer cells, grade 2
-Protoporphyrin accumulation, hepatocyte, grade 1
-Maltese cross under polarized light
-Bright red (birefringent)
-Periportal chronic inflammation, grade 1
-Bile duct proliferation, bile duct, grade 1
-Hepatocellular hypertrophy, grade 1
This finding corresponds to necropsy observation no: 01.
-Fatty change, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
KIDNEYS:
-Hyaline droplets, bilateral, grade 2
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Alveolar macrophages, focal/multifocal, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg MALE

CONT./FF. ANIMAL NO. : 26

THYMUS:
-Cyst (s)
-No histological correlate
This finding corresponds to necropsy observation no: 01.
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: KO
DAYS ON TEST : 28 * ANIMAL NO. : 27

* NECROPSY FINDINGS

LIVER:
01: ENLARGED.
02: DISCOLORATION, BLACK BROWN.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

TRACHEA:
-Mononuclear cell foci, grade 1
LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 3
This finding corresponds to necropsy observations nos: 01,02.
-Protoporphyrin accumulation, Kupffer cells, grade 2
-Protoporphyrin accumulation, hepatocyte, grade 1
-Maltese cross under polarized light
-Bright red (birefringent)
-Periportal chronic inflammation, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg MALE

CONT./FF. ANIMAL NO. : 27

-Bile duct proliferation, bile duct, grade 2
-Hepatocellular hypertrophy, grade 1
This finding corresponds to necropsy observation no: 01.
SPLEEN:
-Extramedullary hemopoiesis, grade 1
KIDNEYS:
-Hyaline droplets, bilateral, grade 1
-Tubular basophilia, bilateral, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Alveolar hemorrhage, focal/multifocal, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, single, unilateral
PARATHYROID GLANDS:
Tissue not present for histologic examination
ADRENAL CORTICES:
-Vacuolation, Zona fasciculata, unilateral, grade 1
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg MALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 28 * ANIMAL NO. : 28

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* NECROPSY FINDINGS

LIVER:
01: DISCOLORATION, BLACK BROWN.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 3
This finding corresponds to necropsy observation no: 01.
-Protoporphyrin accumulation, Kupffer cells, grade 2
-Protoporphyrin accumulation, hepatocyte, grade 1
-Maltese cross under polarized light
-Bright red (birefringent)
-Periportal chronic inflammation, grade 1
-Bile duct proliferation, bile duct, grade 2
SPLEEN:
-Extramedullary hemopoiesis, grade 1
KIDNEYS:
-Hyaline droplets, bilateral, grade 2
-Tubular basophilia, unilateral, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Alveolar hemorrhage, focal/multifocal, grade 1
-Microgranuloma, single, grade 2
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
BONE MARROW (FEMUR):
-Fatty replacement, grade 2

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg MALE

CONT./FF. ANIMAL NO. : 28

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 29

* NECROPSY FINDINGS

LIVER:
01: ENLARGED.
02: DISCOLORATION, BLACK BROWN.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 3
This finding corresponds to necropsy observations nos: 01,02.
-Protoporphyrin accumulation, Kupffer cells, grade 2
-Protoporphyrin accumulation, hepatocyte, grade 1
-Maltese cross under polarized light
-Bright red (birefringent)
-Periportal chronic inflammation, grade 1
-Bile duct proliferation, bile duct, grade 2
-Hepatocellular hypertrophy, grade 1
This finding corresponds to necropsy observations nos: 01,02.
-Fatty change, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 2
KIDNEYS:
-Hyaline droplets, bilateral, grade 2
-Tubular basophilia, bilateral, grade 1
-Tubular simple dilation, bilateral, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg MALE

CONT./FF. ANIMAL NO. : 29

PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
THYMUS:
-Atrophy/involution, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
THYROID GLAND (BOTH LOBES):
-Follicular cell hypertrophy, bilateral, grade 1
ADRENAL CORTICES:
-Vacuolation, Zona fasciculata, bilateral, grade 2
ADRENAL MEDULLAS:
Only one of paired organs examined/present
BONE MARROW (FEMUR):
-Fatty replacement, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 30

* NECROPSY FINDINGS

LIVER:
01: ENLARGED.
02: DISCOLORATION, BLACK BROWN.
NO OTHER NECROPSY OBSERVATIONS NOTED

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg MALE

CONT./FF. ANIMAL NO. : 30

* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 3
This finding corresponds to necropsy observations nos: 01,02.
-Protoporphyrin accumulation, Kupffer cells, grade 2
-Protoporphyrin accumulation, hepatocyte, grade 1
-Maltese cross under polarized light
-Bright red (birefringent)
-Periportal chronic inflammation, grade 1
-Bile duct proliferation, bile duct, grade 2
-Fatty change, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
-Hemosiderin deposits, grade 1
KIDNEYS:
-Hyaline droplets, bilateral, grade 2
-Tubular basophilia, unilateral, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
THYROID GLAND (BOTH LOBES):
-Follicular cell hypertrophy, bilateral, grade 1
PARATHYROID GLANDS:
Tissue not present for histologic examination
ADRENAL CORTICES:
-Vacuolation, Zona fasciculata, bilateral, grade 2
BONE MARROW (FEMUR):
-Fatty replacement, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 31

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* NECROPSY FINDINGS

LIVER:
01: DISCOLORATION, BLACK BROWN.
LYMPH NODES:
01: PORTALES: ENLARGED, D=6 MM.
02: PORTALES: DISCOLORATION, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 3
This finding corresponds to necropsy observation no: 01.
-Protoporphyrin accumulation, Kupffer cells, grade 2
-Protoporphyrin accumulation, hepatocyte, grade 1
-Maltese cross under polarized light
-Bright red (birefringent)
-Periportal chronic inflammation, grade 1
-Bile duct proliferation, bile duct, grade 2
-Fatty change, grade 1
-Inflammatory cell foci, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
KIDNEYS:
-Papillary mineralization, focal/multifocal, unilateral, grade 1
STOMACH:
-Glandular stomach edema, submucosal, grade 2
-Inflammatory cell infiltrate, submucosa, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
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SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg MALE

CONT./FF. ANIMAL NO. : 31

LUNGS:
-Vascular mineralization, focal, grade 1
TESTES:
-Focal tubular atrophy, unilateral, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
LYMPH NODES:
-Erythrophagocytosis, bilateral, grade 2
-Congestion, bilateral
This finding corresponds to necropsy observations nos: 01,02.
-Hemosiderin deposits, bilateral, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 32

* NECROPSY FINDINGS

LIVER:
01: DISCOLORATION, BLACK BROWN.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 3
This finding corresponds to necropsy observation no: 01.
-Protoporphyrin accumulation, Kupffer cells, grade 2
-Protoporphyrin accumulation, hepatocyte, grade 1
-Maltese cross under polarized light

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
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SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg MALE

CONT./FF. ANIMAL NO. : 32

-Bright red (birefringent)
-Periportal chronic inflammation, grade 1
-Bile duct proliferation, bile duct, grade 2
SPLEEN:
-Extramedullary hemopoiesis, grade 1
KIDNEYS:
-Tubular basophilia, bilateral, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Vascular mineralization, focal, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, unilateral
PARATHYROID GLANDS:
Only one of paired organs examined/present
ADRENAL CORTICES:
-Vacuolation, Zona fasciculata, bilateral, grade 2
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 33

* NECROPSY FINDINGS

LIVER:
01: DISCOLORATION, BLACK BROWN.
NO OTHER NECROPSY OBSERVATIONS NOTED

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.:* 21061 IHI
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SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg MALE

CONT./FF. ANIMAL NO. : 33

* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 3
This finding corresponds to necropsy observation no: 01.
-Protoporphyrin accumulation, Kupffer cells, grade 2
-Protoporphyrin accumulation, hepatocyte, grade 1
-Maltese cross under polarized light
-Bright red (birefringent)
-Periportal chronic inflammation, grade 1
-Bile duct proliferation, bile duct, grade 2
SPLEEN:
-Extramedullary hemopoiesis, grade 1
-Hemosiderin deposits, grade 1
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
LUNGS:
-Alveolar macrophages, focal/multifocal, grade 1
-Vascular mineralization, focal, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 34

* NECROPSY FINDINGS

LIVER:
01: DISCOLORATION, BLACK BROWN.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 3
This finding corresponds to necropsy observation no: 01.
-Protoporphyrin accumulation, Kupffer cells, grade 1
-Protoporphyrin accumulation, hepatocyte, grade 1
-Maltese cross under polarized light
-Bright red (birefringent)
-Periportal chronic inflammation, grade 1
-Bile duct proliferation, bile duct, grade 2
-Fatty change, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
THYMUS:
-Cyst (s)
-Atrophy/involution, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
PARATHYROID GLANDS:
Only one of paired organs examined/present
PROSTATE GLAND:
-Mononuclear infiltration, focal, grade 1
BONE MARROW (FEMUR):
-Fatty replacement, grade 2

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SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg MALE

CONT./FF. ANIMAL NO. : 34

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 35

* NECROPSY FINDINGS

LIVER:
01: DISCOLORATION, BLACK BROWN.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 3
This finding corresponds to necropsy observation no: 01.
-Protoporphyrin accumulation, Kupffer cells, grade 2
-Protoporphyrin accumulation, hepatocyte, grade 1
-Maltese cross under polarized light
-Bright red (birefringent)
-Periportal chronic inflammation, grade 1
-Bile duct proliferation, bile duct, grade 2
-Inflammatory cell foci, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
KIDNEYS:
-Tubular basophilia, bilateral, grade 1
-Papillary mineralization, focal/multifocal, unilateral, grade 1
PEYER'S PATCHES (JEJUNUM):
Tissue not present for histologic examination

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SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg MALE

CONT./FF. ANIMAL NO. : 35

PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Vascular mineralization, focal, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
PARATHYROID GLANDS:
Only one of paired organs examined/present
BONE MARROW (FEMUR):
-Fatty replacement, grade 1
PITUITARY GLAND:
-Cyst, single, pars distalis
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
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SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg FEMALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 28 * ANIMAL NO. : 61

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* NECROPSY FINDINGS

LIVER:
01: DISCOLORATION, DARK BROWN.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
-Inflammatory cell foci, grade 1
-Hematopoietic foci, grade 1
-No histological correlate
This finding corresponds to necropsy observation no: 01.
SPLEEN:
-Extramedullary hemopoiesis, grade 1
-Hemosiderin deposits, grade 1
KIDNEYS:
-Hyaline casts, unilateral, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Alveolar hemorrhage, focal/multifocal, grade 1
-Vascular mineralization, focal, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
PARATHYROID GLANDS:
Only one of paired organs examined/present
VAGINA:
-Diestrus phase of the estrous cycle
-Mucification, grade 2
BONE MARROW (FEMUR):
-Fatty replacement, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 61

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: KO
DAYS ON TEST : 28 * ANIMAL NO. : 62

* NECROPSY FINDINGS

LIVER:
01: ENLARGED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

TRACHEA:
-Mononuclear cell foci, grade 1
LIVER:
-Hepatocellular hypertrophy, grade 1
This finding corresponds to necropsy observation no: 01.
-Fatty change, grade 2
-Inflammatory cell foci, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 2
-Hemosiderin deposits, grade 1
KIDNEYS:
-Hyaline casts, bilateral, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Vascular mineralization, focal, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 62

MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
PARATHYROID GLANDS:
Tissue not present for histologic examination
VAGINA:
-Metestrus phase of the estrus cycle
BONE MARROW (FEMUR):
-Fatty replacement, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 63

* NECROPSY FINDINGS

LIVER:
01: DISCOLORATION, BLACK BROWN.
02: ENLARGED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 3
This finding corresponds to necropsy observation no: 01.
-Maltese cross under polarized light
-Bright red (birefringent)
-Periportal chronic inflammation, grade 1
-Bile duct proliferation, bile duct, grade 1
-Hepatocellular hypertrophy, grade 1
This finding corresponds to necropsy observation no: 02.
-Inflammatory cell foci, grade 1

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SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 63

SPLEEN:
-Extramedullary hemopoiesis, grade 2
-Hemosiderin deposits, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, single, bilateral
PARATHYROID GLANDS:
Only one of paired organs examined/present
VAGINA:
-Diestrus phase of the estrous cycle
-Mucification, grade 1
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: KO
DAYS ON TEST : 28 * ANIMAL NO. : 64

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
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SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 64

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 2
-Hemosiderin deposits, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
THYMUS:
-Hemorrhage, focal, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
THYROID GLAND (BOTH LOBES):
-Follicular cell hypertrophy, unilateral, grade 1
PARATHYROID GLANDS:
Only one of paired organs examined/present
VAGINA:
-Diestrus phase of the estrous cycle
-Mucification, grade 2
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg FEMALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 28 * ANIMAL NO. : 65

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

HEART WITH AURICLES:
-Mononuclear cell foci, grade 1
LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 1
-Maltese cross under polarized light
-Bright red (birefringent)
-Periportal chronic inflammation, grade 1
-Hepatocellular hypertrophy, centrilobular, grade 1
-Increased hepatocytic glycogen deposits, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
-Hemosiderin deposits, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Vascular mineralization, focal, grade 1
THYMUS:
-Cyst (s)
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, single, unilateral
PARATHYROID GLANDS:
Tissue not present for histologic examination
VAGINA:
-Diestrus phase of the estrous cycle
-Mucification, grade 1

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TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 65

BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 66

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 2
-Maltese cross under polarized light
-Bright red (birefringent)
-Periportal chronic inflammation, grade 1
-Fatty change, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
-Hemosiderin deposits, grade 1
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
PEYER'S PATCHES (JEJUNUM):
Tissue not present for histologic examination
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Vascular mineralization, focal, grade 1

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TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
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SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 66

THYMUS:
-Atrophy/involution, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
PARATHYROID GLANDS:
Only one of paired organs examined/present
VAGINA:
-Metestrus phase of the estrus cycle
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 67

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Fatty change, grade 1
-Increased hepatocytic glycogen deposits, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
-Hemosiderin deposits, grade 2
PEYER'S PATCHES (JEJUNUM):
Tissue not present for histologic examination
THYMUS:
-Cyst (s)

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SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 67

MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
-Lymphoid hyperplasia, unilateral, grade 1
THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, unilateral
PARATHYROID GLANDS:
Only one of paired organs examined/present
VAGINA:
-Diestrus phase of the estrous cycle
BONE MARROW (FEMUR):
-Fatty replacement, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 68

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 1
-Maltese cross under polarized light
-Bright red (birefringent)
-Increased hepatocytic glycogen deposits, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
-Hemosiderin deposits, grade 1

PATHOLOGY REPORT PAGE : 131/ 134
INDIVIDUAL ANIMAL DATA Harlan Laboratories C53655

TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 68

PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Vascular mineralization, focal, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
THYROID GLAND (BOTH LOBES):
-Ultimobranchial cyst, unilateral
PARATHYROID GLANDS:
Only one of paired organs examined/present
VAGINA:
-Diestrus phase of the estrous cycle
BONE MARROW (FEMUR):
-Fatty replacement, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 69

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

HEART WITH AURICLES:
-Mononuclear cell foci, perivascular, grade 1
-Valvular hemocyst, grade 2
LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 2
-Maltese cross under polarized light
-Bright red (birefringent), under polarized light

PATHOLOGY REPORT PAGE : 132/ 134
INDIVIDUAL ANIMAL DATA Harlan Laboratories C53655

TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 69

.....

-Periportal chronic inflammation, grade 1
-Fatty change, grade 1
-Increased hepatocytic glycogen deposits, grade 1
SPLEEN:
-Extramedullary hemopoiesis, grade 1
-Hemosiderin deposits, grade 1
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
-Papillary mineralization, focal/multifocal, unilateral, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Vascular mineralization, focal, grade 1
THYMUS:
-Cyst (s)
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
PARATHYROID GLANDS:
Tissue not present for histologic examination
VAGINA:
-Metestrus phase of the estrus cycle
BONE MARROW (FEMUR):
-Fatty replacement, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT PAGE : 133/ 134
INDIVIDUAL ANIMAL DATA Harlan Laboratories C53655

TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg FEMALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 70

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Protoporphyrin accumulation, intrahepatic bile duct, grade 1
-Maltese cross under polarized light
-Bright red (birefringent)
-Fatty change, grade 1
-Increased hepatocytic glycogen deposits, grade 1
SPLEEN:
-Hemosiderin deposits, grade 1
KIDNEYS:
-Hyaline casts, unilateral, grade 1
-Papillary mineralization, focal/multifocal, unilateral, grade 1
PEYER'S PATCHES (JEJUNUM):
-Lymphoid hyperplasia, grade 1
PEYER'S PATCHES (ILEUM):
-Lymphoid hyperplasia, grade 1
LUNGS:
-Alveolar macrophages, focal/multifocal, grade 1
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
PARATHYROID GLANDS:
Only one of paired organs examined/present
VAGINA:
-Estrus phase of the estrous cycle
BONE MARROW (FEMUR):
-Fatty replacement, grade 1

PATHOLOGY REPORT PAGE : 134/ 134
INDIVIDUAL ANIMAL DATA Harlan Laboratories C53655

TEST ARTICLE : OCTAMETHYLTRISILOXANE(L3) *PATHOL. NO.*: 21061 IHI
TEST SYSTEM : RAT, 28-Day, Oral (Gavage) *DATE* : 20-JUL-10
SPONSOR : SEHSC *PathData©System V6.2b5*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 05, 1000 mg/kg FEMALE

CONT./FF. ANIMAL NO. : 70

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

APPENDIX VII - IMMUNOHISTOCHEMISTRY

BIOTECHNICS
FOCUSED EXPERTISE

Silicones Environmental, Health and Safety Council (SEHSC)

Harlan Laboratories Study C53655

28-Day Oral Toxicity (Gavage) Study in the Sprague-Dawley Rat with OCTAMETHYLTRISILOXANE (L3)

IMMUNOHISTOCHEMISTRY REPORT

FINAL REPORT DATE: 16 July 2010

Submitted by:
Molly H. Boyle, DVM MPH, DACVP
310 Millstone Drive, Hillsborough, N.C. 27278

Silicones Environmental Health and Safety Council (SEHSC)

Harlan Laboratories Study C53655

28-Day Oral Toxicity (Gavage) Study in the Sprague-Dawley Rat with

OCTAMETHYLTRISILOXANE (L3)

IMMUNOHISTOCHEMISTRY REPORT

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Harlan Laboratories Study C53655 OCTAMETHYLTRISILOXANE (L3)

GLP STATEMENT OF COMPLIANCE

The findings in this report were compiled by the undersigned pathologist and accurately reflect the raw data.

This phase of the study was conducted in compliance with the Good Laboratory Practice Regulations of the United States Food and Drug Administration as set forth in 21 CFR Part 58 and subsequent amendments. There were no deviations that would have an adverse impact on the integrity of the data.

16 Jul 2010
Date

Molly H. Boyle, DVM MPH, DACVP
Principal Investigator
Biotechnics LLC
310 Millstone Drive
Hillsborough, NC 27278 USA

Harlan Laboratories Study C53655 OCTAMETHYLTRISILOXANE (L3)

QUALITY ASSURANCE STATEMENT

Quality Assurance surveillance of this study phase was conducted in compliance with the Good Laboratory Practice Regulations of the United States Food and Drug Administration as set forth in 21 CFR Part 58 and subsequent amendments.

Phase Audited	Date of Audit	Date Reported to Principal Investigator	Date Reported to Management	Date Reported to Study Director
Immunohistochemical Staining	3May10	4May10	7May10	16Jul10
Histology Documentation	7May10	7May10	7May10	16Jul10
IHC Report	12May10	12May10	12May10	16Jul10

J West

Jaimie West, BS
Head of Quality Assurance
Biotechnics LLC
310 Millstone Drive
Hillsborough, NC 27278 USA

16 July 2010
Date

Harlan Laboratories Study C53655 OCTAMETHYLTRISILOXANE (L3)

1. INTRODUCTION:

The purpose of this oral toxicity study was to assess the cumulative toxicity of OCTAMETHYLTRISILOXANE (L3) when administered daily to rats by gavage for a period of 28 days. The reversibility of test item-related changes was assessed after a treatment-free 14-day recovery period.

2. EXPERIMENTAL DESIGN:

Hsd:Sprague Dawley®™SD®™ rats were administered vehicle or L3 via oral gavage for 28 consecutive days as indicated in the following table. The recovery period was 14 days.

Text Table 1. Experimental Design

Group	Treatment	Dosage Level (mg/kg/day)	Number of Animals			
			Main		Recovery	
			Males	Females	Males	Females
1.	Control*	0	5	5	5	5
2.	L3	5	5	5	-	-
3.	L3	25	5	5	-	-
4.	L3	250	5	5	-	-
5.	L3	1000	5	5	5	5

* Group 1 (Control) animals were administered vehicle only (corn oil)

2.1 Macroscopic Examination

At the appropriate scheduled time of sacrifice, all animals were anesthetized by intraperitoneal injection of pentobarbitone and euthanized by exsanguination. All animals were subjected to a complete necropsy examination including external and internal examination and identification of all clinically-recorded lesions.

2.2 Microscopic Examination

Following fixation in neutral phosphate buffered 4% formaldehyde solution, samples of the kidneys (100-300 mg) were transferred to 70% ethanol within 48 hours. Kidney samples for immunohistochemical evaluation were subjected to standard histologic processing and embedded in paraffin wax. Paraffin blocks were sent to Biotechnics, LLC, where they were sectioned and stained, as described in the table below, for the determination of possible alpha-2μ globulin

accumulation in the kidney. Females kidney samples were not sectioned and stained due to absence of alpha-2μ globulin accumulation in the kidney.

Text Table 2. Alpha-2μ Globulin Immunohistochemistry Staining Procedure

Step	Procedure
1	Deparaffinize and rehydrate paraffin sections
2	Wash in automation buffer (Dako, Carpinteria, CA, Lot No. 10037757, expiration date 12/10)
3	Block endogenous peroxidase activity with 0.03% H_2O_2 in PBS with sodium azide for 15 minutes (Kerr Drug, NC, Lot No. 9DF07744, expiration date 04/11).
4	Wash in automation buffer (Dako, Carpinteria, CA, Lot No.10037757, expiration date 12/10)
5	Incubate primary antibody Alpha-2μ Globulin Clone 129736, R&D Systems 1:100 for 40 minutes, R&D Systems, Minneapolis, MN, Lot GWP010, expiration date 04/11)
6	Wash in automation buffer (Dako, Carpinteria, CA, Lot No.10037757, expiration date 12/10)
7	Incubate goat anti rabbit secondary at a 1:500 dilution for 30 minutes (Jackson Immuno Research, West Grove, PA, Lot No. 75225, expiration date 08/10)
8	Wash in automation buffer (Dako, Carpinteria, CA, Lot No.10037757, expiration date 12/10)
9	Incubate Streptavidin for 30 minutes (Vector Labs, Burlingame, CA, Lot No. V0112, expiration date 06/11)
10	Wash in automation buffer (Dako, Carpinteria, CA, Lot No.10037757, expiration date 12/10)
11	Peroxidase development- diaminobenzidine for 8 minutes (DAKO, Carpinteria, CA, Lot No.10035585, expiration date09/11)
12	Wash in automation buffer (Dako, Carpinteria, CA, Lot No.10037757, expiration date 12/10)
13	Counterstain with hematoxylin for 7 minutes (DAKO Corporation, Carpinteria, CA. Lot No.10034184, expiration date 08/10)
14	Dehydrate through 70%, 80%, 95% and 100% ethanol followed by xylene
15	Coverslip

Immunohistochemical evaluation via light microscopy was performed on all male kidneys. Positive alpha-2μ-globulin staining was subcategorized as punctate or globular patterns. Punctate staining consisted of small round to ovoid structures that were the approximate size of lysosomes. Globular staining consisted of larger positively stained bodies that varied in size and shape, and often were associated with intraluminal accumulations of positively stained amorphous material. Each type of staining was graded on a 0-4 scale, with 0 being negative, 1 being the least discernible staining, and 4 being the most pronounced staining seen in the present study. The histologic sections were of adequate size and quality for the detection of treatment-related changes. The tabulation of tissues examined and histologic findings in those tissues serves as the basis for this narrative report., and is presented in Appendix 1.

3. IMMUNOHISTOCHEMICAL EVALUATION

3.1 Main study

Summaries of alpha-2μ-globulin staining in male rats from the Main Study are presented in Text Tables 3 and 4.

Harlan Laboratories Study C53655 OCTAMETHYLTRISILOXANE (L3)

The mean levels of punctate staining in test article-treated groups and the control group and the absence of a dose response suggests there was no biological difference based on the occurrence of α-2μ globulin of the punctate staining pattern. There was a higher level of α-2μ globulin of the globular staining pattern in all test article-treated males. However, the highest mean staining level was noted in the 250 mg/kg/day males. Absence of a dose response raises suspicion as to the toxicologic significance of the α-2μ globulin immunohistochemical staining results.

Text Table 3. Summary Of Immunohistochemical Findings, Punctate Staining Pattern Main Study Males

L3 Dosage level (mg/kg/day):	0	5	25	250	1000
Kidney[a]	5	5	5	5	5
Mean Stain Score	4.0	4.0	3.4	3.4	4.0

[a] = Number of tissues examined.

Text Table 4. Summary Of Immunohistochemical Findings, Globular Staining Pattern Main Study Males

L3 Dosage Level (mg/kg/day):	0	5	25	250	1000
Kidney[a]	5	5	5	5	5
Mean Stain Score	0.4	1.2	2.2	3.2	3.0

[a] = Number of tissues examined.

3.2 Recovery

Summaries of alpha-2μ-globulin staining in the Recovery male rats are presented in Text Tables 5 and 6. Recovery males were analyzed to assess the reversibility of test item-related changes after a treatment-free 14-day recovery period.

Staining for alpha-2μ-globulin of the punctate pattern was present equally in male rats from the 0 and 1000 mg/kg/day recovery groups. Mean alpha-2μ-globulin staining of the punctate pattern was the same in males from the control group and 1000 mg/kg/day recovery group as compared to males from the same dosage groups in the Main Study.

Alpha-2μ-globulin staining of the globular pattern was only rarely present in male rats from the 0 mg/kg/day group, but was present to a more substantial degree in male rats from the 1000 mg/kg/day group. A decrease in the mean stain score for alpha-2μ-globulin of the globular pattern

in recovery males from the 1000 mg/kg/day group as compared to the mean stain at the main necropsy suggests some recovery in the accumulation of alpha-2μ-globulin in the kidneys.

Text Table 5. Summary Of Immunohistochemical Findings, Punctate Staining Pattern Recovery Males

L3 Dosage level (mg/kg/day):	0	5	25	250	1000
Kidney[a]	5	N/A	N/A	N/A	5
Mean Stain Score	4.0	N/A	N/A	N/A	4.0

[a] = Number of animals examined.

Text Table 6. Summary Of Immunohistochemical Findings, Globular Staining Pattern Recovery Males

L3 Dosage level (mg/kg/day):	0	5	25	250	1000
Kidney[a]	5	N/A	N/A	N/A	5
Mean Stain Score	0.4	N/A	N/A	N/A	1.6

[a] = Number of animals examined.

4. DISCUSSION:

Presence of a higher mean level of α-2μ globulin of the globular staining pattern in the kidneys of male rats that received the test article raises suspicion of a test article-related effect, but presence of the highest level of α-2μ globulin staining in the 250 mg/kg/day group rather than the 1000 mg/kg/day group raises questions as to the toxicologic relevance of the difference in immunohistochemical staining intensity. The punctate staining pattern was interpreted as the normal physiologic processing of alpha-2μ-globulin in the kidney. The globular staining pattern may be interpreted as a pathologic accumulation of alpha-2μ-globulin in the kidney, which may be seen as hyaline droplet accumulation/degeneration in routinely stained kidney sections. Slight staining of the globular pattern in control male rats from the recovery group was interpreted as an early manifestation of spontaneous nephropathy of laboratory rats, which is known to include an element of hyaline droplet accumulation. The immunohistochemical staining results should be viewed in conjunction with results of routine histopathological evaluation in arriving at a final conclusion regarding a test article-related effect on α-2μ globulin accumulation in the kidneys.

Harlan Laboratories Study C53655 OCTAMETHYLTRISILOXANE (L3)

5. CONCLUSION:

Octamethyltrisiloxane (L3) was administered daily to male and female rats by gavage for a period of 28 days at dosage levels of 0, 5, 25, 250 or 1000 mg/kg/day. Kidney sections from male rats were stained by immunohistochemical staining methods to reveal the presence of alpha-2μ globulin. While there was a higher level of α-2μ globulin, globular pattern staining in the kidneys of test article-treated male rats, the pattern of staining relative to dose levels raised questions regarding the toxicologic relevance of the increased α-2μ globulin content in the kidneys of male rats. There was evidence of recovery in the accumulation of alpha-2μ-globulin in the recovery group males from the 1000 mg/kg/day group.

Submitted by: _____ Date: 16 Jul 2010
Molly H. Boyle, DVM MPH, DACVP

Reviewed by: _____ Date: 16 Jul 2010
George A. Parker, DVM, PhD, DACVP, DABT

Harlan Laboratories Study C53655 OCTAMETHYLTRISILOXANE (L3)

Appendix 1: Immunohistochemical staining scores in individual animals

Main Study Animals

Animal No.	Punctate staining	Globular staining
Group 1M (0 mg/kg/day L3)		
1	4	1
2	4	0
3	4	0
4	4	0
5	4	1
Group 1M Mean	**4.0**	**0.4**
Group 2M (5 mg/kg/day L3)		
11	4	1
12	4	2
13	4	0
14	4	1
15	4	2
Group 2M Mean	**4.0**	**1.2**
Group 3M (25 mg/kg/day L3)		
16	3	0
17	3	4
18	3	4
19	4	0
20	4	3
Group 3M Mean	**3.4**	**2.2**
Group 4M (250 mg/kg/day L3)		
21	4	3
22	4	4
23	3	3
24	2	3
25	4	3
Group 4M Mean	**3.4**	**3.2**
Group 5M (1000 mg/kg/day L3)		
26	4	3
27	4	2
28	4	3
29	4	3
30	4	4
Group 5M Mean	**4.0**	**3.0**

Harlan Laboratories Study C53655 OCTAMETHYLTRISILOXANE (L3)

Recovery Animals

Animal No.	Punctate staining	Globular staining
Group 1M (0 mg/kg/day L3)		
6	4	1
7	4	0
8	4	0
9	4	0
10	4	1
Group 1M Mean	**4.0**	**0.4**
Group 5M (1000 mg/kg/day L3)		
31	4	3
32	4	0
33	4	1
34	4	2
35	4	2
Group 5M Mean	**4.0**	**1.6**

BIOTECHNICS
FOCUSED EXPERTISE

STUDY NUMBER: C53655 **Date:** 12 May 2010

PATHOLOGY REPORT & MICROSCOPIC DATA ENTRY QA REPORT

☑ Verify information from protocol:
Study number & title, Sponsor, Test Article, Species, Tissue lists, Dosage groups and method

☑ Verify animal information on ~~StarTox Summarized STAR Pages~~: Staining ~~Scores~~ Scores appendix (a)
Animal number and/or Accession number, Group assignment, Sex, ~~Date code, Days on test~~ (a)
No double entries
~~Track gross lesions or tissues missing in STAR back to necropsy/trimming~~ (a)

☒ N/A Review StarTox Outline Pages and Incidence Tables for omission

☑ Compare numerical references and tables in narrative report to ~~Microscopic Incidence Pages~~ Staining Scores appendix (a)

☑ Check pagination, table of contents, headers and footers for dates and draft in narrative ~~and StarTox tables~~ (a)

☑ No findings
☐ Findings listed below; Date forwarded to Pathologist _____

(a) not applicable to this study. N West 12 May 10

QA Findings:	Pathologist Responses:
none.	12 May 2010 Study Pathologist (signature/date)

N West 12 May 2010
QA Auditor (signature/date)

Date forwarded for review to: ☐ Study Director and/or ☒ Laboratory Manager 12 May 2010

12 May 10
Reviewer (signature/date)

N West 12 May 2010
QA Verification (signature/date)

BIOTECHNICS
FOCUSED EXPERTISE

STUDY NUMBER: C53655

Phase: HISTOLOGY DOCUMENTATION **Date:** 7 May 2010

10% review of all histology documentation	**No Finding**	**Finding**	**NA/Not Inspected**
T69 100% QC Review of Histology Documentation is completed and submitted to QA			(a)
HPRs are correctly labeled with group and animal numbers (verified against animal list)	✓		
Animal IDs are verified on HPR			✓ Rec'd blocks.
Initial/date spaces are filled in for trimming, embedding, microtomy, and QC (as appropriate)	✓		
Decal dates are complete (date in and date out)			✓
Footnotes have initials/date and track back to appropriate tissues	✓		
"Not present at trimming" ("NPT") are verified by another technician with initials/date			✓
Appropriate gross lesions have been processed (verify against necropsy records)			✓
All HPRs are present (verified against animal list)	✓		
Histology QC worksheets (T 12—blue recut sheets) are completed properly and present			✓
Special or IHC stain documentation is complete (if applicable)	✓		
Slide/block match was performed	✓		
Inventory/transmittal records are appropriately completed	✓		
Work is completed in accordance with protocol, all amendments, Study Director Notification, etc…	✓		
Path recut request documentation is appropriately completed			✓

☑ **No findings** ☐ **Findings listed below** ☐ **Findings listed on attached report**

(a) not yet active procedure pW 7May10

M West
QA Auditor (signature)

Date forwarded to Principal Investigator 7 May 10

7May10
Principal Investigator (signature/date)

Date forwarded to Laboratory Manager 7 May 10

7May10
Laboratory Manager (signature/date)

M West 7May10
QA Verification (signature/date)

Biotechnics Form QA.1 **Revised: 5 May 2010**

09009e538081ef49

BIOTECHNICS
FOCUSED EXPERTISE

STUDY NUMBER: C53655

Phase: AUTOMATED IMMUNOHISTOCHEMICAL STAINING & COVERSLIPPING **Date:** 3 May 2010

Personnel: K. Scully	**No Finding**	**Finding**	**Not Inspected**
IHC report from Dako Autostainer signed and dated	✓		
Annual preventative maintenance up-to-date for Dako Autostainer (In-use Equipment Maintenance Log)	✓		
Reagents and solutions labeled to indicate identity, concentration, expiration date and storage requirements.	✓		
Reagents are accurately listed on IHC report	✓		
Bar-coded stickers generated by Autostainer match information originally printed on slide (is applicable) not applicable			✓
Verify that Autostainer vials are accurately labeled with contents, and match Reagent Layout Map placement in vial racks.	✓		
Pipettes used have been properly calibrated	✓		
Separate pipette tips are used for each reagent to prevent mixing	✓		
Autostainer carboys (buffer, DI water and hazardous/non-hazardous waste) are appropriately labeled and match labels on lids; black hazardous waste line is attached to appropriate carboy	✓		
Microtomy was within 2 weeks of staining for optimum IHC staining results (if applicable)	✓		
Antibody validation in IHC & Special Procedures log matches dilution and lot number of currently used antibody	✓		
Flammable reagents kept in an approved storage cabinet	✓		
IHC refrigerator thermometer temperature is recorded in Temperature Records Log	✓		
Area is clean and there is adequate separation of operations to prevent mixing	✓		
The reservoir of mounting medium is filled with clear, clean fluid	✓		
Coverslips completely cover all tissue sections on the slides	✓		
Excess mounting medium is removed by appropriate means	✓		
Slides are allowed to dry adequately before they are placed vertically	✓		
Ventilators are in use and there is no excessive accumulation of fumes	✓		

☑ **No findings** ☐ **Findings listed on attached report**

QA Auditor (signature)
Date forwarded to Principal Investigator 4 May 10

7 May 10
Principal Investigator (signature/date)

Date forwarded to Laboratory Manager 7 May 10

7 May 10
Laboratory Manager (signature/date)

7 May 10
QA Verification (signature/date)