8EHQ-0404-15548

Ciba Specialty Chemicals
North America

8EHQ-04-15548

Ciba

April 7, 2004

Via Federal Express

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Document Control Office (7407M)
U.S. Environmental Protection Agency
Attention: TSCA Section 8(e) Submission
Office of Pollution Prevention and Toxics
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

Subject: TSCA 8(e) Notice – ZLI 3331 (TKA 40291)

Dear Section 8(e) Coordinator:

This letter does not contain Confidential Business Information.

In accordance with EPA's March 16, 1978 Policy Statement on Section 8(e) reporting under the Toxic Substances Control Act (TSCA), the EPA's June, 1991 TSCA Section 8(e) Reporting Guide, Ciba Specialty Chemicals Corporation wishes to bring to the attention of the Environmental Protection Agency the results observed in a 28-Day Oral Toxicity Study in the Wistar Rat with ZLI 3331, ZLI 3331 a commercial (L89-113) photoinitiator is chemically 100% 2-propenoic acid, 2-[4-(2-hydroxy-2-methyl-1-oxopropyl)phenoxy]ethyl ester, CASRN 110430-09-6.

Oral administration of ZLI 3331 (TKA 40291) to Wistar rats at doses of 50, 200 and 1000 mg/kg/day, for 28 days did not result in mortality, or behavioral effects in the functional observational battery. In addition, there were no treatment effects upon mean food consumption or mean body weights, locomotor activity, hematology, and urinalysis parameters.

Treatment-related findings in clinical biochemistry were elevated sodium levels and inorganic phosphate levels and lower potassium levels and calcium levels at 1000 mg/kg/day.

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At the high dose level liver, kidney and adrenal gland weights were increased. Spleen weights in females were elevated at 200 and 1000 mg/kg/day.

Morphological changes were detected at all dose levels in males and females in fore-stomach, glandular stomach, liver and in male adrenal glands. The effect on fore-stomach consisted of squamous cell hyperplasia and hyperkeratosis of the epithelium in males and females of all treated groups. In addition, in the fore-stomach of females at 1000 mg/kg/day erosion or ulceration were observed. This effect was reversible during the recovery period. The glandular stomach showed diffuse epithelial hyperplasia in males and females at 1000 mg/kg/day. This finding was reversible after the recovery period. After the 14-day recovery period, glycogen deposition was decreased in liver of both sexes at 1000 mg/kg/day. This finding correlated with the decreased liver weight observed in the males of this group. Adrenal cortical fatty change was increased in males at 1000 mg/kg/day. This correlated with the increased average relative adrenal gland weight observed in the males of this group. This finding was reversible after the 14-day recovery period.

Based on the results of this study, a NOEL could not be established. The NOAEL was considered to be 200 mg/kg body weight/day.

540 White Plains Road
Tarrytown, New York 10591

Tel. 914-785-4536
Fax 914-785-4147

88040000121

274528

Ciba Specialty Chemicals
North America

Ciba

We are enclosing a copy of the study "*ZLI 3331 (TK 40291)* 28-Day Oral Toxicity Study in the Wistar Rat" RCC LTD. Itingen, Switzerland; Study Number 8481774.

Based upon current EPA guidelines, it is felt these results warrant reporting under TSCA 8(e). Please call the undersigned if you have any questions concerning this submittal.

Respectfully yours,

James Osmundsen
Sr. Product Compliance Specialist

540 White Plains Road
Tarrytown, New York 10591

Tel. 914-785-4536
Fax 914-785-4147

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RCC Study Number 848174

TKA 40291 (ZLI 3331):

28-Day Oral Toxicity (Gavage) Study in the Wistar Rat

Report (Part I of II)

Authors: W.H. Braun, Dr. D. Flade,
Dr. A. Brändli-Baiocco

Sponsor Ciba Specialty Chemicals Inc.
Segment Coating Effects
P.O. Box, WRO-1045.1.35
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1 PREFACE

1.1 GENERAL

Title	TKA 40291 (ZLI 3331): 28-Day Oral Toxicity (Gavage) Study in the Wistar Rat
Sponsor	Ciba Specialty Chemicals Inc. Segment Coating Effects P.O. Box, WRO-1045.1.35 CH 4002 Basel / Switzerland
Study Monitor	Dr. Moung Sook Lee
Test Facility	a) RCC Ltd Toxicology CH – 4452 Itingen / Switzerland
	b) RCC Ltd Toxicology CH – 4332 Stein / Switzerland
Test Site(s)	c) RCC Ltd Environmental Chemistry & Pharmanalytics CH – 4452 Itingen / Switzerland
Lead QAU	RCC Ltd Quality Assurance Unit Toxicology CH – 4452 Itingen / Switzerland

1.2 RESPONSIBILITIES

Study Director	W. H. Braun (a)
Deputy Study Director	Dr. B. Damme (a)
Laboratory Coordinator	P. Althaus Ravenstijn (a)
Clinical Laboratory Investigations	P. Gretener (b)
Necropsy/Histotechnique	Dr. K. Weber (a)
Study Pathologist	Dr. A. Brändli-Baiocco (a)
Head of Lead Quality Assurance	I. Wüthrich
Principal Investigator: Analytical Phase	Dr. D. Flade (c)

1.3 SCHEDULE

Experimental Starting Date	07 April 2003
Experimental Completion Date	02 June 2003
Delivery of Animals	14 April 2003
Acclimatization/Pretest	14 to 20 April 2003
Administration/Treatment	21 April to 18 May 2003
Recovery	19 May to 01 June 2003
Termination (Necropsy)	19 May 2003 (Allocation A) 02 June 2003 (Allocation B)
Study Completion Date	12 November 2003

1.4 ARCHIVING

RCC Ltd (CH-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. Wet tissue samples will be archived at RCC Ltd for a minimum of five years. Thereafter, in agreement with the Sponsor, these samples may be further archived at RCC Ltd or transferred to another GLP archive facility for the remainder of the prescribed period. No data will be discarded without the Sponsor's consent.

1.5 TEST GUIDELINES

The study procedures described in this report meet or exceed with the following guidelines:

Directive 96 / 54 / EC, B. 7. "Repeated dose (28 days) toxicity (oral)", September 30, 1996.

"Repeated Dose 28-Day Oral Toxicity Study in Rodents", OECD Guidelines for the Testing of Chemicals, Section 4, Health Effects, Number 407, July 27, 1995.

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

1.6 ANIMAL WELFARE

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

1.7 ACCREDITATION

"RCC Ltd, Toxicology" is accredited according to ISO/IEC 17025 under accreditation number STS 085 by the Swiss Accreditation Service.[1]

[1] In the scope of the accreditation, the clinical laboratory investigations are temporarily subcontracted to the clinical laboratory located at RCC Ltd, Toxicology, CH-4332 Stein

1.8 SIGNATURES

Study Director: W.H. Braun

date: 12 Nov 2003

Management: Dr. H. Fankhauser

date: 12 November 2003

The signatures of Dr. D. Flade (Analytical Chemistry) and Dr. A. Brändli-Baiocco (Study Pathologist) are included in the relevant attached reports.

GOOD LABORATORY PRACTICE

1.9 STATEMENT OF COMPLIANCE / GLP GUIDELINES

RCC STUDY NUMBER:	848174
TEST ITEM:	TKA 40291 (ZLI 3331)
STUDY DIRECTOR:	W.H. Braun
TITLE:	TKA 40291 (ZLI 3331): 28-day Oral Toxicity (Gavage) Study in the Wistar Rat

This study has been performed in compliance with the:

Swiss Ordinance relating to Good Laboratory Practice, adopted February 2nd, 2000 [RS 813.016.5] This Ordinance is based on the OECD Principles of Good Laboratory Practice, as revised in 1997 and adopted 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: 12 Nov 2003

1.10 QUALITY ASSURANCE UNIT

RCC Ltd, Toxicology, CH-4452 Itingen / Switzerland

STATEMENT

RCC STUDY NUMBER:	848174
TEST ITEM:	TKA 40291 (ZLI 3331)
STUDY DIRECTOR:	W.H. Braun
TITLE:	TKA 40291 (ZLI 3331): 28-day Oral Toxicity (Gavage) Study in the Wistar Rat

The general facilities and activities are inspected periodically 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 Unit. The dates are given below.

Dates and Types of QA Inspections		Dates of Reports to the Study Director and to Management
04 April 2003	Study plan	04 April 2003
21 April 2003	Test system, dose preparation, raw data, treatment	21 April 2003
19 May 2003	Process-based (histotechnology)	19 May 2003
02 June 2003	Necropsy	02 June 2003
03 June 2003	Process-based (clinical laboratory investigations)	03 June 2003
11-14 August 2003	Report	14 August 2003

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

In addition, this final report includes a QAU-Statement issued by the Test Site Quality Assurance Unit.

Quality Assurance

J.-P. Wili

J.P. Wili

.....

Date: 12-Nov-2003

2 SUMMARY

GENERAL

In this subacute toxicity study, TKA 40291 (ZLI 3331) was administered daily by oral gavage to SPF-bred Wistar rats of both sexes at dose levels of 50, 200 and 1000 mg/kg body weight/day for a period of 28 days. A control group was treated similarly with the vehicle, PEG 300, only.

The groups comprised 5 animals per sex which were sacrificed 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 sacrificed.

Clinical signs, outside cage observation, food consumption and body weights were recorded periodically during pretest, the treatment and recovery periods. Functional observational battery, locomotor activity and grip strength were performed 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 stomach of all animals, bone marrow of females and adrenal glands of males were examined to establish a no-effect level.

DOSE FORMULATION ANALYSIS

Initial difficulties (ie column blockage and difficult separation of test item and matrix peaks) required some adaptation of the original analytical method. Despite method improvements, the initial results of samples taken after experimental start were inconsistent. Samples prepared in the analytical laboratory were found to be unstable when frozen for 24 hours. Unfrozen samples stored for the same duration revealed good recoveries. Subsequent samples prepared in the analytical laboratory showed that the formulated test item (ie. in PEG 300) degrades within hours and that the dose formulations are not stable for 7 days under these conditions. In conclusion, the mixtures administered probably contained mostly degradation products of the test item.

MORTALITY / VIABILITY

All animals survived until scheduled necropsy.

CLINICAL SIGNS

During daily observations, soft feces was noted from day 7 of treatment at 1000 mg/kg/day and were considered to be test item-related. At 1000 mg/kg/day, salivation was noted in one male on day 16, one female on day 14, two males and one female on day 27 and two males and three females on day 28 of treatment, and were considered to be test item related.

During detailed clinical observations, salivation was noted at 1000 mg/kg/day in two males/one female during week 2 and in one male during week 3. This minor finding was considered to be test item-related.

All other animals were without changes of toxicological relevance at daily and weekly observations.

FUNCTIONAL OBSERVATIONAL BATTERY

During week 4, salivation was noted in three males and three females treated with 1000 mg/kg/day. This finding was considered to be test item-related.

All other animals were without changes of toxicological relevance during the functional observational battery.

Grip Strength

The mean fore- and hindlimb grip strength of the test item-treated rats was unaffected.

Locomotor Activity

No test item-related differences in the mean locomotor activity were noted at any dose level.

FOOD CONSUMPTION

The mean daily food consumption was not affected by the treatment with the test item.

BODY WEIGHT

Differences noted in the mean body weights of the test item-treated males were not seen in the females and therefore considered unlikely to be test item-related.

CLINICAL LABORATORY INVESTIGATIONS

Hematology

No differences of toxicological significance were noted in the hematology parameters after four weeks' treatment or two weeks' recovery.

Clinical Biochemistry

Elevated sodium levels and inorganic phosphate levels and lower potassium levels and calcium levels noted in males treated with 1000 mg/kg/day for four weeks were considered likely to be related to the treatment with the test item.

All other differences noted in the clinical biochemistry parameters after four weeks' treatment and two weeks' recovery were considered to be fortuitous.

Urinalysis

No differences of toxicological significance were noted in the urinalysis parameters after four weeks' treatment or two weeks' recovery.

ORGAN WEIGHTS

Elevated mean absolute liver weights were noted in the females treated with 1000 mg/kg/day and elevated mean liver-to-body weight ratios were noted in males and females treated with 1000 mg/kg/day. Elevated liver-to-brain weight ratios were noted in females treated with 1000 mg/kg/day. Further test item-related weight increases in the mean organ to body weight ratios were noted in the kidneys and adrenals of males treated with 1000 mg/kg/day.

All other organ weights and ratios were considered to be unaffected by treatment.

MACROSCOPIC / MICROSCOPIC FINDINGS

At microscopic examination, TKA 40291 (ZLI 3331) produced morphologic changes in male and female forestomach, glandular stomach and liver as well as in male adrenal glands.

In the forestomach, squamous cell hyperplasia and hyperkeratosis were observed in all test item-treated animals. These findings were still present after the 14-day recovery period, but their severity was decreased. In addition, in the forestomach of females at 1000 mg/kg/day, erosion or ulceration were observed. These findings were reversible after the 14-day recovery period.

The glandular stomach showed diffuse epithelial hyperplasia in males and females at 1000 mg/kg/day. This finding was reversible after the recovery period.

In the adrenal glands, cortical fatty change were increased in incidence and severity in males at 1000 mg/kg. This finding was reversible after the 14-day recovery period.

Glycogen deposition was decreased in animals at 1000 mg/kg after the 14-day recovery period.

3 ASSESSMENT AND DISCUSSION

Oral administration of TKA 40291 (ZLI 3331) to Wistar rats at doses of 50, 200 and 1000 mg/kg/day, for 28 days resulted in no deaths, no differences in mean fore- and hindlimb grip strength, no differences in mean locomotor activity, no differences in mean food consumption or mean body weights, no differences of toxicological significance in the hematology or urinalysis parameters,

Test item-related findings noted after four weeks' treatment were generally restricted to changes in sodium and inorganic phosphate levels (elevated) and potassium and calcium levels (lower) in males treated with 1000 mg/kg/day for four weeks, elevated absolute and/or relative liver weights in males and females treated with 1000 mg/kg/day, increased mean kidney- and adrenal to body weight ratios in males treated with 1000 mg/kg/day, and macroscopic changes (surface irregularities) in the stomachs of rats treated with 1000 mg/kg/day.

Morphological changes were detected at all dose levels in male and female forestomach, glandular stomach, liver as well as in male adrenal glands. The effect on forestomach consisted in squamous cell hyperplasia and hyperkeratosis of the epithelium in males and females of all treated groups. These findings correlated with the irregular surface of the forestomach reported at necropsy in all animals treated at 1000 mg/kg and were still present after the 14-day recovery period, but their severity was decreased. In addition, in the forestomach of females at 1000 mg/kg erosion or ulceration were observed. These findings were reversible after the 14-day recovery period. The glandular stomach showed diffuse epithelial hyperplasia in males and females at 1000 mg/kg. This finding was reversible after the recovery period. Glycogen deposition was decreased in liver of animals of either sex at 1000 mg/kg after the 14-day recovery period. This finding correlated with the decreased liver weight observed in the males of this group. Adrenal cortical fatty change was increased in males at 1000 mg/kg. This correlated with the increased average relative adrenal gland weight observed in the males of this group. This finding was reversible after the 14-day recovery period.

Based on the results of this study, a no-observed-effect-level (NOEL) could not be established.

Erosion and ulceration in the forestomachs of some females after four weeks' treatment with 1000 mg(kg/day were considered to be adverse effects, although they were reversible after the recovery period. Squamous cell hyperplasia and hyperkeratosis of the forestomach epithelium in males and females of all treated groups were dose-related in incidence and severity after four weeks' treatment, but were considered to be an adaptive response to a potent local irritant. These findings were still present after the two-week recovery period in rats previously treated with 1000 mg/kg/day, but the severity was less when compared to the rats which were necropsied after four weeks' treatment, suggesting that reversibility may be a factor of time.

Assuming a treatment duration not exceeding 28 days, the no-observed-adverse-effect-level (NOAEL) of TKA 40291 (ZLI 3331) was considered to be 200 mg/kg/day.

The results of the dose formulation analysis, however, indicated that the test item was stable for a short time, resulting in variable exposure to the test item. Despite this, marked test item-related (or degradation product-related) changes of toxicological significance were noted at all dose levels, but these changes (chiefly morphological) showed indications of reversibility that, given sufficient time, would likely result in full reversibility.

4 OBJECTIVE

4.1 PURPOSE AND RATIONALE

The purpose of this oral toxicity study was to assess the cumulative toxicity of TKA 40291 (ZLI 3331) 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.

This study should provide a rational basis for toxicological risk assessment in man. The results of this study should indicate potential target organs and should identify chemicals with neurotoxic potential.

5 MATERIALS AND METHODS

5.1 TEST SYSTEM

Test system	Rat, HanBrl:WIST (SPF)
Rationale	Recognized by the international guidelines as the recommended test system.
Source	RCC Ltd Laboratory Animal Services CH-4414 Füllinsdorf / Switzerland
Total number of animals per group	Groups 1 and 4: 10 males; 10 females Groups 2 and 3: 5 males; 5 females
Total number of animals	30 males and 30 females
Age at delivery	6 weeks
Body weight range at acclimatization	Males: 136.8 - 159.7 grams (mean 147.1 grams) Females: 114.7 - 129.5 grams (mean 121.0 grams)
Identification	Cage card and individual ear tattoo
Randomization	Computer-generated random algorithm
Acclimatization	Under test conditions after health examination. Only animals without any visible signs of illness were used for the study.

5.2 ALLOCATION

Allocation And Dose Levels	Group 1* 0 mg/kg/day	Group 2 50 mg/kg/day	Group 3 200 mg/kg/day	Group 4 1000 mg/kg/day
Males A	1 - 5	11 - 15	16 - 20	21 – 25
Males B	6 - 10			26 - 30
Females A	31 – 35	41 - 45	46 - 50	51 – 55
Females B	36 - 40			56 - 60

A - Toxicity testing (termination after 28 treatment days)
B - Recovery testing (termination after an additional 14-day recovery period)
* - Control animals were treated with the vehicle, PEG 300, only

5.3 HUSBANDRY

Room number	E15, RCC Itingen
Conditions	Standard Laboratory Conditions. Air-conditioned with 10-15 air changes per hour, and continuously monitored environment with a target range for temperature of 20 ± 3 °C and for relative humidity between 30-70 %. 12 hours fluorescent light / 12 hours dark, music during the light period.
Accommodation	In groups of five in Makrolon type-4 cages with wire mesh tops and standardized softwood bedding ('Lignocel' Schill AG, CH-4132 Muttenz/Switzerland).
Diet	Pelleted standard Provimi Kliba 3433 (batch no. 84/02) rat maintenance diet (Provimi Kliba AG, CH-4303 Kaiseraugst/ Switzerland) was available *ad libitum*. The feed batch was analyzed for contaminants (see Appendix III, pp. 242 - 244).
Water	Community tap-water from Itingen was available *ad libitum* in water bottles. Results of bacteriological assay, chemical and contaminant analyses of representative samples are attached to this report (see Appendix II, pp. 238 - 241).
	None of the contaminants analyzed in the water and diet is considered to have been present at a concentration which would have affected the validity of the results.

5.4 TEST ITEM

Identity	TKA 40291 (ZLI 3331)
Description	white solid
Batch number	RSSL 2002.086.13.A
Purity	88.9%
Composition	Product by process
Stability of test item	Stable under storage conditions
Expiry date	01 March 2004
Storage conditions	at room temperature (17-23°C) in the original container away from direct sunlight
Safety precautions	Routine hygienic procedures (gloves, goggles, face mask)

The test item information was supplied by the sponsor.

5.5 TEST ITEM PREPARATION

The test item formulations were prepared weekly.

TKA 40291 (ZLI 3331) was weighed into a glass beaker on a tared Mettler balance and the vehicle added. The mixtures were prepared using a magnetic stirrer and stored at room temperature (17-23°C).

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

5.5.1 ANALYSIS OF DOSE FORMULATIONS

Concentration, homogeneity and stability (after 2 hours and 7 days) of the dose formulations were determined in samples taken after experimental start. Concentration and homogeneity of the dose formulations were determined in samples taken during week 3 of the treatment. The analyses were performed by RCC Ltd (Environmental Chemistry & Pharmanalytics Division) according to a HPLC method supplied by the Sponsor. The results are presented in Appendix V.

See pp. 327 - 344

5.6 VEHICLE AND CONTROL ITEMS

Identity	PEG 300
Suppplier	Fluka AG
Batch number	442989/1 54802033 and 442989/1 54502013

Expiry date	27 Feb 2008 and 12 Dec 2007
Storage conditions	At room temperature (17-23°C) in the original container in the dark
Safety precautions	Routine hygienic procedures (gloves, goggles, face mask)

5.7 TREATMENT

Method	Oral, by gavage.
Rationale	Accidental oral ingestion is a possible route of human exposure.
Daily dose levels	Group 1: 0 mg/kg body weight Group 2: 50 mg/kg body weight Group 3: 200 mg/kg body weight Group 4: 1000 mg/kg body weight Dose levels are expressed in terms of the test item as supplied.
Rationale for dose level selection	Based upon the results of a non-GLP 5-day dose-range-finding study (RCC Study Number 848175) in which TKA 40291 (ZLI 3331) was administered by gavage to 2 rats per group and sex.
Frequency of administration	Daily
Dose volume	5 ml/kg body weight
Duration of acclimatization period	7 days
Duration of treatment	28 days
Duration of recovery	14 days

5.8 OBSERVATIONS

5.8.1 MORTALITY / VIABILITY

Observations for mortality/viability were recorded twice daily.

5.8.2 GENERAL CAGESIDE OBSERVATIONS (DAILY)

The animals were observed for clinical signs once before commencement of administration; twice daily on days 1-3; as well as once daily on days 4-28, and once daily during days 29-42 (recovery).

5.8.3 DETAILED CLINICAL OBSERVATIONS (WEEKLY)

The animals were observed in their home cages, outside their home cages in a standard arena and in the hand. These observations were performed in random sequence once before commencement of administration and once weekly (weeks 1-3) thereafter.

5.8.4 FOOD CONSUMPTION

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

5.8.5 BODY WEIGHTS

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

5.8.6 FUNCTIONAL OBSERVATIONAL BATTERY

During week 4, relevant parameters (presented in Appendix I) from a modified Irwin screen test were evaluated in all animals.

NB. The results of the Functional Observational Battery are presented in the summary and individual tables of the Detailed Clinical Observations (Weekly) under week 4. This method of data presentation permits a clear evaluation and assessment of weekly clinical signs observed during the study.

GRIP STRENGTH

Forelimb and hind limb 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 Activity Monitor AM 1052 system (Benwick Electronic Equipment Design Manufacture, England). Animals were randomized and 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 15-minute intervals as well as the total activity of the measuring period.

5.9 CLINICAL LABORATORY INVESTIGATIONS

Blood and urine sampling:

after 4 weeks	19 May 2003 (Allocation A and B)
after 6 weeks	02 June 2003 (Allocation B)

Blood samples for hematology and clinical biochemistry were collected 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*. Blood 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-hour fasting period into a specimen vial.

The assays were performed at RCC Ltd (Stein) under internal laboratory quality control conditions to assure reliable test results.

In the summary and individual tables the names of some parameters have been abbreviated. Any abbreviation has been defined in Appendix IV.

Detailed methodology, abbreviations and general remarks are described in Appendix IV.

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

5.9.1 HEMATOLOGY

The following hematology parameters were determined:

Erythrocyte count
Hemoglobin
Hematocrit
Mean corpuscular volume
Red cell volume distribution width
Mean corpuscular hemoglobin
Mean corpuscular hemoglobin concentration
Hemoglobin concentration distribution width
Platelet (thrombocyte) count
Reticulocyte count
Reticulocyte maturity index
Methemoglobin
Total leukocyte count
Differential leukocyte count
Coagulation:
Thromboplastin time
Activated partial thromboplastin time

5.9.2 CLINICAL BIOCHEMISTRY

The following clinical biochemistry parameters were determined:

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

5.9.3 URINALYSIS

The following urinalysis parameters were determined:

Volume (18 hours)
Specific gravity (relative density)
Color
Appearance
pH
Nitrite
Protein
Glucose
Ketones
Urobilinogen
Bilirubin
Erythrocytes
Leukocytes

5.10 PATHOLOGY

5.10.1 NECROPSY

Sacrifice:

after 4 weeks	19 May 2003 (Allocation A)
after 6 weeks	02 June 2003 (Allocation B)

All animals were weighed and necropsied. Descriptions of all macroscopic abnormalities were recorded.

All animals were anesthetized by intraperitoneal injection of sodium pentobarbitone and killed by exsanguination.

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

Adrenal glands
Aorta
Bone (sternum, femur including joint)
Bone marrow (femur)
Brain (cerebrum, cerebellum, brain stem)
Cecum
Colon
Duodenum
Epididymides (fixed in Bouin's solution)
Esophagus
Eyes with optic nerve (fixed in Davidson's solution)
Harderian gland (fixed in Davidson's solution)
Heart
Ileum, with Peyer's patches
Jejunum with Peyer's patches
Kidneys
Larynx
Lacrimal gland (exorbital)
Liver
Lungs (infused with formalin at necropsy)
Lymph nodes (mesenteric, mandibular)
Mammary gland area
Nasal cavity
Ovaries
Pancreas
Pituitary gland
Prostate gland
Rectum
Salivary glands (mandibular, sublingual)
Sciatic nerve
Seminal vesicles
Skeletal muscle
Skin
Spinal cord (cervical, midthoracic, lumbar)
Spleen
Stomach
Testes (fixed in Bouin's solution)
Thymus
Thyroid (incl. parathyroid gland)
Tongue
Trachea
Urinary bladder (infused with formalin at necropsy)
Uterus
Vagina
Gross lesions

5.10.2 ABSOLUTE AND RELATIVE ORGAN WEIGHTS

The following organ weights were recorded on the scheduled dates of necropsy:

Brain	Thymus	Spleen	Ovaries
Heart	Kidneys	Testes	
Liver	Adrenals	Epididymides	

The organ to terminal body weight ratios as well as organ to brain weight ratios were determined.

The determination of the terminal body weight was performed immediately prior to necropsy.

5.10.3 HISTOTECHNIQUE

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

5.10.4 HISTOPATHOLOGY

Slides of all organs and tissues listed in boldface type (see Necropsy, above) which were collected at scheduled sacrifice from the animals of control and high-dose groups were examined by a pathologist.

As test item-related morphologic changes were detected in the organs of high-dose animals, the same organs (liver and stomach of all animals, bone marrow of females and adrenal glands of males) from animals of the mid- and low-dose groups were examined.

5.11 DATA COMPILATION

5.11.1 GENERAL

The following data were recorded on-line: food consumption, body weights, organ weights and macroscopic findings at necropsy and histopathology. Locomotor activity was recorded on-line, and the results were printed and transcribed for compilation and analysis into the computer system.

Clinical laboratory data were recorded on-line (Bayer Advia 120 Hematology System, Hitachi 917 Discrete Random-Access Analyzer, OSM3 Hemoximeter, Roche STA-compact analyzer, Roche Miditron M Semi-Automated Urine Chemistry Analyzer or on data sheets (various light microscopes and refractometers) and then transferred to the computer system.

Cageside and detailed clinical signs, data from the functional observational battery and grip strength were recorded on data sheets and transcribed for compilation and analysis into the computer system.

The computer-generated values which appear in the tables represent the rounded-off results of the raw data values or of calculations which used the exact raw data values.

Group means were calculated according to the definition of any mean value using the individual values per animal and the number of animals.

5.12 DATA CALCULATION

5.12.1 FOOD CONSUMPTION

The food consumption was calculated per rat and per food consumption interval. It expresses the average food consumed per animal and per day over the food consumption interval.

$$FC = \frac{C}{AD}$$

where

FC is Food consumption in grams of food per animal and day;
C is measured food consumption in grams per cage over the consumption interval and
AD is total consumption days over all animals in the cage during the consumption interval.

5.12.2 RELATIVE FOOD CONSUMPTION

The relative food consumption was calculated according to the following formula:

$$RFC = \left[\frac{FC}{BW(i)}\right] \times 1000$$

where

BW(i) is the most ideal body weight in grams or the body weight (of the corresponding rats) recorded on the day most close to the middle of the food consumption interval. In cases of equal "closeness" of two body weight records the later one was chosen;
RFC is relative food consumption in grams of food per kg body weight and day, and
FC is food consumption in grams of food per animal and day.

5.13 STATISTICAL ANALYSIS

The following statistical methods were used to analyze the grip strength, locomotor activity, body weight, organ weights and ratios, as well as:

- The Dunnett-test (many to one t-test) based on a pooled variance estimate were 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 (many-one rank test) were applied instead of the Dunnett-test when the data can not be assumed to follow a normal distribution.
- Fisher's exact-test were applied to the macroscopic findings.

The following statistical methods were used for statistical analysis of clinical laboratory data:

- Quantitative data were analyzed by a one-way analysis of variance (ANOVA) when the variances are considered homogeneous according to Bartlett. Alternatively, if the variances are considered to be heterogenous ($p \leq 0.05$), a non-parametric Kruskal-Wallis test was used. Treated groups were compared to the control groups using Dunnett's test if the ANOVA was significant at the 5% level and by Dunn's test in the case of a significant Kruskal-Wallis test ($p \leq 0.05$).

References :

C.W. Dunnett: A Multiple Comparison Procedure for Comparing Several Treatments with a Control, J. Amer. Stat. Assoc. 50, 1096-1121 (1955).

S.C. Gad and C.S. Weil: Statistics and Experimental Design for Toxicologists. The Telford Press,Caldwell, New Jersey, 43-45 (1986).

W.H. Kruskal and W.A. Wallis: Use of ranks in one-criterion variance analysis. Journal of the American Statistical Association, 47, 583-621 (1952).

O.J. Dunn: Multiple comparisons using rank sums. Technometrics 6, 241-252 (1964).

R.G. Miller: Simultaneous Statistical Inference, Springer Verlag, New York (1981).

R.A. Fisher: Statistical Methods for Research Workers, Oliver and Boyd, Edinburgh (1950).

6 RESULTS

6.1 RESULTS OF DOSE FORMULATION ANALYSIS

The analysis of TKA 40291 in PEG 300 with the method delivered by the sponsor caused some implementation problems at RCC, including blockage of column by PEG 300 (assumed) and difficult separation of the test item peak from matrix peaks. These problems were solved and the reproducibility of peak areas was improved.

Although the development of a suitable analytical method was successful, inconsistent results were obtained within the range-finding study and within this study with the first samples taken after experimental start.

To confirm the dose formulation procedure of samples and to test the freezing stability (approx. – 20°C) of dose formulations, samples were prepared freshly and were partially stored deep-frozen for 24 hours. The analytical results showed a good recovery for the two unfrozen samples (103.5% and 92.0%), but the recoveries obtained for the frozen samples was found to be very low (10.0% and 5.2%). Thus, the dose formulations are assumed to be not stable at – 20°C which were the storage conditions for all samples taken for analytical purposes. Additionally, the results for the 0-hours samples showed that the application mixtures can be prepared correctly under light protection.

As it is mentioned in the study plan, the application mixtures were stored at ambient temperature. Fresh samples (concentrations of 10 mg/mL and 200 mg/mL) were prepared under light protection in the analytical laboratory to test whether the application mixtures are stable at 4°C for 7 days under light protection. The results showed that the test item in PEG 300 degrades within hours and that the dose formulations are not stable for 7 days under these conditions.

In conclusion, the mixtures administered probably contained mostly degradation products of the test item.

See pp. 327 - 344

6.2 VIABILITY/MORTALITY

All animals survived until scheduled necropsy.

See pp. 92 - 99

6.3 OBSERVATIONS

6.3.1 GENERAL CAGESIDE OBSERVATIONS (DAILY)

Soft feces was noted from day 7 of treatment in the males and females at 1000 mg/kg/day when compared with the controls. These changes were considered to be test item-related. At 1000 mg/kg/day, salivation was noted in one male on day 16, one female on day 14, two males and one female on day 27 and two males and three females on day 28 of treatment, and were considered to be test item related.

Localised external findings (hair loss and/or scabs) were seen in up to four males of the control group. Insofar as these findings were restricted to one cage, they were considered to be the result of internecine conflict.

See pp. 40 - 47, 100 - 159

6.3.2 DETAILED CLINICAL OBSERVATIONS (WEEKLY)

During weeks 2 and 3, salivation was noted in two males/one female, and one male, respectively, treated with 1000 mg/kg/day. This minor finding was considered to be test item-related.

All other findings (hair loss in three control males during weeks 2 and 3) were considered to be test item-unrelated.

See pp. 48 - 49, 160 - 171

6.3.3 FUNCTIONAL OBSERVATIONAL BATTERY

During week 4, salivation was noted in three males and three females treated with 1000 mg/kg/day. This finding was considered to be test item-related.

All other findings (hair loss in four control males) were considered to be test item-unrelated.

See pp. 172 - 174

Grip Strength

The mean fore- and hindlimb grip strength of the test item-treated rats compared favorably with those of the controls.

See pp. 50, 175

Locomotor Activity

No test item-related differences in the mean locomotor activity were noted at any dose level. Significantly reduced ($p<0.05$) locomotor activity was noted from 15-30 minutes in the males treated with 1000 mg/kg/day, but the overall locomotor activity was generally similar to that of the control males. In females, significantly reduced locomotor activity was noted from 0-15 minutes at 1000 mg/kg/day ($p<0.01$), and from 0-15 minutes ($p<0.05$), 15-30 minutes ($p<0.05$) and 0-60 minutes ($p<0.01$) at 50 mg/kg/day. The locomotor activity of the females treated with 200 mg/kg/day exceeded that of the control females. These contrary findings were considered to be incidental.

See pp. 51 - 52, 176 - 177

6.4 FOOD CONSUMPTION

The mean daily food consumption of the test item-treated males and females compared favorably with the respective control values during the treatment and recovery periods.

See pp. 31 - 34, 53 - 64, 178 - 193

6.5 BODY WEIGHTS

Differences noted in the mean body weights of the test item-treated males were not seen in the females and therefore considered unlikely to be test item-related.

The mean body weights of the test item-treated males were generally lower than those of the control males. On day 28 of treatment, the difference was significantly lower ($p<0.05$) than that of the controls, but a clear dose-response relationship was not seen in any of the test time-treated males. The mean body weight gain of the all test item-treated males was significantly lower ($p<0.05$) on day 15, whereas significant differences were noted on days 22 and 28 in males treated with 200 mg/kg/day, and on day 28 in males treated with 50 mg/kg/day.

The slightly lower body weight and body weight gain of the males treated with 1000 mg/kg/day was also noted during the recovery period. These differences were considered to be due to high control values.

The mean body weights of the test item-treated females were unaffected. The mean body weight gain of the females treated with 1000 mg/kg/day was significantly elevated ($p<0.05$) on day 15 of treatment. The body weight development of all females compared favorably during the recovery period.

See pp. 35 - 38, 65 - 76, 194 - 209

6.6 CLINICAL LABORATORY INVESTIGATIONS

6.6.1 HEMATOLOGY

Hemoglobin levels were significantly increased ($p<0.01$) and mean cell hemoglobin concentration were significantly decreased ($p<0.05$) after four weeks' treatment in males at 1000 mg/kg/day when compared with controls. Although these differences marginally exceeded those of the historical control data, they were considered to be unrelated to the treatment with the test item as concommitent changes in related parameters were not seen. Similarly, the relative number of "large unstained cells" were significantly increased ($p<0.05$) after four weeks' treatment in males treated at 200 mg/kg/day, but this change was not seen at 1000 mg/kg/day and therefore considered to be incidental.

Hematocrit was significantly increased ($p<0.01$) after four weeks' treatment in males at 1000 mg/kg/day when compared with the control males, but remained within the range of the historical control data and is therefore considered to be fortuitous.

Males treated with 1000 mg/kg/day showed significantly "left-shifted" reticulocyte maturity indices towards high fluorescence reticuloctes (decreased medium fluorescent reticulocytes, $p<0.01$; increased high fluorescent reticulocytes, $p<0.01$) after four weeks' treatment. These differences remained within the ranges of the historical control values. High fluorescent reticulocytes were significantly reduced after four weeks' treatment in males ($p<0.05$) treated with 50 mg/kg/day. This difference, in the absence of a dose-response relationship, was considered to be incidental.

The red cell distribution width was significantly increased ($p<0.01$) after four weeks' treatment in females at 1000 mg/kg/day, but this finding was not accompanied by concommitent changes in related parameters and considered to be incidental.

The relative neutrophil counts were significantly increased after four weeks' treatment in males ($p<0.05$) and females ($p<0.05$) treated at 1000 mg/kg/day, and the absolute neutrophil counts were significantly increased after four weeks' treatment in males treated at 200 mg/kg/day ($p<0.05$) and both sexes treated at 1000 mg/kg/day (males: $p<0.01$; females: $p<0.05$). The relative number of eosinophils was significantly decreased ($p<0.05$) after four weeks' treatment in males treated at 1000 mg/kg/day. All differences remained within the ranges of the historical control data and were considered to be fortuitous.

Contrary changes in activated partial thromboplastin time after four weeks' treatment noted in females at 200 mg/kg/day (prolonged, $p<0.05$) and 1000 mg/kg/day (foreshortened, $p<0.01$) were considered to be unrelated to the test item.

All differences noted after the recovery period (significantly decreased relative monocytes ($p<0.05$) in males previously treated at 1000 mg/kg/day; decreased medium fluorescent reticulocytes ($p<0.01$) in females treated previously at 1000 mg/kg/day) were considered to be incidental changes unrelated to the treatment with the test item.

See pp. 245 - 326

6.6.2 CLINICAL BIOCHEMISTRY

Significantly elevated sodium levels ($p<0.01$) and inorganic phosphate levels ($p<0.01$) were noted in males treated with 1000 mg/kg/day for four weeks. These differences exceeded those of the historical control data. Significantly lower potassium levels ($p<0.05$) and calcium levels ($p<0.01$) were noted in males treated with 1000 mg/kg/day when compared with the control males, but these data remained with the ranges of the historical conrol data. Still, changes in the electrolytes were considered likely to be related to the treatment with the test item.

After four weeks' treatment with 1000 mg/kg/day, mean glucose levels were lower in males ($p<0.01$) and in females(not significant) when compared with the respective controls. Total bilirubin levels were significantly higher in females treated with 1000 mg/kg/day ($p<0.05$) after four weeks' treatment. Significantly lower globulin levels ($p<0.05$) were noted in males treated with 1000 mg/kg/day and a significant increase in the albumin/globulin ratio ($p<0.01$) was seen accordingly. These diiferences were within the ranges of the historical control data.

The clinical biochemistry values noted in the females after four weeks' treatment were similar to those of the controls.

After the recovery period, all changes were considered to be unrelated to treatment (increased urea ($p<0.05$) in males previously treated at 1000 mg/kg/day; decreased cholesterol ($p<0.05$) in males previously treated at 1000 mg/kg/day; decreased phospholipids ($p<0.05$) in males previously treated at 1000 mg/kg/day; significantly lower total bilirubin levels in females previously treated with 1000 mg/kg/day ($p<0.05$); reduced calcium ($p<0.01$), reduced protein ($p<0.01$) and reduced albumin ($p<0.05$) in females previously treated with 1000 mg/kg/day).

See pp. 245 - 326

6.6.3 URINALYSIS

No differences of statistical or toxicological significance were noted in the urinalysis parameters after four weeks' treatment or two weeks' recovery.

See pp. 245 - 326

6.7 PATHOLOGY

6.7.1 ORGAN WEIGHTS

After 4 Weeks

Significantly elevated mean absolute liver weights ($p<0.05$) were noted in the females treated with 1000 mg/kg/day. Significantly elevated mean liver-to-body weight ratios were noted in males ($p<0.05$) and females ($p<0.05$) treated with 1000 mg/kg/day, and significantly elevated liver-to-brain weight ratios were noted in females treated with 1000 mg/kg/day.

Further test item-related changes in the mean organ to body weight ratios were noted in the kidneys ($p<0.05$) and adrenals ($p<0.01$) of males treated with 1000 mg/kg/day.

All other organ weights and ratios were unaffected.

After 6 Weeks

Significantly reduced mean absolute and relative liver weights ($p<0.01$ or $p<0.05$) were noted in the males treated previously with 1000 mg/kg/day.

All other organ weights were generally similar to those of the respective controls.

See pp. 79 - 90, 218 - 234

6.7.2 MACROSCOPIC FINDINGS

Surface irregularities were noted macroscopically in the stomachs of five male and five female rats treated with 1000 mg/kg/day. This finding was considered to be test item-related.

All remaining macroscopical changes (thymic size reduction in one male treated with 200 mg/kg/day, and pelvic dilation in one female treated with 50 mg/kg/day) were considered to be incidental.

See pp. 77 - 78, 210 - 217

6.7.3 MICROSCOPIC FINDINGS

The detailed incidence data for all organs and tables of selected changes including their severity appear in the tables "Number of Animals with Microscopic Findings by Organ/Group/Sex" and "Summary Incidence of Grading by Organ/Sex/Group".

Forestomach

Squamous cell hyperplasia and hyperkeratosis were observed in all test item-treated animals. Squamous cell hyperplasia was minimal in males and females at 50 and in males at 200 mg/kg, minimal to slight in females at 200 mg/kg and moderate to marked in males and females at 1000 mg/kg. Hyperkeratosis was minimal to slight in males and females at 50 and 200 mg/kg and moderate to marked in males and females at 1000 mg/kg. These findings were still present after the 14-day recovery period, but their severity was decreased.

In addition, erosion or ulceration of the mucosa were observed in females at 1000 mg/kg.

Glandular stomach

Minimal to slight diffuse epithelial hyperplasia was observed in males and females at 1000 mg/kg. This finding was reversible after the 14-day recovery period.

Adrenal glands

Cortical fatty change was slightly increased in incidence and severity in males at 1000 mg/kg. No differences were seen between control and test item-treated males after the 14-day recovery period.

Liver

Glycogen deposition was slightly decreased in incidence and grading in males and females at 1000 mg/kg after the 14-day recovery period.

Incidental microscopic findings

Mineralization was observed in the Peyer's patches of males at 1000 mg/kg. This finding is known to occur spontaneously and therefore it is considered incidental.

Fatty atrophy of minimal to slight degree was observed in bone marrow of females at 1000 mg/kg after the 14-day recovery period. Since no changes were observed in the other treated groups, this finding was considered incidental.

A variety of other changes was found in this study. They commonly occur in laboratory rats of this strain and age, and, neither their incidences nor their distribution or morphologic appearance gave any indication of a test item-related association.

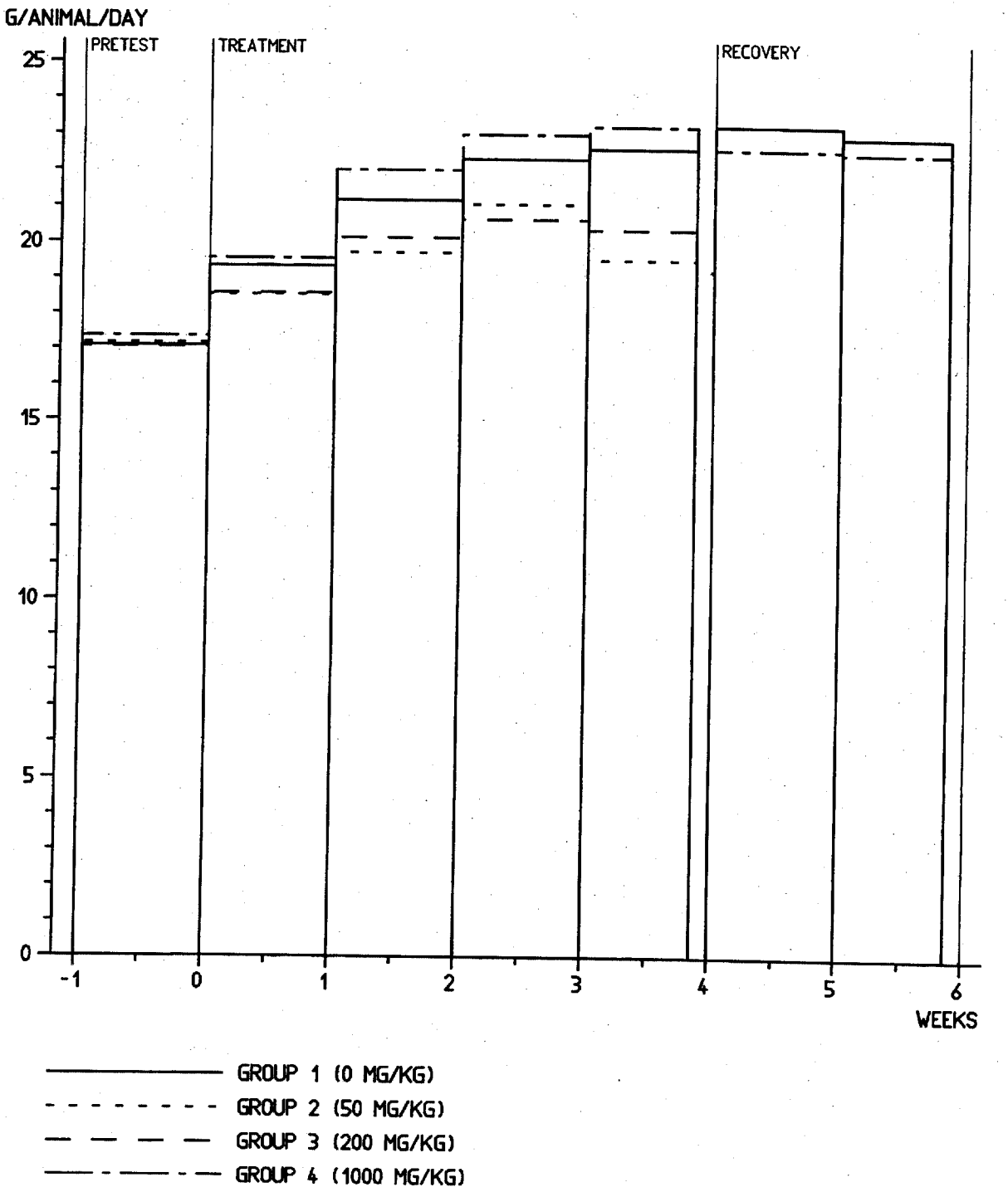
See pp. 345 - 442

7 FIGURES

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

FC-SPLT - 1
06-JUN-03

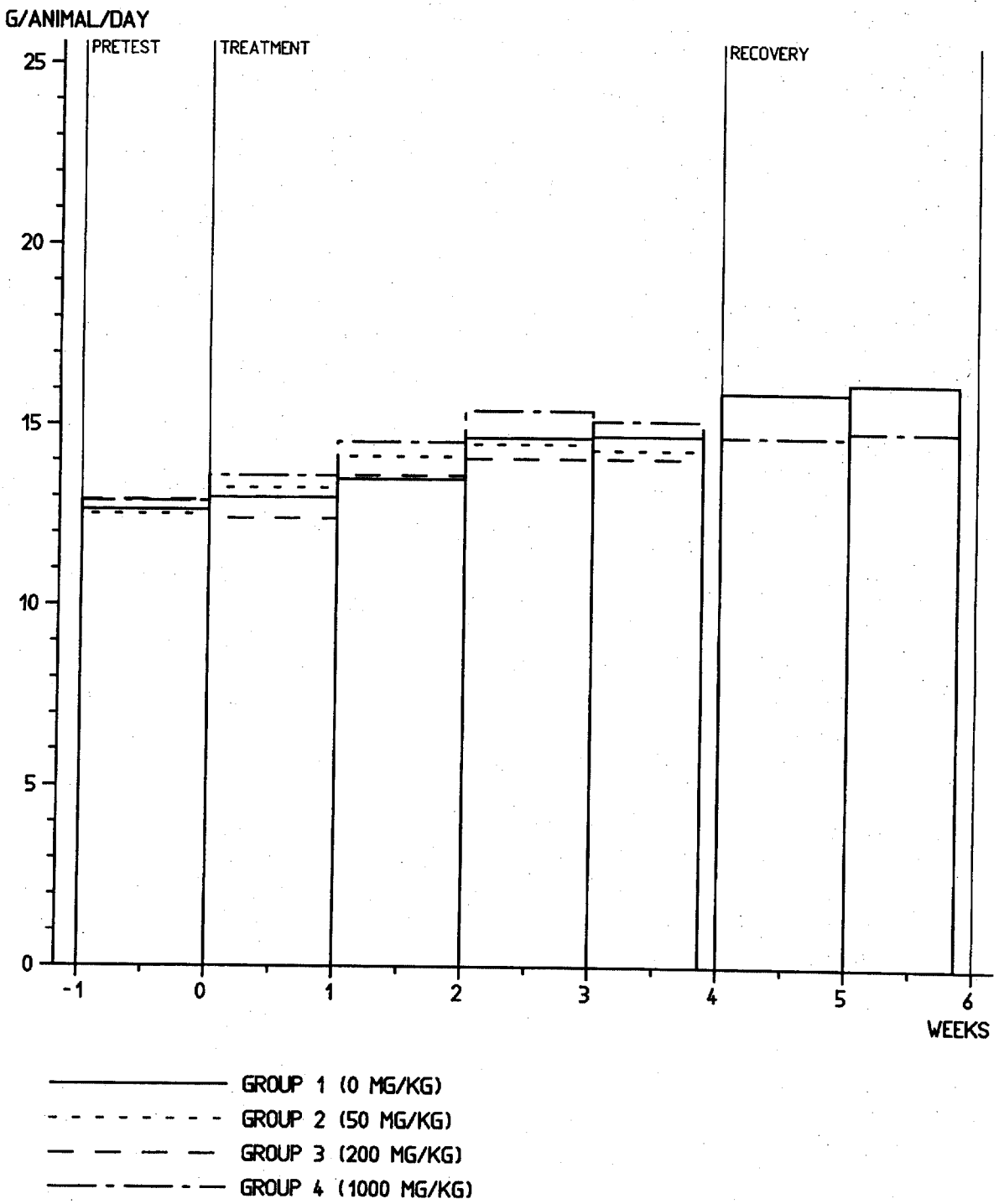
FOOD CONSUMPTION
MALES



RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

FC-SPLT - 2
06-JUN-03

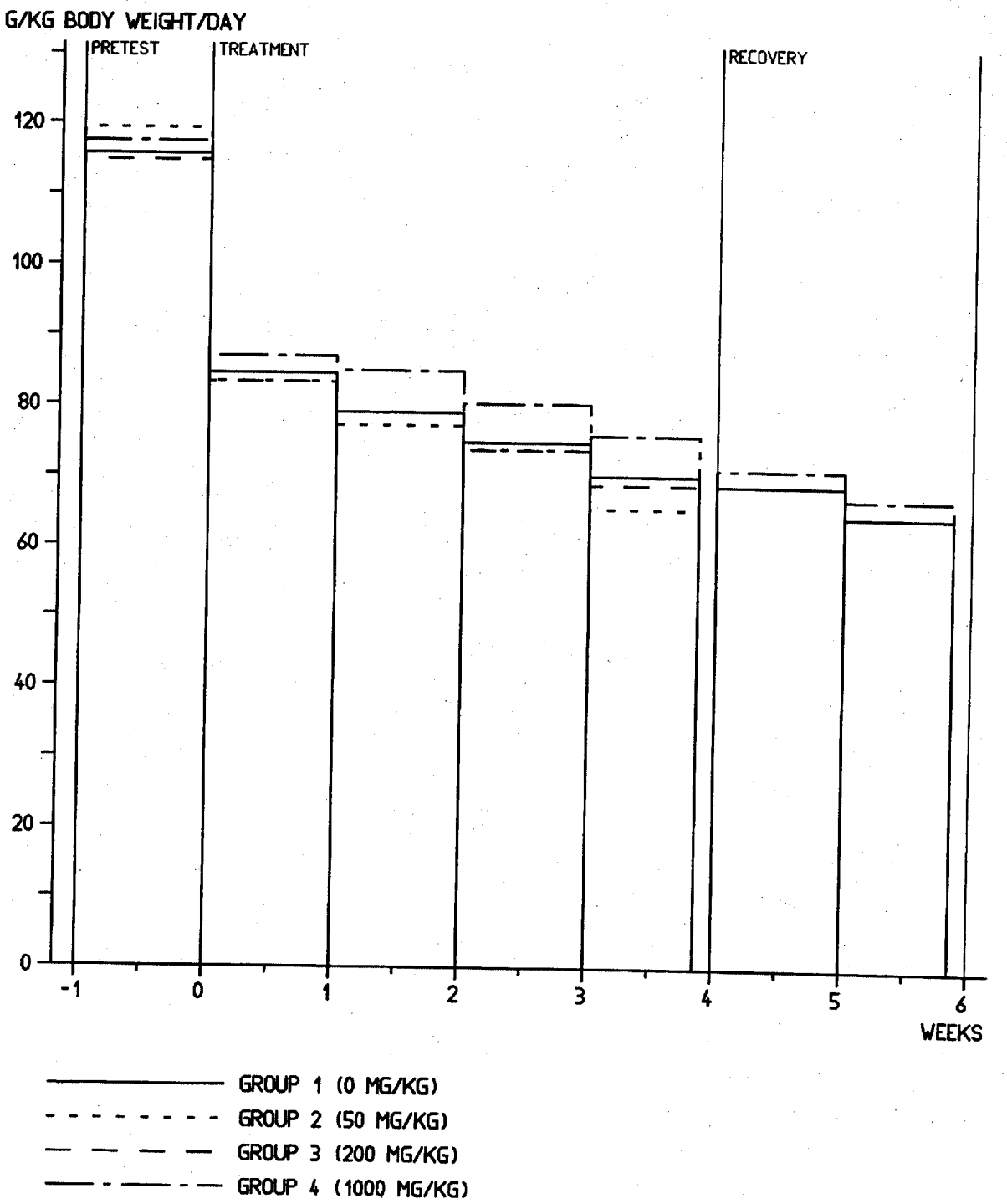
FOOD CONSUMPTION
FEMALES



RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

RFC-SPLT - 1
06-JUN-03

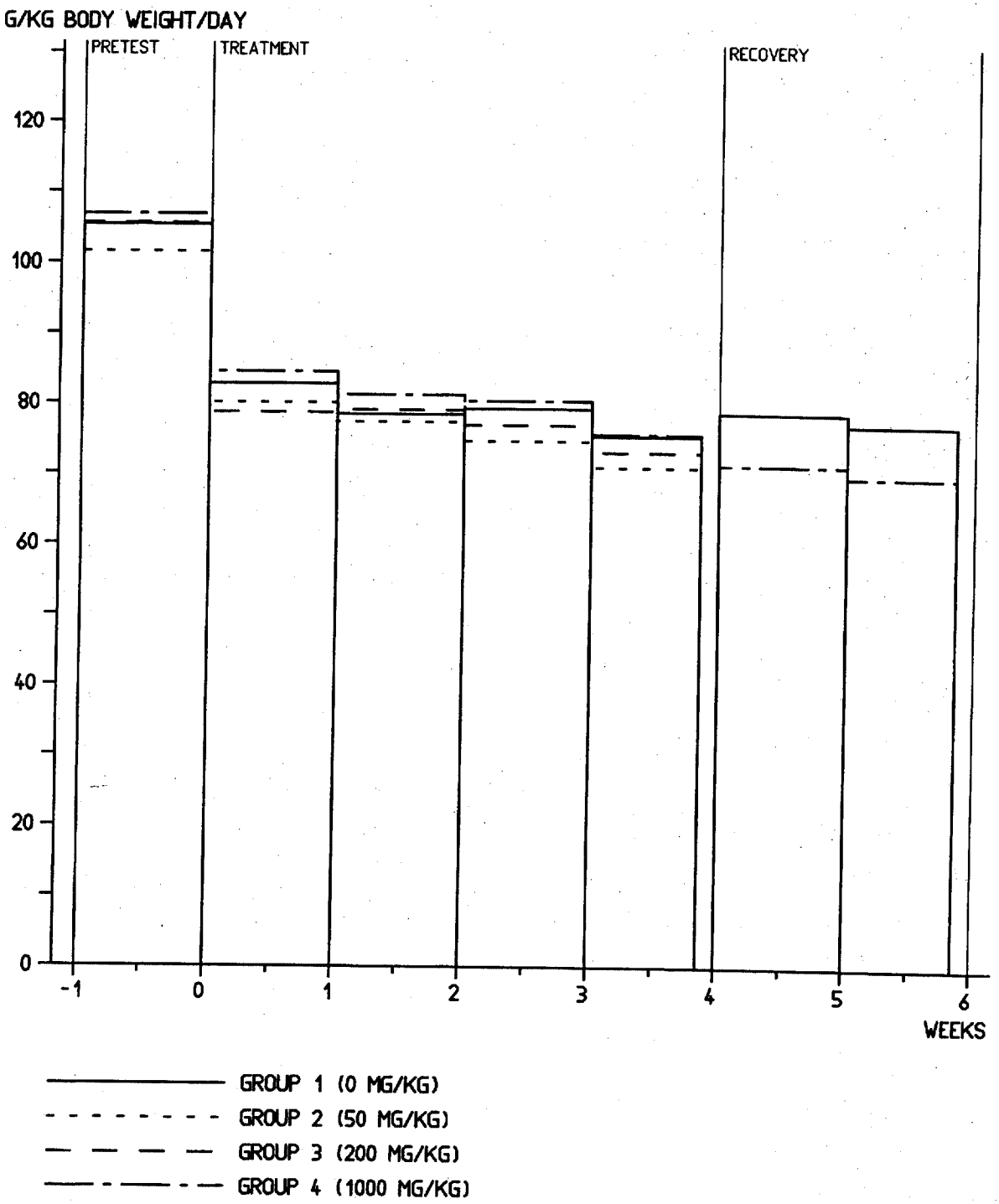
RELATIVE FOOD CONSUMPTION
MALES



RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

RFC-SPLT - 2
06-JUN-03

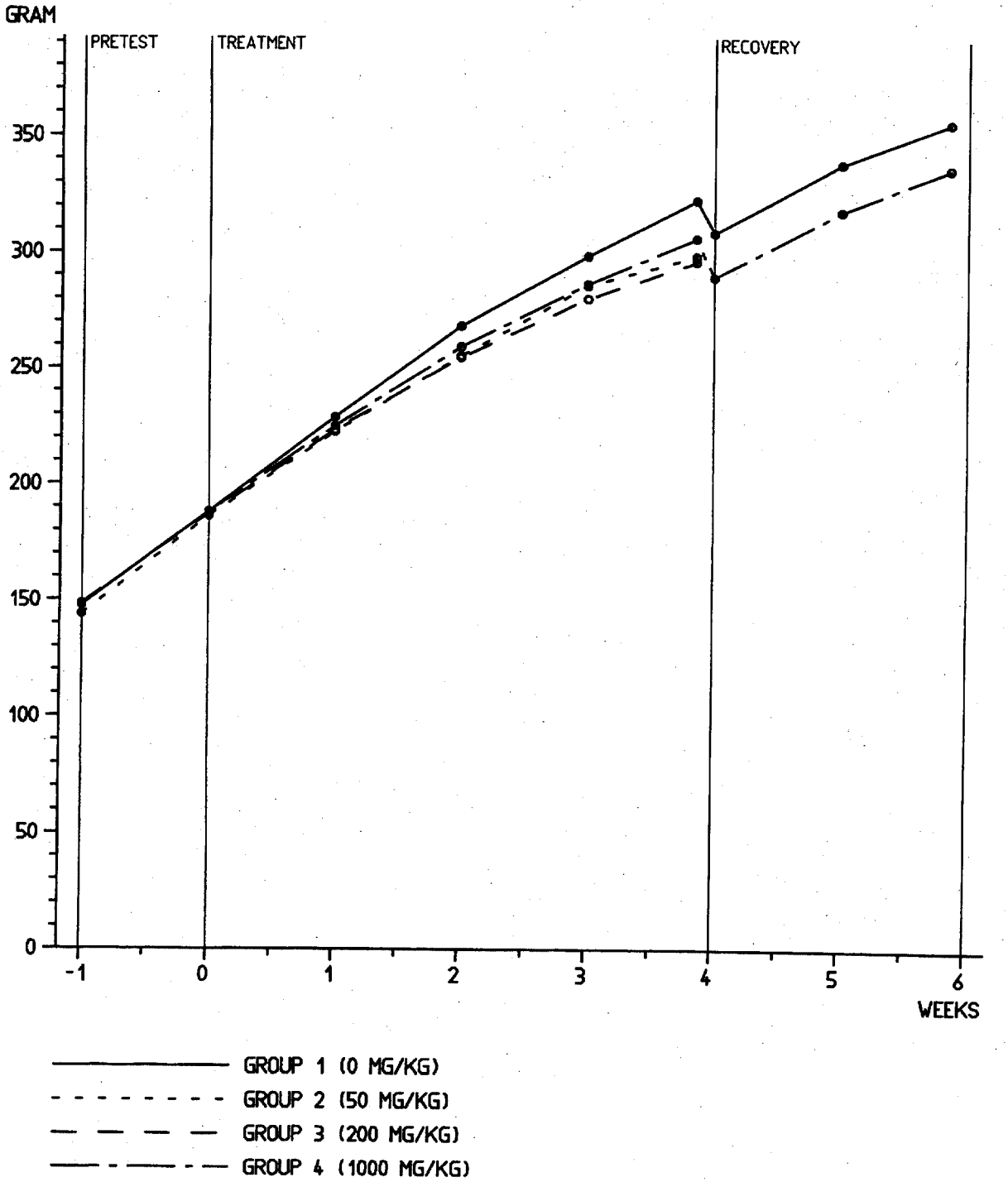
RELATIVE FOOD CONSUMPTION
FEMALES



RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

BW-SPLT - 1
06-JUN-03

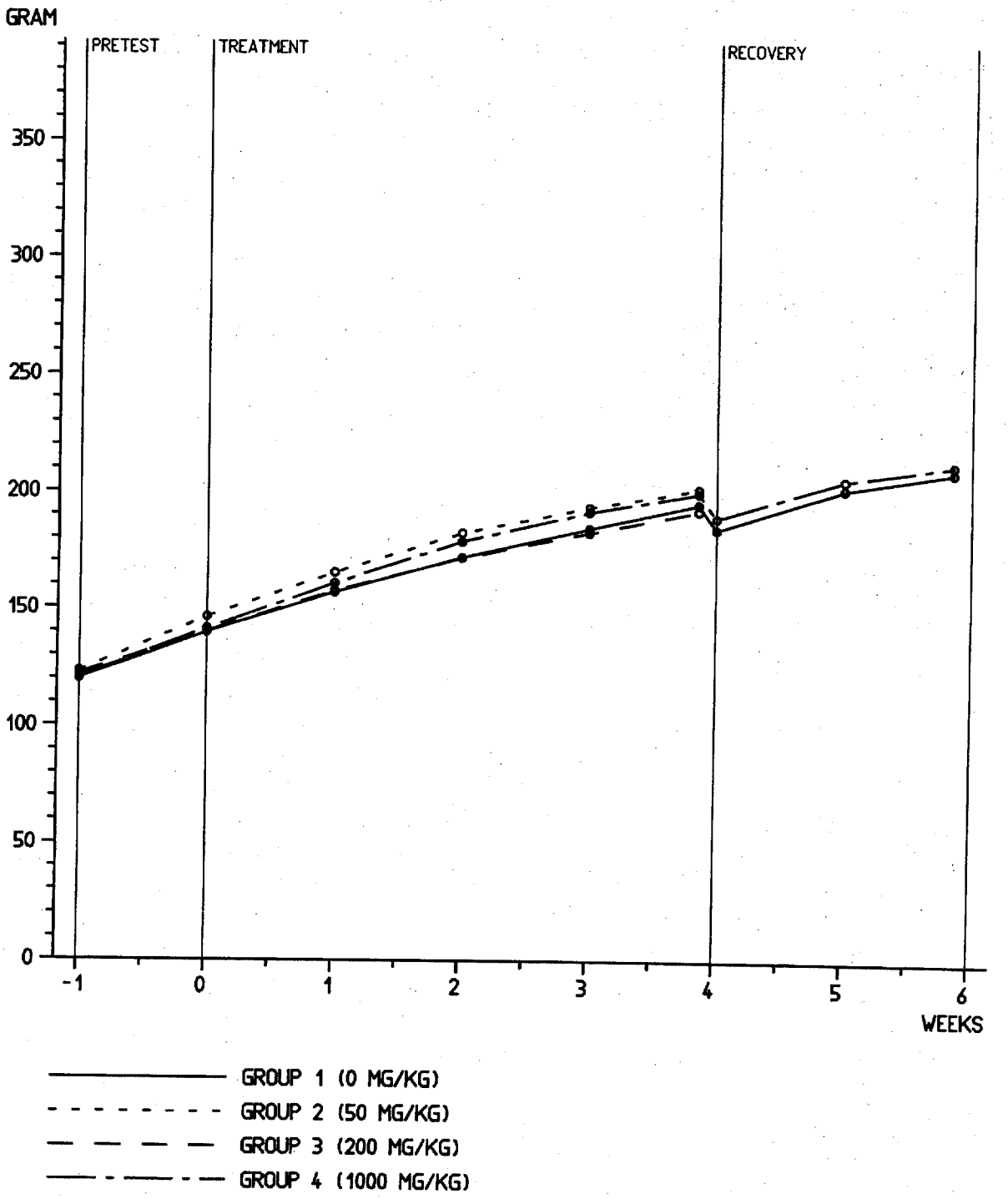
BODY WEIGHTS
MALES



RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

BW-SPLT - 2
06-JUN-03

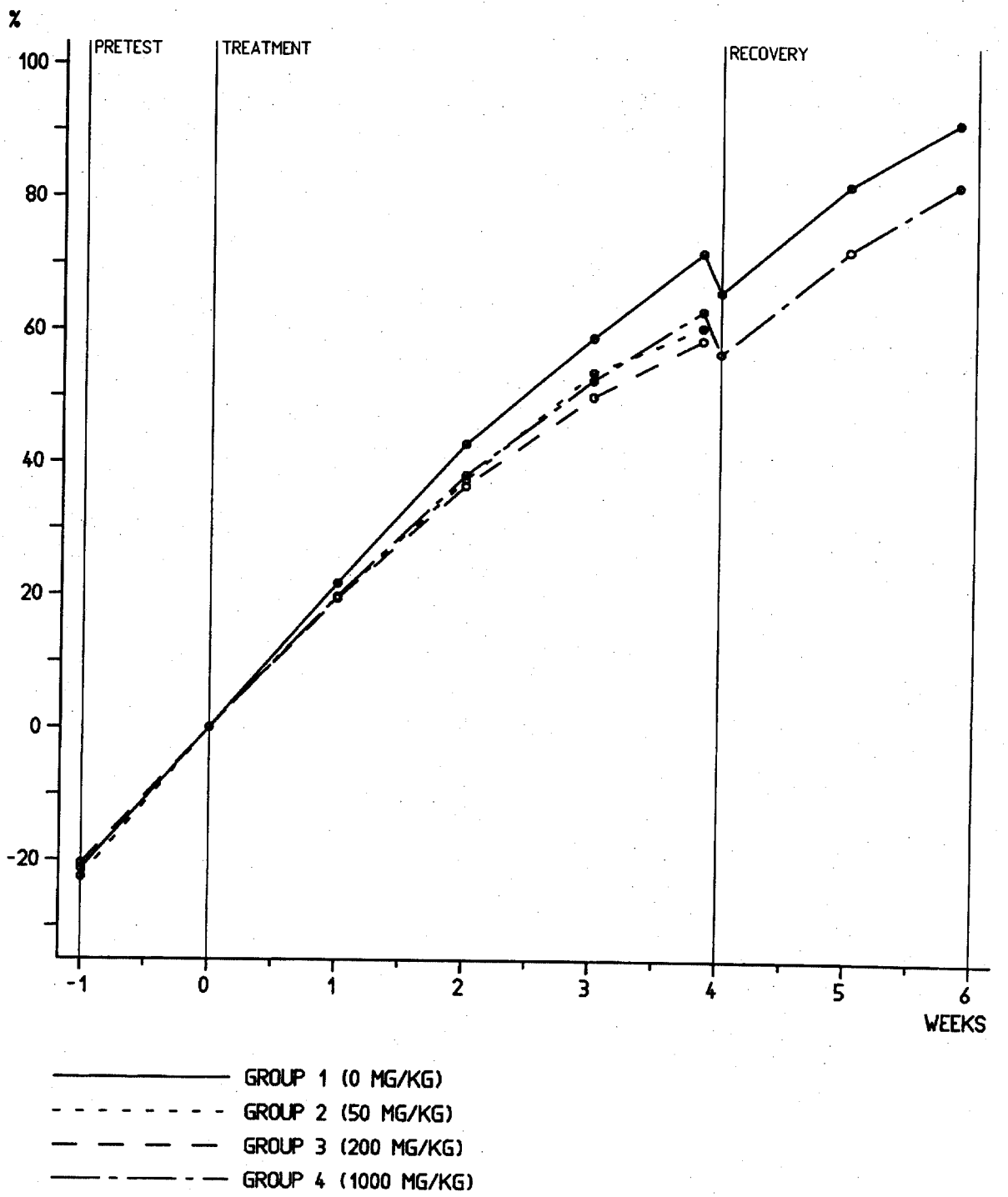
BODY WEIGHTS
FEMALES



RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

BWG-SPLT - 1
06-JUN-03

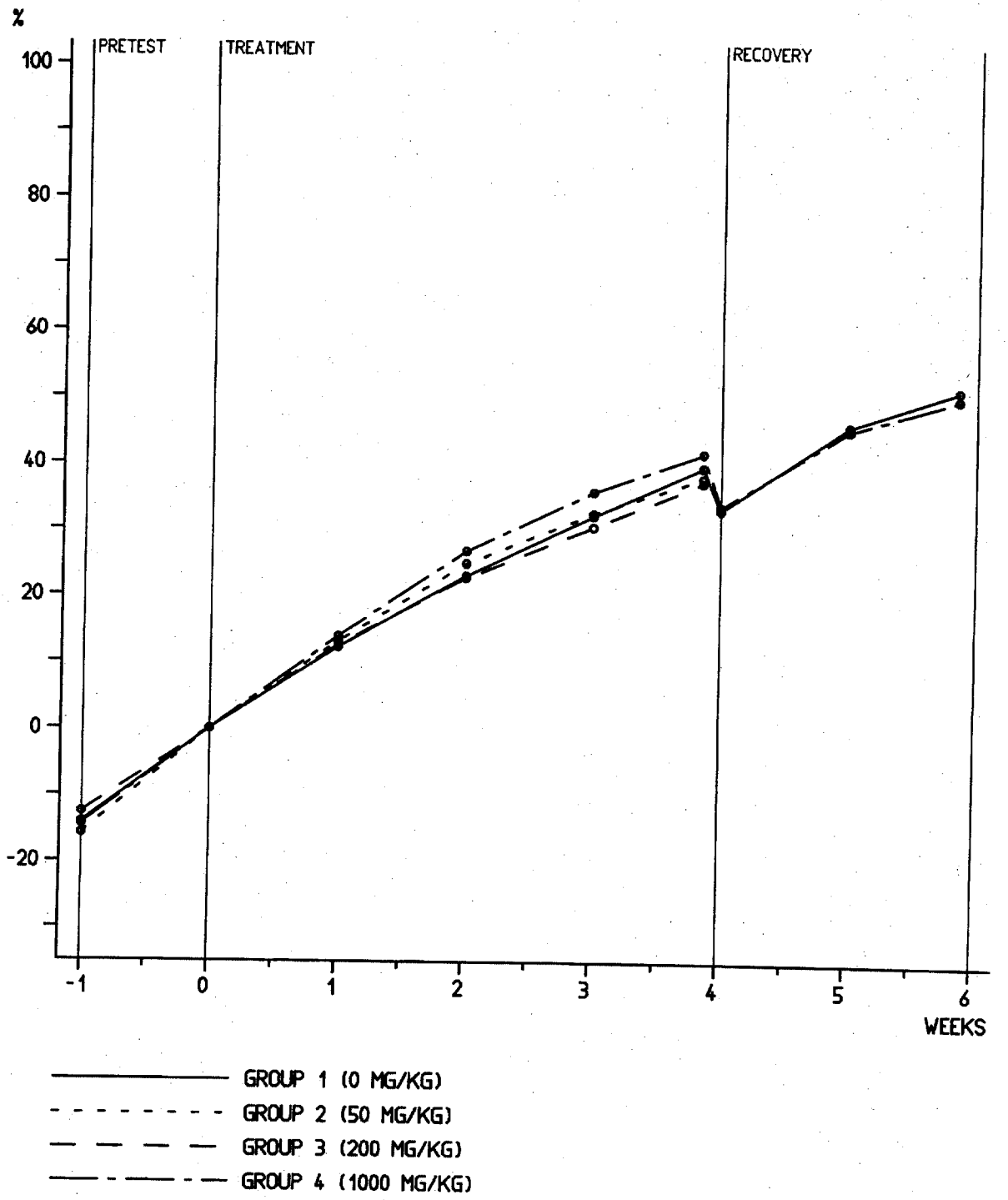
BODY WEIGHT GAIN
MALES



RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

BWG-SPLT - 2
06-JUN-03

BODY WEIGHT GAIN
FEMALES



8 SUMMARY TABLES

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, SUMMARY

GROUP 1 (CONTROL), MALES

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
	No of animals in gr.		10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3				2-	2-	3-	3-	3-	3-	3-	3-	3-	3-	3-	3-	3-	3-	3-	3-	3-	3-	3-
	Crust	1-3																			1-	1-	1-	1-
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

			Treatment							Study day / recovery													
	PARAMETER	SCORE	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
	No of animals in gr.		10	10	10	10	10	10	10	5	5	5	5	5	5	5	5	5	5	5	5	5	5
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3	3-	3-	4-	4-	4-	4-	4-														
	Crust	1-3	1-	1-	1-	1-	1-	1-	1-														
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3																					

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

[ ] = No animals affected

n = Number of affected animals
n- = Mean severity between 1.00 and 1.67
n+ = Mean severity between 1.68 and 2.33
n! = Mean severity between 2.34 and 3.00

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, SUMMARY

GROUP 2 (LOW DOSE), MALES

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
	No of animals in gr.		5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

			Treatment						
	PARAMETER	SCORE	22	23	24	25	26	27	28
	No of animals in gr.		5	5	5	5	5	5	5
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, SUMMARY

GROUP 3 (MID DOSE), MALES

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
	No of animals in gr.		5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

			Treatment						
	PARAMETER	SCORE	22	23	24	25	26	27	28
	No of animals in gr.		5	5	5	5	5	5	5
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, SUMMARY

GROUP 4 (HIGH DOSE), MALES

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
	No of animals in gr.		10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
APP	Piloerection	1-3																						
	Salivation	1-3																	1-					
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								10-	10-	10-	10-	10-	10-	10-	10-	10-	10-	10-	10-	10-	10-	10-

			Treatment							Study day / recovery													
	PARAMETER	SCORE	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
	No of animals in gr.		10	10	10	10	10	10	10	5	5	5	5	5	5	5	5	5	5	5	5	5	5
APP	Piloerection	1-3																					
	Salivation	1-3						2-	2-														
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3	10-	10-	10-	10-	10-	10-	10-	5-													

Abbreviations:

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, SUMMARY

GROUP 1 (CONTROL), FEMALES

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
	No of animals in gr.		10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

			Treatment							Study day / recovery													
	PARAMETER	SCORE	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
	No of animals in gr.		10	10	10	10	10	10	10	5	5	5	5	5	5	5	5	5	5	5	5	5	5
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3																					

Abbreviations:

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, SUMMARY

GROUP 2 (LOW DOSE), FEMALES

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
	No of animals in gr.		5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

			Treatment						
	PARAMETER	SCORE	22	23	24	25	26	27	28
	No of animals in gr.		5	5	5	5	5	5	5
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

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RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

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n = Number of affected animals
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n! = Mean severity between 2.34 and 3.00

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, SUMMARY

GROUP 3 (MID DOSE), FEMALES

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
	No of animals in gr.		5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

			Treatment						
	PARAMETER	SCORE	22	23	24	25	26	27	28
	No of animals in gr.		5	5	5	5	5	5	5
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, SUMMARY

GROUP 4 (HIGH DOSE), FEMALES

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
	No of animals in gr.		10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
APP	Piloerection	1-3																						
	Salivation	1-3															1-							
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								10-	10-	10-	10-	10-	10-	10-	10-	10-	10-	10-	10-	10-	10-	10-

			Treatment							Study day / recovery													
	PARAMETER	SCORE	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
	No of animals in gr.		10	10	10	10	10	10	10	5	5	5	5	5	5	5	5	5	5	5	5	5	5
APP	Piloerection	1-3																					
	Salivation	1-3						1-	3-														
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3	10-	10-	10-	10-	10-	10-	10-	5-													

Abbreviations:

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n! = Mean severity between 2.34 and 3.00

WEEKLY OUTSIDE CAGE OBSERVATIONS, SUMMARY DATA

MALES

			GROUP 1					GROUP 2					GROUP 3					GROUP 4				
NUMBER OF ANIMALS IN GR.			10	10	10	10	10	5	5	5	5	5	5	5	5	5	5	10	10	10	10	10
FINDINGS / STUDY WEEK		SCORE	P	1	2	3	4	P	1	2	3	4	P	1	2	3	4	P	1	2	3	4
APP	Piloerection	1-3																				
	Salivation	1-3																		2-	1-	3-
	Hunched posture	1																				
	Hair Loss	1-3			3-	3-	4-															
MOT	Ataxia	1-3																				
	Tremor/twitching	1-3																				
	Prostration	1																				
	Circling	1																				
	Spasm	1-3																				
BEH	Hyperactivity	1-3																				
	Somnolence	1-3																				
	Inc. exploration	1-3																				
	Red. grooming	1-3																				
	Vocalization	1-3																				
RES	Dyspnea	1																				
	Tachypnea	1																				
	Bradypnea	1																				
REF	Blink	1																				
	Pinna	1																				
	Iridic light reflex	1																				
	Push-off (hind legs)	1																				
	Pain response	1																				
	Startle / hearing	1																				
MIS	Lacrimation	1-3																				
	Limbs cyanotic	1																				
	Mydriasis	1																				
	Miosis	1																				
	Exophthalmos	1																				
	Red. muscle tone	1-3																				

Abbreviations:

APP = Appearance
MOT = Motor
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RES = Respiration
MIS = Miscellaneous
REF = Reflexes
P = Pretest examination (during acclimatization)

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WEEKLY OUTSIDE CAGE OBSERVATIONS, SUMMARY DATA

FEMALES

			GROUP 1					GROUP 2					GROUP 3					GROUP 4				
NUMBER OF ANIMALS IN GR.			10	10	10	10	10	5	5	5	5	5	5	5	5	5	5	10	10	10	10	10
FINDING / STUDY WEEK		SCORE	P	1	2	3	4	P	1	2	3	4	P	1	2	3	4	P	1	2	3	4
APP	Piloerection	1-3																				
	Salivation	1-3																				
	Hunched posture	1																		1-		3-
	Hair Loss	1-3																				
MOT	Ataxia	1-3																				
	Tremor/twitching	1-3																				
	Prostration	1																				
	Circling	1																				
	Spasm	1-3																				
BEH	Hyperactivity	1-3																				
	Somnolence	1-3																				
	Inc. exploration	1-3																				
	Red. grooming	1-3																				
	Vocalization	1-3																				
RES	Dyspnea	1																				
	Tachypnea	1																				
	Bradypnea	1																				
REF	Blink	1																				
	Pinna	1																				
	Iridic light reflex	1																				
	Push-off (hind legs)	1																				
	Pain response	1																				
	Startle / hearing	1																				
MIS	Lacrimation	1-3																				
	Limbs cyanotic	1																				
	Mydriasis	1																				
	Miosis	1																				
	Exophthalmos	1																				
	Red. muscle tone	1-3																				

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

GRIP STRENGTH , SUMMARY AT WEEK 4

	MALES	Mean (g)	FEMALES	Mean (g)
GROUP 1				
0 mg/kg	**Forelimb**	**Hindlimb**	**Forelimb**	**Hindlimb**
Mean	1248	905	929	665
St.dev.	78	61	65	37
N	10	10	0	10
GROUP 2				
50 mg/kg	**Forelimb**	**Hindlimb**	**Forelimb**	**Hindlimb**
Mean	1261	869	919	656
St.dev.	73	86	55	32
N	5	5	5	5
GROUP 3				
200 mg/kg	**Forelimb**	**Hindlimb**	**Forelimb**	**Hindlimb**
Mean	1226	877	901	647
St.dev.	29	37	55	32
N	5	5	5	5
GROUP 4				
1000 mg/kg	**Forelimb**	**Hindlimb**	**Forelimb**	**Hindlimb**
Mean	1269	903	939	656
St.dev.	89	72	43	22
N	10	10	10	10

*/** T-Test sig. at 5% or 1% level

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

LOCOMOTOR ACTIVITY, SUMMARY

LOW BEAMS COUNT **MALES** **4 WEEKS**

GROUP 1	15 min.	30 min.	45 min.	60 min.	Total
0 mg/kg					
Mean	1019	670	468	419	2576
St.dev.	172	96	234	157	347
N	10	10	10	10	10

GROUP 2	15 min.	30 min.	45 min.	60 min.	Total
50 mg/kg					
Mean	809	468	283	284	1845
St.dev.	368	186	166	100	711
N	5	5	5	5	5

GROUP 3	15 min.	30 min.	45 min.	60 min.	Total
200 mg/kg					
Mean	1267	712	562	349	2890
St.dev.	402	328	338	250	1258
N	5	5	5	5	5

GROUP 4	15 min.	30 min.	45 min.	60 min.	Total
1000 mg/kg					
Mean	936	552 *	392	347	2227
St.dev.	269	134	195	186	495
N	10	10	10	10	10

*/** T-Test sig. at 5% or 1% level

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

LOCOMOTOR ACTIVITY, SUMMARY

LOW BEAMS COUNT FEMALES 4 WEEKS

GROUP 1	15 min.	30 min.	45 min.	60 min.	Total
0 mg/kg					
Mean	841	355	190	160	1545
St.dev.	195	149	263	190	575
N	10	10	10	10	10

GROUP 2	15 min.	30 min.	45 min.	60 min.	Total
50 mg/kg					
Mean	582 *	143 *	64	29	818 **
St.dev.	162	143	85	51	230
N	5	5	5	5	5

GROUP 3	15 min.	30 min.	45 min.	60 min.	Total
200 mg/kg					
Mean	1053	675	255	341	2324
St.dev.	286	361	268	399	1211
N	5	5	5	5	5

GROUP 4	15 min.	30 min.	45 min.	60 min.	Total
1000 mg/kg					
Mean	593 **	360	158	54	1166
St.dev.	175	245	154	51	479
N	10	10	10	10	10

*/** T-Test sig. at 5% or 1% level

FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
MALES

PRETEST		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAYS 1-8	MEAN	17.1	17.2	17.0	17.3
WEEKS 1/2	ST.DEV.	0.1	---	---	0.2
	N (CAGE)	2	1	1	2

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
MALES

TREATMENT		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAYS 1-8 WEEKS 1/2	MEAN	19.3	18.5	18.6	19.5
	ST.DEV.	0.7	---	---	0.3
	N (CAGE)	2	1	1	2
DAYS 8-15 WEEKS 2/3	MEAN	21.2	19.7	20.1	22.0
	ST.DEV.	0.5	---	---	0.0
	N (CAGE)	2	1	1	2
DAYS 15-22 WEEKS 3/4	MEAN	22.3	21.1	20.6	23.0
	ST.DEV.	0.1	---	---	0.4
	N (CAGE)	2	1	1	2
DAYS 22-28 WEEK 4	MEAN	22.6	19.5	20.4	23.2
	ST.DEV.	0.1	---	---	0.8
	N (CAGE)	2	1	1	2
MEAN OF MEANS OVER TREATMENT		21.4	19.7	19.9	21.9

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
MALES

RECOVERY		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAYS 1-8	MEAN	23.2	---	---	22.6
WEEKS 1/2	ST.DEV.	---	---	---	---
	N (CAGE)	1	0	0	1
DAYS 8-14	MEAN	22.9	---	---	22.5
WEEK 2	ST.DEV.	---	---	---	---
	N (CAGE)	1	0	0	1
MEAN OF MEANS OVER RECOVERY		23.1	---	---	22.6

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
FEMALES

PRETEST		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAYS 1-8	MEAN	12.6	12.5	12.9	12.9
WEEKS 1/2	ST.DEV.	0.2	---	---	0.3
	N (CAGE)	2	1	1	2

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
FEMALES

TREATMENT		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAYS 1-8 WEEKS 1/2	MEAN	13.0	13.2	12.4	13.6
	ST.DEV.	0.0	---	---	0.1
	N (CAGE)	2	1	1	2
DAYS 8-15 WEEKS 2/3	MEAN	13.5	14.1	13.6	14.5
	ST.DEV.	0.2	---	---	0.5
	N (CAGE)	2	1	1	2
DAYS 15-22 WEEKS 3/4	MEAN	14.6	14.5	14.1	15.4
	ST.DEV.	0.2	---	---	0.1
	N (CAGE)	2	1	1	2
DAYS 22-28 WEEK 4	MEAN	14.7	14.3	14.1	15.1
	ST.DEV.	0.1	---	---	0.1
	N (CAGE)	2	1	1	2
MEAN OF MEANS OVER TREATMENT		13.9	14.0	13.5	14.7

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
FEMALES

RECOVERY		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAYS 1-8	MEAN	15.9	---	---	14.7
WEEKS 1/2	ST.DEV.	---	---	---	---
	N (CAGE)	1	0	0	1
DAYS 8-14	MEAN	16.2	---	---	14.8
WEEK 2	ST.DEV.	---	---	---	---
	N (CAGE)	1	0	0	1
MEAN OF MEANS OVER RECOVERY		16.0	---	---	14.8

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

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

PRETEST		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAYS 1-8	MEAN	116	119	115	117
WEEKS 1/2	ST.DEV.	0.8	---	---	2.4
	N (CAGE)	2	1	1	2

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

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

TREATMENT		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAYS 1-8	MEAN	85	83	83	87
WEEKS 1/2	ST.DEV.	1.6	---	---	0.8
	N (CAGE)	2	1	1	2
DAYS 8-15	MEAN	79	77	79	85
WEEKS 2/3	ST.DEV.	1.0	---	---	1.8
	N (CAGE)	2	1	1	2
DAYS 15-22	MEAN	75	74	74	80
WEEKS 3/4	ST.DEV.	0.0	---	---	2.4
	N (CAGE)	2	1	1	2
DAYS 22-28	MEAN	70	65	69	76
WEEK 4	ST.DEV.	0.4	---	---	2.6
	N (CAGE)	2	1	1	2
MEAN OF MEANS OVER TREATMENT		77	75	76	82

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

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

RECOVERY		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAYS 1-8	MEAN	69	---	---	71
WEEKS 1/2	ST.DEV.	---	---	---	---
	N (CAGE)	1	0	0	1
DAYS 8-14	MEAN	64	---	---	67
WEEK 2	ST.DEV.	---	---	---	---
	N (CAGE)	1	0	0	1
MEAN OF MEANS OVER RECOVERY		67	---	---	69

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

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

PRETEST		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAYS 1-8	MEAN	105	102	106	107
WEEKS 1/2	ST.DEV.	2.4	---	---	4.0
	N (CAGE)	2	1	1	2

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

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

TREATMENT		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAYS 1-8 WEEKS 1/2	MEAN	83	80	79	85
	ST.DEV.	0.9	---	---	0.9
	N (CAGE)	2	1	1	2
DAYS 8-15 WEEKS 2/3	MEAN	78	77	79	81
	ST.DEV.	1.9	---	---	3.0
	N (CAGE)	2	1	1	2
DAYS 15-22 WEEKS 3/4	MEAN	79	75	77	80
	ST.DEV.	2.0	---	---	1.1
	N (CAGE)	2	1	1	2
DAYS 22-28 WEEK 4	MEAN	75	71	73	76
	ST.DEV.	1.7	---	---	0.6
	N (CAGE)	2	1	1	2
MEAN OF MEANS OVER TREATMENT		79	76	77	80

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

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

RECOVERY		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAYS 1-8	MEAN	79	---	---	71
WEEKS 1/2	ST.DEV.	---	---	---	---
	N (CAGE)	1	0	0	1
DAYS 8-14	MEAN	77	---	---	70
WEEK 2	ST.DEV.	---	---	---	---
	N (CAGE)	1	0	0	1
MEAN OF MEANS OVER RECOVERY		78	---	---	71

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHTS (GRAM) SUMMARY
MALES

PRETEST		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAY 1	MEAN	148	144	148	148
WEEK 1	ST.DEV.	7.2	5.1	5.6	7.4
	N	10	5	5	10

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHTS (GRAM) SUMMARY
MALES

TREATMENT		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAY 1	MEAN	188	186	187	188
WEEK 1	ST.DEV.	7.4	5.0	4.3	7.6
	N	10	5	5	10
DAY 8	MEAN	229	222	223	225
WEEK 2	ST.DEV.	9.6	7.4	4.8	10.2
	N	10	5	5	10
DAY 15	MEAN	268	255	255	259
WEEK 3	ST.DEV.	10.4	10.6	10.3	13.8
	N	10	5	5	10
DAY 22	MEAN	298	286	280	286
WEEK 4	ST.DEV.	12.2	12.1	16.5	17.7
	N	10	5	5	10
DAY 28	MEAN	322	298	296 *	306
WEEK 4	ST.DEV.	13.8	21.6	18.4	19.9
	N	10	5	5	10

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHTS (GRAM) SUMMARY
MALES

RECOVERY		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAY 1	MEAN	308	---	---	289
WEEK 1	ST.DEV.	11.7	---	---	11.6
	N	5	0	0	5
DAY 8	MEAN	338	---	---	318
WEEK 2	ST.DEV.	14.1	---	---	16.9
	N	5	0	0	5
DAY 14	MEAN	356	---	---	337
WEEK 2	ST.DEV.	17.6	---	---	18.6
	N	5	0	0	5

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHTS (GRAM) SUMMARY
FEMALES

PRETEST		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAY 1	MEAN	120	123	122	121
WEEK 1	ST.DEV.	2.9	5.5	5.1	4.5
	N	10	5	5	10

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHTS (GRAM) SUMMARY
FEMALES

TREATMENT		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAY 1	MEAN	140	146	140	141
WEEK 1	ST.DEV.	6.0	5.0	8.4	7.3
	N	10	5	5	10
DAY 8	MEAN	157	165	157	161
WEEK 2	ST.DEV.	8.2	5.7	9.1	8.4
	N	10	5	5	10
DAY 15	MEAN	172	182	172	179
WEEK 3	ST.DEV.	8.8	6.4	10.9	9.9
	N	10	5	5	10
DAY 22	MEAN	184	194	183	191
WEEK 4	ST.DEV.	10.0	7.7	13.3	11.6
	N	10	5	5	10
DAY 28	MEAN	195	202	192	200
WEEK 4	ST.DEV.	12.5	8.5	14.4	11.7
	N	10	5	5	10

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHTS (GRAM) SUMMARY
FEMALES

RECOVERY		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAY 1	MEAN	184	---	---	189
WEEK 1	ST.DEV.	11.6	---	---	13.2
	N	5	0	0	5
DAY 8	MEAN	202	---	---	206
WEEK 2	ST.DEV.	10.9	---	---	16.4
	N	5	0	0	5
DAY 14	MEAN	210	---	---	213
WEEK 2	ST.DEV.	7.9	---	---	15.3
	N	5	0	0	5

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHT GAIN (%) SUMMARY
MALES

PRETEST		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAY 1	MEAN	-21.5	-22.6	-20.5	-21.4
WEEK 1	ST.DEV.	1.2	1.3	2.2	1.5
	N	10	5	5	10

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHT GAIN (%) SUMMARY
MALES

TREATMENT		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAY 1	MEAN	0.0	0.0	0.0	0.0
WEEK 1	ST.DEV.	0.0	0.0	0.0	0.0
	N	10	5	5	10
DAY 8	MEAN	21.6	19.5	19.3	19.7
WEEK 2	ST.DEV.	1.9	1.4	1.8	2.0
	N	10	5	5	10
DAY 15	MEAN	42.7	37.3 *	36.4 *	38.0 *
WEEK 3	ST.DEV.	3.4	3.2	6.0	3.3
	N	10	5	5	10
DAY 22	MEAN	58.8	53.6	49.9 *	52.4
WEEK 4	ST.DEV.	5.0	5.0	9.9	5.5
	N	10	5	5	10
DAY 28	MEAN	71.7	60.4 *	58.5 *	62.9
WEEK 4	ST.DEV.	6.7	9.8	10.9	6.7
	N	10	5	5	10

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHT GAIN (%) SUMMARY
MALES

RECOVERY		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAY 1	MEAN	65.8	---	---	56.5
WEEK 1	ST.DEV.	7.4	---	---	4.8
	N	5	0	0	5
DAY 8	MEAN	82.0	---	---	72.1
WEEK 2	ST.DEV.	10.4	---	---	6.9
	N	5	0	0	5
DAY 14	MEAN	91.6	---	---	82.2
WEEK 2	ST.DEV.	13.0	---	---	8.7
	N	5	0	0	5

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHT GAIN (%) SUMMARY
FEMALES

PRETEST		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAY 1	MEAN	-14.1	-15.8	-12.6	-14.4
WEEK 1	ST.DEV.	3.0	1.6	2.6	3.5
	N	10	5	5	10

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHT GAIN (%) SUMMARY
FEMALES

TREATMENT		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAY 1	MEAN	0.0	0.0	0.0	0.0
WEEK 1	ST.DEV.	0.0	0.0	0.0	0.0
	N	10	5	5	10
DAY 8	MEAN	12.2	13.1	12.5	13.9
WEEK 2	ST.DEV.	2.1	0.5	1.6	2.2
	N	10	5	5	10
DAY 15	MEAN	23.0	24.9	22.6	26.7 *
WEEK 3	ST.DEV.	2.1	2.6	2.1	3.4
	N	10	5	5	10
DAY 22	MEAN	32.1	32.5	30.5	35.8
WEEK 4	ST.DEV.	3.4	3.6	3.2	4.9
	N	10	5	5	10
DAY 28	MEAN	39.6	37.9	37.3	41.7
WEEK 4	ST.DEV.	4.1	1.9	4.1	4.9
	N	10	5	5	10

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHT GAIN (%) SUMMARY
FEMALES

RECOVERY		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
DAY 1	MEAN	33.1	---	---	33.7
WEEK 1	ST.DEV.	4.6	---	---	5.8
	N	5	0	0	5
DAY 8	MEAN	46.0	---	---	45.4
WEEK 2	ST.DEV.	3.2	---	---	7.0
	N	5	0	0	5
DAY 14	MEAN	51.6	---	---	50.3
WEEK 2	ST.DEV.	2.8	---	---	6.3
	N	5	0	0	5

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

MACROSCOPICAL FINDINGS SUMMARY
MALES

	GROUP 1 0 MG/KG		GROUP 2 50 MG/KG		GROUP 3 200 MG/KG		GROUP 4 1000 MG/KG	
ANIMALS EXAMINED	10		5		5		10	
ANIMALS WITHOUT FINDINGS	10		5		4		5	
ANIMALS AFFECTED:								
STOMACH.....								
IRREGULAR SURFACE	0	0%	0	0%	0	0%	5	50%
THYMUS.....								
REDUCED IN SIZE	0	0%	0	0%	1	20%	0	0%

MACROSCOPICAL FINDINGS SUMMARY
FEMALES

	GROUP 1 0 MG/KG		GROUP 2 50 MG/KG		GROUP 3 200 MG/KG		GROUP 4 1000 MG/KG	
ANIMALS EXAMINED	10		5		5		10	
ANIMALS WITHOUT FINDINGS	10		4		5		5	
ANIMALS AFFECTED:								
STOMACH.....								
IRREGULAR SURFACE	0	0%	0	0%	0	0%	5	50%
KIDNEYS.....								
PELVIC DILATION	0	0%	1	20%	0	0%	0	0%

ORGAN WEIGHTS (GRAM) SUMMARY
AFTER 4 WEEKS
MALES

		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
BODY W.	MEAN	296.29	274.08	269.49	274.59
	ST.DEV.	14.64	20.03	17.13	22.07
	N	5	5	5	5
BRAIN	MEAN	1.96	1.93	1.92	1.95
	ST.DEV.	0.03	0.10	0.10	0.09
	N	5	5	5	5
HEART	MEAN	0.978	0.913	0.997	1.016
	ST.DEV.	0.072	0.045	0.104	0.085
	N	5	5	5	5
LIVER	MEAN	8.80	7.65	8.24	9.15
	ST.DEV.	0.67	0.80	0.73	0.95
	N	5	5	5	5
THYMUS	MEAN	0.46	0.48	0.40	0.49
	ST.DEV.	0.10	0.14	0.11	0.13
	N	5	5	5	5
KIDNEYS	MEAN	2.10	1.91	1.91	2.23
	ST.DEV.	0.23	0.15	0.11	0.20
	N	5	5	5	5
ADRENALS	MEAN	0.065	0.067	0.065	0.080
	ST.DEV.	0.009	0.008	0.003	0.014
	N	5	5	5	5
SPLEEN	MEAN	0.708	0.645	0.619	0.620
	ST.DEV.	0.069	0.051	0.054	0.107
	N	5	5	5	5
TESTES	MEAN	3.49	3.60	3.40	3.45
	ST.DEV.	0.09	0.17	0.18	0.21
	N	5	5	5	5
EPIDIDYMIDES	MEAN	1.022	1.044	1.015	1.017
	ST.DEV.	0.121	0.121	0.066	0.066
	N	5	5	5	5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

ORGAN/BODY WEIGHT RATIOS SUMMARY
AFTER 4 WEEKS
MALES

		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
BODY W. (GRAM)	MEAN	296.29	274.08	269.49	274.59
	ST.DEV.	14.64	20.03	17.13	22.07
	N	5	5	5	5
BRAIN (%)	MEAN	0.66	0.71	0.71	0.71
	ST.DEV.	0.04	0.05	0.03	0.03
	N	5	5	5	5
HEART (%)	MEAN	0.330	0.334	0.371	0.372
	ST.DEV.	0.015	0.017	0.044	0.044
	N	5	5	5	5
LIVER (%)	MEAN	2.97	2.79	3.05	3.34 *
	ST.DEV.	0.13	0.18	0.09	0.32
	N	5	5	5	5
THYMUS (%)	MEAN	0.16	0.18	0.15	0.18
	ST.DEV.	0.03	0.05	0.03	0.03
	N	5	5	5	5
KIDNEYS (%)	MEAN	0.71	0.70	0.71	0.81 *
	ST.DEV.	0.05	0.02	0.05	0.07
	N	5	5	5	5
ADRENALS (%)	MEAN	0.022	0.024	0.024	0.029 **
	ST.DEV.	0.003	0.001	0.002	0.005
	N	5	5	5	5
SPLEEN (%)	MEAN	0.239	0.236	0.230	0.226
	ST.DEV.	0.018	0.019	0.027	0.032
	N	5	5	5	5
TESTES (%)	MEAN	1.18	1.32	1.27	1.26
	ST.DEV.	0.05	0.08	0.14	0.05
	N	5	5	5	5
EPIDIDYMIDES (%)	MEAN	0.344	0.380	0.378	0.372
	ST.DEV.	0.031	0.027	0.036	0.035
	N	5	5	5	5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

ORGAN/BRAIN WEIGHT RATIOS SUMMARY
AFTER 4 WEEKS
MALES

		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
BRAIN (GRAM)	MEAN	1.96	1.93	1.92	1.95
	ST.DEV.	0.03	0.10	0.10	0.09
	N	5	5	5	5
HEART (%)	MEAN	49.836	47.305	52.086	52.151
	ST.DEV.	4.253	2.683	6.296	5.191
	N	5	5	5	5
LIVER (%)	MEAN	448.58	396.29	429.03	469.33
	ST.DEV.	36.93	39.53	23.58	48.75
	N	5	5	5	5
THYMUS (%)	MEAN	23.50	25.05	20.53	24.81
	ST.DEV.	5.08	6.95	4.63	5.23
	N	5	5	5	5
KIDNEYS (%)	MEAN	107.10	98.79	99.73	114.35
	ST.DEV.	11.77	7.63	3.99	10.15
	N	5	5	5	5
ADRENALS (%)	MEAN	3.309	3.468	3.419	4.088
	ST.DEV.	0.525	0.317	0.271	0.678
	N	5	5	5	5
SPLEEN (%)	MEAN	36.035	33.436	32.309	31.759
	ST.DEV.	3.518	2.828	3.411	5.028
	N	5	5	5	5
TESTES (%)	MEAN	177.83	186.81	177.52	176.94
	ST.DEV.	5.25	13.79	14.64	5.93
	N	5	5	5	5
EPIDIDYMIDES (%)	MEAN	52.037	53.964	53.079	52.234
	ST.DEV.	6.222	5.203	4.962	4.006
	N	5	5	5	5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

ORGAN WEIGHTS (GRAM) SUMMARY
AFTER 4 WEEKS
FEMALES

		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
BODY W.	MEAN	177.17	184.39	173.03	177.31
	ST.DEV.	12.05	5.67	14.33	9.83
	N	5	5	5	5
BRAIN	MEAN	1.83	1.84	1.83	1.82
	ST.DEV.	0.07	0.08	0.06	0.06
	N	5	5	5	5
HEART	MEAN	0.694	0.654	0.661	0.694
	ST.DEV.	0.028	0.064	0.052	0.051
	N	5	5	5	5
LIVER	MEAN	5.17	5.37	5.17	5.79 *
	ST.DEV.	0.43	0.29	0.33	0.39
	N	5	5	5	5
THYMUS	MEAN	0.42	0.46	0.38	0.41
	ST.DEV.	0.03	0.04	0.07	0.07
	N	5	5	5	5
KIDNEYS	MEAN	1.30	1.30	1.27	1.34
	ST.DEV.	0.07	0.10	0.05	0.10
	N	5	5	5	5
ADRENALS	MEAN	0.072	0.068	0.073	0.078
	ST.DEV.	0.010	0.006	0.003	0.010
	N	5	5	5	5
SPLEEN	MEAN	0.467	0.490	0.470	0.480
	ST.DEV.	0.047	0.037	0.049	0.051
	N	5	5	5	5
OVARIES	MEAN	0.093	0.084	0.093	0.095
	ST.DEV.	0.010	0.006	0.011	0.021
	N	5	5	5	5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

ORGAN/BODY WEIGHT RATIOS SUMMARY
AFTER 4 WEEKS
FEMALES

		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
BODY W. (GRAM)	MEAN	177.17	184.39	173.03	177.31
	ST.DEV.	12.05	5.67	14.33	9.83
	N	5	5	5	5
BRAIN (%)	MEAN	1.04	1.00	1.07	1.03
	ST.DEV.	0.06	0.06	0.10	0.04
	N	5	5	5	5
HEART (%)	MEAN	0.393	0.355	0.382	0.392
	ST.DEV.	0.026	0.035	0.008	0.028
	N	5	5	5	5
LIVER (%)	MEAN	2.92	2.91	3.00	3.27 *
	ST.DEV.	0.17	0.15	0.17	0.24
	N	5	5	5	5
THYMUS (%)	MEAN	0.24	0.25	0.22	0.23
	ST.DEV.	0.02	0.03	0.03	0.03
	N	5	5	5	5
KIDNEYS (%)	MEAN	0.73	0.71	0.74	0.75
	ST.DEV.	0.05	0.06	0.07	0.05
	N	5	5	5	5
ADRENALS (%)	MEAN	0.041	0.037	0.042	0.044
	ST.DEV.	0.006	0.003	0.005	0.004
	N	5	5	5	5
SPLEEN (%)	MEAN	0.264	0.266	0.272	0.271
	ST.DEV.	0.024	0.022	0.015	0.022
	N	5	5	5	5
OVARIES (%)	MEAN	0.053	0.046	0.054	0.054
	ST.DEV.	0.006	0.005	0.007	0.012
	N	5	5	5	5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

ORGAN/BRAIN WEIGHT RATIOS SUMMARY
AFTER 4 WEEKS
FEMALES

		GROUP 1 0 MG/KG	GROUP 2 50 MG/KG	GROUP 3 200 MG/KG	GROUP 4 1000 MG/KG
BRAIN (GRAM)	MEAN	1.83	1.84	1.83	1.82
	ST.DEV.	0.07	0.08	0.06	0.06
	N	5	5	5	5
HEART (%)	MEAN	37.966	35.499	36.028	38.154
	ST.DEV.	2.282	3.003	2.785	3.066
	N	5	5	5	5
LIVER (%)	MEAN	282.54	291.56	282.39	318.33 *
	ST.DEV.	21.95	13.36	24.76	23.08
	N	5	5	5	5
THYMUS (%)	MEAN	23.20	25.13	20.68	22.73
	ST.DEV.	1.99	2.80	3.66	3.11
	N	5	5	5	5
KIDNEYS (%)	MEAN	70.85	70.60	69.53	73.48
	ST.DEV.	4.38	4.58	3.87	5.15
	N	5	5	5	5
ADRENALS (%)	MEAN	3.945	3.672	3.968	4.277
	ST.DEV.	0.525	0.342	0.221	0.414
	N	5	5	5	5
SPLEEN (%)	MEAN	25.520	26.593	25.656	26.351
	ST.DEV.	2.302	1.100	2.889	2.271
	N	5	5	5	5
OVARIES (%)	MEAN	5.107	4.553	5.075	5.196
	ST.DEV.	0.671	0.395	0.541	1.034
	N	5	5	5	5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

ORGAN WEIGHTS (GRAM) SUMMARY
AFTER 6 WEEKS
MALES

		GROUP 1 0 MG/KG	GROUP 4 1000 MG/KG
BODY W.	MEAN	328.10	313.09
	ST.DEV.	12.72	19.91
	N	5	5
BRAIN	MEAN	1.97	2.02
	ST.DEV.	0.06	0.06
	N	5	5
HEART	MEAN	1.035	0.959
	ST.DEV.	0.070	0.110
	N	5	5
LIVER	MEAN	10.94	9.32 **
	ST.DEV.	0.85	0.54
	N	5	5
THYMUS	MEAN	0.41	0.41
	ST.DEV.	0.05	0.04
	N	5	5
KIDNEYS	MEAN	2.25	2.03
	ST.DEV.	0.20	0.13
	N	5	5
ADRENALS	MEAN	0.071	0.062
	ST.DEV.	0.011	0.014
	N	5	5
SPLEEN	MEAN	0.669	0.607
	ST.DEV.	0.069	0.065
	N	5	5
TESTES	MEAN	3.66	3.46
	ST.DEV.	0.16	0.22
	N	5	5
EPIDIDYMIDES	MEAN	1.273	1.212
	ST.DEV.	0.144	0.034
	N	5	5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

ORGAN/BODY WEIGHT RATIOS SUMMARY
AFTER 6 WEEKS
MALES

		GROUP 1 0 MG/KG	GROUP 4 1000 MG/KG
BODY W. (GRAM)	MEAN ST.DEV. N	328.10 12.72 5	313.09 19.91 5
BRAIN (%)	MEAN ST.DEV. N	0.60 0.02 5	0.65 0.04 5
HEART (%)	MEAN ST.DEV. N	0.316 0.022 5	0.306 0.026 5
LIVER (%)	MEAN ST.DEV. N	3.33 0.18 5	2.98 * 0.19 5
THYMUS (%)	MEAN ST.DEV. N	0.12 0.01 5	0.13 0.02 5
KIDNEYS (%)	MEAN ST.DEV. N	0.68 0.05 5	0.65 0.06 5
ADRENALS (%)	MEAN ST.DEV. N	0.022 0.003 5	0.020 0.004 5
SPLEEN (%)	MEAN ST.DEV. N	0.204 0.016 5	0.195 0.028 5
TESTES (%)	MEAN ST.DEV. N	1.12 0.06 5	1.11 0.10 5
EPIDIDYMIDES (%)	MEAN ST.DEV. N	0.388 0.041 5	0.388 0.020 5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

ORGAN/BRAIN WEIGHT RATIOS SUMMARY
AFTER 6 WEEKS
MALES

		GROUP 1 0 MG/KG	GROUP 4 1000 MG/KG
BRAIN (GRAM)	MEAN	1.97	2.02
	ST.DEV.	0.06	0.06
	N	5	5
HEART (%)	MEAN	52.780	47.470
	ST.DEV.	4.724	5.326
	N	5	5
LIVER (%)	MEAN	557.32	462.27 **
	ST.DEV.	46.96	36.23
	N	5	5
THYMUS (%)	MEAN	20.68	20.46
	ST.DEV.	1.92	1.69
	N	5	5
KIDNEYS (%)	MEAN	114.37	100.50
	ST.DEV.	10.68	8.53
	N	5	5
ADRENALS (%)	MEAN	3.593	3.051
	ST.DEV.	0.461	0.689
	N	5	5
SPLEEN (%)	MEAN	33.999	30.095
	ST.DEV.	2.908	3.303
	N	5	5
TESTES (%)	MEAN	186.68	171.61
	ST.DEV.	10.79	12.95
	N	5	5
EPIDIDYMIDES (%)	MEAN	64.877	60.014
	ST.DEV.	8.046	2.137
	N	5	5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

ORGAN WEIGHTS (GRAM) SUMMARY
AFTER 6 WEEKS
FEMALES

		GROUP 1 0 MG/KG	GROUP 4 1000 MG/KG
BODY W.	MEAN	194.44	192.88
	ST.DEV.	12.73	22.37
	N	5	5
BRAIN	MEAN	1.77	1.84
	ST.DEV.	0.06	0.09
	N	5	5
HEART	MEAN	0.710	0.700
	ST.DEV.	0.036	0.040
	N	5	5
LIVER	MEAN	6.71	6.57
	ST.DEV.	0.27	0.73
	N	5	5
THYMUS	MEAN	0.39	0.36
	ST.DEV.	0.02	0.06
	N	5	5
KIDNEYS	MEAN	1.22	1.34
	ST.DEV.	0.06	0.13
	N	5	5
ADRENALS	MEAN	0.066	0.073
	ST.DEV.	0.004	0.011
	N	5	5
SPLEEN	MEAN	0.483	0.516
	ST.DEV.	0.040	0.028
	N	5	5
OVARIES	MEAN	0.105	0.101
	ST.DEV.	0.010	0.020
	N	5	5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

ORGAN/BODY WEIGHT RATIOS SUMMARY
AFTER 6 WEEKS
FEMALES

		GROUP 1 0 MG/KG	GROUP 4 1000 MG/KG
BODY W. (GRAM)	MEAN ST.DEV. N	194.44 12.73 5	192.88 22.37 5
BRAIN (%)	MEAN ST.DEV. N	0.91 0.07 5	0.96 0.08 5
HEART (%)	MEAN ST.DEV. N	0.366 0.034 5	0.365 0.026 5
LIVER (%)	MEAN ST.DEV. N	3.46 0.17 5	3.41 0.21 5
THYMUS (%)	MEAN ST.DEV. N	0.20 0.02 5	0.19 0.02 5
KIDNEYS (%)	MEAN ST.DEV. N	0.63 0.07 5	0.70 0.04 5
ADRENALS (%)	MEAN ST.DEV. N	0.034 0.003 5	0.038 0.003 5
SPLEEN (%)	MEAN ST.DEV. N	0.249 0.018 5	0.269 0.021 5
OVARIES (%)	MEAN ST.DEV. N	0.054 0.005 5	0.054 0.014 5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

ORGAN/BRAIN WEIGHT RATIOS SUMMARY
AFTER 6 WEEKS
FEMALES

		GROUP 1 0 MG/KG	GROUP 4 1000 MG/KG
BRAIN (GRAM)	MEAN	1.77	1.84
	ST.DEV.	0.06	0.09
	N	5	5
HEART (%)	MEAN	40.130	37.996
	ST.DEV.	2.647	2.219
	N	5	5
LIVER (%)	MEAN	379.43	356.04
	ST.DEV.	16.96	30.04
	N	5	5
THYMUS (%)	MEAN	22.27	19.67
	ST.DEV.	1.72	2.84
	N	5	5
KIDNEYS (%)	MEAN	69.11	72.57
	ST.DEV.	3.16	3.82
	N	5	5
ADRENALS (%)	MEAN	3.730	3.961
	ST.DEV.	0.147	0.430
	N	5	5
SPLEEN (%)	MEAN	27.317	27.991
	ST.DEV.	2.598	0.563
	N	5	5
OVARIES (%)	MEAN	5.919	5.540
	ST.DEV.	0.606	1.232
	N	5	5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

9 INDIVIDUAL TABLES

MORTALITY DATA
MALES
GROUP 1 (0 MG/KG)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
1	19-MAY-03	21-APR-03	18-MAY-03
2	19-MAY-03	21-APR-03	18-MAY-03
3	19-MAY-03	21-APR-03	18-MAY-03
4	19-MAY-03	21-APR-03	18-MAY-03
5	19-MAY-03	21-APR-03	18-MAY-03
6	02-JUN-03	21-APR-03	18-MAY-03
7	02-JUN-03	21-APR-03	18-MAY-03
8	02-JUN-03	21-APR-03	18-MAY-03
9	02-JUN-03	21-APR-03	18-MAY-03
10	02-JUN-03	21-APR-03	18-MAY-03

MORTALITY DATA
MALES
GROUP 2 (50 MG/KG)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
11	19-MAY-03	21-APR-03	18-MAY-03
12	19-MAY-03	21-APR-03	18-MAY-03
13	19-MAY-03	21-APR-03	18-MAY-03
14	19-MAY-03	21-APR-03	18-MAY-03
15	19-MAY-03	21-APR-03	18-MAY-03

MORTALITY DATA
MALES
GROUP 3 (200 MG/KG)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
16	19-MAY-03	21-APR-03	18-MAY-03
17	19-MAY-03	21-APR-03	18-MAY-03
18	19-MAY-03	21-APR-03	18-MAY-03
19	19-MAY-03	21-APR-03	18-MAY-03
20	19-MAY-03	21-APR-03	18-MAY-03

MORTALITY DATA
MALES
GROUP 4 (1000 MG/KG)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
21	19-MAY-03	21-APR-03	18-MAY-03
22	19-MAY-03	21-APR-03	18-MAY-03
23	19-MAY-03	21-APR-03	18-MAY-03
24	19-MAY-03	21-APR-03	18-MAY-03
25	19-MAY-03	21-APR-03	18-MAY-03
26	02-JUN-03	21-APR-03	18-MAY-03
27	02-JUN-03	21-APR-03	18-MAY-03
28	02-JUN-03	21-APR-03	18-MAY-03
29	02-JUN-03	21-APR-03	18-MAY-03
30	02-JUN-03	21-APR-03	18-MAY-03

MORTALITY DATA
FEMALES
GROUP 1 (0 MG/KG)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
31	19-MAY-03	21-APR-03	18-MAY-03
32	19-MAY-03	21-APR-03	18-MAY-03
33	19-MAY-03	21-APR-03	18-MAY-03
34	19-MAY-03	21-APR-03	18-MAY-03
35	19-MAY-03	21-APR-03	18-MAY-03
36	02-JUN-03	21-APR-03	18-MAY-03
37	02-JUN-03	21-APR-03	18-MAY-03
38	02-JUN-03	21-APR-03	18-MAY-03
39	02-JUN-03	21-APR-03	18-MAY-03
40	02-JUN-03	21-APR-03	18-MAY-03

MORTALITY DATA
FEMALES
GROUP 2 (50 MG/KG)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
41	19-MAY-03	21-APR-03	18-MAY-03
42	19-MAY-03	21-APR-03	18-MAY-03
43	19-MAY-03	21-APR-03	18-MAY-03
44	19-MAY-03	21-APR-03	18-MAY-03
45	19-MAY-03	21-APR-03	18-MAY-03

MORTALITY DATA
FEMALES
GROUP 3 (200 MG/KG)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
46	19-MAY-03	21-APR-03	18-MAY-03
47	19-MAY-03	21-APR-03	18-MAY-03
48	19-MAY-03	21-APR-03	18-MAY-03
49	19-MAY-03	21-APR-03	18-MAY-03
50	19-MAY-03	21-APR-03	18-MAY-03

MORTALITY DATA
FEMALES
GROUP 4 (1000 MG/KG)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
51	19-MAY-03	21-APR-03	18-MAY-03
52	19-MAY-03	21-APR-03	18-MAY-03
53	19-MAY-03	21-APR-03	18-MAY-03
54	19-MAY-03	21-APR-03	18-MAY-03
55	19-MAY-03	21-APR-03	18-MAY-03
56	02-JUN-03	21-APR-03	18-MAY-03
57	02-JUN-03	21-APR-03	18-MAY-03
58	02-JUN-03	21-APR-03	18-MAY-03
59	02-JUN-03	21-APR-03	18-MAY-03
60	02-JUN-03	21-APR-03	18-MAY-03

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), MALES

ANIMAL No. 1

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3				1	1	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3	2	1	1	1	1	1	1
	Crust	1-3							
MOT	Ataxia	1-2							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

[ ] = No abnormal findings noted

n = Severity of findings

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), MALES

ANIMAL No. 2

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3						1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3	1	1	1	1	1	1	1
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
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P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
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DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), MALES

ANIMAL No. 3

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

			Treatment						
	PARAMETER	SCORE	22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3			1	1	1	1	1
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

[ ] = No abnormal findings noted

n = Severity of findings

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DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), MALES

ANIMAL No. 4

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

[ ] = No abnormal findings noted

n = Severity of findings

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), MALES

ANIMAL No. 5

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3				1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	2	1	1
	Crust	1-3																			1	1	1	1
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3	1	1	1	1	1	1	1
	Crust	1-3	1	1	1	1	1	1	1
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

[ ] = No abnormal findings noted

n = Severity of findings

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), MALES

ANIMAL No. 6

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment							Study day / recovery													
			22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3																					

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

[ ] = No abnormal findings noted

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), MALES

ANIMAL No. 7

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment							Study day / recovery													
			22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3																					

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

[ ] = No abnormal findings noted

n = Severity of findings

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), MALES

ANIMAL No. 8

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment							Study day / recovery													
			22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3																					

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), MALES

ANIMAL No. 9

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment							Study day / recovery													
			22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3																					

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), MALES

ANIMAL No. 10

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment							Study day / recovery													
			22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3																					

Abbreviations:

APP = Appearance
MOT = Motor
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 2 (LOW DOSE), MALES

ANIMAL No. 11

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 2 (LOW DOSE), MALES

ANIMAL No. 12

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

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MOT = Motor
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 2 (LOW DOSE), MALES

ANIMAL No. 13

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

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MOT = Motor
BEH = Behavioral
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MIS = Miscellaneous
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 2 (LOW DOSE), MALES

ANIMAL No. 14

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

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MOT = Motor
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 2 (LOW DOSE), MALES

ANIMAL No. 15

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

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MOT = Motor
BEH = Behavioral
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 3 (MID DOSE), MALES

ANIMAL No. 16

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

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MOT = Motor
BEH = Behavioral
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 3 (MID DOSE), MALES

ANIMAL No. 17

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

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BEH = Behavioral
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 3 (MID DOSE), MALES

ANIMAL No. 18

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

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MOT = Motor
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P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 3 (MID DOSE), MALES

ANIMAL No. 19

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

[ ] = No abnormal findings noted

n = Severity of findings

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 3 (MID DOSE), MALES

ANIMAL No. 20

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), MALES

ANIMAL No. 21

	PARAMETER	SCORE	Study day / treatment																						
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3	1	1	1	1	1	1	1

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), MALES

ANIMAL No. 22

	PARAMETER	SCORE	Study day / treatment																						
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3	1	1	1	1	1	1	1

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), MALES

ANIMAL No. 23

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																	1					
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

			Treatment						
	PARAMETER	SCORE	22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3	1	1	1	1	1	1	1

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), MALES

ANIMAL No. 24

	PARAMETER	SCORE	Study day / treatment																						
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3	1	1	1	1	1	1	1

Abbreviations:

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MOT = Motor
BEH = Behavioral
RES = Respiration
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), MALES

ANIMAL No. 25

	PARAMETER	SCORE	Study day / treatment																						
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3						1	1
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3	1	1	1	1	1	1	1

Abbreviations:

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), MALES

ANIMAL No. 26

	PARAMETER	SCORE	Study day / treatment																						
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

	PARAMETER	SCORE	Treatment							Study day / recovery													
			22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3	1	1	1	1	1	1	1	1													

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), MALES

ANIMAL No. 27

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

	PARAMETER	SCORE	Treatment							Study day / recovery													
			22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3	1	1	1	1	1	1	1	1													

Abbreviations:

APP = Appearance
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MIS = Miscellaneous
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), MALES

ANIMAL No. 28

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

	PARAMETER	SCORE	Treatment							Study day / recovery													
			22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3	1	1	1	1	1	1	1	1													

Abbreviations:

APP = Appearance
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), MALES

ANIMAL No. 29

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

	PARAMETER	SCORE	Treatment							Study day / recovery													
			22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3	1	1	1	1	1	1	1	1													

Abbreviations:

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), MALES

ANIMAL No. 30

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

	PARAMETER	SCORE	Treatment							Study day / recovery													
			22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3						1	1														
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3	1	1	1	1	1	1	1	1													

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
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P = Pretest examination (during acclimatization)

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TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), FEMALES

ANIMAL No. 31

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
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RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), FEMALES

ANIMAL No. 32

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

[ ] = No abnormal findings noted

n = Severity of findings

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), FEMALES

ANIMAL No. 33

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), FEMALES

ANIMAL No. 34

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), FEMALES

ANIMAL No. 35

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), FEMALES

ANIMAL No. 36

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment							Study day / recovery													
			22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3																					

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
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P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), FEMALES

ANIMAL No. 37

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment							Study day / recovery													
			22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3																					

Abbreviations:

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), FEMALES

ANIMAL No. 38

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment							Study day / recovery													
			22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3																					

Abbreviations:

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), FEMALES

ANIMAL No. 39

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

			Treatment							Study day / recovery													
	PARAMETER	SCORE	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3																					

Abbreviations:

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 1 (CONTROL), FEMALES

ANIMAL No. 40

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

			Treatment							Study day / recovery													
	PARAMETER	SCORE	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3																					

Abbreviations:

APP = Appearance
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 2 (LOW DOSE), FEMALES

ANIMAL No. 41

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

			Treatment						
	PARAMETER	SCORE	22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

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RES = Respiration
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 2 (LOW DOSE), FEMALES

ANIMAL No. 42

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

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MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 2 (LOW DOSE), FEMALES

ANIMAL No. 43

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

			Treatment						
	PARAMETER	SCORE	22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

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RES = Respiration
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 2 (LOW DOSE), FEMALES

ANIMAL No. 44

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

			Treatment						
	PARAMETER	SCORE	22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

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MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 2 (LOW DOSE), FEMALES

ANIMAL No. 45

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 3 (MID DOSE), FEMALES

ANIMAL No. 46

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

[ ] = No abnormal findings noted

n = Severity of findings

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 3 (MID DOSE), FEMALES

ANIMAL No. 47

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

[ ] = No abnormal findings noted

n = Severity of findings

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 3 (MID DOSE), FEMALES

ANIMAL No. 48

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 3 (MID DOSE), FEMALES

ANIMAL No. 49

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 3 (MID DOSE), FEMALES

ANIMAL No. 50

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3																						

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3							

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), FEMALES

ANIMAL No. 51

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3	1	1	1	1	1	1	1

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), FEMALES

ANIMAL No. 52

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

			Treatment						
	PARAMETER	SCORE	22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3	1	1	1	1	1	1	1

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), FEMALES

ANIMAL No. 53

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3															1							
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

			Treatment						
	PARAMETER	SCORE	22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3	1	1	1	1	1	1	1

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), FEMALES

ANIMAL No. 54

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3	1	1	1	1	1	1	1

Abbreviations:

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BEH = Behavioral
RES = Respiration
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), FEMALES

ANIMAL No. 55

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

	PARAMETER	SCORE	Treatment						
			22	23	24	25	26	27	28
APP	Piloerection	1-3							
	Salivation	1-3							1
	Hunched posture	1							
	Hair Loss	1-3							
	Crust	1-3							
MOT	Ataxia	1-3							
	Tremor/twitching	1-3							
	Prostration	1							
BEH	Hyperactivity	1-3							
	Somnolence	1-3							
RES	Dyspnea	1							
	Tachypnea	1							
	Bradypnea	1							
MIS	Soft Feces	1-3	1	1	1	1	1	1	1

Abbreviations:

APP = Appearance
MOT = Motor
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), FEMALES

ANIMAL No. 56

	PARAMETER	SCORE	Study day / treatment																						
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

	PARAMETER	SCORE	Treatment							Study day / recovery													
			22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3	1	1	1	1	1	1	1	1													

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), FEMALES

ANIMAL No. 57

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

	PARAMETER	SCORE	Treatment							Study day / recovery													
			22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3							1														
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3	1	1	1	1	1	1	1	1													

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), FEMALES

ANIMAL No. 58

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

	PARAMETER	SCORE	Treatment							Study day / recovery													
			22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3	1	1	1	1	1	1	1	1													

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
MIS = Miscellaneous
P = Pretest examination (during acclimatization)

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RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), FEMALES

ANIMAL No. 59

			Study day / treatment																					
	PARAMETER	SCORE	P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

			Treatment							Study day / recovery													
	PARAMETER	SCORE	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3																					
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3	1	1	1	1	1	1	1	1													

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n = Severity of findings

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

DAILY CAGE-SIDE OBSERVATIONS, INDIVIDUAL DATA

GROUP 4 (HIGH DOSE), FEMALES

ANIMAL No. 60

	PARAMETER	SCORE	Study day / treatment																					
			P	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
APP	Piloerection	1-3																						
	Salivation	1-3																						
	Hunched posture	1																						
	Hair Loss	1-3																						
	Crust	1-3																						
MOT	Ataxia	1-3																						
	Tremor/twitching	1-3																						
	Prostration	1																						
BEH	Hyperactivity	1-3																						
	Somnolence	1-3																						
RES	Dyspnea	1																						
	Tachypnea	1																						
	Bradypnea	1																						
MIS	Soft Feces	1-3								1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

	PARAMETER	SCORE	Treatment							Study day / recovery													
			22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
APP	Piloerection	1-3																					
	Salivation	1-3						1	1														
	Hunched posture	1																					
	Hair Loss	1-3																					
	Crust	1-3																					
MOT	Ataxia	1-3																					
	Tremor/twitching	1-3																					
	Prostration	1																					
BEH	Hyperactivity	1-3																					
	Somnolence	1-3																					
RES	Dyspnea	1																					
	Tachypnea	1																					
	Bradypnea	1																					
MIS	Soft Feces	1-3	1	1	1	1	1	1	1	1													

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RCC PROJECT 848174
TKA 40291 (ZLI 3331)

WEEKLY OUTSIDE CAGE OBSERVATIONS, INDIVIDUAL DATA

PRETEST

GROUP 1 (CONTROL)

			MALES										FEMALES									
FINDINGS / ANIMAL NO		SCORE	1	2	3	4	5	6	7	8	9	10	31	32	33	34	35	36	37	38	39	40
APP	Piloerection	1-3																				
	Salivation	1-3																				
	Hunched posture	1																				
	Hair Loss	1-3																				
MOT	Ataxia	1-3																				
	Tremor/twitching	1-3																				
	Prostration	1																				
	Circling	1																				
	Spasm	1-3																				
BEH	Hyperactivity	1-3																				
	Somnolence	1-3																				
	Inc. exploration	1-3																				
	Red. grooming	1-3																				
	Vocalization	1-3																				
RES	Dyspnea	1																				
	Tachypnea	1																				
	Bradypnea	1																				
REF	Blink	1																				
	Pinna	1																				
	Iridic light reflex	1																				
	Push-off (hind legs)	1																				
	Pain response	1																				
	Startle / hearing	1																				
MIS	Lacrimation	1-3																				
	Limbs cyanotic	1																				
	Mydriasis	1																				
	Miosis	1																				
	Exophthalmos	1																				
	Red. muscle tone	1-3																				

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WEEKLY OUTSIDE CAGE OBSERVATIONS, INDIVIDUAL DATA

PRETEST

			GROUP 2 (LOW DOSE)										GROUP 3 (MID DOSE)									
			MALES					FEMALES					MALES					FEMALES				
FINDINGS / ANIMAL NO		SCORE	11	12	13	14	15	41	42	43	44	45	16	17	18	19	20	46	47	48	49	50
APP	Piloerection	1-3																				
	Salivation	1-3																				
	Hunched posture	1																				
	Hair Loss	1-3																				
MOT	Ataxia	1-3																				
	Tremor/twitching	1-3																				
	Prostration	1																				
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RCC PROJECT 848174
TKA 40291 (ZLI 3331)

WEEKLY OUTSIDE CAGE OBSERVATIONS, INDIVIDUAL DATA

PRETEST

GROUP 4 (HIGH DOSE)

			MALES										FEMALES									
FINDINGS / ANIMAL NO		SCORE	21	22	23	24	25	26	27	28	29	30	51	52	53	54	55	56	57	58	59	60
APP	Piloerection	1-3																				
	Salivation	1-3																				
	Hunched posture	1																				
	Hair Loss	1-3																				
MOT	Ataxia	1-3																				
	Tremor/twitching	1-3																				
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RCC PROJECT 848174
TKA 40291 (ZLI 3331)

WEEKLY OUTSIDE CAGE OBSERVATIONS, INDIVIDUAL DATA

WEEK 1

GROUP 1 (CONTROL)

			MALES										FEMALES									
FINDINGS / ANIMAL NO		SCORE	1	2	3	4	5	6	7	8	9	10	31	32	33	34	35	36	37	38	39	40
APP	Piloerection	1-3																				
	Salivation	1-3																				
	Hunched posture	1																				
	Hair Loss	1-3																				
MOT	Ataxia	1-3																				
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WEEKLY OUTSIDE CAGE OBSERVATIONS, INDIVIDUAL DATA

WEEK 1

			GROUP 2 (LOW DOSE)										GROUP 3 (MID DOSE)									
			MALES					FEMALES					MALES					FEMALES				
FINDINGS / ANIMAL NO		SCORE	11	12	13	14	15	41	42	43	44	45	16	17	18	19	20	46	47	48	49	50
APP	Piloerection	1-3																				
	Salivation	1-3																				
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WEEKLY OUTSIDE CAGE OBSERVATIONS, INDIVIDUAL DATA

WEEK 1

GROUP 4 (HIGH DOSE)

			MALES										FEMALES									
FINDINGS / ANIMAL NO		SCORE	21	22	23	24	25	26	27	28	29	30	51	52	53	54	55	56	57	58	59	60
APP	Piloerection	1-3																				
	Salivation	1-3																				
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WEEKLY OUTSIDE CAGE OBSERVATIONS, INDIVIDUAL DATA

WEEK 2

GROUP 1 (CONTROL)

			MALES										FEMALES									
FINDINGS / ANIMAL NO		SCORE	1	2	3	4	5	6	7	8	9	10	31	32	33	34	35	36	37	38	39	40
APP	Piloerection	1-3																				
	Salivation	1-3																				
	Hunched posture	1																				
	Hair Loss	1-3	1	1			1															
MOT	Ataxia	1-3																				
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WEEKLY OUTSIDE CAGE OBSERVATIONS, INDIVIDUAL DATA

WEEK 2

			GROUP 2 (LOW DOSE)										GROUP 3 (MID DOSE)									
			MALES					FEMALES					MALES					FEMALES				
FINDINGS / ANIMAL NO		SCORE	11	12	13	14	15	41	42	43	44	45	16	17	18	19	20	46	47	48	49	50
APP	Piloerection	1-3																				
	Salivation	1-3																				
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WEEKLY OUTSIDE CAGE OBSERVATIONS, INDIVIDUAL DATA

WEEK 2

GROUP 4 (HIGH DOSE)

			MALES										FEMALES									
FINDINGS / ANIMAL NO		SCORE	21	22	23	24	25	26	27	28	29	30	51	52	53	54	55	56	57	58	59	60
APP	Piloerection	1-3																				
	Salivation	1-3							1			1			1							
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RCC PROJECT 848174
TKA 40291 (ZLI 3331)

WEEKLY OUTSIDE CAGE OBSERVATIONS, INDIVIDUAL DATA

WEEK 3

GROUP 1 (CONTROL)

			MALES										FEMALES									
FINDINGS / ANIMAL NO		SCORE	1	2	3	4	5	6	7	8	9	10	31	32	33	34	35	36	37	38	39	40
APP	Piloerection	1-3																				
	Salivation	1-3																				
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RCC PROJECT 848174
TKA 40291 (ZLI 3331)

WEEKLY OUTSIDE CAGE OBSERVATIONS, INDIVIDUAL DATA

WEEK 3

			GROUP 2 (LOW DOSE)										GROUP 3 (MID DOSE)									
			MALES					FEMALES					MALES					FEMALES				
FINDINGS / ANIMAL NO		SCORE	11	12	13	14	15	41	42	43	44	45	16	17	18	19	20	46	47	48	49	50
APP	Piloerection	1-3																				
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WEEKLY OUTSIDE CAGE OBSERVATIONS, INDIVIDUAL DATA

WEEK 3

GROUP 4 (HIGH DOSE)

			MALES										FEMALES									
FINDINGS / ANIMAL NO		SCORE	21	22	23	24	25	26	27	28	29	30	51	52	53	54	55	56	57	58	59	60
APP	Piloerection	1-3																				
	Salivation	1-3										1										
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RCC PROJECT 848174
TKA 40291 (ZLI 3331)

WEEKLY OUTSIDE CAGE OBSERVATIONS, INDIVIDUAL DATA

WEEK 4

GROUP 1 (CONTROL)

			MALES										FEMALES									
FINDINGS / ANIMAL NO		SCORE	1	2	3	4	5	6	7	8	9	10	31	32	33	34	35	36	37	38	39	40
APP	Piloerection	1-3																				
	Salivation	1-3																				
	Hunched posture	1																				
	Hair Loss	1-3	1	1	1		1															
MOT	Ataxia	1-3																				
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REF = Reflexes
MIS = Miscellaneous

[ ] = No abnormal findings noted

n = Severity of findings

RCC PROJECT 848174
TKA 40291 (ZLI 3331)

WEEKLY OUTSIDE CAGE OBSERVATIONS, INDIVIDUAL DATA

WEEK 4

			GROUP 2 (LOW DOSE)										GROUP 3 (MID DOSE)									
			MALES					FEMALES					MALES					FEMALES				
FINDINGS / ANIMAL NO		SCORE	11	12	13	14	15	41	42	43	44	45	16	17	18	19	20	46	47	48	49	50
APP	Piloerection	1-3																				
	Salivation	1-3																				
	Hunched posture	1																				
	Hair Loss	1-3																				
MOT	Ataxia	1-3																				
	Tremor/twitching	1-3																				
	Prostration	1																				
	Circling	1																				
	Spasm	1-3																				
BEH	Hyperactivity	1-3																				
	Somnolence	1-3																				
	Inc. exploration	1-3																				
	Red. grooming	1-3																				
	Vocalization	1-3																				
RES	Dyspnea	1																				
	Tachypnea	1																				
	Bradypnea	1																				
REF	Blink	1																				
	Pinna	1																				
	Iridic light reflex	1																				
	Push-off (hind legs)	1																				
	Pain response	1																				
	Startle / hearing	1																				
MIS	Lacrimation	1-3																				
	Limbs cyanotic	1																				
	Mydriasis	1																				
	Miosis	1																				
	Exophthalmos	1																				
	Red. muscle tone	1-3																				

Abbreviations:

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MOT = Motor
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REF = Reflexes
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RCC PROJECT 848174
TKA 40291 (ZLI 3331)

WEEKLY OUTSIDE CAGE OBSERVATIONS, INDIVIDUAL DATA

WEEK 4

GROUP 4 (HIGH DOSE)

			MALES										FEMALES									
FINDINGS / ANIMAL NO		SCORE	21	22	23	24	25	26	27	28	29	30	51	52	53	54	55	56	57	58	59	60
APP	Piloerection	1-3																				
	Salivation	1-3	1				1					1			1		1				1	
	Hunched posture	1																				
	Hair Loss	1-3																				
MOT	Ataxia	1-3																				
	Tremor/twitching	1-3																				
	Prostration	1																				
	Circling	1																				
	Spasm	1-3																				
BEH	Hyperactivity	1-3																				
	Somnolence	1-3																				
	Inc. exploration	1-3																				
	Red. grooming	1-3																				
	Vocalization	1-3																				
RES	Dyspnea	1																				
	Tachypnea	1																				
	Bradypnea	1																				
REF	Blink	1																				
	Pinna	1																				
	Iridic light reflex	1																				
	Push-off (hind legs)	1																				
	Pain response	1																				
	Startle / hearing	1																				
MIS	Lacrimation	1-3																				
	Limbs cyanotic	1																				
	Mydriasis	1																				
	Miosis	1																				
	Exophthalmos	1																				
	Red. muscle tone	1-3																				

Abbreviations:

APP = Appearance
MOT = Motor
BEH = Behavioral
RES = Respiration
REF = Reflexes
MIS = Miscellaneous

[ ] = No abnormal findings noted

n = Severity of findings

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

GRIP STRENGTH , INDIVIDUAL DATA AT WEEK 4

GROUP 1 0 mg/kg

MALES Animal No.	Forelimb	Hindlimb	FEMALES Animal No.	Forelimb	Hindlimb
1	1223	940	31	950	657
2	1173	847	32	1013	693
3	1223	993	33	1030	723
4	1217	877	34	880	593
5	1223	880	35	930	633
6	1340	1017	36	927	687
7	1240	890	37	890	653
8	1183	840	38	873	687
9	1227	853	39	970	683
10	1430	917	40	823	643

GROUP 2 50 mg/kg

Animal No.	Forelimb	Hindlimb	Animal No.	Forelimb	Hindlimb
11	1243	833	41	903	650
12	1367	990	42	833	610
13	1283	907	43	947	700
14	1167	760	44	937	657
15	1243	857	45	977	663

GROUP 3 200 mg/kg

Animal No.	Forelimb	Hindlimb	Animal No.	Forelimb	Hindlimb
16	1227	883	46	947	623
17	1200	833	47	910	650
18	1253	853	48	880	687
19	1257	930	49	950	667
20	1193	883	50	817	607

GROUP 4 1000 mg/kg

Animal No.	Forelimb	Hindlimb	Animal No.	Forelimb	Hindlimb
21	1223	880	51	927	623
22	1273	970	52	993	650
23	1383	907	53	950	667
24	1213	843	54	943	673
25	1387	1013	55	943	663
26	1187	850	56	933	670
27	1153	813	57	983	677
28	1247	887	58	927	660
29	1397	1013	59	833	610
30	1223	850	60	953	670

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

LOCOMOTOR ACTIVITY, INDIVIDUAL DATA

LOW BEAMS COUNT MALES 4 WEEKS

Animal No	15 min.	30 min.	45 min.	60 min.	Total
Group 1 0 mg/kg					
1	1144	736	486	539	2905
2	1057	676	285	652	2670
3	1205	700	649	283	2837
4	951	685	235	162	2033
5	829	675	684	584	2772
6	801	556	823	237	2417
7	888	543	583	384	2398
8	903	623	56	456	2038
9	1318	880	355	484	3037
10	1093	627	524	411	2655
Group 2 50 mg/kg					
11	646	249	6	306	1207
12	787	504	419	192	1902
13	572	516	289	230	1607
14	1451	733	404	448	3036
15	591	340	297	246	1474
Group 3 200 mg/kg					
16	876	592	215	218	1901
17	813	254	279	72	1418
18	1658	1078	744	416	3896
19	1619	974	1034	736	4363
20	1369	663	536	305	2873
Group 4 1000 mg/kg					
21	745	523	596	333	2197
22	703	509	481	432	2125
23	685	509	448	77	1719
24	761	465	320	385	1931
25	902	346	466	359	2073
26	1378	632	5	252	2267
27	1308	855	413	681	3257
28	1078	580	147	89	1894
29	1130	611	655	550	2946
30	665	487	393	316	1861

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

LOCOMOTOR ACTIVITY, INDIVIDUAL DATA

LOW BEAMS COUNT FEMALES 4 WEEKS

Animal No	15 min.	30 min.	45 min.	60 min.	Total
Group 1 0 mg/kg					
31	673	267	0	9	949
32	1004	380	19	61	1464
33	821	107	658	151	1737
34	866	315	10	84	1275
35	894	338	461	500	2193
36	390	268	11	40	709
37	795	267	52	84	1198
38	1020	547	569	520	2656
39	1046	618	36	16	1716
40	905	438	79	135	1557
Group 2 50 mg/kg					
41	449	384	131	7	971
42	438	19	4	2	463
43	794	63	2	12	871
44	714	151	181	2	1048
45	513	98	4	120	735
Group 3 200 mg/kg					
46	730	464	28	32	1254
47	861	165	32	15	1073
48	1445	1078	683	815	4021
49	1006	800	299	737	2842
50	1225	868	231	108	2432
Group 4 1000 mg/kg					
51	412	427	78	102	1019
52	860	635	30	44	1569
53	689	746	448	102	1985
54	677	153	263	70	1163
55	525	191	19	24	759
56	879	584	231	2	1696
57	444	274	342	155	1215
58	570	445	116	10	1141
59	428	3	22	10	463
60	450	146	30	22	648

FOOD CONSUMPTION (G/ANIMAL/DAY)
MALES

GROUP 1 (0 MG/KG)

	PRETEST	TREATMENT				RECOVERY	
DAYS	1-8	1-8	8-15	15-22	22-28	1-8	8-14
WEEKS	1/2	1/2	2/3	3/4	4	1/2	2
CAGE							
1	17.1	19.8	21.5	22.4	22.7	---	---
2	17.0	18.8	20.8	22.2	22.5	23.2	22.9

FOOD CONSUMPTION (G/ANIMAL/DAY)
MALES

GROUP 2 (50 MG/KG)

	PRETEST	TREATMENT				RECOVERY	
DAYS	1-8	1-8	8-15	15-22	22-28	1-8	8-14
WEEKS	1/2	1/2	2/3	3/4	4	1/2	2
CAGE							
3	17.2	18.5	19.7	21.1	19.5	---	---

FOOD CONSUMPTION (G/ANIMAL/DAY)
MALES

GROUP 3 (200 MG/KG)

	PRETEST	TREATMENT				RECOVERY	
DAYS	1-8	1-8	8-15	15-22	22-28	1-8	8-14
WEEKS	1/2	1/2	2/3	3/4	4	1/2	2
CAGE							
4	17.0	18.6	20.1	20.6	20.4	---	---

FOOD CONSUMPTION (G/ANIMAL/DAY)
MALES

GROUP 4 (1000 MG/KG)

	PRETEST	TREATMENT				RECOVERY	
DAYS	1-8	1-8	8-15	15-22	22-28	1-8	8-14
WEEKS	1/2	1/2	2/3	3/4	4	1/2	2
CAGE							
5	17.5	19.8	22.0	22.7	22.7	---	---
6	17.2	19.3	22.0	23.3	23.8	22.6	22.5

FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES

GROUP 1 (0 MG/KG)

	PRETEST	TREATMENT				RECOVERY	
DAYS	1-8	1-8	8-15	15-22	22-28	1-8	8-14
WEEKS	1/2	1/2	2/3	3/4	4	1/2	2
CAGE							
7	12.5	13.0	13.4	14.5	14.6	---	---
8	12.8	13.0	13.6	14.8	14.7	15.9	16.2

FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES

GROUP 2 (50 MG/KG)

	PRETEST	TREATMENT				RECOVERY	
DAYS	1-8	1-8	8-15	15-22	22-28	1-8	8-14
WEEKS	1/2	1/2	2/3	3/4	4	1/2	2
CAGE							
9	12.5	13.2	14.1	14.5	14.3	---	---

FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES

GROUP 3 (200 MG/KG)

	PRETEST	TREATMENT				RECOVERY	
DAYS	1-8	1-8	8-15	15-22	22-28	1-8	8-14
WEEKS	1/2	1/2	2/3	3/4	4	1/2	2
CAGE							
10	12.9	12.4	13.6	14.1	14.1	---	---

FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES

GROUP 4 (1000 MG/KG)

	PRETEST	TREATMENT				RECOVERY	
DAYS	1-8	1-8	8-15	15-22	22-28	1-8	8-14
WEEKS	1/2	1/2	2/3	3/4	4	1/2	2
CAGE							
11	13.1	13.7	14.9	15.4	15.1	---	---
12	12.7	13.5	14.2	15.4	15.2	14.7	14.8

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

GROUP 1 (0 MG/KG)

	PRETEST	TREATMENT				RECOVERY	
DAYS	1-8	1-8	8-15	15-22	22-28	1-8	8-14
WEEKS	1/2	1/2	2/3	3/4	4	1/2	2
CAGE							
1	115	86	80	75	70	---	---
2	116	83	78	75	70	69	64

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

GROUP 2 (50 MG/KG)

	PRETEST	TREATMENT				RECOVERY	
DAYS	1-8	1-8	8-15	15-22	22-28	1-8	8-14
WEEKS	1/2	1/2	2/3	3/4	4	1/2	2
CAGE							
3	119	83	77	74	65	---	---

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

GROUP 3 (200 MG/KG)

	PRETEST	TREATMENT				RECOVERY	
DAYS	1-8	1-8	8-15	15-22	22-28	1-8	8-14
WEEKS	1/2	1/2	2/3	3/4	4	1/2	2
CAGE							
4	115	83	79	74	69	---	---

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

GROUP 4 (1000 MG/KG)

	PRETEST	TREATMENT				RECOVERY	
DAYS	1-8	1-8	8-15	15-22	22-28	1-8	8-14
WEEKS	1/2	1/2	2/3	3/4	4	1/2	2
CAGE							
5	116	86	84	79	74	---	---
6	119	88	86	82	78	71	67

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

GROUP 1 (0 MG/KG)

	PRETEST	TREATMENT				RECOVERY	
DAYS	1-8	1-8	8-15	15-22	22-28	1-8	8-14
WEEKS	1/2	1/2	2/3	3/4	4	1/2	2
CAGE							
7	104	82	77	78	74	---	---
8	107	83	80	81	77	79	77

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

GROUP 2 (50 MG/KG)

	PRETEST	TREATMENT				RECOVERY	
DAYS	1-8	1-8	8-15	15-22	22-28	1-8	8-14
WEEKS	1/2	1/2	2/3	3/4	4	1/2	2
CAGE							
9	102	80	77	75	71	---	---

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

GROUP 3 (200 MG/KG)

	PRETEST	TREATMENT				RECOVERY	
DAYS	1-8	1-8	8-15	15-22	22-28	1-8	8-14
WEEKS	1/2	1/2	2/3	3/4	4	1/2	2
CAGE							
10	106	79	79	77	73	---	---

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

GROUP 4 (1000 MG/KG)

	PRETEST	TREATMENT				RECOVERY	
DAYS	1-8	1-8	8-15	15-22	22-28	1-8	8-14
WEEKS	1/2	1/2	2/3	3/4	4	1/2	2
CAGE							
11	110	85	83	81	76	---	---
12	104	84	79	80	75	71	70

BODY WEIGHTS (GRAM)
MALES

GROUP 1 (0 MG/KG)

	PRETEST	TREATMENT					RECOVERY
DAYS	1	1	8	15	22	28	
WEEKS	1	1	2	3	4	4	1
ANIMAL							1
1	151	189	234	274	307	335	---
2	143	186	229	267	297	324	---
3	137	178	215	253	279	304	---
4	160	201	244	291	321	346	---
5	154	194	235	268	295	316	---
6	137	177	219	265	298	325	310
7	149	192	238	275	310	334	324
8	153	193	231	269	296	315	304
9	148	184	218	257	284	302	292
10	144	184	223	263	297	323	311

	RECOVERY	
DAYS	8	14
WEEKS	2	2
ANIMAL		
1	---	---
2	---	---
3	---	---
4	---	---
5	---	---
6	347	372
7	351	370
8	330	345
9	318	331
10	346	362

BODY WEIGHTS (GRAM)
MALES

GROUP 2 (50 MG/KG)

	PRETEST	TREATMENT					RECOVERY
DAYS	1	1	8	15	22	28	
WEEKS	1	1	2	3	4	4	1
ANIMAL							1
11	138	183	220	248	278	269	---
12	148	192	229	268	298	319	---
13	144	185	223	262	298	319	---
14	150	190	229	257	282	297	---
15	139	180	211	241	272	287	---

	RECOVERY	
DAYS	8	14
WEEKS	2	2
ANIMAL		
11	---	---
12	---	---
13	---	---
14	---	---
15	---	---

BODY WEIGHTS (GRAM)
MALES

GROUP 3 (200 MG/KG)

	PRETEST	TREATMENT					RECOVERY
DAYS	1	1	8	15	22	28	
WEEKS	1	1	2	3	4	4	1
ANIMAL							1
16	148	191	231	267	296	313	---
17	146	181	219	255	288	304	---
18	143	185	222	262	290	309	---
19	158	191	224	249	268	282	---
20	147	186	219	241	257	271	---

	RECOVERY	
DAYS	8	14
WEEKS	2	2
ANIMAL		
16	---	---
17	---	---
18	---	---
19	---	---
20	---	---

BODY WEIGHTS (GRAM)
MALES

GROUP 4 (1000 MG/KG)

	PRETEST	TREATMENT					RECOVERY
DAYS	1	1	8	15	22	28	
WEEKS	1	1	2	3	4	4	1
ANIMAL							1
21	146	184	220	249	267	284	---
22	159	202	249	290	326	347	---
23	148	189	227	264	287	305	---
24	145	185	221	251	269	284	---
25	158	194	227	260	293	310	---
26	151	194	228	263	292	313	292
27	137	179	218	251	282	303	286
28	137	176	212	244	275	295	280
29	148	191	228	271	300	328	308
30	148	184	218	249	272	292	280

	RECOVERY	
DAYS	8	14
WEEKS	2	2
ANIMAL		
21	---	---
22	---	---
23	---	---
24	---	---
25	---	---
26	324	340
27	317	340
28	305	324
29	343	364
30	300	315

BODY WEIGHTS (GRAM)
FEMALES

GROUP 1 (0 MG/KG)

	PRETEST	TREATMENT					RECOVERY
DAYS	1	1	8	15	22	28	
WEEKS	1	1	2	3	4	4	1
ANIMAL							1
31	125	143	158	171	179	194	---
32	123	152	176	193	209	223	---
33	119	140	154	170	187	194	---
34	115	132	151	165	177	188	---
35	119	137	152	168	179	187	---
36	117	139	156	169	180	194	179
37	121	139	152	170	185	188	187
38	119	145	166	181	193	211	203
39	118	135	151	167	179	186	179
40	122	133	151	164	177	184	173

	RECOVERY	
DAYS	8	14
WEEKS	2	2
ANIMAL		
31	---	---
32	---	---
33	---	---
34	---	---
35	---	---
36	204	206
37	204	216
38	218	219
39	194	207
40	190	199

BODY WEIGHTS (GRAM)
FEMALES

GROUP 2 (50 MG/KG)

	PRETEST	TREATMENT					RECOVERY
DAYS	1	1	8	15	22	28	
WEEKS	1	1	2	3	4	4	1
ANIMAL							1
41	127	148	168	182	197	208	---
42	118	140	158	178	188	190	---
43	128	153	172	188	197	210	---
44	117	142	160	174	183	196	---
45	127	148	167	189	203	205	---

	RECOVERY	
DAYS	8	14
WEEKS	2	2
ANIMAL		
41	---	---
42	---	---
43	---	---
44	---	---
45	---	---

BODY WEIGHTS (GRAM)
FEMALES

GROUP 3 (200 MG/KG)

	PRETEST	TREATMENT					RECOVERY
DAYS	1	1	8	15	22	28	
WEEKS	1	1	2	3	4	4	1
ANIMAL							1
46	118	137	157	169	185	197	---
47	125	147	162	176	190	200	---
48	130	150	170	188	199	208	---
49	117	129	146	160	166	171	---
50	122	136	152	165	173	185	---

	RECOVERY	
DAYS	8	14
WEEKS	2	2
ANIMAL		
46	---	---
47	---	---
48	---	---
49	---	---
50	---	---

BODY WEIGHTS (GRAM)
FEMALES

GROUP 4 (1000 MG/KG)

	PRETEST	TREATMENT					RECOVERY
DAYS	1	1	8	15	22	28	
WEEKS	1	1	2	3	4	4	1
ANIMAL							1
51	117	131	151	171	184	193	---
52	126	142	163	180	194	201	---
53	122	156	175	193	203	215	---
54	116	135	155	173	183	193	---
55	115	139	157	175	186	187	---
56	120	140	164	183	197	207	197
57	121	134	149	166	176	185	172
58	121	145	160	177	188	198	185
59	119	138	158	173	187	198	185
60	129	149	173	198	216	221	207

	RECOVERY	
DAYS	8	14
WEEKS	2	2
ANIMAL		
51	---	---
52	---	---
53	---	---
54	---	---
55	---	---
56	209	218
57	188	195
58	201	208
59	200	206
60	232	236

BODY WEIGHT GAIN (%)
MALES

GROUP 1 (0 MG/KG)

	PRETEST	TREATMENT					RECOVERY
DAYS	1	1	8	15	22	28	
WEEKS	1	1	2	3	4	4	1
ANIMAL							1
1	-20.2	0.0	23.6	44.7	62.3	77.4	---
2	-23.0	0.0	23.3	43.8	59.9	74.6	---
3	-23.0	0.0	20.7	42.1	56.5	70.3	---
4	-20.5	0.0	21.6	44.7	59.9	72.2	---
5	-20.8	0.0	20.8	37.6	51.6	62.4	---
6	-22.4	0.0	23.7	49.5	68.2	83.4	75.0
7	-22.7	0.0	23.6	43.0	61.2	73.6	68.7
8	-20.4	0.0	20.1	39.9	53.5	63.8	57.6
9	-19.8	0.0	18.0	39.3	53.9	64.0	58.6
10	-21.7	0.0	21.1	42.5	61.3	75.1	68.8

	RECOVERY	
DAYS	8	14
WEEKS	2	2
ANIMAL		
1	---	---
2	---	---
3	---	---
4	---	---
5	---	---
6	96.0	110.4
7	82.8	92.3
8	71.3	79.4
9	72.4	79.6
10	87.4	96.6

BODY WEIGHT GAIN (%)
MALES

GROUP 2 (50 MG/KG)

	PRETEST	TREATMENT					RECOVERY
DAYS	1	1	8	15	22	28	
WEEKS	1	1	2	3	4	4	1
ANIMAL							1
11	-24.4	0.0	20.1	35.2	51.5	47.0	---
12	-23.0	0.0	19.1	39.3	55.0	66.2	---
13	-21.9	0.0	20.6	41.9	61.5	73.0	---
14	-21.1	0.0	20.6	35.7	48.8	56.6	---
15	-22.8	0.0	17.2	34.2	51.1	59.5	---

	RECOVERY	
DAYS	8	14
WEEKS	2	2
ANIMAL		
11	---	---
12	---	---
13	---	---
14	---	---
15	---	---

BODY WEIGHT GAIN (%)
MALES

GROUP 3 (200 MG/KG)

	PRETEST	TREATMENT					RECOVERY
DAYS	1	1	8	15	22	28	
WEEKS	1	1	2	3	4	4	1
ANIMAL							1
16	-22.5	0.0	21.0	39.9	55.4	64.4	---
17	-19.2	0.0	20.9	40.6	59.0	67.7	---
18	-22.7	0.0	19.8	41.5	56.9	67.1	---
19	-17.5	0.0	16.9	30.3	39.9	47.6	---
20	-20.7	0.0	18.0	29.5	38.5	45.7	---

	RECOVERY	
DAYS	8	14
WEEKS	2	2
ANIMAL		
16	---	---
17	---	---
18	---	---
19	---	---
20	---	---

BODY WEIGHT GAIN (%)
MALES

GROUP 4 (1000 MG/KG)

	PRETEST	TREATMENT					RECOVERY
DAYS	1	1	8	15	22	28	1
WEEKS	1	1	2	3	4	4	1
ANIMAL							
21	-20.3	0.0	19.8	35.4	45.3	54.9	---
22	-21.1	0.0	23.7	44.1	61.7	72.4	---
23	-21.8	0.0	19.7	39.1	51.6	61.1	---
24	-21.7	0.0	19.7	35.8	45.8	53.3	---
25	-18.6	0.0	16.7	33.9	50.7	59.7	---
26	-22.0	0.0	17.6	35.6	50.5	61.5	50.7
27	-23.5	0.0	21.9	40.0	57.6	69.0	60.0
28	-22.4	0.0	20.0	38.3	56.1	67.1	58.8
29	-22.5	0.0	19.1	41.7	57.0	71.5	61.2
30	-19.6	0.0	18.3	35.5	47.9	58.6	52.0

	RECOVERY	
DAYS	8	14
WEEKS	2	2
ANIMAL		
21	---	---
22	---	---
23	---	---
24	---	---
25	---	---
26	67.1	75.3
27	77.3	90.2
28	73.2	83.8
29	79.7	90.5
30	63.2	71.2

BODY WEIGHT GAIN (%)
FEMALES

GROUP 1 (0 MG/KG)

	PRETEST	TREATMENT					RECOVERY
DAYS	1	1	8	15	22	28	
WEEKS	1	1	2	3	4	4	1
ANIMAL							1
31	-12.6	0.0	10.4	19.4	24.6	35.5	---
32	-19.4	0.0	15.8	26.8	37.3	46.6	---
33	-14.7	0.0	9.7	21.5	33.6	38.6	---
34	-12.9	0.0	14.3	24.6	34.3	42.7	---
35	-13.0	0.0	10.8	22.7	30.7	36.5	---
36	-16.0	0.0	12.1	21.4	29.2	38.9	---
37	-13.1	0.0	9.7	22.7	33.0	35.6	28.6
38	-17.8	0.0	14.4	25.0	33.6	45.9	34.5
39	-12.6	0.0	11.6	23.1	32.0	37.4	40.4
40	-8.6	0.0	13.3	23.0	32.9	38.0	31.9
							30.3

	RECOVERY	
DAYS	8	14
WEEKS	2	2
ANIMAL		
31	---	---
32	---	---
33	---	---
34	---	---
35	---	---
36	46.2	48.1
37	46.9	55.3
38	50.8	51.6
39	43.3	53.1
40	42.9	49.8

BODY WEIGHT GAIN (%)
FEMALES

GROUP 2 (50 MG/KG)

	PRETEST	TREATMENT					RECOVERY
DAYS	1	1	8	15	22	28	
WEEKS	1	1	2	3	4	4	1
ANIMAL							1
41	-14.2	0.0	13.8	23.4	33.4	40.7	---
42	-16.0	0.0	13.1	27.3	34.7	35.7	---
43	-16.1	0.0	12.7	23.2	29.0	37.3	---
44	-18.1	0.0	12.6	22.4	28.7	37.4	---
45	-14.5	0.0	13.0	28.0	36.8	38.6	---

	RECOVERY	
DAYS	8	14
WEEKS	2	2
ANIMAL		
41	---	---
42	---	---
43	---	---
44	---	---
45	---	---

BODY WEIGHT GAIN (%)
FEMALES

GROUP 3 (200 MG/KG)

	PRETEST	TREATMENT					RECOVERY
DAYS	1	1	8	15	22	28	
WEEKS	1	1	2	3	4	4	1
ANIMAL							1
46	-14.3	0.0	13.9	23.1	34.8	43.4	---
47	-15.2	0.0	10.1	20.0	29.5	36.3	---
48	-13.6	0.0	13.6	25.3	32.7	38.6	---
49	-9.3	0.0	13.4	23.8	28.5	32.6	---
50	-10.5	0.0	11.7	21.0	26.9	35.4	---

	RECOVERY	
DAYS	8	14
WEEKS	2	2
ANIMAL		
46	---	---
47	---	---
48	---	---
49	---	---
50	---	---

BODY WEIGHT GAIN (%)
FEMALES

GROUP 4 (1000 MG/KG)

	PRETEST	TREATMENT					RECOVERY
DAYS	1	1	8	15	22	28	
WEEKS	1	1	2	3	4	4	1
ANIMAL							1
51	-10.9	0.0	15.2	30.3	40.4	46.8	---
52	-11.3	0.0	14.9	26.5	36.2	41.5	---
53	-21.7	0.0	12.3	24.0	30.8	38.0	---
54	-14.4	0.0	15.0	27.8	35.5	42.8	---
55	-17.4	0.0	13.1	25.8	33.8	34.5	---
56	-14.4	0.0	17.1	30.1	40.1	47.5	40.4
57	-10.0	0.0	10.9	23.2	31.1	38.0	28.2
58	-16.8	0.0	10.2	21.7	29.7	35.9	27.6
59	-13.9	0.0	14.2	25.5	35.1	43.3	33.7
60	-13.6	0.0	15.7	32.4	44.9	48.3	38.6

	RECOVERY	
DAYS	8	14
WEEKS	2	2
ANIMAL		
51	---	---
52	---	---
53	---	---
54	---	---
55	---	---
56	48.7	55.1
57	39.6	45.4
58	38.4	43.4
59	44.8	49.2
60	55.4	58.2

MACROSCOPICAL FINDINGS
MALES
GROUP 1 (0 MG/KG)

ANIMAL 1 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 2 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 3 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 4 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 5 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 6 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

ANIMAL 7 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

ANIMAL 8 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

ANIMAL 9 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

ANIMAL 10 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

MACROSCOPICAL FINDINGS
MALES
GROUP 2 (50 MG/KG)

ANIMAL 11 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 12 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 13 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 14 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 15 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

MACROSCOPICAL FINDINGS
MALES
GROUP 3 (200 MG/KG)

ANIMAL 16 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 17 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 18 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 19 (SCHEDULED NECROPSY, 19-MAY-2003)

THYMUS..... REDUCED IN SIZE.

ANIMAL 20 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

MACROSCOPICAL FINDINGS
MALES
GROUP 4 (1000 MG/KG)

ANIMAL 21 (SCHEDULED NECROPSY, 19-MAY-2003)

STOMACH..... FORESTOMACH, MUCOSA: IRREGULAR SURFACE.

ANIMAL 22 (SCHEDULED NECROPSY, 19-MAY-2003)

STOMACH..... FORESTOMACH, MUCOSA: IRREGULAR SURFACE.

ANIMAL 23 (SCHEDULED NECROPSY, 19-MAY-2003)

STOMACH..... FORESTOMACH, MUCOSA: IRREGULAR SURFACE.

ANIMAL 24 (SCHEDULED NECROPSY, 19-MAY-2003)

STOMACH..... FORESTOMACH, MUCOSA: IRREGULAR SURFACE.

ANIMAL 25 (SCHEDULED NECROPSY, 19-MAY-2003)

STOMACH..... FORESTOMACH, MUCOSA: IRREGULAR SURFACE.

ANIMAL 26 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

ANIMAL 27 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

ANIMAL 28 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

ANIMAL 29 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

ANIMAL 30 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

MACROSCOPICAL FINDINGS
FEMALES
GROUP 1 (0 MG/KG)

ANIMAL 31 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 32 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 33 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 34 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 35 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 36 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

ANIMAL 37 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

ANIMAL 38 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

ANIMAL 39 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

ANIMAL 40 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

MACROSCOPICAL FINDINGS
FEMALES
GROUP 2 (50 MG/KG)

ANIMAL 41 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 42 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 43 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 44 (SCHEDULED NECROPSY, 19-MAY-2003)

KIDNEYS..... RIGHT SIDE: PELVIC DILATION.

ANIMAL 45 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

MACROSCOPICAL FINDINGS
FEMALES
GROUP 3 (200 MG/KG)

ANIMAL 46 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 47 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 48 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 49 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

ANIMAL 50 (SCHEDULED NECROPSY, 19-MAY-2003)

NO FINDINGS NOTED

MACROSCOPICAL FINDINGS
FEMALES
GROUP 4 (1000 MG/KG)

ANIMAL 51 (SCHEDULED NECROPSY, 19-MAY-2003)

STOMACH..... FORESTOMACH, MUCOSA: IRREGULAR SURFACE.

ANIMAL 52 (SCHEDULED NECROPSY, 19-MAY-2003)

STOMACH..... FORESTOMACH, MUCOSA: IRREGULAR SURFACE.

ANIMAL 53 (SCHEDULED NECROPSY, 19-MAY-2003)

STOMACH..... FORESTOMACH, MUCOSA: IRREGULAR SURFACE.

ANIMAL 54 (SCHEDULED NECROPSY, 19-MAY-2003)

STOMACH..... FORESTOMACH, MUCOSA: IRREGULAR SURFACE.

ANIMAL 55 (SCHEDULED NECROPSY, 19-MAY-2003)

STOMACH..... FORESTOMACH, MUCOSA: IRREGULAR SURFACE.

ANIMAL 56 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

ANIMAL 57 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

ANIMAL 58 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

ANIMAL 59 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

ANIMAL 60 (SCHEDULED NECROPSY, 02-JUN-2003)

NO FINDINGS NOTED

ORGAN WEIGHTS (GRAM)
AFTER 4 WEEKS
MALES

GROUP 1 (0 MG/KG)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
1	304.53	1.92	1.059	8.71	0.50	1.96	0.078	0.657
2	296.42	1.98	0.911	8.55	0.61	2.14	0.068	0.779
3	275.85	1.98	0.898	8.35	0.40	1.91	0.060	0.648
4	314.56	1.96	1.036	9.99	0.36	2.48	0.066	0.787
5	290.11	1.99	0.985	8.43	0.43	2.03	0.052	0.667

ANIMAL NUMBER	TESTES	EPIDIDYMID
1	3.43	0.933
2	3.44	0.987
3	3.44	0.952
4	3.65	1.233
5	3.50	1.003

GROUP 2 (50 MG/KG)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
11	246.91	1.95	0.858	6.42	0.37	1.67	0.059	0.634
12	293.37	2.05	0.980	8.22	0.72	2.05	0.071	0.708
13	292.99	1.94	0.895	7.79	0.40	2.00	0.075	0.670
14	274.72	1.96	0.922	8.44	0.41	1.97	0.071	0.569
15	262.43	1.77	0.910	7.40	0.52	1.85	0.059	0.646

ANIMAL NUMBER	TESTES	EPIDIDYMID
11	3.36	0.889
12	3.57	1.134
13	3.63	1.085
14	3.82	1.166
15	3.63	0.944

GROUP 3 (200 MG/KG)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
16	284.07	1.95	1.004	8.91	0.44	1.82	0.065	0.631
17	276.74	1.90	0.947	8.44	0.42	1.87	0.069	0.541
18	283.47	2.07	1.004	8.91	0.54	2.10	0.062	0.629
19	257.59	1.84	1.157	7.57	0.27	1.91	0.068	0.691
20	245.58	1.84	0.874	7.36	0.31	1.86	0.062	0.601

ORGAN WEIGHTS (GRAM)
AFTER 4 WEEKS
MALES

GROUP 3 (200 MG/KG)

ANIMAL NUMBER	TESTES	EPIDIDYMID
16	3.29	0.940
17	3.15	1.116
18	3.43	0.985
19	3.61	1.036
20	3.50	1.000

GROUP 4 (1000 MG/KG)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
21	255.21	1.88	0.913	8.00	0.42	1.93	0.070	0.681
22	308.93	2.06	1.022	10.31	0.65	2.44	0.081	0.760
23	274.31	1.93	0.961	9.01	0.43	2.29	0.102	0.625
24	255.28	1.85	1.136	9.88	0.35	2.35	0.066	0.490
25	279.20	2.04	1.046	8.55	0.59	2.14	0.080	0.545

ANIMAL NUMBER	TESTES	EPIDIDYMID
21	3.27	1.050
22	3.76	1.091
23	3.28	0.922
24	3.40	1.040
25	3.55	0.984

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

GROUP 1 (0 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
1	304.53	0.63	0.348	2.86	0.17	0.64	0.026	0.216
2	296.42	0.67	0.307	2.88	0.21	0.72	0.023	0.263
3	275.85	0.72	0.326	3.03	0.15	0.69	0.022	0.235
4	314.56	0.62	0.329	3.17	0.12	0.79	0.021	0.250
5	290.11	0.69	0.340	2.91	0.15	0.70	0.018	0.230

ANIMAL NUMBER	TESTES	EPIDIDYMID
1	1.12	0.306
2	1.16	0.333
3	1.25	0.345
4	1.16	0.392
5	1.20	0.346

GROUP 2 (50 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
11	246.91	0.79	0.347	2.60	0.15	0.68	0.024	0.257
12	293.37	0.70	0.334	2.80	0.24	0.70	0.024	0.241
13	292.99	0.66	0.306	2.66	0.14	0.68	0.026	0.229
14	274.72	0.71	0.336	3.07	0.15	0.72	0.026	0.207
15	262.43	0.68	0.347	2.82	0.20	0.71	0.022	0.246

ANIMAL NUMBER	TESTES	EPIDIDYMID
11	1.36	0.360
12	1.22	0.387
13	1.24	0.370
14	1.39	0.424
15	1.38	0.360

GROUP 3 (200 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
16	284.07	0.69	0.353	3.14	0.16	0.64	0.023	0.222
17	276.74	0.69	0.342	3.05	0.15	0.68	0.025	0.195
18	283.47	0.73	0.354	3.14	0.19	0.74	0.022	0.222
19	257.59	0.71	0.449	2.94	0.11	0.74	0.026	0.268
20	245.58	0.75	0.356	3.00	0.13	0.76	0.025	0.245

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

GROUP 3 (200 MG/KG)

ANIMAL NUMBER	TESTES	EPIDIDYMID
16	1.16	0.331
17	1.14	0.403
18	1.21	0.347
19	1.40	0.402
20	1.43	0.407

GROUP 4 (1000 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
21	255.21	0.74	0.358	3.13	0.17	0.75	0.028	0.267
22	308.93	0.67	0.331	3.34	0.21	0.79	0.026	0.246
23	274.31	0.70	0.350	3.28	0.16	0.84	0.037	0.228
24	255.28	0.73	0.445	3.87	0.14	0.92	0.026	0.192
25	279.20	0.73	0.374	3.06	0.21	0.77	0.029	0.195

ANIMAL NUMBER	TESTES	EPIDIDYMID
21	1.28	0.411
22	1.22	0.353
23	1.20	0.336
24	1.33	0.407
25	1.27	0.352

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

GROUP 1 (0 MG/KG)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN	TESTES
1	1.92	55.189	454.05	26.23	102.01	4.061	34.249	178.55
2	1.98	46.100	432.39	31.00	108.08	3.419	39.403	174.06
3	1.98	45.376	421.85	20.29	96.37	3.047	32.737	174.08
4	1.96	52.963	510.59	18.52	126.81	3.380	40.257	186.63
5	1.99	49.550	424.02	21.44	102.23	2.636	33.528	175.85

ANIMAL NUMBER	EPIDIDYMID
1	48.642
2	49.929
3	48.130
4	63.041
5	50.440

GROUP 2 (50 MG/KG)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN	TESTES
11	1.95	43.968	328.95	19.02	85.52	3.044	32.498	172.26
12	2.05	47.922	401.82	35.03	100.11	3.481	34.618	174.42
13	1.94	46.216	402.35	20.88	103.15	3.872	34.579	187.31
14	1.96	47.109	431.02	20.70	100.65	3.642	29.038	195.25
15	1.77	51.311	417.30	29.60	104.49	3.299	36.446	204.80

ANIMAL NUMBER	EPIDIDYMID
11	45.582
12	55.442
13	55.994
14	59.552
15	53.251

GROUP 3 (200 MG/KG)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN	TESTES
16	1.95	51.580	457.65	22.82	93.43	3.360	32.412	169.15
17	1.90	49.908	444.90	21.90	98.72	3.619	28.486	166.14
18	2.07	48.526	430.66	26.24	101.51	3.016	30.409	165.72
19	1.84	62.999	412.56	14.83	104.02	3.715	37.622	196.56
20	1.84	47.418	399.39	16.86	100.99	3.385	32.614	190.01

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

GROUP 3 (200 MG/KG)

ANIMAL NUMBER	EPIDIDYMID
16	48.282
17	58.811
18	47.607
19	56.441
20	54.253

GROUP 4 (1000 MG/KG)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN	TESTES
21	1.88	48.621	425.60	22.44	102.56	3.742	36.250	174.27
22	2.06	49.701	501.05	31.47	118.48	3.938	36.949	182.80
23	1.93	49.852	467.28	22.30	119.00	5.266	32.425	170.07
24	1.85	61.279	533.31	18.83	126.57	3.551	26.449	183.53
25	2.04	51.303	419.42	28.99	105.14	3.945	26.721	174.02

ANIMAL NUMBER	EPIDIDYMID
21	55.898
22	53.060
23	47.829
24	56.109
25	48.275

ORGAN WEIGHTS (GRAM)
AFTER 4 WEEKS
FEMALES

GROUP 1 (0 MG/KG)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
31	171.37	1.84	0.731	4.94	0.43	1.28	0.069	0.459
32	198.50	1.86	0.711	5.68	0.45	1.34	0.071	0.503
33	174.55	1.93	0.657	5.25	0.39	1.30	0.080	0.488
34	169.75	1.76	0.683	4.57	0.45	1.19	0.058	0.389
35	171.70	1.77	0.689	5.42	0.39	1.38	0.084	0.497

ANIMAL NUMBER	OVARIES
31	0.081
32	0.095
33	0.090
34	0.092
35	0.109

GROUP 2 (50 MG/KG)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
41	188.49	1.91	0.730	5.84	0.40	1.44	0.078	0.534
42	177.44	1.94	0.636	5.24	0.50	1.29	0.061	0.520
43	190.34	1.76	0.564	5.12	0.50	1.19	0.068	0.463
44	179.43	1.80	0.641	5.20	0.46	1.37	0.064	0.448
45	186.23	1.80	0.700	5.45	0.45	1.22	0.068	0.486

ANIMAL NUMBER	OVARIES
41	0.075
42	0.090
43	0.082
44	0.089
45	0.082

GROUP 3 (200 MG/KG)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
46	176.19	1.85	0.685	5.00	0.29	1.25	0.076	0.439
47	181.21	1.74	0.672	5.65	0.42	1.31	0.072	0.513
48	190.16	1.90	0.728	5.36	0.46	1.28	0.069	0.533
49	153.99	1.85	0.598	4.92	0.35	1.32	0.076	0.434
50	163.62	1.83	0.620	4.91	0.36	1.21	0.072	0.431

ORGAN WEIGHTS (GRAM)
AFTER 4 WEEKS
FEMALES

GROUP 3 (200 MG/KG)

ANIMAL NUMBER	OVARIES
46	0.081
47	0.087
48	0.106
49	0.088
50	0.104

GROUP 4 (1000 MG/KG)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
51	173.48	1.87	0.653	5.74	0.42	1.36	0.083	0.457
52	181.73	1.79	0.758	6.31	0.34	1.46	0.078	0.444
53	192.37	1.90	0.709	5.75	0.52	1.36	0.091	0.561
54	170.81	1.76	0.632	5.23	0.40	1.19	0.066	0.440
55	168.17	1.78	0.716	5.91	0.39	1.32	0.072	0.498

ANIMAL NUMBER	OVARIES
51	0.130
52	0.081
53	0.092
54	0.091
55	0.079

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

GROUP 1 (0 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
31	171.37	1.07	0.427	2.88	0.25	0.74	0.040	0.268
32	198.50	0.94	0.358	2.86	0.23	0.68	0.036	0.254
33	174.55	1.11	0.376	3.01	0.23	0.74	0.046	0.280
34	169.75	1.04	0.402	2.69	0.27	0.70	0.034	0.229
35	171.70	1.03	0.401	3.15	0.23	0.80	0.049	0.289

ANIMAL NUMBER	OVARIES
31	0.047
32	0.048
33	0.051
34	0.054
35	0.063

GROUP 2 (50 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
41	188.49	1.02	0.387	3.10	0.21	0.76	0.041	0.283
42	177.44	1.09	0.359	2.95	0.28	0.73	0.034	0.293
43	190.34	0.92	0.296	2.69	0.26	0.62	0.036	0.243
44	179.43	1.00	0.357	2.90	0.26	0.76	0.035	0.250
45	186.23	0.97	0.376	2.92	0.24	0.65	0.036	0.261

ANIMAL NUMBER	OVARIES
41	0.040
42	0.051
43	0.043
44	0.050
45	0.044

GROUP 3 (200 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
46	176.19	1.05	0.389	2.84	0.17	0.71	0.043	0.249
47	181.21	0.96	0.371	3.12	0.23	0.72	0.040	0.283
48	190.16	1.00	0.383	2.82	0.24	0.67	0.036	0.280
49	153.99	1.20	0.388	3.20	0.23	0.85	0.049	0.282
50	163.62	1.12	0.379	3.00	0.22	0.74	0.044	0.263

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

GROUP 3 (200 MG/KG)

ANIMAL NUMBER	OVARIES
46	0.046
47	0.048
48	0.056
49	0.057
50	0.063

GROUP 4 (1000 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
51	173.48	1.08	0.377	3.31	0.24	0.78	0.048	0.263
52	181.73	0.98	0.417	3.47	0.19	0.80	0.043	0.244
53	192.37	0.99	0.368	2.99	0.27	0.71	0.047	0.292
54	170.81	1.03	0.370	3.06	0.23	0.69	0.038	0.257
55	168.17	1.06	0.426	3.51	0.23	0.78	0.043	0.296

ANIMAL NUMBER	OVARIES
51	0.075
52	0.045
53	0.048
54	0.053
55	0.047

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

GROUP 1 (0 MG/KG)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN	OVARIES
31	1.84	39.742	268.76	23.20	69.40	3.757	24.963	4.393
32	1.86	38.291	305.94	24.44	72.29	3.803	27.118	5.134
33	1.93	33.991	271.73	20.45	67.22	4.116	25.282	4.644
34	1.76	38.817	259.97	25.62	67.54	3.315	22.121	5.226
35	1.77	38.990	306.30	22.27	77.80	4.734	28.112	6.137

GROUP 2 (50 MG/KG)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN	OVARIES
41	1.91	38.122	304.73	20.84	75.01	4.047	27.897	3.901
42	1.94	32.879	270.91	25.61	66.64	3.162	26.885	4.640
43	1.76	32.099	291.68	28.67	67.67	3.874	26.386	4.694
44	1.80	35.618	288.64	25.57	76.14	3.527	24.888	4.965
45	1.80	38.776	301.82	24.99	67.53	3.752	26.909	4.567

GROUP 3 (200 MG/KG)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN	OVARIES
46	1.85	36.949	269.66	15.88	67.32	4.082	23.686	4.373
47	1.74	38.681	325.34	24.42	75.60	4.127	29.517	4.996
48	1.90	38.268	281.92	24.28	67.43	3.605	28.015	5.549
49	1.85	32.338	266.23	18.94	71.12	4.115	23.480	4.780
50	1.83	33.902	268.80	19.87	66.20	3.913	23.581	5.675

GROUP 4 (1000 MG/KG)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN	OVARIES
51	1.87	34.947	307.12	22.44	72.74	4.446	24.440	6.977
52	1.79	42.356	352.45	19.04	81.56	4.382	24.823	4.544
53	1.90	37.340	302.94	27.62	71.73	4.806	29.567	4.859
54	1.76	35.943	297.62	22.80	67.41	3.725	25.003	5.158
55	1.78	40.181	331.55	21.74	73.98	4.028	27.924	4.443

ORGAN WEIGHTS (GRAM)
AFTER 6 WEEKS
MALES

GROUP 1 (0 MG/KG)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
6	339.54	1.98	1.109	11.86	0.42	2.49	0.081	0.763
7	342.49	2.00	1.022	11.67	0.42	2.31	0.076	0.670
8	317.76	2.01	0.932	9.80	0.41	1.94	0.077	0.660
9	313.93	1.86	1.092	10.89	0.33	2.17	0.055	0.570
10	326.80	1.98	1.022	10.49	0.45	2.32	0.066	0.681

ANIMAL NUMBER	TESTES	EPIDIDYMID
6	3.72	1.212
7	3.58	1.422
8	3.46	1.053
9	3.68	1.328
10	3.88	1.350

GROUP 4 (1000 MG/KG)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
26	323.64	2.06	0.987	9.45	0.38	2.07	0.059	0.554
27	314.76	2.03	1.100	9.79	0.44	2.16	0.082	0.705
28	301.42	1.91	0.906	9.71	0.36	2.13	0.051	0.594
29	338.64	2.04	0.995	9.24	0.44	1.89	0.070	0.548
30	286.97	2.05	0.805	8.43	0.44	1.89	0.047	0.636

ANIMAL NUMBER	TESTES	EPIDIDYMID
26	3.12	1.233
27	3.73	1.256
28	3.48	1.191
29	3.53	1.207
30	3.46	1.171

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

GROUP 1 (0 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
6	339.54	0.58	0.327	3.49	0.13	0.73	0.024	0.225
7	342.49	0.58	0.298	3.41	0.12	0.68	0.022	0.196
8	317.76	0.63	0.293	3.08	0.13	0.61	0.024	0.208
9	313.93	0.59	0.348	3.47	0.10	0.69	0.017	0.182
10	326.80	0.61	0.313	3.21	0.14	0.71	0.020	0.208

ANIMAL NUMBER	TESTES	EPIDIDYMID
6	1.09	0.357
7	1.05	0.415
8	1.09	0.331
9	1.17	0.423
10	1.19	0.413

GROUP 4 (1000 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
26	323.64	0.64	0.305	2.92	0.12	0.64	0.018	0.171
27	314.76	0.65	0.349	3.11	0.14	0.68	0.026	0.224
28	301.42	0.63	0.301	3.22	0.12	0.71	0.017	0.197
29	338.64	0.60	0.294	2.73	0.13	0.56	0.021	0.162
30	286.97	0.72	0.281	2.94	0.15	0.66	0.016	0.222

ANIMAL NUMBER	TESTES	EPIDIDYMID
26	0.96	0.381
27	1.18	0.399
28	1.15	0.395
29	1.04	0.356
30	1.21	0.408

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

GROUP 1 (0 MG/KG)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN	TESTES
6	1.98	56.064	599.38	21.48	125.67	4.095	38.562	187.85
7	2.00	51.213	584.90	21.23	115.87	3.788	33.574	179.41
8	2.01	46.442	488.33	20.40	96.64	3.822	32.898	172.44
9	1.86	58.639	584.66	17.57	116.54	2.932	30.611	197.80
10	1.98	51.543	529.31	22.71	117.12	3.329	34.349	195.91

ANIMAL NUMBER	EPIDIDYMID
6	61.276
7	71.272
8	52.477
9	71.290
10	68.072

GROUP 4 (1000 MG/KG)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN	TESTES
26	2.06	47.936	458.91	18.31	100.68	2.865	26.906	151.29
27	2.03	54.081	481.22	21.83	106.00	4.031	34.661	183.24
28	1.91	47.435	508.38	18.95	111.52	2.670	31.099	182.25
29	2.04	48.679	452.05	21.67	92.27	3.425	26.810	172.58
30	2.05	39.219	410.80	21.54	92.02	2.265	31.000	168.68

ANIMAL NUMBER	EPIDIDYMID
26	59.883
27	61.750
28	62.356
29	59.031
30	57.050

ORGAN WEIGHTS (GRAM)
AFTER 6 WEEKS
FEMALES

GROUP 1 (0 MG/KG)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
36	186.78	1.73	0.676	6.78	0.38	1.26	0.060	0.500
37	205.39	1.81	0.668	7.09	0.38	1.20	0.069	0.536
38	210.79	1.73	0.723	6.75	0.39	1.14	0.066	0.475
39	182.50	1.86	0.729	6.58	0.38	1.28	0.070	0.427
40	186.73	1.72	0.753	6.35	0.43	1.23	0.066	0.476

ANIMAL NUMBER	OVARIES
36	0.115
37	0.105
38	0.111
39	0.103
40	0.089

GROUP 4 (1000 MG/KG)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
56	190.57	1.77	0.728	6.25	0.40	1.23	0.065	0.486
57	172.40	1.82	0.636	5.58	0.35	1.31	0.071	0.501
58	186.56	1.90	0.714	6.85	0.32	1.33	0.070	0.531
59	183.85	1.76	0.685	6.64	0.30	1.28	0.067	0.506
60	231.03	1.97	0.737	7.54	0.45	1.56	0.093	0.557

ANIMAL NUMBER	OVARIES
56	0.110
57	0.104
58	0.119
59	0.108
60	0.067

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

GROUP 1 (0 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
36	186.78	0.93	0.362	3.63	0.20	0.68	0.032	0.268
37	205.39	0.88	0.325	3.45	0.19	0.59	0.033	0.261
38	210.79	0.82	0.343	3.20	0.19	0.54	0.031	0.225
39	182.50	1.02	0.399	3.61	0.21	0.70	0.038	0.234
40	186.73	0.92	0.403	3.40	0.23	0.66	0.036	0.255

ANIMAL NUMBER	OVARIES
36	0.062
37	0.051
38	0.053
39	0.057
40	0.048

GROUP 4 (1000 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
56	190.57	0.93	0.382	3.28	0.21	0.64	0.034	0.255
57	172.40	1.05	0.369	3.24	0.20	0.76	0.041	0.291
58	186.56	1.02	0.382	3.67	0.17	0.71	0.038	0.284
59	183.85	0.96	0.373	3.61	0.16	0.69	0.036	0.275
60	231.03	0.85	0.319	3.26	0.20	0.67	0.040	0.241

ANIMAL NUMBER	OVARIES
56	0.058
57	0.060
58	0.064
59	0.058
60	0.029

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

GROUP 1 (0 MG/KG)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN	OVARIES
36	1.73	39.019	391.70	21.77	73.03	3.476	28.885	6.647
37	1.81	36.957	392.39	21.28	66.62	3.795	29.654	5.831
38	1.73	41.668	389.32	22.50	65.58	3.775	27.385	6.398
39	1.86	39.201	354.20	20.69	68.79	3.744	22.965	5.552
40	1.72	43.805	369.55	25.11	71.50	3.857	27.696	5.166

GROUP 4 (1000 MG/KG)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN	OVARIES
56	1.77	41.014	352.08	22.35	69.22	3.670	27.393	6.218
57	1.82	34.996	306.95	18.99	72.14	3.921	27.545	5.703
58	1.90	37.640	361.11	16.91	70.00	3.714	27.996	6.288
59	1.76	39.002	378.05	17.14	72.57	3.790	28.803	6.118
60	1.97	37.329	382.00	22.93	78.92	4.712	28.220	3.374

Segment PA Support Process Issue Date: July 2003	**Handling of Chemical Specific Reporting Requirements and Trade Restrictions** Process Owner: **Manager, Regulatory & Product Compliance**	Ciba

1. PURPOSE

The Toxic Substances Control Act (TSCA) authorizes the Environmental Protection Agency (EPA) to require manufacturers, importers, processors and distributors of specific chemicals to create and maintain records and submit information to the EPA. In addition, other agencies of the US Government, such as the Departments of State, Treasury, or Commerce, may require reporting, notification, or place trade restrictions (such as requiring trade licenses) or embargoes on materials. This procedure is used to ensure knowledge of, and compliance with, all regulations.

The Agency that issues the regulation or rule may communicate a reporting requirement or other action directly or may publicly announce the requirement in the Federal Register. The Manager of Regulatory & Product Compliance is responsible for knowing about and acting upon the requirement.

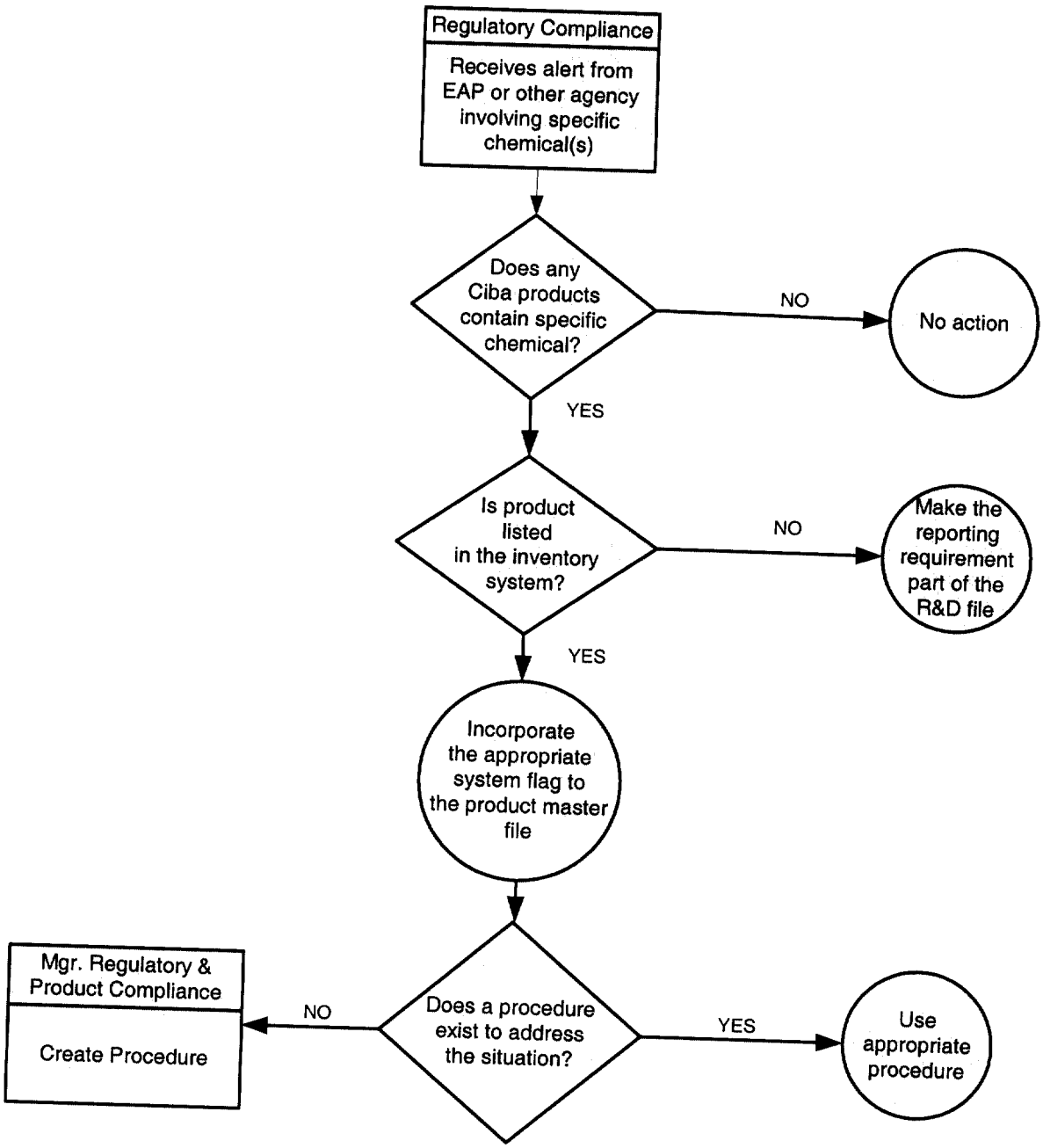
The following specific procedures apply:

- Export Notification Procedure (TSCA 12(b))
- Voluntary Product Restriction
- Distribution of products convered under a TSCA 5(e) consent order
- Processing Orders and Sample Requests for Products Regulated by TSCA 5(f)
- Recording and Reporting Adverse Effects Information and Allegations (TSCA 8(c))
- Substantial Risk Assessment (TSCA 8(e))
- Export Restrictions
- Tracking and Reporting Materials Required by the Chemical Weapons Convention

Products covered under a Significant New Use Rule (SNUR) are not addressed by this procedure; see:

- Preparation and Prosecution of a Pre-manufacture Notification.

2. PROCESS



3. PROCESS MEASUREMENT(S)

All requirements and rules are identified and in compliance.

4. HISTORY

Anne Christian	Original Issue

END OF DOCUMENT

RCC Study Number 848174

TKA 40291 (ZLI 3331):

28-Day Oral Toxicity (Gavage) Study in the Wistar Rat

Report (Part II of II)

Authors: W.H. Braun, Dr. D. Flade,
Dr. A. Brändli-Baiocco

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APPENDIX I:

OBSERVATIONS

SUMMARY OF PARAMETERS (MINIMUM REQUIREMENT FOR EACH ANIMAL)									
OBSERVATIONS: DAILY CAGE-SIDE (D), PRETEST (P), WEEKLY (W) AND FOB (F)									
	SCORE	PARAMETER	D	P	W 1	W 2	W 3	F 4	Comments
APPEARANCE	1-3	Piloerection	X	X	X	X	X	X	None
	1-3	Salivation	X	X	X	X	X	X	None
	1	Hunched posture	X	X	X	X	X	X	None
MOTOR	1-3	Ataxia	X	X	X	X	X	X	None
	1-3	Tremor/twitching	X	X	X	X	X	X	None
	1	Prostration	X	X	X	X	X	X	None
	1	Circling		X	X	X	X	X	None
	1-3	Spasm		X	X	X	X	X	None
BEHAVIOR	1-3	Hyperactivity	X	X	X	X	X	X	None
	1-3	Somnolence	X	X	X	X	X	X	None
	1-3	Increased exploration		X	X	X	X	X	None
	1-3	Reduced grooming		X	X	X	X	X	None
	1-3	Vocalisation		X	X	X	X	X	None
RESPIRATION	1	Dyspnea	X	X	X	X	X	X	None
	1	Tachypnea	X	X	X	X	X	X	None
	1	Bradypnea	X	X	X	X	X	X	None
REFLEXES	1	Blink		X	X	X	X	X	None
	1	Pinna		X	X	X	X	X	None
	1	Iridic light reflex		X	X	X	X	X	None
	1	Push-off (hind leg)		X	X	X	X	X	None
	1	Pain response		X	X	X	X	X	None
	1	Startle/hearing		X	X	X	X	X	None
Miscellaneous	1-3	Lacrimation		X	X	X	X	X	None
	1	Limbs cyanotic		X	X	X	X	X	None
	1	Mydriasis		X	X	X	X	X	None
	1	Miosis		X	X	X	X	X	None
	1	Exophthalmos		X	X	X	X	X	None
	1-3	Reduced muscle tone		X	X	X	X	X	None

NB. Findings described as 'Study-specific' include abnormal findings which were detected during daily observation of the standard parameters and subsequently tracked throughout the study for onset in other animals and progression/regression in the afflicted animals. Parameters marked with 'X' were specifically observed for presence or absence. 'Study specific' findings marked with 'X' were observed in the week noted, and no longer evident if 'X' did not appear in subsequent weeks. 'Cage-specific' findings (if present) refer to observations which could not be ascribed to a single animal in the cage and were therefore ascribed to all individuals in the cage.

X: observed

APPENDIX II:

DRINKING WATER ANALYSES

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

BACTERIOLOGICAL ASSAY OF DRINKING WATER, ITINGEN

Official Laboratory	Liestal, 16.01.2003
Basel-Landschaft	Ref.no. 200023141
Sampling point:	59.99.N Net water RCC Ltd, Itingen, Room No. 10
Sampled on:	16.01.2003
Sample:	
Time of sampling	7.50-8.25
Water temperature (°C)	11.4

BACTERIOLOGICAL TEST:

Aerobic mesophilic bacteria / ml	7
E.coli / 100 ml	0
Enterococci / 100 ml	0

ASSESSMENT:

At the time of sampling, the tested bacteriological parameters met the requirements for drinking water according to article 275 of the "Eidg. Lebensmittelverordnung".

Official Laboratory
The Official Chemist

(signed Dr. N. Jagou)

KANTONALES LABORATORIUM BASEL-LANDSCHAFT

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

CHEMICAL WATER ANALYSIS, ITINGEN

Official Laboratory Basel-Landschaft	Liestal, 16.01.2003 Ref.no. 200023142
Sampling point:	59.99.N, Net water RCC Ltd, Itingen, Room no. 10
Sampled on:	16.01.2003
Time of sampling	7.50-8.25
Water temperature (°C)	11.4

CHEMICAL TEST:

Appearance			clear, colourless
Odor			not remarkable
Taste			not remarkable
UV-absorption at 254 nm/100 cm			1.32
Conductivity		µS/cm	702.0
Oxygen demand	($KMnO_4$ cons.)	mg/l	1.8
Turbidity	FNU		0.14
Chloride	Cl^-	mg/l	17.5
Nitrate	NO_3^-	mg/l	20.2
Sulphate	SO_4^{--}	mg/l	87.2
Nitrite	NO_2^-	mg/l	<0.005
Total hardness		fr.H°	39.3
Alkaline hardness		fr.H°	29.5
Non carbonate hardness		fr.H°	9.8
Calcium	Ca^{++}	mg/l	138.1
Magnesium	Mg^{++}	mg/l	11.7

ASSESSMENT:

At the time of sampling, the tested chemical parameters met the requirements for drinking water according to article 275 of the "Eidg. Lebensmittelverordnung".

Official Laboratory
The Official Chemist

(signed Dr. N. Maggi)

CONTAMINANT ASSAY OF DRINKING WATER, ITINGEN

RCC Study No.: 904994

Date of Sampling: 16.01.2003

Sample: H_2O, RCC 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	23	1500
PCBs (28, 52, 101, 138, 153, 180)	< 0.05	0.1
Nitrosamines, total (DMN, DEN, NPIP, NMORPH)	< 0.002	---

< 0.05 = less than 0.05 microgram per liter

* Schweizer Lebensmittelbuch

March 05, 2003

signed K. Biedermann

APPENDIX III:

CHEMICAL ANALYSIS OF FEED

RCC STUDY NUMBER 848174
TKA 40291 (ZLI 3331)

ANALYTICAL TEST REPORT

RCC Study 842160
16.12.02

Prepared for	PROVIMI KLIBA AG 4303 Kaiseraugst
Attention of	Dr. Isler
Materials tested	KLIBA-NAFAG 3433, Batch 84/02 vom 04.12.02
Test performed	AAS, GC, GC-MS, HPLC
Test results	See attached Table 1
Submitted	E. Dettwiler
Issued by	K. Biedermann

.....
December 24, 2002/msh

ATTACHMENT

RCC Study 842160
16.12.02

Table 1 - Test Results

KLIBA-NAFAG 3433,
Batch 84/02 vom 04.12.02

PARAMETER	ASSAY LEVEL mg/kg	LIMIT* mg/kg
Aflatoxins (B1, B2, G1, G2), total	< 0.001	0.005
Estrogens (DES, Hexestrol, Dienestrol), total	< 0.001	0.001
Lindane	< 0.005	0.02
Heptachlor	< 0.005	0.02
Malathion	< 0.5	2.5
DDT, total	< 0.025	0.100
Dieldrin	< 0.005	0.02
Cadmium	0.03	0.160
Arsenic	0.16	1.0
Lead	0.57	1.5
Mercury	< 0.05	0.1
Selenium	< 0.15	0.6
Copper	29	----
PCBs	< 0.025	0.05
Nitrosamines (DMN, DEN, NPIP, NMORPH), total	< 0.002	0.010

< 0.001 = less than 0.001 milligram per kilogram
* = USP EPA, Federal Register, Vol. 44, No. 91, May 9, 1979

APPENDIX IV:

CLINICAL LABORATORY INVESTIGATIONS

RCC Study Number 848174

TKA 40291 (ZLI 3331):

28-Day Oral Toxicity (Gavage) Study in the Wistar Rat

Author: Peter Gretener
Dr. med. vet. FVH

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1.1 CLINICAL LABORATORY INVESTIGATIONS

Blood and urine sampling: After 4 weeks: 19 May 2003 (Allocation A and B)
After 6 weeks: 02 June 2003 (Allocation B)

Blood samples for hematology and clinical chemistry were collected 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. Blood 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 micro-hematocrit glass capillary tubes.

Urine was collected into specimen vials during the 18-hour fasting period while animals were housed in metabolism cages.

The assays were performed at RCC Ltd (Stein) under internal laboratory quality control conditions to assure reliable test results.

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	kg	kilogram	μ	micro (10^{-6})
sec	second	T	tera (10^{12})	n	nano (10^{-9})
		G	giga (10^{9})	p	pico (10^{-12})
				f	femto (10^{-15})

General remarks:

n.d. = not determined, no value measured for this parameter
Reference values generally depend on the method used for analysis. The assignment is given by a method code.

1.1.1 HEMATOLOGY

The following anticoagulants were used during blood collection:

Complete blood cell count	Di-potassium-EDTA
Methemoglobin	Lithium heparin
Coagulation	Sodium citrate, 3.8% (1 part anticoagulant to 9 parts blood)

Complete blood cell count Parameter	Abbreviation	Unit		Method code	Instrumentation
Erythrocyte count	RBC	T/l		M01	Advia 120[1]
Hemoglobin	Hb	mmol/l		M01	Advia 120
Hematocrit	Hct	rel.1		M01	Advia 120
Mean corpuscular volume	MCV	fl		M01	Advia 120
Red cell volume distribution width	RDW	rel.1		M01	Advia 120
Mean corpuscular hemoglobin	MCH	fmol		M01	Advia 120
Mean corpuscular hemoglobin concentration	MCHC	mmol/l		M01	Advia 120
Hemoglobin concentration distribution width	HDW	mmol/l		M01	Advia 120
		relative	absolute		
Reticulocyte count	Reti	rel.1	G/l	M02	Advia 120
Reticulocyte maturity index	L Reti	rel.1		M01	Advia 120
(low, medium, high fluorescence)	M Reti	rel.1		M01	Advia 120
	H Reti	rel.1		M01	Advia 120
Leukocyte count, total	WBC	G/l		M01	Advia 120
Differential leukocyte count		relative	absolute		Advia 120
Neutrophils	Neut	rel.1	G/l	M01	Advia 120
Eosinophils	Eos	rel.1	G/l	M01	Advia 120
Basophils	Baso	rel.1	G/l	M01	Advia 120
Lymphocytes	Lympho	rel.1	G/l	M01	Advia 120
Monocytes	Mono	rel.1	G/l	M01	Advia 120
Large unstained cells	Luc	rel.1	G/l	M01	Advia 120
Platelet count	Plt	G/l		M01	Advia 120

[1] ADVIA 120 hematology system (Bayer)

Hemoglobin derivatives

Parameter	Abbreviation	Unit	Method	Method code	Instru-mentation
Methemoglobin	MetHb	rel. 1	Spectrometry, results given as ratio of total hemoglobin	M01	OSM3[2]

Coagulation

Parameter	Abbreviation	Unit	Method	Method code	Instru-mentation
Prothrombin time (=Thromboplastin time)	PT	rel. 1	Clotting assay, recombinant thromboplastin reagent Results as ratio of normal activity	M01	STA[3]
Activated partial thromboplastin time	PTT	sec	Clotting assay, synthetic phospholipid reagent, colloidal silica activator	M01	STA

1.1.2 CLINICAL CHEMISTRY

Lithium heparin was used as anticoagulant during blood collection.

Parameter	Abbre-viation	Unit	Method	Method code	Instru-mentation
Glucose	Gluc	mmol/l	Hexokinase/G6P-DH	M01	Hitachi 917[4]
Urea	Urea	mmol/l	Urease/GLDH	M01	Hitachi 917
Creatinine	Creat	µmol/l	Enzymatic colorimetric test	M01	Hitachi 917
Bilirubin, total	Bili-tot	µmol/l	Reaction with 2,5-Dichloro-phenyl-diazonium salt	M01	Hitachi 917
Cholesterol, total	Chol	mmol/l	Enzymatic, CHOD/PAP	M01	Hitachi 917
Triglycerides	Trigly	mmol/l	Glycerol-Kinase GPO/PAP method	M01	Hitachi 917
Phospholipids	Phos-Lip	mmol/l	Phospholipase-Cholinoxidase-Peroxidase-reaction	M01	Hitachi 917
Aspartate aminotransferase EC 2.6.1.1	ASAT	U/l 37°C	MDH/NADH coupled reaction	M01	Hitachi 917

---

2 Hemoximeter OSM3

3 STA-compact analyzer (Roche Diagnostics)

4 Hitachi 917 analyzer, Roche Diagnostics

Parameter	Abbre-viation	Unit	Method	Method code	Instru-mentation
Alanine aminotransferase EC 2.6.1.2	ALAT	U/l 37°C	LDH/NADH coupled reaction	M01	Hitachi 917
Lactate dehydrogenase EC 1.1.1.27	LDH	U/l 37°C	NADH/LDH coupled reaction using pyruvate as substrate	M01	Hitachi 917
Glutamate dehydrogenase EC 1.4.1.3	GLDH	U/l 37°C	Standard method, optimized (DGKC)	M01	Hitachi 917
Alkaline phosphatase EC 3.1.3.1	AIP	U/l 37°C	p-Nitrophenyl-phosphate as substrate	M01	Hitachi 917
Gamma-glutamyl transferase EC 2.3.2.2	GGT	U/l 37°C	Substrate: L-gamma-glutamyl-3-carboxy-4-nitroanilide	M01	Hitachi 917
Creatine kinase EC 2.7.3.2	CK	U/l 37°C	HK/ATP and G6P-DH/NADPH coupled reaction method	M01	Hitachi 917
Sodium	Na+	mmol/l	Ion selective electrode	M01	Hitachi 917
Potassium	K+	mmol/l	Ion selective electrode	M01	Hitachi 917
Chloride	Cl^-	mmol/l	Ion selective electrode	M01	Hitachi 917
Calcium	Ca++	mmol/l	o-Cresolphthalein complexone method	M01	Hitachi 917
Phosphorus inorganic	PO4-in	mmol/l	Phosphomolybdate reaction	M01	Hitachi 917
Protein, total	Prot	g/l	Biuret reaction	M01	Hitachi 917
Albumin	Alb	g/l	Bromocresol green method	M02	Hitachi 917
Globulin	Glob	g/l	Calculated value (Total protein minus Albumin)	M02	
Albumin/Globulin Ratio	A/G	rel.1	Calculated value (Albumin/Globulin)	M02	

1.1.3 URINALYSIS

Physical examination

Parameter	Abbreviation		Unit	Method / Instrumentation	Method code
Urine volume (18-hour)	Volume		ml	Gravimetric[5]	M01
Relative Density (= Specific gravity)	Rel dens		rel.1	Refractometer[6]	M01
Color	Color			Visual inspection	
	NORMAL				
	COLESS	colorless			
	YE/BR	yellow-brown			
	YE/GR	yellow-green			
	RED				
	BROWN				
	RE/BR	red-brown			
Appearance	Appear			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	Abbrevition	Unit	Set points	Method code	Instru-mentation
pH-value	pH		5.0, 6.0, 6.5, 7.0, 8.0, 9.0	M01	Miditron[7]
Nitrite	NIT	score	0 (negative), 1 (positive)	M01	Miditron
Protein	PRO	g/l	0, 0.25, 0.75, 1.50, 5.00	M01	Miditron
Glucose	GLU	mmol/l	0, 3, 6, 17, 56	M01	Miditron
Ketones	KET	mmol/l	0, 0.5, 1.5, 5.0, 15.0	M01	Miditron
Urobilinogen	UBG	µmol/l	0, 17, 68, 135, 203	M01	Miditron
Bilirubin	BIL	µmol/l	0, 17, 50, 100	M01	Miditron
Erythrocytes	ERY	per µl	0, 10, 25, 50, 150, 250	M01	Miditron
Leukocytes	LEU	per µl	0, 25, 100, 500	M01	Miditron

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5 Mettler balance

6 Clinical Refractometer SU-202, Krenco

7 Miditron semi-automated urine chemistry analyzer and reagent test strips, Roche Diagnostics

1.2 HEMATOLOGY (MEANS)

MALES

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
RBC	T/l					
WEEK 5		MEAN	8.158 a	8.326	8.402	8.447
		S.D.	0.207	0.331	0.236	0.185
		N	10	5	5	10
WEEK 7		MEAN	8.524 a			8.376
		S.D.	0.176			0.136
		N	5			5
Hb	mmol/l					
WEEK 5		MEAN	10.05ad	10.22	10.24	10.41**
		S.D.	0.20	0.25	0.34	0.24
		N	10	5	5	10
WEEK 7		MEAN	10.26 a			10.30
		S.D.	0.09			0.25
		N	5			5
Hct	rel. 1					
WEEK 5		MEAN	0.4400ad	0.4440	0.4460	0.4620**
		S.D.	0.0105	0.0114	0.0134	0.0114
		N	10	5	5	10
WEEK 7		MEAN	0.4540 a			0.4580
		S.D.	0.0055			0.0164
		N	5			5
MCV	fl					
WEEK 5		MEAN	54.00 a	53.34	53.24	54.72
		S.D.	1.34	1.29	1.37	1.07
		N	10	5	5	10

Statistical key: a=ANOVA ad=ANOVA + Dunnett ** = p<0.01

Hematology (means)

MALES

		Group	Group 1	Group 2	Group 3	Group 4
		Group Name	Control			
		Dose Level	0 mg/kg	50 mg/kg	200 mg/kg	1000 mg/kg
MCV	fl					
WEEK 7		MEAN	53.30 a			54.74
		S.D.	1.63			1.30
		N	5			5
RDW	rel. 1					
WEEK 5		MEAN	0.1146 a	0.1116	0.1122	0.1138
		S.D.	0.0038	0.0022	0.0036	0.0028
		N	10	5	5	10
WEEK 7		MEAN	0.1220 a			0.1216
		S.D.	0.0046			0.0021
		N	5			5
MCH	fmol					
WEEK 5		MEAN	1.232 a	1.230	1.220	1.231
		S.D.	0.024	0.034	0.024	0.030
		N	10	5	5	10
WEEK 7		MEAN	1.204 a			1.228
		S.D.	0.031			0.026
		N	5			5
MCHC	mmol/l					
WEEK 5		MEAN	22.807ad	23.026	22.906	22.493*
		S.D.	0.300	0.216	0.246	0.247
		N	10	5	5	10
WEEK 7		MEAN	22.594 a			22.472
		S.D.	0.294			0.222
		N	5			5

Statistical key: a=ANOVA ad=ANOVA + Dunnett * = $p<0.05$

Hematology (means)

MALES

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
HDW	mmol/l					
WEEK 5		MEAN	1.484 a	1.520	1.608	1.491
		S.D.	0.068	0.104	0.122	0.081
		N	10	5	5	10
WEEK 7		MEAN	1.586 a			1.546
		S.D.	0.129			0.075
		N	5			5
Reti	rel. 1					
WEEK 5		MEAN	0.0293 k	0.0238	0.0272	0.0308
		S.D.	0.0030	0.0093	0.0022	0.0043
		N	10	5	5	10
WEEK 7		MEAN	0.0264 a			0.0284
		S.D.	0.0044			0.0030
		N	5			5
Reti	G/l					
WEEK 5		MEAN	238.8kd	195.2	229.6	261.4
		S.D.	19.8	69.2	18.5	35.0
		N	10	5	5	10
WEEK 7		MEAN	226.2 a			236.6
		S.D.	34.3			24.0
		N	5			5
L Reti	rel. 1					
WEEK 5		MEAN	0.4020kd	0.4696	0.4076	0.3656
		S.D.	0.0297	0.0803	0.0108	0.0348
		N	10	5	5	10

Statistical key: a=ANOVA k=Kruskal-Wallis kd=Kruskal-Wallis + Dunn

Hematology (means)

MALES

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
L Reti	rel. 1					
WEEK 7		MEAN	0.3976 a			0.3896
		S.D.	0.0416			0.0264
		N	5			5
M Reti	rel. 1					
WEEK 5		MEAN	0.3512ad	0.3560	0.3750	0.3150**
		S.D.	0.0257	0.0187	0.0265	0.0208
		N	10	5	5	10
WEEK 7		MEAN	0.3130 a			0.3082
		S.D.	0.0175			0.0204
		N	5			5
H Reti	rel. 1					
WEEK 5		MEAN	0.2465ad	0.1744*	0.2172	0.3193**
		S.D.	0.0492	0.0671	0.0212	0.0481
		N	10	5	5	10
WEEK 7		MEAN	0.2894 a			0.3022
		S.D.	0.0556			0.0336
		N	5			5
WBC	G/l					
WEEK 5		MEAN	6.338ad	5.300	6.216	7.234
		S.D.	0.930	1.091	0.827	0.417
		N	10	5	5	10
WEEK 7		MEAN	6.708 a			6.134
		S.D.	0.830			0.459
		N	5			5

Statistical key: a=ANOVA ad=ANOVA + Dunnett * = p<0.05 ** = p<0.01

Hematology (means)

MALES

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Neut	rel. 1					
WEEK 5		MEAN	0.1235ad	0.1222	0.1816*	0.1663*
		S.D.	0.0260	0.0279	0.0662	0.0255
		N	10	5	5	10
WEEK 7		MEAN	0.1370 a			0.1244
		S.D.	0.0230			0.0190
		N	5			5
Eos	rel. 1					
WEEK 5		MEAN	0.0168ad	0.0166	0.0126	0.0116*
		S.D.	0.0058	0.0044	0.0029	0.0033
		N	10	5	5	10
WEEK 7		MEAN	0.0122 a			0.0144
		S.D.	0.0027			0.0032
		N	5			5
Baso	rel. 1					
WEEK 5		MEAN	0.0025 a	0.0022	0.0024	0.0022
		S.D.	0.0007	0.0008	0.0005	0.0006
		N	10	5	5	10
WEEK 7		MEAN	0.0028 a			0.0024
		S.D.	0.0015			0.0005
		N	5			5
Lympho	rel. 1					
WEEK 5		MEAN	0.8329ad	0.8312	0.7726*	0.7929
		S.D.	0.0288	0.0363	0.0669	0.0262
		N	10	5	5	10

Statistical key: a=ANOVA ad=ANOVA + Dunnett * = p<0.05

Hematology (means)

MALES

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Lympho	rel. 1					
WEEK 7		MEAN	0.8196 a			0.8368
		S.D.	0.0243			0.0200
		N	5			5
Mono	rel. 1					
WEEK 5		MEAN	0.0173 a	0.0186	0.0212	0.0190
		S.D.	0.0029	0.0071	0.0026	0.0049
		N	10	5	5	10
WEEK 7		MEAN	0.0190ad			0.0160*
		S.D.	0.0021			0.0014
		N	5			5
Luc	rel. 1					
WEEK 5		MEAN	0.0067ad	0.0096	0.0098*	0.0082
		S.D.	0.0021	0.0015	0.0028	0.0024
		N	10	5	5	10
WEEK 7		MEAN	0.0088 a			0.0058
		S.D.	0.0046			0.0037
		N	5			5
Neut	G/l					
WEEK 5		MEAN	0.771ad	0.652	1.110*	1.208**
		S.D.	0.119	0.193	0.335	0.230
		N	10	5	5	10
WEEK 7		MEAN	0.918 a			0.764
		S.D.	0.185			0.136
		N	5			5

Statistical key: a=ANOVA ad=ANOVA + Dunnett * = p<0.05 ** = p<0.01

Hematology (means)

MALES

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Eos	G/l					
WEEK 5		MEAN	0.105 a	0.084	0.078	0.082
		S.D.	0.031	0.015	0.022	0.023
		N	10	5	5	10
WEEK 7		MEAN	0.082 a			0.090
		S.D.	0.018			0.025
		N	5			5
Baso	G/l					
WEEK 5		MEAN	0.015ad	0.012	0.012	0.019
		S.D.	0.005	0.004	0.004	0.006
		N	10	5	5	10
WEEK 7		MEAN	0.022 a			0.016
		S.D.	0.011			0.005
		N	5			5
Lympho	G/l					
WEEK 5		MEAN	5.294kd	4.410	4.818	5.731
		S.D.	0.896	0.947	0.859	0.276
		N	10	5	5	10
WEEK 7		MEAN	5.500 a			5.130
		S.D.	0.737			0.364
		N	5			5
Mono	G/l					
WEEK 5		MEAN	0.108ad	0.098	0.132	0.136
		S.D.	0.015	0.029	0.022	0.037
		N	10	5	5	10

Statistical key: a=ANOVA ad=ANOVA + Dunnett kd=Kruskal-Wallis + Dunn

Hematology (means)

MALES

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Mono	G/l					
WEEK 7		MEAN	0.128 a			0.102
		S.D.	0.022			0.013
		N	5			5
Luc	G/l					
WEEK 5		MEAN	0.043 a	0.050	0.062	0.058
		S.D.	0.018	0.016	0.018	0.015
		N	10	5	5	10
WEEK 7		MEAN	0.058 a			0.036
		S.D.	0.029			0.021
		N	5			5
Plt	G/l					
WEEK 5		MEAN	1008.5 a	1008.4	1041.4	963.9
		S.D.	97.5	110.5	85.7	76.2
		N	10	5	5	10
WEEK 7		MEAN	967.4 a			977.4
		S.D.	118.4			75.6
		N	5			5
MetHb	rel. 1					
WEEK 5		MEAN	0.0079 a	0.0078	0.0074	0.0080
		S.D.	0.0007	0.0008	0.0009	0.0005
		N	10	5	5	10
WEEK 7		MEAN	0.0092 a			0.0088
		S.D.	0.0011			0.0004
		N	5			5

Statistical key: a=ANOVA

Hematology (means)

MALES

		Group	Group 1	Group 2	Group 3	Group 4
		Group Name	Control			
		Dose Level	0 mg/kg	50 mg/kg	200 mg/kg	1000 mg/kg
PT	rel. 1					
WEEK 5		MEAN	0.795 a	0.792	0.836	0.780
		S.D.	0.050	0.038	0.043	0.046
		N	10	5	5	10
WEEK 7		MEAN	0.708 a			0.692
		S.D.	0.026			0.011
		N	5			5
PTT	sec					
WEEK 5		MEAN	18.22 a	18.26	18.20	17.85
		S.D.	0.90	0.45	0.58	0.91
		N	10	5	5	10
WEEK 7		MEAN	19.42 a			18.74
		S.D.	0.88			0.69
		N	5			5

Statistical key: a=ANOVA

FEMALES

Hematology (means)

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
RBC	T/l					
WEEK 5		MEAN	8.098 a	7.816	8.318	8.135
		S.D.	0.377	0.288	0.226	0.357
		N	10	5	5	10
WEEK 7		MEAN	8.096 a			7.784
		S.D.	0.329			0.442
		N	5			5
Hb	mmol/l					
WEEK 5		MEAN	9.84ad	9.56	9.70	9.99
		S.D.	0.26	0.19	0.27	0.32
		N	10	5	5	10
WEEK 7		MEAN	9.96 k			9.86
		S.D.	0.05			0.30
		N	5			5
Hct	rel. 1					
WEEK 5		MEAN	0.4260ad	0.4100	0.4200	0.4390
		S.D.	0.0107	0.0100	0.0100	0.0145
		N	10	5	5	10
WEEK 7		MEAN	0.4400 a			0.4360
		S.D.	0.0100			0.0152
		N	5			5
MCV	fl					
WEEK 5		MEAN	52.75ad	52.72	50.70	54.01
		S.D.	1.88	0.90	1.10	1.56
		N	10	5	5	10

Statistical key: a=ANOVA ad=ANOVA + Dunnett k=Kruskal-Wallis

FEMALES

Hematology (means)

	Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
MCV	fl				
WEEK 7	MEAN	54.26 a			56.06
	S.D.	1.17			1.51
	N	5			5
RDW	rel. 1				
WEEK 5	MEAN	0.1056ad	0.1070	0.1064	0.1111**
	S.D.	0.0037	0.0030	0.0034	0.0037
	N	10	5	5	10
WEEK 7	MEAN	0.1350 a			0.1274
	S.D.	0.0082			0.0063
	N	5			5
MCH	fmol				
WEEK 5	MEAN	1.213ad	1.226	1.164	1.231
	S.D.	0.042	0.034	0.033	0.046
	N	10	5	5	10
WEEK 7	MEAN	1.232 a			1.272
	S.D.	0.042			0.041
	N	5			5
MCHC	mmol/l				
WEEK 5	MEAN	23.007ad	23.252	22.966	22.797
	S.D.	0.282	0.289	0.286	0.271
	N	10	5	5	10
WEEK 7	MEAN	22.716 a			22.642
	S.D.	0.338			0.187
	N	5			5

Statistical key: a=ANOVA ad=ANOVA + Dunnett ** = p<0.01

FEMALES

Hematology (means)

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
HDW	mmol/l					
WEEK 5		MEAN	1.372 a	1.350	1.416	1.344
		S.D.	0.054	0.054	0.098	0.051
		N	10	5	5	10
WEEK 7		MEAN	1.356 a			1.334
		S.D.	0.036			0.053
		N	5			5
Reti	rel. 1					
WEEK 5		MEAN	0.0280 a	0.0272	0.0264	0.0302
		S.D.	0.0036	0.0019	0.0035	0.0044
		N	10	5	5	10
WEEK 7		MEAN	0.0254 a			0.0268
		S.D.	0.0031			0.0045
		N	5			5
Reti	G/l					
WEEK 5		MEAN	225.9 a	212.6	219.2	245.4
		S.D.	27.7	17.6	28.7	36.1
		N	10	5	5	10
WEEK 7		MEAN	208.6 a			208.2
		S.D.	31.8			27.1
		N	5			5
L Reti	rel. 1					
WEEK 5		MEAN	0.4034 a	0.4130	0.4082	0.3667
		S.D.	0.0515	0.0660	0.0423	0.0468
		N	10	5	5	10

Statistical key: a=ANOVA

FEMALES

Hematology (means)

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
L Reti	rel. 1					
WEEK 7		MEAN	0.4618 a			0.4046
		S.D.	0.0819			0.0487
		N	5			5
M Reti	rel. 1					
WEEK 5		MEAN	0.3200 a	0.3444	0.3286	0.3025
		S.D.	0.0292	0.0251	0.0529	0.0246
		N	10	5	5	10
WEEK 7		MEAN	0.3278ad			0.2860**
		S.D.	0.0171			0.0185
		N	5			5
H Reti	rel. 1					
WEEK 5		MEAN	0.2766 a	0.2426	0.2632	0.3307
		S.D.	0.0683	0.0828	0.0914	0.0629
		N	10	5	5	10
WEEK 7		MEAN	0.2106 a			0.3094
		S.D.	0.0748			0.0605
		N	5			5
WBC	G/l					
WEEK 5		MEAN	5.073 a	4.678	5.570	5.503
		S.D.	1.283	1.017	1.016	1.231
		N	10	5	5	10
WEEK 7		MEAN	4.214 a			4.344
		S.D.	0.454			0.688
		N	5			5

Statistical key: a=ANOVA ad=ANOVA + Dunnett ** = p<0.01

FEMALES

Hematology (means)

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Neut	rel. 1					
WEEK 5		MEAN	0.1521ad	0.1392	0.1558	0.2273*
		S.D.	0.0621	0.0229	0.0619	0.0817
		N	10	5	5	10
WEEK 7		MEAN	0.1226 a			0.1348
		S.D.	0.0123			0.0339
		N	5			5
Eos	rel. 1					
WEEK 5		MEAN	0.0173 k	0.0160	0.0232	0.0128
		S.D.	0.0081	0.0044	0.0284	0.0030
		N	10	5	5	10
WEEK 7		MEAN	0.0162 a			0.0148
		S.D.	0.0019			0.0029
		N	5			5
Baso	rel. 1					
WEEK 5		MEAN	0.0019 a	0.0018	0.0016	0.0016
		S.D.	0.0007	0.0004	0.0009	0.0008
		N	10	5	5	10
WEEK 7		MEAN	0.0026 a			0.0020
		S.D.	0.0013			0.0007
		N	5			5
Lympho	rel. 1					
WEEK 5		MEAN	0.8029 a	0.8192	0.7978	0.7320
		S.D.	0.0712	0.0254	0.0865	0.0836
		N	10	5	5	10

Statistical key: a=ANOVA ad=ANOVA + Dunnett k=Kruskal-Wallis * = p<0.05

FEMALES

Hematology (means)

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Lympho	rel. 1					
WEEK 7		MEAN	0.8324 a			0.8226
		S.D.	0.0142			0.0333
		N	5			5
Mono	rel. 1					
WEEK 5		MEAN	0.0192 a	0.0168	0.0148	0.0198
		S.D.	0.0060	0.0023	0.0036	0.0060
		N	10	5	5	10
WEEK 7		MEAN	0.0204 a			0.0200
		S.D.	0.0059			0.0069
		N	5			5
Luc	rel. 1					
WEEK 5		MEAN	0.0065 a	0.0070	0.0072	0.0063
		S.D.	0.0019	0.0016	0.0023	0.0016
		N	10	5	5	10
WEEK 7		MEAN	0.0058 a			0.0056
		S.D.	0.0028			0.0011
		N	5			5
Neut	G/l					
WEEK 5		MEAN	0.756kd	0.636	0.880	1.228*
		S.D.	0.317	0.055	0.395	0.494
		N	10	5	5	10
WEEK 7		MEAN	0.512 k			0.590
		S.D.	0.022			0.218
		N	5			5

Statistical key: a=ANOVA k=Kruskal-Wallis kd=Kruskal-Wallis + Dunn * = p<0.05

FEMALES

Hematology (means)

	Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Eos	G/l				
WEEK 5	MEAN	0.087 k	0.076	0.120	0.070
	S.D.	0.046	0.027	0.140	0.023
	N	10	5	5	10
WEEK 7	MEAN	0.070 a			0.066
	S.D.	0.012			0.022
	N	5			5
Baso	G/l				
WEEK 5	MEAN	0.008 a	0.008	0.010	0.010
	S.D.	0.006	0.004	0.000	0.005
	N	10	5	5	10
WEEK 7	MEAN	0.012 a			0.010
	S.D.	0.004			0.000
	N	5			5
Lympho	G/l				
WEEK 5	MEAN	4.086 a	3.848	4.442	4.059
	S.D.	1.161	0.937	0.889	1.213
	N	10	5	5	10
WEEK 7	MEAN	3.516 a			3.568
	S.D.	0.429			0.547
	N	5			5
Mono	G/l				
WEEK 5	MEAN	0.099 a	0.080	0.082	0.103
	S.D.	0.050	0.019	0.026	0.024
	N	10	5	5	10

Statistical key: a=ANOVA k=Kruskal-Wallis

FEMALES

Hematology (means)

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Mono	G/l					
WEEK 7		MEAN	0.084 a			0.082
		S.D.	0.022			0.018
		N	5			5
Luc	G/l					
WEEK 5		MEAN	0.032 a	0.032	0.038	0.037
		S.D.	0.017	0.008	0.019	0.013
		N	10	5	5	10
WEEK 7		MEAN	0.022 a			0.024
		S.D.	0.013			0.009
		N	5			5
Plt	G/l					
WEEK 5		MEAN	981.6 a	1072.6	987.8	1042.4
		S.D.	122.5	141.4	93.3	61.8
		N	10	5	5	10
WEEK 7		MEAN	1053.4 a			988.0
		S.D.	43.2			72.2
		N	5			5
MetHb	rel. 1					
WEEK 5		MEAN	0.0078 a	0.0080	0.0080	0.0078
		S.D.	0.0006	0.0007	0.0007	0.0008
		N	10	5	5	10
WEEK 7		MEAN	0.0092 a			0.0094
		S.D.	0.0008			0.0005
		N	5			5

Statistical key: a=ANOVA

FEMALES

Hematology (means)

	Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
PT	rel. 1				
WEEK 5	MEAN	0.899 a	0.918	0.918	0.911
	S.D.	0.049	0.031	0.041	0.043
	N	10	5	5	10
WEEK 7	MEAN	0.864 a			0.860
	S.D.	0.044			0.040
	N	5			5
PTT	sec				
WEEK 5	MEAN	19.07ad	18.56	20.10*	17.88**
	S.D.	0.65	0.61	0.34	0.70
	N	10	5	5	10
WEEK 7	MEAN	18.76 a			18.66
	S.D.	0.90			0.32
	N	5			5

Statistical key: a=ANOVA ad=ANOVA + Dunnett * = $p<0.05$ ** = $p<0.01$

1.3 BLOOD CHEMISTRY (MEANS)

MALES

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Gluc	mmol/l					
WEEK 5		MEAN	5.016ad	5.086	4.602	4.036**
		S.D.	0.606	0.484	0.473	0.648
		N	10	5	5	10
WEEK 7		MEAN	5.176 a			4.716
		S.D.	0.355			0.565
		N	5			5
Urea	mmol/l					
WEEK 5		MEAN	7.093ad	6.144	6.680	7.926
		S.D.	1.048	1.187	0.701	1.398
		N	10	5	5	10
WEEK 7		MEAN	4.964ad			5.906*
		S.D.	0.394			0.770
		N	5			5
Creat	µmol/l					
WEEK 5		MEAN	22.23 a	21.90	22.26	23.30
		S.D.	1.38	2.49	1.24	2.49
		N	10	5	5	10
WEEK 7		MEAN	23.34 a			25.38
		S.D.	2.01			1.93
		N	5			5
Bili-tot	µmol/l					
WEEK 5		MEAN	1.348 a	1.278	1.214	1.265
		S.D.	0.227	0.281	0.190	0.273
		N	10	5	5	10

Statistical key: a=ANOVA ad=ANOVA + Dunnett * = $p<0.05$ ** = $p<0.01$

MALES

Blood chemistry (means)

	Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Bili-tot µmol/l					
WEEK 7	MEAN	1.250 a			1.310
	S.D.	0.262			0.192
	N	5			5
Chol mmol/l					
WEEK 5	MEAN	1.756 a	1.782	1.892	1.767
	S.D.	0.267	0.610	0.190	0.260
	N	10	5	5	10
WEEK 7	MEAN	1.720ad			1.350*
	S.D.	0.212			0.210
	N	5			5
Trigly mmol/l					
WEEK 5	MEAN	0.467 a	0.320	0.400	0.391
	S.D.	0.212	0.049	0.163	0.151
	N	10	5	5	10
WEEK 7	MEAN	0.536 a			0.636
	S.D.	0.136			0.078
	N	5			5
Phos-Lip mmol/l					
WEEK 5	MEAN	1.691 a	1.586	1.696	1.551
	S.D.	0.193	0.353	0.108	0.134
	N	10	5	5	10
WEEK 7	MEAN	1.686ad			1.444*
	S.D.	0.113			0.132
	N	5			5

Statistical key: a=ANOVA ad=ANOVA + Dunnett * = $p<0.05$

MALES

Blood chemistry (means)

	Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
ASAT	U/l				
WEEK 5	MEAN	76.93kd	66.04	68.78	83.12
	S.D.	8.98	5.61	3.87	16.10
	N	10	5	5	10
WEEK 7	MEAN	73.76 a			77.54
	S.D.	8.89			5.73
	N	5			5
ALAT	U/l				
WEEK 5	MEAN	26.88 a	24.52	25.54	33.15
	S.D.	5.54	5.65	3.78	10.91
	N	10	5	5	10
WEEK 7	MEAN	25.94 a			29.36
	S.D.	3.25			3.90
	N	5			5
LDH	U/l				
WEEK 5	MEAN	163.91 a	148.38	156.80	173.08
	S.D.	31.45	57.79	34.45	56.48
	N	10	5	5	10
WEEK 7	MEAN	148.80 a			143.20
	S.D.	47.18			48.53
	N	5			5
GLDH	U/l				
WEEK 5	MEAN	6.63kd	5.82	7.20	9.18
	S.D.	1.01	0.62	1.43	4.18
	N	10	5	5	10

Statistical key: a=ANOVA kd=Kruskal-Wallis + Dunn

MALES

Blood chemistry (means)

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
GLDH	U/l					
WEEK 7		MEAN	6.52 a			7.12
		S.D.	0.77			0.50
		N	5			5
AlP	U/l					
WEEK 5		MEAN	102.67 a	111.20	99.10	110.12
		S.D.	24.71	27.25	15.91	31.88
		N	10	5	5	10
WEEK 7		MEAN	78.90 a			89.44
		S.D.	15.76			18.83
		N	5			5
GGT	U/l					
WEEK 5		MEAN	0.00 a	0.00	0.00	0.00
		S.D.	0.00	0.00	0.00	0.00
		N	10	5	5	10
WEEK 7		MEAN	0.00 a			0.00
		S.D.	0.00			0.00
		N	5			5
CK	U/l					
WEEK 5		MEAN	180.37 k	190.70	172.72	213.90
		S.D.	31.48	93.48	35.13	58.63
		N	10	5	5	10
WEEK 7		MEAN	135.46 a			152.48
		S.D.	50.85			37.75
		N	5			5

Statistical key: a=ANOVA k=Kruskal-Wallis

MALES

Blood chemistry (means)

	Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Na+ mmol/l					
WEEK 5	MEAN	145.62ad	145.66	146.48	147.25**
	S.D.	0.87	1.22	0.53	1.00
	N	10	5	5	10
WEEK 7	MEAN	143.54 a			144.88
	S.D.	1.06			1.32
	N	5			5
K+ mmol/l					
WEEK 5	MEAN	3.714ad	3.870	3.950*	3.501*
	S.D.	0.172	0.170	0.250	0.118
	N	10	5	5	10
WEEK 7	MEAN	3.386 a			3.600
	S.D.	0.164			0.273
	N	5			5
Cl- mmol/l					
WEEK 5	MEAN	100.59ad	101.40	99.74	98.98
	S.D.	1.63	1.48	1.09	1.53
	N	10	5	5	10
WEEK 7	MEAN	99.80 a			101.38
	S.D.	1.11			1.31
	N	5			5
Ca++ mmol/l					
WEEK 5	MEAN	2.940ad	2.880	2.998	2.848**
	S.D.	0.036	0.056	0.057	0.076
	N	10	5	5	10

Statistical key: a=ANOVA ad=ANOVA + Dunnett * = $p<0.05$ ** = $p<0.01$

MALES

Blood chemistry (means)

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Ca++	mmol/l					
WEEK 7		MEAN	2.828 a			2.772
		S.D.	0.072			0.054
		N	5			5
P04-in	mmol/l					
WEEK 5		MEAN	2.494ad	2.380	2.554	2.759**
		S.D.	0.148	0.155	0.105	0.142
		N	10	5	5	10
WEEK 7		MEAN	2.196 a			2.388
		S.D.	0.098			0.282
		N	5			5
Prot	g/l					
WEEK 5		MEAN	66.374 a	64.934	66.946	65.892
		S.D.	1.776	1.172	2.049	1.650
		N	10	5	5	10
WEEK 7		MEAN	67.052 a			65.426
		S.D.	2.938			1.325
		N	5			5
Alb	g/l					
WEEK 5		MEAN	42.102 a	41.428	41.722	43.201
		S.D.	1.295	0.641	1.341	1.538
		N	10	5	5	10
WEEK 7		MEAN	42.370 a			41.234
		S.D.	0.952			0.737
		N	5			5

Statistical key: a=ANOVA ad=ANOVA + Dunnett ** = p<0.01

MALES

Blood chemistry (means)

	Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Glob	g/l				
WEEK 5	MEAN	24.272ad	23.506	25.224	22.691*
	S.D.	1.526	0.626	1.679	0.918
	N	10	5	5	10
WEEK 7	MEAN	24.682 a			24.192
	S.D.	2.374			1.022
	N	5			5
A/G	rel. 1				
WEEK 5	MEAN	1.740ad	1.762	1.660	1.907**
	S.D.	0.130	0.033	0.130	0.114
	N	10	5	5	10
WEEK 7	MEAN	1.726 a			1.708
	S.D.	0.157			0.075
	N	5			5

Statistical key: a=ANOVA ad=ANOVA + Dunnett * = $p<0.05$ ** = $p<0.01$

FEMALES

Blood chemistry (means)

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Gluc	mmol/l					
WEEK 5		MEAN	4.254 a	4.112	4.026	3.775
		S.D.	0.629	0.395	0.316	0.627
		N	10	5	5	10
WEEK 7		MEAN	4.226 a			5.026
		S.D.	0.469			0.647
		N	5			5
Urea	mmol/l					
WEEK 5		MEAN	7.467 a	6.916	7.774	7.863
		S.D.	0.869	0.786	1.765	0.922
		N	10	5	5	10
WEEK 7		MEAN	7.016 a			6.296
		S.D.	1.298			0.717
		N	5			5
Creat	µmol/l					
WEEK 5		MEAN	26.00 a	27.44	26.82	27.72
		S.D.	1.55	1.63	2.34	2.64
		N	10	5	5	10
WEEK 7		MEAN	26.72 a			26.60
		S.D.	3.36			1.79
		N	5			5
Bili-tot	µmol/l					
WEEK 5		MEAN	1.663ad	1.818	1.498	1.174*
		S.D.	0.502	0.477	0.446	0.291
		N	10	5	5	10

Statistical key: a=ANOVA ad=ANOVA + Dunnett * = $p<0.05$

FEMALES

Blood chemistry (means)

	Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Bili-tot µmol/l					
WEEK 7	MEAN	1.368ad			1.142*
	S.D.	0.150			0.147
	N	5			5
Chol mmol/l					
WEEK 5	MEAN	1.664ad	1.644	1.584	2.128
	S.D.	0.387	0.307	0.355	0.523
	N	10	5	5	10
WEEK 7	MEAN	1.730 a			1.646
	S.D.	0.605			0.446
	N	5			5
Trigly mmol/l					
WEEK 5	MEAN	0.258 a	0.244	0.218	0.270
	S.D.	0.049	0.053	0.056	0.069
	N	10	5	5	10
WEEK 7	MEAN	0.346 a			0.380
	S.D.	0.072			0.113
	N	5			5
Phos-Lip mmol/l					
WEEK 5	MEAN	1.705 a	1.748	1.584	1.951
	S.D.	0.292	0.218	0.272	0.384
	N	10	5	5	10
WEEK 7	MEAN	1.934 a			1.802
	S.D.	0.526			0.382
	N	5			5

Statistical key: a=ANOVA ad=ANOVA + Dunnett * = $p<0.05$

Blood chemistry (means)

FEMALES

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
ASAT	U/l					
WEEK 5		MEAN	68.17 a	66.58	73.96	74.82
		S.D.	4.11	5.58	9.56	7.11
		N	10	5	5	10
WEEK 7		MEAN	69.40 a			63.80
		S.D.	11.73			6.34
		N	5			5
ALAT	U/l					
WEEK 5		MEAN	20.22ad	18.22	22.10	23.88
		S.D.	3.06	1.71	2.12	4.25
		N	10	5	5	10
WEEK 7		MEAN	23.68 a			19.72
		S.D.	3.25			2.57
		N	5			5
LDH	U/l					
WEEK 5		MEAN	153.26 k	140.74	214.04	183.84
		S.D.	18.26	15.80	136.46	45.24
		N	10	5	5	10
WEEK 7		MEAN	161.04 k			133.94
		S.D.	77.42			15.76
		N	5			5
GLDH	U/l					
WEEK 5		MEAN	5.78 a	5.76	5.44	6.62
		S.D.	1.58	0.61	0.81	1.48
		N	10	5	5	10

Statistical key: a=ANOVA ad=ANOVA + Dunnett k=Kruskal-Wallis

FEMALES

Blood chemistry (means)

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
GLDH	U/l					
WEEK 7		MEAN	10.90 k			6.10
		S.D.	7.44			0.87
		N	5			5
AlP	U/l					
WEEK 5		MEAN	49.90 a	61.38	41.72	53.20
		S.D.	13.05	16.84	3.33	13.28
		N	10	5	5	10
WEEK 7		MEAN	41.16 a			43.78
		S.D.	9.76			13.33
		N	5			5
GGT	U/l					
WEEK 5		MEAN	0.00 a	0.00	0.00	0.00
		S.D.	0.00	0.00	0.00	0.00
		N	10	5	5	10
WEEK 7		MEAN	0.00 a			0.00
		S.D.	0.00			0.00
		N	5			5
CK	U/l					
WEEK 5		MEAN	159.93 k	135.70	193.22	190.55
		S.D.	26.94	21.21	97.12	55.40
		N	10	5	5	10
WEEK 7		MEAN	115.14 a			118.12
		S.D.	17.85			9.18
		N	5			5

Statistical key: a=ANOVA k=Kruskal-Wallis

FEMALES

Blood chemistry (means)

	Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Na+ mmol/l					
WEEK 5	MEAN	145.71 a	146.06	145.58	146.47
	S.D.	0.95	0.36	0.87	0.58
	N	10	5	5	10
WEEK 7	MEAN	144.28 a			144.26
	S.D.	0.47			0.44
	N	5			5
K+ mmol/l					
WEEK 5	MEAN	3.561 a	3.402	3.694	3.330
	S.D.	0.235	0.170	0.385	0.268
	N	10	5	5	10
WEEK 7	MEAN	3.492 a			3.220
	S.D.	0.285			0.248
	N	5			5
Cl- mmol/l					
WEEK 5	MEAN	102.05 a	102.70	102.98	102.21
	S.D.	1.35	1.69	2.12	2.08
	N	10	5	5	10
WEEK 7	MEAN	103.06 a			102.84
	S.D.	1.15			0.68
	N	5			5
Ca++ mmol/l					
WEEK 5	MEAN	2.831 a	2.788	2.808	2.792
	S.D.	0.067	0.044	0.062	0.059
	N	10	5	5	10

Statistical key: a=ANOVA

FEMALES

Blood chemistry (means)

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Ca++	mmol/l					
WEEK 7		MEAN	2.798ad			2.706**
		S.D.	0.022			0.051
		N	5			5
PO4-in	mmol/l					
WEEK 5		MEAN	2.083 a	2.048	2.204	1.959
		S.D.	0.167	0.151	0.194	0.259
		N	10	5	5	10
WEEK 7		MEAN	1.824 a			1.734
		S.D.	0.153			0.139
		N	5			5
Prot	g/l					
WEEK 5		MEAN	66.416 a	66.160	66.366	66.299
		S.D.	2.352	1.919	2.277	2.006
		N	10	5	5	10
WEEK 7		MEAN	69.212ad			65.460**
		S.D.	1.705			1.234
		N	5			5
Alb	g/l					
WEEK 5		MEAN	45.618 a	45.762	44.660	45.375
		S.D.	2.346	1.686	2.331	1.772
		N	10	5	5	10
WEEK 7		MEAN	46.960ad			43.784*
		S.D.	2.318			1.628
		N	5			5

Statistical key: a=ANOVA ad=ANOVA + Dunnett * = p<0.05 ** = p<0.01

FEMALES

Blood chemistry (means)

	Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Glob	g/l				
WEEK 5	MEAN	20.798 a	20.398	21.706	20.924
	S.D.	1.431	0.919	0.805	1.245
	N	10	5	5	10
WEEK 7	MEAN	22.252 a			21.676
	S.D.	0.971			0.956
	N	5			5
A/G	rel. 1				
WEEK 5	MEAN	2.205 a	2.248	2.060	2.177
	S.D.	0.201	0.127	0.147	0.167
	N	10	5	5	10
WEEK 7	MEAN	2.116 a			2.028
	S.D.	0.177			0.148
	N	5			5

Statistical key: a=ANOVA

1.4 URINE ANALYSIS (MEANS)

MALES

	Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Volume	ml				
WEEK 5	MEAN	9.78 a	10.34	8.74	11.30
	S.D.	2.10	1.57	3.18	2.31
	N	10	5	5	10
WEEK 7	MEAN	8.32 a			7.46
	S.D.	0.98			1.69
	N	5			5
Rel dens	rel. 1				
WEEK 5	MEAN	1.0706 a	1.0566	1.0720	1.0750
	S.D.	0.0126	0.0075	0.0171	0.0136
	N	10	5	5	10
WEEK 7	MEAN	1.0412 k			1.0438
	S.D.	0.0020			0.0110
	N	5			5
Color	Choice				
WEEK 5					
NORMAL	N	10	5	5	10
WEEK 7					
NORMAL	N	5			5
Appear	Choice				
WEEK 5					
NORMAL	N	8	4	4	6
CLOUDY	N	0	0	0	3
TURBID	N	2	1	1	1
WEEK 7					
NORMAL	N	3			3
CLOUDY	N	1			2
TURBID	N	1			0

Statistical key: a=ANOVA k=Kruskal-Wallis

MALES

Urine analysis (means)

	Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
pH					
WEEK 5	MEAN	6.50 k	6.90	6.50	6.55
	S.D.	0.33	0.22	0.00	0.28
	N	10	5	5	10
WEEK 7	MEAN	7.20 k			6.80
	S.D.	0.45			0.27
	N	5			5
NIT Score					
WEEK 5	MEAN	0.0 k	0.0	0.0	0.0
	S.D.	0.0	0.0	0.0	0.0
	N	10	5	5	10
WEEK 7	MEAN	0.0 k			0.0
	S.D.	0.0			0.0
	N	5			5
PRO g/l					
WEEK 5	MEAN	0.400 k	0.250	0.550	0.400
	S.D.	0.242	0.000	0.274	0.242
	N	10	5	5	10
WEEK 7	MEAN	0.250 k			0.450
	S.D.	0.000			0.274
	N	5			5
GLU mmol/l					
WEEK 5	MEAN	0.0 k	0.0	0.0	0.0
	S.D.	0.0	0.0	0.0	0.0
	N	10	5	5	10

Statistical key: k=Kruskal-Wallis

MALES

Urine analysis (means)

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
GLU	mmol/l					
WEEK 7		MEAN	0.0 k			0.0
		S.D.	0.0			0.0
		N	5			5
KET	mmol/l					
WEEK 5		MEAN	0.20 k	0.10	0.40	0.15
		S.D.	0.26	0.22	0.65	0.24
		N	10	5	5	10
WEEK 7		MEAN	0.90 k			0.70
		S.D.	0.55			0.45
		N	5			5
UBG	µmol/l					
WEEK 5		MEAN	0.0 k	0.0	0.0	0.0
		S.D.	0.0	0.0	0.0	0.0
		N	10	5	5	10
WEEK 7		MEAN	0.0 k			0.0
		S.D.	0.0			0.0
		N	5			5
BIL	µmol/l					
WEEK 5		MEAN	0.0 k	0.0	0.0	0.0
		S.D.	0.0	0.0	0.0	0.0
		N	10	5	5	10
WEEK 7		MEAN	0.0 k			0.0
		S.D.	0.0			0.0
		N	5			5

Statistical key: k=Kruskal-Wallis

MALES

Urine analysis (means)

	Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
ERY per µl					
WEEK 5	MEAN	1.0 k	2.0	2.0	1.0
	S.D.	3.2	4.5	4.5	3.2
	N	10	5	5	10
WEEK 7	MEAN	2.0 k			4.0
	S.D.	4.5			5.5
	N	5			5
LEU per µl					
WEEK 5	MEAN	70.0kd	55.0	100.0	32.5
	S.D.	38.7	41.1	0.0	23.7
	N	10	5	5	10
WEEK 7	MEAN	85.0 k			55.0
	S.D.	33.5			41.1
	N	5			5

Statistical key: k=Kruskal-Wallis kd=Kruskal-Wallis + Dunn

FEMALES

Urine analysis (means)

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
Volume	ml					
WEEK 5		MEAN	7.12 a	5.10	6.96	6.71
		S.D.	3.76	1.52	2.33	2.47
		N	10	5	5	10
WEEK 7		MEAN	6.58 a			6.42
		S.D.	1.08			2.25
		N	5			5
Rel dens	rel. 1					
WEEK 5		MEAN	1.0585 a	1.0692	1.0614	1.0691
		S.D.	0.0174	0.0152	0.0150	0.0141
		N	10	5	5	10
WEEK 7		MEAN	1.0380 a			1.0368
		S.D.	0.0034			0.0081
		N	5			5
Color	Choice					
WEEK 5						
NORMAL		N	10	5	5	10
WEEK 7						
NORMAL		N	5			5
Appear	Choice					
WEEK 5						
NORMAL		N	9	4	5	9
TURBID		N	1	1	0	1
WEEK 7						
NORMAL		N	4			4
CLOUDY		N	1			1
pH						
WEEK 5		MEAN	5.90kd	6.10	6.70*	5.65
		S.D.	0.52	0.22	0.27	0.71
		N	10	5	5	10

Statistical key: a=ANOVA kd=Kruskal-Wallis + Dunn * = p<0.05

FEMALES

Urine analysis (means)

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
pH						
WEEK 7		MEAN	6.20 k			6.50
		S.D.	0.45			0.50
		N	5			5
NIT	Score					
WEEK 5		MEAN	0.0 k	0.0	0.0	0.0
		S.D.	0.0	0.0	0.0	0.0
		N	10	5	5	10
WEEK 7		MEAN	0.0 k			0.0
		S.D.	0.0			0.0
		N	5			5
PRO	g/l					
WEEK 5		MEAN	0.325 k	0.350	0.200	0.450
		S.D.	0.237	0.224	0.112	0.258
		N	10	5	5	10
WEEK 7		MEAN	0.250 k			0.200
		S.D.	0.000			0.112
		N	5			5
GLU	mmol/l					
WEEK 5		MEAN	0.0 k	0.0	0.0	0.0
		S.D.	0.0	0.0	0.0	0.0
		N	10	5	5	10
WEEK 7		MEAN	0.0 k			0.0
		S.D.	0.0			0.0
		N	5			5

Statistical key: k=Kruskal-Wallis

FEMALES

Urine analysis (means)

	Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
KET mmol/l					
WEEK 5	MEAN	0.00 k	0.20	0.10	0.15
	S.D.	0.00	0.27	0.22	0.24
	N	10	5	5	10
WEEK 7	MEAN	0.20 k			0.20
	S.D.	0.27			0.27
	N	5			5
UBG µmol/l					
WEEK 5	MEAN	0.0 k	3.4	0.0	1.7
	S.D.	0.0	7.6	0.0	5.4
	N	10	5	5	10
WEEK 7	MEAN	0.0 k			0.0
	S.D.	0.0			0.0
	N	5			5
BIL µmol/l					
WEEK 5	MEAN	5.1 k	0.0	0.0	0.0
	S.D.	8.2	0.0	0.0	0.0
	N	10	5	5	10
WEEK 7	MEAN	0.0 k			3.4
	S.D.	0.0			7.6
	N	5			5
ERY per µl					
WEEK 5	MEAN	3.5 k	2.0	0.0	0.0
	S.D.	8.2	4.5	0.0	0.0
	N	10	5	5	10

Statistical key: k=Kruskal-Wallis

FEMALES

Urine analysis (means)

	Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 50 mg/kg	Group 3 200 mg/kg	Group 4 1000 mg/kg
ERY per µl					
WEEK 7	MEAN	2.0 k			2.0
	S.D.	4.5			4.5
	N	5			5
LEU per µl					
WEEK 5	MEAN	22.5 k	25.0	25.0	22.5
	S.D.	7.9	0.0	0.0	7.9
	N	10	5	5	10
WEEK 7	MEAN	15.0 k			15.0
	S.D.	13.7			13.7
	N	5			5

Statistical key: k=Kruskal-Wallis

1.5 HEMATOLOGY (INDIVIDUALS)

WEEK 5

MALES

AN_NO	RBC	Hb	Hct	MCV	RDW	MCH	MCHC	HDW	Reti	Reti	L Reti	M Reti
	T/l	mmol/l	rel. 1	fl	rel. 1	fmol	mmol/l	mmol/l	rel. 1	G/l	rel. 1	rel. 1
Group 1 (0 mg/kg)												
1 M	8.34	10.2	0.440	52.6	0.116	1.23	23.30	1.55	0.026	218	0.434	0.390
2 M	7.79	9.7	0.420	54.1	0.112	1.24	22.96	1.41	0.032	251	0.407	0.340
3 M	8.03	10.1	0.440	55.2	0.110	1.26	22.80	1.45	0.028	226	0.396	0.363
4 M	8.24	10.3	0.460	55.3	0.116	1.25	22.55	1.51	0.032	263	0.414	0.351
5 M	8.25	9.9	0.440	53.1	0.122	1.20	22.68	1.57	0.027	225	0.380	0.368
6 M	7.91	9.9	0.430	54.5	0.113	1.25	22.88	1.38	0.033	258	0.360	0.303
7 M	8.11	9.9	0.440	54.8	0.117	1.22	22.25	1.58	0.032	259	0.385	0.327
8 M	8.49	10.1	0.440	51.6	0.117	1.19	23.03	1.48	0.024	204	0.447	0.380
9 M	8.15	10.3	0.450	55.7	0.109	1.26	22.59	1.48	0.030	244	0.366	0.351
10 M	8.27	10.1	0.440	53.1	0.114	1.22	23.03	1.43	0.029	240	0.431	0.339
Group 2 (50 mg/kg)												
11 M	8.73	10.4	0.460	52.1	0.112	1.20	22.94	1.45	0.011	96	0.581	0.326
12 M	8.11	9.8	0.430	53.2	0.109	1.21	22.69	1.38	0.024	191	0.490	0.358
13 M	7.93	10.2	0.440	55.3	0.115	1.28	23.20	1.56	0.037	290	0.373	0.359
14 M	8.59	10.4	0.450	52.3	0.111	1.21	23.10	1.64	0.022	188	0.491	0.359
15 M	8.27	10.3	0.440	53.8	0.111	1.25	23.20	1.57	0.025	211	0.413	0.378
Group 3 (200 mg/kg)												
16 M	8.43	10.2	0.440	52.1	0.114	1.21	23.16	1.58	0.025	215	0.408	0.396
17 M	8.17	9.9	0.440	53.7	0.113	1.21	22.53	1.59	0.025	205	0.392	0.381
18 M	8.15	10.1	0.440	54.4	0.106	1.24	22.81	1.45	0.030	247	0.411	0.389
19 M	8.64	10.8	0.470	54.5	0.113	1.25	22.97	1.63	0.028	243	0.422	0.329
20 M	8.62	10.2	0.440	51.5	0.115	1.19	23.06	1.79	0.028	238	0.405	0.380
Group 4 (1000 mg/kg)												
21 M	8.82	10.4	0.460	52.5	0.114	1.18	22.43	1.56	0.030	267	0.398	0.313
22 M	8.34	10.4	0.460	55.2	0.113	1.24	22.56	1.45	0.032	267	0.335	0.269
23 M	8.55	10.6	0.470	54.7	0.119	1.24	22.66	1.60	0.033	282	0.338	0.319
24 M	8.43	10.2	0.450	53.9	0.108	1.21	22.42	1.55	0.022	186	0.405	0.326
25 M	8.29	10.4	0.460	55.6	0.114	1.25	22.55	1.41	0.029	243	0.389	0.312
26 M	8.47	10.7	0.480	56.2	0.112	1.26	22.39	1.43	0.030	257	0.391	0.313
27 M	8.34	10.7	0.460	55.3	0.115	1.28	23.07	1.61	0.028	234	0.342	0.321
28 M	8.17	9.9	0.440	54.4	0.113	1.21	22.26	1.45	0.038	310	0.333	0.304
29 M	8.43	10.5	0.470	55.4	0.115	1.24	22.41	1.39	0.035	297	0.319	0.320
30 M	8.63	10.3	0.470	54.0	0.115	1.20	22.18	1.46	0.031	271	0.406	0.353

WEEK 5

Hematology (individuals)

MALES

AN_NO	H Reti	WBC	Neut	Eos	Baso	Lympho	Mono	Luc	Neut	Eos	Baso	Lympho
	rel. 1	G/l	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	G/l	G/l	G/l	G/l
Group 1 (0 mg/kg)												
1 M	0.176	5.79	0.147	0.030	0.004	0.795	0.020	0.004	0.85	0.17	0.02	4.61
2 M	0.253	6.37	0.102	0.011	0.003	0.861	0.016	0.007	0.65	0.07	0.02	5.48
3 M	0.241	6.47	0.116	0.016	0.002	0.843	0.015	0.007	0.75	0.11	0.01	5.45
4 M	0.235	8.39	0.102	0.011	0.002	0.860	0.016	0.009	0.86	0.09	0.02	7.22
5 M	0.252	6.28	0.109	0.021	0.002	0.844	0.016	0.007	0.68	0.13	0.01	5.30
6 M	0.336	5.00	0.182	0.018	0.003	0.775	0.019	0.003	0.91	0.09	0.01	3.87
7 M	0.287	6.87	0.122	0.017	0.002	0.834	0.014	0.010	0.84	0.12	0.02	5.74
8 M	0.173	6.34	0.142	0.012	0.002	0.816	0.021	0.007	0.90	0.08	0.01	5.17
9 M	0.282	6.59	0.107	0.019	0.002	0.851	0.014	0.007	0.71	0.12	0.02	5.61
10 M	0.230	5.28	0.106	0.013	0.003	0.850	0.022	0.006	0.56	0.07	0.01	4.49
Group 2 (50 mg/kg)												
11 M	0.092	5.58	0.096	0.015	0.001	0.859	0.017	0.012	0.54	0.08	0.01	4.79
12 M	0.152	4.04	0.094	0.018	0.003	0.865	0.013	0.008	0.38	0.07	0.01	3.49
13 M	0.269	6.21	0.136	0.016	0.003	0.819	0.017	0.009	0.85	0.10	0.02	5.09
14 M	0.150	4.27	0.160	0.023	0.002	0.775	0.031	0.010	0.69	0.10	0.01	3.31
15 M	0.209	6.40	0.125	0.011	0.002	0.838	0.015	0.009	0.80	0.07	0.01	5.37
Group 3 (200 mg/kg)												
16 M	0.196	6.28	0.159	0.011	0.002	0.799	0.019	0.010	1.00	0.07	0.01	5.01
17 M	0.227	5.65	0.138	0.009	0.003	0.814	0.024	0.013	0.78	0.05	0.01	4.60
18 M	0.200	6.48	0.132	0.012	0.002	0.823	0.018	0.012	0.85	0.08	0.01	5.33
19 M	0.248	7.41	0.185	0.015	0.003	0.768	0.023	0.007	1.37	0.11	0.02	5.69
20 M	0.215	5.26	0.294	0.016	0.002	0.659	0.022	0.007	1.55	0.08	0.01	3.46
Group 4 (1000 mg/kg)												
21 M	0.289	6.74	0.125	0.012	0.003	0.841	0.012	0.008	0.84	0.08	0.02	5.66
22 M	0.395	6.85	0.142	0.014	0.002	0.809	0.024	0.009	0.97	0.09	0.01	5.54
23 M	0.342	7.27	0.195	0.018	0.002	0.756	0.023	0.007	1.42	0.13	0.02	5.50
24 M	0.269	7.10	0.164	0.010	0.001	0.792	0.027	0.006	1.16	0.07	0.01	5.63
25 M	0.298	7.92	0.173	0.013	0.002	0.784	0.022	0.006	1.37	0.10	0.02	6.21
26 M	0.297	6.87	0.172	0.010	0.003	0.783	0.018	0.013	1.18	0.07	0.02	5.38
27 M	0.337	7.67	0.187	0.011	0.003	0.771	0.018	0.010	1.44	0.08	0.03	5.92
28 M	0.364	6.84	0.143	0.012	0.002	0.820	0.013	0.010	0.98	0.08	0.02	5.61
29 M	0.361	7.45	0.206	0.005	0.002	0.767	0.015	0.005	1.53	0.04	0.02	5.71
30 M	0.241	7.63	0.156	0.011	0.002	0.806	0.018	0.008	1.19	0.08	0.02	6.15

Hematology (individuals)

WEEK 5 MALES

AN_NO	Mono G/l	Luc G/l	Plt G/l	MetHb rel. 1	PT rel. 1	PTT sec
Group 1 (0 mg/kg)						
1 M	0.12	0.02	986	0.008	0.83	18.0
2 M	0.10	0.05	954	0.008	0.80	17.9
3 M	0.10	0.04	945	0.009	0.82	17.7
4 M	0.13	0.07	930	0.007	0.72	19.5
5 M	0.10	0.04	1089	0.008	0.87	18.6
6 M	0.09	0.02	1117	0.009	0.78	16.7
7 M	0.10	0.07	1126	0.007	0.75	19.6
8 M	0.13	0.05	1017	0.008	0.74	18.8
9 M	0.09	0.04	1093	0.008	0.86	17.7
10 M	0.12	0.03	828	0.007	0.78	17.7
Group 2 (50 mg/kg)						
11 M	0.10	0.07	1179	0.009	0.79	18.0
12 M	0.05	0.03	915	0.008	0.75	17.9
13 M	0.11	0.05	1060	0.008	0.76	18.8
14 M	0.13	0.04	951	0.007	0.83	18.7
15 M	0.10	0.06	937	0.007	0.83	17.9
Group 3 (200 mg/kg)						
16 M	0.12	0.06	1090	0.008	0.83	18.0
17 M	0.13	0.08	1123	0.008	0.78	19.2
18 M	0.12	0.08	1097	0.008	0.84	17.7
19 M	0.17	0.05	947	0.006	0.90	18.1
20 M	0.12	0.04	950	0.007	0.83	18.0
Group 4 (1000 mg/kg)						
21 M	0.08	0.05	959	0.008	0.74	19.3
22 M	0.17	0.06	899	0.008	0.83	18.1
23 M	0.16	0.05	934	0.008	0.75	18.4
24 M	0.19	0.04	895	0.008	0.70	19.0
25 M	0.17	0.05	909	0.008	0.85	16.4
26 M	0.12	0.09	1049	0.007	0.78	17.6
27 M	0.14	0.07	969	0.008	0.78	16.7
28 M	0.09	0.07	915	0.008	0.77	17.8
29 M	0.11	0.04	974	0.008	0.77	17.6
30 M	0.13	0.06	1136	0.009	0.83	17.6

WEEK 5

Hematology (individuals)

FEMALES

AN_NO	RBC	Hb	Hct	MCV	RDW	MCH	MCHC	HDW	Reti	Reti	L Reti	M Reti
	T/l	mmol/l	rel. 1	fl	rel. 1	fmol	mmol/l	mmol/l	rel. 1	G/l	rel. 1	rel. 1
Group 1 (0 mg/kg)												
31 F	7.72	9.7	0.420	54.8	0.109	1.25	22.83	1.38	0.033	252	0.339	0.269
32 F	7.73	9.8	0.430	55.6	0.098	1.26	22.73	1.26	0.025	195	0.410	0.292
33 F	8.45	10.3	0.440	52.1	0.108	1.21	23.31	1.41	0.028	238	0.361	0.301
34 F	7.96	10.1	0.430	54.4	0.105	1.27	23.31	1.38	0.028	225	0.430	0.293
35 F	8.16	9.7	0.410	50.7	0.108	1.18	23.35	1.46	0.032	260	0.396	0.335
36 F	8.50	9.8	0.430	51.0	0.104	1.15	22.48	1.39	0.029	242	0.363	0.349
37 F	8.33	9.9	0.430	51.7	0.106	1.19	22.98	1.39	0.027	229	0.405	0.354
38 F	7.71	9.5	0.410	53.2	0.101	1.23	23.05	1.37	0.023	174	0.391	0.323
39 F	8.69	10.1	0.440	50.2	0.109	1.16	23.13	1.31	0.023	200	0.527	0.345
40 F	7.73	9.5	0.420	53.8	0.108	1.23	22.90	1.37	0.032	244	0.412	0.339
Group 2 (50 mg/kg)												
41 F	7.84	9.5	0.410	52.3	0.107	1.21	23.08	1.28	0.029	231	0.336	0.300
42 F	8.11	9.9	0.420	52.3	0.106	1.22	23.42	1.33	0.024	191	0.513	0.352
43 F	7.58	9.5	0.400	53.4	0.104	1.26	23.56	1.33	0.028	212	0.387	0.362
44 F	8.08	9.5	0.420	51.7	0.112	1.18	22.84	1.40	0.028	229	0.394	0.355
45 F	7.47	9.4	0.400	53.9	0.106	1.26	23.36	1.41	0.027	200	0.435	0.353
Group 3 (200 mg/kg)												
46 F	8.41	10.0	0.430	51.3	0.109	1.19	23.12	1.52	0.030	251	0.356	0.258
47 F	8.36	9.9	0.430	51.7	0.107	1.19	22.96	1.44	0.022	186	0.419	0.303
48 F	7.99	9.3	0.410	51.3	0.104	1.16	22.67	1.29	0.025	201	0.372	0.322
49 F	8.23	9.7	0.410	50.2	0.110	1.17	23.36	1.49	0.030	247	0.447	0.369
50 F	8.60	9.6	0.420	49.0	0.102	1.11	22.72	1.34	0.025	211	0.447	0.391
Group 4 (1000 mg/kg)												
51 F	7.82	9.3	0.420	53.1	0.114	1.19	22.46	1.40	0.029	228	0.389	0.304
52 F	8.23	9.8	0.430	52.7	0.113	1.19	22.66	1.44	0.033	273	0.380	0.320
53 F	7.97	10.2	0.440	55.1	0.111	1.28	23.29	1.32	0.029	229	0.335	0.309
54 F	8.59	10.5	0.470	54.5	0.108	1.22	22.49	1.31	0.025	218	0.400	0.309
55 F	8.61	10.2	0.450	52.0	0.107	1.19	22.80	1.28	0.028	240	0.436	0.323
56 F	7.82	10.1	0.440	56.1	0.112	1.30	23.09	1.32	0.029	226	0.352	0.255
57 F	8.58	10.1	0.450	52.2	0.115	1.18	22.66	1.38	0.037	314	0.315	0.317
58 F	8.08	9.9	0.430	53.8	0.112	1.22	22.68	1.34	0.031	250	0.322	0.304
59 F	8.03	10.0	0.430	54.1	0.104	1.25	23.07	1.29	0.024	191	0.429	0.323
60 F	7.62	9.8	0.430	56.5	0.115	1.29	22.77	1.36	0.037	285	0.309	0.261

Hematology (individuals)

WEEK 5

FEMALES

AN_NO	H Reti	WBC	Neut	Eos	Baso	Lympho	Mono	Luc	Neut	Eos	Baso	Lympho
	rel. 1	G/l	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	G/l	G/l	G/l	G/l
Group 1 (0 mg/kg)												
31 F	0.392	5.56	0.099	0.009	0.002	0.871	0.012	0.008	0.55	0.05	0.01	4.84
32 F	0.299	7.46	0.111	0.009	0.002	0.846	0.022	0.010	0.83	0.07	0.02	6.31
33 F	0.338	6.60	0.167	0.027	0.002	0.766	0.031	0.007	1.10	0.18	0.01	5.05
34 F	0.276	4.49	0.122	0.013	0.003	0.839	0.018	0.005	0.55	0.06	0.01	3.77
35 F	0.268	3.45	0.174	0.014	0.002	0.785	0.020	0.006	0.60	0.05	0.01	2.70
36 F	0.288	4.73	0.300	0.033	0.001	0.638	0.023	0.004	1.42	0.16	0.00	3.02
37 F	0.240	3.30	0.130	0.022	0.001	0.821	0.021	0.004	0.43	0.07	0.00	2.71
38 F	0.287	5.50	0.104	0.011	0.002	0.863	0.011	0.008	0.57	0.06	0.01	4.75
39 F	0.128	4.79	0.113	0.014	0.003	0.850	0.013	0.007	0.54	0.07	0.01	4.07
40 F	0.250	4.85	0.201	0.021	0.001	0.750	0.021	0.006	0.97	0.10	0.00	3.64
Group 2 (50 mg/kg)												
41 F	0.364	3.98	0.145	0.016	0.001	0.814	0.019	0.005	0.58	0.06	0.00	3.24
42 F	0.135	4.48	0.133	0.021	0.002	0.822	0.015	0.007	0.60	0.10	0.01	3.68
43 F	0.251	3.55	0.176	0.017	0.002	0.779	0.017	0.009	0.62	0.06	0.01	2.76
44 F	0.251	5.31	0.124	0.009	0.002	0.843	0.014	0.008	0.66	0.05	0.01	4.47
45 F	0.212	6.07	0.118	0.017	0.002	0.838	0.019	0.006	0.72	0.11	0.01	5.09
Group 3 (200 mg/kg)												
46 F	0.385	4.58	0.113	0.011	0.001	0.848	0.017	0.009	0.52	0.05	0.01	3.89
47 F	0.279	4.89	0.239	0.074	0.003	0.663	0.018	0.005	1.17	0.37	0.01	3.24
48 F	0.306	5.29	0.081	0.012	0.002	0.890	0.010	0.007	0.43	0.06	0.01	4.71
49 F	0.184	5.95	0.159	0.010	0.001	0.813	0.012	0.005	0.95	0.06	0.01	4.84
50 F	0.162	7.14	0.187	0.009	0.001	0.775	0.017	0.010	1.33	0.06	0.01	5.53
Group 4 (1000 mg/kg)												
51 F	0.307	4.84	0.311	0.012	0.000	0.638	0.030	0.008	1.51	0.06	0.00	3.09
52 F	0.300	5.22	0.313	0.014	0.001	0.647	0.018	0.007	1.63	0.07	0.01	3.38
53 F	0.355	5.37	0.198	0.017	0.001	0.756	0.021	0.007	1.07	0.09	0.01	4.06
54 F	0.291	5.74	0.225	0.019	0.001	0.729	0.021	0.005	1.29	0.11	0.01	4.18
55 F	0.241	8.14	0.106	0.012	0.002	0.861	0.010	0.009	0.87	0.10	0.02	7.01
56 F	0.393	5.99	0.204	0.012	0.002	0.766	0.013	0.004	1.22	0.07	0.01	4.59
57 F	0.368	6.50	0.356	0.009	0.002	0.610	0.018	0.004	2.32	0.06	0.01	3.97
58 F	0.374	5.18	0.129	0.011	0.003	0.833	0.017	0.007	0.67	0.05	0.01	4.32
59 F	0.248	4.47	0.176	0.011	0.002	0.780	0.024	0.006	0.79	0.05	0.01	3.49
60 F	0.430	3.58	0.255	0.011	0.002	0.700	0.026	0.006	0.91	0.04	0.01	2.50

Hematology (individuals)

WEEK 5 FEMALES

AN_NO	Mono G/l	Luc G/l	Plt G/l	MetHb rel. 1	PT rel. 1	PTT sec
Group 1 (0 mg/kg)						
31 F	0.07	0.04	1158	0.007	0.89	18.5
32 F	0.16	0.07	960	0.007	0.84	18.7
33 F	0.21	0.04	933	0.009	0.92	20.0
34 F	0.08	0.02	880	0.007	0.87	17.7
35 F	0.07	0.02	874	0.008	0.97	19.1
36 F	0.11	0.02	770	0.008	0.88	19.1
37 F	0.07	0.01	1076	0.008	0.98	19.5
38 F	0.06	0.04	1132	0.008	0.85	19.2
39 F	0.06	0.03	1002	0.008	0.86	19.7
40 F	0.10	0.03	1031	0.008	0.93	19.2
Group 2 (50 mg/kg)						
41 F	0.08	0.02	944	0.008	0.89	19.1
42 F	0.07	0.03	1080	0.009	0.89	19.3
43 F	0.06	0.03	1061	0.008	0.91	18.4
44 F	0.08	0.04	974	0.008	0.94	17.9
45 F	0.11	0.04	1304	0.007	0.96	18.1
Group 3 (200 mg/kg)						
46 F	0.08	0.04	1112	0.007	0.90	19.9
47 F	0.09	0.02	883	0.008	0.98	20.6
48 F	0.05	0.03	937	0.008	0.87	19.8
49 F	0.07	0.03	1055	0.009	0.91	20.3
50 F	0.12	0.07	952	0.008	0.93	19.9
Group 4 (1000 mg/kg)						
51 F	0.15	0.04	1071	0.007	0.83	18.2
52 F	0.09	0.04	1088	0.008	0.96	17.8
53 F	0.11	0.04	1032	0.008	0.87	17.8
54 F	0.12	0.03	1146	0.007	0.95	16.9
55 F	0.08	0.07	970	0.008	0.92	19.2
56 F	0.07	0.03	1063	0.007	0.94	17.4
57 F	0.12	0.03	1079	0.009	0.90	18.2
58 F	0.09	0.04	976	0.009	0.90	17.1
59 F	0.11	0.03	1052	0.007	0.88	18.6
60 F	0.09	0.02	947	0.008	0.96	17.6

Hematology (individuals)

WEEK 7 MALES

AN_NO	RBC	Hb	Hct	MCV	RDW	MCH	MCHC	HDW	Reti	Reti	L Reti	M Reti
	T/l	mmol/l	rel. 1	fl	rel. 1	fmol	mmol/l	mmol/l	rel. 1	G/l	rel. 1	rel. 1
Group 1 (0 mg/kg)												
6 M	8.42	10.3	0.450	53.4	0.121	1.23	22.97	1.47	0.031	265	0.366	0.293
7 M	8.39	10.3	0.460	54.5	0.130	1.22	22.42	1.79	0.028	238	0.362	0.317
8 M	8.79	10.3	0.450	51.2	0.121	1.17	22.84	1.60	0.020	179	0.462	0.340
9 M	8.40	10.3	0.460	55.2	0.119	1.23	22.29	1.59	0.029	245	0.383	0.311
10 M	8.62	10.1	0.450	52.2	0.119	1.17	22.45	1.48	0.024	204	0.415	0.304
Group 4 (1000 mg/kg)												
26 M	8.50	10.7	0.480	55.9	0.121	1.26	22.56	1.53	0.026	219	0.420	0.288
27 M	8.43	10.4	0.470	55.9	0.125	1.23	22.10	1.66	0.030	251	0.383	0.290
28 M	8.23	10.1	0.440	53.8	0.122	1.22	22.69	1.51	0.033	272	0.354	0.308
29 M	8.23	10.2	0.450	55.1	0.120	1.24	22.53	1.46	0.027	223	0.380	0.318
30 M	8.49	10.1	0.450	53.0	0.120	1.19	22.48	1.57	0.026	218	0.411	0.337

Hematology (individuals)

WEEK 7 MALES

AN_NO	H Reti	WBC	Neut	Eos	Baso	Lympho	Mono	Luc	Neut	Eos	Baso	Lympho
	rel. 1	G/l	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	G/l	G/l	G/l	G/l
Group 1 (0 mg/kg)												
6 M	0.341	7.05	0.169	0.011	0.005	0.789	0.019	0.006	1.19	0.08	0.04	5.56
7 M	0.321	6.89	0.148	0.014	0.001	0.805	0.016	0.017	1.02	0.10	0.01	5.54
8 M	0.198	7.47	0.111	0.008	0.003	0.849	0.021	0.007	0.83	0.06	0.02	6.35
9 M	0.306	6.84	0.120	0.014	0.002	0.838	0.018	0.007	0.82	0.10	0.02	5.73
10 M	0.281	5.29	0.137	0.014	0.003	0.817	0.021	0.007	0.73	0.07	0.02	4.32
Group 4 (1000 mg/kg)												
26 M	0.292	5.95	0.149	0.014	0.003	0.811	0.018	0.005	0.89	0.09	0.02	4.83
27 M	0.327	6.55	0.141	0.015	0.002	0.822	0.016	0.003	0.92	0.10	0.02	5.38
28 M	0.338	6.02	0.112	0.014	0.002	0.844	0.016	0.012	0.67	0.09	0.01	5.08
29 M	0.302	5.52	0.110	0.010	0.002	0.861	0.014	0.003	0.61	0.05	0.01	4.75
30 M	0.252	6.63	0.110	0.019	0.003	0.846	0.016	0.006	0.73	0.12	0.02	5.61

Hematology (individuals)

WEEK 7 MALES

AN_NO	Mono G/l	Luc G/l	Plt G/l	MetHb rel. 1	PT rel. 1	PTT sec
Group 1 (0 mg/kg)						
6 M	0.14	0.04	1023	0.010	0.73	19.2
7 M	0.11	0.11	1052	0.009	0.73	20.0
8 M	0.16	0.05	995	0.008	0.68	20.6
9 M	0.12	0.05	1008	0.009	0.72	18.4
10 M	0.11	0.04	759	0.009	0.68	18.9
Group 4 (1000 mg/kg)						
26 M	0.11	0.03	996	0.008	0.68	19.0
27 M	0.11	0.02	1005	0.009	0.68	19.4
28 M	0.10	0.07	929	0.009	0.70	19.3
29 M	0.08	0.02	880	0.009	0.70	18.0
30 M	0.11	0.04	1077	0.009	0.70	18.0

WEEK 7

Hematology (individuals)

FEMALES

AN_NO	RBC	Hb	Hct	MCV	RDW	MCH	MCHC	HDW	Reti	Reti	L Reti	M Reti
	T/l	mmol/l	rel. 1	fl	rel. 1	fmol	mmol/l	mmol/l	rel. 1	G/l	rel. 1	rel. 1
Group 1 (0 mg/kg)												
36 F	8.40	10.0	0.440	52.8	0.136	1.19	22.62	1.40	0.024	206	0.555	0.331
37 F	8.24	10.0	0.450	54.3	0.139	1.22	22.39	1.35	0.027	222	0.374	0.348
38 F	7.81	9.9	0.430	55.3	0.123	1.26	22.82	1.36	0.024	191	0.488	0.301
39 F	7.68	9.9	0.430	55.5	0.132	1.29	23.25	1.37	0.022	170	0.514	0.326
40 F	8.35	10.0	0.450	53.4	0.145	1.20	22.50	1.30	0.030	254	0.378	0.333
Group 4 (1000 mg/kg)												
56 F	7.31	9.6	0.420	58.1	0.128	1.32	22.72	1.35	0.031	227	0.346	0.281
57 F	8.37	10.2	0.450	54.1	0.138	1.22	22.52	1.30	0.021	179	0.472	0.294
58 F	8.09	10.0	0.450	55.2	0.124	1.24	22.38	1.31	0.030	239	0.433	0.308
59 F	7.45	9.5	0.420	56.2	0.125	1.28	22.75	1.29	0.029	215	0.385	0.289
60 F	7.70	10.0	0.440	56.7	0.122	1.30	22.84	1.42	0.023	181	0.387	0.258

WEEK 7

Hematology (individuals)

FEMALES

AN_NO	H Reti	WBC	Neut	Eos	Baso	Lympho	Mono	Luc	Neut	Eos	Baso	Lympho
	rel. 1	G/l	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	G/l	G/l	G/l	G/l
Group 1 (0 mg/kg)												
36 F	0.115	4.76	0.113	0.016	0.005	0.847	0.016	0.003	0.54	0.08	0.02	4.03
37 F	0.278	3.50	0.143	0.014	0.002	0.814	0.023	0.004	0.50	0.05	0.01	2.85
38 F	0.211	4.24	0.125	0.015	0.002	0.831	0.020	0.007	0.53	0.07	0.01	3.53
39 F	0.160	4.34	0.116	0.017	0.002	0.846	0.014	0.005	0.50	0.07	0.01	3.68
40 F	0.289	4.23	0.116	0.019	0.002	0.824	0.029	0.010	0.49	0.08	0.01	3.49
Group 4 (1000 mg/kg)												
56 F	0.373	4.17	0.147	0.017	0.001	0.811	0.017	0.006	0.61	0.07	0.01	3.38
57 F	0.234	5.30	0.181	0.018	0.002	0.780	0.012	0.006	0.96	0.10	0.01	4.14
58 F	0.259	4.71	0.093	0.013	0.002	0.869	0.017	0.005	0.44	0.06	0.01	4.09
59 F	0.326	3.49	0.141	0.011	0.002	0.814	0.029	0.004	0.49	0.04	0.01	2.84
60 F	0.355	4.05	0.112	0.015	0.003	0.839	0.025	0.007	0.45	0.06	0.01	3.39

Hematology (individuals)

WEEK 7 FEMALES

AN_NO	Mono G/l	Luc G/l	Plt G/l	MetHb rel. 1	PT rel. 1	PTT sec
Group 1 (0 mg/kg)						
36 F	0.08	0.01	1005	0.008	0.87	18.5
37 F	0.08	0.01	1063	0.010	0.93	18.6
38 F	0.08	0.03	1114	0.009	0.84	19.3
39 F	0.06	0.02	1019	0.010	0.87	17.5
40 F	0.12	0.04	1066	0.009	0.81	19.9
Group 4 (1000 mg/kg)						
56 F	0.07	0.03	1062	0.009	0.87	18.7
57 F	0.06	0.03	993	0.009	0.79	19.1
58 F	0.08	0.02	876	0.010	0.89	18.2
59 F	0.10	0.01	1038	0.010	0.88	18.7
60 F	0.10	0.03	971	0.009	0.87	18.6

1.6 BLOOD CHEMISTRY (INDIVIDUALS)

WEEK 5 MALES

AN_NO	Gluc	Urea	Creat	Bili-tot	Chol	Trigly	Phos-Lip	ASAT	ALAT	LDH	GLDH	AIP
	mmol/l	mmol/l	µmol/l	µmol/l	mmol/l	mmol/l	mmol/l	U/l	U/l	U/l	U/l	U/l
Group 1 (0 mg/kg)												
1 M	4.81	5.96	21.4	1.49	1.77	0.39	1.69	69.1	20.2	140.1	5.8	104.1
2 M	4.44	8.02	22.2	1.45	2.05	0.38	1.90	81.5	27.3	158.5	7.6	107.2
3 M	4.41	7.08	22.8	1.13	1.51	0.64	1.53	85.7	32.1	218.4	7.1	93.0
4 M	6.39	8.12	21.9	1.43	1.29	0.27	1.41	86.8	37.1	209.1	7.8	157.8
5 M	4.71	7.81	21.2	1.26	2.02	0.70	1.86	70.1	32.2	117.7	6.0	91.7
6 M	5.03	5.02	20.5	0.88	1.64	0.40	1.60	67.8	23.2	169.0	5.7	87.1
7 M	5.67	6.22	23.4	1.52	2.18	0.91	2.05	72.1	23.9	137.3	5.3	115.4
8 M	5.17	7.03	25.4	1.67	1.69	0.30	1.57	68.1	20.3	153.1	6.8	61.8
9 M	4.77	7.81	21.6	1.23	1.76	0.40	1.61	75.8	27.8	156.2	6.0	95.9
10 M	4.76	7.86	21.9	1.42	1.65	0.28	1.69	92.3	24.7	179.7	8.2	112.7
Group 2 (50 mg/kg)												
11 M	5.25	8.13	25.8	1.06	1.20	0.33	1.23	75.6	28.2	246.3	6.6	107.4
12 M	5.52	5.92	20.0	0.92	1.12	0.26	1.19	62.7	18.5	130.4	5.9	84.3
13 M	4.38	4.93	22.6	1.47	1.90	0.39	1.72	66.0	21.4	97.3	6.2	120.4
14 M	5.47	5.77	19.6	1.59	2.52	0.33	1.95	64.4	32.4	119.4	5.1	91.0
15 M	4.81	5.97	21.5	1.35	2.17	0.29	1.84	61.5	22.1	148.5	5.3	152.9
Group 3 (200 mg/kg)												
16 M	4.95	7.72	23.5	1.44	1.67	0.43	1.56	67.3	28.3	147.7	9.5	99.9
17 M	5.01	5.87	23.3	1.25	1.89	0.35	1.71	73.7	30.0	108.6	6.4	121.9
18 M	3.91	6.41	20.5	0.93	1.74	0.65	1.69	70.6	25.4	149.0	7.6	104.3
19 M	4.32	6.42	21.6	1.30	2.10	0.37	1.86	63.3	23.5	198.3	5.9	89.7
20 M	4.82	6.98	22.4	1.15	2.06	0.20	1.66	69.0	20.5	180.4	6.6	79.7
Group 4 (1000 mg/kg)												
21 M	4.42	9.20	22.3	1.20	2.12	0.20	1.68	84.3	29.8	303.8	6.4	66.0
22 M	4.62	6.81	22.7	1.02	1.88	0.27	1.54	72.9	30.1	153.2	6.7	80.0
23 M	3.61	5.53	22.5	1.86	1.90	0.53	1.70	83.2	25.8	238.3	7.4	127.7
24 M	4.86	6.90	20.4	1.29	1.23	0.65	1.27	70.6	26.4	140.9	7.0	168.7
25 M	4.57	9.14	19.6	1.36	2.03	0.25	1.67	74.1	24.5	162.0	8.8	129.4
26 M	3.83	7.11	25.5	0.84	1.57	0.53	1.52	78.8	36.4	157.6	12.5	127.7
27 M	3.15	7.13	23.9	1.41	1.87	0.31	1.57	126.1	60.7	174.9	19.9	132.5
28 M	4.55	8.96	24.0	1.37	1.55	0.32	1.39	72.2	26.5	150.4	7.0	81.1
29 M	3.67	8.68	28.4	1.20	1.74	0.51	1.59	84.5	30.6	110.7	9.1	96.4
30 M	3.08	9.80	23.7	1.10	1.78	0.34	1.58	84.5	40.7	139.0	7.0	91.7

Blood chemistry (individuals)

WEEK 5 MALES

AN_NO	GGT U/l	CK U/l	Na+ mmol/l	K+ mmol/l	Cl- mmol/l	Ca++ mmol/l	PO4-in mmol/l	Prot g/l	Alb g/l	Glob g/l	A/G rel. 1
Group 1 (0 mg/kg)											
1 M	0.0	195.2	145.2	3.77	97.5	3.00	2.75	66.52	40.02	26.50	1.51
2 M	0.0	186.7	146.3	3.61	102.3	2.97	2.51	66.32	42.38	23.94	1.77
3 M	0.0	231.9	144.9	4.06	102.1	2.97	2.68	64.56	41.22	23.34	1.77
4 M	0.0	195.1	145.3	3.71	101.0	2.90	2.51	66.42	42.96	23.46	1.83
5 M	0.0	116.9	145.9	3.82	99.0	2.96	2.44	66.69	41.64	25.05	1.66
6 M	0.0	183.2	145.5	3.56	101.9	2.91	2.36	65.61	41.26	24.35	1.69
7 M	0.0	207.6	143.8	3.90	102.4	2.93	2.33	69.73	44.85	24.88	1.80
8 M	0.0	167.4	146.5	3.57	100.2	2.95	2.41	65.91	42.88	23.03	1.86
9 M	0.0	160.6	146.6	3.55	99.7	2.92	2.33	68.50	41.99	26.51	1.58
10 M	0.0	159.1	146.2	3.59	99.8	2.89	2.62	63.48	41.82	21.66	1.93
Group 2 (50 mg/kg)											
11 M	0.0	348.2	147.2	4.06	102.3	2.83	2.24	63.56	40.44	23.12	1.75
12 M	0.0	114.7	145.9	3.86	102.7	2.83	2.23	64.09	41.28	22.81	1.81
13 M	0.0	125.7	145.8	3.60	102.4	2.94	2.36	65.62	41.96	23.66	1.77
14 M	0.0	180.0	143.8	3.95	100.1	2.94	2.48	66.49	42.03	24.46	1.72
15 M	0.0	184.9	145.6	3.88	99.5	2.86	2.59	64.91	41.43	23.48	1.76
Group 3 (200 mg/kg)											
16 M	0.0	174.0	146.4	3.93	101.4	2.94	2.44	65.23	39.89	25.34	1.57
17 M	0.0	133.2	146.2	3.90	100.2	3.01	2.44	67.88	41.12	26.76	1.54
18 M	0.0	178.9	145.8	3.57	99.4	3.09	2.62	69.45	42.64	26.81	1.59
19 M	0.0	151.2	147.1	4.21	99.1	2.98	2.65	67.70	43.34	24.36	1.78
20 M	0.0	226.3	146.9	4.14	98.6	2.97	2.62	64.47	41.62	22.85	1.82
Group 4 (1000 mg/kg)											
21 M	0.0	303.1	148.0	3.42	98.6	2.92	2.93	65.07	42.69	22.38	1.91
22 M	0.0	224.9	146.8	3.51	100.1	2.78	2.48	63.86	40.48	23.38	1.73
23 M	0.0	205.5	146.9	3.73	96.2	2.88	2.73	66.61	45.45	21.16	2.15
24 M	0.0	140.0	145.5	3.47	98.5	2.72	2.77	63.63	41.54	22.09	1.88
25 M	0.0	304.9	147.5	3.31	100.9	2.92	2.88	67.90	44.75	23.15	1.93
26 M	0.0	228.8	146.6	3.46	97.7	2.93	2.88	66.96	44.27	22.69	1.95
27 M	0.0	239.7	146.5	3.59	98.0	2.86	2.58	64.29	42.10	22.19	1.90
28 M	0.0	142.5	147.4	3.43	100.8	2.74	2.71	66.50	42.94	23.56	1.82
29 M	0.0	173.0	148.4	3.62	98.6	2.85	2.85	68.33	44.02	24.31	1.81
30 M	0.0	176.6	148.9	3.47	100.4	2.88	2.78	65.77	43.77	22.00	1.99

Blood chemistry (individuals)

WEEK 5 FEMALES

AN_NO	Gluc	Urea	Creat	Bili-tot	Chol	Trigly	Phos-Lip	ASAT	ALAT	LDH	GLDH	AlP
	mmol/l	mmol/l	µmol/l	µmol/l	mmol/l	mmol/l	mmol/l	U/l	U/l	U/l	U/l	U/l
Group 1 (0 mg/kg)												
31 F	4.10	7.19	25.0	1.40	1.72	0.27	1.88	61.3	19.8	143.8	4.6	35.2
32 F	4.89	6.77	26.2	2.52	2.35	0.36	2.13	75.3	25.3	186.1	8.0	53.9
33 F	3.43	6.04	24.7	2.26	1.49	0.28	1.48	71.5	18.6	149.9	4.7	42.8
34 F	3.82	7.94	25.5	1.92	1.40	0.22	1.39	65.9	18.6	128.1	5.2	45.9
35 F	4.94	8.21	23.7	1.59	1.80	0.22	1.87	65.2	20.7	134.9	4.2	43.5
36 F	3.40	8.42	26.3	0.94	1.24	0.23	1.40	67.3	20.1	167.4	6.5	79.2
37 F	4.09	6.49	26.2	0.99	2.22	0.29	2.02	66.9	17.6	145.7	4.8	36.1
38 F	4.99	8.63	29.5	1.53	1.22	0.21	1.33	70.7	17.4	140.7	9.0	55.0
39 F	3.98	7.17	27.0	1.87	1.78	0.29	1.91	71.9	26.0	167.3	5.3	47.0
40 F	4.90	7.81	25.9	1.61	1.42	0.21	1.64	65.7	18.1	168.7	5.5	60.4
Group 2 (50 mg/kg)												
41 F	4.11	7.13	27.9	2.56	1.23	0.30	1.49	61.0	18.6	132.6	6.2	45.6
42 F	3.81	6.47	28.3	1.43	1.48	0.16	1.59	74.0	19.4	144.4	5.4	45.3
43 F	4.78	8.06	28.7	1.90	2.04	0.27	2.05	62.9	17.1	121.1	5.4	66.4
44 F	4.03	6.96	24.6	1.37	1.79	0.23	1.80	70.9	20.1	163.8	6.6	85.8
45 F	3.83	5.96	27.7	1.83	1.68	0.26	1.81	64.1	15.9	141.8	5.2	63.8
Group 3 (200 mg/kg)												
46 F	4.37	6.71	25.5	0.75	1.53	0.20	1.36	64.7	25.7	163.2	6.8	44.0
47 F	3.60	6.28	27.0	1.68	2.17	0.26	2.00	75.3	21.4	181.3	4.6	38.2
48 F	4.17	6.48	28.6	1.66	1.50	0.29	1.56	70.1	21.1	144.9	5.2	39.0
49 F	4.19	9.67	23.6	1.48	1.52	0.15	1.67	70.0	20.2	125.5	5.3	41.3
50 F	3.80	9.73	29.4	1.92	1.20	0.19	1.33	89.7	22.1	455.3	5.3	46.1
Group 4 (1000 mg/kg)												
51 F	3.89	9.08	31.6	0.83	1.62	0.23	1.60	75.6	19.3	187.9	6.1	50.0
52 F	4.86	8.51	24.1	1.38	2.88	0.25	2.50	70.6	23.1	184.5	6.0	47.4
53 F	3.90	8.41	29.8	0.87	1.84	0.31	1.91	75.2	22.9	102.9	5.7	52.9
54 F	2.89	7.95	28.0	1.60	2.87	0.33	2.49	79.6	21.0	254.4	6.3	65.4
55 F	3.25	7.93	28.5	1.51	2.08	0.21	1.85	69.8	34.0	151.7	10.5	37.2
56 F	3.33	8.00	30.2	1.23	2.39	0.25	2.01	86.3	23.6	243.8	7.7	77.8
57 F	3.86	8.46	26.1	1.42	1.37	0.14	1.31	70.4	19.7	213.5	6.3	34.9
58 F	3.69	5.94	26.7	1.08	2.54	0.36	2.29	74.2	27.3	170.2	5.5	44.4
59 F	3.36	6.72	23.4	0.96	1.72	0.35	1.72	62.5	24.1	149.7	6.1	60.9
60 F	4.72	7.63	28.8	0.86	1.97	0.27	1.83	84.0	23.8	179.8	6.0	61.1

Blood chemistry (individuals)

WEEK 5

FEMALES

AN_NO	GGT	CK	Na+	K+	Cl-	Ca++	PO4-in	Prot	Alb	Glob	A/G
	U/l	U/l	mmol/l	mmol/l	mmol/l	mmol/l	mmol/l	g/l	g/l	g/l	rel. 1
Group 1 (0 mg/kg)											
31 F	0.0	154.1	147.0	3.64	101.9	2.77	2.04	62.61	43.46	19.15	2.27
32 F	0.0	207.2	144.3	3.65	101.0	2.83	2.18	64.60	45.18	19.42	2.33
33 F	0.0	152.5	145.2	3.33	100.4	2.96	2.10	68.33	47.67	20.66	2.31
34 F	0.0	134.9	146.2	3.28	99.9	2.79	2.21	66.00	45.68	20.32	2.25
35 F	0.0	123.0	144.2	3.32	102.5	2.77	1.78	66.34	43.07	23.27	1.85
36 F	0.0	142.5	146.5	3.90	102.4	2.81	2.09	64.13	41.44	22.69	1.83
37 F	0.0	159.2	145.1	3.89	101.7	2.94	1.80	68.93	48.38	20.55	2.35
38 F	0.0	156.2	146.3	3.55	104.2	2.79	2.25	65.00	45.88	19.12	2.40
39 F	0.0	203.0	146.2	3.34	103.2	2.83	2.19	68.91	47.88	21.03	2.28
40 F	0.0	166.7	146.1	3.71	103.3	2.82	2.19	69.31	47.54	21.77	2.18
Group 2 (50 mg/kg)											
41 F	0.0	165.7	146.3	3.25	102.4	2.83	2.25	65.59	46.03	19.56	2.35
42 F	0.0	137.7	145.7	3.32	104.5	2.74	2.13	64.22	44.89	19.33	2.32
43 F	0.0	107.4	146.5	3.64	103.1	2.77	1.85	67.08	45.64	21.44	2.13
44 F	0.0	127.2	145.7	3.52	103.5	2.76	1.99	64.89	43.86	21.03	2.09
45 F	0.0	140.5	146.1	3.28	100.0	2.84	2.02	69.02	48.39	20.63	2.35
Group 3 (200 mg/kg)											
46 F	0.0	142.0	144.7	3.84	100.1	2.80	2.52	64.91	42.17	22.74	1.85
47 F	0.0	191.0	145.1	4.05	101.9	2.91	1.99	66.68	45.96	20.72	2.22
48 F	0.0	174.8	145.5	3.72	104.6	2.79	2.20	63.30	42.07	21.23	1.98
49 F	0.0	102.3	147.0	3.04	105.4	2.74	2.15	68.83	46.57	22.26	2.09
50 F	0.0	356.0	145.6	3.82	102.9	2.80	2.16	68.11	46.53	21.58	2.16
Group 4 (1000 mg/kg)											
51 F	0.0	166.0	146.6	3.20	100.5	2.73	2.24	68.04	46.51	21.53	2.16
52 F	0.0	194.1	146.0	3.68	101.7	2.82	1.54	67.86	47.84	20.02	2.39
53 F	0.0	116.9	145.8	3.50	101.9	2.74	1.93	65.76	46.74	19.02	2.46
54 F	0.0	263.0	146.7	3.49	99.0	2.84	2.11	63.72	42.54	21.18	2.01
55 F	0.0	168.1	146.8	3.68	104.3	2.84	2.07	68.62	46.47	22.15	2.10
56 F	0.0	296.0	147.2	3.33	102.2	2.79	2.17	64.00	42.79	21.21	2.02
57 F	0.0	176.4	147.3	3.03	104.7	2.74	1.98	68.32	46.49	21.83	2.13
58 F	0.0	211.9	145.7	3.23	102.3	2.76	1.60	65.41	45.48	19.93	2.28
59 F	0.0	127.0	145.9	3.31	100.1	2.91	2.24	63.71	44.19	19.52	2.26
60 F	0.0	186.1	146.7	2.85	105.4	2.75	1.71	67.55	44.70	22.85	1.96

Blood chemistry (individuals)

WEEK 7 MALES

AN_NO	Gluc	Urea	Creat	Bili-tot	Chol	Trigly	Phos-Lip	ASAT	ALAT	LDH	GLDH	AlP
	mmol/l	mmol/l	µmol/l	µmol/l	mmol/l	mmol/l	mmol/l	U/l	U/l	U/l	U/l	U/l
Group 1 (0 mg/kg)												
6 M	5.56	5.56	21.6	1.18	1.67	0.65	1.70	66.2	27.5	122.5	6.2	73.7
7 M	4.96	5.03	26.2	1.59	2.07	0.51	1.86	80.4	25.4	232.1	6.8	90.6
8 M	5.55	4.58	24.7	1.10	1.51	0.55	1.56	63.4	22.7	125.5	5.7	54.2
9 M	5.01	5.02	22.1	0.94	1.73	0.65	1.69	74.7	30.7	141.0	6.2	82.8
10 M	4.80	4.63	22.1	1.44	1.62	0.32	1.62	84.1	23.4	122.9	7.7	93.2
Group 4 (1000 mg/kg)												
26 M	5.15	5.06	26.7	1.46	1.07	0.71	1.29	77.0	30.0	226.8	7.9	101.4
27 M	5.09	5.47	24.5	1.17	1.58	0.60	1.56	83.9	32.3	125.2	6.9	116.2
28 M	5.14	6.57	23.9	1.32	1.22	0.58	1.36	68.9	24.5	106.1	6.6	70.3
29 M	4.17	5.57	28.1	1.07	1.36	0.56	1.41	76.5	26.3	116.2	7.3	79.1
30 M	4.03	6.86	23.7	1.53	1.52	0.73	1.60	81.4	33.7	141.7	6.9	80.2

Blood chemistry (individuals)

WEEK 7 MALES

AN_NO	GGT	CK	Na+	K+	Cl-	Ca++	PO4-in	Prot	Alb	Glob	A/G
	U/l	U/l	mmol/l	mmol/l	mmol/l	mmol/l	mmol/l	g/l	g/l	g/l	rel. 1
Group 1 (0 mg/kg)											
6 M	0.0	120.8	142.1	3.28	98.4	2.87	2.17	67.30	42.10	25.20	1.67
7 M	0.0	226.0	143.9	3.45	99.1	2.87	2.33	69.88	43.35	26.53	1.63
8 M	0.0	109.8	142.8	3.64	99.9	2.88	2.19	66.45	43.24	23.21	1.86
9 M	0.0	112.5	144.3	3.33	100.3	2.81	2.06	69.21	42.12	27.09	1.55
10 M	0.0	108.2	144.6	3.23	101.3	2.71	2.23	62.42	41.04	21.38	1.92
Group 4 (1000 mg/kg)											
26 M	0.0	200.6	143.0	4.03	100.0	2.75	2.54	64.57	41.42	23.15	1.79
27 M	0.0	145.9	144.7	3.45	100.5	2.85	2.42	64.73	40.72	24.01	1.70
28 M	0.0	96.6	144.5	3.30	101.7	2.70	2.20	67.74	41.97	25.77	1.63
29 M	0.0	152.0	145.7	3.63	101.3	2.78	2.75	64.76	40.24	24.52	1.64
30 M	0.0	167.3	146.5	3.59	103.4	2.78	2.03	65.33	41.82	23.51	1.78

WEEK 7 — Blood chemistry (individuals) — FEMALES

AN_NO	Gluc	Urea	Creat	Bili-tot	Chol	Trigly	Phos-Lip	ASAT	ALAT	LDH	GLDH	AlP
	mmol/l	mmol/l	µmol/l	µmol/l	mmol/l	mmol/l	mmol/l	U/l	U/l	U/l	U/l	U/l
Group 1 (0 mg/kg)												
36 F	4.22	7.94	28.9	1.11	1.19	0.28	1.45	64.9	21.3	136.2	5.9	55.1
37 F	3.99	6.35	26.2	1.45	2.65	0.40	2.63	81.9	25.2	132.6	16.8	28.9
38 F	5.03	8.53	30.3	1.49	1.33	0.28	1.45	74.1	25.1	142.1	20.8	42.3
39 F	3.85	7.02	26.7	1.41	1.45	0.44	1.83	51.4	19.4	98.2	3.9	43.7
40 F	4.04	5.24	21.5	1.38	2.03	0.33	2.31	74.7	27.4	296.1	7.1	35.8
Group 4 (1000 mg/kg)												
56 F	4.88	7.40	28.3	1.09	2.06	0.41	2.07	69.6	16.9	147.9	5.8	62.2
57 F	4.15	6.36	27.5	1.25	0.91	0.18	1.15	59.5	19.1	106.9	7.6	28.6
58 F	5.26	6.40	24.2	1.00	1.87	0.43	2.09	65.2	23.8	140.6	5.5	34.3
59 F	5.93	5.75	25.2	1.34	1.58	0.45	1.84	55.2	18.6	138.2	5.5	50.9
60 F	4.91	5.57	27.8	1.03	1.81	0.43	1.86	69.5	20.2	136.1	6.1	42.9

WEEK 7 — Blood chemistry (individuals) — FEMALES

AN_NO	GGT	CK	Na+	K+	Cl-	Ca++	PO4-in	Prot	Alb	Glob	A/G
	U/l	U/l	mmol/l	mmol/l	mmol/l	mmol/l	mmol/l	g/l	g/l	g/l	rel. 1
Group 1 (0 mg/kg)											
36 F	0.0	117.5	144.9	3.53	103.5	2.76	1.84	66.89	43.09	23.80	1.81
37 F	0.0	94.5	144.2	3.15	103.1	2.81	1.59	69.95	48.33	21.62	2.24
38 F	0.0	113.0	143.9	3.52	104.7	2.80	1.92	68.38	47.11	21.27	2.21
39 F	0.0	107.6	144.6	3.34	101.7	2.81	1.78	69.40	47.17	22.23	2.12
40 F	0.0	143.1	143.8	3.92	102.3	2.81	1.99	71.44	49.10	22.34	2.20
Group 4 (1000 mg/kg)											
56 F	0.0	125.5	144.7	2.90	103.4	2.63	1.57	63.85	41.66	22.19	1.88
57 F	0.0	110.4	144.6	3.45	103.5	2.76	1.90	67.05	46.14	20.91	2.21
58 F	0.0	128.7	144.3	3.46	102.7	2.73	1.64	64.92	43.90	21.02	2.09
59 F	0.0	118.4	143.6	3.04	102.8	2.68	1.85	65.23	44.09	21.14	2.09
60 F	0.0	107.6	144.1	3.25	101.8	2.73	1.71	66.25	43.13	23.12	1.87

1.7 URINE ANALYSIS (INDIVIDUALS)

WEEK 5

MALES

AN_NO	Volume ml	Rel dens rel. 1	Color Choice	Appear Choice	pH	NIT Score	PRO g/l	GLU mmol/l	KET mmol/l	UBG µmol/l	BIL µmol/l	ERY per µl
Group 1 (0 mg/kg)												
1 M	11.7	1.063	NORMAL	TURBID	6.0	0	0.25	0	0.0	0	0	0
2 M	9.1	1.076	NORMAL	NORMAL	6.0	0	0.25	0	0.0	0	0	0
3 M	9.5	1.079	NORMAL	NORMAL	6.5	0	0.25	0	0.0	0	0	0
4 M	9.8	1.075	NORMAL	NORMAL	6.5	0	0.25	0	0.5	0	0	0
5 M	7.4	1.090	NORMAL	NORMAL	6.5	0	0.75	0	0.5	0	0	0
6 M	14.1	1.044	NORMAL	TURBID	6.5	0	0.25	0	0.0	0	0	0
7 M	10.0	1.068	NORMAL	NORMAL	7.0	0	0.25	0	0.5	0	0	10
8 M	7.1	1.074	NORMAL	NORMAL	6.5	0	0.75	0	0.0	0	0	0
9 M	10.9	1.060	NORMAL	NORMAL	6.5	0	0.25	0	0.0	0	0	0
10 M	8.2	1.077	NORMAL	NORMAL	7.0	0	0.75	0	0.5	0	0	0
Group 2 (50 mg/kg)												
11 M	9.5	1.057	NORMAL	NORMAL	7.0	0	0.25	0	0.0	0	0	0
12 M	13.1	1.049	NORMAL	NORMAL	7.0	0	0.25	0	0.0	0	0	0
13 M	9.4	1.063	NORMAL	NORMAL	6.5	0	0.25	0	0.0	0	0	0
14 M	9.6	1.065	NORMAL	NORMAL	7.0	0	0.25	0	0.0	0	0	0
15 M	10.1	1.049	NORMAL	TURBID	7.0	0	0.25	0	0.5	0	0	10
Group 3 (200 mg/kg)												
16 M	9.4	1.073	NORMAL	NORMAL	6.5	0	0.25	0	0.0	0	0	0
17 M	13.9	1.045	NORMAL	TURBID	6.5	0	0.25	0	0.0	0	0	10
18 M	7.7	1.072	NORMAL	NORMAL	6.5	0	0.75	0	0.5	0	0	0
19 M	7.0	1.078	NORMAL	NORMAL	6.5	0	0.75	0	0.0	0	0	0
20 M	5.7	1.092	NORMAL	NORMAL	6.5	0	0.75	0	1.5	0	0	0
Group 4 (1000 mg/kg)												
21 M	9.5	1.098	NORMAL	NORMAL	6.5	0	0.75	0	0.5	0	0	0
22 M	10.7	1.080	NORMAL	NORMAL	7.0	0	0.25	0	0.0	0	0	0
23 M	17.0	1.049	NORMAL	TURBID	6.0	0	0.25	0	0.0	0	0	10
24 M	10.7	1.071	NORMAL	NORMAL	7.0	0	0.25	0	0.0	0	0	0
25 M	12.8	1.066	NORMAL	NORMAL	6.5	0	0.25	0	0.0	0	0	0
26 M	11.3	1.069	NORMAL	CLOUDY	6.5	0	0.25	0	0.0	0	0	0
27 M	11.8	1.073	NORMAL	CLOUDY	6.5	0	0.25	0	0.0	0	0	0
28 M	10.0	1.074	NORMAL	NORMAL	6.5	0	0.75	0	0.0	0	0	0
29 M	10.5	1.078	NORMAL	CLOUDY	6.5	0	0.25	0	0.5	0	0	0
30 M	8.7	1.092	NORMAL	NORMAL	6.5	0	0.75	0	0.5	0	0	0

Urine analysis (individuals)

WEEK 5

MALES

ANIMAL NO	LEU per µl
Group 1 (0 mg/kg)	
1 M	25
2 M	25
3 M	100
4 M	25
5 M	100
6 M	25
7 M	100
8 M	100
9 M	100
10 M	100
Group 2 (50 mg/kg)	
11 M	25
12 M	25
13 M	25
14 M	100
15 M	100
Group 3 (200 mg/kg)	
16 M	100
17 M	100
18 M	100
19 M	100
20 M	100
Group 4 (1000 mg/kg)	
21 M	100
22 M	25
23 M	25
24 M	25
25 M	25
26 M	25
27 M	25
28 M	25
29 M	25
30 M	25

WEEK 5

Urine analysis (individuals)

FEMALES

AN_NO	Volume	Rel dens	Color	Appear	pH	NIT	PRO	GLU	KET	UBG	BIL	ERY
	ml	rel. 1	Choice	Choice		Score	g/l	mmol/l	mmol/l	µmol/l	µmol/l	per µl
Group 1 (0 mg/kg)												
31 F	3.8	1.094	NORMAL	TURBID	6.5	0	0.75	0	0.0	0	17	25
32 F	5.6	1.070	NORMAL	NORMAL	5.0	0	0.25	0	0.0	0	17	0
33 F	16.5	1.027	NORMAL	NORMAL	6.0	0	0.00	0	0.0	0	0	0
34 F	7.8	1.052	NORMAL	NORMAL	6.0	0	0.25	0	0.0	0	0	0
35 F	6.4	1.053	NORMAL	NORMAL	6.0	0	0.25	0	0.0	0	0	0
36 F	6.4	1.058	NORMAL	NORMAL	6.5	0	0.25	0	0.0	0	0	10
37 F	5.8	1.060	NORMAL	NORMAL	5.0	0	0.25	0	0.0	0	17	0
38 F	9.9	1.048	NORMAL	NORMAL	6.0	0	0.25	0	0.0	0	0	0
39 F	3.8	1.070	NORMAL	NORMAL	6.0	0	0.75	0	0.0	0	0	0
40 F	5.2	1.053	NORMAL	NORMAL	6.0	0	0.25	0	0.0	0	0	0
Group 2 (50 mg/kg)												
41 F	4.3	1.078	NORMAL	NORMAL	6.0	0	0.25	0	0.5	17	0	0
42 F	4.8	1.057	NORMAL	TURBID	6.0	0	0.25	0	0.5	0	0	10
43 F	5.2	1.072	NORMAL	NORMAL	6.0	0	0.25	0	0.0	0	0	0
44 F	7.6	1.051	NORMAL	NORMAL	6.5	0	0.25	0	0.0	0	0	0
45 F	3.6	1.088	NORMAL	NORMAL	6.0	0	0.75	0	0.0	0	0	0
Group 3 (200 mg/kg)												
46 F	8.2	1.052	NORMAL	NORMAL	6.5	0	0.25	0	0.0	0	0	0
47 F	10.4	1.040	NORMAL	NORMAL	7.0	0	0.00	0	0.0	0	0	0
48 F	6.2	1.073	NORMAL	NORMAL	6.5	0	0.25	0	0.0	0	0	0
49 F	4.8	1.067	NORMAL	NORMAL	7.0	0	0.25	0	0.5	0	0	0
50 F	5.2	1.075	NORMAL	NORMAL	6.5	0	0.25	0	0.0	0	0	0
Group 4 (1000 mg/kg)												
51 F	5.5	1.076	NORMAL	NORMAL	6.5	0	0.75	0	0.5	0	0	0
52 F	4.9	1.092	NORMAL	NORMAL	5.0	0	0.75	0	0.5	0	0	0
53 F	5.9	1.084	NORMAL	NORMAL	6.5	0	0.75	0	0.0	17	0	0
54 F	8.2	1.052	NORMAL	NORMAL	6.0	0	0.25	0	0.0	0	0	0
55 F	5.1	1.076	NORMAL	NORMAL	5.0	0	0.25	0	0.0	0	0	0
56 F	9.3	1.055	NORMAL	NORMAL	5.0	0	0.25	0	0.0	0	0	0
57 F	8.2	1.057	NORMAL	NORMAL	6.0	0	0.25	0	0.0	0	0	0
58 F	10.6	1.053	NORMAL	NORMAL	5.0	0	0.25	0	0.0	0	0	0
59 F	2.2	1.070	NORMAL	TURBID	5.0	0	0.75	0	0.5	0	0	0
60 F	7.2	1.076	NORMAL	NORMAL	6.5	0	0.25	0	0.0	0	0	0

Urine analysis (individuals)

WEEK 5

FEMALES

AN_NO	LEU per µl
Group 1 (0 mg/kg)	
31 F	25
32 F	25
33 F	0
34 F	25
35 F	25
36 F	25
37 F	25
38 F	25
39 F	25
40 F	25
Group 2 (50 mg/kg)	
41 F	25
42 F	25
43 F	25
44 F	25
45 F	25
Group 3 (200 mg/kg)	
46 F	25
47 F	25
48 F	25
49 F	25
50 F	25
Group 4 (1000 mg/kg)	
51 F	25
52 F	25
53 F	25
54 F	0
55 F	25
56 F	25
57 F	25
58 F	25
59 F	25
60 F	25

WEEK 7

Urine analysis (individuals)

MALES

AN_NO	Volume	Rel dens	Color	Appear	pH	NIT	PRO	GLU	KET	UBG	BIL	ERY
	ml	rel. 1	Choice	Choice		Score	g/l	mmol/l	mmol/l	µmol/l	µmol/l	per µl
Group 1 (0 mg/kg)												
6 M	9.4	1.041	NORMAL	NORMAL	7.0	0	0.25	0	0.5	0	0	0
7 M	8.9	1.038	NORMAL	CLOUDY	8.0	0	0.25	0	1.5	0	0	0
8 M	6.8	1.043	NORMAL	NORMAL	7.0	0	0.25	0	0.5	0	0	0
9 M	8.2	1.041	NORMAL	TURBID	7.0	0	0.25	0	0.5	0	0	10
10 M	8.3	1.043	NORMAL	NORMAL	7.0	0	0.25	0	1.5	0	0	0
Group 4 (1000 mg/kg)												
26 M	10.0	1.032	NORMAL	CLOUDY	7.0	0	0.25	0	0.5	0	0	0
27 M	7.7	1.038	NORMAL	NORMAL	7.0	0	0.25	0	0.5	0	0	10
28 M	7.2	1.047	NORMAL	NORMAL	6.5	0	0.75	0	0.5	0	0	0
29 M	7.1	1.041	NORMAL	CLOUDY	7.0	0	0.25	0	1.5	0	0	10
30 M	5.3	1.061	NORMAL	NORMAL	6.5	0	0.75	0	0.5	0	0	0

WEEK 7

Urine analysis (individuals)

MALES

AN_NO	LEU
	per µl
Group 1 (0 mg/kg)	
6 M	100
7 M	100
8 M	100
9 M	100
10 M	25
Group 4 (1000 mg/kg)	
26 M	100
27 M	25
28 M	100
29 M	25
30 M	25

WEEK 7

Urine analysis (individuals)

FEMALES

AN_NO	Volume	Rel dens	Color	Appear	pH	NIT	PRO	GLU	KET	UBG	BIL	ERY
	ml	rel. 1	Choice	Choice		Score	g/l	mmol/l	mmol/l	µmol/l	µmol/l	per µl
Group 1 (0 mg/kg)												
36 F	5.4	1.042	NORMAL	NORMAL	6.0	0	0.25	0	0.5	0	0	10
37 F	7.3	1.035	NORMAL	NORMAL	6.0	0	0.25	0	0.0	0	0	0
38 F	5.7	1.040	NORMAL	NORMAL	6.0	0	0.25	0	0.5	0	0	0
39 F	8.0	1.034	NORMAL	CLOUDY	7.0	0	0.25	0	0.0	0	0	0
40 F	6.5	1.039	NORMAL	NORMAL	6.0	0	0.25	0	0.0	0	0	0
Group 4 (1000 mg/kg)												
56 F	5.4	1.041	NORMAL	NORMAL	6.5	0	0.25	0	0.5	0	0	0
57 F	4.6	1.039	NORMAL	NORMAL	7.0	0	0.25	0	0.0	0	0	10
58 F	5.0	1.044	NORMAL	NORMAL	6.0	0	0.25	0	0.0	0	17	0
59 F	10.1	1.023	NORMAL	CLOUDY	7.0	0	0.00	0	0.0	0	0	0
60 F	7.0	1.037	NORMAL	NORMAL	6.0	0	0.25	0	0.5	0	0	0

WEEK 7

Urine analysis (individuals)

FEMALES

AN_NO	LEU
	per µl
Group 1 (0 mg/kg)	
36 F	25
37 F	0
38 F	25
39 F	25
40 F	0
Group 4 (1000 mg/kg)	
56 F	25
57 F	0
58 F	0
59 F	25
60 F	25

1.8 REFERENCE VALUES - HEMATOLOGY

SPECIES RAT
STRAIN HanBr1:WIST(SPF)
SUPPLIER RCC Ltd.
STUDY TYPE [ALL]
DOSE ROUTE [ALL]
DATES: [ALL]

MALE

PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES N	5%	MEDIAN	95%	RANGE OF STUDY MEANS N	MIN	MAX
RBC	T/l	M01	9 TO 12	734	739	7.69	8.33	9.01	82	7.65	8.86
			13 TO 16	255	255	7.90	8.62	9.46	46	7.82	9.51
Hb	mmol/l	M01	9 TO 12	734	739	9.2	9.8	10.4	82	8.8	10.4
			13 TO 16	255	255	9.2	9.9	10.5	46	9.2	10.4
Hct	rel. 1	M01	9 TO 12	734	739	0.438	0.470	0.504	82	0.438	0.502
			13 TO 16	255	255	0.440	0.476	0.511	46	0.438	0.506
MCV	fl	M01	9 TO 12	734	739	53.0	56.4	60.0	82	52.0	60.5
			13 TO 16	255	255	51.6	55.1	59.0	46	52.0	58.6
RDW	rel. 1	M01	9 TO 12	734	739	0.103	0.112	0.157	82	0.104	0.140
			13 TO 16	255	255	0.112	0.126	0.175	46	0.115	0.163
MCH	fmol	M01	9 TO 12	734	739	1.10	1.17	1.26	82	1.08	1.26
			13 TO 16	255	255	1.07	1.14	1.24	46	1.08	1.21
MCHC	mmol/l	M01	9 TO 12	734	739	19.78	20.76	22.13	82	18.81	22.80
			13 TO 16	255	255	19.61	20.68	22.26	46	19.47	22.64
HDW	mmol/l	M01	9 TO 12	734	739	1.21	1.46	1.74	82	1.23	1.84
			13 TO 16	255	255	1.31	1.48	1.77	46	1.35	1.75
Reti	rel. 1	M02	9 TO 12	406	406	0.020	0.026	0.037	48	0.022	0.051
			13 TO 16	137	137	0.018	0.024	0.031	27	0.018	0.028
Reti	G/l	M02	9 TO 12	406	406	169.	216.	294.	48	183.	409.
			13 TO 16	137	137	157.	204.	259.	27	150.	242.
L Reti	rel. 1	M01	9 TO 12	391	391	0.285	0.417	0.521	46	0.281	0.517
			13 TO 16	132	132	0.327	0.461	0.565	26	0.328	0.562
M Reti	rel. 1	M01	9 TO 12	391	391	0.238	0.361	0.408	46	0.233	0.409
			13 TO 16	132	132	0.269	0.365	0.411	26	0.268	0.397
H Reti	rel. 1	M01	9 TO 12	391	391	0.097	0.221	0.477	46	0.109	0.484
			13 TO 16	132	132	0.060	0.168	0.395	26	0.069	0.403
WBC	G/l	M01	9 TO 12	734	739	4.96	7.28	10.57	82	4.99	12.53
			13 TO 16	255	255	4.66	6.92	10.06	46	4.19	10.61

Reference values - Hematology

SPECIES RAT
STRAIN HanBrl:WIST(SPF)
SUPPLIER RCC Ltd.
STUDY TYPE [ALL]
DOSE ROUTE [ALL]
DATES: [ALL]

MALE

PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES N	5%	MEDIAN	95%	RANGE OF STUDY MEANS N	MIN	MAX
Neut	rel. 1	M01	9 TO 12	733	738	0.086	0.144	0.243	82	0.085	0.210
			13 TO 16	255	255	0.096	0.148	0.229	46	0.109	0.207
Eos	rel. 1	M01	9 TO 12	733	738	0.007	0.012	0.025	82	0.008	0.038
			13 TO 16	255	255	0.008	0.013	0.023	46	0.009	0.029
Baso	rel. 1	M01	9 TO 12	733	738	0.002	0.003	0.012	82	0.002	0.020
			13 TO 16	255	255	0.001	0.003	0.011	46	0.001	0.013
Lympho	rel. 1	M01	9 TO 12	733	738	0.707	0.805	0.869	82	0.730	0.873
			13 TO 16	255	255	0.699	0.794	0.856	46	0.727	0.841
Mono	rel. 1	M01	9 TO 12	733	738	0.012	0.022	0.043	82	0.014	0.043
			13 TO 16	255	255	0.013	0.022	0.051	46	0.014	0.049
Luc	rel. 1	M01	9 TO 12	733	738	0.003	0.007	0.022	82	0.003	0.034
			13 TO 16	255	255	0.002	0.007	0.021	46	0.003	0.020
Neut	G/l	M01	9 TO 12	733	738	0.59	1.05	1.74	82	0.59	2.50
			13 TO 16	255	255	0.60	1.03	1.73	46	0.62	1.62
Eos	G/l	M01	9 TO 12	733	738	0.05	0.09	0.18	82	0.05	0.19
			13 TO 16	255	255	0.05	0.09	0.18	46	0.05	0.19
Baso	G/l	M01	9 TO 12	733	738	0.01	0.03	0.09	82	0.01	0.19
			13 TO 16	255	255	0.01	0.02	0.09	46	0.01	0.10
Lympho	G/l	M01	9 TO 12	733	738	3.81	5.83	8.69	82	3.82	9.44
			13 TO 16	255	255	3.60	5.41	8.14	46	3.38	8.87
Mono	G/l	M01	9 TO 12	733	738	0.08	0.16	0.38	82	0.08	0.39
			13 TO 16	255	255	0.08	0.16	0.41	46	0.08	0.45
Luc	G/l	M01	9 TO 12	733	738	0.02	0.05	0.20	82	0.02	0.32
			13 TO 16	255	255	0.02	0.05	0.18	46	0.02	0.19
Plt	G/l	M01	9 TO 12	734	739	779.	969.	1187.	82	809.	1189.
			13 TO 16	255	255	724.	916.	1136.	46	757.	1081.

Reference values - Hematology

SPECIES RAT
STRAIN HanBrl:WIST(SPF)
SUPPLIER RCC Ltd.
STUDY TYPE [ALL]
DOSE ROUTE [ALL]
DATES: [ALL]

MALE

PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES N	5%	MEDIAN	95%	RANGE OF STUDY MEANS N	MIN	MAX
PT	rel. 1	M01	9 TO 12	614	619	0.64	0.85	1.01	70	0.40	1.18
			13 TO 16	197	197	0.45	0.82	0.95	40	0.38	0.91
PTT	sec	M01	9 TO 12	412	417	14.3	17.7	20.6	47	14.4	20.4
			13 TO 16	122	122	14.6	18.2	20.7	25	15.3	20.0
MetHb	rel. 1	M01	9 TO 12	368	368	0.006	0.009	0.010	44	0.004	0.011
			13 TO 16	126	126	0.007	0.009	0.010	26	0.006	0.010

Reference values - Hematology

SPECIES RAT
STRAIN HanBrl:WIST(SPF)
SUPPLIER RCC Ltd.
STUDY TYPE [ALL]
DOSE ROUTE [ALL]
DATES: [ALL]

FEMALE

PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES N	5%	MEDIAN	95%	RANGE OF STUDY MEANS N	MIN	MAX
RBC	T/l	M01	9 TO 12	690	695	7.25	7.92	8.60	75	7.26	8.52
			13 TO 16	246	246	7.22	7.95	8.87	45	7.29	8.79
Hb	mmol/l	M01	9 TO 12	690	695	8.7	9.3	10.0	75	8.5	10.1
			13 TO 16	246	246	8.9	9.6	10.2	45	9.1	10.0
Hct	rel. 1	M01	9 TO 12	690	695	0.410	0.441	0.472	75	0.409	0.472
			13 TO 16	246	246	0.420	0.456	0.490	45	0.422	0.486
MCV	fl	M01	9 TO 12	690	695	52.5	56.0	59.4	75	51.6	60.4
			13 TO 16	246	246	53.8	57.3	61.1	45	54.3	60.6
RDW	rel. 1	M01	9 TO 12	690	695	0.097	0.106	0.155	75	0.095	0.143
			13 TO 16	246	246	0.105	0.129	0.160	45	0.104	0.153
MCH	fmol	M01	9 TO 12	690	695	1.11	1.18	1.25	75	1.12	1.24
			13 TO 16	246	246	1.12	1.21	1.30	45	1.13	1.27
MCHC	mmol/l	M01	9 TO 12	690	695	19.90	21.08	22.49	75	19.77	23.15
			13 TO 16	246	246	19.98	21.00	22.55	45	19.83	22.77
HDW	mmol/l	M01	9 TO 12	690	695	1.13	1.30	1.53	75	1.15	1.62
			13 TO 16	246	246	1.09	1.21	1.45	45	1.11	1.56
Reti	rel. 1	M02	9 TO 12	398	398	0.022	0.029	0.039	47	0.024	0.051
			13 TO 16	138	138	0.017	0.025	0.034	27	0.016	0.031
Reti	G/l	M02	9 TO 12	398	398	171.	224.	296.	47	186.	366.
			13 TO 16	138	138	136.	192.	254.	27	132.	232.
L Reti	rel. 1	M01	9 TO 12	383	383	0.282	0.413	0.527	45	0.284	0.507
			13 TO 16	133	133	0.308	0.456	0.595	26	0.312	0.550
M Reti	rel. 1	M01	9 TO 12	383	383	0.222	0.326	0.387	45	0.220	0.388
			13 TO 16	133	133	0.249	0.340	0.407	26	0.242	0.391
H Reti	rel. 1	M01	9 TO 12	383	383	0.105	0.261	0.488	45	0.106	0.496
			13 TO 16	133	133	0.068	0.185	0.441	26	0.073	0.446
WBC	G/l	M01	9 TO 12	690	695	3.32	5.11	7.77	75	2.67	7.65
			13 TO 16	246	246	2.66	4.24	6.81	45	2.20	5.90

Reference values - Hematology

SPECIES RAT
STRAIN HanBrl:WIST(SPF)
SUPPLIER RCC Ltd.
STUDY TYPE [ALL]
DOSE ROUTE [ALL]
DATES: [ALL]

FEMALE

PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES N	5%	MEDIAN	95%	RANGE OF STUDY MEANS N	MIN	MAX
Neut	rel. 1	M01	9 TO 12	690	695	0.082	0.156	0.287	75	0.092	0.225
			13 TO 16	246	246	0.090	0.154	0.302	45	0.105	0.296
Eos	rel. 1	M01	9 TO 12	690	695	0.007	0.013	0.026	75	0.007	0.028
			13 TO 16	246	246	0.008	0.015	0.031	45	0.011	0.035
Baso	rel. 1	M01	9 TO 12	690	695	0.001	0.003	0.009	75	0.001	0.014
			13 TO 16	246	246	0.001	0.003	0.010	45	0.001	0.009
Lympho	rel. 1	M01	9 TO 12	690	695	0.663	0.793	0.878	75	0.689	0.873
			13 TO 16	246	246	0.633	0.798	0.867	45	0.655	0.855
Mono	rel. 1	M01	9 TO 12	690	695	0.011	0.021	0.041	75	0.013	0.041
			13 TO 16	246	246	0.012	0.022	0.046	45	0.012	0.043
Luc	rel. 1	M01	9 TO 12	690	695	0.003	0.007	0.022	75	0.003	0.032
			13 TO 16	246	246	0.002	0.006	0.017	45	0.002	0.017
Neut	G/l	M01	9 TO 12	690	695	0.42	0.81	1.57	75	0.46	1.24
			13 TO 16	246	246	0.34	0.64	1.35	45	0.38	1.06
Eos	G/l	M01	9 TO 12	690	695	0.03	0.07	0.14	75	0.05	0.15
			13 TO 16	246	246	0.03	0.06	0.13	45	0.04	0.13
Baso	G/l	M01	9 TO 12	690	695	0.00	0.01	0.05	75	0.01	0.10
			13 TO 16	246	246	0.00	0.01	0.04	45	0.00	0.05
Lympho	G/l	M01	9 TO 12	690	695	2.46	4.03	6.25	75	1.96	6.52
			13 TO 16	246	246	2.05	3.27	5.48	45	1.47	4.94
Mono	G/l	M01	9 TO 12	690	695	0.05	0.11	0.23	75	0.05	0.23
			13 TO 16	246	246	0.04	0.10	0.22	45	0.03	0.20
Luc	G/l	M01	9 TO 12	690	695	0.01	0.03	0.12	75	0.01	0.18
			13 TO 16	246	246	0.01	0.03	0.09	45	0.01	0.09
Plt	G/l	M01	9 TO 12	690	695	811.	1026.	1283.	75	819.	1218.
			13 TO 16	246	246	721.	974.	1236.	45	709.	1323.

Reference values - Hematology

SPECIES RAT
STRAIN HanBr1:WIST(SPF)
SUPPLIER RCC Ltd.
STUDY TYPE [ALL]
DOSE ROUTE [ALL]
DATES: [ALL]

FEMALE

PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES N	5%	MEDIAN	95%	RANGE OF STUDY MEANS N	MIN	MAX
PT	rel. 1	M01	9 TO 12	609	614	0.85	0.98	1.29	69	0.87	1.33
			13 TO 16	195	195	0.80	0.95	1.18	40	0.81	1.21
PTT	sec	M01	9 TO 12	409	414	14.6	17.9	20.8	46	14.9	21.7
			13 TO 16	124	124	14.8	18.1	21.2	25	14.4	21.0
MetHb	rel. 1	M01	9 TO 12	373	373	0.005	0.008	0.010	44	0.003	0.010
			13 TO 16	128	128	0.007	0.009	0.011	26	0.007	0.010
Heinz B	rel. 1	M01	9 TO 12	20	20	0.000	0.000	0.000	1	0.000	0.000

1.9 REFERENCE VALUES - BLOOD CHEMISTRY

SPECIES RAT
STRAIN HanBrl:WIST(SPF) MALE
SUPPLIER RCC Ltd.
STUDY TYPE [ALL]
DOSE ROUTE [ALL]
DATES: [ALL]

PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES N	5%	MEDIAN	95%	RANGE OF STUDY MEANS N	MIN	MAX
Gluc	mmol/l	M01	9 TO 12	725	730	3.96	6.01	9.63	79	3.48	9.24
			13 TO 16	247	247	4.20	6.78	9.83	45	4.08	9.18
Urea	mmol/l	M01	9 TO 12	725	730	4.76	6.08	8.22	79	4.98	9.40
			13 TO 16	247	247	4.73	5.82	7.13	45	4.83	7.21
Creat	µmol/l	M01	9 TO 12	695	700	17.9	22.6	30.4	73	18.8	33.3
			13 TO 16	247	247	18.8	24.8	34.0	45	19.8	38.2
Bili-tot	µmol/l	M01	9 TO 12	695	700	0.84	1.32	1.97	73	1.01	1.95
			13 TO 16	247	247	0.86	1.42	2.02	45	0.98	2.02
Prot	g/l	M01	9 TO 12	725	730	61.16	65.61	69.56	79	60.62	69.79
			13 TO 16	247	247	62.46	66.57	71.35	45	62.33	70.94
Alb	g/l	M02	9 TO 12	366	371	38.50	41.02	44.05	43	39.14	44.05
			13 TO 16	136	136	38.34	41.48	43.99	27	39.10	43.51
Glob	g/l	M02	9 TO 12	366	371	20.26	24.04	26.87	43	19.66	26.32
			13 TO 16	136	136	22.11	24.76	28.41	27	21.94	28.10
A/G	rel. 1	M02	9 TO 12	366	371	1.51	1.72	2.05	43	1.54	2.13
			13 TO 16	136	136	1.41	1.67	1.93	27	1.42	1.90
Chol	mmol/l	M01	9 TO 12	725	730	1.11	1.57	2.21	79	1.23	2.23
			13 TO 16	247	247	1.08	1.55	2.17	45	1.24	2.11
Trigly	mmol/l	M01	9 TO 12	605	610	0.27	0.58	1.26	64	0.31	1.45
			13 TO 16	207	207	0.30	0.60	1.20	37	0.36	1.06
Phos-Lip	mmol/l	M01	9 TO 12	460	465	1.22	1.55	1.98	45	1.29	2.07
			13 TO 16	172	172	1.21	1.52	1.90	30	1.29	1.87
Na+	mmol/l	M01	9 TO 12	724	729	139.2	142.4	146.2	79	138.9	147.2
			13 TO 16	247	247	139.0	142.5	146.8	45	138.7	147.2
K+	mmol/l	M01	9 TO 12	725	730	3.19	3.73	4.41	79	3.26	5.13
			13 TO 16	247	247	3.01	3.70	4.48	45	2.95	4.67
Ca++	mmol/l	M01	9 TO 12	695	700	2.60	2.76	2.93	73	2.59	2.99
			13 TO 16	247	247	2.54	2.71	2.91	45	2.52	2.91

Reference values - Blood chemistry

SPECIES RAT
STRAIN HanBrl:WIST(SPF)
SUPPLIER RCC Ltd.
STUDY TYPE [ALL]
DOSE ROUTE [ALL]
DATES: [ALL]

MALE

PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES N	5%	MEDIAN	95%	RANGE OF STUDY MEANS N	MIN	MAX
Cl-	mmol/l	M01	9 TO 12	700	705	95.8	100.0	105.9	74	95.3	107.3
			13 TO 16	247	247	96.5	100.3	107.4	45	93.5	107.9
PO4-in	mmol/l	M01	9 TO 12	700	705	1.92	2.30	2.67	74	1.91	2.87
			13 TO 16	247	247	1.60	2.00	2.37	45	1.69	2.44
ASAT	U/l	M01	9 TO 12	725	730	61.6	74.8	99.6	79	60.5	99.7
			13 TO 16	247	247	60.6	72.6	94.5	45	63.2	95.1
ALAT	U/l	M01	9 TO 12	725	730	20.9	28.5	46.5	79	19.4	64.2
			13 TO 16	247	247	21.6	29.9	48.2	45	21.2	42.1
AlP	U/l	M01	9 TO 12	725	730	81.0	116.6	181.1	79	78.7	178.6
			13 TO 16	246	246	63.9	88.7	122.1	45	60.8	113.0
GGT	U/l	M01	9 TO 12	580	585	0.0	0.0	0.0	64	0.0	0.9
			13 TO 16	192	192	0.0	0.0	0.0	34	0.0	0.0
GLDH	U/l	M01	9 TO 12	124	124	4.6	6.4	8.8	15	4.9	9.5
			13 TO 16	49	49	4.3	5.9	9.4	9	5.3	7.7
CK	U/l	M01	9 TO 12	397	402	121.1	171.4	339.9	44	138.6	287.8
			13 TO 16	132	132	96.3	135.9	271.2	26	108.1	185.9
LDH	U/l	M01	9 TO 12	397	402	81.3	127.1	230.0	44	81.1	246.8
			13 TO 16	122	122	75.5	125.1	255.1	25	76.0	265.2

Reference values - Blood chemistry

SPECIES RAT
STRAIN HanBrl:WIST(SPF)
SUPPLIER RCC Ltd.
STUDY TYPE [ALL]
DOSE ROUTE [ALL]
DATES: [ALL]

FEMALE

PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES N	5%	MEDIAN	95%	RANGE OF STUDY MEANS N	MIN	MAX
Gluc	mmol/l	M01	9 TO 12	688	693	4.16	5.69	9.11	72	3.59	9.07
			13 TO 16	247	247	4.25	6.30	9.57	45	4.29	9.40
Urea	mmol/l	M01	9 TO 12	688	693	5.55	7.04	9.16	72	5.81	9.99
			13 TO 16	247	247	5.65	7.01	8.58	45	6.20	8.02
Creat	µmol/l	M01	9 TO 12	683	688	20.8	25.7	33.5	71	21.6	38.2
			13 TO 16	247	247	22.4	28.1	36.6	45	22.4	40.6
Bili-tot	µmol/l	M01	9 TO 12	683	688	1.01	1.61	2.41	71	1.21	2.39
			13 TO 16	247	247	1.05	1.53	2.43	45	1.13	2.60
Prot	g/l	M01	9 TO 12	688	693	61.43	66.39	71.21	72	60.27	70.48
			13 TO 16	247	247	62.91	68.62	73.78	45	62.82	73.16
Alb	g/l	M02	9 TO 12	363	368	41.18	44.85	49.23	42	42.34	47.57
			13 TO 16	139	139	41.76	46.10	50.22	27	42.60	48.69
Glob	g/l	M02	9 TO 12	363	368	18.62	21.69	24.42	42	16.27	23.89
			13 TO 16	139	139	19.39	22.57	25.31	27	19.76	25.27
A/G	rel. 1	M02	9 TO 12	363	368	1.79	2.07	2.45	42	1.86	2.71
			13 TO 16	139	139	1.77	2.05	2.40	27	1.81	2.34
Chol	mmol/l	M01	9 TO 12	688	693	0.97	1.43	2.04	72	1.01	1.85
			13 TO 16	247	247	0.98	1.41	2.11	45	0.99	1.83
Trigly	mmol/l	M01	9 TO 12	594	599	0.19	0.31	0.57	62	0.22	0.99
			13 TO 16	209	209	0.23	0.35	0.61	37	0.25	0.79
Phos-Lip	mmol/l	M01	9 TO 12	463	468	1.18	1.59	2.05	45	1.20	2.08
			13 TO 16	174	174	1.22	1.62	2.21	30	1.42	1.97
Na+	mmol/l	M01	9 TO 12	685	690	139.0	142.0	146.2	72	138.4	147.1
			13 TO 16	247	247	138.0	141.6	145.5	45	137.9	145.3
K+	mmol/l	M01	9 TO 12	688	693	2.76	3.40	4.08	72	2.74	4.11
			13 TO 16	247	247	2.53	3.32	3.96	45	2.63	4.24
Ca++	mmol/l	M01	9 TO 12	683	688	2.55	2.72	2.90	71	2.57	2.90
			13 TO 16	247	247	2.49	2.68	2.86	45	2.53	2.92

Reference values - Blood chemistry

SPECIES RAT
STRAIN HanBrl:WIST(SPF)
SUPPLIER RCC Ltd.
STUDY TYPE [ALL]
DOSE ROUTE [ALL]
DATES: [ALL]

FEMALE

PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES N	5%	MEDIAN	95%	RANGE OF STUDY MEANS N	MIN	MAX
Cl-	mmol/l	M01	9 TO 12	683	688	97.6	102.5	107.9	71	97.3	108.9
			13 TO 16	247	247	98.2	102.7	108.2	45	98.5	108.6
PO4-in	mmol/l	M01	9 TO 12	683	688	1.37	1.90	2.30	71	1.45	2.36
			13 TO 16	247	247	1.05	1.51	1.97	45	1.19	1.92
ASAT	U/l	M01	9 TO 12	688	693	58.8	70.5	90.1	72	60.4	80.8
			13 TO 16	247	247	55.7	66.4	87.4	45	56.4	95.8
ALAT	U/l	M01	9 TO 12	688	693	15.1	20.5	33.5	72	15.4	38.2
			13 TO 16	247	247	15.3	20.9	32.0	45	16.8	31.1
AlP	U/l	M01	9 TO 12	688	693	34.8	57.9	101.7	72	34.7	92.2
			13 TO 16	247	247	26.2	41.0	71.8	45	28.4	64.8
GGT	U/l	M01	9 TO 12	544	549	0.0	0.0	0.0	57	0.0	0.3
			13 TO 16	194	194	0.0	0.0	0.0	34	0.0	0.2
GLDH	U/l	M01	9 TO 12	125	125	4.1	5.8	9.1	15	4.6	8.2
			13 TO 16	50	50	3.6	5.1	17.7	9	4.8	13.2
CK	U/l	M01	9 TO 12	394	399	95.2	143.1	288.4	43	116.1	422.1
			13 TO 16	134	134	87.9	120.5	241.7	26	106.1	222.5
LDH	U/l	M01	9 TO 12	394	399	76.4	123.7	233.0	43	79.8	276.2
			13 TO 16	124	124	70.3	119.8	190.3	25	78.7	203.9

1.10 REFERENCE VALUES - URINE ANALYSIS

SPECIES RAT
STRAIN HanBrl:WIST(SPF)
SUPPLIER RCC Ltd.
STUDY TYPE [ALL]
DOSE ROUTE [ALL]
DATES: [ALL]

MALE

PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES N	5%	MEDIAN	95%	RANGE OF STUDY MEANS N	MIN	MAX
Volume	ml	M01	9 TO 12	636	641	1.7	5.5	11.1	62	1.8	10.7
			13 TO 16	237	237	1.5	4.9	10.4	44	1.6	10.3
Rel dens	rel. 1	M01	9 TO 12	636	641	1.025	1.042	1.094	62	1.030	1.093
			13 TO 16	237	237	1.027	1.043	1.090	44	1.032	1.098
pH		M01	9 TO 12	635	640	6.0	6.5	7.0	62	5.6	7.4
			13 TO 16	237	237	6.0	6.5	7.0	44	5.7	7.1
NIT	Score	M01	9 TO 12	296	301	0.	0.	1.	28	0.	1.
			13 TO 16	104	104	0.	0.	1.	21	0.	1.
PRO	g/l	M01	9 TO 12	635	640	0.25	0.25	0.75	62	0.13	0.85
			13 TO 16	237	237	0.25	0.25	0.75	44	0.20	1.05
GLU	mmol/l	M01	9 TO 12	635	640	0.	0.	0.	62	0.	0.
			13 TO 16	237	237	0.	0.	0.	44	0.	0.
KET	mmol/l	M01	9 TO 12	635	640	0.0	0.5	1.5	62	0.1	2.0
			13 TO 16	237	237	0.0	0.5	1.5	44	0.2	2.2
UBG	µmol/l	M01	9 TO 12	635	640	0.	0.	17.	62	0.	15.
			13 TO 16	237	237	0.	0.	17.	44	0.	24.
BIL	µmol/l	M01	9 TO 12	635	640	0.	0.	17.	62	0.	14.
			13 TO 16	237	237	0.	0.	17.	44	0.	17.
ERY	per µl	M01	9 TO 12	635	640	0.	10.	25.	62	2.	54.
			13 TO 16	237	237	0.	10.	25.	44	2.	61.
LEU	per µl	M01	9 TO 12	635	640	0.	25.	100.	62	11.	85.
			13 TO 16	237	237	0.	25.	100.	44	0.	85.

Reference values - Urine analysis

SPECIES RAT
STRAIN HanBrl:WIST(SPF)
SUPPLIER RCC Ltd.
STUDY TYPE [ALL]
DOSE ROUTE [ALL]
DATES: [ALL]

FEMALE

PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES N	5%	MEDIAN	95%	RANGE OF STUDY MEANS N	MIN	MAX
Volume	ml	M01	9 TO 12	632	637	1.3	4.2	8.2	61	1.6	16.0
			13 TO 16	237	237	1.1	4.1	9.7	44	1.2	9.3
Rel dens	rel. 1	M01	9 TO 12	632	637	1.026	1.043	1.094	61	1.029	1.095
			13 TO 16	237	237	1.023	1.042	1.084	44	1.029	1.089
pH		M01	9 TO 12	631	636	5.0	6.0	7.0	61	5.3	7.1
			13 TO 16	237	237	5.0	6.0	7.0	44	5.3	6.9
NIT	Score	M01	9 TO 12	298	303	0.	0.	1.	28	0.	0.
			13 TO 16	104	104	0.	0.	0.	21	0.	0.
PRO	g/l	M01	9 TO 12	631	636	0.00	0.25	0.75	61	0.08	0.65
			13 TO 16	237	237	0.00	0.25	0.75	44	0.05	0.75
GLU	mmol/l	M01	9 TO 12	631	636	0.	0.	0.	61	0.	0.
			13 TO 16	237	237	0.	0.	0.	44	0.	0.
KET	mmol/l	M01	9 TO 12	631	636	0.0	0.5	1.5	61	0.0	1.0
			13 TO 16	237	237	0.0	0.5	1.5	44	0.0	1.3
UBG	µmol/l	M01	9 TO 12	631	636	0.	0.	17.	61	0.	10.
			13 TO 16	237	237	0.	0.	17.	44	0.	20.
BIL	µmol/l	M01	9 TO 12	631	636	0.	0.	17.	61	0.	12.
			13 TO 16	237	237	0.	0.	17.	44	0.	17.
ERY	per µl	M01	9 TO 12	631	636	0.	10.	25.	61	0.	19.
			13 TO 16	237	237	0.	10.	25.	44	0.	25.
LEU	per µl	M01	9 TO 12	631	636	0.	25.	25.	61	0.	44.
			13 TO 16	237	237	0.	0.	25.	44	0.	60.

APPENDIX V:

ANALYSIS OF DOSE FORMULATIONS

ANALYTICAL PHASE REPORT

Study Title:

TKA 40291 (ZLI 3331):
28-DAY ORAL TOXICITY (GAVAGE) STUDY IN THE WISTAR RAT

Title of Analytical Phase:

Determination of Concentration, Homogeneity and Stability of TKA 40291 (ZLI 3331) in PEG 300

Study Director:

W. H. Braun (RCC Ltd, Toxicology, Itingen)

Principal Investigator Analytical Phase:

Dr. D. Flade

Completion Date of Analytical Phase Report:

October 23, 2003

Test Site:

RCC Ltd
Environmental Chemistry & Pharmanalytics
CH-4452 Itingen/Switzerland

RCC Study No.:

848174

GOOD LABORATORY PRACTICE

STATEMENT OF COMPLIANCE

RCC Study Number :	848174
Study Director :	W. H. Braun, RCC Ltd, Toxicology, Itingen / Switzerland
Test Item :	TKA 40291 (ZLI 3331)
Principal Investigator Analytical Phase :	Dr. D. Flade
Title of Analytical Phase :	Determination of Concentration, Homogeneity, and Stability of TKA 40291 (ZLI 3331) in PEG 300

The analytical phase has been performed in compliance with the Swiss Ordinance relating to Good Laboratory Practice, adopted February 2nd, 2000 [RS 813.016.5]. This Ordinance is based on the OECD Principles of Good Laboratory Practice, as revised in 1997 and adopted November 26th, 1997 by decision of the OECD Council [C(97)186/Final].

Principal Investigator
Analytical Phase: Dr. D. Flade

D. Flade
.....
Date: October, 23, 2003

SIGNATURES

Principal Investigator
Analytical Phase: Dr. D. Flade

D. Flade
.....
Date: October 23, 2003

Management: Dr. J. Schreitmüller

J. Schreitmüller
.....
Date: October 23, 2003

QUALITY ASSURANCE UNIT

RCC Ltd, Environmental Chemistry & Pharmanalytics, CH-4452 Itingen / Switzerland

STATEMENT

RCC Study Number :	848174
Study Director :	W. H. Braun, RCC Ltd, Toxicology, Itingen / Switzerland
Test Item :	TKA 40291 (ZLI 3331)
Principal Investigator Analytical Phase :	Dr. D. Flade
Title of Analytical Phase :	Determination of Concentration, Homogeneity, and Stability of TKA 40291 (ZLI 3331) in PEG 300

The general facilities and activities are inspected periodically and the results are reported to the responsible person and the management.

Study procedures were periodically inspected and this analytical phase report was audited by the Quality Assurance Unit. The dates are given below.

Dates and Types of QAU Inspections		Dates of Reports to the Principal Investigator Analytical Phase and to the Management*
June 04, 2003	Process based (Analytical work)	June 04, 2003
August 11, 2003	Final analytical phase report	August 11, 2003

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

* A summary report of study related inspections (if applicable) was issued to the study director, lead QA and test facility management.

Quality Assurance: for H. Schneylin

D. Bohnz

Date: October 23, 2003

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PREFACE

GENERAL

Title of Analytical Phase:	Determination of Concentration, Homogeneity, and Stability of TKA 40291 (ZLI 3331) in PEG 300
Sponsor:	Ciba Specialty Chemicals Inc. Segment Coating Effects P.O. Box, WRO-1045.1.35 CH-4002 Basel / Switzerland
Study Director: (Test Facility)	W H. Braun RCC Ltd Toxicology CH-4452 Itingen / Switzerland
Test Site:	RCC Ltd Environmental Chemistry & Pharmanalytics Zelgliweg 1 CH-4452 Itingen / Switzerland

RESPONSIBILITIES

Principal Investigator Analytical Phase:	Dr. D. Flade
Head of RCC Quality Assurance:	I. Wüthrich

SCHEDULE OF ANALYTICAL PHASE

Experimental Starting Date:	April 29, 2003
Experimental Completion Date:	July 02, 2003
Completion Date of Analytical Phase Report:	October 23, 2003

ARCHIVING

RCC Ltd, CH-4452 Itingen/Switzerland will retain a copy of the study plan, the raw data, and the analytical phase report of the present study for at least ten years. No data will be discarded without the sponsor's consent.

1 PURPOSE

This phase report describes the analytical method employed and the results obtained for concentration, homogeneity, and stability of TKA 40291 (ZLI 3331) in PEG 300. The analyses were performed by a HPLC method.

Analysis of homogeneity was performed by analysing samples of each dose group from three different segments (top, middle, bottom) of the respective mixing container.

Evaluation of stability was performed by analysing samples of each dose group over storage periods of two hours and seven days at room temperature and protected from light.

2 MATERIALS AND METHODS

2.1 TEST ITEM

Detailed information on the test item TKA 40291 (ZLI 3331) as used for analytical purposes is given in the toxicology report.

2.2 SAMPLE PREPARATION AND STORAGE

Test item/vehicle mixtures were prepared by RCC Ltd, Toxicology, Itingen and about 2 g (weighed to the third decimal place) of each mixture was delivered to the analytical laboratory of RCC Ltd, Environmental Chemistry & Pharmanalytics. These samples for analysis of concentration and homogeneity were stored deep-frozen (about -20 °C) until analysis. Storage stability samples were collected after storage periods of two hours and seven days at room temperature and protected from light. These samples were delivered to the analytical laboratory where they were stored deep-frozen until analysis.
Additional samples were prepared by RCC Ltd, Environmental Chemistry and Pharmanalytics, Itingen for further testing of the analytical method and stability of dose formulations. Storage conditions changed according to purposes. Detailed information is given in the raw data.

2.3 ANALYTICAL PROCEDURE

2.3.1 Reagents

Aceton:	Baker no. 9254
Toluol:	Merck no. 8389
Polyethylenglycol (PEG 300):	Fluka no. 81160

2.3.2 Standard Solutions

Stock solutions of the test item in Toluene with concentrations in the range from 216 µg/mL to 297 µg/mL and in Acetone with concentrations in the range from 220 µg/mL to 257 µg/mL were prepared by weighing appropriate amounts of the test item accurately into 100-mL volumetric flasks. Then, about 70 mL of purified water was added to each volumetric flask and dissolution was achieved using an ultrasonic bath. The flasks were filled to the mark with Toluene and Acetone, respectively. Finally, various standard solutions were prepared by respective dilution of these stock solutions with Toluene or Acetone to yield concentrations in the range from 0.794 µg/mL to 148.7 µg/mL. These standard solutions as well as the stock solutions were used for calibration of the HPLC.

2.3.3 Analysis of Samples

The delivered and slef-prepared samples were dissolved in about 70 mL of Toluene or Acetone using an ultrasonic bath. Then, the 100-mL volumetric flasks were filled to the mark with Toluene or Acetone. Depending on the dose group, the latter sample solutions were further diluted with Toluene or Acetone to yield concentrations within the calibration range. Finally, a defined aliquot was quantified by HPLC.

2.3.4 Gas Chromatographic Determination

Apparatus:	Hewlett Packard 6890 Series and HP Chemstation Version G 2070 AA
Column:	DB-5, 17 m x 0.53 mm, 1.5 µm film thickness
Carrier gas:	Helium, 2.5 mL/min
Temperatures:	Injector: Oven track on Detector: 340 °C Oven: 95 °C for 1 min at 10 °C/min to 220 °C 220 °C for 6.5 min at 30 °C/min to 325 °C 325 °C for 10 min
Injection:	1 µl, on column
Detector:	FID

2.3.5 Evaluation of Results

Injected samples were quantified by the peak areas (counts) of the test item with reference to the calibration curve. The latter was obtained by correlation of the peak areas of the standard solutions with their corresponding concentrations (µg/mL), using the following equation 1 or 2:

$$Y = a + b \cdot X \qquad (1)$$

where

Y = Peak areas of test item in injected sample [counts]
a = Y-axis intercept
b = Slope
X = Concentration of test item in injected sample [µg/mL]

or

$$Y = a \cdot X^{b} \qquad (2)$$

where

Y = Peak area of test item in injected sample [counts]
a = Constant factor
b = Exponent
X = Concentration of test item in injected sample [µg/mL]

The concentrations of test item in vehicle were calculated according to equation 3:

$$C = \frac{X \cdot V \cdot D \cdot Q}{W \cdot 1000} \qquad (3)$$

where

C = Concentration of test item in vehicle [mg/mL]
X = Concentration of test item in injected sample calculated by equation 1 [µg/mL]
V = Final volume [mL]
D = Dilution factor
Q = Density of test item/vehicle mixtures [1.12 g/mL; as provided by the supplier]
W = Weight of sample [about 2 g, weighed to the third decimal place]

3 RESULTS

This chemical analysis determined concentration, homogeneity, and stability of TKA 40291 (ZLI 3331) in Polyethylene glycol (PEG 300).

The analysis of TKA 40291 in PEG 300 with the method, delivered by the sponsor, caused some implementation problems at RCC, naming blockage of column by PEG 300 (assumed) and separation of the test item peak from matrix peaks. These problems were solved and the reproducibility of peak areas was improved. An example of a calibration curve is shown in Table 1.

Although the development of a suitable analytical method was successful, inconsistent results were obtained within the Range-finding study (RCC-Study-no. 848175) performed before (see Table 2) and within this study with the first samples taken after experimental start (see Table 3).

To confirm the right preparation procedure of samples at the toxicology and to test the freezing stability (approx. – 20°C) of dose formulations, samples were prepared freshly and were partially stored deep-frozen for 24 hours. The analytical results showed a good recovery for the two unfrozen samples with 103.5% and 92.0%, but for the frozen samples the recovery was found to be 10.0% and 5.2% (see Table 4). Thus, the dose formulations are asumed to be not stable at – 20°C, which were the storage conditions for all samples, taken at the toxicology for analytical purposes. Additionally, the results for the 0 hours-samples showed that the application mixtures can be prepared correctly under light protection.

As it is mentioned in the study plan, the application mixtures were stored at ambient temperature in light-protected containers at the toxicology site. Hence, it was tried to approve with freshly in the analytical laboratory prepared samples with concentrations of 10 mg/mL and 200 mg/mL, whether the application mixtures are stable for 7 days under light protection at 4°C. The results obtained show a fast degradation rate for the test item in PEG 300 within hours and that the dose formulations are not stable under these conditions for one week (see Table 5).

In conclusion, the mixtures applicated within the toxicity study contained for the most part degradation products of the test item.

For the preparation of dose formulations with TKA 40291 in PEG 300 light protection seems to be very important. The stability data show, that the dose formulations should be prepared daily and analysed immediately after application.

An example of a calibration curve is shown in Table 1 and typical chromatograms of standard solutions and test samples are presented in Figures 1 and 2.

The tabulated values represent rounded-off results by calculations based on the exact raw data.

Table 1: Example of Calibration Curve

Date of analysis: July 03, 2003

Concentrations (µg/mL)	Peak area (counts)	Concentration corrected (µg/mL)	Peak area corrected (counts)	Bias (%)
6.60	5059	6.30	5427	-7.3%
11.0	10034	10.4	10737	-7.0%
22.0	22406	20. 7	24011	-7.2%
44.0	54328	47.1	50559	6.9%
66.0	79152	67.7	77107	2.6%
7.10	6542	7.52	6028	7.9%
11.8	12968	12.9	11738	9.5%
23.7	24470	22.4	26014	-6.3%
71.0	79777	68.2	83116	-4.2%

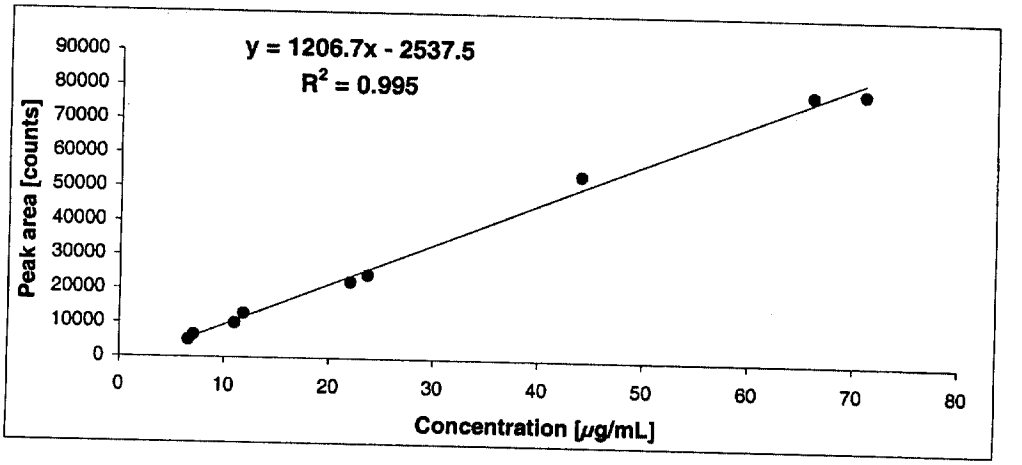


Table 2: Concentration, Homogeneity, and Stability of Test Item in Vehicle (RCC Study no. 848175)

Dose Group	Nominal Conc. (mg/mL)	T M B	Time of Storage[1]	Date of Analysis	Concentration Found			
					(mg/mL)	% of Nom.	Mean % of Nom.	± Dev. in % of Mean
Date of Preparation: 21-MAR-03 (RCC Study no. 848175)								
1	---	--	0 h	25-APR-03	0.00	---	---	---
2	40	T M B	0 h 0 h 0 h	25-APR-03 25-APR-03 25-APR-03	46.87 41.01 45.85	117.2 102.5 114.6	111.4	-8/+5
		--	2 h 7 d	25-APR-03 25-APR-03	22.82 33.99	57.1* 85.0	---	---
3	120	T M B	0 h 0 h 0 h	25-APR-03 25-APR-03 25-APR-03	103.7 83.9 99.4	86.4 69.9* 82.8	79.7	-12/+8
		--	2 h 7 d	25-APR-03 25-APR-03	100.9 75.6	84.0 63.0*	---	---
4	200	T M B	0 h 0 h 0 h	25-APR-03 25-APR-03 25-APR-03	181.1 172.2 188.5	90.5 86.1 94.3	90.3	-5/+4
		--	2 h 7 d	25-APR-03 25-APR-03	181.3 136.2	90.7 68.1*	---	---

T/M/B: Top/Middle/Bottom (segment of mixing container)
h/d: hours/days
1 Under storage conditions
* Results were approved by repeated analysis

Table 3: Concentration, Homogeneity, and Stability of Test Item in Vehicle

Dose Group	Nominal Conc. (mg/mL)	T M B	Time of Storage[1]	Date of Analysis	Concentration Found			
					(mg/mL)	% of Nom.	Mean % of Nom.	± Dev. in % of Mean
Date of Preparation: 07-APR-03								
1	---	--	0 h	29-APR-03	0.00	---	---	---
2	10	T M B	0 h 0 h 0 h	29-APR-03 29-APR-03 29-APR-03	18.43 9.351 8.504	184.3 93.5 85.0	121.0	-30/+52
		--	2 h 7 d	29-APR-03 29-APR-03	6.130 4.058	61.3 40.6	---	---
3	40	T M B	0 h 0 h 0 h	29-APR-03 29-APR-03 29-APR-03	17.4 15.6 11.3	43.6 38.9 28.2	36.9	-24/+18
		--	2 h 7 d	29-APR-03 29-APR-03	5.97 5.29	14.9 13.2	---	---
4	200	T M B	0 h 0 h 0 h	29-APR-03 29-APR-03 29-APR-03	87.6 82.1 87.3	43.8 41.0 43.6	42.8	-4/+2
		--	2 h 7 d	29-APR-03 29-APR-03	0.00 0.00	0 0	---	---

T/M/B: Top/Middle/Bottom (segment of mixing container)
h/d: hours/days
1 Under storage conditions

Table 4: 24 h-Freezing Stability of Test Item in Vehicle

Dose Group	Nominal Conc. (mg/mL)	TMB	Time of Storage[1]	Date of Analysis	Concentration Found			
					(mg/mL)	% of Nom.	Mean % of Nom.	± Dev. in % of Mean
Date of Preparation: 18-JUN-03								
1	5.18	--	0 h	18-JUN-03	5.359	103.5	---	---
			0 h	18-JUN-03	4.765	92.0		
	5.18	--	24 h	19-JUN-03	0.520	10.0	---	---
			24 h	19-JUN-03	0.269	5.2		

Table 5: Concentration, Homogeneity, and Stability of Test Item in Vehicle

Dose Group	Nominal Conc. (mg/mL)	T M B	Time of Storage[1]	Date of Analysis	Concentration Found			
					(mg/mL)	% of Nom.	Mean % of Nom.	± Dev. in % of Mean
Date of Preparation: 24-JUN-03								
1	---	--	0 h	03-JUL-03	0.00	---	---	---
2	5.405	T M B	0 h 0 h 0 h	03-JUL-03 03-JUL-03 03-JUL-03	5.30 1.98 1.98	98.0 36.6 36.7	57.1	n. a.
		--	2 h 7 d	03 JUL-03 03-JUL-03	1.05 0.63	19.4 11.7	---	---
4	200.1	T M B	0 h 0 h 0 h	03-JUL-03 03-JUL-03 03-JUL-03	173.6 134.1 127.5	86.7 67.0 63.7	72.5	n. a.
		--	2 h 7 d	03-JUL-03 03-JUL-03	107.4 97.2	53.7 48.6	---	---

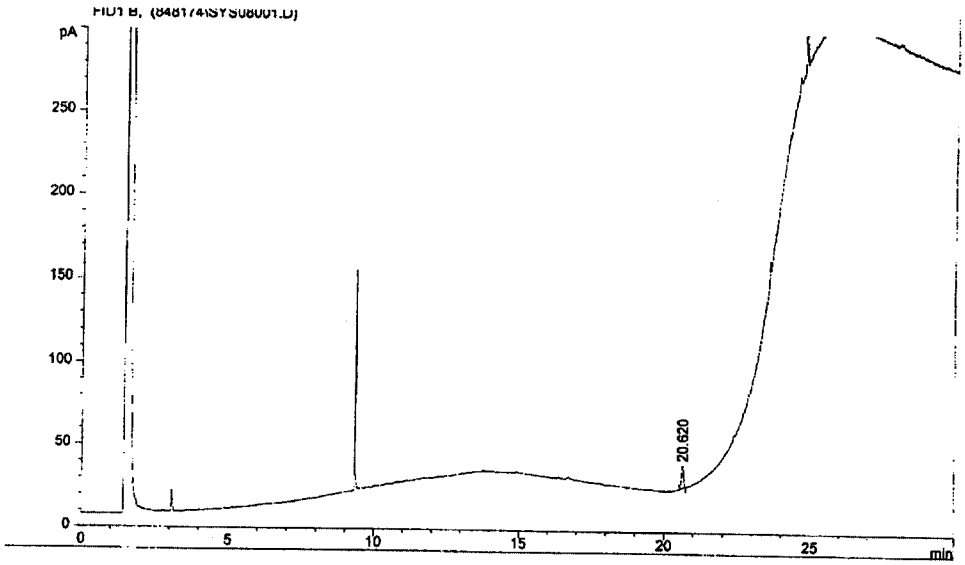
T/M/B: Top/Middle/Bottom (segment of mixing container)
h/d: hours/days
1 Under storage conditions

Figure 1: Typical Chromatograms of Standard Solutions

(A) Standard solution: 6.60 μg/mL
(B) Standard solution: 66.0 μg/mL

Date of analysis: July 03, 2003

(A)



(B)

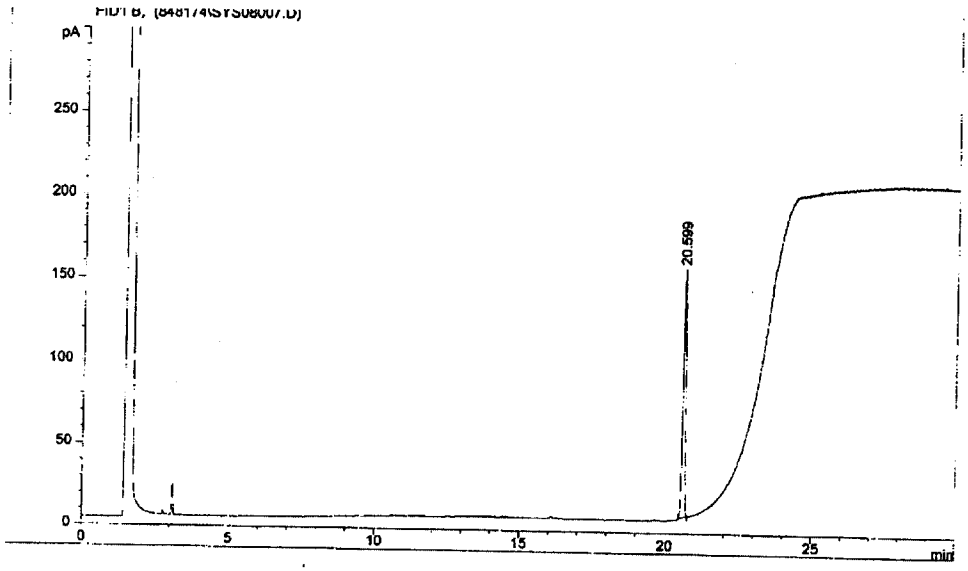
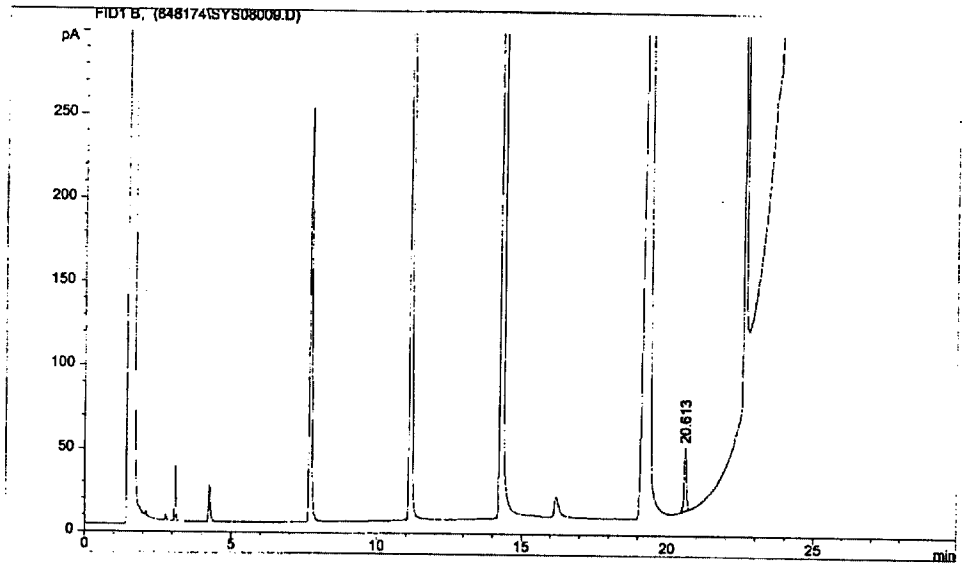


Figure 2: Typical Chromatograms of Test Samples

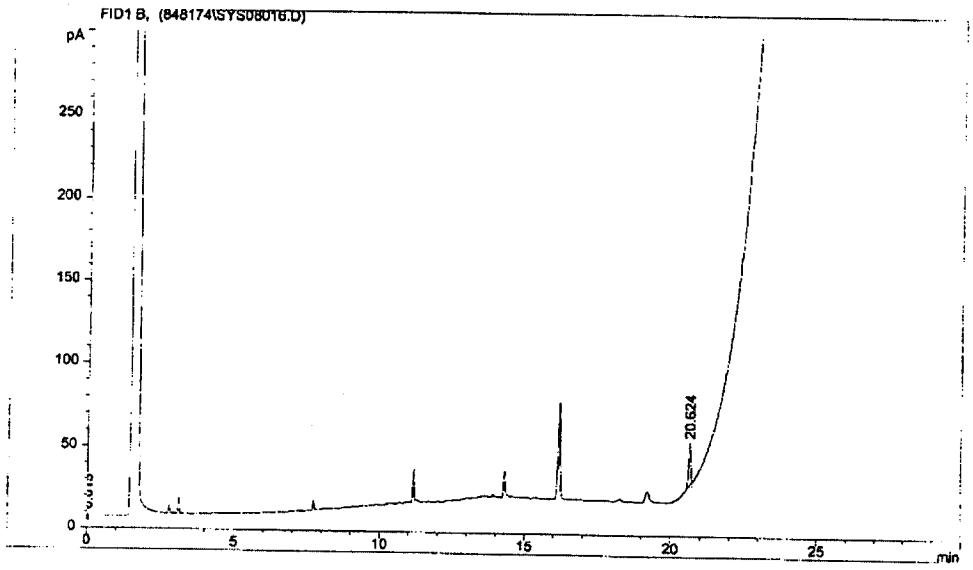
(A) Dose group 2 (top), nominal concentration: 5.4 mg/mL, 5x diluted
(B) Dose group 4 (top), nominal concentration: 200.1 mg/mL, 200x diluted

Date of analysis: July 03, 2003

(A)



(B)



APPENDIX VI:

PATHOLOGY REPORT

PATHOLOGY REPORT		RCC STUDY NUMBER 848174	
TEST ITEM	: TKA 40291 (ZLI 3331)	PATH. NO	: 70009 BBA
TEST SYSTEM	: Rat	DATE	: 23-OCT-03
STUDY TYPE	: Oral (Gavage)	SPONSOR	: Ciba Specialty Chemicals

Prepared by:

Dr. Annamaria Braendli-Baiocco, Pathologist FVH
Veterinary Pathologist

TEST ITEM	: TKA 40291 (ZLI 3331)	PATH. NO.	: 70009 BBA
TEST SYSTEM	: Rat, Oral (Gavage)	DATE	: 23-OCT-03
SPONSOR	: Ciba Specialty Chemicals		

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[1] Animal organ finding table

TEST ITEM	: TKA 40291 (ZLI 3331)	PATH. NO.	: 70009 BBA
TEST SYSTEM	: Rat, Oral (Gavage)	DATE	: 23-OCT-03
SPONSOR	: Ciba Specialty Chemicals		

Authentication

I, the undersigned hereby declare that the histopathology data (Principal Section and Tables) in this report were compiled by me, and that they accurately reflect the primary data records.

Prepared by:

Dr. A. Braendli-Baiocco, Pathologist FVH
Veterinary Pathologist

for .....
Date: October 23, 2003

Cross-checked by:

Dr. Ph. Schaetti
Toxicologic Pathologist

Ph. Schaetti
.....
Date: October 23, 2003

TEST ITEM	: TKA 40291 (ZLI 3331)	PATH. NO.	: 70009 BBA
TEST SYSTEM	: Rat, Oral (Gavage)	DATE	: 23-OCT-03
SPONSOR	: Ciba Specialty Chemicals		

SUMMARY

The purpose of this oral toxicity study was to assess the cumulative toxicity of TKA 40291 (ZLI 3331) when administered daily to rats by gavage for a period of 28 days.

Forty rats were assigned to four dose groups for further pathological examination, each group containing five animals per sex. The animals received the test item once daily by gavage at the dose of 0, 50, 200, 1000 mg/kg body weight (groups 1, 2, 3 and 4) for 28 days (allocation A). The control animals of group 1 received only the vehicle. In addition, five rats per sex were assigned, respectively, to group 1 and 4, for a 14-day recovery period following the treatment period (allocation B).

At the end of the treatment and recovery periods, all animals were sacrificed, necropsied and examined post mortem. Histological examination was performed on all tissues selected in the study plan from all rats of groups 1 and 4, as well as on liver and stomach of all animals, bone marrow of female and adrenal glands of male animals.

There were no unscheduled deaths.

At the end of the 28-day treatment period the following mean organ weights were increased: absolute liver weight in females at 1000 mg/kg, liver weight relative to body weight in males and female at 1000 mg/kg, liver weight relative to brain weight in females at 1000 mg/kg as well as kidney and adrenal gland weight relative to body weight in males at 1000 mg/kg.

At the end of the 14-day recovery period, the absolute and relative liver weight relative to body weight were decreased in males at 1000 mg/kg.

At necropsy, at the end of the 28-day treatment period, the mucosa of the forestomach presented with an irregular surface in all animals administered with TKA 40291 (ZLI 3331) at 1000 mg/kg.

At microscopic examination, TKA 40291 (ZLI 3331) produced morphologic changes in male and female forestomach, glandular stomach and liver as well as in male adrenal glands.

In the forestomach squamous cell hyperplasia and hyperkeratosis were observed in all treated animals. These findings were still present after the 14-day recovery period, but their severity was decreased. In addition, in the forestomach of females at 1000 mg/kg erosion or ulceration were observed. These findings were reversible after the 14-day recovery period.

The glandular stomach showed diffuse epithelial hyperplasia in males and females at 1000 mg/kg. This finding was reversible after the recovery period.

In the adrenal glands, cortical fatty change were increased in incidence and severity in males at 1000 mg/kg. This finding was reversible after the 14-day recovery period.

Glycogen deposition was decreased in animals at 1000 mg/kg after the 14-day recovery period.

TEST ITEM	: TKA 40291 (ZLI 3331)	PATH. NO.	: 70009 BBA
TEST SYSTEM	: Rat, Oral (Gavage)	DATE	: 23-OCT-03
SPONSOR	: Ciba Specialty Chemicals		

Based on the results of pathology, the No-Observed-Effect-Level (NOEL) for TKA 40291 (ZLI 3331) could not be established.

TEST ITEM	: TKA 40291 (ZLI 3331)	PATH. NO.	: 70009 BBA
TEST SYSTEM	: Rat, Oral (Gavage)	DATE	: 23-OCT-03
SPONSOR	: Ciba Specialty Chemicals		

MATERIALS AND METHODS

Group Allocation

	Group 1* 0 mg/kg/day	Group 2 50 mg/kg/day	Group 3 200 mg/kg/day	Group 4 1000 mg/kg/day
Males A	1 - 5	11 - 15	16 - 20	21 - 25
Males B	6 – 10			26 - 30
Females A	31 – 35	41 - 45	46 - 50	51 - 55
Females B	21 – 26			56 - 60

A - Toxicity testing (termination after 28 treatment days)

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

* - Control animals received vehicle only

Necropsy and Histopathology

Necropsies and histological preparation of the tissues were performed at RCC Ltd, Itingen / Switzerland.

Paraffin sections were stained with hematoxylin & eosin and examined by light microscope. From all groups 1 and 4 allocation A and B animals, the following sections were examined:

Adrenal glands
Bone marrow (femur)
Brain (cerebrum, cerebellum, pons)
Cecum
Colon
Duodenum
Epididymides
Heart
Ileum, with Peyer's patches
Jejunum, with Peyer's patches
Kidneys
Liver
Lungs
Lymph nodes - mesenteric, mandibular
Ovaries
Prostate gland
Rectum
Sciatic nerve
Seminal vesicles
Spinal cord - cervical, midthoracic, lumbar
Spleen
Stomach
Testes
Thymus
Thyroid incl. parathyroid gland
Trachea
Urinary bladder
Uterus
Vagina
Gross lesions

Because of possible test-item related findings noted in animals of group 4, to establish a no-effect level, liver and stomach of all animals as well as bone marrow of female and adrenal glands of male animals were processed and submitted to microscopic examination.

TEST ITEM	: TKA 40291 (ZLI 3331)	PATH. NO.	: 70009 BBA
TEST SYSTEM	: Rat, Oral (Gavage)	DATE	: 23-OCT-03
SPONSOR	: Ciba Specialty Chemicals		

Data Compilation

The animal data and necropsy findings were transferred electronically via transfer file into the PathData System V6.1b5.

The microscopic findings were directly entered into the PathData during the microscopy sessions. The slides were evaluated during June 2003.

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". In paired organs, findings occurred sometimes bilaterally and were of different degrees of severity. When this occurred, the higher degree was recorded.

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 macroscopic and microscopic findings.

Data Cross Checking

Stomach and liver of male and female animals as well as adrenal glands of male and bone marrow of female animals were reviewed by Dr. Ph. Schaetti (RCC Itingen, Department of Pathology). The assessment of the study pathologist and reviewing pathologist compared favorably.

TEST ITEM	: TKA 40291 (ZLI 3331)	PATH. NO.	: 70009 BBA
TEST SYSTEM	: Rat, Oral (Gavage)	DATE	: 23-OCT-03
SPONSOR	: Ciba Specialty Chemicals		

RESULTS

Mortality

There were no unscheduled deaths.

Organ weights

The following mean organ weights were increased after the 28-day treatment period:

Liver: absolute in females at 1000 mg/kg, relative to body weight in males and females at 1000 mg/kg and relative to brain weight in females at 1000 mg/kg.

Kidneys: relative to body weight in males at 1000 mg/kg.

Adrenal glands: relative to body weight in males at 1000 mg/kg.

The absolute and relative liver weight relative to body weight was decreased in males at 1000 mg/kg after the 14-day recovery period.

Macroscopic Findings

After the 28-day treatment period, the mucosa of the forestomach presented with irregular surface in all animals treated at 1000 mg/kg.

A few other macroscopic findings were observed in this study. They occurred in low number in various experimental groups and were similar to those occurring spontaneously in laboratory rats of this strain and age. Thus, no experimental relevance is attributed to these findings.

Microscopic Findings

The detailed incidence data for all organs and tables of selected changes including their severity appear in the tables "NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX" and "SUMMARY INCIDENCE OF GRADING BY ORGAN/SEX/GROUP".

Forestomach

Squamous cell hyperplasia and hyperkeratosis were observed in all treated animals. Squamous cell hyperplasia was minimal in males and females at 50 and in males at 200 mg/kg, minimal to slight in females at 200 mg/kg and moderate to marked in males and females at 1000 mg/kg. Hyperkeratosis was minimal to slight in males and females at 50 and 200 mg/kg and moderate to marked in males and females at 1000 mg/kg. These findings were still present after the 14-day recovery period, but their severity was decreased.

In addition, erosion or ulceration of the mucosa were observed in females at 1000 mg/kg.

TEST ITEM	: TKA 40291 (ZLI 3331)	PATH. NO.	: 70009 BBA
TEST SYSTEM	: Rat, Oral (Gavage)	DATE	: 23-OCT-03
SPONSOR	: Ciba Specialty Chemicals		

Glandular stomach

Minimal to slight diffuse epithelial hyperplasia was observed in males and females at 1000 mg/kg. This finding was reversible after the 14-day recovery period.

Adrenal glands

Cortical fatty change was slightly increased in incidence and severity in males at 1000 mg/kg. No differences were seen between control and treated males after the 14-day recovery period.

Liver

Glycogen deposition was slightly decreased in incidence and grading in males and females at 1000 mg/kg after the 14-day recovery period.

Incidental microscopic findings

Mineralization was observed in the Peyer's patches of males at 1000 mg/kg. This finding is known to occur spontaneously and therefore it is considered incidental.

Fatty atrophy of minimal to slight degree was observed in bone marrow of females at 1000 mg/kg after the 14-day recovery period. Since no changes were observed in the other treated groups, this finding was considered incidental.

A variety of other changes was found in this study. They commonly occur in laboratory rats of this strain and age, and, neither their incidences nor their distribution or morphologic appearance gave any indication of a test item-related association.

TEST ITEM	: TKA 40291 (ZLI 3331)	PATH. NO.	: 70009 BBA
TEST SYSTEM	: Rat, Oral (Gavage)	DATE	: 23-OCT-03
SPONSOR	: Ciba Specialty Chemicals		

CONCLUSIONS

Under the condition of this experiment, the test item TKA 40291 (ZLI 3331) produced morphological changes in male and female forestomach, glandular stomach, liver as well as in male adrenal glands.

The effect on forestomach consisted in squamous cell hyperplasia and hyperkeratosis of the epithelium in males and females of all treated groups. These findings correlated with the irregular surface of the forestomach reported at necropsy in all animals treated at 1000 mg/kg. These findings were still present after the 14-day recovery period, but their severity was decreased. In addition, in the forestomach of females at 1000 mg/kg erosion or ulceration were observed. These findings were reversible after the 14-day recovery period.

The glandular stomach showed diffuse epithelial hyperplasia in males and females at 1000 mg/kg. This finding was reversible after the recovery period.

Glycogen deposition was decreased in liver of animals of either sex at 1000 mg/kg after the 14-day recovery period. This finding correlates with the decreased liver weight observed in the males of this group.

Adrenal cortical fatty change was increased in males at 1000 mg/kg. This correlate with the increased average relative adrenal gland weight observed in the males of this group. This finding was reversible after the 14-day recovery period.

Based on the results of pathology, the No-Observed-Effect-Level (NOEL) for TKA 40291 (ZLI 3331) could not be established.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

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
* = Comment in text of individual animal data
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
GRADE 4 = Marked / many / large
P = Finding present, severity not scored
(= Finding unilateral in paired organs
* = Comment in text of individual animal data

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0
TEST ITEM-RELATED FINDINGS

SEX :					MALE
DOSE GROUP:	1	2	3	4	
NO.ANIMALS:	5	5	5	5	
ADRENAL GLANDS :	5	5	5	5	
- CHANGE FATTY CORT.					
GRADE 1 :	2	3	2	2	
GRADE 2 :	-	-	-	2	
TOTAL AFFECTED :	2	3	2	4	
MEAN SEVERITY :	1.0	1.0	1.0	1.5	
FORESTOMACH :	5	5	5	5	
- HYPERPLAS. SQUAMOUS					
GRADE 1 :	-	3	5	-	
GRADE 3 :	-	-	-	1	
GRADE 4 :	-	-	-	4	
TOTAL AFFECTED :	-	3	5	5	
MEAN SEVERITY :	-	1.0	1.0	3.8	
- HYPERKERATOSIS					
GRADE 1 :	2	3	4	-	
GRADE 2 :	-	1	1	-	
GRADE 3 :	-	-	-	2	
GRADE 4 :	-	-	-	3	
TOTAL AFFECTED :	2	4	5	5	
MEAN SEVERITY :	1.0	1.3	1.2	3.6	
GLANDULAR STOMACH :	5	5	5	5	
- HYPERPLAS.EPITHELIAL					
GRADE 1 :	-	-	-	4	
TOTAL AFFECTED :	-	-	-	4	
MEAN SEVERITY :	-	-	-	1.0	

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0
TEST ITEM-RELATED FINDINGS

FEMALE

SEX :				
DOSE GROUP:	1	2	3	4
NO.ANIMALS:	5	5	5	5
ADRENAL GLANDS :	5	-	-	5
- CHANGE FATTY CORT.				
GRADE 1 :	1	-	-	1
TOTAL AFFECTED :	1	-	-	1
MEAN SEVERITY :	1.0	-	-	1.0
FORESTOMACH :	5	5	5	5
- HYPERPLAS. SQUAMOUS				
GRADE 1 :	1	5	4	-
GRADE 2 :	-	-	1	-
GRADE 3 :	-	-	-	4
GRADE 4 :	-	-	-	1
TOTAL AFFECTED :	1	5	5	5
MEAN SEVERITY :	1.0	1.0	1.2	3.2
- HYPERKERATOSIS				
GRADE 1 :	2	2	3	-
GRADE 2 :	-	3	1	-
GRADE 3 :	-	-	-	2
GRADE 4 :	-	-	-	3
TOTAL AFFECTED :	2	5	4	5
MEAN SEVERITY :	1.0	1.6	1.3	3.6
- EROSION				
GRADE 1 :	-	-	-	1
GRADE 2 :	-	-	-	1
TOTAL AFFECTED :	-	-	-	2
MEAN SEVERITY :	-	-	-	1.5

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0
TEST ITEM-RELATED FINDINGS

SEX :					FEMALE
DOSE GROUP:	1	2	3	4	
NO.ANIMALS:	5	5	5	5	
FORESTOMACH CONT'D.	5	5	5	5	
- ULCERATION					
GRADE 2 :	-	-	-	1	
TOTAL AFFECTED :	-	-	-	1	
MEAN SEVERITY :	-	-	-	2.0	
GLANDULAR STOMACH :	5	5	5	5	
- HYPERPLAS.EPITHELIAL					
GRADE 1 :	-	-	-	4	
GRADE 2 :	-	-	-	1	
TOTAL AFFECTED :	-	-	-	5	
MEAN SEVERITY :	-	-	-	1.2	

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1
TEST ITEM-RELATED FINDINGS

SEX :					MALE
DOSE GROUP:	1	2	3	4	
NO.ANIMALS:	5	-	-	5	
ADRENAL GLANDS :	5	-	-	5	
- CHANGE FATTY CORT.					
GRADE 1 :	3	-	-	3	
GRADE 2 :	1	-	-	-	
TOTAL AFFECTED :	4	-	-	3	
MEAN SEVERITY :	1.3	-	-	1.0	
FORESTOMACH :	5	-	-	5	
- HYPERPLAS. SQUAMOUS					
GRADE 2 :	-	-	-	5	
TOTAL AFFECTED :	-	-	-	5	
MEAN SEVERITY :	-	-	-	2.0	
- HYPERKERATOSIS					
GRADE 1 :	2	-	-	-	
GRADE 2 :	-	-	-	5	
TOTAL AFFECTED :	2	-	-	5	
MEAN SEVERITY :	1.0	-	-	2.0	
LIVER :	5	-	-	5	
- DEPOS. OF GLYCOGEN					
GRADE 1 :	3	-	-	1	
GRADE 2 :	2	-	-	-	
TOTAL AFFECTED :	5	-	-	1	
MEAN SEVERITY :	1.4	-	-	1.0	

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1
TEST ITEM-RELATED FINDINGS

SEX :					FEMALE
DOSE GROUP:	1	2	3	4	
NO.ANIMALS:	5	-	-	5	
ADRENAL GLANDS :	5	-	-	5	
- CHANGE FATTY CORT.					
GRADE 1 :	3	-	-	3	
TOTAL AFFECTED :	3	-	-	3	
MEAN SEVERITY :	1.0	-	-	1.0	
FORESTOMACH :	5	-	-	5	
- HYPERPLAS. SQUAMOUS					
GRADE 2 :	-	-	-	5	
TOTAL AFFECTED :	-	-	-	5	
MEAN SEVERITY :	-	-	-	2.0	
- HYPERKERATOSIS					
GRADE 1 :	1	-	-	1	
GRADE 2 :	-	-	-	4	
TOTAL AFFECTED :	1	-	-	5	
MEAN SEVERITY :	1.0	-	-	1.8	
LIVER :	5	-	-	5	
- DEPOS. OF GLYCOGEN					
GRADE 1 :	2	-	-	2	
GRADE 2 :	3	-	-	1	
TOTAL AFFECTED :	5	-	-	3	
MEAN SEVERITY :	1.6	-	-	1.3	

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

SEX :					MALE
DOSE GROUP:	1	2	3	4	
NO.ANIMALS:	5	5	5	5	
ADRENAL GLANDS :	5	5	5	5	
- CHANGE FATTY CORT. :	2	3	2	4	
BONE MARROW :	5	-	-	5	
- ATROPHY FATTY :	1	-	-	1	
EPIDIDYMIDES :	5	-	-	5	
- INFILT. INFLAM. CELL:	1	-	-	-	
FORESTOMACH :	5	5	5	5	
- HYPERPLAS. SQUAMOUS :	-	3	5	5	
- HYPERKERATOSIS :	2	4	5	5	
GLANDULAR STOMACH :	5	5	5	5	
- HYPERPLAS.EPITHELIAL:	-	-	-	4	
KIDNEYS :	5	-	-	5	
- CHANGE HYALINE TUB. :	1	-	-	3	
- BASOPHILIA TUBULAR :	3	-	-	2	
- MINERALIZATION :	-	-	-	1	
LIVER :	5	5	5	5	
- INFILT. INFLAM. CELL:	3	3	2	3	
- CHANGE FATTY :	-	-	-	1	
LUNG :	5	-	-	5	
- MINERALIZ. VASCULAR :	2	-	-	-	
- INFILT. INFLAM. CELL:	1	-	-	-	
PARATHYROID GLANDS :	4	-	-	4	
- FIBROSIS :	-	-	-	1	
PEYER'S PATCHES :	5	-	-	5	
- MINERALIZATION :	-	-	-	3	
PROSTATE GLAND :	5	-	-	5	
- INFILT. INFLAM. CELL:	1	-	-	-	

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

SEX :					MALE
DOSE GROUP:	1	2	3	4	
NO.ANIMALS:	5	5	5	5	
SPLEEN :	5	-	-	5	
- EXMED. HEMATOPOIESIS:	4	-	-	3	
THYMUS :	5	-	1	5	
- HYPERPLAS.EPITHELIAL:	1	-	-	1	
- ATROPHY :	-	-	1	-	
THYROID GLAND :	5	-	-	5	
- HYPERTROPHY FOLLIC. :	2	-	-	1	
- ACCESSORY THYMUS :	1	-	-	-	
TRACHEA :	5	-	-	5	
- DILATATION GLANDULAR:	3	-	-	2	

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

SEX :					FEMALE
DOSE GROUP:	1	2	3	4	
NO.ANIMALS:	5	5	5	5	
ADRENAL GLANDS :	5	-	-	5	
- CHANGE FATTY CORT. :	1	-	-	1	
BONE MARROW :	5	5	5	5	
- ATROPHY FATTY :	1	-	1	1	
FORESTOMACH :	5	5	5	5	
- HYPERPLAS. SQUAMOUS :	1	5	5	5	
- HYPERKERATOSIS :	2	5	4	5	
- INFILT. INFLAM. CELL:	-	-	1	-	
- EROSION :	-	-	-	2	
- ULCERATION :	-	-	-	1	
GLANDULAR STOMACH :	5	5	5	5	
- HYPERPLAS.EPITHELIAL:	-	-	-	5	
KIDNEYS :	5	1	-	5	
- BASOPHILIA TUBULAR :	1	-	-	1	
- DILATATION PELVIC :	-	1	-	1	
- MINERALIZ.CORTICOMED:	-	1	-	-	
- MINERALIZATION :	1	-	-	-	
LIVER :	5	5	5	5	
- INFILT. INFLAM. CELL:	2	1	3	-	
- CHANGE FATTY :	-	1	-	1	
LUNG :	5	-	-	5	
- MINERALIZ. VASCULAR :	1	-	-	-	
- INFILT. LYMPHOHIST. :	1	-	-	1	
MANDIB.LYMPH NODES :	5	-	-	5	
- ATROPHY LYMPH. TISS.:	1	-	-	-	
SCIATIC NERVE, LEFT :	5	-	-	5	
- DEGENERATING FIBERS :	1	-	-	1	

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: KO

SEX :					FEMALE
DOSE GROUP:	1	2	3	4	
NO.ANIMALS:	5	5	5	5	
SPLEEN :	5	-	-	5	
- HEMOSIDEROSIS :	4	-	-	3	
- EXMED. HEMATOPOIESIS:	4	-	-	3	
THYMUS :	5	-	-	5	
- HYPERPLAS.EPITHELIAL:	1	-	-	1	
THYROID GLAND :	5	-	-	5	
- ACCESSORY THYMUS :	1	-	-	-	
TRACHEA :	5	-	-	5	
- DILATATION GLANDULAR:	1	-	-	-	
VAGINA :	5	-	-	5	
- PROESTRUS :	1	-	-	2	
- METESTRUS :	1	-	-	2	
- DIESTRUS :	3	-	-	1	

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1

SEX :					MALE
DOSE GROUP:	1	2	3	4	
NO.ANIMALS:	5	-	-	5	
ADRENAL GLANDS :	5	-	-	5	
- CHANGE FATTY CORT. :	4	-	-	3	
BONE MARROW :	5	-	-	5	
- ATROPHY FATTY :	1	-	-	-	
FORESTOMACH :	5	-	-	5	
- HYPERPLAS. SQUAMOUS :	-	-	-	5	
- HYPERKERATOSIS :	2	-	-	5	
KIDNEYS :	5	-	-	5	
- CHANGE HYALINE TUB. :	4	-	-	3	
- BASOPHILIA TUBULAR :	3	-	-	2	
- MINERALIZATION :	1	-	-	-	
- INFILT. LYMPHOHIST. :	1	-	-	-	
LIVER :	5	-	-	5	
- DEPOS. OF GLYCOGEN :	5	-	-	1	
- INFILT. INFLAM. CELL:	2	-	-	4	
LUNG :	5	-	-	5	
- MINERALIZ. VASCULAR :	1	-	-	1	
- FOAM CELLS :	-	-	-	1	
MANDIB.LYMPH NODES :	5	-	-	5	
- HYPERPL.REACT.CHR :	1	-	-	-	
PARATHYROID GLANDS :	4	-	-	3	
- FIBROSIS :	1	-	-	-	
SPLEEN :	5	-	-	5	
- EXMED. HEMATOPOIESIS:	4	-	-	5	
THYMUS :	5	-	-	5	
- HYPERPLAS.EPITHELIAL:	1	-	-	1	

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1

SEX :					MALE
DOSE GROUP:	1	2	3	4	
NO.ANIMALS:	5	-	-	5	
THYROID GLAND :	5	-	-	5	
- HYPERTROPHY FOLLIC. :	3	-	-	3	
- ACCESSORY THYMUS :	-	-	-	1	
TRACHEA :	5	-	-	5	
- DILATATION GLANDULAR:	2	-	-	3	

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1

FEMALE

SEX :				
DOSE GROUP:	1	2	3	4
NO.ANIMALS:	5	-	-	5
ADRENAL GLANDS :	5	-	-	5
- CHANGE FATTY CORT. :	3	-	-	3
BONE MARROW :	5	-	-	5
- ATROPHY FATTY :	-	-	-	4
FORESTOMACH :	5	-	-	5
- HYPERPLAS. SQUAMOUS :	-	-	-	5
- HYPERKERATOSIS :	1	-	-	5
- CYST EPIDERMAL :	-	-	-	1
KIDNEYS :	5	-	-	5
- MINERALIZATION :	-	-	-	1
LIVER :	5	-	-	5
- DEPOS. OF GLYCOGEN :	5	-	-	3
- INFILT. INFLAM. CELL:	-	-	-	1
LUNG :	5	-	-	5
- INFILT. INFLAM. CELL:	1	-	-	1
- INFILT. LYMPHOHIST. :	1	-	-	1
OVARIES :	5	-	-	5
- DILATATION OF RETE :	-	-	-	1
PARATHYROID GLANDS :	5	-	-	3
- FIBROSIS :	2	-	-	-
SCIATIC NERVE, LEFT :	5	-	-	5
- DEGENERATING FIBERS :	-	-	-	1
SPLEEN :	5	-	-	5
- HEMOSIDEROSIS :	4	-	-	4
- EXMED. HEMATOPOIESIS:	2	-	-	3
THYMUS :	5	-	-	5
- HYPERPLAS.EPITHELIAL:	3	-	-	-

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
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NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1

SEX :					FEMALE
DOSE GROUP:	1	2	3	4	
NO.ANIMALS:	5	-	-	5	
THYROID GLAND :	5	-	-	5	
- CYST DEVELOPMENTAL :	-	-	-	1	
TRACHEA :	5	-	-	5	
- DILATATION GLANDULAR:	1	-	-	1	
VAGINA :	5	-	-	5	
- ESTRUS :	1	-	-	-	
- PROESTRUS :	1	-	-	-	
- METESTRUS :	-	-	-	2	
- DIESTRUS :	3	-	-	3	

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
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PathData® System V6.1b

CORRELATION TABLE: NECROPSY - MICROSCOPY

DOSE GROUP 2, FEMALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 44
KIDNEYS	
- 01: RIGHT SIDE: PELVIC DILATION.	- PELVIC DILATATION, unilateral, grade 3.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
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PathData® System V6.1b

CORRELATION TABLE: NECROPSY - MICROSCOPY

DOSE GROUP 3, MALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 19
THYMUS	
- 01: REDUCED IN SIZE.	- ATROPHY, grade 1.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
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PathData® System V6.1b

CORRELATION TABLE: NECROPSY - MICROSCOPY

DOSE GROUP 4, MALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 21
FORESTOMACH	
Finding 01 in STOMACH	- HYPERKERATOSIS, grade 3.
Finding 01 in STOMACH	- SQUAMOUS CELL HYPERPLASIA, grade 4.
STOMACH	
- 01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.	- SEE UNDER: FORESTOMACH.
	ANIMAL NO: 22
FORESTOMACH	
Finding 01 in STOMACH	- HYPERKERATOSIS, grade 4.
Finding 01 in STOMACH	- SQUAMOUS CELL HYPERPLASIA, grade 4.
STOMACH	
- 01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.	- SEE UNDER: FORESTOMACH.
	ANIMAL NO: 23
FORESTOMACH	
Finding 01 in STOMACH	- HYPERKERATOSIS, grade 4.
Finding 01 in STOMACH	- SQUAMOUS CELL HYPERPLASIA, grade 3.
STOMACH	
- 01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.	- SEE UNDER: FORESTOMACH.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

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PathData® System V6.1b

CORRELATION TABLE: NECROPSY - MICROSCOPY — DOSE GROUP 4, MALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 24
FORESTOMACH	
Finding 01 in STOMACH	- HYPERKERATOSIS, grade 3.
Finding 01 in STOMACH	- SQUAMOUS CELL HYPERPLASIA, grade 4.
STOMACH	
- 01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.	- SEE UNDER: FORESTOMACH.
	ANIMAL NO: 25
FORESTOMACH	
Finding 01 in STOMACH	- HYPERKERATOSIS, grade 4.
Finding 01 in STOMACH	- SQUAMOUS CELL HYPERPLASIA, grade 4.
STOMACH	
- 01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.	- SEE UNDER: FORESTOMACH.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
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CORRELATION TABLE: NECROPSY - MICROSCOPY

DOSE GROUP 4, FEMALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 51
FORESTOMACH	
Finding 01 in STOMACH	- HYPERKERATOSIS, grade 3.
Finding 01 in STOMACH	- SQUAMOUS CELL HYPERPLASIA, grade 3.
STOMACH	
- 01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.	- SEE UNDER: FORESTOMACH.
	ANIMAL NO: 52
FORESTOMACH	
Finding 01 in STOMACH	- HYPERKERATOSIS, grade 4.
Finding 01 in STOMACH	- SQUAMOUS CELL HYPERPLASIA, grade 3.
STOMACH	
- 01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.	- SEE UNDER: FORESTOMACH.
	ANIMAL NO: 53
FORESTOMACH	
Finding 01 in STOMACH	- HYPERKERATOSIS, grade 3.
Finding 01 in STOMACH	- SQUAMOUS CELL HYPERPLASIA, grade 3.
STOMACH	
- 01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.	- SEE UNDER: FORESTOMACH.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

CORRELATION TABLE: NECROPSY - MICROSCOPY

DOSE GROUP 4, FEMALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 54
FORESTOMACH	
Finding 01 in STOMACH	- HYPERKERATOSIS, grade 4.
Finding 01 in STOMACH	- SQUAMOUS CELL HYPERPLASIA, grade 3.
STOMACH	
- 01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.	- SEE UNDER: FORESTOMACH.
	ANIMAL NO: 55
FORESTOMACH	
Finding 01 in STOMACH	- HYPERKERATOSIS, grade 4.
Finding 01 in STOMACH	- SQUAMOUS CELL HYPERPLASIA, grade 4.
STOMACH	
- 01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.	- SEE UNDER: FORESTOMACH.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 1, 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
ADRENAL GLANDS	+	-	-	-	+	+	+	+	+	-
- CHANGE FATTY CORT.	1.	.	.	.	1.	1.	(1.	2.	1.	.
BONE MARROW	-	-	-	-	+	-	-	+	-	-
- ATROPHY FATTY	.	.	.	.	1.	.	.	1.	.	.
BRAIN	-	-	-	-	-	-	-	-	-	-
CECUM	-	-	-	-	-	-	-	-	-	-
COLON	-	-	-	-	-	-	-	-	-	-
DUODENUM	-	-	-	-	-	-	-	-	-	-
EPIDIDYMIDES	+	-	-	-	-	-	-	-	-	-
- INFILT. INFLAM. CELL	(1.	.	.	.	.	.	.	.	.	.
FORESTOMACH	-	+	+	-	-	+	-	+	-	-
- HYPERKERATOSIS	.	1.	1.	.	.	1.	.	1.	.	.
GLANDULAR STOMACH	-	-	-	-	-	-	-	-	-	-
HEART	-	-	-	-	-	-	-	-	-	-
ILEUM	-	-	-	-	-	-	-	-	-	-
JEJUNUM	-	-	-	-	-	-	-	-	-	-
KIDNEYS	+	+	+	+	-	+	+	+	+	-
- CHANGE HYALINE TUB.	.	.	1.	.	.	2.	1.	1.	1.	.
- BASOPHILIA TUBULAR	(1.	(1.	.	(1.	.	.	1.	(1.	2.	.
- MINERALIZATION	.	.	.	.	.	.	.	.	(1.	.
- INFILT. LYMPHOHIST.	.	.	.	.	.	.	(1.	.	.	.
LIVER	+	-	+	+	-	+	+	+	+	+
- DEPOS. OF GLYCOGEN	.	.	.	.	.	1.	2.	1.	2.	1.
- INFILT. INFLAM. CELL	1.	.	1.	1.	.	.	.	.	1.	1.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 1, 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
LUNG	-	-	-	+	+	-	-	-	-	+
- MINERALIZ. VASCULAR	.	.	.	1.	1.	.	.	.	.	1.
- INFILT. INFLAM. CELL	.	.	.	1.	.	.	.	.	.	.
MANDIB.LYMPH NODES	-	-	-	-	-	-	-	-	-	+
- HYPERPL.REACT.CHR	.	.	.	.	.	.	.	.	.	2.
MESENT. LYMPH NODE	-	-	-	-	-	-	-	-	-	-
PARATHYROID GLANDS	0	-	-	-	-	-	0	+	-	-
- FIBROSIS	.	.	.	.	.	.	.	2.	.	.
PEYER'S PATCHES	-	-	-	-	-	-	-	-	0	0
PROSTATE GLAND	-	-	+	-	-	-	-	-	-	-
- INFILT. INFLAM. CELL	.	.	1.	.	.	.	.	.	.	.
RECTUM	-	-	-	-	-	-	-	-	-	-
SCIATIC NERVE, LEFT	-	-	-	-	-	-	-	-	-	-
SEMINAL VESICLES	-	-	-	-	-	-	-	-	-	-
SPINAL CORD	-	-	-	-	-	-	-	-	-	-
SPLEEN	+	+	+	-	+	+	+	+	+	-
- EXMED. HEMATOPOIESIS	1.	1.	2.	.	1.	1.	2.	1.	1.	.
STOMACH	-	-	-	-	-	-	-	-	-	-
TESTES	-	-	-	-	-	-	-	-	-	-
THYMUS	-	-	-	+	-	-	-	-	-	+
- HYPERPLAS.EPITHELIAL	.	.	.	1.	.	.	.	.	.	1.
THYROID GLAND	+	-	+	-	+	-	+	-	+	+
- HYPERTROPHY FOLLIC.	1.	.	1.	.	.	.	1.	.	1.	1.
- ACCESSORY THYMUS	.	.	.	.	P.	.	.	.	.	.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 1, 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
TRACHEA	-	-	+	+	+	-	-	-	+	+
- DILATATION GLANDULAR	.	.	1.	1.	1.	.	.	.	1.	1.
URINARY BLADDER	-	-	-	-	-	-	-	-	-	-

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 1, 0 MG/KG

ANIMAL NUMBER :	31	32	33	34	35	36	37	38	39	40
	FK0	FK0	FK0	FK0	FK0	FR1	FR1	FR1	FR1	FR1
ADRENAL GLANDS	-	-	+	-	-	+	-	+	-	+
- CHANGE FATTY CORT.	.	.	1.	.	.	1.	.	1.	.	1.
BONE MARROW	+	-	-	-	-	-	-	-	-	-
- ATROPHY FATTY	1.	.	.	.	.	.	.	.	.	.
BRAIN	-	-	-	-	-	-	-	-	-	-
CECUM	-	-	-	-	-	-	-	-	-	-
COLON	-	-	-	-	-	-	-	-	-	-
DUODENUM	-	-	-	-	-	-	-	-	-	-
FORESTOMACH	-	-	-	+	+	+	-	-	-	-
- HYPERPLAS. SQUAMOUS	.	.	.	1.	.	.	.	.	.	.
- HYPERKERATOSIS	.	.	.	1.	1.	1.	.	.	.	.
GLANDULAR STOMACH	-	-	-	-	-	-	-	-	-	-
HEART	-	-	-	-	-	-	-	-	-	-
ILEUM	-	-	-	-	-	-	-	-	-	-
JEJUNUM	-	-	-	-	-	-	-	-	-	-
KIDNEYS	-	+	-	+	-	-	-	-	-	-
- BASOPHILIA TUBULAR	.	.	.	(1.	.	.	.	.	.	.
- MINERALIZATION	.	(1.	.	.	.	.	.	.	.	.
LIVER	-	-	+	-	+	+	+	+	+	+
- DEPOS. OF GLYCOGEN	.	.	.	.	.	2.	1.	2.	2.	1.
- INFILT. INFLAM. CELL	.	.	1.	.	1.	.	.	.	.	.
LUNG	+	-	+	-	-	-	-	+	-	+
- MINERALIZ. VASCULAR	1.	.	.	.	.	.	.	.	.	.
- INFILT. INFLAM. CELL	.	.	.	.	.	.	.	1.	.	.
- INFILT. LYMPHOHIST.	.	.	1.	.	.	.	.	.	.	1.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 1, 0 MG/KG

ANIMAL NUMBER :	31	32	33	34	35	36	37	38	39	40
	FK0	FK0	FK0	FK0	FK0	FR1	FR1	FR1	FR1	FR1
MANDIB.LYMPH NODES	-	+	-	-	-	-	-	-	-	-
- ATROPHY LYMPH. TISS.	.	2.	.	.	.	.	.	.	.	.
MESENT. LYMPH NODE	-	-	-	-	-	-	-	-	-	-
OVARIES	-	-	-	-	-	-	-	-	-	-
PARATHYROID GLANDS	-	-	0	-	-	+	+	-	-	-
- FIBROSIS	.	.	.	.	.	1.	1.	.	.	.
PEYER'S PATCHES	-	-	-	-	-	-	-	-	-	-
RECTUM	-	-	-	0	-	-	-	-	-	-
SCIATIC NERVE, LEFT	-	-	-	-	+	-	-	-	-	-
- DEGENERATING FIBERS	.	.	.	.	1.	.	.	.	.	.
SPINAL CORD	-	-	-	-	-	-	-	-	-	-
SPLEEN	+	+	+	+	+	+	+	+	-	+
- HEMOSIDEROSIS	.	1.	1.	1.	1.	1.	1.	1.	.	1.
- EXMED. HEMATOPOIESIS	2.	1.	.	1.	1.	.	1.	.	.	1.
STOMACH	-	-	-	-	-	-	-	-	-	-
THYMUS	-	+	-	-	-	+	-	-	+	+
- HYPERPLAS.EPITHELIAL	.	1.	.	.	.	1.	.	.	1.	1.
THYROID GLAND	+	-	-	-	-	-	-	-	-	-
- ACCESSORY THYMUS	P.	.	.	.	.	.	.	.	.	.
TRACHEA	-	-	-	-	+	-	-	-	+	-
- DILATATION GLANDULAR	.	.	.	.	1.	.	.	.	1.	.
URINARY BLADDER	-	-	-	-	-	-	-	-	-	-
UTERUS	-	-	-	-	-	-	-	-	-	-

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 1, 0 MG/KG

ANIMAL NUMBER :

	31	32	33	34	35	36	37	38	39	40
	FK0	FK0	FK0	FK0	FK0	FR1	FR1	FR1	FR1	FR1
VAGINA	+	+	+	+	+	+	+	+	+	+
- ESTRUS	.	.	.	.	.	.	.	.	P.	.
- PROESTRUS	P.	.	.	.	.	.	P.	.	.	.
- METESTRUS	.	.	.	.	P.	.	.	.	.	.
- DIESTRUS	.	P.	P.	P.	.	P.	.	P.	.	P.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 2, 50 MG/KG

ANIMAL NUMBER :

	11	12	13	14	15	41	42	43	44	45
	MK0	MK0	MK0	MK0	MK0	FK0	FK0	FK0	FK0	FK0
ADRENAL GLANDS	+	-	+	-	+	'	'	'	'	'
- CHANGE FATTY CORT.	1.	.	(1.	.	1.					
BONE MARROW	'	'	'	'	'	-	-	-	-	-
FORESTOMACH	+	+	-	+	+	+	+	+	+	+
- HYPERPLAS. SQUAMOUS	.	1.	.	1.	1.	1.	1.	1.	1.	1.
- HYPERKERATOSIS	1.	2.	.	1.	1.	2.	1.	1.	2.	2.
GLANDULAR STOMACH	-	-	-	-	-	-	-	-	-	-
KIDNEYS	'	'	'	'	'	'	'	'	(+G	'
- DILATATION PELVIC									(3.	
- MINERALIZ.CORTICOMED									(1.	
LIVER	+	+	+	-	-	+	+	-	-	-
- INFILT. INFLAM. CELL	1.	1.	1.	.	.	1.	.	.	.	.
- CHANGE FATTY	.	.	.	.	.	.	1.	.	.	.
STOMACH	-	-	-	-	-	-	-	-	-	-

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 3, 200 MG/KG

ANIMAL NUMBER :	16 MK0	17 MK0	18 MK0	19 MK0	20 MK0	46 FK0	47 FK0	48 FK0	49 FK0	50 FK0
ADRENAL GLANDS	+	-	-	+	-	'	'	'	'	'
- CHANGE FATTY CORT.	1.	.	.	(1.	.					
BONE MARROW	'	'	'	'	'	-	-	-	+	-
- ATROPHY FATTY						.	.	.	2.	.
FORESTOMACH	+	+	+	+	+	+	+	+	+	+
- HYPERPLAS. SQUAMOUS	1.	1.	1.	1.	1.	1.	2.	1.	1.	1.
- HYPERKERATOSIS	1.	2.	1.	1.	1.	1.	1.	1.	.	2.
- INFILT. INFLAM. CELL	.	.	.	.	.	.	2.	.	.	.
GLANDULAR STOMACH	-	-	-	-	-	-	-	-	-	-
LIVER	-	-	+	+	-	+	-	+	-	+
- INFILT. INFLAM. CELL	.	.	1.	1.	.	2.	.	1.	.	1.
STOMACH	-	-	-	-	-	-	-	-	-	-
THYMUS	'	'	'	+G	'	'	'	'	'	'
- ATROPHY				1.						

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 4, 1000 MG/KG

ANIMAL NUMBER :	21	22	23	24	25	26	27	28	29	30
	MK0	MK0	MK0	MK0	MK0	MR1	MR1	MR1	MR1	MR1
ADRENAL GLANDS	+	+	+	-	+	+	-	-	+	+
- CHANGE FATTY CORT.	2.	1.	2.	.	1.	1.	.	.	1.	(1.
BONE MARROW	-	-	-	+	-	-	-	-	-	-
- ATROPHY FATTY	.	.	.	2.	.	.	.	.	.	.
BRAIN	-	-	-	-	-	-	-	-	-	-
CECUM	-	-	-	-	-	-	-	-	-	-
COLON	-	-	-	-	-	-	-	-	-	-
DUODENUM	-	-	-	-	-	-	-	-	-	-
EPIDIDYMIDES	-	-	-	-	-	-	-	-	-	-
FORESTOMACH	+	+	+	+	+	+	+	+	+	+
- HYPERPLAS. SQUAMOUS	4.	4.	3.	4.	4.	2.	2.	2.	2.	2.
- HYPERKERATOSIS	3.	4.	4.	3.	4.	2.	2.	2.	2.	2.
GLANDULAR STOMACH	+	+	+	+	-	-	-	-	-	-
- HYPERPLAS.EPITHELIAL	1.	1.	1.	1.	.	.	.	.	.	.
HEART	-	-	-	-	-	-	-	-	-	-
ILEUM	-	-	-	-	-	-	-	-	-	-
JEJUNUM	-	-	-	-	-	-	-	-	-	-
KIDNEYS	+	+	+	+	+	+	+	+	-	+
- CHANGE HYALINE TUB.	1.	.	1.	1.	.	1.	1.	1.	.	.
- BASOPHILIA TUBULAR	.	(1.	.	1.	.	.	(1.	.	.	(1.
- MINERALIZATION	.	.	.	.	(1.	.	.	.	.	.
LIVER	-	+	+	+	+	-	+	+	+	+
- DEPOS. OF GLYCOGEN	.	.	.	.	.	.	.	.	1.	.
- INFILT. INFLAM. CELL	.	1.	1.	.	1.	.	1.	1.	1.	1.
- CHANGE FATTY	.	.	.	1.	.	.	.	.	.	.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 4, 1000 MG/KG

ANIMAL NUMBER :	21	22	23	24	25	26	27	28	29	30
	MK0	MK0	MK0	MK0	MK0	MR1	MR1	MR1	MR1	MR1
LUNG	-	-	-	-	-	-*	-	-	+	+
- MINERALIZ. VASCULAR	.	.	.	.	.	.	.	.	.	1.
- FOAM CELLS	.	.	.	.	.	.	.	.	1.	.
MANDIB.LYMPH NODES	-	-	-	-	-	-	-	-	-	-
MESENT. LYMPH NODE	-	-	-	-	-	-	-	-	-	-
PARATHYROID GLANDS	-	+	-	0	-	0	0	-	-	-
- FIBROSIS	.	1.	.	.	.	.	.	.	.	.
PEYER'S PATCHES	-	+	+	+	-	-	-	-	-	-
- MINERALIZATION	.	2*	1*	1*	.	.	.	.	.	.
PROSTATE GLAND	-	-	-	-	-	-	-	-	-	-
RECTUM	-	-	-	-	-	-	-	-	-	-
SCIATIC NERVE, LEFT	-	-	-	-	-	-	-	-	-	-
SEMINAL VESICLES	-	-	-	-	-	-	-	-	-	-
SPINAL CORD	-	-	-	-	-	-	-	-	-	-
SPLEEN	-	+	+	-	+	+	+	+	+	+
- EXMED. HEMATOPOIESIS	.	1.	1.	.	2.	1.	2.	1.	1.	1.
STOMACH	-G	-G	-G	-G	-G	-	-	-	-	-
TESTES	-	-	-	-	-	-	-	-	-	-
THYMUS	-	+	-	-	-	-	+	-	-	-
- HYPERPLAS.EPITHELIAL	.	1.	.	.	.	.	1.	.	.	.
THYROID GLAND	-	-	+	-	-	+	+	-	+	+
- HYPERTROPHY FOLLIC.	.	.	1.	.	.	1.	1.	.	1.	.
- ACCESSORY THYMUS	.	.	.	.	.	.	.	.	.	P.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 4, 1000 MG/KG

ANIMAL NUMBER :

	21	22	23	24	25	26	27	28	29	30
	MK0	MK0	MK0	MK0	MK0	MR1	MR1	MR1	MR1	MR1
TRACHEA	-	-	+	-	+	-	-	+	+	+
- DILATATION GLANDULAR	.	.	1.	.	1.	.	.	1.	1.	1.
URINARY BLADDER	-	-	-	-	-	-	-	-	-	-

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 4, 1000 MG/KG

ANIMAL NUMBER :	51	52	53	54	55	56	57	58	59	60
	FK0	FK0	FK0	FK0	FK0	FR1	FR1	FR1	FR1	FR1
ADRENAL GLANDS	-	-	-	-	+	+	+	+	-	-
- CHANGE FATTY CORT.	.	.	.	.	1.	1.	1.	1.	.	.
BONE MARROW	-	-	-	-	+	+	-	+	+	+
- ATROPHY FATTY	.	.	.	.	1.	2.	.	1.	1.	1.
BRAIN	-	-	-	-	-	-	-	-	-	-
CECUM	-	-	-	-	-	-	-	-	-	-
COLON	-	-	-	-	-	-	-	-	-	-
DUODENUM	-	-	-	-	-	-	-	-	-	-
FORESTOMACH	+	+	+	+	+	+	+	+	+	+
- HYPERPLAS. SQUAMOUS	3.	3.	3.	3.	4.	2.	2.	2.	2.	2.
- HYPERKERATOSIS	3.	4.	3.	4.	4.	1.	2.	2.	2.	2.
- CYST EPIDERMAL	.	.	.	.	.	.	.	.	2.	.
- EROSION	.	2.	1.	.	.	.	.	.	.	.
- ULCERATION	.	.	.	2.	.	.	.	.	.	.
GLANDULAR STOMACH	+	+	+	+	+	-	-	-	-	-
- HYPERPLAS.EPITHELIAL	1.	1.	2.	1.	1.	.	.	.	.	.
HEART	-	-	-	-	-	-	-	-	-	-
ILEUM	-	-	-	-	-	-	-	-	-	-
JEJUNUM	-	-	-	-	-	-	-	-	-	-
KIDNEYS	-	+	-	-	-	-	-	-	+	-
- BASOPHILIA TUBULAR	.	(1.	.	.	.	.	.	.	.	.
- DILATATION PELVIC	.	(1.	.	.	.	.	.	.	.	.
- MINERALIZATION	.	.	.	.	.	.	.	.	(1.	.
LIVER	+	-	-	-	-	-	+	+	+	-
- DEPOS. OF GLYCOGEN	.	.	.	.	.	.	1.	2.	1.	.
- INFILT. INFLAM. CELL	.	.	.	.	.	.	.	1.	.	.
- CHANGE FATTY	1.	.	.	.	.	.	.	.	.	.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 4, 1000 MG/KG

ANIMAL NUMBER :	51	52	53	54	55	56	57	58	59	60
	FK0	FK0	FK0	FK0	FK0	FR1	FR1	FR1	FR1	FR1
LUNG	-	-	-	-	+	+	-	-	+	-
- INFILT. INFLAM. CELL	.	.	.	.	.	1.	.	.	.	.
- INFILT. LYMPHOHIST.	.	.	.	.	1.	.	.	.	1.	.
MANDIB.LYMPH NODES	-	-	-	-	-	-	-	-	-	-
MESENT. LYMPH NODE	-	-	-	-	-	-	-	-	-	-
OVARIES	-	-	-	-	-	-	+*	-	-	-
- DILATATION OF RETE	.	.	.	.	.	.	(P.	.	.	.
PARATHYROID GLANDS	-	0	-	-	0	-	-	-	0	0
PEYER'S PATCHES	-	-	-	-	-	-	-	-	-	-
RECTUM	-	-	-	-	-	-	-	-	-	-
SCIATIC NERVE, LEFT	-	-	-	+	-	+	-	-	-	-
- DEGENERATING FIBERS	.	.	.	1.	.	1.	.	.	.	.
SPINAL CORD	-	-	-	-	-	-	-	-	-	-
SPLEEN	+	+	+	+	-	+	+	+	+	+
- HEMOSIDEROSIS	1.	1.	.	1.	.	1.	1.	1.	1.	.
- EXMED. HEMATOPOIESIS	1.	1.	1.	.	.	.	.	1.	1.	1.
STOMACH	-G	-G	-G	-G	-G	-	-	-	-	-
THYMUS	-	-	+	-	-	-	-	-	-	-
- HYPERPLAS.EPITHELIAL	.	.	1.	.	.	.	.	.	.	.
THYROID GLAND	-	-	-	-	-	-	+	-	-	-
- CYST DEVELOPMENTAL	.	.	.	.	.	.	P.	.	.	.
TRACHEA	-	-	-	-	-	-	-	-	-	+
- DILATATION GLANDULAR	.	.	.	.	.	.	.	.	.	2.
URINARY BLADDER	-	-	-	-	-	-	-	-	-	-

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 4, 1000 MG/KG

ANIMAL NUMBER :

	51	52	53	54	55	56	57	58	59	60
	FK0	FK0	FK0	FK0	FK0	FR1	FR1	FR1	FR1	FR1
UTERUS	-	-	-	-	-	-	-	-	-	-
VAGINA	+	+	+	+	+	+	+	+	+	+
- PROESTRUS	.	.	P.	P.	.	.	.	.	.	.
- METESTRUS	P.	P.	.	.	.	P.	.	.	P.	.
- DIESTRUS	.	.	.	.	P.	.	P.	P.	.	P.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

ANIMAL HEADING DATA
DOSE GROUP : 1, 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	21-APR-03	18-MAY-03	19-MAY-03
2	M	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
3	M	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
4	M	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
5	M	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
6	M	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
7	M	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
8	M	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
9	M	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
10	M	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
31	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
32	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
33	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
34	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
35	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
36	F	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
37	F	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
38	F	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
39	F	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
40	F	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 1, 0 MG/KG

MALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 28

* ANIMAL NO. : 1

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
EPIDIDYMIDES:
-INFLAMMATORY CELL INFILTRATION, unilateral, grade 1
KIDNEYS:
-TUBULAR BASOPHILIA, unilateral, grade 1
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1
PARATHYROID GLANDS:
Tissue not present for histologic examination
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
THYROID GLAND (BOTH LOBES):
-FOLLICULAR CELL HYPERTROPHY, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 1, 0 MG/KG

MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 2

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

FORESTOMACH:
-HYPERKERATOSIS, grade 1
KIDNEYS:
-TUBULAR BASOPHILIA, unilateral, grade 1
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 3

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

FORESTOMACH:
-HYPERKERATOSIS, grade 1
KIDNEYS:
-TUBULAR HYALINE CHANGE, bilateral, grade 1
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 1, 0 MG/KG

MALE

CONT./FF. ANIMAL NO. : 3

PROSTATE GLAND:
-INFLAMMATORY CELL INFILTRATION, grade 1
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 2
THYROID GLAND (BOTH LOBES):
-FOLLICULAR CELL HYPERTROPHY, bilateral, grade 1
TRACHEA:
-GLANDULAR DILATATION, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 4

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:
-TUBULAR BASOPHILIA, unilateral, grade 1
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1
LUNG:
-VASCULAR MINERALIZATION, grade 1
-INFLAMMATORY CELL INFILTRATION, grade 1
THYMUS:
-EPITHELIAL HYPERPLASIA, TUBULES AND CORDS, grade 1
TRACHEA:
-GLANDULAR DILATATION, grade 1

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 1, 0 MG/KG

MALE

CONT./FF. ANIMAL NO. : 4

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: KO
DAYS ON TEST : 28

* ANIMAL NO. : 5

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
BONE MARROW:
-FATTY ATROPHY, grade 1
LUNG:
-VASCULAR MINERALIZATION, grade 1
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
THYROID GLAND (BOTH LOBES):
-ACCESSORY THYMUS, bilateral
TRACHEA:
-GLANDULAR DILATATION, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 1, 0 MG/KG

MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 6

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
FORESTOMACH:
-HYPERKERATOSIS, grade 1
KIDNEYS:
-TUBULAR HYALINE CHANGE, bilateral, grade 2
LIVER:
-DEPOSITION OF GLYCOGEN, grade 1
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, 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.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 1, 0 MG/KG

MALE

CONT./FF. ANIMAL NO. : 7

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, unilateral, grade 1
KIDNEYS:
-TUBULAR HYALINE CHANGE, bilateral, grade 1
-TUBULAR BASOPHILIA, bilateral, grade 1
-LYMPHOHISTIOCYTIC INFILTRATION, unilateral, grade 1
LIVER:
-DEPOSITION OF GLYCOGEN, grade 2
PARATHYROID GLANDS:
Tissue not present for histologic examination
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 2
THYROID GLAND (BOTH LOBES):
-FOLLICULAR CELL HYPERTROPHY, bilateral, grade 1
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

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 2
BONE MARROW:
-FATTY ATROPHY, grade 1

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 1, 0 MG/KG

MALE

CONT./FF. ANIMAL NO. : 8

FORESTOMACH:
-HYPERKERATOSIS, grade 1
KIDNEYS:
-TUBULAR HYALINE CHANGE, bilateral, grade 1
-TUBULAR BASOPHILIA, unilateral, grade 1
LIVER:
-DEPOSITION OF GLYCOGEN, grade 1
PARATHYROID GLANDS:
-FIBROSIS, bilateral, grade 2
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
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

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
KIDNEYS:
-TUBULAR HYALINE CHANGE, bilateral, grade 1
-TUBULAR BASOPHILIA, bilateral, grade 2
-MINERALIZATION, unilateral, grade 1
LIVER:
-DEPOSITION OF GLYCOGEN, grade 2
-INFLAMMATORY CELL INFILTRATION, grade 1

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 1, 0 MG/KG

MALE

CONT./FF. ANIMAL NO. : 9

PEYER'S PATCHES:
Tissue not present for histologic examination
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
THYROID GLAND (BOTH LOBES):
-FOLLICULAR CELL HYPERTROPHY, bilateral, grade 1
TRACHEA:
-GLANDULAR DILATATION, 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

LIVER:
-DEPOSITION OF GLYCOGEN, grade 1
-INFLAMMATORY CELL INFILTRATION, grade 1
LUNG:
-VASCULAR MINERALIZATION, grade 1
MANDIBULAR LYMPH NODES:
-CHRONIC REACTIVE HYPERPLASIA, bilateral, grade 2
PEYER'S PATCHES:
Tissue not present for histologic examination
THYMUS:
-EPITHELIAL HYPERPLASIA, TUBULES AND CORDS, grade 1

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 1, 0 MG/KG

MALE

CONT./FF. ANIMAL NO. : 10

THYROID GLAND (BOTH LOBES):
-FOLLICULAR CELL HYPERTROPHY, bilateral, grade 1
TRACHEA:
-GLANDULAR DILATATION, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 1, 0 MG/KG

FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 31

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

BONE MARROW:
-FATTY ATROPHY, grade 1
LUNG:
-VASCULAR MINERALIZATION, grade 1
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 2
THYROID GLAND (BOTH LOBES):
-ACCESSORY THYMUS, bilateral
VAGINA:
-PROESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 32

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 1, 0 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 32

* MICROSCOPIC FINDINGS

KIDNEYS:
-MINERALIZATION, unilateral, grade 1
MANDIBULAR LYMPH NODES:
-ATROPHY OF LYMPHATIC TISSUE, bilateral, grade 2
SPLEEN:
-HEMOSIDEROSIS, grade 1
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
THYMUS:
-EPITHELIAL HYPERPLASIA, TUBULES AND CORDS, grade 1
VAGINA:
-DIESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28

* ANIMAL NO. : 33

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1
LUNG:
-LYMPHOHISTIOCYTIC INFILTRATION, grade 1

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 1, 0 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 33

PARATHYROID GLANDS:
Tissue not present for histologic examination
SPLEEN:
-HEMOSIDEROSIS, grade 1
VAGINA:
-DIESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28

* ANIMAL NO. : 34

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
-HYPERKERATOSIS, grade 1
KIDNEYS:
-TUBULAR BASOPHILIA, unilateral, grade 1
RECTUM:
Tissue not present for histologic examination
SPLEEN:
-HEMOSIDEROSIS, grade 1
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
VAGINA:
-DIESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 1, 0 MG/KG

FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 35

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

FORESTOMACH:
-HYPERKERATOSIS, grade 1
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1
SCIATIC NERVE (LEFT):
-DEGENERATING NERVE FIBERS, grade 1
SPLEEN:
-HEMOSIDEROSIS, grade 1
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
TRACHEA:
-GLANDULAR DILATATION, grade 1
VAGINA:
-METESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 36

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 1, 0 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 36

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
FORESTOMACH:
-HYPERKERATOSIS, grade 1
LIVER:
-DEPOSITION OF GLYCOGEN, grade 2
PARATHYROID GLANDS:
-FIBROSIS, bilateral, grade 1
SPLEEN:
-HEMOSIDEROSIS, grade 1
THYMUS:
-EPITHELIAL HYPERPLASIA, TUBULES AND CORDS, grade 1
VAGINA:
-DIESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: R1
DAYS ON TEST : 28

* ANIMAL NO. : 37

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-DEPOSITION OF GLYCOGEN, grade 1
PARATHYROID GLANDS:
-FIBROSIS, bilateral, grade 1

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 1, 0 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 37

SPLEEN:
-HEMOSIDEROSIS, grade 1
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
VAGINA:
-PROESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: R1
DAYS ON TEST : 28

* ANIMAL NO. : 38

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
LIVER:
-DEPOSITION OF GLYCOGEN, grade 2
LUNG:
-INFLAMMATORY CELL INFILTRATION, grade 1
SPLEEN:
-HEMOSIDEROSIS, grade 1
VAGINA:
-DIESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 1, 0 MG/KG

FEMALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 39

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-DEPOSITION OF GLYCOGEN, grade 2
THYMUS:
-EPITHELIAL HYPERPLASIA, TUBULES AND CORDS, grade 1
TRACHEA:
-GLANDULAR DILATATION, grade 1
VAGINA:
-ESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 40

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
LIVER:
-DEPOSITION OF GLYCOGEN, grade 1

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 1, 0 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 40

LUNG:
-LYMPHOHISTIOCYTIC INFILTRATION, grade 1
SPLEEN:
-HEMOSIDEROSIS, grade 1
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
THYMUS:
-EPITHELIAL HYPERPLASIA, TUBULES AND CORDS, grade 1
VAGINA:
-DIESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

ANIMAL HEADING DATA
DOSE GROUP : 2, 50 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	21-APR-03	18-MAY-03	19-MAY-03
12	M	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
13	M	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
14	M	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
15	M	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
41	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
42	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
43	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
44	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
45	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 2, 50 MG/KG

MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 11

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
FORESTOMACH:
-HYPERKERATOSIS, grade 1
LIVER:
-INFLAMMATORY CELL INFILTRATION, 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

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
-HYPERKERATOSIS, grade 2
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 2, 50 MG/KG

MALE

CONT./FF. ANIMAL NO. : 12

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28

* ANIMAL NO. : 13

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, unilateral, grade 1
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28

* ANIMAL NO. : 14

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 2, 50 MG/KG

MALE

CONT./FF. ANIMAL NO. : 14

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
-HYPERKERATOSIS, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28

* ANIMAL NO. : 15

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
-HYPERKERATOSIS, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 2, 50 MG/KG

FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 41

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
-HYPERKERATOSIS, grade 2
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 42

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
-HYPERKERATOSIS, grade 1
LIVER:
-FATTY CHANGE, HEPATOCELLULAR PERILOBULAR, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 2, 50 MG/KG

FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 43

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
-HYPERKERATOSIS, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 44

* NECROPSY FINDINGS

KIDNEYS:
01: RIGHT SIDE: PELVIC DILATION.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
-HYPERKERATOSIS, grade 2
KIDNEYS:
Only one of paired organs examined/present
-PELVIC DILATATION, unilateral, grade 3
This finding corresponds to necropsy observation no: 01.
-CORTICOMEDULLARY MINERALIZATION, unilateral, grade 1

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 2, 50 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 44

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28

* ANIMAL NO. : 45

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
-HYPERKERATOSIS, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

ANIMAL HEADING DATA
DOSE GROUP : 3, 200 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	21-APR-03	18-MAY-03	19-MAY-03
17	M	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
18	M	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
19	M	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
20	M	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
46	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
47	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
48	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
49	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
50	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 3, 200 MG/KG

MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 16

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
-HYPERKERATOSIS, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 17

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
-HYPERKERATOSIS, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 3, 200 MG/KG

MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 18

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
-HYPERKERATOSIS, grade 1
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 19

* NECROPSY FINDINGS

THYMUS:
01: REDUCED IN SIZE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, unilateral, grade 1
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
-HYPERKERATOSIS, grade 1

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 3, 200 MG/KG

MALE

CONT./FF. ANIMAL NO. : 19

LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1
THYMUS:
-ATROPHY, grade 1
This finding corresponds to necropsy observation no: 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28

* ANIMAL NO. : 20

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
-HYPERKERATOSIS, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 3, 200 MG/KG

FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 46

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
-HYPERKERATOSIS, grade 1
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 47

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 2
-HYPERKERATOSIS, grade 1
-INFLAMMATORY CELL INFILTRATION, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 3, 200 MG/KG

FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 48

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
-HYPERKERATOSIS, grade 1
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 49

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

BONE MARROW:
-FATTY ATROPHY, grade 2
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 3, 200 MG/KG

FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28

* ANIMAL NO. : 50

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 1
-HYPERKERATOSIS, grade 2
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

ANIMAL HEADING DATA
DOSE GROUP : 4, 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
21	M	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
22	M	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
23	M	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
24	M	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
25	M	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
26	M	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
27	M	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
28	M	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
29	M	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
30	M	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
51	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
52	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
53	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
54	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
55	F	K0	K0	28	21-APR-03	18-MAY-03	19-MAY-03
56	F	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
57	F	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
58	F	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
59	F	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03
60	F	R1	R1	28	21-APR-03	18-MAY-03	02-JUN-03

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

MALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 28 * ANIMAL NO. : 21

* NECROPSY FINDINGS

STOMACH:
01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 2
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 4
This finding corresponds to necropsy observation no.: 01
in the STOMACH.
-HYPERKERATOSIS, grade 3
This finding corresponds to necropsy observation no.: 01
in the STOMACH.
GLANDULAR STOMACH:
-EPITHELIAL HYPERPLASIA, DIFFUSE, grade 1
KIDNEYS:
-TUBULAR HYALINE CHANGE, bilateral, grade 1
STOMACH:
For diagnosis of necropsy observation no. 01 see under: FORESTOMACH.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

MALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 28 * ANIMAL NO. : 22

* NECROPSY FINDINGS

STOMACH:
01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 4
This finding corresponds to necropsy observation no.: 01 in the STOMACH.
-HYPERKERATOSIS, grade 4
This finding corresponds to necropsy observation no.: 01 in the STOMACH.
GLANDULAR STOMACH:
-EPITHELIAL HYPERPLASIA, DIFFUSE, grade 1
KIDNEYS:
-TUBULAR BASOPHILIA, unilateral, grade 1
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1
PARATHYROID GLANDS:
-FIBROSIS, bilateral, grade 1
PEYER'S PATCHES:
-MINERALIZATION, grade 2
SEE SLIDE NO. 26
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
STOMACH:
For diagnosis of necropsy observation no. 01 see under: FORESTOMACH.
THYMUS:
-EPITHELIAL HYPERPLASIA, TUBULES AND CORDS, grade 1

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

MALE

CONT./FF. ANIMAL NO. : 22

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: KO
DAYS ON TEST : 28

* ANIMAL NO. : 23

* NECROPSY FINDINGS

STOMACH:
01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 2
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 3
This finding corresponds to necropsy observation no.: 01 in the STOMACH.
-HYPERKERATOSIS, grade 4
This finding corresponds to necropsy observation no.: 01 in the STOMACH.
GLANDULAR STOMACH:
-EPITHELIAL HYPERPLASIA, DIFFUSE, grade 1
KIDNEYS:
-TUBULAR HYALINE CHANGE, bilateral, grade 1
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1
PEYER'S PATCHES:
-MINERALIZATION, grade 1
SEE SLIDE NO. 26

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

MALE

CONT./FF. ANIMAL NO. : 23

SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
STOMACH:
For diagnosis of necropsy observation no. 01 see under: FORESTOMACH.
THYROID GLAND (BOTH LOBES):
-FOLLICULAR CELL HYPERTROPHY, bilateral, grade 1
TRACHEA:
-GLANDULAR DILATATION, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 28

* ANIMAL NO. : 24

* NECROPSY FINDINGS

STOMACH:
01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

BONE MARROW:
-FATTY ATROPHY, grade 2
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 4
This finding corresponds to necropsy observation no.: 01
in the STOMACH.
-HYPERKERATOSIS, grade 3
This finding corresponds to necropsy observation no.: 01
in the STOMACH.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

MALE

CONT./FF. ANIMAL NO. : 24

GLANDULAR STOMACH:
-EPITHELIAL HYPERPLASIA, DIFFUSE, grade 1
KIDNEYS:
-TUBULAR HYALINE CHANGE, bilateral, grade 1
-TUBULAR BASOPHILIA, bilateral, grade 1
LIVER:
-FATTY CHANGE, HEPATOCELLULAR DIFFUSE, grade 1
PARATHYROID GLANDS:
Tissue not present for histologic examination
PEYER'S PATCHES:
-MINERALIZATION, grade 1
SEE SLIDE NO. 27
STOMACH:
For diagnosis of necropsy observation no. 01 see under: FORESTOMACH.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 25

* NECROPSY FINDINGS

STOMACH:
01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 4
This finding corresponds to necropsy observation no.: 01

in the STOMACH.
-HYPERKERATOSIS, grade 4
This finding corresponds to necropsy observation no.: 01
in the STOMACH.
KIDNEYS:
-MINERALIZATION, unilateral, grade 1
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 2
STOMACH:
For diagnosis of necropsy observation no. 01 see under: FORESTOMACH.
TRACHEA:
-GLANDULAR DILATATION, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: R1
DAYS ON TEST : 28 * ANIMAL NO. : 26

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 2
-HYPERKERATOSIS, grade 2

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

MALE

CONT./FF. ANIMAL NO. : 26

KIDNEYS:
-TUBULAR HYALINE CHANGE, bilateral, grade 1
LUNG:
SMALL EXOPHYTIC PROLIFERATION ARISING IN THE BRONCHIOLUS.
THE LESION IS COMPOSED OF POLYGONAL CELLS.
PARATHYROID GLANDS:
Tissue not present for histologic examination
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
THYROID GLAND (BOTH LOBES):
-FOLLICULAR CELL HYPERTROPHY, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: R1
DAYS ON TEST : 28

* ANIMAL NO. : 27

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 2
-HYPERKERATOSIS, grade 2
KIDNEYS:
-TUBULAR HYALINE CHANGE, bilateral, grade 1
-TUBULAR BASOPHILIA, unilateral, grade 1
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

MALE

CONT./FF. ANIMAL NO. : 27

PARATHYROID GLANDS:
Tissue not present for histologic examination
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 2
THYMUS:
-EPITHELIAL HYPERPLASIA, TUBULES AND CORDS, grade 1
THYROID GLAND (BOTH LOBES):
-FOLLICULAR CELL HYPERTROPHY, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: R1
DAYS ON TEST : 28

* ANIMAL NO. : 28

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 2
-HYPERKERATOSIS, grade 2
KIDNEYS:
-TUBULAR HYALINE CHANGE, bilateral, grade 1
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
TRACHEA:
-GLANDULAR DILATATION, grade 1

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

MALE

CONT./FF. ANIMAL NO. : 28

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1
DAYS ON TEST : 28

* ANIMAL NO. : 29

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 2
-HYPERKERATOSIS, grade 2
LIVER:
-DEPOSITION OF GLYCOGEN, grade 1
-INFLAMMATORY CELL INFILTRATION, grade 1
LUNG:
-FOAM CELLS, grade 1
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
THYROID GLAND (BOTH LOBES):
-FOLLICULAR CELL HYPERTROPHY, bilateral, grade 1
TRACHEA:
-GLANDULAR DILATATION, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 28

* ANIMAL NO. : 30

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, unilateral, grade 1
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 2
-HYPERKERATOSIS, grade 2
KIDNEYS:
-TUBULAR BASOPHILIA, unilateral, grade 1
LIVER:
-INFLAMMATORY CELL INFILTRATION, grade 1
LUNG:
-VASCULAR MINERALIZATION, grade 1
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
THYROID GLAND (BOTH LOBES):
-ACCESSORY THYMUS, bilateral
TRACHEA:
-GLANDULAR DILATATION, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 51

* NECROPSY FINDINGS

STOMACH:
01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 3
This finding corresponds to necropsy observation no.: 01 in the STOMACH.
-HYPERKERATOSIS, grade 3
This finding corresponds to necropsy observation no.: 01 in the STOMACH.
GLANDULAR STOMACH:
-EPITHELIAL HYPERPLASIA, DIFFUSE, grade 1
LIVER:
-FATTY CHANGE, HEPATOCELLULAR PERILOBULAR, grade 1
SPLEEN:
-HEMOSIDEROSIS, grade 1
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
STOMACH:
For diagnosis of necropsy observation no. 01 see under: FORESTOMACH.
VAGINA:
-METESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

FEMALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 28

* ANIMAL NO. : 52

* NECROPSY FINDINGS

STOMACH:
01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 3
This finding corresponds to necropsy observation no.: 01 in the STOMACH.
-HYPERKERATOSIS, grade 4
This finding corresponds to necropsy observation no.: 01 in the STOMACH.
-EROSION, grade 2
GLANDULAR STOMACH:
-EPITHELIAL HYPERPLASIA, DIFFUSE, grade 1
KIDNEYS:
-TUBULAR BASOPHILIA, unilateral, grade 1
-PELVIC DILATATION, unilateral, grade 1
PARATHYROID GLANDS:
Tissue not present for histologic examination
SPLEEN:
-HEMOSIDEROSIS, grade 1
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
STOMACH:
For diagnosis of necropsy observation no. 01 see under: FORESTOMACH.
VAGINA:
-METESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28

* ANIMAL NO. : 53

* NECROPSY FINDINGS

STOMACH:
01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 3
This finding corresponds to necropsy observation no.: 01 in the STOMACH.
-HYPERKERATOSIS, grade 3
This finding corresponds to necropsy observation no.: 01 in the STOMACH.
-EROSION, grade 1
GLANDULAR STOMACH:
-EPITHELIAL HYPERPLASIA, DIFFUSE, grade 2
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
STOMACH:
For diagnosis of necropsy observation no. 01 see under: FORESTOMACH.
THYMUS:
-EPITHELIAL HYPERPLASIA, TUBULES AND CORDS, grade 1
VAGINA:
-PROESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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PATHOL. NO. : 70009 BBA
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PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28

* ANIMAL NO. : 54

* NECROPSY FINDINGS

STOMACH:
01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 3
This finding corresponds to necropsy observation no.: 01 in the STOMACH.
-HYPERKERATOSIS, grade 4
This finding corresponds to necropsy observation no.: 01 in the STOMACH.
-ULCERATION, grade 2
GLANDULAR STOMACH:
-EPITHELIAL HYPERPLASIA, DIFFUSE, grade 1
SCIATIC NERVE (LEFT):
-DEGENERATING NERVE FIBERS, grade 1
SPLEEN:
-HEMOSIDEROSIS, grade 1
STOMACH:
For diagnosis of necropsy observation no. 01 see under: FORESTOMACH.
VAGINA:
-PROESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
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PATHOL. NO. : 70009 BBA
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TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28

* ANIMAL NO. : 55

* NECROPSY FINDINGS

STOMACH:
01: FORESTOMACH, MUCOSA: IRREGULAR SURFACE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
BONE MARROW:
-FATTY ATROPHY, grade 1
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 4
This finding corresponds to necropsy observation no.: 01 in the STOMACH.
-HYPERKERATOSIS, grade 4
This finding corresponds to necropsy observation no.: 01 in the STOMACH.
GLANDULAR STOMACH:
-EPITHELIAL HYPERPLASIA, DIFFUSE, grade 1
LUNG:
-LYMPHOHISTIOCYTIC INFILTRATION, grade 1
PARATHYROID GLANDS:
Tissue not present for histologic examination
STOMACH:
For diagnosis of necropsy observation no. 01 see under: FORESTOMACH.
VAGINA:
-DIESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
TEST SYSTEM : RAT, 28-DAY, Oral(Gavage)
SPONSOR : Ciba Specialty Chemicals

PATHOL. NO.: 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

FEMALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 28

* ANIMAL NO. : 56

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
BONE MARROW:
-FATTY ATROPHY, grade 2
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 2
-HYPERKERATOSIS, grade 1
LUNG:
-INFLAMMATORY CELL INFILTRATION, grade 1
SCIATIC NERVE (LEFT):
-DEGENERATING NERVE FIBERS, grade 1
SPLEEN:
-HEMOSIDEROSIS, grade 1
VAGINA:
-METESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
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PATHOL. NO. : 70009 BBA
DATE : 23-OCT-03
PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

FEMALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 28

* ANIMAL NO. : 57

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 2
-HYPERKERATOSIS, grade 2
LIVER:
-DEPOSITION OF GLYCOGEN, grade 1
OVARIES:
SMALL NESTS OF BASOPHILIC CELLS UNILATERAL, PROBABLY EMBRYONIC REMNANTS OF RETE OVARII
-DILATATION OF RETE OVARII, unilateral
SPLEEN:
-HEMOSIDEROSIS, grade 1
THYROID GLAND (BOTH LOBES):
-DEVELOPMENTAL CYST, bilateral
VAGINA:
-DIESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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PATHOL. NO. : 70009 BBA
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PathData® System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

FEMALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 28

* ANIMAL NO. : 58

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-CORTICAL FATTY CHANGE, DIFFUSE, bilateral, grade 1
BONE MARROW:
-FATTY ATROPHY, grade 1
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 2
-HYPERKERATOSIS, grade 2
LIVER:
-DEPOSITION OF GLYCOGEN, grade 2
-INFLAMMATORY CELL INFILTRATION, grade 1
SPLEEN:
-HEMOSIDEROSIS, grade 1
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
VAGINA:
-DIESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

FEMALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 28

* ANIMAL NO. : 59

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

BONE MARROW:
-FATTY ATROPHY, grade 1
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 2
-HYPERKERATOSIS, grade 2
-EPIDERMAL CYST, grade 2
KIDNEYS:
-MINERALIZATION, unilateral, grade 1
LIVER:
-DEPOSITION OF GLYCOGEN, grade 1
LUNG:
-LYMPHOHISTIOCYTIC INFILTRATION, grade 1
PARATHYROID GLANDS:
Tissue not present for histologic examination
SPLEEN:
-HEMOSIDEROSIS, grade 1
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
VAGINA:
-METESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : TKA 40291 (ZLI 3331)
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TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000 MG/KG

FEMALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 28

* ANIMAL NO. : 60

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

BONE MARROW:
-FATTY ATROPHY, grade 1
FORESTOMACH:
-SQUAMOUS CELL HYPERPLASIA, grade 2
-HYPERKERATOSIS, grade 2
PARATHYROID GLANDS:
Tissue not present for histologic examination
SPLEEN:
-EXTRAMEDULLARY HEMATOPOIESIS, grade 1
TRACHEA:
-GLANDULAR DILATATION, grade 2
VAGINA:
-DIESTRUS
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.