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March 25, 2004

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EPA East – Room 6428 Attn: Section 8(e)
Office of Pollution Prevention and Toxics
US EPA
1200 Pennsylvania Avenue NW
Washington DC 20460-0001

RE: TSCA 8(E) SUPPLEMENTAL SUBMISSION:
Docket No. 8EHQ-03-15463

Dear Docket Coordinators:

On October 28, 2003, 3M provided EPA with preliminary results from a combined repeated dose toxicity study with a reproduction/developmental toxicity screening test in rats conducted with 1-butanesulfonamide, 1,1,2,2,3,3,4,4,4-nonafluoro-n-methyl (CAS 68298-12-4, N-MePFBA) indicating reproductive and possible neurotoxic effects. The final report for this study contains results that are consistent with the previously reported information.

Enclosed please find the following final report on CD-Rom:

- Combined Repeated Dose Toxicity Study with Reproduction/Developmental Toxicity Screening Test with T-7601 Administered by Oral Gavage in Wister Rats

Please contact Paul Lieder (651-737-2678) if you have any questions or if we can provide additional information.

Sincerely,

Larry R. Johnson

Larry R. Johnson
Director, Corporate Toxicology and Regulatory Services

Enclosure

CONTAINS NO CBI

bcc (cover letter only):

Cheri Kedrowski – CT&RS – 220-2E-02
Paul Lieder – CT&RS – 220-2E-02
Paul Loudas – SMMD EHS&R – 236-1B-10

bcc (with attachments):

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File Information

TSCA 8(e) file number: 67
Toxicology number: T-7601.8

REPORT

Study Title

COMBINED REPEATED DOSE TOXICITY STUDY WITH REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST WITH T-7601 ADMINISTERED BY ORAL GAVAGE IN WISTAR RATS

Author

Drs. M.E.W. Beekhuijzen

Study completion date

12 February 2004

Test Facility

NOTOX B.V.
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The Netherlands

Laboratory Project Identification

NOTOX Project 385717
NOTOX Substance 113769/B

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2. STATEMENT OF GLP COMPLIANCE

NOTOX B.V., 's-Hertogenbosch, The Netherlands

The study described in this report has been correctly reported and was conducted in compliance with:

The Organization for Economic Cooperation and Development (OECD) Good Laboratory Practice Guidelines (1997).

Which essentially conform to:

United States Environmental Protection Agency (FIFRA). Title 40 Code of Federal Regulations Part 160.
United States Environmental Protection Agency (TSCA). Title 40 Code of Federal Regulations Part 792.
United States Food and Drug Administration. Title 21 Code of Federal Regulations Part 58.
Japanese Ministry of Agriculture, Forestry and Fisheries. 59 NohSan, Notifications No. 3850.
Japanese Ministry of Economy, Trade and Industry. Kanpogyo No. 39 Environmental Agency, Kikyoku No. 85.
Japanese Ministry of Health, Labor and Welfare. Ordinance No.21.

The GLP statement from the test site for histopathology is included in Appendix 4 of this report.

NOTOX B.V.

Drs. M.E.W. Beekhuijzen
Study Director

Date: 12 February 2004

W.J.A.M. Frieling DVM
Head of Department

Date: 16 February 2004

3. QUALITY ASSURANCE STATEMENT

NOTOX B.V., 's-Hertogenbosch, The Netherlands

This report was inspected by the NOTOX Quality Assurance Unit to confirm that the methods and results accurately and completely reflect the raw data.

The dates of Quality Assurance inspections are given below.
During the on-site process inspections procedures applicable to this type of study were inspected

Type of inspections	Phase / Section	Start Inspection date(s)	End Inspection date(s)	Reporting date
Protocol (Study)		26-Jun-03	26-Jun-03	26-Jun-03
On-site (Process)	SPF Unit	07-Jul-03	11-Jul-03	15-Jul-03
On-site (Process)	Clinical Pathology	02-Sep-03	12-Sep-03	12-Sep-03
On-site (Process)	Pathology	11-Aug-03	25-Aug-03	25-Aug-03
On-site (Process)	Analytical & Physical Chem.	30-Jun-03	03-Jul-03	07-Jul-03
On-site (Study)	dosing	25-Jul-03	25-Jul-03	25-Jul-03
On-site (Study)	necropsy	02-Sep-03	02-Sep-03	02-Sep-03
Report (Study)		15-Dec-03	30-Dec-03	31-Dec-03

The Quality Assurance programme for histopathology was performed by the Quality Assurance appointed by the test site management and a Quality Assurance statement is included in the histopathology report (see Appendix 4).

Head of Quality Assurance
C.J.Mitchell B.Sc.

Date: 23-2-04

4. SUMMARY

Combined repeated dose toxicity study with reproduction/developmental toxicity screening test with T-7601 administered by oral gavage in Wistar rats.

The study was based on the following guideline:
OECD "Guidelines for Testing of Chemicals", Section 4, Health Effects, No. 422, "Combined Repeated Dose Toxicity Study With The Reproduction/Developmental Toxicity Screening Test", 22 March 1996.

Dose levels for this study, based on a dose range finding study with T-7601 in the rat, were selected to be: 0, 50, 150, and 1000 mg/kg body weight/day.

The test substance T-7601 formulated in propylene glycol was administered daily for at least 28 days up to the day prior to necropsy. The study period for the males consisted of two weeks pre-mating, mating, and post-mating for the remainder of the 28 days. The study period for the females consisted of two weeks pre-mating, mating, post-coitum, and at least 4 days of lactation. The females that showed to be non-pregnant were also treated for at least 28 days. All groups consisted of ten males and ten females.

The following parameters were evaluated: mortality, clinical signs, functional observations, body weights, food consumption, reproduction processes, offspring observations, clinical pathology, macroscopy, organ weights and histopathology.

4.1 Results

Formulation analysis revealed that the formulations were prepared accurately, were homogeneous and stable for at least 4 hours at room temperature.

The following changes were considered to be related to treatment:

<u>at 50 mg/kg body weight/day:</u>
- No treatment-related findings.

<u>at 150 mg/kg body weight/day:</u>
- Clinical signs (salivation and diarrhoea).

<u>at 1000 mg/kg body weight/day:</u>
- The death of two males and two females were likely incidental, however a possible relationship to treatment could not be excluded.
- Clinical signs (lethargy, hunched posture, uncoordinated movements, decreased locomotor activity, ventro-lateral recumbency, quick breathing, laboured respiration, rales, shallow respiration, swelling of the genital region and abdomen, piloerection, red discolouration of urine, diarrhoea, salivation, chromodacryorrhoea of the eye and snout, lean appearance and ptosis).
- Decreased body weight gain and incidentally severe body weight loss for both sexes.
- Reduced food consumption for both sexes.
- Affected haematology parameters (increased erythrocytes count, haemoglobin concentration, and haematocrit for both sexes, and increased mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, and red cell distribution width for males).
- Affected clinical biochemistry parameters (increased alanine aminotransferase, alkaline phosphatase, urea, triglyceride, chloride, and inorganic phosphorus for males, and decreased aspartate aminotransferase, decreased bilirubin, and increased albumin for females).

- At necropsy, four males showed a yellowish nodule(s) on the epididymides.
- Decreased terminal body weight and increased liver weights for both sexes, and increased spleen and epididymides weights for the males.
- Minimal/slight hepatocyte hypertrophy in the liver of both sexes, increased severity of hematopoiesis in the spleen of males, increased severity of hemosiderosis in the spleen of females, slight/moderate sperm granuloma in the epididymides of males.
- Other findings in the testes (tubular atrophy, dilation, giant cells) and epididymides (reduced spermatozoa, cellular debris) of high dose animals were secondary to the blockage caused by the sperm granulomas.
- Meningitis was present in the brain and spinal cord of two high dose females. A possible relationship to treatment could not be totally excluded, however these findings were considered most likely to be incidental.
- Minimal centrilobular degeneration in the liver (two decedent males), slight adrenal cortical vacuolation (two males), minimal/slight atrophy in the thymus (one male and female), and minimal/slight acanthosis and hyperkeratosis in the stomach (one male and one female) were considered to be due to inanition or stress, rather than direct effects of the compound.
- Decreased fertility index, conception rate and gestation index.
- It is difficult to assess breeding data as this group consisted of only 3 litters. However, there seems to be a tendency for poor breeding performance regarding postnatal loss between days 0 to 4 post partum.
- It is difficult to assess pup development as this group consisted of only 3 litters. Decreased pup weight and increased incidence of clinical signs of the pups (small, pale, cold, and little milk) were observed in these litters.

4.2 Conclusion

Gavage treatment of male and female Wistar rats with T-7601 at dose levels of 50, 150 or 1000 mg/kg body weight/day during at least 28 days, revealed parental toxicity at 150 and 1000 mg/kg body weight/day. Reproductive, breeding, and developmental toxicity was observed at 1000 mg/kg body weight/day.

Based on the results in this combined repeated dose toxicity study with reproduction / developmental toxicity screening test:

- The definitive parental No Observed Adverse Effect Level (NOAEL) was established as being 50 mg/kg body weight/day.
- The definitive reproductive, breeding and development NOAEL was established as being 150 mg/kg body weight/day.

5. INTRODUCTION

5.1 Preface

Sponsor	3M Corporate Toxicology 3M Center, Building 220-2E-02 P.O. Box 33220 ST. PAUL, MINNESOTA 55133-3220 U.S.A.
Study Monitor	Dr. P. Lieder 3M Medical Department Corporate Toxicology 3M Center, Building 220-2E-02 P.O. Box 33220 ST. PAUL, MINNESOTA 55144-1000 U.S.A.
Test Facility	NOTOX B.V. Hambakenwetering 7 5231 DD 's-Hertogenbosch The Netherlands
Test site: Histopathology	Pre-Clinical Safety Consultants Ltd. Dr. D.E. Prentice (Managing Director and overall responsibility) Contact Office: P.O. Box 184 Huntingdon, Cambs., PE17 2AB, England

5.2 Project staff

Study Director	Drs. M.E.W. Beekhuijzen (NOTOX)
Coordinating Biotechnician	H.J. Bessels (NOTOX)
Clinical Pathology	J.E. van Kesteren (NOTOX)
Necropsy/Histotechnology	J.H. van den Brink, DVM (NOTOX)
Analytical Chemistry	Ir. M.J.C. Brekelmans (Principal Scientist, NOTOX)
Histopathology	Dr. R.H. Alison (Principal Investigator, PCS)

5.3 Study schedule

Acclimatisation	16 July 2003
Start treatment	21 July 2003
Start mating	04 August 2003
Necropsy of males	18 August 2003
Delivery of litters	27-31 August 2003
Necropsy of females and pups	01-05 September 2003

5.4 Project numbers

Due to the complexity of the study several project numbers were generated. These numbers were only used for online data collection. Eventually, all data were reported under NOTOX Project 385717.

Project number	Description
385717	General (protocol, report)
385741	Pre-mating online
385752	Reproduction online (mating, pregnancy, lactation of females, post-mating of males, necropsy offspring)
385739	Clinical signs online (clinical signs, clinical pathology, functional observations, necropsy parental animals)

5.5 Aims of the study

The purpose of this study was to assess the toxic potential, and effect on the general reproductive performance of T-7601 when administered to rats by daily oral gavage over a relatively limited period.

This study should provide part of a rational basis for toxicological risk assessment in man, and initial information on possible effects on male and female reproductive performance. The oral route was selected, as this will be the route of possible human exposure during manufacture, handling or use of the test substance.

5.6 Guidelines

The protocol was reviewed and agreed by the Laboratory Animal Welfare Officer and the Ethical Committee of NOTOX (DEC NOTOX 03-30) as required by the Dutch Act on Animal Experimentation (February 1997).

The study procedures described in this report were based on the following guideline:

1) OECD "Guidelines for Testing of Chemicals", Section 4, Health Effects, No. 422, "Combined Repeated Dose Toxicity Study With The Reproduction/Developmental Toxicity Screening Test", 22 March 1996.

5.7 Storage and retention of records and materials

Records and materials pertaining to the study including protocol, raw data, specimens (except specimens requiring refrigeration or freezing) and the final report are retained in the NOTOX archives for a period of at least 10 years after finalization of the report. After this period, the sponsor will be contacted to determine whether raw data and specimens should be returned to them, retained or destroyed on their behalf.

Those specimens requiring refrigeration or freezing will be retained by NOTOX for as long as the quality of the specimens permits evaluation but no longer than three months after finalization of the report.

NOTOX will retain a test substance sample until the expiry date, but no longer than 10 years after finalization of the report. After this period the sample will be destroyed.

6. MATERIALS AND METHODS

6.1 Test Substance

Identification	T-7601
CAS Number	68298-12-4 (1-Butanesulfonamide, 1,1,2,2,3,3,4,4,4-nonafluoro-n-methyl)
Description	Light yellow waxy powder (determined at Notox)
Batch	Lot 3 (taken from label)
Purity	>95% 1-Butanesulfonamide, 1,1,2,2,3,3,4,4,4-nonafluoro-n-methyl, 95% < 5% N-Methyl-4-hydrido-perfluorobutylsulfonamide
Test substance storage	At room temperature in the dark
Stability under storage conditions	Not indicated
Expiry date	17 June 2004 (allocated by NOTOX, 1 year after receipt of the test substance)
Specific Gravity	1.65

The sponsor is responsible for all test substance data unless determined by NOTOX.

6.2 Vehicle

Vehicle	Propylene glycol, specific gravity 1.036
Rationale for vehicle	Based on trial formulations performed at NOTOX.
Stability of test substance in vehicle	Stable for at least 4 hours at room temperature (determined during this project).
Method of formulation	Formulations (w/w) were prepared daily within 4 hours prior to dosing (with some exceptions; see protocol deviation number 11) and were homogenised to visually acceptable levels. Adjustment was made for specific gravity of the test substance and vehicle.
Storage conditions	At ambient temperature.

6.3 Chemical analysis of dose preparations

Analyses were done according a validated method (NOTOX Project number 385752) on the samples specified below.

Week	Group	Analysis
1	1	acc (M)
	2	acc (M), hom (TMB), stab t=4h RT (M)
	3	acc (M)
	4	acc (M), hom (TMB), stab t=4h RT (M)
4	1	acc (M)
	2	acc (M), hom (TMB)
	3	acc (M)
	4	acc (M), hom (TMB)

Triplicate samples were analysed

Type of sample R=Random, T=Top, M=Middle, B=Bottom position of container

Analysis acc=accuracy, hom=homogeneity, stab=stability, RT=Room temperature

6.4 Test System

Test System	Rat: male and female Wistar rats Crl: (WI) BR (outbred, SPF-Quality). Untreated animals and virgin females were used at initiation of the study. Recognised by international guidelines as the recommended test system (e.g. EPA, FDA, OECD, EEC).
Source	Charles River Deutschland, Sulzfeld, Germany
Age at start F_0-treatment	Approximately 8 weeks
Number of F_0-animals	40 females and 40 males
Acclimatisation F_0	At least 5 days prior to start of treatment
Health check F_0	A health inspection was performed prior to commencement of treatment to ensure that the animals were in a good state of health.
Randomisation F_0	At least 5 days before study start, by computer-generated random algorithm according to body weight, with all animals within ± 20% of the sex mean.
Identification F_0	By tattoo on the tail and earmark.
Mating procedures F_0	Females were paired on a one-to-one-basis with males from the same treatment group. Each morning following pairing, the trays under the cages were checked for ejected copulation plugs. The day on which a copulation plug is found was designated day 0 of gestation (=day 0 *post-coitum*). Once mating occurred, the males and females were separated.
Parturition F_0	The females were allowed to litter normally. Day 1 of lactation was defined as the day when a litter is found completed (i.e. membranes, placentas cleaned up, nest build up and/or feeding of pups started). Females that were littering were left undisturbed.
Lactation F_0	Deficiencies in maternal care, such as inadequate construction or cleaning of the nest, pups left scattered and cold, physical abuse of pups or apparently inadequate lactation or feeding, were recorded.
Identification offspring	The offspring was individually identified by means of intracutaneous injection of Indian ink.

6.5 Allocation

Group	Dose level mg/kg b.w./day	Number of animals		Animals numbers	
		F_0 males	F_0 females	males	females
1	0	10	10	01-10	41-50
2	50	10	10	11-20	51-60
3	150	10	10	21-30	61-70
4	1000	10	10	31-40	71-80

*These dose levels were chosen based on a dose range finding study (See Appendix 5).

6.6 Animal Husbandry

Conditions
Animals were housed in a controlled environment, in which optimal conditions were considered to be approximately 15 air changes per hour, a temperature of 21 ± 3^{0}C (actual range: 18.1 – 23.5^{0}C), a relative humidity of 30 – 70% (actual range: 42 – 87%) and 12 hours artificial light and 12 hours darkness per day. Temporary fluctuations from the light/dark cycle (with a maximum of 1 hour) occurred due to performance of functional observations in the room. Cleaning procedures in the room might have caused the temporary fluctuations above the optimal level of 70% for relative humidity.
Based on laboratory historical data these conditions were considered not to have affected the study integrity.

Accommodation
Upon arrival, animals were housed in groups of 5 animals/sex/cage in suspended stainless steel cages.
During the mating procedures, females were caged together with males on a one-to-one-basis in suspended stainless steel cages with wire mesh floors.
Mated females and males were individually housed in labelled polycarbonate cages containing sawdust (SAWI bedding, Jelu Werk, Rosenberg, Germany) as bedding material. Certificates of analysis were examined and then retained in the NOTOX archives.
Offspring was kept with the dam until termination.
In order to reduce environmental influences as much as possible, cages were arranged in a latin square design over the cage rack during the study period. Each cage was identified with a colour-coded label according to dose group, showing the study number, animal identifications, and other experimental details. From arrival until mating, males and females were not housed in separate rooms (see protocol deviation number 9). During the final stage of the pregnancy period (from approximately day 16 of gestation onwards) and during lactation, paper (Enviro-dri, BMI, Helmond, The Netherlands) was supplied to each dam for incorporation in the nest. The paper was analysed for contaminants. This was replaced when soiled.

Diet
Free access was allowed to standard pelleted laboratory animal diet (from Altromin (code VRF 1), Lage, Germany). Each batch was analysed for nutrients and contaminants were analysed on a regular basis. Results were examined and then retained in the NOTOX archives. Fresh diet was provided on a weekly basis, or at periodic intervals during pregnancy.

Water
Free access was allowed to tap water. Certificates of analysis (performed quarterly) were examined and then retained in the NOTOX archives.

Analysis of diet, sawdust, nesting material, and water were found to be within normal limits.

6.7 Treatment Parental Animals

Method	Oral gavage, using a rubber catheter attached to a plastic disposable syringe.
Frequency	Once daily, at approximately the same time each day.
Exposure period	The males and females were exposed for 2 weeks prior to mating, during mating, and up to the day prior to necropsy. Exposure period was at least until the minimum total dosing period of 28 days had been completed.
Dose levels	Group 1: 0 mg/kg b.w./day (vehicle) Group 2: 50 mg/kg b.w./day Group 3: 150 mg/kg b.w./day Group 4: 1000 mg/kg b.w./day These dose levels were chosen based on a dose range finding study (See Appendix 5).
Dose volume	5 ml/kg body weight. Actual dose volumes were calculated according to the latest body weight.

6.8 Observations Parental Animals

Mortality / Viability	At least twice daily. Animals showing pain, distress or discomfort, which was considered not transient in nature or was likely to become more severe, were sacrificed for humane reasons based on OECD guidance document on humane endpoints (ENV/JM/MONO/ 2000/7). The time of death was recorded as precisely as possible.
Clinical signs	At least once daily, detailed clinical observations were made in all animals. Arena observations were not performed (see protocol deviation number 10). The symptoms were graded according to fixed scales and the time of onset, degree and duration were recorded: - Fixed scale with maximum grade 1 : grade 0 = absent, grade 1 = present. - Fixed scale with max. grade 3 or 4 : grade 1 = slight, grade 2 = moderate, grade 3 = severe, grade 4 = very severe. Cage debris of pregnant females was examined to detect abortion or premature birth.

Functional Observations	The following tests were performed in 5 males and 5 females, randomly selected from each group: - hearing ability, pupillary reflex, static righting reflex and grip strength (Score 0 = normal/present, score 1 = abnormal/absent). - motor activity test (recording period: 12 hours during overnight for individual animals, using a computerised monitoring system, Pearson Technical Services, Debenham, Stowmarket, England). During the motor activity test, males were caged individually and females were caged with their offspring. The assigned males were tested during week 4 of treatment and the assigned females were tested during lactation (all before blood sampling). The study director selected the animals and informed the involved personnel by protocol amendment. The motor activity test was performed for a second time for female 75 as the results of the first test showed very low values. In order to avoid hypothermia of pups, dams were removed from the pups for not more than 30-40 minutes.
Body weights	Males and females were weighed on the first day of exposure and weekly thereafter. Mated females were weighed on days 0, 7, 14 and 21 of gestation, and during lactation on days 1 and 4.
Food consumption	Weekly, for males and females. During the mating period measurement of food consumption was suspended. Food consumption of mated females was measured on gestation days 0, 7, 14 and 21, and during lactation on days 1 and 4.
Water consumption	Subjective appraisal was maintained during the study, but no quantitative investigation introduced as no effect was suspected.
Reproduction processes	Male number paired with, mating date, confirmation of pregnancy, and delivery day were recorded.

6.9 Observations Offspring

Each litter was examined to determine the following if practically possible:

- The numbers of live and dead pups at the First Litter Check (= check at day 1 of lactation) and daily thereafter (if possible, defects or cause of death were evaluated)
- The individual weight of all live pups on days 1 and 4 of lactation
- Sex of all pups (by assessment of the ano-genital distance)
- The number of pups with physical or behavioural abnormalities daily

6.10 Clinical Laboratory Investigations

Blood samples were collected from 5 males and 5 females randomly selected from each group under iso-flurane anaesthesia immediately prior to scheduled *post mortem* examination, between 7.30 and 9.30 a.m. The study director selected the animals and informed the involved personnel by protocol amendment. The animals were fasted overnight (with a maximum of 20 hours for the females, and 22 hours for the males; see protocol deviation number 6) before blood sampling, but water was provided. Blood samples were drawn from the retro-orbital sinus of all rats/sex/group and collected into tubes prepared with EDTA for haematological parameters (0.5 ml), with citrate for clotting tests (1.0 ml) and Li-heparin treated tubes for clinical biochemistry parameters (0.5 ml). The following parameters were determined:

Parameter	Unit
Haematology [a]	
Erythrocytes count	10^{12}/l
Haemoglobin	mmol/l
Haematocrit	l/l
Mean corpuscular volume	fl
Mean corpuscular haemoglobin	fmol
Mean corpuscular haemoglobin concentration	mmol/l
Platelets count	10^{9}/l
Red cell distribution width	%
Total leucocytes count	10^{9}/l
Differential leucocyte count	%WBC
Clotting Potential [b]	
Prothrombin time	s
Partial thromboplastin time	s
Clinical Biochemistry [c]	
Alanine aminotransferase	U/l
Alkaline phosphatase	U/l
Aspartate aminotransferase	U/l
Bilirubin, total	µmol/l
Chloride	mmol/l
Cholesterol, total	mmol/l
Creatinine	µmol/l
Glucose	mmol/l
Phosphorus	mmol/l
Protein, total	g/l
Protein, albumin	g/l
Triglycerides	mmol/l
Urea	mmol/l
Calcium	mmol/l
Potassium	mmol/l
Sodium	mmol/l

[a] Instrumentation: ADVIA120 (Bayer Diagnostics).

[b] Instrumentation: STA Compact (Roche Diagnostics).

[c] Instrumentation: Olympus AU400 (Goffin Meyvis). Samples were occasionally stored at ≤-75°C prior to analysis.

6.11 Pathology

6.11.1 Parental animals - Termination

All animals were fasted overnight (with a maximum of 20 hours) prior to necropsy, but water was provided.

All animals surviving to the end of the observation period and all moribund animals were anaesthetised using iso-flurane and subsequently exsanguinated.

Males were killed after the mating period at least until the minimum total dosing period of 28 days had been completed.
Females were killed at day 4 *post partum* or shortly thereafter.

In case a female was not pregnant, the uterus was stained using the Salewski technique in order to determine any very early post-implantation losses (=implantation site scars).

6.11.2 Parental animals - Macroscopic examination

After sacrifice or death all parental animals were subjected to macroscopic examination of the cranial, thoracic and abdominal tissues and organs, with special attention being paid to the reproductive organs. Descriptions of all macroscopic abnormalities were recorded.

From all females, the number of implantation sites and corpora lutea were recorded.

Samples of the following tissues and organs were collected and fixed in neutral phosphate buffered 4% formaldehyde solution (except the epididymides and testes):

From 5 surviving animals/sex/group*,
and from all animals that died spontaneously or were killed in extremis:

Identification marks: not processed
Adrenal glands
(Aorta)
Brain (cerebellum, hippocampus, cortex)
Caecum
(Cervix)
Clitoral gland
Colon
Coagulation gland
Duodenum
Epididymides (fixed in Bouin's**)
(Eyes with optic nerve and Harderian gland)
(Female mammary gland area)
(Femur including joint)
Heart
Ileum
Jejunum
Kidneys
(Larynx)
(Lacrimal gland, exorbital)
Liver
Lung, infused with formalin
Lymph nodes - mandibular, mesenteric
(Nasopharynx)
(Oesophagus)
Ovaries
(Pancreas)
Peyer's patches (jejunum, ileum) if detectable
Pituitary gland
Preputial gland
Prostate gland
Rectum
(Salivary glands - mandibular, sublingual)
Sciatic nerve
Seminal vesicles
(Skeletal muscle)
(Skin)
Spinal cord -cervical, midthoracic, lumbar
Spleen
Sternum with bone marrow
Stomach
Testes (fixed in Bouin's**)
Thymus
Thyroid including parathyroid
(Tongue)
Trachea
Urinary bladder
Uterus
(Vagina)
All gross lesions

* The study director selected the animals and informed the involved personnel by protocol amendment.

From all adult animals:

Cervix
Clitoral gland
Coagulation gland
Epididymides (fixed in Bouin's**)
Ovaries
Preputial gland
Prostate gland
Seminal vesicles
Testes (fixed in Bouin's**)
Uterus
Vagina
All gross lesions

** = transferred to formalin after fixation for at least 24 hours.

6.11.3 Parental animals - Organ weights

The following organ weights (and terminal body weight) were recorded:

From 5 surviving animals/sex/group*:

Adrenal glands
Brain
Epididymides (total weight for both)
Heart
Kidneys
Liver
Spleen
Testes
Thymus

* The study director selected the animals and informed the involved personnel by protocol amendment.

From all adult males:

Epididymides (total weight for both)
Testes

6.11.4 Parental animals - Histotechnology

All organ and tissue samples, as defined under Histopathology (following), were processed, embedded and cut at a thickness of 2-4 micrometers and stained with haematoxylin and eosin.

Of the selected 5 males/group of the control and high dose group, additional slides of the testes were prepared to examine staging of spermatogenesis. The testes were processed, sectioned at 3-4 microns, and stained with PAS/hematoxylin.

6.11.5 Parental animals - Histopathology

The following slides were examined by a pathologist:
- The preserved organs and tissues of the selected animals of groups 1 and 4.
- Liver, spleen, testes, epididymides, brain, spinal cord, thymus, stomach and adrenals of all remaining animals (on detection of treatment-related morphological changes in these organs of any animal in the high dose group)
- The additional slides of the testes of the selected 5 males/group of groups 1 and 4 to examine staging of spermatogenesis
- The preserved organs and tissues of the animals of all dose groups which died spontaneously or were killed *in extremis*
- all gross lesions of all animals (all dose groups)
- The reproductive organs of all non-pregnant females and animals suspected of infertility

All abnormalities were described and included in the report.
Tissues mentioned within brackets were not examined as there were no signs of toxicity or target organ involvement.

6.11.6 Offspring - Termination

Pups were killed by decapitation on day 4 of lactation or shortly thereafter.

6.11.7 Offspring - Macroscopic examination

All offspring were sexed and externally examined if practically possible. The stomach was examined for the presence of milk.
Descriptions of all macroscopic abnormalities were recorded.
If possible, defects or cause of death were evaluated. Any abnormal pup was preserved in neutral phosphate buffered 4% formaldehyde solution, bouin or 96% ethanol, as appropriate.
No further examination of these pups was performed.

6.12 Calculation of Reproduction Parameters

For each dose group reproduction parameters were expressed in two ways:
- As a mean (with standard deviation) of the number observed for each litter
- Relative to a second parameter and calculated on a total group basis

For each group the following calculations were performed:

Percentage mating	$\frac{\text{Number of females mated}}{\text{Number of females paired}} \times 100$
Fertility index	$\frac{\text{Number of pregnant females}}{\text{Number of females paired}} \times 100$
Conception rate	$\frac{\text{Number of pregnant females}}{\text{Number of females mated}} \times 100$
Gestation index	$\frac{\text{Number of females bearing live pups}}{\text{Number of pregnant females}} \times 100$
Duration of gestation	Number of days between confirmation of mating and the beginning of parturition
Percentage live males at First Litter Check	$\frac{\text{Number of live male pups at First Litter Check}}{\text{Number of live pups at First Litter Check}} \times 100$
Percentage live females at First Litter Check	$\frac{\text{Number of live female pups at First Litter Check}}{\text{Number of live pups at First Litter Check}} \times 100$
Percentage of postnatal loss days 0-4 *post partum*	$\frac{\text{Number of dead pups on day 4 } \textit{post partum}}{\text{Number of live pups at First Litter Check}} \times 100$
Viability index	$\frac{\text{Number of live pups on day 4 } \textit{post partum}}{\text{Number of pups born alive}} \times 100$

6.13 Statistical Analysis

The following statistical methods were used to analyse the data:

If the variables could assumed to follow a normal distribution, the Dunnett-test (many-to-one t-test) based on a pooled variance estimate was applied for the comparison of the treated groups and the control groups.

The Steel-test (many-to-one rank test) was applied instead of the Dunnett-test if the data could not assumed to follow a normal distribution.

The exact Fisher-test was applied for 2x2 tables if variables could dichotomized without loss of information.

All tests were two-sided and in all cases $p < 0.05$ was accepted as the lowest level of significance.

Additional methods of statistical analysis were used at the discretion of the statistician. The methods and the results were described in the report.

References:

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

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

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

6.14 List of Protocol Deviations

1. Body weight on day 1 of mating of female 80 was determined two days before this day.
2. Body weight on day 1 of mating of female 74 was determined one day afterward.
3. One adrenal gland of animal 3 and no parathyroid of animal 46 were available for histopathology.
4. Full instead of limited necropsy and histology was performed on animal 6.
5. During the pilot study, the animals were dosed using a stainless steel stomach tube.
6. Males were fasted overnight for 22 hours before blood sampling.
7. Animals were delivered on 16 July 2003 instead of 09 July 2003.
8. Raw data of clinical pathology was collected under NOTOX Project 385739 instead of NOTOX Project 385717.
9. From arrival until mating, males and females were not housed in separate rooms.
10. Arena observations were not performed once prior to start of treatment and one week thereafter.
11. On seven occasions, formulations were not prepared daily within 4 hours prior to dosing, but ranged from 4 hours and fifteen minutes to five hours and thirty-seven minutes.
12. For several days project number 385717 was used for online data collection of clinical symptoms (instead of 385739). All results were transferred to the correct project number. However, as during the first two days no symptoms were noted, the tables of individual clinical symptoms do not show any dots for the first two days of observation.
13. Body weight of female 77 (139 gram) was determined on the day of sacrifice (killed in extremis).
14. Project number 385717 was used for online data collection of functional observations (instead of 385739).
15. Hearing ability, pupillary reflex, static righting reflex and grip strength tests were performed for female 75 on 02 September 2003 instead of 30 August 2003.

Evaluations:

1. Body weight increase over two days is very slight.
2. Body weight increase over one day is very slight.
3. Sufficient tissues are available for evaluation.
4. Additional information.
5. This is a correct method of dosing when treatment is only for five days.
6. This deviation is only very slight.
7. Acclimatisation period was adequate.
8. A note to file with explanation was added to the raw data.
9. Regularity of the oestrus cycle was not determined during this project.
10. Standard clinical observations did not reveal any symptom of concern for groups 1-3, for group 4 standard clinical observations were adequate to show their bad health.
11. As formulations analyses showed the formulations to be stable for at least 4 hours, it can be assumed that they are also stable for five hours and thirty-seven minutes.
12. A note of explanation is added to 7.2.2. (results clinical signs) of this report.
13. Additional information.
14. All results were transferred to the correct project number.
15. These tests were performed during lactation.

Based on the above evaluations, these deviations were considered not to have affected the integrity of the study.

7. RESULTS

7.1 Analysis of dose preparations (See also APPENDIX 3)

Test substance formulations in propylene glycol were noted as stable for at least 4 hours and formed a homogeneous suspension at the concentrations tested. Analysis of the accuracy of dose preparations revealed values within the range of 85-111% of nominal, which was considered to represent an acceptable level of accuracy for formulations of this type.

7.2 Observations

7.2.1 Mortality

There were 6 unscheduled deaths:

At 150 mg/kg b.w./day:
Female 65: moribund sacrifice, cause of death uterine prolapse just after delivery;
At 1000 mg/kg b.w./day:
Male 33: found dead, cause of death gavage error,
Male 34: found dead, cause of death not evident,
Male 38: moribund sacrifice, cause of death not evident,
Female 77: moribund sacrifice, cause of death meningitis,
Female 78: found dead, cause of death meningitis.

The death of animals 65 (mid dose) and 33 (high dose) were considered to be incidental findings. The deaths of animals 34, 38, 77 and 78 are also likely to be incidental findings, however a possible relationship to treatment cannot entirely be excluded.

7.2.2 Clinical signs

Treatment related clinical signs were noted in the mid dose group (150 mg/kg) and the high dose group (1000 mg/kg).
At 1000 mg/kg, these consisted of lethargy, hunched posture, uncoordinated movements, decreased locomotor activity, ventro-lateral recumbency, quick breathing, laboured respiration, rales, shallow respiration, swelling of the genital region and abdomen, piloerection, red discolouration of urine, diarrhoea, salivation, chromodacryorrhoea of both eyes and the snout, lean appearance and ptosis.
At 150 mg/kg, these consisted of salivation and diarrhoea.

Rales and salivation were also observed in the other groups, however at a much lower incidence. Alopecia was observed at a low incidence in the control group and at 150 and 1000 mg/kg. This is within the limits of historical control data of rats of this strain and age that are housed and treated under the conditions of this study.

For several days a different project number was used for online data collection of clinical symptoms (see protocol deviation number 12). All results were transferred to the correct project number. However, as during the first two days no symptoms were noted, the tables of individual clinical symptoms do not show any dots for the first two days of observation.

7.2.3 Functional observations

No changes were observed in hearing ability, papillary reflex, static righting reflex and grip strength in the treated animals, when compared to control animals.
The variation in motor activity did not indicate a relation with treatment.

7.2.4 Body weights

Body weights and body weight gain of males of the 1000 mg/kg dose group were statistically significantly decreased during treatment. Several males in this group also showed severe body weight loss.

Females of the highest dose group showed statistically significantly decreased body weights and body weight gain during the pre-mating period. Three females also showed a body weight loss in this period. Body weights of females of the highest dose group were also decreased during pregnancy and lactation. This decrease was not statistically significant due to the limited number of females in this group.

No treatment related effects on body weights and body weight gain were observed at 50 and 150 mg/kg body weight/day.

7.2.5 Food consumption

At 1000 mg/kg, absolute and relative food consumption were decreased during the complete treatment period. Statistical significance was reached for food consumption and relative food consumption during pre-mating (males), and for food consumption during post-mating (males) and lactation (females).

No treatment related effect on food consumption and relative food consumption were observed at mid and low dose groups.

7.3 Clinical laboratory investigations

7.3.1 Haematology

The following statistically significant differences of haematology parameters were recorded in the highest dose group at the end of treatment:

- decreased neutrophils count (females)
- increased erythrocytes count (males and females)
- increased haemoglobin concentration (males and females)
- increased haematocrit (males and females)
- increased mean corpuscular volume (males)
- increased mean corpuscular haemoglobin (males)
- increased mean corpuscular haemoglobin concentration (males)
- increased red cell distribution width (males).

These findings were considered to be treatment related.

In the 50 mg/kg dose group a statistically significantly increase for platelets count in females was recorded. As no dose relationship was observed, this finding was considered to be caused by chance.

No other statistically significant effects upon haematology parameters were noted.

7.3.2 Clinical biochemistry

The following statistically significant differences of clinical biochemistry parameters were recorded in the highest dose group at the end of treatment:

- increased alanine aminotransferase (males)
- increased alkaline phosphatase (males)
- increased urea (males)
- increased triglyceride (males)
- increased chloride (males)
- increased inorganic phosphorus (males)
- decreased aspartate aminotransferase (females)
- decreased bilirubin (females)
- increased albumin (females).

These findings were considered to be treatment related.

Inorganic phosphorus was decreased in females of all treatment groups to the same extent. Since no dose-relationship or correlative findings were noted, the inorganic phosphorus decrease was considered to be of no toxicological significance.

7.4 Pathology

7.4.1 Macroscopic findings

At necropsy, respectively, three, four, seven and fifteen animals (out of twenty animals) in the control, 50, 150 and 1000 mg/kg dose groups showed abnormalities.

Four males in the highest dose group appeared to have yellowish nodule(s) on the epididymides. This finding correlated with the microscopic finding of sperm granuloma, and was considered to be treatment-related.

Three animals of the 1000 mg/kg dose group died spontaneously. Male 33 was partly cannibalised and showed isolated dark red foci on the thymus, dark red discolouration of lungs and left mandibular lymphnode. Male 34 was partly cannibalised, showed beginning autolysis, reddish discolouration of the stomach and many dark red foci on both sides of the thymus. Female 78 showed dark red discolouration of the mesenteric lymph node and the left adrenal gland grown together with the kidney.
Two animals of the 1000 mg/kg group were killed in extremis. Male 38 was emaciated, showed a thickened limiting ridge of the stomach, an irregular surface of the forestomach, reddish discoloured caecum, accentuated lobular pattern of the liver, enlarged liver and dark red contents of the urinary bladder. Female 77 was emaciated and showed a forestomach with many crateriform retractions.
In the 150 mg/kg dose group, female 65 was killed in extremis and showed a prolapse of the uterus.

Incidental findings that were observed in the highest dose group included pelvic dilation of the kidney(s), reddish discolouration of the duodenum, watery-clear cysts on the uterus, reddish discolouration of the thymus, dark red discolouration of right mandibular lymph node.
Incidental findings observed in the other groups consisted of isolated/many dark red foci on the thymus, several reddish foci on thymus, light red discolouration of the thymus, dark red discolouration of the liver and right mandibular lymph node, accentuated lobular pattern of the liver, pelvic dilation of the kidney(s), alopecia in throat region, isolated/several gray-white foci on adrenal glands, exophtalmus of right eye, constricted spleen and several tan foci on the clitoral glands.
These finding are observed in rats of this age and strain that are housed and treated under the conditions of this study. At the incidence observed, these signs were therefore considered to be of no toxicological significance.

The finding of an uterus containing fluid, was noted for female 71 and 79 of the highest dose group. This finding is related to an oestrus cycle stage and therefore a physiologic finding.

7.4.2 Organ weights

The following treatment-related changes were present:

Males:
1000 mg/kg body weight/day
- decreased terminal body weight
- increased relative liver weight
- increased relative spleen weight
- increased relative epididymides weight

Females:
1000 mg/kg body weight/day
- decreased terminal body weight
- increased absolute and relative liver weight

The increased statistically significantly relative brain, heart, and testes weights observed in animals of the highest dose group were considered to be due to the lower terminal body weights, and thus not related to treatment.
Males of the 1000 mg/kg dose group showed statistically significantly decreased absolute thymus weights. In the absence of histopathological effects, this finding was considered not to be toxicologically relevant.

7.4.3 Microscopic examination (See also APPENDIX 4)

Primary treatment-related findings were confined to the liver, spleen and epididymides of high dose animals:

Liver: minimal/slight hepatocyte hypertrophy in males and females,
Spleen: increased severity of hematopoiesis in males,
increased severity of hemosiderosis in females,
Epididymides: slight/moderate sperm granuloma in males.

Other findings in the testes (tubular atrophy, dilation, giant cells) and epididymides (reduced spermatozoa, cellular debris) of high dose animals were secondary to the blockage caused by the sperm granulomas. An unilateral sperm granuloma in a single low dose animal was considered an incidental finding.
Meningitis was present in the brain and spinal cord of two high dose females. A possible relationship to treatment could not be totally excluded, however these findings were considered most likely to be incidental.
Minimal centrilobular degeneration in the liver (two high dose decedent males), slight adrenal cortical vacuolation in the adrenals (two high dose males), minimal/slight atrophy in the thymus (one high dose male and one high dose female), and minimal/slight acanthosis and hyperkeratosis in the stomach (one high dose male and one high dose female) were considered to be due to inanition or stress, rather than direct effects of the compound.

Staging of spermatogenesis:
The assessment of the integrity of the spermatogenetic cycle did not provide any evidence of impaired spermatogenesis.

Other microscopic findings observed were within the range of background pathology encountered in rats of this strain and age.

7.5 Reproduction

Table I. Reproduction Data

Number of females	Group 1 Control	Group 2 50 mg/kg	Group 3 150 mg/kg	Group 4 1000 mg/kg
Paired	10	10	10	9
Mated	10	10	10	9
Pregnant	10	9	8	4
Litters with living pups	10	9	8	3

All females mated within four days of pairing.

Reproduction of females of the 1000 mg/kg dose group was negatively affected. This was shown by four pregnancies out of nine mated females. One of these pregnant females (female 78) died spontaneously on day 12 *post-coitum*; at necropsy this female showed implantation sites after Salewski staining. As a result only three litters with living pups were recorded in this group. This gave rise to a decreased fertility index, conception rate and gestation index in the highest dose group.

Reproduction parameters up to 150 mg/kg body weight/day were found to be within normal limits.

7.6 Breeding data

Duration of gestation was not affected by treatment.

In all treatment groups, postnatal loss was statistically significantly increased. This resulted in a statistically significantly decreased viability index for all treatment groups. However, these findings were considered unrelated to treatment at 50 and 150 mg/kg, and are difficult to asses at 1000 mg/kg.
At 50 and 150 mg/kg, increased postnatal loss was mainly due to the loss of one complete litter in each group (consisting of 13 pups at 50 mg/kg and 5 pups at 150 mg/kg), and as the number of living pups on day 4 of lactation was considered to be normal, the changes in postnatal loss and viability index were regarded to be unaffected by the test item at these dose levels.
At 1000 mg/kg, it is difficult to assess breeding data as this group consists of only 3 litters. However, there seems to be a tendency for poor breeding performance regarding postnatal loss between days 0 to 4 post partum.

7.7 Pup development

Mean body weights of pups per group in the highest dose group were statistically significantly decreased on days 1 and 4 during lactation.

In the 50 mg/kg dose group, statistically significantly decreased body weights were measured on day 1 (female pups) and day 4 (male and female pups). This finding was not considered to be treatment-related, since pup body weights in the control group were very close to the upper limit of historical control data. Moreover, no dose-relationship was noted.

Other effects upon pup body weights during lactation period were not established.

Clinical signs were noted in all groups, but the incidence in the 1000 mg/kg group was slightly increased. Findings consisted of a small, cold or pale appearance, and little or no milk. One pup of the control group showed an absent tail.
Macroscopic examination of pups revealed small appearance, no milk and cannibalism. The incidence of small pups was increased in the highest dose group. This corresponded with the observed decreased body weights in this group.

8. DISCUSSION AND CONCLUSION

T-7601 was administered to four groups of ten male and ten female Wistar rats by daily oral gavage at dose levels of 0 (propylene glycol), 50, 150 and 1000 mg/kg body weight/day for at least 28 days.
The study period for the males consisted of two weeks pre-mating, mating, and post-mating for the remainder of the 28 days. The study period for the females consisted of two weeks pre-mating, mating, post-coitum, and at least 4 days of lactation. The females that showed to be non-pregnant were also treated for at least 28 days.

Six rats died unexpectedly. One female treated at 150 mg/kg died just after delivery due to prolapse of the uterus. The death of one male of the 1000 mg/kg dose group was caused by a gavage error. These deaths were considered to be incidental. At 1000 mg/kg, the cause of death of two males could not be established and two females died due to meningitis. These deaths were also likely to be incidental findings, however a possible relationship to treatment could not entirely be excluded.

Treatment related clinical signs were noted in the mid dose group (150 mg/kg) and the high dose group (1000 mg/kg). At 1000 mg/kg, these consisted of lethargy, hunched posture, uncoordinated movements, decreased locomotor activity, ventro-lateral recumbency, quick breathing, laboured respiration, rales, shallow respiration, swelling of the genital region and abdomen, piloerection, red discolouration of urine, diarrhoea, salivation, chromodacryorrhoea of the eye and snout, lean appearance and ptosis. At 150 mg/kg, these consisted of salivation and diarrhoea.

Functional observations were unaffected with treatment of T-7601.

Body weight gain and food consumption were decreased during treatment for both sexes at 1000 mg/kg. Incidental severe body weight loss was observed at this dose level.

At 1000 mg/kg, clinical laboratory investigations showed affected parameters. For haematology, these consisted of increased erythrocytes count, haemoglobin concentration, and haematocrit for both sexes, and increased mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, and red cell distribution width for males. For clinical biochemistry, these consisted of increased alanine aminotransferase, alkaline phosphatase, urea, triglyceride, chloride, and inorganic phosphorus for males, and decreased aspartate aminotransferase, decreased bilirubin, and increased albumin for females.
The observed increases in haemoglobin concentration (both sexes), haematocrit (both sexes), and albumin (females) might be indicative for dehydration, which is in accordance with the retarded condition of the animals. However, no clear explanation can be given for all other affected clinical laboratory parameters.

At necropsy, four males treated at 1000 mg/kg showed a yellowish nodule(s) on the epididymides.

At 1000 mg/kg, decreased terminal body weight and increased liver weights for both sexes, and increased spleen and epididymides weights for the males were noted.

At 1000 mg/kg b.w./day, microscopic examination revealed the following:
Minimal/slight hepatocyte hypertrophy in the liver of both sexes, increased severity of hematopoiesis in the spleen of males, increased severity of hemosiderosis in the spleen of females, slight/moderate sperm granuloma in the epididymides of males.
Other findings in the testes (tubular atrophy, dilation, giant cells) and epididymides (reduced spermatozoa, cellular debris) of high dose animals were secondary to the blockage caused by the sperm granulomas.
Meningitis was present in the brain and spinal cord of two high dose females. A possible relationship to treatment could not be totally excluded, however these findings were considered most likely to be incidental.
Minimal centrilobular degeneration in the liver (two decedent males), slight adrenal cortical vacuolation in the adrenals (two males), minimal/slight atrophy in the thymus (one male and female), and minimal/slight acanthosis and hyperkeratosis in the stomach (one male and one female) were considered to be due to inanition or stress, rather than direct effects of the compound.

Fertility index, conception rate and gestation index were decreased at the highest dose group.

Duration of gestation was not affected by treatment with T-7601.

Based on only three litters, at 1000 mg/kg, increased postnatal loss between days 0 to 4 post partum, decreased pup weight, and increased incidence of clinical signs of the pups (small, pale, cold, and little milk) were observed.

Gavage treatment of male and female Wistar rats with T-7601 at dose levels of 50, 150 or 1000 mg/kg body weight/day during at least 28 days, revealed parental toxicity at 150 and 1000 mg/kg body weight/day. Reproductive, breeding, and developmental toxicity was observed at 1000 mg/kg body weight/day.

Based on the results in this combined repeated dose toxicity study with reproduction / developmental toxicity screening test:

- The definitive parental No Observed Adverse Effect Level (NOAEL) was established as being 50 mg/kg body weight/day.
- The definitive reproductive, breeding and development NOAEL was established as being 150 mg/kg body weight/day.

APPENDIX 1 SUMMARY TABLES

CLINICAL SIGNS SUMMARY, WEEKLY
MALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT WEEKS: 1	4
GROUP 1 (CONTROL)		
Breathing		
Rales (3)	G:	. 1. .
	%:	. 2. .
Secretion / excretion		
Salivation (3)	G:	. 111
	%:	. 311
GROUP 2 (50 MG/KG)		
Secretion / excretion		
Salivation (3)	G:	111
	%:	. 111
GROUP 3 (150 MG/KG)		
Breathing		
Rales (3)	G:	. . 1.
	%:	. . 1.
Skin / fur / plumage		
Alopecia (3)	G:	. . . 1
(Forelegs)	%:	. . . 1
Secretion / excretion		
Diarrhoea (1)	G:	. 111
	%:	. 552
Salivation (3)	G:	. 111
	%:	. 888
GROUP 4 (1000 MG/KG)		
Behavior		
Lethargy (3)	G:	1112
	%:	4991
Posture		
Hunched posture (1)	G:	1111
	%:	AAAA
Gait / motility		
Uncoordinated movements (3)	G:	111.
	%:	321.
Decreased locomotor activity (3)	G:	1. . .
	%:	1. . .
Breathing		
Quick breathing (1)	G:	. . . 1
	%:	. . . 1
Laboured respiration (3)	G:	111.
	%:	211.
Rales (3)	G:	1111
	%:	1143
Shallow respiration (3)	G:	. 11.
	%:	. 11.
Skin / fur / plumage		
Swelling (3)	G:	. . . 2
(Genital region)	%:	. . . 1
Piloerection (1)	G:	1111
	%:	2345
Alopecia (3)	G:	1112
(Back)	%:	1233
Alopecia (3)	G:	1. . .
(Inguinal region right)	%:	1. . .

G: Median value of the highest individual weekly grades
%: Percent of affected animals (0=less than 5%, 1=between 5% and 15%,..., A=more than 95%)
.: Observation performed, sign not present

CLINICAL SIGNS SUMMARY, WEEKLY
MALES

SIGN (MAX. GRADE) (LOCATION)		TREATMENT WEEKS: 1 4
GROUP 4 (1000 MG/KG)		
Alopecia (3)	G:	2
(Hindleg left)	%:	1
Alopecia (3)	G:	1
(Hindleg right)	%:	1
Red discolouration (1)	G:	1111
(Urine)	%:	1111
Secretion / excretion		
Diarrhoea (1)	G:	111
	%:	899
Salivation (3)	G:	1111
	%:	AAAA
Chromodacryorrhoea (3)	G:	1
(Eye left)	%:	1
Chromodacryorrhoea (3)	G:	1
(Eye right)	%:	1
Chromodacryorrhoea (3)	G:	1
(Snout)	%:	1
Various		
Lean (1)	G:	1111
	%:	1661
Ptosis (3)	G:	11
	%:	11

FEMALES

SIGN (MAX. GRADE) (LOCATION)		TREATMENT WEEKS: 1 4
GROUP 1 (CONTROL)		
Breathing		
Rales (3)	G:	1
	%:	1
Skin / fur / plumage		
Alopecia (3)	G:	111
(Cervical region)	%:	112
Alopecia (3)	G:	22333
(Abdomen)	%:	11112
Alopecia (3)	G:	22333
(Chest)	%:	11112
Alopecia (3)	G:	2222
(Thigh hind left)	%:	1112
Alopecia (3)	G:	2222
(Thigh hind right)	%:	1112
Alopecia (3)	G:	2333
(Forelegs)	%:	1112
GROUP 2 (50 MG/KG)		
No clinical signs noted		

G: Median value of the highest individual weekly grades
%: Percent of affected animals (0=less than 5%, 1=between 5% and 15%, ..., A=more than 95%)
: Observation performed, sign not present

CLINICAL SIGNS SUMMARY, WEEKLY
FEMALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT WEEKS:	1	2	3	4
GROUP 3 (150 MG/KG)					
Skin / fur / plumage					
Alopecia (3)	G:	.	.	.	1
(Foreleg right)	%:	.	.	.	1
Secretion / excretion					
Salivation (3)	G:	.	1	1	1
	%:	.	A	A	A
GROUP 4 (1000 MG/KG)					
Behavior					
Lethargy (3)	G:	.	3	.	.
	%:	.	1	.	.
Posture					
Ventro-lateral recumbency (1)	G:	.	.	.	1
	%:	.	.	.	1
Hunched posture (1)	G:	1	1	1	1
	%:	A	A	A	A
Gait / motility					
Decreased locomotor activity (3)	G:	.	1	.	.
	%:	.	1	.	.
Breathing					
Laboured respiration (3)	G:	.	1	1	.
	%:	.	1	1	.
Rales (3)	G:	.	.	1	1
	%:	.	.	1	1
Skin / fur / plumage					
Swelling (3)	G:	.	1	1	1
(Abdomen)	%:	.	1	1	1
Piloerection (1)	G:	.	1	.	.
	%:	.	1	.	.
Alopecia (3)	G:	1	1	1	2
(Back)	%:	1	3	3	1
Secretion / excretion					
Diarrhoea (1)	G:	.	1	.	.
	%:	.	1	.	.
Salivation (3)	G:	1	1	1	1
	%:	A	A	A	9
Various					
Lean (1)	G:	1	1	1	1
	%:	1	2	1	1
Ptosis (3)	G:	.	1	.	.
	%:	.	1	.	.

G: Median value of the highest individual weekly grades
%: Percent of affected animals (0=less than 5%, 1=between 5% and 15%, ..., A=more than 95%)
.: Observation performed, sign not present

FUNCTIONAL OBSERVATIONS
MALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
WEEK 4					
HEARING	MEDIAN	0	0	0	0
SCORE 0/1	N	5	5	5	5
PUPIL L	MEDIAN	0	0	0	0
SCORE 0/1	N	5	5	5	5
PUPIL R	MEDIAN	0	0	0	0
SCORE 0/1	N	5	5	5	5
STATIC R	MEDIAN	0	0	0	0
SCORE 0/1	N	5	5	5	5
GRIP	MEDIAN	0	0	0	0
SCORE 0/1	N	5	5	5	5

FEMALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
WEEK 4					
HEARING	MEDIAN	0	0	0	0
SCORE 0/1	N	5	5	5	5
PUPIL L	MEDIAN	0	0	0	0
SCORE 0/1	N	5	5	5	5
PUPIL R	MEDIAN	0	0	0	0
SCORE 0/1	N	5	5	5	5
STATIC R	MEDIAN	0	0	0	0
SCORE 0/1	N	5	5	5	5
GRIP	MEDIAN	0	0	0	0
SCORE 0/1	N	5	5	5	5

+/++ Steel-test significant at 5% (+) or 1% (++) level

BODY WEIGHTS (GRAM) SUMMARY
MALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
PRE-MATING					
DAY 1	MEAN	257	258	257	250
WEEK 1	ST.DEV	8.5	9.7	9.8	12.3
	N	10	10	10	10
DAY 8	MEAN	302	301	302	243 **
WEEK 2	ST.DEV	16.0	9.3	16.7	20.0
	N	10	10	10	9

FEMALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
PRE-MATING					
DAY 1	MEAN	185	184	183	186
WEEK 1	ST.DEV	6.5	9.4	9.5	9.8
	N	10	10	10	10
DAY 8	MEAN	210	209	206	192 **
WEEK 2	ST.DEV	8.2	7.5	8.1	15.0
	N	10	10	10	10

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

BODY WEIGHTS (GRAM) SUMMARY
MALES
F0-GENERATION

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
MATING					
DAY 1	MEAN	344	339	341	276 **
	ST.DEV.	28.7	13.5	20.4	17.2
	N	10	10	10	8
POST MATING					
DAY 1	MEAN	374	373	371	313 **
	ST.DEV.	32.9	16.9	21.7	11.8
	N	10	10	10	8
DAY 7	MEAN	402	399	395	314 **
	ST.DEV.	37.2	20.6	27.7	15.8
	N	10	10	10	7

FEMALES
F0-GENERATION

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
MATING					
DAY 1	MEAN	230	228	227	224
	ST.DEV.	10.8	10.0	12.8	5.5
	N	10	10	10	9
POST COITUM					
DAY 0	MEAN	237	238	233	230
	ST.DEV.	8.5	10.7	7.6	9.3
	N	10	9	8	3
DAY 7	MEAN	287	284	281	279
	ST.DEV.	10.3	9.9	9.9	20.8
	N	10	9	8	3
DAY 14	MEAN	339	330	324	324
	ST.DEV.	12.6	13.2	15.4	19.0
	N	10	9	8	3
DAY 21	MEAN	441	441	415	396
	ST.DEV.	32.2	15.7	40.6	11.4
	N	10	9	8	3
LACTATION					
DAY 1	MEAN	338	323	322	311
	ST.DEV.	22.1	17.4	15.7	21.5
	N	10	9	7	3
DAY 4	MEAN	345	331	331	318
	ST.DEV.	18.1	16.4	18.7	21.5
	N	10	9	7	3

*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level
Explanations for excluded data are listed in the tables of the individual values

BODY WEIGHT GAIN (%) SUMMARY
MALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
PRE-MATING					
DAY 1	MEAN	0	0	0	0
WEEK 1	ST.DEV	0.0	0.0	0.0	0.0
	N	10	10	10	10
DAY 8	MEAN	18	17	17	-3 **
WEEK 2	ST.DEV	4.3	2.3	3.6	9.8
	N	10	10	10	9

FEMALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
PRE-MATING					
DAY 1	MEAN	0	0	0	0
WEEK 1	ST.DEV	0.0	0.0	0.0	0.0
	N	10	10	10	10
DAY 8	MEAN	14	14	13	3 **
WEEK 2	ST.DEV	4.3	3.8	5.0	7.4
	N	10	10	10	10

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

BODY WEIGHT GAIN (%) SUMMARY
MALES
F0-GENERATION

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
MATING					
DAY 1	MEAN	0	0	0	0
	ST.DEV.	0.0	0.0	0.0	0.0
	N	10	10	10	8
POST MATING					
DAY 1	MEAN	0	0	0	0
	ST.DEV.	0.0	0.0	0.0	0.0
	N	10	10	10	8
DAY 7	MEAN	7	7	7	-1 **
	ST.DEV.	1.4	1.5	1.9	5.0
	N	10	10	10	7

FEMALES
F0-GENERATION

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
MATING					
DAY 1	MEAN	0	0	0	0
	ST.DEV.	0.0	0.0	0.0	0.0
	N	10	10	10	9
POST COITUM					
DAY 0	MEAN	0	0	0	0
	ST.DEV.	0.0	0.0	0.0	0.0
	N	10	9	8	3
DAY 7	MEAN	21	19	21	22
	ST.DEV.	2.2	4.7	2.6	4.1
	N	10	9	8	3
DAY 14	MEAN	44	39	40	41
	ST.DEV.	4.5	6.2	5.5	3.4
	N	10	9	8	3
DAY 21	MEAN	86	86	78	73
	ST.DEV.	14.3	8.1	18.2	5.4
	N	10	9	8	3
LACTATION					
DAY 1	MEAN	0	0	0	0
	ST.DEV.	0.0	0.0	0.0	0.0
	N	10	9	7	3
DAY 4	MEAN	2	3	3	2
	ST.DEV.	3.8	3.3	3.6	5.1
	N	10	9	7	3

*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level
Explanations for excluded data are listed in the tables of the individual values

FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
MALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
PRE-MATING					
DAYS 1-8	MEAN	30	29	28	18 **
WEEKS 1-2	ST.DEV	0.7	1.4	1.8	0.5
	N (CAGE)	2	2	2	2
DAYS 8-15	MEAN	32	30	29	19 *
WEEKS 2-3	ST.DEV	1.2	1.0	0.1	4.6
	N (CAGE)	2	2	2	2
MEAN OF MEANS					
OVER PRE-MATING	MEAN	31	29	29	18

FEMALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
PRE-MATING					
DAYS 1-8	MEAN	22	21	21	16
WEEKS 1-2	ST.DEV	2.2	1.8	1.1	1.6
	N (CAGE)	2	2	2	2
DAYS 8-15	MEAN	23	23	22	21
WEEKS 2-3	ST.DEV	1.3	1.1	0.1	1.4
	N (CAGE)	2	2	2	2
MEAN OF MEANS					
OVER PRE-MATING	MEAN	22	22	22	18

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

FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
MALES
F0-GENERATION

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
POST MATING					
DAYS 1-7	MEAN	35	33	33	24 **
	ST.DEV.	3.0	2.4	3.1	10.2
	N	10	10	10	8

FEMALES
F0-GENERATION

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
POST COITUM					
DAYS 0-7	MEAN	27	26	27	26
	ST.DEV.	2.1	1.8	1.8	2.1
	N	10	9	8	3
DAYS 7-14	MEAN	32	30	30	30
	ST.DEV.	2.1	2.6	2.0	1.7
	N	10	9	8	3
DAYS 14-21	MEAN	33	33	32	30
	ST.DEV.	3.0	2.1	2.7	3.6
	N	10	9	8	3
MEAN OF MEANS		31	30	30	29
LACTATION					
DAYS 1-4	MEAN	38	34	34	24 *
	ST.DEV.	8.3	6.9	7.3	6.1
	N	10	9	6	3

*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level
Explanations for excluded data are listed in the tables of the individual values

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

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
PRE-MATING					
DAYS 1-8	MEAN	100	95	93	73 **
WEEKS 1-2	ST.DEV	1.4	5.2	6.4	0.9
	N (CAGE)	2	2	2	2
DAYS 8-15	MEAN	105	99	97	78
WEEKS 2-3	ST.DEV	3.1	3.8	0.3	21.9
	N (CAGE)	2	2	2	2
MEAN OF MEANS OVER PRE-MATING	MEAN	103	97	95	75

FEMALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
PRE-MATING					
DAYS 1-8	MEAN	103	99	102	81
WEEKS 1-2	ST.DEV	8.3	7.7	4.2	2.8
	N (CAGE)	2	2	2	2
DAYS 8-15	MEAN	108	110	108	111
WEEKS 2-3	ST.DEV	3.7	4.3	1.6	0.5
	N (CAGE)	2	2	2	2
MEAN OF MEANS OVER PRE-MATING	MEAN	105	104	105	96

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

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY) SUMMARY
MALES
F0-GENERATION

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
POST MATING					
DAYS 1-7	MEAN	87	84	84	87
	ST.DEV.	5.4	6.1	4.8	16.0
	N	10	10	10	7

FEMALES
F0-GENERATION

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
POST COITUM					
DAYS 0-7	MEAN	94	93	95	92
	ST.DEV.	5.0	6.1	4.2	1.9
	N	10	9	8	3
DAYS 7-14	MEAN	95	92	93	93
	ST.DEV.	3.1	5.7	4.4	3.8
	N	10	9	8	3
DAYS 14-21	MEAN	76	74	77	76
	ST.DEV.	6.8	4.6	4.1	9.6
	N	10	9	8	3
MEAN OF MEANS		89	86	88	87
LACTATION					
DAYS 1-4	MEAN	109	104	102	75 *
	ST.DEV.	23.7	18.9	18.5	14.4
	N	10	9	6	3

*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level
Explanations for excluded data are listed in the tables of the individual values

HAEMATOLOGY SUMMARY
MALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
END OF TREATMENT					
WBC	MEAN	7.4	8.2	8.4	9.9
10E9/l	ST.DEV	2.0	2.8	1.8	2.0
	N	5	5	5	5
Band Neutro	MEAN	0	0	0	1
%WBC	ST.DEV	0	0	0	1
	N	5	5	5	5
NEUT	MEAN	16.4	17.2	13.8	16.4
%WBC	ST.DEV	3.9	3.6	4.4	5.5
	N	5	5	5	5
EOS	MEAN	0.8	1.4	1.2	0.8
%WBC	ST.DEV	1.3	0.5	0.4	0.8
	N	5	5	5	5
BASO	MEAN	0.0	0.0	0.0	0.0
%WBC	ST.DEV	0.0	0.0	0.0	0.0
	N	5	5	5	5
MONO	MEAN	1.4	2.4	1.0	1.6
%WBC	ST.DEV	1.5	1.5	1.2	1.3
	N	5	5	5	5
LYMPHO	MEAN	81.2	78.8	83.8	80.4
%WBC	ST.DEV	5.0	4.4	5.4	5.8
	N	5	5	5	5
RBC	MEAN	7.57	7.59	7.50	8.65 **
10E12/l	ST.DEV	0.42	0.18	0.28	0.48
	N	5	5	5	5
HGB	MEAN	9.2	9.0	9.2	11.4 **
mmol/l	ST.DEV	0.3	0.2	0.2	0.7
	N	5	5	5	5
HCT	MEAN	0.428	0.419	0.427	0.521 **
l/l	ST.DEV	0.016	0.013	0.016	0.031
	N	5	5	5	5
MCV	MEAN	56.7	55.3	56.9	60.3 **
fl	ST.DEV	2.0	0.8	1.6	0.7
	N	5	5	5	5
MCH	MEAN	1.21	1.18	1.22	1.32 **
fmol	ST.DEV	0.05	0.01	0.02	0.02
	N	5	5	5	5
MCHC	MEAN	21.38	21.41	21.51	21.93 **
mmol/l	ST.DEV	0.10	0.17	0.39	0.14
	N	5	5	5	5
PLT	MEAN	907	857	952	781
10E9/l	ST.DEV	147	131	153	143
	N	5	5	5	4
RDW	MEAN	11.4	11.9	11.4	16.1 **
%	ST.DEV	0.4	0.7	0.6	1.3
	N	5	5	5	5

+/++ Steel-test significant at 5% (+) or 1% (++) level
*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

HAEMATOLOGY SUMMARY
MALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
END OF TREATMENT					
PT	MEAN	17.4	17.5	18.5	18.1
s	ST.DEV	1.0	0.1	1.0	0.8
	N	5	4	4	5
APTT	MEAN	13.1	12.8	11.7	13.1
s	ST.DEV	1.4	1.9	1.4	2.5
	N	5	4	4	5

+/++ Steel-test significant at 5% (+) or 1% (++) level
*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

HAEMATOLOGY SUMMARY
FEMALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
END OF TREATMENT					
WBC	MEAN	6.4	6.1	5.5	7.3
10E9/l	ST.DEV	1.5	1.4	1.1	0.8
	N	5	4	5	5
Band Neutro	MEAN	0	0	0	0
%WBC	ST.DEV	1	1	0	0
	N	5	4	5	5
NEUT	MEAN	21.6	23.0	19.0	13.6 +
%WBC	ST.DEV	4.4	5.4	5.8	2.5
	N	5	4	5	5
EOS	MEAN	0.6	0.8	0.6	2.0
%WBC	ST.DEV	0.5	1.0	0.9	1.6
	N	5	4	5	5
BASO	MEAN	0.0	0.0	0.0	0.0
%WBC	ST.DEV	0.0	0.0	0.0	0.0
	N	5	4	5	5
MONO	MEAN	1.6	2.0	1.8	4.0
%WBC	ST.DEV	1.5	0.8	0.8	3.2
	N	5	4	5	5
LYMPHO	MEAN	75.8	74.0	78.6	80.2
%WBC	ST.DEV	4.2	4.7	6.5	3.8
	N	5	4	5	5
RBC	MEAN	7.14	7.04	7.29	8.66 **
10E12/l	ST.DEV	0.44	0.26	0.34	0.46
	N	5	4	5	5
HGB	MEAN	9.0	8.7	9.1	11.4 **
mmol/l	ST.DEV	0.6	0.4	0.2	0.6
	N	5	4	5	5
HCT	MEAN	0.423	0.410	0.432	0.526 **
l/l	ST.DEV	0.023	0.017	0.014	0.028
	N	5	4	5	5
MCV	MEAN	59.3	58.3	59.3	60.7
fl	ST.DEV	1.8	1.1	1.8	2.6
	N	5	4	5	5
MCH	MEAN	1.26	1.24	1.25	1.32
fmol	ST.DEV	0.02	0.01	0.05	0.05
	N	5	4	5	5
MCHC	MEAN	21.23	21.25	21.10	21.74
mmol/l	ST.DEV	0.42	0.48	0.39	0.20
	N	5	4	5	5
PLT	MEAN	999	1298 *	1179	802
10E9/l	ST.DEV	114	55	226	114
	N	5	4	5	5
RDW	MEAN	12.1	12.5	12.1	12.7
%	ST.DEV	0.8	0.2	0.8	0.3
	N	5	4	5	5

+/++ Steel-test significant at 5% (+) or 1% (++) level
*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

HAEMATOLOGY SUMMARY
FEMALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
END OF TREATMENT					
PT	MEAN	17.3	17.6	17.5	16.7
s	ST.DEV	0.4	0.9	0.8	0.5
	N	5	5	5	5
APTT	MEAN	12.5	12.2	12.5	14.4
s	ST.DEV	1.5	1.1	0.9	2.1
	N	5	5	5	5

+/++ Steel-test significant at 5% (+) or 1% (++) level
*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

CLINICAL BIOCHEMISTRY SUMMARY
MALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
END OF TREATMENT					
ALAT	MEAN	35.6	28.7	33.6	67.3 **
U/l	ST.DEV	1.5	4.9	5.3	21.9
	N	5	5	5	5
ASAT	MEAN	71.9	66.7	75.5	88.1
U/l	ST.DEV	6.1	5.6	7.3	27.2
	N	5	5	5	5
ALP	MEAN	125	98	127	230 **
U/l	ST.DEV	29	10	12	41
	N	5	5	5	5
BILIRUBIN	MEAN	3.1	3.1	2.7	3.4
umol/l	ST.DEV	0.9	0.6	0.5	0.7
	N	5	5	5	5
UREA	MEAN	6.0	6.0	7.4	9.6 **
mmol/l	ST.DEV	1.3	1.0	1.8	1.0
	N	5	5	5	5
CREATININE	MEAN	41.4	31.2	35.6	33.5
umol/l	ST.DEV	9.3	6.8	9.2	7.5
	N	5	5	5	5
GLUCOSE	MEAN	6.68	6.26	5.72	6.36
mmol/l	ST.DEV	0.91	0.31	0.52	1.00
	N	5	5	5	5
CHOLESTEROL	MEAN	1.39	1.27	1.29	1.62
mmol/l	ST.DEV	0.18	0.19	0.40	0.34
	N	5	5	5	5
TRIGLYCERIDES	MEAN	0.34	0.42	0.31	0.64 **
mmol/l	ST.DEV	0.08	0.08	0.10	0.12
	N	5	5	5	5
SODIUM	MEAN	141.9	141.6	141.3	140.7
mmol/l	ST.DEV	0.5	1.2	0.8	0.8
	N	5	5	5	5
POTASSIUM	MEAN	3.61	3.78	3.61	3.74
mmol/l	ST.DEV	0.18	0.40	0.07	0.29
	N	5	5	5	5
CALCIUM	MEAN	2.81	2.79	2.86	2.90
mmol/l	ST.DEV	0.05	0.04	0.06	0.08
	N	5	5	5	5
CHLORIDE	MEAN	102	103	103	106 **
mmol/l	ST.DEV	1	2	1	2
	N	5	5	5	5
INORG.PHOS	MEAN	2.38	2.19	2.28	2.68 **
mmol/l	ST.DEV	0.14	0.08	0.08	0.17
	N	5	5	5	5
TOTAL PROTEIN	MEAN	58.9	59.6	59.5	56.3
g/l	ST.DEV	2.9	0.9	2.0	2.2
	N	5	5	5	5

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

CLINICAL BIOCHEMISTRY SUMMARY
MALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
END OF TREATMENT					
ALBUMIN	MEAN	31.4	31.6	31.2	32.5
g/l	ST.DEV	1.5	0.7	0.5	1.8
	N	5	5	5	5

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

CLINICAL BIOCHEMISTRY SUMMARY
FEMALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
END OF TREATMENT					
ALAT	MEAN	64.9	60.5	59.4	77.1
U/l	ST.DEV	8.7	23.6	3.8	25.9
	N	5	5	5	5
ASAT	MEAN	80.1	72.6	66.1	55.1 **
U/l	ST.DEV	14.2	11.8	5.7	9.3
	N	5	5	5	5
ALP	MEAN	120	97	85	107
U/l	ST.DEV	25	34	18	15
	N	5	5	5	5
BILIRUBIN	MEAN	3.5	3.9	3.7	3.0 *
umol/l	ST.DEV	0.5	0.2	0.3	0.2
	N	5	5	5	5
UREA	MEAN	8.5	8.2	7.6	7.5
mmol/l	ST.DEV	1.1	1.9	1.1	0.7
	N	5	5	5	5
CREATININE	MEAN	43.1	42.4	39.8	41.5
umol/l	ST.DEV	2.2	1.6	0.9	3.5
	N	5	5	5	5
GLUCOSE	MEAN	5.43	6.20	5.98	5.56
mmol/l	ST.DEV	0.48	1.50	0.77	0.51
	N	5	5	5	5
CHOLESTEROL	MEAN	1.94	1.78	2.02	2.02
mmol/l	ST.DEV	0.44	0.28	0.56	0.48
	N	5	5	5	5
TRIGLYCERIDES	MEAN	0.68	0.51	0.60	0.89
mmol/l	ST.DEV	0.33	0.11	0.23	0.25
	N	5	5	5	5
SODIUM	MEAN	139.9	139.3	140.2	139.0
mmol/l	ST.DEV	1.3	2.5	0.9	1.2
	N	5	5	5	5
POTASSIUM	MEAN	3.78	3.55	3.53	3.44
mmol/l	ST.DEV	0.20	0.45	0.29	0.28
	N	5	5	5	5
CALCIUM	MEAN	2.99	2.87	2.88	3.04
mmol/l	ST.DEV	0.11	0.11	0.08	0.05
	N	5	5	5	5
CHLORIDE	MEAN	98	100	101	100
mmol/l	ST.DEV	3	2	2	1
	N	5	5	5	5
INORG.PHOS	MEAN	2.82	2.04 **	2.07 **	2.02 **
mmol/l	ST.DEV	0.37	0.15	0.21	0.17
	N	5	5	5	5
TOTAL PROTEIN	MEAN	61.7	63.7	63.9	65.4
g/l	ST.DEV	1.5	3.5	3.5	1.7
	N	5	5	5	5

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

CLINICAL BIOCHEMISTRY SUMMARY
FEMALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
END OF TREATMENT					
ALBUMIN	MEAN	32.5	33.4	33.0	38.2 **
g/l	ST.DEV	1.2	1.5	1.5	1.7
	N	5	5	5	5

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

MACROSCOPIC FINDINGS SUMMARY
MALES

	GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
ALL NECROPSIES				
Animals examined	10	10	10	10
Animals without findings	9	9	7	3
Animals affected	1	1	3	7
General observations				
Emaciated	0	0	0	1
Cannibalism:organ missing	0	0	0	2
Beginning autolysis	0	0	0	1
Lungs				
Discolouration	0	0	0	1
Stomach				
Thickened	0	0	0	1
Irregular surface	0	0	0	1
Discolouration	0	0	0	1
Duodenum				
Discolouration	0	0	0	1
Caecum				
Discolouration	0	0	0	1
Liver				
Accentuated lobular pattern	0	0	0	1
Enlarged	0	0	0	1
Discolouration	0	1	0	0
Kidneys				
Pelvic dilation	0	0	2	2
Urinary bladder				
Contents:	0	0	0	1
Epididymides				
Nodule(s)	0	0	0	4
Thymus				
Focus/foci	1	0	2	2
Mandibular l.node				
Discolouration	0	0	0	1

FEMALES

	GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
ALL NECROPSIES				
Animals examined	10	10	10	10
Animals without findings	8	7	6	2
Animals affected	2	3	4	8
General observations				
Emaciated	0	0	0	1
Stomach				
Crateriform retraction	0	0	0	1
Liver				
Accentuated lobular pattern	0	1	0	0
Kidneys				
Pelvic dilation	0	0	0	1

/ ## Fisher's Exact test significant at 5% (#) or 1% (##) level

MACROSCOPIC FINDINGS SUMMARY
FEMALES

	GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
ALL NECROPSIES				
Uterus				
Prolapse of the uterus.	0	0	1	0
Cyst(s)	0	0	0	1
Contains fluid	0	0	0	2
Clitoral glands				
Focus/foci	0	0	1	0
Adrenal glands				
Focus/foci	0	1	0	0
Grown together with:	0	0	0	1
Spleen				
Constricted.	0	0	1	0
Thymus				
Discolouration	1	0	0	1
Mesenteric l.node				
Discolouration	0	0	0	1
Mandibular l.node				
Discolouration	1	2	2	1
Skin				
Alopecia	1	0	0	0
Eyes				
Right side : exophtalmus.	0	1	0	0

/ ## Fisher's Exact test significant at 5% (#) or 1% (##) level

ORGAN WEIGHTS (GRAM) SUMMARY
MALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
END OF TREATMENT					
BODY W.	MEAN	361	360	358	279 **
(GRAM)	ST.DEV	32	17	20	14
	N	10	10	10	7
BRAIN	MEAN	2.05	2.10	2.11	1.95
(GRAM)	ST.DEV	0.10	0.13	0.16	0.04
	N	5	5	5	5
HEART	MEAN	1.208	1.162	1.186	1.108
(GRAM)	ST.DEV	0.066	0.095	0.067	0.044
	N	5	5	5	5
LIVER	MEAN	10.48	10.46	10.16	11.72
(GRAM)	ST.DEV	0.90	0.55	0.72	0.87
	N	5	5	5	5
THYMUS	MEAN	0.491	0.487	0.472	0.299 **
(GRAM)	ST.DEV	0.065	0.081	0.116	0.054
	N	5	5	5	5
KIDNEYS	MEAN	3.02	3.00	3.02	2.67
(GRAM)	ST.DEV	0.30	0.29	0.26	0.12
	N	5	5	5	5
ADRENALS	MEAN	0.078	0.079	0.073	0.062
(GRAM)	ST.DEV	0.011	0.013	0.009	0.011
	N	5	5	5	5
SPLEEN	MEAN	0.792	0.876	0.814	0.719
(GRAM)	ST.DEV	0.012	0.085	0.064	0.049
	N	5	5	5	5
TESTES	MEAN	3.47	3.69	3.74	3.40
(GRAM)	ST.DEV	0.28	0.41	0.37	0.54
	N	10	10	10	7
EPIDIDYMIDES	MEAN	1.091	1.141	1.131	1.054
(GRAM)	ST.DEV	0.125	0.155	0.116	0.161
	N	10	10	10	7

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

ORGAN/BODY WEIGHT RATIOS (%) SUMMARY
MALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
END OF TREATMENT					
BODY W.	MEAN	361	360	358	279 **
(GRAM)	ST.DEV	32	17	20	14
	N	10	10	10	7
BRAIN	MEAN	0.58	0.58	0.60	0.70 **
(%)	ST.DEV	0.05	0.04	0.03	0.05
	N	5	5	5	5
HEART	MEAN	0.342	0.323	0.338	0.399 *
(%)	ST.DEV	0.032	0.029	0.027	0.023
	N	5	5	5	5
LIVER	MEAN	2.96	2.91	2.89	4.21 **
(%)	ST.DEV	0.15	0.18	0.09	0.26
	N	5	5	5	5
THYMUS	MEAN	0.138	0.136	0.134	0.107
(%)	ST.DEV	0.010	0.023	0.031	0.015
	N	5	5	5	5
KIDNEYS	MEAN	0.85	0.84	0.86	0.96
(%)	ST.DEV	0.06	0.12	0.04	0.05
	N	5	5	5	5
ADRENALS	MEAN	0.022	0.022	0.021	0.023
(%)	ST.DEV	0.004	0.005	0.003	0.005
	N	5	5	5	5
SPLEEN	MEAN	0.224	0.244	0.232	0.259 *
(%)	ST.DEV	0.014	0.033	0.008	0.014
	N	5	5	5	5
TESTES	MEAN	0.97	1.03	1.05	1.23 **
(%)	ST.DEV	0.11	0.10	0.09	0.25
	N	10	10	10	7
EPIDIDYMIDES	MEAN	0.305	0.317	0.316	0.380 **
(%)	ST.DEV	0.045	0.043	0.032	0.072
	N	10	10	10	7

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

ORGAN WEIGHTS (GRAM) SUMMARY
FEMALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
END OF TREATMENT					
BODY W.	MEAN	321	302	301	288 *
(GRAM)	ST.DEV	24	16	18	22
	N	6	6	6	5
BRAIN	MEAN	2.01	1.98	1.95	1.97
(GRAM)	ST.DEV	0.10	0.12	0.07	0.05
	N	5	5	5	5
HEART	MEAN	1.049	0.985	1.054	1.108
(GRAM)	ST.DEV	0.048	0.047	0.144	0.088
	N	5	5	5	5
LIVER	MEAN	10.72	10.79	11.24	13.80 **
(GRAM)	ST.DEV	1.01	1.06	1.46	1.41
	N	5	5	5	5
THYMUS	MEAN	0.321	0.301	0.331	0.366
(GRAM)	ST.DEV	0.040	0.073	0.072	0.067
	N	5	5	5	5
KIDNEYS	MEAN	2.24	2.34	2.31	2.24
(GRAM)	ST.DEV	0.08	0.24	0.27	0.15
	N	5	5	5	5
ADRENALS	MEAN	0.103	0.098	0.102	0.087
(GRAM)	ST.DEV	0.019	0.012	0.006	0.009
	N	5	5	5	5
SPLEEN	MEAN	0.845	0.748	0.751	0.714
(GRAM)	ST.DEV	0.119	0.085	0.132	0.106
	N	5	5	5	5

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

ORGAN/BODY WEIGHT RATIOS (%) SUMMARY
FEMALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
END OF TREATMENT					
BODY W.	MEAN	321	302	301	288 *
(GRAM)	ST.DEV	24	16	18	22
	N	6	6	6	5
BRAIN	MEAN	0.64	0.66	0.66	0.69
(%)	ST.DEV	0.02	0.04	0.02	0.04
	N	5	5	5	5
HEART	MEAN	0.337	0.326	0.356	0.386 *
(%)	ST.DEV	0.016	0.019	0.040	0.032
	N	5	5	5	5
LIVER	MEAN	3.44	3.56	3.79	4.80 **
(%)	ST.DEV	0.23	0.22	0.37	0.35
	N	5	5	5	5
THYMUS	MEAN	0.103	0.099	0.112	0.127
(%)	ST.DEV	0.014	0.021	0.023	0.021
	N	5	5	5	5
KIDNEYS	MEAN	0.72	0.77	0.78	0.78
(%)	ST.DEV	0.01	0.06	0.06	0.04
	N	5	5	5	5
ADRENALS	MEAN	0.033	0.033	0.034	0.030
(%)	ST.DEV	0.006	0.003	0.001	0.003
	N	5	5	5	5
SPLEEN	MEAN	0.271	0.247	0.253	0.249
(%)	ST.DEV	0.035	0.024	0.038	0.042
	N	5	5	5	5

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

REPRODUCTION PROCESSES
F0-GENERATION - POST COITUM

FEMALE NUMBER	MALE NUMBER	MATING DATE	PREGNANT	SCHEDULE	DELIVERY RECORDED	WEANING DATE	NECROPSY DATE
GROUP 1 (CONTROL)							
41	1	06AUG2003	YES	BREEDING	27AUG2003	01SEP2003	01SEP2003
42	2	08AUG2003	YES	BREEDING	30AUG2003	04SEP2003	04SEP2003
43	3	08AUG2003	YES	BREEDING	30AUG2003	04SEP2003	04SEP2003
44	4	05AUG2003	YES	BREEDING	27AUG2003	01SEP2003	01SEP2003
45	5	07AUG2003	YES	BREEDING	28AUG2003	02SEP2003	02SEP2003
46	6	05AUG2003	YES	BREEDING	27AUG2003	01SEP2003	01SEP2003
47	7	07AUG2003	YES	BREEDING	28AUG2003	02SEP2003	02SEP2003
48	8	05AUG2003	YES	BREEDING	27AUG2003	01SEP2003	01SEP2003
49	9	06AUG2003	YES	BREEDING	28AUG2003	02SEP2003	02SEP2003
50	10	08AUG2003	YES	BREEDING	30AUG2003	04SEP2003	04SEP2003
GROUP 2 (50 MG/KG)							
51	11	07AUG2003	YES	BREEDING	28AUG2003	02SEP2003	02SEP2003
52	12	06AUG2003	YES	BREEDING	27AUG2003	01SEP2003	01SEP2003
53	13	06AUG2003	YES	BREEDING	27AUG2003	01SEP2003	01SEP2003
54	14	06AUG2003	YES	BREEDING	28AUG2003	02SEP2003	02SEP2003
55	15	06AUG2003	YES	BREEDING	28AUG2003	02SEP2003	02SEP2003
56	16	08AUG2003	YES	BREEDING	29AUG2003	03SEP2003	03SEP2003
57 <NP>	17	05AUG2003	NO	---	---	---	05SEP2003
58	18	08AUG2003	YES	BREEDING	30AUG2003	04SEP2003	04SEP2003
59	19	06AUG2003	YES	BREEDING	27AUG2003	01SEP2003	01SEP2003
60	20	08AUG2003	YES	BREEDING	30AUG2003	04SEP2003	04SEP2003
GROUP 3 (150 MG/KG)							
61	21	05AUG2003	YES	BREEDING	27AUG2003	01SEP2003	01SEP2003
62	22	08AUG2003	YES	BREEDING	30AUG2003	04SEP2003	04SEP2003
63	23	06AUG2003	YES	BREEDING	27AUG2003	01SEP2003	01SEP2003
64	24	06AUG2003	YES	BREEDING	28AUG2003	02SEP2003	02SEP2003
65	25	08AUG2003	YES	BREEDING	31AUG2003	---	01SEP2003
66	26	05AUG2003	YES	BREEDING	26AUG2003	01SEP2003	01SEP2003
67	27	08AUG2003	YES	BREEDING	30AUG2003	04SEP2003	04SEP2003
68 <NP>	28	05AUG2003	NO	---	---	---	05SEP2003
69	29	06AUG2003	YES	BREEDING	28AUG2003	02SEP2003	02SEP2003
70 <NP>	30	05AUG2003	NO	---	---	---	05SEP2003
GROUP 4 (1000 MG/KG)							
71 <NP>	31	08AUG2003	NO	---	---	---	05SEP2003
72 <NP>	32	08AUG2003	NO	---	---	---	05SEP2003
73 <NP>	35	07AUG2003	NO	---	---	---	05SEP2003
74	36	06AUG2003	YES	BREEDING	27AUG2003	01SEP2003	01SEP2003
75	37	07AUG2003	YES	BREEDING	29AUG2003	05SEP2003	05SEP2003
76 <NP>	38	06AUG2003	NO	---	---	---	05SEP2003
78 <SD>	39	06AUG2003	YES	---	---	---	18AUG2003
79 <NP>	40	07AUG2003	NO	---	---	---	05SEP2003
80	39	09AUG2003	YES	BREEDING	31AUG2003	05SEP2003	05SEP2003

<SD> Spontaneous death
<NP> Non-pregnant

MATING PERFORMANCE
F0-GENERATION - POST COITUM

DAY OF THE PAIRING PERIOD	GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
NUMBER OF FEMALES MATED DURING THE FIRST PAIRING PERIOD				
1	3	1	4	-
2	2	5	3	3
3	2	1	-	4
4	3	3	3	2
MEDIAN PRECOITAL TIME	3	2	2	3
MEAN PRECOITAL TIME	2.5	2.6	2.2	2.9
N	10	10	10	9

+/++ Steel-test significant at 5% (+) or 1% (++) level

BREEDING DATA PER GROUP
FEMALES
F0-GENERATION - LACTATION

	GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
LITTERS				
TOTAL	10	9	8	3
DURATION OF GESTATION				
MEAN (+)	21.7	21.4	21.9	21.7
ST.DEV.	0.48	0.53	0.64	0.58
N	10	9	8	3
DEAD PUPS AT FIRST LITTER CHECK				
LITTERS AFFECTED (#)	2	1	0	0
TOTAL	2	1	0	0
MEAN (+)	0.2	0.1	0.0	0.0
ST.DEV.	0.42	0.33	0.00	0.00
N	10	9	8	3
LIVING PUPS AT FIRST LITTER CHECK				
% OF MALES / FEMALES (#)	46 / 54	43 / 57	53 / 47	48 / 52
TOTAL	122	140	87	25
MEAN (+)	12.2	15.6	10.9	8.3
ST.DEV.	5.03	1.67	4.97	6.81
N	10	9	8	3
POSTNATAL LOSS DAYS 0 - 4				
% OF LIVING PUPS	1.6	15.0	13.8	48.0
LITTERS AFFECTED (#)	2	5	3	2
TOTAL (#)	2	21 ##	12 ##	12 ##
MEAN (+)	0.2	2.3	1.5	4.0
ST.DEV.	0.42	4.21	2.51	4.58
N	10	9	8	3
LIVING PUPS DAY 4 P.P.				
TOTAL	120	119	75	13
MEAN (+)	12.0	13.2	9.4	4.3
ST.DEV.	4.92	5.21	5.60	3.79
N	10	9	8	3
VIABILITY INDEX (#)	98.4	85.0 ##	86.2 ##	52.0 ##

/ ## Fisher's Exact test significant at 5% (#) or 1% (##) level
+/++ Steel-test significant at 5% (+) or 1% (++) level
Viability index = (Number of alive pups on day 4 p.p. / Number of pups born alive) *100

MEAN BODY WEIGHTS OF PUPS PER GROUP (GRAM)
F0-GENERATION - LACTATION

DAY	SEX		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 1000 MG/KG
1	M	MEAN	7.1	6.5	6.9	5.1 **
		ST.DEV.	0.8	0.5	0.5	1.2
		N	10	9	7	3
	F	MEAN	6.8	6.0 *	6.7	4.6 **
		ST.DEV.	0.7	0.5	0.6	0.8
		N	10	9	7	3
	M+F	MEAN	6.9	6.2	6.8	4.8 **
		ST.DEV.	0.7	0.5	0.5	0.8
		N	10	9	7	3
4	M	MEAN	10.6	9.0 *	10.0	6.4 **
		ST.DEV.	1.3	0.7	1.3	2.3
		N	10	8	7	2
	F	MEAN	9.9	8.3 *	9.4	5.5 **
		ST.DEV.	1.2	0.9	1.5	1.6
		N	10	8	7	2
	M+F	MEAN	10.2	8.6 *	9.7	5.8 **
		ST.DEV.	1.2	0.7	1.3	1.6
		N	10	8	7	2

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

APPENDIX 2 INDIVIDUAL TABLES

MORTALITY DATA
MALES

ANIMAL	SCHEDULED NECROPSY	SPONTANEOUS DEATH	KILLED IN EXTREMIS	TREATMENT FROM	TO
GROUP 1 (CONTROL)					
1	18AUG03			21JUL03	17AUG03
2	18AUG03			21JUL03	17AUG03
3	18AUG03			21JUL03	17AUG03
4	18AUG03			21JUL03	17AUG03
5	18AUG03			21JUL03	17AUG03
6	18AUG03			21JUL03	17AUG03
7	18AUG03			21JUL03	17AUG03
8	18AUG03			21JUL03	17AUG03
9	18AUG03			21JUL03	17AUG03
10	18AUG03			21JUL03	17AUG03
GROUP 2 (50 MG/KG)					
11	18AUG03			21JUL03	17AUG03
12	18AUG03			21JUL03	17AUG03
13	18AUG03			21JUL03	17AUG03
14	18AUG03			21JUL03	17AUG03
15	18AUG03			21JUL03	17AUG03
16	18AUG03			21JUL03	17AUG03
17	18AUG03			21JUL03	17AUG03
18	18AUG03			21JUL03	17AUG03
19	18AUG03			21JUL03	17AUG03
20	18AUG03			21JUL03	17AUG03
GROUP 3 (150 MG/KG)					
21	18AUG03			21JUL03	17AUG03
22	18AUG03			21JUL03	17AUG03
23	18AUG03			21JUL03	17AUG03
24	18AUG03			21JUL03	17AUG03
25	18AUG03			21JUL03	17AUG03
26	18AUG03			21JUL03	17AUG03
27	18AUG03			21JUL03	17AUG03
28	18AUG03			21JUL03	17AUG03
29	18AUG03			21JUL03	17AUG03
30	18AUG03			21JUL03	17AUG03
GROUP 4 (1000 MG/KG)					
31	18AUG03			21JUL03	17AUG03
32	18AUG03			21JUL03	17AUG03
33		01AUG03		21JUL03	01AUG03
34		27JUL03		21JUL03	26JUL03
35	18AUG03			21JUL03	17AUG03
36	18AUG03			21JUL03	17AUG03
37	18AUG03			21JUL03	17AUG03
38			13AUG03	21JUL03	13AUG03
39	18AUG03			21JUL03	17AUG03
40	18AUG03			21JUL03	17AUG03

MORTALITY DATA
FEMALES

ANIMAL	SCHEDULED NECROPSY	SPONTANEOUS DEATH	KILLED IN EXTREMIS	TREATMENT FROM	TO
GROUP 1 (CONTROL)					
41	01SEP03			21JUL03	31AUG03
42	04SEP03			21JUL03	03SEP03
43	04SEP03			21JUL03	03SEP03
44	01SEP03			21JUL03	31AUG03
45	02SEP03			21JUL03	01SEP03
46	01SEP03			21JUL03	31AUG03
47	02SEP03			21JUL03	01SEP03
48	01SEP03			21JUL03	31AUG03
49	02SEP03			21JUL03	01SEP03
50	04SEP03			21JUL03	03SEP03
GROUP 2 (50 MG/KG)					
51	02SEP03			21JUL03	01SEP03
52	01SEP03			21JUL03	31AUG03
53	01SEP03			21JUL03	31AUG03
54	02SEP03			21JUL03	01SEP03
55	02SEP03			21JUL03	01SEP03
56	03SEP03			21JUL03	02SEP03
57	05SEP03			21JUL03	04SEP03
58	04SEP03			21JUL03	03SEP03
59	01SEP03			21JUL03	31AUG03
60	04SEP03			21JUL03	03SEP03
GROUP 3 (150 MG/KG)					
61	01SEP03			21JUL03	31AUG03
62	04SEP03			21JUL03	03SEP03
63	01SEP03			21JUL03	31AUG03
64	02SEP03			21JUL03	01SEP03
65			01SEP03	21JUL03	31AUG03
66	01SEP03			21JUL03	31AUG03
67	04SEP03			21JUL03	03SEP03
68	05SEP03			21JUL03	04SEP03
69	02SEP03			21JUL03	01SEP03
70	05SEP03			21JUL03	04SEP03
GROUP 4 (1000 MG/KG)					
71	05SEP03			21JUL03	04SEP03
72	05SEP03			21JUL03	04SEP03
73	05SEP03			21JUL03	04SEP03
74	01SEP03			21JUL03	31AUG03
75	05SEP03			21JUL03	04SEP03
76	05SEP03			21JUL03	04SEP03
77			03AUG03	21JUL03	03AUG03
78		18AUG03		21JUL03	17AUG03
79	05SEP03			21JUL03	04SEP03
80	05SEP03			21JUL03	04SEP03

CLINICAL SIGNS
MALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT WEEKS: 1 ... 4 DAYS: 3456712345671234567123456712345671234567123456712345671234
GROUP 1 (CONTROL)	
ANIMAL 1	
Breathing	
Rales (3)	G: .....1..111.....
ANIMAL 2	
Secretion / excretion	
Salivation (3)	G: .....1111111111111..
ANIMAL 3	
Secretion / excretion	
Salivation (3)	G: .....1.....
ANIMAL 4	
Secretion / excretion	
Salivation (3)	G: .....1.....
ANIMAL 5	
No clinical signs noted	
ANIMAL 6	
No clinical signs noted	
ANIMAL 7	
No clinical signs noted	
ANIMAL 8	
No clinical signs noted	
ANIMAL 9	
Breathing	
Rales (3)	G: .....1..111.....
ANIMAL 10	
No clinical signs noted	
GROUP 2 (50 MG/KG)	
ANIMAL 11	
No clinical signs noted	
ANIMAL 12	
Secretion / excretion	
Salivation (3)	G: .....11..11111111111111...
ANIMAL 13	
No clinical signs noted	
ANIMAL 14	
No clinical signs noted	
ANIMAL 15	
No clinical signs noted	
ANIMAL 16	
No clinical signs noted	
ANIMAL 17	
No clinical signs noted	
ANIMAL 18	
No clinical signs noted	
ANIMAL 19	
No clinical signs noted	
ANIMAL 20	
No clinical signs noted	
GROUP 3 (150 MG/KG)	
ANIMAL 21	
Secretion / excretion	
Diarrhoea (1)	G: .....1111.....
Salivation (3)	G: 1111111111111111

G: Highest daily grades
.: Observation performed, sign not present

CLINICAL SIGNS
MALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT	
	WEEKS:	1. . . . . 4. . . . .
	DAYS:	3456712345671234567123456712345671234567123456712345671234
GROUP 3 (150 MG/KG)		
ANIMAL 22		
Secretion / excretion		
Diarrhoea (1)	G:	. . . . . 1111. . . . .
ANIMAL 23		
Skin / fur / plumage		
Alopecia (3) (Forelegs)	G:	 1111111
Secretion / excretion		
Diarrhoea (1)	G:	. . . . . 1111. . . . .
Salivation (3)	G:	 1111111111111111
ANIMAL 24		
Secretion / excretion		
Diarrhoea (1)	G:	. . . . . 111111111. . . . .
ANIMAL 25		
Breathing		
Rales (3)	G:	. . . . . 111111. . . . .
Secretion / excretion		
Diarrhoea (1)	G:	. . . . . 111111111. . . . .
Salivation (3)	G:	 1111111111111111
ANIMAL 26		
Secretion / excretion		
Salivation (3)	G:	. . . . . 1111111111111. . .
ANIMAL 27		
Secretion / excretion		
Salivation (3)	G:	 1111111111111111
ANIMAL 28		
Secretion / excretion		
Salivation (3)	G:	 1111111111111111
ANIMAL 29		
Secretion / excretion		
Salivation (3)	G:	 1111111111111111
ANIMAL 30		
Secretion / excretion		
Salivation (3)	G:	 1111111111111111
GROUP 4 (1000 MG/KG)		
ANIMAL 31		
Behavior		
Lethargy (3)	G:	. . . 1111111111111111. . . . .
Posture		
Hunched posture (1)	G:	. . 11111111111111111111111
Skin / fur / plumage		
Piloerection (1)	G:	. . . 11111111111111111111
Secretion / excretion		
Salivation (3)	G:	. 111111111111111111111111
Various		
Lean (1)	G:	. . . . . 1. . 1111. . . . .
ANIMAL 32		
Behavior		
Lethargy (3)	G:	. . . . . 1. . 1111111111. . . . .
Posture		
Hunched posture (1)	G:	. . 11111111111111111111111
Breathing		
Rales (3)	G:	 11111111111
Secretion / excretion		

G: Highest daily grades
.: Observation performed, sign not present

CLINICAL SIGNS
MALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT WEEKS: 1 . . . . . 4 . . . . . DAYS: 345671234567123456712345671234567123456712345671234
GROUP 4 (1000 MG/KG)	
Diarrhoea (1)	G: . . . . . 111111111. . . . .
Salivation (3)	G: . 111111111111111111111111
Various	
Lean (1)	G: . . . . . 1. . 111111. . . . .
ANIMAL 33	
Behavior	
Lethargy (3)	G: . . . . . 1. . 1
Posture	
Hunched posture (1)	G: . . 11111111
Secretion / excretion	
Salivation (3)	G: . 111111111
ANIMAL 34	
Behavior	
Lethargy (3)	G: . . . 11
Posture	
Hunched posture (1)	G: . . 111
Gait / motility	
Uncoordinated movements (3)	G: . . . 11
Decreased locomotor activity (3)	G: . . . 11
Breathing	
Laboured respiration (3)	G: . . . 11
Skin / fur / plumage	
Alopecia (3) (Inguinal region right)	G: . 1111
Secretion / excretion	
Salivation (3)	G: . 1111
Various	
Lean (1)	G: . . . 11
ANIMAL 35	
Behavior	
Lethargy (3)	G: . . . . . 1. . 1111111111. . . . .
Posture	
Hunched posture (1)	G: . . 111111111111111111111111
Breathing	
Rales (3)	G: 11111111111
Skin / fur / plumage	
Piloerection (1)	G: . . . . . 1. . 1111111111111111
Secretion / excretion	
Diarrhoea (1)	G: . . . . . 111111111. . . . .
Salivation (3)	G: . 111111111111111111111111
Various	
Lean (1)	G: . . . . . 1. . 111111. . . . .
Ptosis (3)	G: . . . . . 1. . 111111. . . . .
ANIMAL 36	
Behavior	
Lethargy (3)	G: . . . 1111111111111111. . . . .
Posture	
Hunched posture (1)	G: . . 111111111111111111111111
Gait / motility	
Uncoordinated movements (3)	G: . . . 1111111111. . . . .
Skin / fur / plumage	
Alopecia (3) (Back)	G: . . . . 1111111111111111. . . . .
Alopecia (3) (Hindleg left)	G: 222222

G: Highest daily grades
.: Observation performed, sign not present

CLINICAL SIGNS
MALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT WEEKS: 1 . . . . . 4 . . . . . DAYS: 345671234567123456712345671234567123456712345671234
GROUP 4 (1000 MG/KG)	
Alopecia (3)	G: 111111
(Hindleg right)	
Red discolouration (1)	G: . . . 1111111111. . . . .
(Urine)	
Secretion / excretion	
Diarrhoea (1)	G: . . . . . 111111111. . . . .
Salivation (3)	G: . 111111111111111111111111
Various	
Lean (1)	G: . . . . . 1. . 1111. . . . .
ANIMAL 37	
Posture	
Hunched posture (1)	G: . . 111111111111111111111111
Breathing	
Rales (3)	G: . 1. . . . . 11. 11111. . . . .
Secretion / excretion	
Diarrhoea (1)	G: . . . . . 1. . 11111111111. . . . .
Salivation (3)	G: . 111111111111111111111111
ANIMAL 38	
Behavior	
Lethargy (3)	G: . . . . . 1. . 1111111111. . 2
Posture	
Hunched posture (1)	G: . . 111111111111111111
Breathing	
Quick breathing (1)	G: 1
Skin / fur / plumage	
Swelling (3)	G: 2
(Genital region)	
Piloerection (1)	G: 1
Red discolouration (1)	G: 1
(Urine)	
Secretion / excretion	
Diarrhoea (1)	G: . . . . . 1111111111.
Salivation (3)	G: . 111111111111111111111
Various	
Lean (1)	G: 1
ANIMAL 39	
Behavior	
Lethargy (3)	G: . . . . . 1. . 1111111111. . . . .
Posture	
Hunched posture (1)	G: . . 111111111111111111111111
Secretion / excretion	
Diarrhoea (1)	G: . . . . . 111111111. . . . .
Salivation (3)	G: . 111111111111111111111111
ANIMAL 40	
Behavior	
Lethargy (3)	G: . . . 1112112111111111. . . . .
Posture	
Hunched posture (1)	G: . . 111111111111111111111111
Gait / motility	
Uncoordinated movements (3)	G: . . . . 11111111. . . . .
Breathing	
Laboured respiration (3)	G: . . . . 111111111111111. . . . .
Shallow respiration (3)	G: . . . . . 1. . 1111111111. . . . .
Skin / fur / plumage	
Piloerection (1)	G: 1111111111111111111

G: Highest daily grades
.: Observation performed, sign not present

CLINICAL SIGNS
MALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT WEEKS: 1 ... 4 DAYS: 3456712345671234567123456712345671234567123456712345671234
GROUP 4 (1000 MG/KG)	
Alopecia (3) (Back)	G: .....1..11111111111112222
Secretion / excretion	
Diarrhoea (1)	G: .....111111111.....
Salivation (3)	G: .111111111111111111111111
Chromodacryorrhoea (3) (Eye left)	G: .....1..111.....
Chromodacryorrhoea (3) (Eye right)	G: .....1..111.....
Chromodacryorrhoea (3) (Snout)	G: .....1..111.....
Various	
Lean (1)	G: .....1..1111.....

FEMALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT WEEKS: 1 ... 4 DAYS: 3456712345671234567123456712345671234567123456712345671234
GROUP 1 (CONTROL)	
ANIMAL 41	
No clinical signs noted	
ANIMAL 42	
No clinical signs noted	
ANIMAL 43	
No clinical signs noted	
ANIMAL 44	
No clinical signs noted	
ANIMAL 45	
Skin / fur / plumage	
Alopecia (3) (Abdomen)	G: 221222222222223333333333333333
Alopecia (3) (Chest)	G: 111222222222223333333333333333
Alopecia (3) (Thigh hind left)	G: 222222222222222222222
Alopecia (3) (Thigh hind right)	G: 222222222222222222222
Alopecia (3) (Forelegs)	G: 222222222223333333333
ANIMAL 46	
No clinical signs noted	
ANIMAL 47	
Breathing	
Rales (3)	G: .....1.....
Skin / fur / plumage	
Alopecia (3) (Cervical region)	G: 11111111111111
ANIMAL 48	
No clinical signs noted	

G: Highest daily grades
.: Observation performed, sign not present

CLINICAL SIGNS
FEMALES

SIGN (MAX. GRADE) (LOCATION)		TREATMENT WEEKS:1 . . . . . 4 . . . . . DAYS: 345671234567123456712345671234567123456712345671234
GROUP 1 (CONTROL)		
ANIMAL 49		
No clinical signs noted		
ANIMAL 50		
No clinical signs noted		
GROUP 2 (50 MG/KG)		
ANIMAL 51		
No clinical signs noted		
ANIMAL 52		
No clinical signs noted		
ANIMAL 53		
No clinical signs noted		
ANIMAL 54		
No clinical signs noted		
ANIMAL 55		
No clinical signs noted		
ANIMAL 56		
No clinical signs noted		
ANIMAL 57		
No clinical signs noted		
ANIMAL 58		
No clinical signs noted		
ANIMAL 59		
No clinical signs noted		
ANIMAL 60		
No clinical signs noted		
GROUP 3 (150 MG/KG)		
ANIMAL 61		
Secretion / excretion		
Salivation (3)	G:	 1111111111111111111111111111111
ANIMAL 62		
Secretion / excretion		
Salivation (3)	G:	 1111111111111111111111111111111
ANIMAL 63		
Secretion / excretion		
Salivation (3)	G:	 1111111111111111111111111111111
ANIMAL 64		
Secretion / excretion		
Salivation (3)	G:	 1111111111111111111111111111111
ANIMAL 65		
Secretion / excretion		
Salivation (3)	G:	 1111111111111111111111111111111
ANIMAL 66		
Secretion / excretion		
Salivation (3)	G:	 1111111111111111111111111111111
ANIMAL 67		
Secretion / excretion		
Salivation (3)	G:	 1111111111111111111111111111111
ANIMAL 68		
Secretion / excretion		
Salivation (3)	G:	 1111111111111111111111111111111

G: Highest daily grades
.: Observation performed, sign not present

CLINICAL SIGNS
FEMALES

SIGN (MAX. GRADE) (LOCATION)		TREATMENT WEEKS: 1 . . . . . 4 . . . . . DAYS: 3456712345671234567123456712345671234567123456712345671234
GROUP 3 (150 MG/KG)		
ANIMAL 69		
Skin / fur / plumage		
Alopecia (3)	G:	 1111111111111
(Foreleg right)		
Secretion / excretion		
Salivation (3)	G:	 1111111111111111111111111111111111
ANIMAL 70		
Secretion / excretion		
Salivation (3)	G:	 1111111111111111111111111111111111111
GROUP 4 (1000 MG/KG)		
ANIMAL 71		
Posture		
Hunched posture (1)	G:	. . 1111111111111111111111. . . . .
Secretion / excretion		
Salivation (3)	G:	. 1111111111111111111111111111111111111111111
ANIMAL 72		
Posture		
Hunched posture (1)	G:	. . 1111111111111111111111. . . . .
Breathing		
Rales (3)	G:	. . . . . 111111111. . . . .
Secretion / excretion		
Salivation (3)	G:	. 1111111111111111111111111111111111111111111
ANIMAL 73		
Posture		
Hunched posture (1)	G:	. . 1111111111111111111111. . . . .
Secretion / excretion		
Salivation (3)	G:	. 1111111111111111111111111111111111111111111
ANIMAL 74		
Posture		
Hunched posture (1)	G:	. . 1111111111111111111111. . . . .
Skin / fur / plumage		
Alopecia (3)	G:	. . . . . 2222222222222221111. . . . .
(Back)		
Secretion / excretion		
Salivation (3)	G:	. 1111111111111111111111111111111111111111111
ANIMAL 75		
Posture		
Hunched posture (1)	G:	. . 1111111111111111111111. . . . .
Secretion / excretion		
Salivation (3)	G:	. 1111111111111111111111111111111111111111111
ANIMAL 76		
Posture		
Hunched posture (1)	G:	. . 1111111111111111111111. . . . .
Secretion / excretion		
Salivation (3)	G:	. 1111111111111111111111111111111111111111111
ANIMAL 77		
Behavior		
Lethargy (3)	G:	 333
Posture		
Hunched posture (1)	G:	. . 1111111111
Gait / motility		
Decreased locomotor activity (3)	G:	 111
Breathing		
Laboured respiration (3)	G:	 111

G: Highest daily grades
.: Observation performed, sign not present

CLINICAL SIGNS
FEMALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT WEEKS: 1 . . . . . 4 . . . . . DAYS: 34567123456712345671234567123456712345671234
GROUP 4 (1000 MG/KG)	
Skin / fur / plumage	
Piloerection (1)	G: 111
Alopecia (3) (Back)	G: 111
Secretion / excretion	
Diarrhoea (1)	G: 1
Salivation (3)	G: . 11111111111
Various	
Lean (1)	G: 111
Ptosis (3)	G: 111
ANIMAL 78	
Posture	
Ventro-lateral recumbency (1)	G: . . . . . 1.
Hunched posture (1)	G: . . 11111111111111111111111.
Breathing	
Laboured respiration (3)	G: . . . . . 1.
Skin / fur / plumage	
Alopecia (3) (Back)	G: . . . 11111111111111111111111.
Secretion / excretion	
Salivation (3)	G: . 11111111111111111111111.
ANIMAL 79	
Posture	
Hunched posture (1)	G: . . 11111111111111111111111. . . . .
Skin / fur / plumage	
Swelling (3) (Abdomen)	G: . . . . . 11. . 111111111111. . . . .
Secretion / excretion	
Salivation (3)	G: . 1111111111111111111111111111111111111111111
ANIMAL 80	
Posture	
Hunched posture (1)	G: . . 11111111111111111111111 . . . . .
Skin / fur / plumage	
Alopecia (3) (Back)	G: . . . . . 11. . 1111111111111111. . . . .
Secretion / excretion	
Salivation (3)	G: . 1111111111111111111111111111111111111111111
Various	
Lean (1)	G: . . . . 1111. 11111111111. . . . .

G: Highest daily grades
.: Observation performed, sign not present

FUNCTIONAL OBSERVATIONS
MALES
WEEK 4

ANIMAL	HEARING SCORE 0/1	PUPIL L SCORE 0/1	PUPIL R SCORE 0/1	STATIC R SCORE 0/1	GRIP SCORE 0/1
GROUP 1 (CONTROL)					
1	0	0	0	0	0
2	0	0	0	0	0
3	0	0	0	0	0
4	0	0	0	0	0
5	0	0	0	0	0
6	---	---	---	---	---
7	---	---	---	---	---
8	---	---	---	---	---
9	---	---	---	---	---
10	---	---	---	---	---
GROUP 2 (50 MG/KG)					
11	0	0	0	0	0
12	0	0	0	0	0
13	0	0	0	0	0
14	0	0	0	0	0
15	0	0	0	0	0
16	---	---	---	---	---
17	---	---	---	---	---
18	---	---	---	---	---
19	---	---	---	---	---
20	---	---	---	---	---
GROUP 3 (150 MG/KG)					
21	0	0	0	0	0
22	0	0	0	0	0
23	0	0	0	0	0
24	0	0	0	0	0
25	0	0	0	0	0
26	---	---	---	---	---
27	---	---	---	---	---
28	---	---	---	---	---
29	---	---	---	---	---
30	---	---	---	---	---
GROUP 4 (1000 MG/KG)					
31	0	0	0	0	0
32	0	0	0	0	0
35	0	0	0	0	0
36	0	0	0	0	0
37	0	0	0	0	0
38	---	---	---	---	---
39	---	---	---	---	---
40	---	---	---	---	---

FUNCTIONAL OBSERVATIONS
FEMALES
WEEK 4

ANIMAL	HEARING SCORE 0/1	PUPIL L SCORE 0/1	PUPIL R SCORE 0/1	STATIC R SCORE 0/1	GRIP SCORE 0/1
GROUP 1 (CONTROL)					
41	0	0	0	0	0
44	0	0	0	0	0
45	0	0	0	0	0
46	0	0	0	0	0
48	0	0	0	0	0
49	---	---	---	---	---
50	---	---	---	---	---
GROUP 2 (50 MG/KG)					
52	0	0	0	0	0
53	0	0	0	0	0
54	0	0	0	0	0
55	0	0	0	0	0
59	0	0	0	0	0
GROUP 3 (150 MG/KG)					
61	0	0	0	0	0
63	0	0	0	0	0
64	0	0	0	0	0
66	0	0	0	0	0
69	0	0	0	0	0
GROUP 4 (1000 MG/KG)					
71	0	0	0	0	0
72	0	0	0	0	0
74	0	0	0	0	0
75	0	0	0	0	0
80	0	0	0	0	0

MOTOR ACTIVITY TEST
MALES
END OF TREATMENT

Animal number	Location of sensor	Counts per sample period (hour) 1	2	3	4	5	6	7	8	9	10	11	12	Total
GROUP 1 (CONTROL)														
1	High	3280	7115	3630	445	375	1493	542	119	490	402	2150	1427	21468
1	Low	800	279	427	413	337	809	278	442	519	334	982	670	6290
2	High	243	160	230	295	73	706	50	136	51	177	149	177	2447
2	Low	525	295	545	452	600	550	451	497	169	272	319	235	4910
3	High	251	23	177	228	39	137	84	195	135	258	182	206	1915
3	Low	396	378	956	272	192	108	341	431	145	92	198	69	3578
4	High	112	314	76	195	103	202	88	334	205	246	335	437	2647
4	Low	285	252	244	442	13	82	0	333	125	237	171	228	2412
5	High	483	127	143	262	95	345	49	179	62	168	341	141	2395
5	Low	816	458	600	543	514	583	132	383	97	219	1028	750	6123
GROUP 2 (50 MG/KG/DAY)														
11	High	387	103	188	153	157	291	73	492	19	207	189	421	2680
11	Low	406	238	735	334	307	49	6	852	0	38	45	175	3185
12	High	216	257	182	419	396	634	179	453	471	177	448	662	4494
12	Low	308	298	556	486	447	792	295	805	406	285	637	973	6288
13	High	297	205	420	119	178	435	161	275	0	101	471	555	3217
13	Low	632	372	490	651	492	787	375	869	107	379	679	912	6745
14	High	367	208	333	730	593	817	215	545	100	431	571	468	5378
14	Low	945	362	628	514	714	425	126	224	193	317	647	702	5797
15	High	605	379	297	103	320	118	342	101	197	128	293	544	3427
15	Low	548	255	380	116	164	105	160	117	394	121	163	337	2860
GROUP 3 (150 MG/KG/DAY)														
21	High	174	254	214	502	672	442	4	95	2	4	410	165	2938
21	Low	251	503	510	738	1569	992	12	240	132	21	567	612	6147
22	High	212	164	184	405	263	120	228	209	54	8	361	440	2648
22	Low	327	313	515	810	505	152	768	663	284	192	935	668	6132
23	High	94	312	333	51	236	57	367	0	151	226	251	471	2549
23	Low	556	713	605	220	661	372	767	162	112	438	681	905	6192
24	High	233	49	188	317	272	214	251	100	533	126	642	314	3239
24	Low	480	412	427	772	684	400	503	271	786	95	884	670	6384
25	High	97	79	131	117	236	178	241	187	192	75	442	266	2241
25	Low	527	253	340	425	360	889	147	150	209	131	969	741	5141
GROUP 4 (1000 MG/KG/DAY)														
31	High	215	372	82	176	102	75	58	137	130	290	309	163	2109
31	Low	182	637	247	489	329	130	216	197	272	374	520	346	3939
32	High	433	1	20	193	306	132	115	239	432	413	477	248	3009
32	Low	849	99	314	453	589	201	342	340	677	684	598	569	5715
35	High	352	2	117	152	249	245	411	505	159	165	501	497	3355
35	Low	1016	23	1117	579	461	529	890	772	491	359	747	981	7965
36	High	49	64	209	32	1	85	2051	844	116	3438	1453	1174	9516
36	Low	482	419	149	81	36	258	431	268	366	360	422	232	3504
37	High	663	106	2	404	339	172	396	465	552	35	334	395	3863
37	Low	258	101	18	260	250	78	766	262	298	97	309	95	2792

MOTOR ACTIVITY TEST
FEMALES
END OF TREATMENT

Animal number	Location of sensor	Counts per sample period (hour) 1	2	3	4	5	6	7	8	9	10	11	12	Total
GROUP 1 (CONTROL)														
41	High	120	122	119	103	108	290	241	75	207	2	226	5	1618
41	Low	449	480	432	574	589	719	383	261	330	0	451	97	4765
44	High	300	151	69	128	236	91	165	146	35	66	99	64	1550
44	Low	296	460	223	294	559	240	313	476	84	292	230	280	3747
45	High	168	15	115	147	243	230	218	1	492	159	144	227	2159
45	Low	617	132	592	567	1158	783	1144	67	1289	745	577	831	8502
46	High	308	17	398	157	221	181	7	383	121	147	208	340	2488
46	Low	1069	67	1617	1164	1940	1331	96	1748	2101	617	1906	1639	15295
48	High	105	50	330	304	57	229	284	62	192	6	220	222	2061
48	Low	597	201	1519	1146	210	585	969	199	797	158	357	774	7512
GROUP 2 (50 MG/KG/DAY)														
52	High	10	317	214	445	426	635	670	729	362	490	323	503	5124
52	Low	98	984	701	2034	2353	2737	3113	2579	1433	1141	555	1709	19437
53	High	276	215	167	157	337	148	448	327	29	106	187	180	2577
53	Low	833	963	694	710	1904	1024	1492	729	252	404	447	609	10061
54	High	209	88	214	8	39	100	50	198	120	268	264	85	1643
54	Low	733	217	1901	82	385	546	213	480	596	1277	841	553	7824
55	High	225	339	422	258	237	133	108	122	136	133	51	136	2300
55	Low	499	467	1772	325	438	296	305	356	432	335	377	529	6131
59	High	481	71	202	798	499	672	798	92	160	37	380	107	4297
59	Low	1098	62	584	1948	1239	1063	2349	67	730	104	606	253	10103
GROUP 3 (150 MG/KG/DAY)														
61	High	103	237	154	320	144	234	93	212	420	393	513	258	3081
61	Low	259	1013	721	956	190	643	703	726	1401	1655	1748	482	10497
63	High	100	203	418	356	402	291	442	319	205	61	162	54	3013
63	Low	259	302	571	579	1117	482	1907	1395	451	225	174	231	7693
64	High	262	138	8	131	308	249	248	180	190	108	190	182	2194
64	Low	473	137	4	530	1052	588	853	514	849	27	1031	630	6688
66	High	77	178	27	176	0	98	192	3	98	0	110	151	1110
66	Low	502	861	189	1090	79	458	850	382	814	174	773	957	7129
69	High	99	176	186	143	183	255	246	146	48	233	26	31	1772
69	Low	312	365	708	687	937	688	382	307	16	905	152	117	5576
GROUP 4 (1000 MG/KG/DAY)														
74	High	1	30	10	70	4	150	214	333	210	1	123	102	1248
74	Low	74	276	564	418	136	965	2001	2482	712	0	636	565	8829
75	High	0	0	91	23	27	116	0	57	58	5	48	46	471
75	Low	2	25	399	264	171	444	12	350	236	142	239	194	2478
71	High	71	35	140	361	253	188	233	124	71	154	308	292	2230
71	low	236	290	377	775	877	489	575	173	363	540	842	848	6385
72	high	181	14	25	33	71	129	202	123	94	114	79	177	1242
72	low	628	79	210	233	649	554	555	702	494	391	771	947	6213
80	high	53	0	28	247	174	219	82	286	203	83	165	405	1945
80	low	385	47	252	1224	493	937	471	898	466	156	268	792	6389
75*	high	216	0	142	253	396	1	434	19	255	462	102	188	2468
75*	low	312	25	370	500	747	3	1116	2	571	427	312	563	4948

* = The motor activity test was performed for a second time for female 75 as the results of the first test showed very low values.

BODY WEIGHTS (GRAM)
MALES

	PRE-MATING	
DAYS	1	8
WEEKS	1	2
ANIMAL		
GROUP 1 (CONTROL)		
1	264	303
2	257	293
3	243	288
4	258	299
5	264	317
6	258	297
7	246	272
8	249	306
9	258	321
10	270	324
GROUP 2 (50 MG/KG)		
11	263	303
12	269	310
13	252	301
14	245	294
15	256	305
16	257	295
17	260	296
18	250	291
19	276	322
20	248	296
GROUP 3 (150 MG/KG)		
21	242	284
22	251	288
23	265	323
24	271	315
25	248	295
26	247	274
27	268	320
28	257	317
29	262	305
30	262	302
GROUP 4 (1000 MG/KG)		
31	271	226
32	232	246
33	255	273
34	235	---
35	251	256
36	258	215
37	260	258
38	238	238
39	245	256
40	253	218

BODY WEIGHTS (GRAM)
FEMALES

	PRE-MATING	
DAYS	1	8
WEEKS	1	2
ANIMAL		
GROUP 1 (CONTROL)		
41	191	217
42	179	205
43	184	207
44	179	193
45	190	214
46	188	205
47	188	219
48	196	219
49	175	216
50	182	209
GROUP 2 (50 MG/KG)		
51	174	201
52	177	208
53	175	211
54	185	212
55	191	220
56	191	211
57	190	207
58	201	218
59	172	194
60	186	209
GROUP 3 (150 MG/KG)		
61	184	209
62	182	205
63	176	210
64	173	208
65	188	209
66	202	210
67	188	205
68	175	193
69	170	194
70	188	221
GROUP 4 (1000 MG/KG)		
71	199	217
72	183	186
73	184	184
74	178	198
75	194	220
76	197	180
77	189	182
78	166	183
79	182	187
80	186	180

BODY WEIGHTS (GRAM)
MALES
F0-GENERATION

	MATING	POST MATING	
DAYS	1	1	7
ANIMAL			
GROUP 1 (CONTROL)			
1	357	395	426
2	326	354	373
3	324	351	373
4	325	353	385
5	368	397	420
6	335	362	387
7	291	316	342
8	348	374	400
9	377	416	455
10	384	420	456
GROUP 2 (50 MG/KG)			
11	345	384	410
12	339	382	407
13	349	374	397
14	326	346	369
15	353	389	417
16	316	358	391
17	337	374	402
18	326	354	366
19	360	401	434
20	338	369	398
GROUP 3 (150 MG/KG)			
21	320	348	364
22	324	352	362
23	364	398	425
24	348	378	409
25	326	362	380
26	307	338	360
27	363	402	431
28	362	386	419
29	352	383	415
30	346	362	388
GROUP 4 (1000 MG/KG)			
31	298	320	327
32	265	312	337
35	289	312	298
36	300	304	307
37	277	321	321
38	263	289	---
39	260	316	293
40	259	327	317

BODY WEIGHTS (GRAM)
FEMALES
F0-GENERATION

	MATING	POST COITUM				LACTATION	
DAYS	1	0	7	14	21	1	4
ANIMAL							
GROUP 1 (CONTROL)							
41	237	233	275	339	457	343	349
42	222	234	286	330	431	307	325
43	222	236	286	340	464	327	354
44	226	223	272	315	387	326	319
45	230	235	286	340	435	333	328
46	215	225	281	346	483	354	359
47	239	247	298	350	450	334	351
48	247	248	297	349	480	360	354
49	244	245	305	358	416	382	378
50	222	239	284	327	402	317	335
GROUP 2 (50 MG/KG)							
51	222	233	273	320	448	313	323
52	230	229	274	303	414	293	309
53	236	237	291	339	449	345	359
54	237	239	298	346	449	339	339
55	244	246	283	331	438	319	326
56	227	237	286	334	450	333	322
57 <NP>	214	230	277	275	284	---	---
58	236	260	298	342	463	332	354
59	215	222	282	332	442	332	330
60	222	240	273	322	419	303	320
GROUP 3 (150 MG/KG)							
61	231	231	269	299	336	305	298
62	224	232	275	327	432	324	335
63	230	229	279	330	445	335	331
64	226	227	276	305	383	308	319
65	224	244	292	337	392	---	---
66	246	239	291	343	444	348	353
67	219	238	295	333	453	326	350
68 <NP>	201	205	261	257	261	---	---
69	220	220	273	321	432	311	331
70 <NP>	244	246	293	313	326	---	---
GROUP 4 (1000 MG/KG)							
71 <NP>	229	263	293	306	302	---	---
72 <NP>	222	230	253	269	278	---	---
73 <NP>	220	233	261	281	280	---	---
74	223	222	261	304	383	287	304
75	221	240	302	342	401	328	343
76 <NP>	237	229	293	312	333	---	---
78 <SD>	222	218	271	---	---	---	---
79 <NP>	223	221	266	265	274	---	---
80	220	227	275	325	404	319	308

<SD> Spontaneous death
<NP> Non-pregnant

BODY WEIGHT GAIN (%)
MALES

	PRE-MATING	
DAYS	1	8
WEEKS	1	2
ANIMAL		
GROUP 1 (CONTROL)		
1	0	15
2	0	14
3	0	19
4	0	16
5	0	20
6	0	15
7	0	11
8	0	23
9	0	24
10	0	20
GROUP 2 (50 MG/KG)		
11	0	15
12	0	15
13	0	19
14	0	20
15	0	19
16	0	15
17	0	14
18	0	16
19	0	17
20	0	19
GROUP 3 (150 MG/KG)		
21	0	17
22	0	15
23	0	22
24	0	16
25	0	19
26	0	11
27	0	19
28	0	23
29	0	16
30	0	15
GROUP 4 (1000 MG/KG)		
31	0	-17
32	0	6
33	0	7
34	0	---
35	0	2
36	0	-17
37	0	-1
38	0	0
39	0	4
40	0	-14

BODY WEIGHT GAIN (%)
FEMALES

	PRE-MATING	
DAYS	1	8
WEEKS	1	2
ANIMAL		
GROUP 1 (CONTROL)		
41	0	14
42	0	15
43	0	13
44	0	8
45	0	13
46	0	9
47	0	16
48	0	12
49	0	23
50	0	15
GROUP 2 (50 MG/KG)		
51	0	16
52	0	18
53	0	21
54	0	15
55	0	15
56	0	10
57	0	9
58	0	8
59	0	13
60	0	12
GROUP 3 (150 MG/KG)		
61	0	14
62	0	13
63	0	19
64	0	20
65	0	11
66	0	4
67	0	9
68	0	10
69	0	14
70	0	18
GROUP 4 (1000 MG/KG)		
71	0	9
72	0	2
73	0	0
74	0	11
75	0	13
76	0	-9
77	0	-4
78	0	10
79	0	3
80	0	-3

BODY WEIGHT GAIN (%)
MALES
F0-GENERATION

	MATING	POST MATING	
DAYS	1	1	7
ANIMAL			
GROUP 1 (CONTROL)			
1	0	0	8
2	0	0	5
3	0	0	6
4	0	0	9
5	0	0	6
6	0	0	7
7	0	0	8
8	0	0	7
9	0	0	9
10	0	0	9
GROUP 2 (50 MG/KG)			
11	0	0	7
12	0	0	7
13	0	0	6
14	0	0	7
15	0	0	7
16	0	0	9
17	0	0	7
18	0	0	3
19	0	0	8
20	0	0	8
GROUP 3 (150 MG/KG)			
21	0	0	5
22	0	0	3
23	0	0	7
24	0	0	8
25	0	0	5
26	0	0	7
27	0	0	7
28	0	0	9
29	0	0	8
30	0	0	7
GROUP 4 (1000 MG/KG)			
31	0	0	2
32	0	0	8
35	0	0	-4
36	0	0	1
37	0	0	0
38	0	0	---
39	0	0	-7
40	0	0	-3

BODY WEIGHT GAIN (%)
FEMALES
F0-GENERATION

	MATING	POST COITUM				LACTATION	
DAYS	1	0	7	14	21	1	4
ANIMAL							
GROUP 1 (CONTROL)							
41	0	0	18	45	96	0	2
42	0	0	22	41	84	0	6
43	0	0	21	44	97	0	8
44	0	0	22	41	74	0	-2
45	0	0	22	45	85	0	-2
46	0	0	25	54	115	0	1
47	0	0	21	42	82	0	5
48	0	0	20	41	94	0	-2
49	0	0	24	46	70	0	-1
50	0	0	19	37	68	0	6
GROUP 2 (50 MG/KG)							
51	0	0	17	37	92	0	3
52	0	0	20	32	81	0	5
53	0	0	23	43	89	0	4
54	0	0	25	45	88	0	0
55	0	0	15	35	78	0	2
56	0	0	21	41	90	0	-3
57 <NP>	0	0	20	20	23	---	---
58	0	0	15	32	78	0	7
59	0	0	27	50	99	0	-1
60	0	0	14	34	75	0	6
GROUP 3 (150 MG/KG)							
61	0	0	16	29	45	0	-2
62	0	0	19	41	86	0	3
63	0	0	22	44	94	0	-1
64	0	0	22	34	69	0	4
65	0	0	20	38	61	---	---
66	0	0	22	44	86	0	1
67	0	0	24	40	90	0	7
68 <NP>	0	0	27	25	27	---	---
69	0	0	24	46	96	0	6
70 <NP>	0	0	19	27	33	---	---
GROUP 4 (1000 MG/KG)							
71 <NP>	0	0	11	16	15	---	---
72 <NP>	0	0	10	17	21	---	---
73 <NP>	0	0	12	21	20	---	---
74	0	0	18	37	73	0	6
75	0	0	26	43	67	0	5
76 <NP>	0	0	28	36	45	---	---
78 <SD>	0	0	24	---	---	---	---
79 <NP>	0	0	20	20	24	---	---
80	0	0	21	43	78	0	-3

<SD> Spontaneous death
<NP> Non-pregnant

FOOD CONSUMPTION (G/ANIMAL/DAY)
MALES

	PRE-MATING	
DAYS	1-8	8-15
WEEKS	1-2	2-3
CAGE		
GROUP 1 (CONTROL)		
1	30	31
2	31	32
GROUP 2 (50 MG/KG)		
3	28	29
4	30	31
GROUP 3 (150 MG/KG)		
5	29	29
6	27	29
GROUP 4 (1000 MG/KG)		
7	18	16
8	17	22

FEMALES

	PRE-MATING	
DAYS	1-8	8-15
WEEKS	1-2	2-3
CAGE		
GROUP 1 (CONTROL)		
9	20	22
10	23	24
GROUP 2 (50 MG/KG)		
11	22	24
12	19	22
GROUP 3 (150 MG/KG)		
13	22	22
14	20	22
GROUP 4 (1000 MG/KG)		
15	17	22
16	14	20

FOOD CONSUMPTION (G/ANIMAL/DAY)
MALES
F0-GENERATION

	POST MATING
DAYS	1-7
ANIMAL	
GROUP 1 (CONTROL)	
1	37
2	32
3	32
4	34
5	34
6	37
7	30
8	39
9	37
10	37
GROUP 2 (50 MG/KG)	
11	35
12	33
13	30
14	32
15	32
16	32
17	36
18	33
19	36
20	38
GROUP 3 (150 MG/KG)	
21	31
22	28
23	38
24	35
25	36
26	29
27	36
28	34
29	33
30	33
GROUP 4 (1000 MG/KG)	
31	28
32	31
35	23
36	37
37	26
38	2
39	24
40	23

FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES
F0-GENERATION

	POST COITUM			LACTATION
DAYS	0-7	7-14	14-21	1-4
ANIMAL				
GROUP 1 (CONTROL)				
41	24	33	36	49
42	26	30	30	38
43	28	33	32	47
44	24	28	31	25
45	26	32	30	38
46	26	33	35	42
47	29	34	34	39
48	30	35	37	40
49	29	35	38	22
50	29	30	31	36
GROUP 2 (50 MG/KG)				
51	25	29	29	36
52	29	26	32	38
53	28	33	35	45
54	27	33	35	23
55	26	32	34	34
56	26	31	34	32
57 <NP>	26	24	21	---
58	25	29	31	42
59	27	32	33	28
60	23	27	30	32
GROUP 3 (150 MG/KG)				
61	27	28	26	24
62	26	30	31	37
63	25	28	31	28
64	25	28	30	31
65	30	32	33	---
66	28	34	35	---
67	29	29	34	41
68 <NP>	23	23	19	---
69	26	31	34	42
70 <NP>	26	28	24	---
GROUP 4 (1000 MG/KG)				
71 <NP>	28	27	23	---
72 <NP>	21	21	21	---
73 <NP>	21	24	23	---
74	23	29	30	23
75	28	32	34	31
76 <NP>	30	31	29	---
78 <SD>	25	14	---	---
79 <NP>	22	22	21	---
80	26	29	26	19

<SD> Spontaneous death
<NP> Non-pregnant

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

	PRE-MATING	
DAYS	1-8	8-15
WEEKS	1-2	2-3
CAGE		
GROUP 1 (CONTROL)		
1	99	102
2	101	107
GROUP 2 (50 MG/KG)		
3	91	96
4	99	102
GROUP 3 (150 MG/KG)		
5	97	98
6	88	97
GROUP 4 (1000 MG/KG)		
7	72	63
8	73	94

FEMALES

	PRE-MATING	
DAYS	1-8	8-15
WEEKS	1-2	2-3
CAGE		
GROUP 1 (CONTROL)		
9	97	105
10	108	111
GROUP 2 (50 MG/KG)		
11	104	113
12	93	107
GROUP 3 (150 MG/KG)		
13	105	107
14	99	109
GROUP 4 (1000 MG/KG)		
15	83	111
16	79	112

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)
MALES
F0-GENERATION

	POST MATING
DAYS	1-7
ANIMAL	
GROUP 1 (CONTROL)	
1	86
2	85
3	86
4	87
5	81
6	94
7	87
8	98
9	82
10	81
GROUP 2 (50 MG/KG)	
11	84
12	80
13	74
14	87
15	78
16	81
17	89
18	89
19	82
20	95
GROUP 3 (150 MG/KG)	
21	84
22	78
23	89
24	86
25	94
26	81
27	83
28	80
29	80
30	85
GROUP 4 (1000 MG/KG)	
31	86
32	92
35	76
36	120
37	80
38	---
39	83
40	72

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)
FEMALES
F0-GENERATION

	POST COITUM			LACTATION
DAYS	0-7	7-14	14-21	1-4
ANIMAL				
GROUP 1 (CONTROL)				
41	88	98	79	139
42	90	92	69	117
43	98	96	70	132
44	90	90	81	79
45	91	93	69	117
46	91	95	72	117
47	96	98	76	111
48	100	100	78	114
49	96	97	91	59
50	103	93	77	106
GROUP 2 (50 MG/KG)				
51	90	90	66	111
52	104	87	77	123
53	98	98	78	125
54	92	96	79	67
55	92	98	77	103
56	92	93	75	99
57 <NP>	94	86	74	---
58	85	84	68	119
59	97	96	75	85
60	85	85	71	100
GROUP 3 (150 MG/KG)				
61	99	94	78	79
62	93	91	73	110
63	89	86	70	84
64	92	93	78	98
65	101	95	83	---
66	97	98	79	---
67	98	88	74	116
68 <NP>	88	89	72	---
69	95	97	78	126
70 <NP>	88	89	73	---
GROUP 4 (1000 MG/KG)				
71 <NP>	97	87	75	---
72 <NP>	84	78	76	---
73 <NP>	81	85	81	---
74	90	96	79	75
75	91	94	84	89
76 <NP>	101	100	86	---
78 <SD>	94	---	---	---
79 <NP>	82	84	78	---
80	94	89	65	61

<SD> Spontaneous death
<NP> Non-pregnant

HAEMATOLOGY
MALES
END OF TREATMENT

ANIMAL	WBC 10E9/l	Band Neutro %WBC	NEUT %WBC	EOS %WBC	BASO %WBC	MONO %WBC	LYMPHO %WBC
GROUP 1 (CONTROL)							
1	9.7	0	22.0	1.0	0.0	3.0	74.0
2	9.3	0	14.0	0.0	0.0	0.0	86.0
3	4.9	0	19.0	0.0	0.0	1.0	80.0
4	6.2	0	14.0	0.0	0.0	0.0	86.0
5	7.0	1	13.0	3.0	0.0	3.0	80.0
GROUP 2 (50 MG/KG)							
11	6.6	1	14.0	2.0	0.0	2.0	81.0
12	10.3	0	22.0	1.0	0.0	5.0	72.0
13	7.7	0	14.0	2.0	0.0	1.0	83.0
14	11.7	0	20.0	1.0	0.0	2.0	77.0
15	4.9	0	16.0	1.0	0.0	2.0	81.0
GROUP 3 (150 MG/KG)							
21	6.8	1	12.0	2.0	0.0	1.0	84.0
22	6.3	0	21.0	1.0	0.0	3.0	75.0
23	10.5	0	9.0	1.0	0.0	0.0	90.0
24	9.4	0	13.0	1.0	0.0	1.0	85.0
25	8.8	0	14.0	1.0	0.0	0.0	85.0
GROUP 4 (1000 MG/KG)							
31	10.4	0	22.0	1.0	0.0	3.0	74.0
32	12.2	0	11.0	2.0	0.0	0.0	87.0
35	6.8	1	19.0	1.0	0.0	1.0	78.0
36	10.5	2	20.0	0.0	0.0	1.0	77.0
37	9.4	1	10.0	0.0	0.0	3.0	86.0

MALES
END OF TREATMENT

ANIMAL	RBC 10E12/l	HGB mmol/l	HCT l/l	MCV fl	MCH fmol	MCHC mmol/l	PLT 10E9/l
GROUP 1 (CONTROL)							
1	7.89	9.7	0.454	57.5	1.22	21.29	1013
2	8.12	9.2	0.432	53.2	1.13	21.30	693
3	7.34	9.1	0.424	57.8	1.24	21.45	1058
4	7.13	8.9	0.413	58.0	1.25	21.53	938
5	7.35	8.9	0.418	56.9	1.21	21.34	832
GROUP 2 (50 MG/KG)							
11	7.45	8.9	0.415	55.8	1.20	21.48	657
12	7.86	9.3	0.435	55.3	1.18	21.30	793
13	7.63	9.1	0.431	56.4	1.19	21.18	920
14	7.59	8.9	0.413	54.5	1.18	21.62	967
15	7.41	8.7	0.403	54.5	1.17	21.49	949
GROUP 3 (150 MG/KG)							
21	7.17	8.8	0.403	56.3	1.23	21.93	902
22	7.87	9.4	0.444	56.4	1.20	21.20	1106
23	7.48	9.1	0.418	55.9	1.21	21.67	769
24	7.31	9.2	0.437	59.8	1.26	21.02	867
25	7.69	9.4	0.432	56.2	1.22	21.75	1117

HAEMATOLOGY
MALES
END OF TREATMENT

ANIMAL	RBC 10E12/l	HGB mmol/l	HCT l/l	MCV fl	MCH fmol	MCHC mmol/l	PLT 10E9/l
GROUP 4 (1000 MG/KG)							
31	8.66	11.7	0.534	61.6	1.36	22.00	---
32	7.88	10.3	0.471	59.8	1.31	21.92	964
35	9.16	12.1	0.549	60.0	1.32	22.08	814
36	8.60	11.2	0.516	60.0	1.30	21.70	710
37	8.94	11.8	0.537	60.0	1.32	21.95	635

MALES
END OF TREATMENT

ANIMAL	RDW %	PT s	APTT s
GROUP 1 (CONTROL)			
1	11.4	17.0	12.5
2	12.0	17.9	12.6
3	11.6	15.8	11.6
4	11.0	18.1	13.5
5	10.9	18.1	15.2
GROUP 2 (50 MG/KG)			
11	11.4	17.4	11.2
12	13.0	---	---
13	11.6	17.6	15.6
14	11.9	17.5	12.0
15	11.5	17.3	12.5
GROUP 3 (150 MG/KG)			
21	11.0	17.5	10.4
22	11.0	19.6	13.6
23	12.2	---	---
24	11.7	19.1	11.6
25	10.9	17.8	11.2
GROUP 4 (1000 MG/KG)			
31	16.4	17.2	16.0
32	14.9	19.2	12.1
35	15.8	18.3	15.5
36	18.1	17.6	10.1
37	15.2	18.2	11.8

FEMALES
END OF TREATMENT

ANIMAL	WBC 10E9/l	Band Neutro %WBC	NEUT %WBC	EOS %WBC	BASO %WBC	MONO %WBC	LYMPHO %WBC
GROUP 1 (CONTROL)							
41	7.9	1	23.0	1.0	0.0	2.0	73.0
44	4.9	0	23.0	0.0	0.0	0.0	77.0
45	8.2	0	20.0	1.0	0.0	0.0	79.0
46	5.4	1	15.0	1.0	0.0	3.0	80.0
48	5.6	0	27.0	0.0	0.0	3.0	70.0

HAEMATOLOGY
FEMALES
END OF TREATMENT

ANIMAL	WBC 10E9/l	Band Neutro %WBC	NEUT %WBC	EOS %WBC	BASO %WBC	MONO %WBC	LYMPHO %WBC
GROUP 2 (50 MG/KG)							
52	6.0	0	31.0	0.0	0.0	2.0	67.0
53	4.1	1	20.0	0.0	0.0	3.0	76.0
54	7.4	0	21.0	2.0	0.0	1.0	76.0
55	6.8	0	20.0	1.0	0.0	2.0	77.0
59	---	---	---	---	---	---	---
GROUP 3 (150 MG/KG)							
61	7.2	0	15.0	0.0	0.0	1.0	84.0
63	4.7	0	17.0	1.0	0.0	1.0	81.0
64	4.6	0	19.0	2.0	0.0	2.0	77.0
66	4.9	0	15.0	0.0	0.0	2.0	83.0
69	6.1	0	29.0	0.0	0.0	3.0	68.0
GROUP 4 (1000 MG/KG)							
71	7.4	0	13.0	1.0	0.0	9.0	77.0
72	8.3	0	12.0	0.0	0.0	5.0	83.0
74	6.5	0	12.0	2.0	0.0	1.0	85.0
75	7.8	1	18.0	3.0	0.0	2.0	76.0
80	6.7	0	13.0	4.0	0.0	3.0	80.0

FEMALES
END OF TREATMENT

ANIMAL	RBC 10E12/l	HGB mmol/l	HCT l/l	MCV fl	MCH fmol	MCHC mmol/l	PLT 10E9/l
GROUP 1 (CONTROL)							
41	7.31	9.4	0.450	61.5	1.29	20.95	1082
44	7.65	9.5	0.434	56.7	1.24	21.78	824
45	6.48	8.1	0.388	59.9	1.24	20.77	942
46	6.95	8.8	0.418	60.2	1.27	21.11	1077
48	7.30	9.2	0.426	58.4	1.26	21.54	1072
GROUP 2 (50 MG/KG)							
52	6.75	8.2	0.395	58.5	1.22	20.86	1353
53	7.08	8.8	0.402	56.7	1.24	21.95	1313
54	7.37	9.2	0.434	58.9	1.24	21.08	1221
55	6.94	8.7	0.410	59.2	1.25	21.10	1304
59	---	---	---	---	---	---	---
GROUP 3 (150 MG/KG)							
61	7.40	9.0	0.429	58.0	1.21	20.90	1005
63	6.81	8.9	0.411	60.3	1.30	21.57	1511
64	7.10	9.2	0.435	61.3	1.30	21.15	1034
66	7.49	9.2	0.449	60.0	1.23	20.55	1025
69	7.66	9.3	0.437	57.0	1.21	21.31	1320
GROUP 4 (1000 MG/KG)							
71	9.12	11.7	0.528	57.9	1.28	22.08	659
72	8.99	12.3	0.568	63.1	1.37	21.73	724
74	8.30	10.6	0.490	59.0	1.27	21.62	856
75	8.06	11.1	0.515	63.9	1.38	21.60	818
80	8.82	11.4	0.527	59.8	1.30	21.69	951

HAEMATOLOGY
FEMALES
END OF TREATMENT

ANIMAL	RDW %	PT s	APTT s
GROUP 1 (CONTROL)			
41	12.6	16.8	14.3
44	11.3	17.8	12.5
45	12.2	16.9	10.4
46	13.1	17.5	13.4
48	11.2	17.4	11.9
GROUP 2 (50 MG/KG)			
52	12.3	19.1	12.8
53	12.5	17.5	13.3
54	12.8	17.2	12.5
55	12.4	17.0	11.8
59	---	17.1	10.5
GROUP 3 (150 MG/KG)			
61	10.9	18.6	12.2
63	13.1	17.8	13.0
64	12.5	17.6	12.4
66	11.8	16.5	13.7
69	12.4	17.1	11.4
GROUP 4 (1000 MG/KG)			
71	12.4	16.6	14.9
72	13.1	16.8	15.5
74	12.6	17.3	11.7
75	12.5	15.9	12.9
80	13.0	17.1	17.0

CLINICAL BIOCHEMISTRY
MALES
END OF TREATMENT

ANIMAL	ALAT U/l	ASAT U/l	ALP U/l	BILIRUBIN umol/l	UREA mmol/l
GROUP 1 (CONTROL)					
1	33.6	73.0	176	2.7	5.2
2	37.6	68.4	114	2.8	5.2
3	34.8	81.4	103	3.1	4.8
4	36.5	65.3	117	4.6	7.8
5	35.7	71.5	116	2.4	6.9
GROUP 2 (50 MG/KG)					
11	27.1	67.0	96	2.5	7.8
12	37.0	70.6	100	3.6	5.8
13	26.8	65.5	83	3.3	5.5
14	28.8	72.4	101	3.7	5.9
15	24.0	58.0	109	2.3	5.1
GROUP 3 (150 MG/KG)					
21	31.4	73.8	135	2.8	5.5
22	26.5	64.7	111	2.4	7.1
23	36.3	81.7	143	2.3	6.4
24	33.2	74.6	121	3.6	7.5
25	40.7	82.7	124	2.4	10.3
GROUP 4 (1000 MG/KG)					
31	55.8	81.1	214	3.8	9.8
32	54.4	63.2	198	3.3	10.5
35	72.3	83.1	196	3.4	7.9
36	50.4	78.2	248	4.3	10.2
37	103.6	134.7	293	2.3	9.4

MALES
END OF TREATMENT

ANIMAL	CREATININE umol/l	GLUCOSE mmol/l	CHOLESTEROL mmol/l	TRIGLYCERIDES mmol/l	SODIUM mmol/l
GROUP 1 (CONTROL)					
1	53.1	6.10	1.67	0.41	141.9
2	40.5	6.02	1.23	0.27	142.4
3	27.1	8.18	1.29	0.36	141.3
4	43.4	6.91	1.49	0.41	142.4
5	42.7	6.20	1.29	0.25	141.6
GROUP 2 (50 MG/KG)					
11	24.1	6.73	1.48	0.50	143.5
12	24.9	6.19	1.07	0.37	140.7
13	39.0	5.94	1.32	0.34	141.2
14	31.2	6.06	1.07	0.38	142.0
15	36.8	6.38	1.39	0.52	140.5
GROUP 3 (150 MG/KG)					
21	24.9	5.82	1.94	0.49	140.0
22	39.0	5.44	1.31	0.25	142.0
23	49.4	5.32	0.89	0.28	141.7
24	32.3	6.58	1.07	0.27	141.7
25	32.3	5.43	1.26	0.27	141.3

CLINICAL BIOCHEMISTRY
MALES
END OF TREATMENT

ANIMAL	CREATININE umol/l	GLUCOSE mmol/l	CHOLESTEROL mmol/l	TRIGLYCERIDES mmol/l	SODIUM mmol/l
GROUP 4 (1000 MG/KG)					
31	36.0	5.82	2.18	0.61	140.6
32	41.2	5.44	1.38	0.66	140.6
35	21.8	7.52	1.31	0.53	141.8
36	37.5	7.37	1.64	0.84	139.5
37	30.8	5.67	1.60	0.58	140.8

MALES
END OF TREATMENT

ANIMAL	POTASSIUM mmol/l	CALCIUM mmol/l	CHLORIDE mmol/l	INORG.PHOS mmol/l	TOTAL PROTEIN g/l	ALBUMIN g/l
GROUP 1 (CONTROL)						
1	3.34	2.87	102	2.43	62.6	33.4
2	3.57	2.85	102	2.16	61.0	32.3
3	3.72	2.81	102	2.34	57.4	30.5
4	3.80	2.79	104	2.44	55.4	29.5
5	3.64	2.73	102	2.51	58.1	31.1
GROUP 2 (50 MG/KG)						
11	4.30	2.73	105	2.29	60.7	31.5
12	4.14	2.81	104	2.20	58.9	32.5
13	3.46	2.83	103	2.24	58.5	30.9
14	3.56	2.80	101	2.12	60.0	31.1
15	3.46	2.78	101	2.10	60.0	32.2
GROUP 3 (150 MG/KG)						
21	3.57	2.86	102	2.19	58.8	31.5
22	3.53	2.93	103	2.27	62.3	31.8
23	3.62	2.82	103	2.42	60.0	31.3
24	3.72	2.79	103	2.28	56.7	30.5
25	3.61	2.92	104	2.26	59.8	31.1
GROUP 4 (1000 MG/KG)						
31	4.24	2.92	105	2.58	58.0	33.8
32	3.47	2.99	108	2.73	56.9	32.3
35	3.67	2.79	105	2.47	54.6	33.0
36	3.60	2.96	108	2.69	58.6	33.7
37	3.73	2.85	104	2.92	53.5	29.5

FEMALES
END OF TREATMENT

ANIMAL	ALAT U/l	ASAT U/l	ALP U/l	BILIRUBIN umol/l	UREA mmol/l
GROUP 1 (CONTROL)					
41	68.7	56.4	149	4.1	9.9
44	53.5	79.5	126	3.4	6.9
45	58.1	89.6	126	2.9	8.7
46	74.3	82.7	121	3.9	8.4
48	70.0	92.4	79	3.4	8.4

CLINICAL BIOCHEMISTRY
FEMALES
END OF TREATMENT

ANIMAL	ALAT U/l	ASAT U/l	ALP U/l	BILIRUBIN umol/l	UREA mmol/l
GROUP 2 (50 MG/KG)					
52	82.1	88.3	118	3.9	8.9
53	59.4	68.1	94	3.5	7.5
54	20.9	56.5	59	3.9	5.6
55	69.0	72.2	142	3.9	10.7
59	71.1	77.9	70	4.1	8.2
GROUP 3 (150 MG/KG)					
61	60.9	76.0	85	3.4	7.6
63	54.9	65.8	92	3.5	8.0
64	55.6	63.4	90	4.2	8.2
66	63.1	62.8	55	3.8	5.6
69	62.3	62.5	101	3.6	8.4
GROUP 4 (1000 MG/KG)					
71	65.8	56.2	115	2.8	6.5
72	82.4	67.3	114	2.9	7.3
74	73.1	56.9	92	3.1	7.8
75	117.2	41.3	123	2.9	8.4
80	47.1	53.8	91	3.2	7.6

FEMALES
END OF TREATMENT

ANIMAL	CREATININE umol/l	GLUCOSE mmol/l	CHOLESTEROL mmol/l	TRIGLYCERIDES mmol/l	SODIUM mmol/l
GROUP 1 (CONTROL)					
41	44.8	4.79	2.69	1.19	140.3
44	41.3	5.42	1.56	0.39	140.9
45	41.3	6.13	1.90	0.42	137.7
46	46.2	5.34	1.87	0.64	139.8
48	42.0	5.49	1.70	0.78	140.7
GROUP 2 (50 MG/KG)					
52	42.7	4.91	1.33	0.36	139.5
53	42.7	5.59	2.09	0.66	140.4
54	40.6	8.73	1.74	0.49	135.0
55	44.8	6.34	1.81	0.55	141.1
59	41.3	5.43	1.91	0.47	140.7
GROUP 3 (150 MG/KG)					
61	39.2	6.28	1.20	0.35	140.3
63	39.9	5.28	2.46	0.39	141.6
64	40.6	6.37	2.61	0.62	140.1
66	38.5	5.09	1.97	0.84	139.4
69	40.6	6.89	1.85	0.81	139.5
GROUP 4 (1000 MG/KG)					
71	44.8	5.89	2.18	0.86	140.6
72	42.6	6.20	2.59	1.27	138.7
74	35.7	5.15	1.82	0.64	139.1
75	43.3	4.97	2.18	0.69	137.3
80	41.1	5.61	1.31	1.00	139.4

CLINICAL BIOCHEMISTRY
FEMALES
END OF TREATMENT

ANIMAL	POTASSIUM mmol/l	CALCIUM mmol/l	CHLORIDE mmol/l	INORG.PHOS mmol/l	TOTAL PROTEIN g/l	ALBUMIN g/l
GROUP 1 (CONTROL)						
41	3.66	3.18	94	3.39	63.1	33.6
44	3.67	2.91	101	2.38	61.9	33.1
45	4.14	2.90	99	2.76	61.7	32.1
46	3.70	3.02	98	2.93	62.4	33.0
48	3.72	2.96	98	2.66	59.2	30.6
GROUP 2 (50 MG/KG)						
52	3.88	2.85	103	2.08	63.3	33.5
53	3.20	2.78	101	2.01	60.0	31.8
54	3.53	2.95	97	1.94	66.5	34.8
55	4.10	3.02	101	2.28	60.6	31.9
59	3.02	2.75	99	1.91	68.0	34.8
GROUP 3 (150 MG/KG)						
61	3.56	2.75	103	1.74	57.9	30.8
63	3.18	2.91	102	2.02	66.3	34.3
64	3.97	2.95	102	2.15	64.9	33.6
66	3.53	2.94	98	2.29	63.7	32.1
69	3.42	2.83	99	2.17	66.5	34.2
GROUP 4 (1000 MG/KG)						
71	3.23	3.10	102	1.87	66.3	39.2
72	3.62	3.07	100	2.18	65.2	39.4
74	3.42	3.01	101	1.85	64.5	36.4
75	3.81	2.97	100	2.21	63.2	36.3
80	3.14	3.04	99	2.01	67.7	39.6

MACROSCOPIC FINDINGS
MALES
ALL NECROPSIES

ANIMAL	ORGAN	FINDING	DAY OF DEATH
GROUP 1 (CONTROL)			
1		No findings noted	Scheduled necropsy, 18Aug2003
2		No findings noted	Scheduled necropsy, 18Aug2003
3		No findings noted	Scheduled necropsy, 18Aug2003
4		No findings noted	Scheduled necropsy, 18Aug2003
5		No findings noted	Scheduled necropsy, 18Aug2003
6		No findings noted	Scheduled necropsy, 18Aug2003
7		No findings noted	Scheduled necropsy, 18Aug2003
8		No findings noted	Scheduled necropsy, 18Aug2003
9	Thymus	Focus/foci, many, dark red.	Scheduled necropsy, 18Aug2003
10		No findings noted	Scheduled necropsy, 18Aug2003
GROUP 2 (50 MG/KG)			
11		No findings noted	Scheduled necropsy, 18Aug2003
12		No findings noted	Scheduled necropsy, 18Aug2003
13		No findings noted	Scheduled necropsy, 18Aug2003
14	Liver	Discolouration, dark red.	Scheduled necropsy, 18Aug2003
15		No findings noted	Scheduled necropsy, 18Aug2003
16		No findings noted	Scheduled necropsy, 18Aug2003
17		No findings noted	Scheduled necropsy, 18Aug2003
18		No findings noted	Scheduled necropsy, 18Aug2003
19		No findings noted	Scheduled necropsy, 18Aug2003
20		No findings noted	Scheduled necropsy, 18Aug2003
GROUP 3 (150 MG/KG)			
21		No findings noted	Scheduled necropsy, 18Aug2003
22		No findings noted	Scheduled necropsy, 18Aug2003
23		No findings noted	Scheduled necropsy, 18Aug2003
24	Kidneys	Right side: pelvic dilation.	Scheduled necropsy, 18Aug2003
25		No findings noted	Scheduled necropsy, 18Aug2003
26		No findings noted	Scheduled necropsy, 18Aug2003
27		No findings noted	Scheduled necropsy, 18Aug2003
28	Thymus	Both sides: focus/foci, many, dark red.	Scheduled necropsy, 18Aug2003
29		No findings noted	Scheduled necropsy, 18Aug2003
30	Kidneys	Right side: pelvic dilation.	Scheduled necropsy, 18Aug2003
	Thymus	Right side: focus/foci, several, Reddish.	
GROUP 4 (1000 MG/KG)			
31		No findings noted	Scheduled necropsy, 18Aug2003
32	Kidneys	Right side: pelvic dilation.	Scheduled necropsy, 18Aug2003
	Epididymides	Left side, head: nodule(s), yellowish. Right side, tail: nodule(s), yellowish.	
33	General observations	Cannibalism:organ missing partly G.i.tractus partly genital region.	Spontaneous death, 01Aug2003
	Lungs	Discolouration, dark red.	
	Thymus	Focus/foci, isolated, dark red.	
	Mandibular l.node	Discolouration, dark red.	
34	General observations	Cannibalism:organ missing partly Genital region partly g.i.tractus and eyes. Beginning autolysis.	Spontaneous death, 27Jul2003
	Stomach	Discolouration, reddish.	
	Thymus	Both sides: focus/foci, many, dark red.	
35	Duodenum	Discolouration, reddish.	Scheduled necropsy, 18Aug2003
	Epididymides	Right side, tail: nodule(s), several, Yellowish, hard.	
36	Epididymides	Left side, tail: nodule(s), yellowish.	Scheduled necropsy, 18Aug2003
37		No findings noted	Scheduled necropsy, 18Aug2003

MACROSCOPIC FINDINGS
MALES
ALL NECROPSIES

ANIMAL	ORGAN	FINDING	DAY OF DEATH
GROUP 4 (1000 MG/KG)			
38	General observations	Emaciated.	Killed in extremis, 13Aug2003
	Stomach	Limiting ridge: thickened. Forestomach: irregular surface.	
	Caecum	Discolouration, reddish.	
	Liver	Accentuated lobular pattern. Enlarged.	
	Urinary bladder	Contents: dark red.	
39		No findings noted	Scheduled necropsy, 18Aug2003
40	Kidneys	Right side: pelvic dilation.	Scheduled necropsy, 18Aug2003
	Epididymides	Left side, tail: nodule(s), yellowish, Soft.	

FEMALES
ALL NECROPSIES

ANIMAL	ORGAN	FINDING	DAY OF DEATH
GROUP 1 (CONTROL)			
41		No findings noted	Scheduled necropsy, 01Sep2003
42		No findings noted	Scheduled necropsy, 04Sep2003
43		No findings noted	Scheduled necropsy, 04Sep2003
44		No findings noted	Scheduled necropsy, 01Sep2003
45	Mandibular l.node	Right side: discolouration, dark red.	Scheduled necropsy, 02Sep2003
	Skin	Throat region: alopecia.	
46	Thymus	Discolouration, light red.	Scheduled necropsy, 01Sep2003
47		No findings noted	Scheduled necropsy, 02Sep2003
48		No findings noted	Scheduled necropsy, 01Sep2003
49		No findings noted	Scheduled necropsy, 02Sep2003
50		No findings noted	Scheduled necropsy, 04Sep2003
GROUP 2 (50 MG/KG)			
51		No findings noted	Scheduled necropsy, 02Sep2003
52		No findings noted	Scheduled necropsy, 01Sep2003
53	Liver	Accentuated lobular pattern.	Scheduled necropsy, 01Sep2003
	Adrenal glands	Left side: focus/foci, isolated, Gray-white. Right side: focus/foci, several, Gray-white.	
54	Mandibular l.node	Right side: discolouration, dark red.	Scheduled necropsy, 02Sep2003
55		No findings noted	Scheduled necropsy, 02Sep2003
56		No findings noted	Scheduled necropsy, 03Sep2003
57		No findings noted	Scheduled necropsy, 05Sep2003
58		No findings noted	Scheduled necropsy, 04Sep2003
59	Mandibular l.node	Right side: discolouration, dark red.	Scheduled necropsy, 01Sep2003
	Eyes	Right side : exophtalmus.	
60		No findings noted	Scheduled necropsy, 04Sep2003
GROUP 3 (150 MG/KG)			
61		No findings noted	Scheduled necropsy, 01Sep2003
62		No findings noted	Scheduled necropsy, 04Sep2003
63	Spleen	Constricted.	Scheduled necropsy, 01Sep2003
64	Mandibular l.node	Right side: discolouration, dark red.	Scheduled necropsy, 02Sep2003
65	Uterus	Prolapse of the uterus.	Killed in extremis, 01Sep2003
66		No findings noted	Scheduled necropsy, 01Sep2003
67		No findings noted	Scheduled necropsy, 04Sep2003

MACROSCOPIC FINDINGS
FEMALES
ALL NECROPSIES

ANIMAL	ORGAN	FINDING	DAY OF DEATH
GROUP 3 (150 MG/KG)			
68		No findings noted	Scheduled necropsy, 05Sep2003
69	Clitoral glands	Both sides: focus/foci, several, tan.	Scheduled necropsy, 02Sep2003
	Mandibular l.node	Right side: discolouration, dark red.	
70		No findings noted	Scheduled necropsy, 05Sep2003
GROUP 4 (1000 MG/KG)			
71	Uterus	Contains fluid.	Scheduled necropsy, 05Sep2003
72		No findings noted	Scheduled necropsy, 05Sep2003
73	Uterus	Right horn: cyst(s), watery-clear.	Scheduled necropsy, 05Sep2003
74		No findings noted	Scheduled necropsy, 01Sep2003
75	Thymus	Right side: discolouration, reddish.	Scheduled necropsy, 05Sep2003
76	Mandibular l.node	Right side: discolouration, dark red.	Scheduled necropsy, 05Sep2003
77	General observations	Emaciated.	Killed in extremis, 03Aug2003
	Stomach	Forestomach: crateriform retraction, Many.	
78	Adrenal glands	Left side: grown together with: kidneys.	Spontaneous death, 18Aug2003
	Mesenteric l.node	Discolouration, dark red.	
79	Uterus	Contains fluid.	Scheduled necropsy, 05Sep2003
80	Kidneys	Pelvic dilation.	Scheduled necropsy, 05Sep2003

ORGAN WEIGHTS (GRAM)
MALES
END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (GRAM)	HEART (GRAM)	LIVER (GRAM)	THYMUS (GRAM)
GROUP 1 (CONTROL)					
1	381	1.94	1.230	11.91	0.556
2	335	2.18	1.230	9.56	0.427
3	334	1.97	1.126	10.36	0.482
4	340	2.04	1.294	9.94	0.429
5	382	2.13	1.159	10.62	0.561
6	350	---	---	---	---
7	315	---	---	---	---
8	358	---	---	---	---
9	400	---	---	---	---
10	412	---	---	---	---
GROUP 2 (50 MG/KG)					
11	364	2.06	1.115	10.99	0.619
12	366	2.31	1.051	9.86	0.410
13	358	2.13	1.140	10.00	0.503
14	332	1.98	1.201	10.44	0.452
15	381	2.03	1.302	11.04	0.453
16	343	---	---	---	---
17	365	---	---	---	---
18	345	---	---	---	---
19	390	---	---	---	---
20	359	---	---	---	---
GROUP 3 (150 MG/KG)					
21	339	2.06	1.285	9.41	0.579
22	328	2.02	1.102	9.69	0.417
23	381	2.33	1.156	11.28	0.608
24	358	2.22	1.200	10.08	0.419
25	351	1.91	1.186	10.33	0.338
26	347	---	---	---	---
27	386	---	---	---	---
28	376	---	---	---	---
29	368	---	---	---	---
30	342	---	---	---	---
GROUP 4 (1000 MG/KG)					
31	288	1.98	1.106	12.67	0.282
32	285	1.98	1.108	11.68	0.345
33	---	---	---	---	---
34	---	---	---	---	---
35	251	2.00	1.088	10.72	0.219
36	280	1.89	1.059	12.52	0.300
37	287	1.93	1.179	10.99	0.351
38	---	---	---	---	---
39	289	---	---	---	---
40	270	---	---	---	---

ORGAN WEIGHTS (GRAM)
MALES
END OF TREATMENT

ANIMAL	KIDNEYS (GRAM)	ADRENALS (GRAM)	SPLEEN (GRAM)	TESTES (GRAM)	EPIDIDYMIDES (GRAM)
GROUP 1 (CONTROL)					
1	3.04	0.062	0.791	3.76	1.118
2	2.60	0.073	0.797	3.48	1.059
3	3.04	0.079	0.777	3.10	0.903
4	2.96	0.089	0.786	3.49	1.078
5	3.45	0.087	0.810	3.31	1.061
6	---	---	---	4.06	1.372
7	---	---	---	3.45	1.160
8	---	---	---	3.23	1.043
9	---	---	---	3.56	0.976
10	---	---	---	3.31	1.144
GROUP 2 (50 MG/KG)					
11	2.88	0.076	0.887	3.68	1.274
12	3.08	0.070	0.832	4.10	1.238
13	2.66	0.073	0.769	3.00	0.844
14	3.44	0.102	0.997	3.66	1.122
15	2.93	0.073	0.897	4.20	1.181
16	---	---	---	3.98	1.311
17	---	---	---	3.38	0.964
18	---	---	---	3.28	1.078
19	---	---	---	4.16	1.319
20	---	---	---	3.52	1.081
GROUP 3 (150 MG/KG)					
21	2.83	0.062	0.811	3.70	1.004
22	2.82	0.076	0.751	3.26	1.250
23	3.35	0.081	0.921	3.84	1.144
24	3.26	0.064	0.809	3.52	0.934
25	2.83	0.082	0.780	3.31	1.148
26	---	---	---	3.40	1.084
27	---	---	---	3.79	1.225
28	---	---	---	4.20	1.231
29	---	---	---	4.26	1.265
30	---	---	---	4.11	1.020
GROUP 4 (1000 MG/KG)					
31	2.85	0.049	0.796	2.57	0.801
32	2.75	0.055	0.722	3.38	1.216
33	---	---	---	---	---
34	---	---	---	---	---
35	2.58	0.077	0.675	4.21	1.275
36	2.58	0.061	0.677	2.89	1.000
37	2.59	0.069	0.727	3.46	1.002
38	---	---	---	---	---
39	---	---	---	3.56	1.113
40	---	---	---	3.71	0.969

ORGAN/BODY WEIGHT RATIOS (%)
MALES
END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (%)	HEART (%)	LIVER (%)	THYMUS (%)
GROUP 1 (CONTROL)					
1	381	0.51	0.323	3.13	0.146
2	335	0.65	0.367	2.85	0.127
3	334	0.59	0.337	3.10	0.144
4	340	0.60	0.381	2.92	0.126
5	382	0.56	0.303	2.78	0.147
6	350	---	---	---	---
7	315	---	---	---	---
8	358	---	---	---	---
9	400	---	---	---	---
10	412	---	---	---	---
GROUP 2 (50 MG/KG)					
11	364	0.57	0.306	3.02	0.170
12	366	0.63	0.287	2.69	0.112
13	358	0.59	0.318	2.79	0.141
14	332	0.60	0.362	3.14	0.136
15	381	0.53	0.342	2.90	0.119
16	343	---	---	---	---
17	365	---	---	---	---
18	345	---	---	---	---
19	390	---	---	---	---
20	359	---	---	---	---
GROUP 3 (150 MG/KG)					
21	339	0.61	0.379	2.78	0.171
22	328	0.62	0.336	2.95	0.127
23	381	0.61	0.303	2.96	0.160
24	358	0.62	0.335	2.81	0.117
25	351	0.54	0.338	2.94	0.096
26	347	---	---	---	---
27	386	---	---	---	---
28	376	---	---	---	---
29	368	---	---	---	---
30	342	---	---	---	---
GROUP 4 (1000 MG/KG)					
31	288	0.69	0.384	4.40	0.098
32	285	0.69	0.389	4.10	0.121
33	---	---	---	---	---
34	---	---	---	---	---
35	251	0.79	0.433	4.27	0.087
36	280	0.67	0.378	4.47	0.107
37	287	0.67	0.411	3.83	0.122
38	---	---	---	---	---
39	289	---	---	---	---
40	270	---	---	---	---

ORGAN/BODY WEIGHT RATIOS (%)
MALES
END OF TREATMENT

ANIMAL	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	EPIDIDYMIDES (%)
GROUP 1 (CONTROL)					
1	0.80	0.016	0.208	0.99	0.293
2	0.78	0.022	0.238	1.04	0.316
3	0.91	0.024	0.233	0.93	0.270
4	0.87	0.026	0.231	1.03	0.317
5	0.90	0.023	0.212	0.87	0.278
6	---	---	---	1.16	0.392
7	---	---	---	1.09	0.368
8	---	---	---	0.90	0.291
9	---	---	---	0.89	0.244
10	---	---	---	0.80	0.278
GROUP 2 (50 MG/KG)					
11	0.79	0.021	0.244	1.01	0.350
12	0.84	0.019	0.227	1.12	0.338
13	0.74	0.020	0.215	0.84	0.236
14	1.04	0.031	0.300	1.10	0.338
15	0.77	0.019	0.235	1.10	0.310
16	---	---	---	1.16	0.382
17	---	---	---	0.92	0.264
18	---	---	---	0.95	0.312
19	---	---	---	1.07	0.338
20	---	---	---	0.98	0.301
GROUP 3 (150 MG/KG)					
21	0.84	0.018	0.239	1.09	0.296
22	0.86	0.023	0.229	0.99	0.381
23	0.88	0.021	0.242	1.01	0.300
24	0.91	0.018	0.226	0.98	0.261
25	0.81	0.023	0.222	0.94	0.327
26	---	---	---	0.98	0.312
27	---	---	---	0.98	0.317
28	---	---	---	1.12	0.327
29	---	---	---	1.16	0.344
30	---	---	---	1.20	0.298
GROUP 4 (1000 MG/KG)					
31	0.99	0.017	0.276	0.89	0.278
32	0.97	0.019	0.253	1.18	0.427
33	---	---	---	---	---
34	---	---	---	---	---
35	1.03	0.031	0.269	1.68	0.508
36	0.92	0.022	0.242	1.03	0.357
37	0.90	0.024	0.253	1.21	0.349
38	---	---	---	---	---
39	---	---	---	1.23	0.385
40	---	---	---	1.37	0.359

ORGAN WEIGHTS (GRAM)
FEMALES
END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (GRAM)	HEART (GRAM)	LIVER (GRAM)	THYMUS (GRAM)
GROUP 1 (CONTROL)					
41	316	2.12	0.984	10.62	0.378
42	---	---	---	---	---
43	---	---	---	---	---
44	295	1.88	1.047	9.07	0.347
45	308	1.94	1.024	10.90	0.286
46	318	2.09	1.090	11.55	0.292
47	---	---	---	---	---
48	320	2.00	1.101	11.49	0.303
49	366	---	---	---	---
50	---	---	---	---	---
GROUP 2 (50 MG/KG)					
51	299	---	---	---	---
52	283	1.87	0.909	9.42	0.267
53	324	1.88	0.975	11.85	0.349
54	313	2.14	1.028	10.54	0.400
55	308	2.06	0.996	11.86	0.215
56	---	---	---	---	---
57	---	---	---	---	---
58	---	---	---	---	---
59	286	1.97	1.015	10.29	0.274
60	---	---	---	---	---
GROUP 3 (150 MG/KG)					
61	278	1.82	0.981	8.97	0.369
62	---	---	---	---	---
63	307	1.98	0.993	12.05	0.284
64	289	1.96	1.104	10.58	0.279
65	325	---	---	---	---
66	314	2.01	1.280	12.28	0.441
67	---	---	---	---	---
68	---	---	---	---	---
69	292	1.98	0.911	12.32	0.283
70	---	---	---	---	---
GROUP 4 (1000 MG/KG)					
71	292	1.96	1.026	13.47	0.366
72	275	2.04	1.075	12.07	0.434
73	---	---	---	---	---
74	271	1.91	1.036	13.05	0.268
75	325	2.02	1.199	15.63	0.422
76	---	---	---	---	---
77	---	---	---	---	---
78	---	---	---	---	---
79	---	---	---	---	---
80	276	1.93	1.205	14.76	0.340

ORGAN WEIGHTS (GRAM)
FEMALES
END OF TREATMENT

ANIMAL	KIDNEYS (GRAM)	ADRENALS (GRAM)	SPLEEN (GRAM)
GROUP 1 (CONTROL)			
41	2.28	0.097	0.955
42	---	---	---
43	---	---	---
44	2.11	0.075	0.690
45	2.26	0.128	0.910
46	2.25	0.104	0.925
47	---	---	---
48	2.31	0.110	0.746
49	---	---	---
50	---	---	---
GROUP 2 (50 MG/KG)			
51	---	---	---
52	1.97	0.091	0.682
53	2.44	0.095	0.887
54	2.62	0.120	0.703
55	2.30	0.094	0.695
56	---	---	---
57	---	---	---
58	---	---	---
59	2.34	0.092	0.775
60	---	---	---
GROUP 3 (150 MG/KG)			
61	2.08	0.098	0.734
62	---	---	---
63	2.57	0.103	0.955
64	2.00	0.095	0.608
65	---	---	---
66	2.59	0.112	0.786
67	---	---	---
68	---	---	---
69	2.30	0.101	0.673
70	---	---	---
GROUP 4 (1000 MG/KG)			
71	2.24	0.091	0.854
72	2.05	0.071	0.693
73	---	---	---
74	2.13	0.089	0.603
75	2.43	0.096	0.631
76	---	---	---
77	---	---	---
78	---	---	---
79	---	---	---
80	2.34	0.089	0.788

ORGAN/BODY WEIGHT RATIOS (%)
FEMALES
END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (%)	HEART (%)	LIVER (%)	THYMUS (%)
GROUP 1 (CONTROL)					
41	316	0.67	0.311	3.36	0.120
42	---	---	---	---	---
43	---	---	---	---	---
44	295	0.64	0.355	3.07	0.118
45	308	0.63	0.332	3.54	0.093
46	318	0.66	0.343	3.63	0.092
47	---	---	---	---	---
48	320	0.63	0.344	3.59	0.095
49	366	---	---	---	---
50	---	---	---	---	---
GROUP 2 (50 MG/KG)					
51	299	---	---	---	---
52	283	0.66	0.321	3.33	0.094
53	324	0.58	0.301	3.66	0.108
54	313	0.68	0.328	3.37	0.128
55	308	0.67	0.323	3.85	0.070
56	---	---	---	---	---
57	---	---	---	---	---
58	---	---	---	---	---
59	286	0.69	0.355	3.60	0.096
60	---	---	---	---	---
GROUP 3 (150 MG/KG)					
61	278	0.66	0.353	3.23	0.133
62	---	---	---	---	---
63	307	0.64	0.323	3.92	0.093
64	289	0.68	0.382	3.66	0.097
65	325	---	---	---	---
66	314	0.64	0.408	3.91	0.140
67	---	---	---	---	---
68	---	---	---	---	---
69	292	0.68	0.312	4.22	0.097
70	---	---	---	---	---
GROUP 4 (1000 MG/KG)					
71	292	0.67	0.351	4.61	0.125
72	275	0.74	0.391	4.39	0.158
73	---	---	---	---	---
74	271	0.71	0.382	4.82	0.099
75	325	0.62	0.369	4.81	0.130
76	---	---	---	---	---
77	---	---	---	---	---
78	---	---	---	---	---
79	---	---	---	---	---
80	276	0.70	0.437	5.35	0.123

ORGAN/BODY WEIGHT RATIOS (%)
FEMALES
END OF TREATMENT

ANIMAL	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)
GROUP 1 (CONTROL)			
41	0.72	0.031	0.302
42	---	---	---
43	---	---	---
44	0.71	0.025	0.234
45	0.73	0.042	0.295
46	0.71	0.033	0.291
47	---	---	---
48	0.72	0.034	0.233
49	---	---	---
50	---	---	---
GROUP 2 (50 MG/KG)			
51	---	---	---
52	0.70	0.032	0.241
53	0.75	0.029	0.274
54	0.84	0.038	0.225
55	0.75	0.031	0.226
56	---	---	---
57	---	---	---
58	---	---	---
59	0.82	0.032	0.271
60	---	---	---
GROUP 3 (150 MG/KG)			
61	0.75	0.035	0.264
62	---	---	---
63	0.84	0.034	0.311
64	0.69	0.033	0.210
65	---	---	---
66	0.82	0.036	0.250
67	---	---	---
68	---	---	---
69	0.79	0.035	0.230
70	---	---	---
GROUP 4 (1000 MG/KG)			
71	0.77	0.031	0.292
72	0.75	0.026	0.252
73	---	---	---
74	0.79	0.033	0.223
75	0.75	0.030	0.194
76	---	---	---
77	---	---	---
78	---	---	---
79	---	---	---
80	0.85	0.032	0.286

BREEDING DATA PER LITTER
FEMALES
F0 GENERATION - LACTATION

LITTER	DURATION OF GESTATION	-- FIRST LITTER CHECK -- DEAD PUPS		LIVING PUPS			P.NATAL LOSS DAYS 0 - 4		LIVING PUPS DAY 4 P.P.		
		M	F	M	F	TOT.	M	F	M	F	TOT.
GROUP 1 (CONTROL)											
41	21	0	0	5	9	14	0	0	5	9	14
42	22	0	0	5	9	14	0	0	5	9	14
43	22	0	0	7	8	15	0	0	7	8	15
44	22	0	0	1	5	6	0	0	1	5	6
45	21	0	0	8	7	15	1	0	7	7	14
46	22	0	0	8	9	17	0	0	8	9	17
47	21	0	1	6	9	15	0	1	6	8	14
48	22	0	0	11	5	16	0	0	11	5	16
49	22	0	0	1	1	2	0	0	1	1	2
50	22	0	1	4	4	8	0	0	4	4	8
TOTAL		0	2	56	66	122	1	1	55	65	120
N	10	10	10	10	10	10	10	10	10	10	10
MEAN	21.7	0.0	0.2	5.6	6.6	12.2	0.1	0.1	5.5	6.5	12.0
ST.DEV.	0.5	0.0	0.4	3.1	2.8	5.0	0.3	0.3	3.1	2.7	4.9
GROUP 2 (50 MG/KG)											
51	21	0	0	5	12	17	0	1	5	11	16
52	21	0	1	7	9	16	0	2	7	7	14
53	21	0	0	9	6	15	0	0	9	6	15
54	22	0	0	6	7	13	6	7	0	0	0
55	22	0	0	3	10	13	0	0	3	10	13
56	21	0	0	7	9	16	0	0	7	9	16
58	22	0	0	8	10	18	1	0	7	10	17
59	21	0	0	9	7	16	1	3	8	4	12
60	22	0	0	6	10	16	0	0	6	10	16
TOTAL		0	1	60	80	140	8	13	52	67	119
N	9	9	9	9	9	9	9	9	9	9	9
MEAN	21.4	0.0	0.1	6.7	8.9	15.6	0.9	1.4	5.8	7.4	13.2
ST.DEV.	0.5	0.0	0.3	1.9	1.9	1.7	2.0	2.4	2.8	3.6	5.2
GROUP 3 (150 MG/KG)											
61	22	0	0	3	1	4	0	0	3	1	4
62	22	0	0	10	3	13	0	0	10	3	13
63	21	0	0	5	10	15	0	6	5	4	9
64	22	0	0	3	3	6	0	0	3	3	6
65	23	0	0	5	0	5	5	0	0	0	0
66	21	0	0	9	5	14	1	0	8	5	13
67	22	0	0	5	9	14	0	0	5	9	14
69	22	0	0	6	10	16	0	0	6	10	16
TOTAL		0	0	46	41	87	6	6	40	35	75
N	8	8	8	8	8	8	8	8	8	8	8
MEAN	21.9	0.0	0.0	5.8	5.1	10.9	0.8	0.8	5.0	4.4	9.4
ST.DEV.	0.6	0.0	0.0	2.5	4.1	5.0	1.8	2.1	3.1	3.5	5.6
GROUP 4 (1000 MG/KG)											
74	21	0	0	9	7	16	4	5	5	2	7
75	22	0	0	1	5	6	0	0	1	5	6
80	22	0	0	2	1	3	2	1	0	0	0
TOTAL		0	0	12	13	25	6	6	6	7	13
N	3	3	3	3	3	3	3	3	3	3	3
MEAN	21.7	0.0	0.0	4.0	4.3	8.3	2.0	2.0	2.0	2.3	4.3
ST.DEV.	0.6	0.0	0.0	4.4	3.1	6.8	2.0	2.6	2.6	2.5	3.8

MEAN BODY WEIGHTS OF PUPS PER LITTER (GRAM)
F0-GENERATION - LACTATION

LITTER	SEX	DAY 1	DAY 4
GROUP 1 (CONTROL)			
41	M	6.8	9.7
	F	6.4	9.1
	M+F	6.6	9.3
42	M	7.0	10.4
	F	6.7	10.0
	M+F	6.8	10.2
43	M	7.1	11.2
	F	7.0	10.4
	M+F	7.1	10.8
44	M	8.3	12.7
	F	7.6	11.6
	M+F	7.7	11.8
45	M	6.1	9.5
	F	6.0	8.6
	M+F	6.1	9.0
46	M	7.1	9.8
	F	6.9	9.4
	M+F	7.0	9.6
47	M	5.8	8.6
	F	5.6	8.3
	M+F	5.7	8.5
48	M	6.8	9.9
	F	6.6	9.3
	M+F	6.8	9.7
49	M	8.1	12.2
	F	7.7	10.9
	M+F	7.9	11.5
50	M	7.6	12.0
	F	7.3	11.7
	M+F	7.4	11.8
GROUP 2 (50 MG/KG)			
51	M	6.3	9.2
	F	6.0	9.0
	M+F	6.1	9.1
52	M	5.6	7.8
	F	5.1	7.3
	M+F	5.3	7.5
53	M	6.4	9.3
	F	5.9	8.4
	M+F	6.2	8.9
54	M	7.4	--
	F	6.8	--
	M+F	7.1	--
55	M	6.8	10.1
	F	6.6	9.7
	M+F	6.7	9.8

MEAN BODY WEIGHTS OF PUPS PER LITTER (GRAM)
F0-GENERATION - LACTATION

LITTER	SEX	DAY 1	DAY 4
GROUP 2 (50 MG/KG)			
56	M	6.3	8.4
	F	5.8	7.4
	M+F	6.0	7.8
58	M	6.6	9.5
	F	6.3	8.9
	M+F	6.5	9.1
59	M	6.5	8.8
	F	5.9	7.1
	M+F	6.2	8.2
60	M	6.2	8.9
	F	5.7	8.4
	M+F	5.9	8.6
GROUP 3 (150 MG/KG)			
61	M	6.5	9.2
	F	6.8	10.1
	M+F	6.6	9.5
62	M	7.2	11.4
	F	7.2	10.6
	M+F	7.2	11.2
63	M	6.4	9.2
	F	6.0	8.3
	M+F	6.2	8.8
64	M	7.5	11.7
	F	7.3	11.2
	M+F	7.4	11.4
66	M	6.5	8.4
	F	6.0	7.2
	M+F	6.3	7.9
67	M	7.6	10.8
	F	7.2	10.3
	M+F	7.3	10.5
69	M	6.5	9.4
	F	6.1	8.3
	M+F	6.3	8.7
GROUP 4 (1000 MG/KG)			
74	M	4.4	4.8
	F	3.9	4.3
	M+F	4.2	4.7
75	M	6.5	8.0
	F	5.5	6.6
	M+F	5.7	6.9
80	M	4.6	--
	F	4.3	--
	M+F	4.5	--

BODY WEIGHTS OF PUPS (GRAM)
F0-GENERATION - LACTATION

LITTER	PUP	SEX	DAY 1	DAY 4
GROUP 1 (CONTROL)				
41	1	M	6.8	10.0
	2	M	7.0	10.7
	3	M	7.0	9.4
	4	M	6.4	8.5
	5	M	7.0	9.9
	6	F	6.1	9.3
	7	F	6.5	9.5
	8	F	6.1	9.0
	9	F	6.9	9.4
	10	F	6.5	8.7
	11	F	6.4	8.3
	12	F	6.5	10.1
	13	F	6.3	8.6
	14	F	6.4	9.2
42	1	M	7.1	10.5
	2	M	7.1	9.9
	3	M	7.3	10.6
	4	M	7.1	11.1
	5	M	6.7	10.2
	6	F	6.4	9.5
	7	F	6.5	10.1
	8	F	6.6	10.5
	9	F	6.7	10.5
	10	F	6.8	9.6
	11	F	6.2	9.2
	12	F	6.4	9.4
	13	F	7.4	11.3
	14	F	7.1	9.9
43	1	M	7.4	11.9
	2	M	6.2	9.7
	3	M	7.1	10.3
	4	M	7.9	13.2
	5	M	6.9	10.7
	6	M	7.6	11.9
	7	M	6.8	10.9
	8	F	7.7	11.7
	9	F	7.4	10.8
	10	F	7.4	11.4
	11	F	6.1	9.0
	12	F	7.0	10.6
	13	F	6.7	9.7
	14	F	7.0	10.1
	15	F	6.8	9.8
44	1	M	8.3	12.7
	2	F	7.7	11.3
	3	F	7.6	11.6
	4	F	7.8	11.8
	5	F	7.4	11.7
	6	F	7.7	11.6
45	1	M	6.5	10.0
	2	M	6.5	9.3
	3	M	6.6	9.7
	4	M	6.4	9.4
	5	M	6.1	9.2
	6	M	4.7	--
	7	M	6.7	10.2
	8	M	5.5	8.6

BODY WEIGHTS OF PUPS (GRAM)
F0-GENERATION - LACTATION

LITTER	PUP	SEX	DAY 1	DAY 4
GROUP 1 (CONTROL)				
	9	F	5.7	8.3
	10	F	6.1	8.7
	11	F	6.0	8.6
	12	F	6.0	9.0
	13	F	6.2	8.9
	14	F	5.8	8.4
	15	F	6.1	8.4
46	1	M	7.5	10.9
	2	M	6.5	9.0
	3	M	6.7	9.6
	4	M	7.3	9.6
	5	M	7.3	10.6
	6	M	7.2	9.5
	7	M	7.3	9.6
	8	M	7.0	9.7
	9	F	6.7	9.8
	10	F	6.9	9.4
	11	F	6.9	9.3
	12	F	6.6	9.0
	13	F	7.5	9.4
	14	F	7.1	9.3
	15	F	6.9	9.8
	16	F	7.1	9.7
	17	F	6.2	8.7
47	1	M	5.5	8.2
	2	M	6.0	9.0
	3	M	5.2	7.8
	4	M	6.1	8.8
	5	M	6.2	9.2
	6	M	6.0	8.9
	7	F	5.6	--
	8	F	5.3	7.6
	9	F	5.9	9.2
	10	F	5.5	8.0
	11	F	5.4	8.7
	12	F	5.8	8.6
	13	F	6.0	8.7
	14	F	5.7	8.3
	15	F	5.5	7.8
	16	F	--	--
48	1	M	7.4	10.3
	2	M	6.6	9.7
	3	M	7.2	11.0
	4	M	6.5	9.1
	5	M	7.1	10.3
	6	M	6.8	9.7
	7	M	6.7	9.7
	8	M	6.1	9.0
	9	M	6.6	9.6
	10	M	7.2	10.0
	11	M	6.9	10.0
	12	F	6.6	8.9
	13	F	6.1	8.8
	14	F	7.0	9.7
	15	F	6.7	9.6
	16	F	6.5	9.2

BODY WEIGHTS OF PUPS (GRAM)
F0-GENERATION - LACTATION

LITTER	PUP	SEX	DAY 1	DAY 4
GROUP 1 (CONTROL)				
49	1	M	8.1	12.2
	2	F	7.7	10.9
50	1	M	7.7	12.4
	2	M	7.9	12.2
	3	M	7.6	11.9
	4	M	7.3	11.5
	5	F	6.9	10.8
	6	F	7.7	13.0
	7	F	7.2	11.5
	8	F	7.3	11.6
	9	F	--	--
GROUP 2 (50 MG/KG)				
51	1	M	6.6	10.5
	2	M	5.3	5.8
	3	M	6.3	9.6
	4	M	6.3	9.9
	5	M	7.0	10.4
	6	F	5.7	--
	7	F	5.7	7.7
	8	F	6.4	8.9
	9	F	6.2	9.2
	10	F	5.8	8.4
	11	F	5.7	9.0
	12	F	6.1	9.3
	13	F	6.4	10.0
	14	F	6.2	8.5
	15	F	5.9	8.6
	16	F	5.8	9.3
	17	F	6.3	9.8
52	1	M	5.7	8.2
	2	M	5.6	7.9
	3	M	5.6	7.7
	4	M	5.6	7.7
	5	M	5.4	6.7
	6	M	5.5	7.8
	7	M	5.6	8.2
	8	F	4.9	7.2
	9	F	4.6	7.0
	10	F	5.3	7.3
	11	F	5.4	7.8
	12	F	4.6	--
	13	F	5.0	--
	14	F	5.5	8.2
	15	F	5.1	7.4
	16	F	5.2	6.4
	17	F	--	--
53	1	M	6.3	9.6
	2	M	6.3	9.4
	3	M	6.2	8.9
	4	M	6.8	10.2
	5	M	6.4	9.6
	6	M	6.3	8.6
	7	M	6.7	9.4
	8	M	6.4	8.5
	9	M	6.3	9.4
	10	F	5.4	8.1

BODY WEIGHTS OF PUPS (GRAM)
F0-GENERATION - LACTATION

LITTER	PUP	SEX	DAY 1	DAY 4
GROUP 2 (50 MG/KG)				
	11	F	6.1	9.0
	12	F	6.1	9.0
	13	F	5.9	8.3
	14	F	6.0	8.9
	15	F	6.0	7.2
54	1	M	7.6	
	2	M	7.8	
	3	M	6.9	
	4	M	7.0	
	5	M	7.2	
	6	M	7.8	
	7	F	6.5	
	8	F	6.9	
	9	F	7.0	
	10	F	7.4	
	11	F	6.7	
	12	F	6.7	
	13	F	6.6	
55	1	M	6.8	9.6
	2	M	7.0	10.7
	3	M	6.6	9.9
	4	F	7.0	10.2
	5	F	6.0	9.0
	6	F	6.7	10.1
	7	F	6.4	9.9
	8	F	6.7	10.1
	9	F	7.2	10.9
	10	F	6.9	10.2
	11	F	6.4	9.1
	12	F	7.0	9.8
	13	F	5.9	7.9
56	1	M	6.4	8.7
	2	M	5.9	7.5
	3	M	6.3	7.1
	4	M	6.3	8.7
	5	M	6.6	9.3
	6	M	6.0	8.5
	7	M	6.5	8.8
	8	F	5.7	8.0
	9	F	6.2	8.0
	10	F	5.9	7.6
	11	F	5.3	6.4
	12	F	6.1	7.3
	13	F	5.6	7.9
	14	F	5.9	7.4
	15	F	5.7	7.0
	16	F	5.9	7.2
58	1	M	6.9	10.8
	2	M	5.7	8.0
	3	M	6.6	9.3
	4	M	7.4	10.0
	5	M	7.1	10.5
	6	M	7.3	10.4
	7	M	6.0	7.6
	8	M	6.2	--
	9	F	6.4	10.0
	10	F	6.8	10.2

BODY WEIGHTS OF PUPS (GRAM)
F0-GENERATION - LACTATION

LITTER	PUP	SEX	DAY 1	DAY 4
GROUP 2 (50 MG/KG)				
	11	F	6.9	10.1
	12	F	4.7	4.7
	13	F	6.6	10.1
	14	F	6.9	9.7
	15	F	7.2	9.4
	16	F	4.7	5.7
	17	F	6.8	9.8
	18	F	6.5	8.9
59	1	M	6.6	10.4
	2	M	6.9	8.3
	3	M	6.1	--
	4	M	6.6	9.2
	5	M	6.7	8.5
	6	M	6.4	9.0
	7	M	6.3	8.1
	8	M	6.3	9.0
	9	M	6.3	8.2
	10	F	5.9	8.4
	11	F	5.7	5.2
	12	F	5.7	7.2
	13	F	6.2	--
	14	F	5.9	7.5
	15	F	5.9	--
	16	F	6.1	--
60	1	M	5.6	8.1
	2	M	6.4	9.3
	3	M	6.3	8.9
	4	M	6.5	9.4
	5	M	6.5	8.7
	6	M	6.2	9.2
	7	F	5.7	8.4
	8	F	6.2	8.9
	9	F	6.3	9.4
	10	F	5.0	7.6
	11	F	5.8	8.6
	12	F	5.8	9.3
	13	F	5.8	8.0
	14	F	5.3	7.0
	15	F	5.4	7.9
	16	F	6.0	8.5
GROUP 3 (150 MG/KG)				
61	1	M	5.3	7.6
	2	M	6.8	9.6
	3	M	7.5	10.5
	4	F	6.8	10.1
62	1	M	7.0	11.2
	2	M	7.4	12.1
	3	M	7.2	11.5
	4	M	7.4	11.6
	5	M	7.1	10.2
	6	M	7.2	11.6
	7	M	7.4	12.0
	8	M	7.1	11.5
	9	M	7.1	11.5
	10	M	7.4	10.9
	11	F	6.9	9.9

BODY WEIGHTS OF PUPS (GRAM)
F0-GENERATION - LACTATION

LITTER	PUP	SEX	DAY 1	DAY 4
GROUP 3 (150 MG/KG)				
	12	F	7.5	10.7
	13	F	7.2	11.3
63	1	M	6.6	9.2
	2	M	6.3	9.4
	3	M	6.4	9.4
	4	M	6.1	8.2
	5	M	6.8	9.6
	6	F	5.9	8.0
	7	F	6.0	--
	8	F	5.9	--
	9	F	6.0	7.4
	10	F	6.1	9.1
	11	F	6.3	--
	12	F	6.2	--
	13	F	5.8	8.5
	14	F	6.2	--
	15	F	5.8	--
64	1	M	7.4	11.9
	2	M	7.1	11.4
	3	M	8.0	11.8
	4	F	7.5	11.2
	5	F	7.1	11.1
	6	F	7.3	11.3
66	1	M	6.2	7.9
	2	M	6.7	--
	3	M	7.1	9.5
	4	M	6.1	7.7
	5	M	6.4	8.3
	6	M	6.4	8.4
	7	M	6.7	8.8
	8	M	6.5	8.4
	9	M	6.5	8.2
	10	F	5.7	7.3
	11	F	6.2	7.3
	12	F	5.5	6.7
	13	F	6.4	7.9
	14	F	6.0	6.9
67	1	M	7.0	10.4
	2	M	7.7	10.8
	3	M	7.8	10.9
	4	M	7.8	11.6
	5	M	7.4	10.3
	6	F	7.6	10.6
	7	F	7.1	10.6
	8	F	6.7	10.1
	9	F	7.1	10.3
	10	F	7.2	9.9
	11	F	7.2	10.3
	12	F	7.2	9.8
	13	F	7.5	10.7
	14	F	7.2	10.8
69	1	M	6.7	10.2
	2	M	6.2	9.0
	3	M	6.3	8.8
	4	M	6.5	8.8

BODY WEIGHTS OF PUPS (GRAM)
F0-GENERATION - LACTATION

LITTER	PUP	SEX	DAY 1	DAY 4
GROUP 3 (150 MG/KG)				
	5	M	6.6	9.4
	6	M	6.9	10.2
	7	F	5.5	7.4
	8	F	5.9	8.9
	9	F	5.9	6.8
	10	F	6.1	9.1
	11	F	6.8	9.3
	12	F	6.5	8.9
	13	F	6.6	8.5
	14	F	6.2	7.7
	15	F	6.2	8.7
	16	F	5.5	8.1
GROUP 4 (1000 MG/KG)				
74	1	M	4.6	5.3
	2	M	4.2	4.8
	3	M	4.1	--
	4	M	4.4	4.9
	5	M	4.5	--
	6	M	4.2	4.2
	7	M	4.5	--
	8	M	4.5	--
	9	M	4.4	4.8
	10	F	4.0	--
	11	F	3.9	3.8
	12	F	3.7	--
	13	F	4.3	--
	14	F	3.6	--
	15	F	4.2	4.9
	16	F	4.0	--
75	1	M	6.5	8.0
	2	F	5.7	7.5
	3	F	5.6	6.5
	4	F	5.0	5.6
	5	F	5.2	6.2
	6	F	6.2	7.4
80	1	M	4.6	
	2	M	4.5	
	3	F	4.3	

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS
GROUP 1 (CONTROL)					
LITTER 41 27AUG03	1	M	DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	2	M	DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	3	M	DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	4	M	DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	5	M	DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	6	F	DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	7	F	DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	8	F	DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	9	F	DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	10	F	DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	11	F	DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	12	F	DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	13	F	DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	14	F	DAY 5	Planned Necropsy	FLC Tail absent DAY 2 Tail absent DAY 3 Tail absent DAY 4 Tail absent DAY 5 Tail absent LLC Tail absent MACRO Tail absent
LITTER 42 30AUG03	1	M	DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	2	M	DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	3	M	DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS	
GROUP 1 (CONTROL)						
	4	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	6	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	7	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	8	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	9	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	10	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	11	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	12	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	13	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	14	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 43 30AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	6	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	7	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS	
GROUP 1 (CONTROL)						
	8	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	9	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	10	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	11	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	12	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	13	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	14	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	15	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 44 27AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	6	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 45 28AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS	
GROUP 1 (CONTROL)						
	5	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	6	M	DAY 4	Missing	FLC	No findings
	7	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	8	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	9	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	10	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	11	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	12	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	13	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	14	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	15	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 46 27AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	6	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	7	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	8	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS	
GROUP 1 (CONTROL)						
	9	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	10	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	11	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	12	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	13	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	14	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	15	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	16	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	17	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 47 28AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	6	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	7	F	DAY 2	Spontaneous death	FLC	No findings
					LLC	No findings
					MACRO	No findings
	8	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	9	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS
GROUP 1 (CONTROL)					
	10	F	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	11	F	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	12	F	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	13	F	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	14	F	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	15	F	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	16	F	DAY 1	Dead at FLC	FLC Dead
					MACRO Cannibalism (except head and frontlegs)
LITTER 48 27AUG03	1	M	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	2	M	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	3	M	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	4	M	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	5	M	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	6	M	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	7	M	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	8	M	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	9	M	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	10	M	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	11	M	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS	
GROUP 1 (CONTROL)						
	12	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	13	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	14	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	15	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	16	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 49 28AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 50 30AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	6	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	7	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	8	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	9	F	DAY 1	Dead at FLC	FLC	Dead
					LLC	No findings
					MACRO	No findings
GROUP 2 (50 MG/KG)						
LITTER 51 28AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS	
GROUP 2 (50 MG/KG)						
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					DAY 4	Small
					LLC	No findings
					MACRO	Small
	3	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	6	F	DAY 4	Missing	FLC	No findings
	7	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	8	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	9	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	10	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	11	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	12	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	13	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	14	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	15	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	16	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	17	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 52 27AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS	
GROUP 2 (50 MG/KG)						
	3	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	6	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	7	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	8	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	9	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	10	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	11	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	12	F	DAY 2	Missing	FLC	No findings
	13	F	DAY 4	Missing	FLC	No findings
	14	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	15	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	16	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	17	F	DAY 1	Dead at FLC	FLC	Dead
					MACRO	Cannibalism (except head)
LITTER 53 27AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS	
GROUP 2 (50 MG/KG)						
	6	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	7	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	8	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	9	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	10	F	DAY 5	Missing	FLC	No findings
	11	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	12	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	13	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	14	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	15	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 54 28AUG03	1	M	DAY 1	Spontaneous death	FLC	No findings
					LLC	Cannibalism
					MACRO	Cannibalism (of foreleg/hindleg, gi-tractus)
	2	M	DAY 1	Missing	FLC	No findings
	3	M	DAY 1	Killed in extremis	FLC	No findings
					LLC	Cannibalism
					MACRO	Cannibalism (of hindleg)
	4	M	DAY 1	Spontaneous death	FLC	No findings
					LLC	Cannibalism
					MACRO	Cannibalism (no organs missing)
	5	M	DAY 1	Missing	FLC	No findings
	6	M	DAY 1	Spontaneous death	FLC	No findings
					LLC	Cannibalism
					MACRO	Cannibalism (of brain, forelegs/hindleg, stomach)
	7	F	DAY 1	Spontaneous death	FLC	No findings
					LLC	Cannibalism
					MACRO	Cannibalism (of forelegs/hindleg, gi-tractus)
	8	F	DAY 1	Missing	FLC	No findings
	9	F	DAY 1	Spontaneous death	FLC	No findings
					LLC	Cannibalism
					MACRO	Cannibalism (of stomach)
	10	F	DAY 1	Spontaneous death	FLC	No findings
					LLC	Cannibalism
					MACRO	Cannibalism (of hindleg/forefoot)
	11	F	DAY 1	Killed in extremis	FLC	No findings
					LLC	Cannibalism
					MACRO	Cannibalism (no organs missing)

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS	
GROUP 2 (50 MG/KG)						
	12	F	DAY 1	Spontaneous death	FLC	No findings
					LLC	Cannibalism
					MACRO	No findings
	13	F	DAY 1	Spontaneous death	FLC	No findings
					LLC	Cannibalism
					MACRO	Cannibalism (of foreleg, small/large bowel)
LITTER 55 28AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	6	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	7	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	8	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	9	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	10	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	11	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	12	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	13	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 56 29AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS	
GROUP 2 (50 MG/KG)						
	4	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	6	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	7	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	8	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	9	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	10	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	11	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	12	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	13	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	14	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	15	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	16	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 58 30AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS
GROUP 2 (50 MG/KG)					
	6	M	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	7	M	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	8	M	DAY 4	Spontaneous death	FLC No findings
					LLC No findings
					MACRO No milk
	9	F	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	10	F	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	11	F	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	12	F	DAY 5	Planned Necropsy	FLC No findings
					DAY 4 Small
					LLC No findings
					MACRO Small
	13	F	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	14	F	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	15	F	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	16	F	DAY 5	Planned Necropsy	FLC No findings
					DAY 4 Small
					LLC No findings
					MACRO No findings
	17	F	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	18	F	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
LITTER 59 27AUG03	1	M	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	2	M	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	3	M	DAY 4	Missing	FLC No findings
	4	M	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings
	5	M	DAY 5	Planned Necropsy	FLC No findings
					LLC No findings
					MACRO No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS	
GROUP 2 (50 MG/KG)						
	6	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	7	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	8	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	9	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	10	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	11	F	DAY 5	Planned Necropsy	FLC	No findings
					DAY 4	Small
					LLC	No findings
					MACRO	Small
	12	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	13	F	DAY 4	Missing	FLC	No findings
	14	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	15	F	DAY 2	Missing	FLC	No findings
	16	F	DAY 2	Spontaneous death	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 60 30AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	6	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	7	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	8	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS	
GROUP 2 (50 MG/KG)						
	9	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	10	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	11	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	12	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	13	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	14	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	15	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	16	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
GROUP 3 (150 MG/KG)						
LITTER 61 27AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 62 30AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS	
GROUP 3 (150 MG/KG)						
	6	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	7	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	8	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	9	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	10	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	11	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	12	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	13	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 63 27AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	6	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	7	F	DAY 4	Missing	FLC	No findings
	8	F	DAY 2	Spontaneous death	FLC	No findings
					LLC	No findings
					MACRO	No findings
	9	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	10	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	11	F	DAY 2	Spontaneous death	FLC	No findings
					LLC	No findings
					MACRO	No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS	
GROUP 3 (150 MG/KG)						
	12	F	DAY 2	Missing	FLC	No findings
	13	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	14	F	DAY 4	Missing	FLC	No findings
	15	F	DAY 4	Missing	FLC	No findings
LITTER 64 28AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	6	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 65 31AUG03	1	M	DAY 1	Killed in extremis	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 1	Killed in extremis	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	M	DAY 1	Killed in extremis	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	M	DAY 1	Killed in extremis	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	M	DAY 1	Killed in extremis	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 66 26AUG03	1	M	DAY 6	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 4	Missing	FLC	No findings
	3	M	DAY 6	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	M	DAY 6	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	M	DAY 6	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	6	M	DAY 6	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS	
GROUP 3 (150 MG/KG)						
	7	M	DAY 6	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	8	M	DAY 6	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	9	M	DAY 6	Planned Necropsy	FLC	Cold, no milk
					LLC	No findings
					MACRO	No findings
	10	F	DAY 6	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	11	F	DAY 6	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	12	F	DAY 6	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	13	F	DAY 6	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	14	F	DAY 6	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 67 30AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	4	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	5	M	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	6	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	7	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	8	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	9	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	10	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 3 (150 MG/KG)			
	11 F	DAY 5 Planned Necropsy	FLC No findings
			LLC No findings
			MACRO No findings
	12 F	DAY 5 Planned Necropsy	FLC No findings
			LLC No findings
			MACRO No findings
	13 F	DAY 5 Planned Necropsy	FLC No findings
			LLC No findings
			MACRO No findings
	14 F	DAY 5 Planned Necropsy	FLC No findings
			LLC No findings
			MACRO No findings
LITTER 69 28AUG03	1 M	DAY 5 Planned Necropsy	FLC No findings
			LLC No findings
			MACRO No findings
	2 M	DAY 5 Planned Necropsy	FLC No findings
			LLC No findings
			MACRO No findings
	3 M	DAY 5 Planned Necropsy	FLC No findings
			LLC No findings
			MACRO No findings
	4 M	DAY 5 Planned Necropsy	FLC No findings
			LLC No findings
			MACRO No findings
	5 M	DAY 5 Planned Necropsy	FLC No findings
			LLC No findings
			MACRO No findings
	6 M	DAY 5 Planned Necropsy	FLC No findings
			LLC No findings
			MACRO Small
	7 F	DAY 5 Planned Necropsy	FLC No findings
			LLC No findings
			MACRO No findings
	8 F	DAY 5 Planned Necropsy	FLC No findings
			LLC No findings
			MACRO No findings
	9 F	DAY 5 Planned Necropsy	FLC No findings
			DAY 4 Small
			LLC No findings
			MACRO Small
	10 F	DAY 5 Planned Necropsy	FLC No findings
			LLC No findings
			MACRO No findings
	11 F	DAY 5 Planned Necropsy	FLC No findings
			LLC No findings
			MACRO No findings
	12 F	DAY 5 Planned Necropsy	FLC No findings
			LLC No findings
			MACRO No findings
	13 F	DAY 5 Planned Necropsy	FLC No findings
			LLC No findings
			MACRO No findings
	14 F	DAY 5 Planned Necropsy	FLC No findings
			LLC No findings
			MACRO No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS	
GROUP 3 (150 MG/KG)						
	15	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	16	F	DAY 5	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	Small
GROUP 4 (1000 MG/KG)						
LITTER 74 27AUG03	1	M	DAY 5	Planned Necropsy	FLC	No findings
					DAY 4	Small
					LLC	No findings
					MACRO	Small
	2	M	DAY 5	Planned Necropsy	FLC	No findings
					DAY 4	Small
					LLC	No findings
					MACRO	Small
	3	M	DAY 4	Missing	FLC	Pale, cold, small
	4	M	DAY 5	Planned Necropsy	FLC	No findings
					DAY 4	Small
					LLC	No findings
					MACRO	Small
	5	M	DAY 4	Missing	FLC	No findings
	6	M	DAY 5	Planned Necropsy	FLC	No findings
					DAY 4	Small
					LLC	No findings
					MACRO	Small
	7	M	DAY 4	Missing	FLC	No findings
	8	M	DAY 4	Missing	FLC	No findings
	9	M	DAY 5	Planned Necropsy	FLC	No findings
					DAY 4	Small
					LLC	No findings
					MACRO	Small
	10	F	DAY 4	Missing	FLC	No findings
	11	F	DAY 5	Missing	FLC	No findings
					DAY 4	Small
	12	F	DAY 4	Missing	FLC	Small
	13	F	DAY 4	Missing	FLC	No findings
	14	F	DAY 4	Missing	FLC	Small
	15	F	DAY 5	Planned Necropsy	FLC	No findings
					DAY 4	Small
					LLC	No findings
					MACRO	Small
	16	F	DAY 4	Missing	FLC	No findings
LITTER 75 29AUG03	1	M	DAY 7	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	2	F	DAY 7	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	3	F	DAY 7	Planned Necropsy	FLC	No findings
					DAY 2	Pale
					LLC	No findings
					MACRO	No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION

LITTER DELIVERY	PUP		END OF P.P. PHASE		FINDINGS	
GROUP 4 (1000 MG/KG)						
	4	F	DAY 7	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	Small
	5	F	DAY 7	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
	6	F	DAY 7	Planned Necropsy	FLC	No findings
					LLC	No findings
					MACRO	No findings
LITTER 80 31AUG03	1	M	DAY 4	Spontaneous death	FLC	Small, little milk
					DAY 2	Small
					DAY 3	Small
					LLC	No findings
					MACRO	No findings
	2	M	DAY 2	Missing	FLC	Small, little milk
	3	F	DAY 2	Missing	FLC	Small, little milk

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

REMARKS AND KEY TO MISSING VALUES CLINICAL LABORATORY INVESTIGATIONS

HAEMATOLOGY

18-Aug-2003:
Animal 12, 23 --- = citrate sample clotted
Animal 31 --- = PLT not reproducible

01-Sep-2003:
Animal 59 --- = EDTA sample clotted

CLINICAL BIOCHEMISTRY
No remarks

Appendix 3

FORMULATION ANALYSIS

NOTOX Project 385717
NOTOX Substance 113769/B

REPORT APPROVAL

PRINCIPAL SCIENTIST: Ir. M.J.C. Brekelmans
(Analytical Chemistry)

Date: January 08, 2004

PREFACE

Study plan (analytical study)	Start: 21 July 2003 Completed: 12 August 2003

PURPOSE

The purpose of the analytical study was to check accuracy of preparation (all concentrations) and to determine stability and homogeneity (lowest and highest concentrations) of T-7601 in propylene glycol and to validate the analytical method used.

NOMINAL AND PREPARED CONCENTRATIONS

Nominal test substance concentration in the formulation (target):

GROUP 1	0 mg/ml =	0 mg/g
GROUP 2	10 mg/ml =	9.62 mg/g
GROUP 3	30 mg/ml =	28.6 mg/g
GROUP 4	200 mg/ml =	180 mg/g

INTERNAL STANDARD

Identification number	AS516
Name	Perfluorobutane sulfonate (L-7038)
Description	White crystalline powder
Molecular formula	$C_4F_9SO_3^-K^+$
CAS number	29420-49-3
Batch number	Lot 2
Article number	-
Purity	97.3%
Expiry Date	17 January 2007
Supplier	3M Environmental Laboratory

The sponsor is responsible for all test substance data unless determined by NOTOX.

REAGENTS

Milli-Q water	Tap water purified by reversed osmosis and subsequently passed over activated carbon and ion-exchange cartridges: Millipore, Bedford, MA, USA
Methanol	HPLC-grade, Labscan, Dublin, Ireland
Ammoniumacetate	Fractopur®, Merck, Darmstadt, Germany
2.0 mM Ammoniumacetate	154 mg Ammoniumacetate in 1000 ml Milli-Q water
Propylene glycol	99.5%, Merck, Darmstadt, Germany

SAMPLING PROCEDURE

Accuracy of dose preparation	Formulations prepared on 22-07-03 (week 1) and on 12-08-03 (week 4) were analysed for test substance concentration.
Homogeneity of formulations	The formulations of Groups 2 and 4 prepared on 22-07-03 (week 1) and on 12-08-03 (week 4) were tested for homogeneity.
Stability of formulations	The formulations of Groups 2 and 4 prepared on 22-07-03 (week 1) were analysed immediately after preparation and after 4 hours of storage at ambient temperature.

The formulations were stirred during sampling. Duplicate samples for the determination of the accuracy and stability were taken at 50% height of the formulation. For the determination of the homogeneity, duplicate samples were taken at 90% height, at 50% height and at 10% height of the formulation.

SAMPLE PRETREATMENT

Samples (approximately 500 mg) were taken from the formulations and weighed accurately into volumetric flasks (20 ml). The flasks were filled up to the mark with methanol. The solutions were further diluted with 50/50 (v/v) methanol/Milli-Q water to obtain concentrations within the calibration range. Internal standard was added to a final concentration of 1.17 mg/l. The propylene glycol concentration in the diluted samples was 0.25 ml/l. If necessary, propylene glycol was added to achieve this concentration.

ANALYTICAL METHOD

Quantitative analyses of T-7601 was based on High Performance Liquid Chromatography with Mass Spectrometric detection (LC-MSMS).

Analytical conditions

Column

Stationary phase	Betasil C18
Dimensions	50 x 2.1 mm; dp = 5 µm
Brand	Thermo Hypersil, Keystone (Cheshire, UK)

Mobile phase

Time (minutes)	2.0 mM Ammoniumacetate (%)	Methanol (%)
0	60	40
2.9	5	95
3.9	5	95
4.4	60	40
6.4	60	40

Flow	300 µl/min
Injection volume	10 µl
Detection	Mass Spectrometric detection using a LCQ Duo mass spectrometer (Thermo Finnigan, San Jose, CA, USA)

T-7601,

Ionisation source	ESI-, Position 3
Acquisition	MS/MS monitoring the reaction: 312 → 100-350 amu
Isolation width	1.5 amu
Normalized collision energy	30 %
Quantitation on mass	188 and 219 amu

Internal standard:

Ionisation source	ESI-, Position 3
Acquisition	MS monitoring: 95 - 350 amu
Quantitation on mass	299 amu

Standard and calibration solutions

Standard solutions of T-7601 were prepared in methanol.

On each day of analysis, calibration solutions in 50/50 (v/v) methanol/Milli-Q water containing 0.25 ml propylene glycol/l were made up from two standard solutions. Internal standard (Perfluorobutane sulfonate) was added to a final concentration of 1.17 mg/l.

VALIDATION OF THE ANALYTICAL METHOD

The high performance liquid chromatographic (HPLC) method was validated for:

Specificity

Blank propylene glycol was pretreated as specified in 'sample pretreatment procedure'. Subsequently the pretreated propylene glycol was injected in triplicate into the HPLC system. The resulting chromatograms were critically evaluated for interfering peaks by comparison with chromatograms of a test substance solution in propylene glycol. Interfering peaks were required to be ≤ 30% of the LOQ.

Linearity

From two standard solutions (1096 and 1116 mg/l), six dilutions were prepared in 50/50 (v/v) methanol/Milli-Q water containing 2.5 ml propylene glycol/l. This resulted in a concentration range of 0.997 – 9.99 mg/l. Each of these solutions was injected in triplicate. Responses were plotted against the concentrations. A linear regression program was used to calculate the regression line from the responses and concentrations. The correlation coefficient was required to be at least 0.99.

Accuracy

Blank propylene glycol (0.5 ml in a 20 ml volumetric flask) was spiked with the test substance at two concentration levels (10 mg/g and 180 mg/g). At each concentration level, six samples were prepared. These samples were treated as described in 'sample pretreatment procedure' and analysed in triplicate. The recovery was calculated for each sample. The mean recovery (n=6) at each concentration level was required to be in the range 70-110%.

Precision -- repeatability

Using the spiked samples prepared for the accuracy test, the coefficient of variation was calculated at all three levels (n=6). The coefficient of variation at all concentration levels was required to be ≤ 20%.

Limit of quantitation (LOQ)

The LOQ was determined as the lowest concentration at which the mean recovery was in the range 70-110% and the coefficient of variation of the recovery was ≤ 20%.

Limit of detection (LOD)

A 0.150 mg/l solution of the test substance in 50/50 (v/v) methanol/Milli-Q water containing 2.5 ml propylene glycol/l was injected in triplicate. In each chromatogram, the test substance peak height (intensity) was measured as well as the noise level of the system (intensity). The LOD was calculated from the mean peak height and the mean noise level.

Stability of the chromatographic system and end solutions

Solutions of the test substance at concentrations of 0.997 mg/l and 9.99 mg/l in 50/50 (v/v) methanol/Milli-Q water containing 0.25 ml propylene glycol/l were injected three times (in triplicate) in a 22-hour time interval, respectively. During this period, the solutions were kept in the autosampler (at room temperature). The maximum deviation of the response (n=9) was calculated for each concentration was required to be ≤20%.

DATA HANDLING –VALIDATION OF THE ANALYTICAL METHOD

Response:

$$R = \frac{\text{Peak area test substance}}{\text{Peak area internal standard}}$$

Mean:

$$\bar{x} = \frac{1}{n}\sum_{i=1}^{n} x_i$$

where:
x_i : measured value
n : number of measurements

Standard deviation:

$$s_{n-1} = \sqrt{\frac{\sum_{i=1}^{n}(x_i - \bar{x})^2}{(n-1)}}$$

Coefficient of variation: (standard deviation / mean value) * 100%

Maximum deviation: [(highest - lowest)/mean] * 100%

where 'mean' is the mean value of the highest and the lowest value.

Linearity

A linear regression program was used to calculate the regression line from the responses and concentrations. Linear regression analysis was performed using the least squares method. A weighting factor ($1/\text{concentration}^2$) was used.

Regression line: $Y = a X + b$

where:
Y : response
X : concentration [mg/l]
a : slope [l/mg]
b : intercept

Recovery :

$$\frac{\text{Concentration analysed}}{\text{Concentration prepared}} * 100\ [\%]$$

Limit of quantification (LOQ): The lowest concentration of T-7601 tested at which an acceptable recovery and coefficient of variation is obtained[1].

Limit of detection (LOD): The limit of detection is defined as the concentration of T-7601 at which its signal (peak height) is three times the noise level (S/N=3).

[1] LOQ criteria see 'Validation of the analytical method'

Limit of detection= ((3 * noise level)/ signal) * conc.

where:
noise level (N) : height of the noise [intensity]
signal (S) : height of the test substance peak [intensity]
conc. : concentration of test substance [mg/l]

DATA HANDLING – SAMPLE ANALYSIS

Response:

$$R = \frac{\text{Peak area test substance}}{\text{Peak area internal standard}}$$

Calibration curve:

The response was correlated with the concentration test substance, using linear regression analysis (least squares method; no weighting factor).

$$R = a * C + b$$

R = response calibration solution
C = concentration of test substance in calibration solution [mg/l]
a = slope [l/mg]
b = intercept

On each day of analysis, two calibration solutions were used for quantification. One calibration solution was injected (in triplicate) before and one calibration solution was injected (in triplicate) after maximum four samples. Using the six responses, a calibration curve was constructed.

Concentration T-7601 analysed in the samples:

$$C = \frac{(R - b) * V * d}{a * w} \quad [mg/g]$$

R = response sample
V = volume volumetric flask [ml]
d = dilution factor
a = slope [l/mg]
b = intercept
w = weight sample [mg]

Accuracy:

$$\frac{\text{Concentration analysed}}{\text{Concentration prepared}} * 100\ [\%]$$

Relative Difference (Relative Diff.):

$$\frac{\text{Mean response } t = 4 - \text{Mean response } t = 0}{\text{Mean response } t = 0} * 100\ [\%]$$

t = time of sampling [hours]

RESULTS –VALIDATION OF THE ANALYTICAL METHOD

The calculations for the validation tests were performed using not-rounded concentrations and responses. Therefore, some differences might be observed when calculating the statistical parameters using the values as mentioned in the tables.

Specificity

Figures 1 and 2 show HPLC chromatograms of a pretreated blank propylene glycol solution (50/50 (v/v) methanol/Milli-Q water containing 0.25 ml propylene glycol/l) and of a pretreated 9.60 mg/g accuracy sample, respectively.

Comparison of these chromatograms indicated that no peak was present at the position of the test substance.

Linearity

The results are summarized in Table 1. The regression line is shown in Figure 4.

Table 1 Linearity

T-7601 Concentration [mg/l]	Response [1]
0.997 [2]	0.182 0.164 0.178
2.00	0.335 0.337 0.333
4.00	0.546 0.529 0.531
6.03	0.709 0.722 0.714
8.00	0.981 0.947 0.949
9.99	1.139 1.115 1.107
Slope Intercept with Y-axis Weighting factor R	0.0993 0.136 1/concentration^2 0.9988

[1] Triplicate measurements
[2] This concentration was not used for calculation of the regression line because the points deviated by more than 50% from the line.

From these results, it was concluded that there is a linear relationship between response and concentration in the concentration range of 2.00 mg/l – 9.99 mg/l using a (1/concentration^2) weighting factor. Unweighted regression and regression using a weighting factor (1/concentration) resulted in a deviation of more than 10% from the calculated line at

concentrations below 2.00 mg/l.

Accuracy and Precision

Propylene glycol samples spiked with T-7601 and pretreated as described in 'sample pretreatment' were analysed. HPLC chromatograms of pretreated samples are shown in Figure 2 and Figure 3. The results are summarised in Table 2.

Table 2 Accuracy and Precision.

Concentration prepared [mg/g]	Concentration analysed [mg/g]	Recovery [1] [%]	Mean Recovery [%]	Coefficient of variation [%]
9.86	10.1	102	100	2.5
9.60	9.42	98		
9.79	9.83	100		
10.0	10.0	100		
9.67	10.1	105		
9.65	9.46	98		
176	193	110	105	4.0
174	189	109		
191	190	99		
180	192	106		
182	194	106		
175	178	101		

[1] Triplicate measurements.

Mean recoveries were between 70% and 110% and the coefficient of variation was below 20% at both concentration levels. Therefore, the analytical method was considered applicable to samples in propylene glycol in the concentration range 10 mg/g – 180 mg/g.

Limit of quantification (LOQ)

At the lowest concentration tested during the accuracy test (i.e. 10 mg/g), the mean recovery was 100% and the coefficient of variation was 2.5% (see Table 2). The LOQ for the samples in propylene glycol is therefore reported as 10 mg/g.

Limit of detection (LOD)

From three chromatograms of a 0.150 mg/l solution of the test substance in 50/50 (v/v) methanol/Milli-Q water containing 2.5 ml propylene glycol/l, the mean noise level (N) was determined to be $15.7 \cdot 10^3$ units (intensity). The test substance signal (S), i.e. the mean height of the test substance peak, was determined to be $117 \cdot 10^3$ units (intensity). Using these values, the limit of detection (S/N=3) was calculated to be 0.06 mg/l at an injection volume of 10 µl. Taking the minimum dilution factor of the formulations (i.e. 4000) into account, the limit of detection for the formulations was 0.24 mg/g.

Stability of the chromatographic system and end solutions

Table 3 Stability of the 0.997 mg/l solution

Elapsed time [hours]	Response
0.0	0.2180
0.1	0.2148
0.2	0.2081
19.3	0.1823
19.4	0.1643
19.5	0.1776
21.8	0.1677
21.9	0.1656
22.0	0.1746
Maximum deviation [%]	28.1

Table 4 Stability of the 9.99 mg/l solution.

Elapsed time [hours]	Response
0.0	1.353
0.1	1.295
0.2	1.431
20.7	1.139
20.8	1.115
20.9	1.107
21.8	1.159
21.9	1.100
22.0	1.129
Maximum deviation [%]	26.2

The results show that responses of solutions kept in the autosampler at room temperature at T-7601 concentrations of 0.997 mg/l and 9.99 mg/l in 50/50 (v/v) methanol/Milli-Q water containing 0.25 ml propylene glycol/l show maximum deviations >20%, which is relatively high. In order to correct as much as possible for LCMSMS sensitivity changes in time, it was decided to inject calibration solutions before and after maximum four samples.

RESULTS - SAMPLE ANALYSIS

The results of the sample analysis of the different tests are summarized in Table 5 - Table 7. All calculations were performed using actual concentrations. In the tables however, values were rounded off. Analysed concentrations were given for duplicate samples. The mean of triplicate analysis was given for each sample. The maximum deviation between the responses (n=3) was <15% for each sample.

HPLC chromatograms of pretreated samples from week 1 at target concentrations of 0 mg/g, 9.62 mg/g, 28.6 mg/g and 180 mg/g are shown in Figure 5 - Figure 8.

Table 5 Accuracy of dose preparation and homogeneity test in week 1

Group	Date of analysis	Sample position	Concentration [mg/g]		Accuracy	Homogeneity (RSD)
			Target	Analysed	[%]	[%]
1	22-07-03		0	n.d. n.d.	n.a. n.a.	
2	22-07-03	90% height	9.62	9.11 8.22	95 85	5.4
		50% height	9.62	8.54 8.36	89 87	
		10% height	9.62	8.98 9.44	93 98	
3	22-07-03	50% height	28.6	28.9 28.4	101 99	
4	22-07-03	90% height	180	193 177	107 98	4.6
		50% height	180	190 200	106 111	
		10% height	180	184 179	102 99	

n.d. Not detected. Analysis showed the absence of test substance in the formulation.

n.a. Not applicable.

Table 6 Test for stability of formulations in week 1

Group	Date of analysis [dd-mm-yy]	Concentration analysed [mg/g]		Relative Diff. [%]
		t=0 hours	t=4 hours	
2	22-07-03	8.45	9.28	10
4	22-07-03	195	189	-3

Table 7 Accuracy of dose preparation and homogeneity test in week 4

Group	Date of analysis	Sample position	Concentration [mg/g]		Accuracy	Homogeneity (RSD)
			Target	Analysed	[%]	[%]
1	12-08-03		0	n.d. n.d.	n.a. n.a.	
2	12-08-03	90% height	9.62	9.83 9.31	102 97	2.7
		50% height	9.62	9.20 9.43	96 98	
		10% height	9.62	9.27 9.14	96 95	
3	12-08-03	50% height	28.6	28.2 28.0	98 98	
4	12-08-03	90% height	180	179 161	99 89	6.3
		50% height	180	179 160	99 89	
		10% height	180	154 171	86 95	

n.d. Not detected. Analysis showed the absence of test substance in the formulation.

n.a. Not applicable.

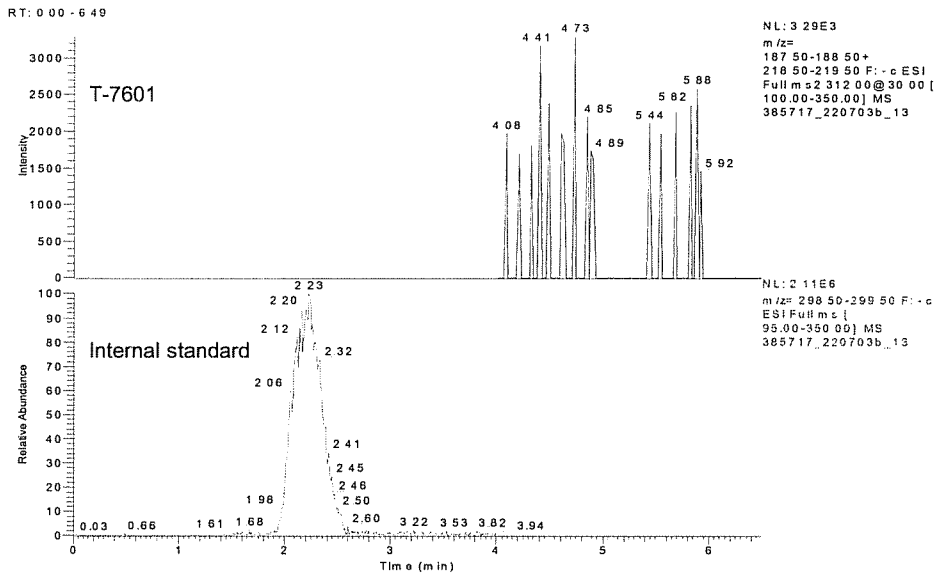

Figure 1 HPLC chromatogram of a pretreated blank propylene glycol sample [res.id. 385717_220703b_13].

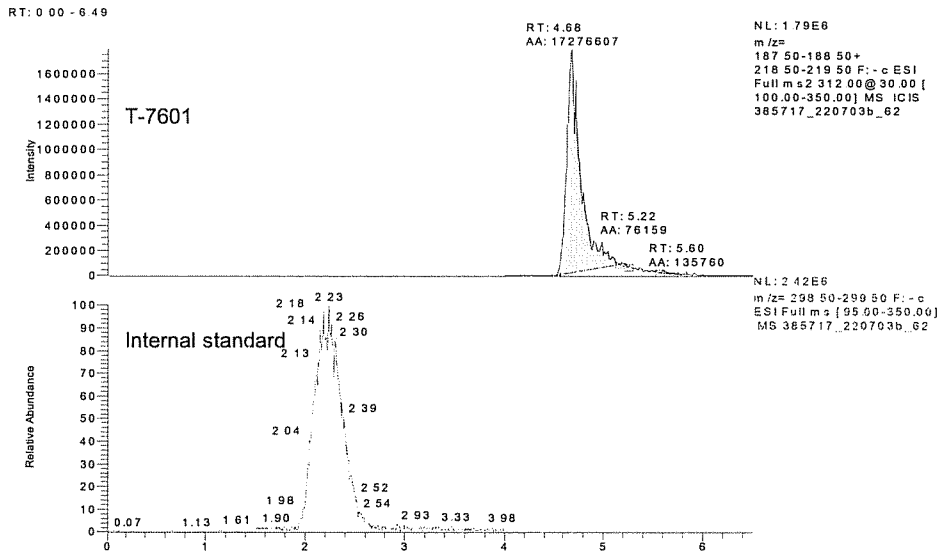

Figure 2 HPLC chromatogram of a pretreated 9.60 mg/g accuracy sample [res.id. 385717_220703b_62].

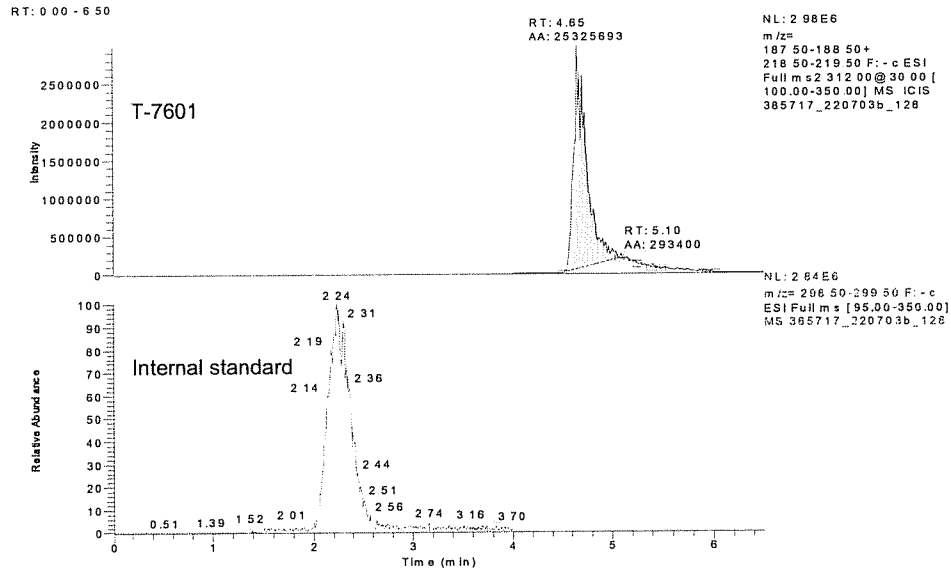

Figure 3 HPLC chromatogram of a pretreated 180 mg/g accuracy sample [res.id. 385717_220703b_128].

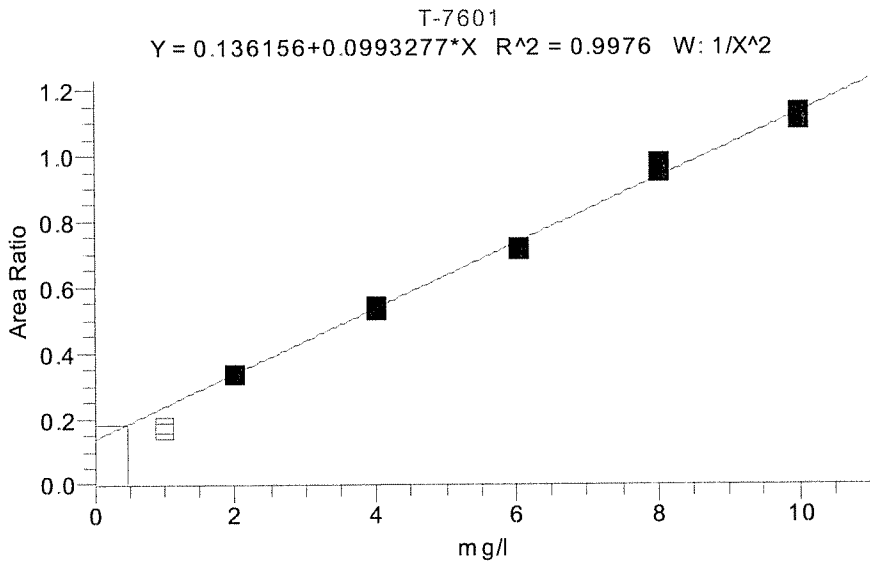

Figure 4 Regression line: Response of T-7601 against concentration.

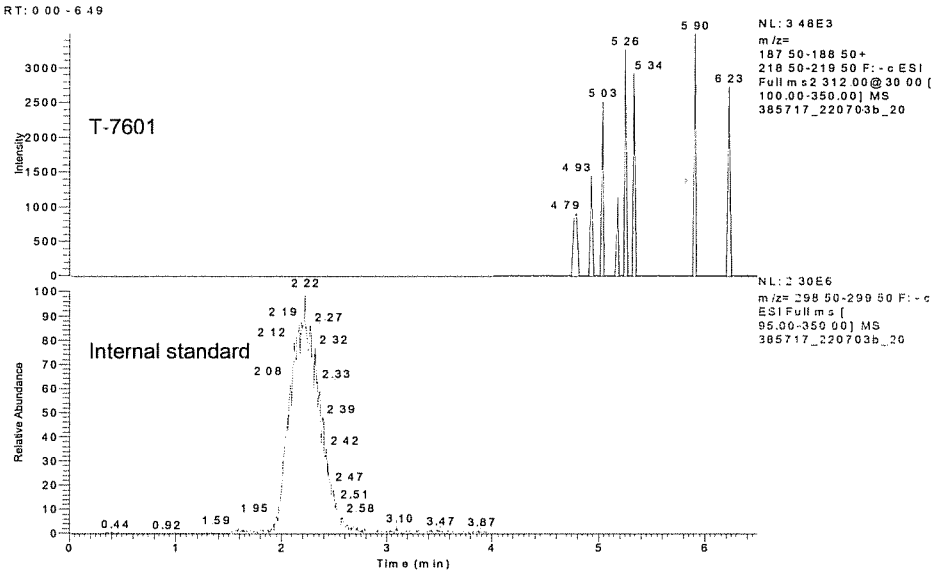

Figure 5 HPLC chromatogram of a pretreated 0 mg/g test sample taken in week 1 (dilution factor 4000) [res.id. 385717_220703b_20].

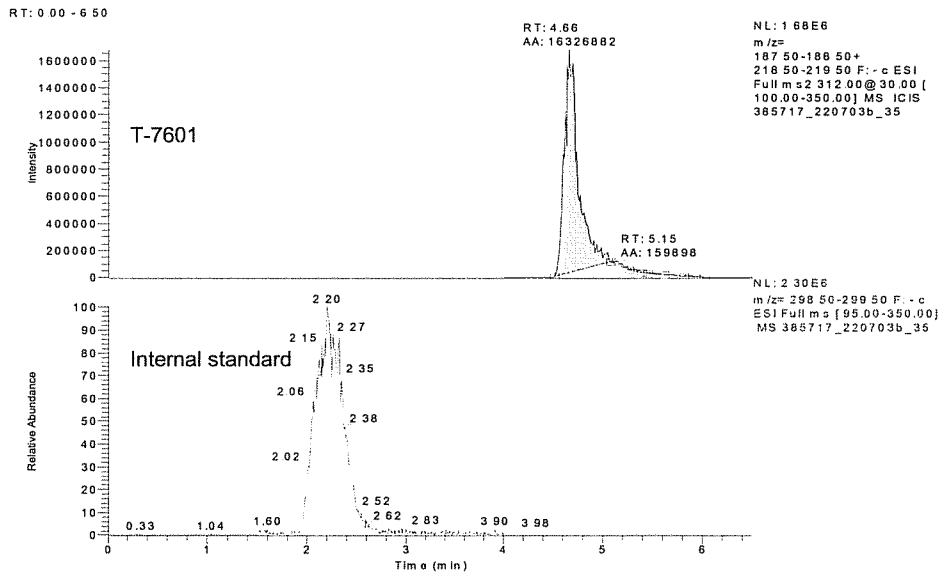

Figure 6 HPLC chromatogram of a pretreated 9.62 mg/g test sample taken in week 1 (dilution factor 4000) [res.id. 385717_220703b_35].

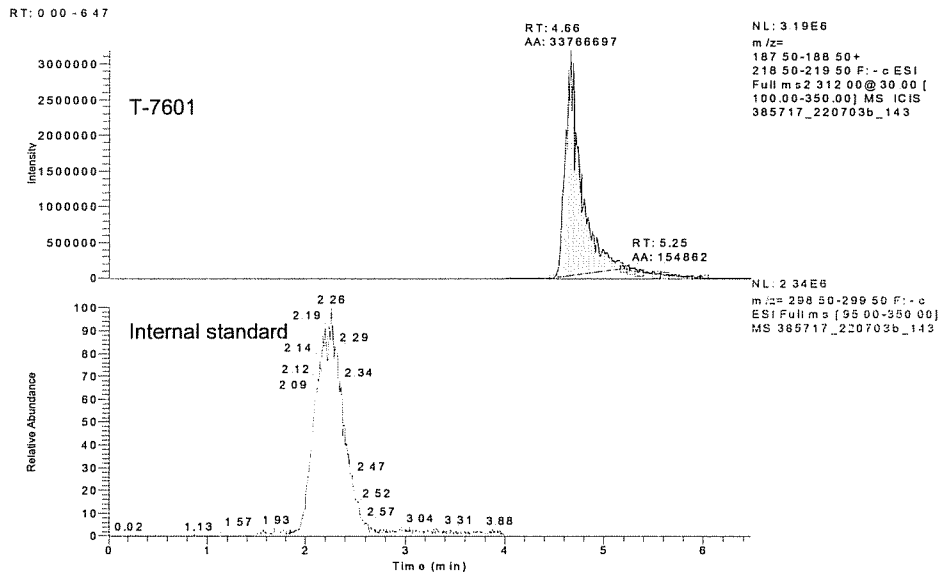

Figure 7 HPLC chromatogram of a pretreated 28.6 mg/g test sample taken in week 1 (dilution factor 4000) [res.id. 385717_220703b_143].

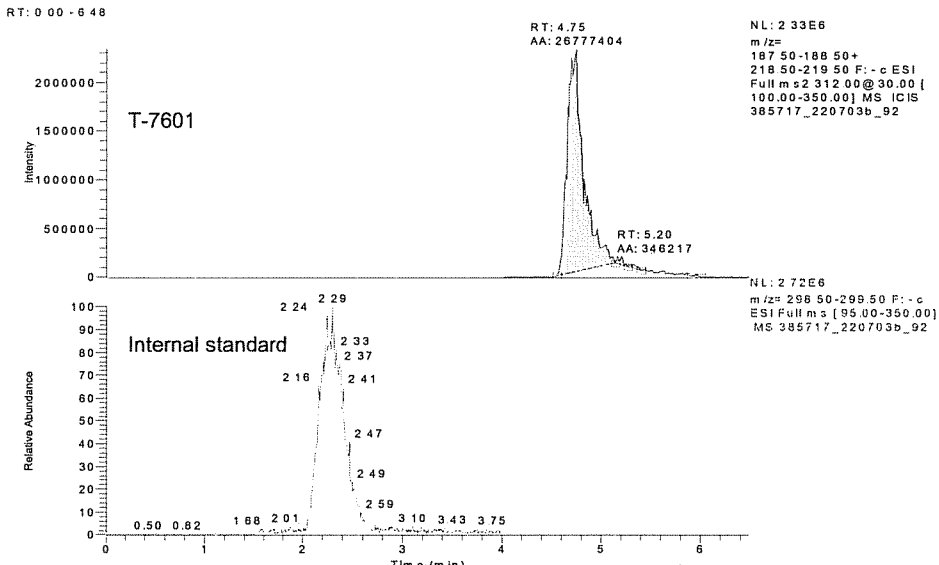

Figure 8 HPLC chromatogram of a pretreated 180 mg/g test sample taken in week 1 (dilution factor 40000) [res.id. 385717_220703b_92].

APPENDIX 4

PATHOLOGY REPORT		**NOTOX Project 385717**	
TEST ITEM	: T-7601	PATHOL. NO	: RHA03019
TEST SYSTEM	: Rat, 28-day + repro, gavage	DATE	: 04-FEBRUARY-2004
SPONSOR	: 3M Corporate Toxicology		

Title: COMBINED REPEATED DOSE TOXICITY STUDY WITH REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST WITH T-7601 ADMINISTERED BY ORAL GAVAGE IN WISTAR RATS

Prepared by: R.H. Alison, BVSc, MRCVS, DiplECVP
Toxicologic Pathologist

Test site: Roger Alison
Baurgorm, Bantry, Co. Cork, Ireland

TEST ITEM : T-7601
TEST SYSTEM : Rat, 28-day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATH. NO. : RHA03019
DATE : 04-FEB-04

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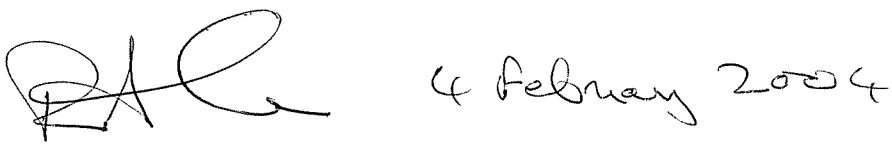
TEST ITEM	: T-7601	PATH. NO.	: RHA03019
TEST SYSTEM	: Rat, 28-day + repro, gavage	DATE	: 04-FEB-04
SPONSOR	: 3M Corporate Toxicology		

AUTHENTICATION

The undersigned hereby declares:

1) That the histopathology data in this report were compiled by him, and that they reflect accurately the primary data records;

2) That all practices and procedures associated with the histopathological evaluation presented in this report comply with the requirements of the OECD Principles of Good Laboratory Practice (ENV/MC/CHEM (98)17, Paris, 1998).



R.H. ALISON, BVSc, MRCVS, DiplECVP

Principal Investigator

Test Site:

Roger Alison
(Consultant for Pre-Clinical Safety Consultants Ltd.)
Baurgorm, Bantry, Co. Cork, IRELAND

TEST ITEM	: T-7601	PATH. NO.	: RHA03019
TEST SYSTEM	: Rat, 28-day + repro, gavage	DATE	: 04-FEB-04
SPONSOR	: 3M Corporate Toxicology		

QUALITY ASSURANCE STATEMENT

The operations of Roger Alison are audited at approximately 6-monthly intervals by the undersigned in compliance with the OECD Principles of Good Laboratory Practice, 1997 Revision (ENV/MC/CHEM (98)17, Paris, 1998), and the Irish National Accreditation Board GLP Compliance Monitoring Programme Publication, Edition 4, March 2000.

Findings are reported both to the Principal Investigator (study pathologist), the Test Facility, and to PCS Consultants management. The Principal Investigator's most recent facility QA audit was 24 March 2003.

This report has been audited in compliance with the above regulations and is considered to be an accurate presentation of the histopathological procedures involved and of the study findings.

Date of audit: 19 November 2003

Date of reporting findings: 19 November 2003

DAVID FORD BSc, PhD, FRQA. 5 February 2004

Quality Assurance Consultant

Goodwin House
Bank Street, Pulham Market
Diss, Norfolk IP21 4TG
UNITED KINGDOM

TEST ITEM	: T-7601	PATH. NO.	: RHA03019
TEST SYSTEM	: Rat, 28-day + repro, gavage	DATE	: 04-FEB-04
SPONSOR	: 3M Corporate Toxicology		

SUMMARY

Groups of 10 male and 10 female Wistar rats received 0, 50, 150, or 1000 mg/kg body weight/day of T-7601 by gavage. Males were exposed from 2 weeks prior to mating for at least 28 days. Females were exposed from 2 weeks prior to mating until termination about 4 days after parturition (for at least 28 days).

The following organs were examined histopathologically:
all organs from five control and high dose animals of each sex and from all decedents;
testes and epididymides from all males;
reproductive organs from non-pregnant animals and those suspected of infertility;
liver, spleen, brain, spinal cord, thymus, stomach, adrenals were examined from all available animals.

Mortality
There were 6 unscheduled deaths, one mid dose female and five high dose animals.

A possible relationship to treatment could not entirely be excluded for four high dose animals: males 34 and 38 (cause of death not evident) and females 77 and 78 (cause of death meningitis).

Necropsy findings

Treatment-related nodules were present in the epididymides of 4/10 high dose males (correlating with microscopic findings of sperm granuloma).

Histopathological findings

Primary treatment-related treatment-related findings were confined to the liver, spleen and epididymides of high dose animals:

Liver: minimal/slight hepatocyte hypertrophy in males and females,

Spleen: increased severity of hematopoiesis in males,
increased severity of hemosiderosis in females.

Epididymides: slight/moderate sperm granuloma in males.

Other findings in the testes (tubular atrophy, dilation, giant cells) and epididymides (reduced spermatozoa, cellular debris) of high dose animals were secondary to the blockage caused by the sperm granulomas. An unilateral sperm granuloma in a single low dose animal was considered an incidental finding.

TEST ITEM	: T-7601	PATH. NO.	: RHA03019
TEST SYSTEM	: Rat, 28-day + repro, gavage	DATE	: 04-FEB-04
SPONSOR	: 3M Corporate Toxicology		

Meningitis was present in the brain and spinal cord of two high dose females. A possible relationship to treatment could not be totally excluded, however these findings were considered most likely to be incidental.

Minimal centrilobular degeneration in the liver (two high dose decedent males), slight adrenal cortical vacuolation in the adrenals (two high dose males), minimal/slight atrophy in the thymus (one high dose male and one high dose female),and minimal/slight acanthosis and hyperkeratosis in the stomach (one high dose male and one high dose female) were considered to be due to inanition or stress, rather than direct effects of the compound.

Staging of spermatogenesis:
The assessment of the integrity of the spermatogenetic cycle did not provide any evidence of impaired spermatogenesis.

Conclusion

On the basis of this histopathological examination, the No Observed Adverse Effect Level (NOAEL) was 150 mg/kg/day.

TEST ITEM	: T-7601	PATH. NO.	: RHA03019
TEST SYSTEM	: Rat, 28-day + repro, gavage	DATE	: 04-FEB-04
SPONSOR	: 3M Corporate Toxicology		

MATERIALS AND METHODS

Introduction

The in-life and necropsy phases of this study, and the slide preparation were performed by NOTOX B.V., Hambakenwetering 7, 5231 DD, 's-Hertogenbosch, The Netherlands.

The histopathological examination was carried out by Roger H. Alison, Preclinical Safety Consultants Ltd. (PCS), Baurgorm, Bantry, Co. Cork, Ireland during October - November 2003.

Group Allocation

Group:	1	2	3	4
Dose (mg/kg/day):	0	50	150	1000
Males :	1 – 10	11 - 20	21 – 30	31 – 40
Females:	41 – 50	51 – 60	61 – 70	71 - 80

The animals received the test item once daily by gavage for at least 28 consecutive days. Controls received the vehicle, propylene glycol.

Necropsy

At the end of the assigned study period, the rats were killed by exsanguination under isofluorane anaesthesia. Complete necropsies were performed on all rats. All macroscopic abnormalities observed were recorded.

The weights of the following organs were recorded from 5 animals/sex/group surviving to the scheduled necropsies:

adrenal glands
brain
heart
kidneys
liver
spleen
thymus

The weight of testes and epididymides was recorded for all males at the terminal sacrifice.

The data were analysed statistically and a copy was provided to the pathologist.

TEST ITEM	: T-7601	PATH. NO.	: RHA03019
TEST SYSTEM	: Rat, 28-day + repro, gavage	DATE	: 04-FEB-04
SPONSOR	: 3M Corporate Toxicology		

Tissue sampling

Representative samples of the following tissues and organs were collected and, unless otherwise indicated, fixed in neutral phosphate buffered 4% formaldehyde solution:

1) from five surviving animals/sex/group (selected by the study director) and from all decedent animals at necropsy:

adrenal glands
aorta
brain
cecum
cervix
clitoral gland
colon
coagulating gland
duodenum
epididymides (fixed in Bouin's)
esophagus
eyes, optic nerves and Harderian glands
female mammary gland area
femur (including joint)
heart
ileum
jejunum
kidneys
lacrimal gland (exorbital)
larynx
liver
lungs
macroscopic abnormalities
mandibular lymph node
mesenteric lymph node
nasopharynx
ovaries
pancreas
Peyer's patches (if detectable)
pituitary gland
preputial gland
prostate gland
rectum
salivary glands (mandibular, sublingual)
sciatic nerve
seminal vesicles
skeletal muscle
skin
spinal cord
spleen
sternum with bone marrow
stomach
testes (fixed in Bouin's)
thymus
thyroid (including parathyroids)
tongue
trachea
urinary bladder
uterus
vagina

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2) From all animals:

cervix
clitoral gland
coagulating gland
epididymides (fixed in Bouin's)
macroscopic abnormalities
ovaries
prostate gland
seminal vesicles
testes (fixed in Bouin's)
uterus
vagina

Tissues examined by the pathologist (listed in **bold** type above) were prepared as 2-4 micron paraffin embedded, hematoxylin and eosin (HE) stained sections.

Additional sections of testis from the selected 5 males from the control and high dose group were were prepared for staging of spermatogenesis. These were sectioned at 3-4 microns and stained with PAS/hematoxylin.

The following tissues were examined:

5 control and high dose animals of each sex:	All organs in **bold type** above (list 1), Testes for staging of spermatogenesis
All available animals	Target organs and potential target organs: Liver, spleen, brain, spinal cord, thymus, stomach, adrenals.
All decedents	All organs in **bold type** above.
All non pregnant females and animals suspected of infertility	Reproductive organs
All animals	All macroscopic abnormalities, testes, epididymides,

Data Compilation

The animal data and macroscopic findings were transferred from the toxicological data management system by an intersystem transfer into the NOTOX PATHDATA system. Necropsy findings were then transferred (also by inter-system transfer) onto the PCS PATHDATA system by the study pathologist. The microscopic findings were recorded by the study pathologist using on-line input into the PCS PATHDATA computer system under pathology number RHA03019.

The main Notox study number was 385717, however necropsy findings for parental animals were collected under project number 385739.

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All macroscopic and microscopic findings are given for each animal in text form under "Text of Gross and Microscopic Findings". The incidence of microscopic findings is also presented in tabular form under "Table of Individual Microscopic Findings". Incidence tables are created by computer.

Histopathological changes were described whenever possible, according to distribution, severity and morphological character.

Severity scores were assigned as follows:
Grade "1": Minimal/very few/very small.
Grade "2": Slight/few/small.
Grade "3": Moderate/moderate number/moderate size.
Grade "4": Marked/many/large.
Grade "5": Massive/extensive number/extensive size.
Grade "P": Finding present, grading not scored.

In the case of non-neoplastic lesions in bilaterally affected paired organs, the severity score of the worst affected organ was recorded.

Staging of spermatogenesis: the presence of selected stages of spermatogenesis (stages I, VIII, XI, XIV) was recorded during this assessment (Russell LD *et al* (1990): Histological and Histopathological Evaluation of the Testis, Cache River Press, Clearwater, Florida).

Archiving

The histological sections and a copy of the final report have been returned to Notox for archiving.

Other raw data relating to the histopathological evaluation of the study will be archived by the study pathologist, R. H. Alison, at Baurgorm, Bantry, Cork, Ireland for at least ten years.

No data will be discarded after this period without the consent of Notox.

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RESULTS

Mortality

There were 6 unscheduled deaths:

mid dose female:
65: moribund sacrifice, cause of death uterine prolapse;
high dose males:
33: found dead, cause of death gavage error;
34: found dead, cause of death not evident,
38: moribund sacrifice, cause of death not evident,
high dose females:
77: moribund sacrifice, cause of death meningitis,
78: found dead, cause of death meningitis.

The death of animals 65 (mid dose) and 33 (high dose) were considered to be incidental findings.

The deaths of animals 34, 38, 77 and 78 are also likely to be incidental findings, however a possible relationship to treatment cannot entirely be excluded.

Necropsy Findings

Treatment-related nodules were present in the epididymides of 4/10 high dose males (correlating with microscopic findings of sperm granuloma).

There were no other treatment-related necropsy findings.

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Microscopic Findings

Primary treatment-related findings were confined to the liver, spleen and epididymides of high dose animals:

Liver: minimal/slight hepatocyte hypertrophy in males and females,

Spleen: increased severity of hematopoiesis in males,
increased severity of hemosiderosis in females.

Epididymides: slight/moderate sperm granuloma in males.

DOSE GROUP:	01		02		03		04	
SEX :	M	F	M	F	M	F	M	F
NO.ANIMALS:	10	10	10	10	10	10	10	10
LIVER :	6	5	5	5	5	6	8	7
- Hepatocyte hypertrop:	-	-	-	-	-	-	6	6
Grade 1:	-	-	-	-	-	-	5	6
Grade 2:	-	-	-	-	-	-	1	-
SPLEEN :	6	5	5	5	5	6	7	7
- Exmed hematopoiesis :	6	5	5	5	5	6	6	7
Grade 1:	1	1	1	2	2	2	1	3
Grade 2:	5	2	3	3	3	3	-	3
Grade 3:	-	2	1	-	-	1	5	1
- Hemosiderosis :	-	-	-	-	-	2	1	5
Grade 1:	-	-	-	-	-	1	-	1
Grade 2:	-	-	-	-	-	1	1	4
EPIDIDYMIDES :	10	-	10	-	10	-	9	-
- Sperm granuloma :	-	-	1	-	-	-	5	-
Grade 2:	-	-	-	-	-	-	2	-
Grade 3:	-	-	1	-	-	-	3	-

Other findings in the testes (tubular atrophy, dilation, giant cells) and epididymides (reduced spermatozoa, cellular debris) of high dose animals were secondary to the blockage caused by the sperm granulomas. An unilateral sperm granuloma in a single low dose animal was considered an incidental finding.

Meningitis was present in the brain and spinal cord of two high dose females. A possible relationship to treatment could not be totally excluded, however these findings were considered most likely to be incidental.

Minimal centrilobular degeneration in the liver (two high dose decedent males), slight adrenal cortical vacuolation in the adrenals (two high dose males), minimal/slight atrophy in the

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thymus (one high dose male and one high dose female),and minimal/slight acanthosis and hyperkeratosis in the stomach (one high dose male and one high dose female) were considered to be due to inanition or stress, rather than direct effects of the compound.

Staging of spermatogenesis:
The assessment of the integrity of the spermatogenetic cycle did not provide any evidence of impaired spermatogenesis.

Other microscopic findings observed were within the range of background pathology encountered in rats of this strain and age.

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CONCLUSIONS

On the basis of this histopathological examination, the No Observed Adverse Effect Level (NOAEL) was 150 mg/kg/day.

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EXPLANATION OF CODES AND SYMBOLS

CODES AND SYMBOLS USED AT ANIMAL LEVEL:

M	= Male animal
F	= Female animal
K0	= Terminal sacrifice group
+	= Intercurrent death/sacrificed moribund
+1	= Found dead
+2	= Sacrificed moribund

CODES AND SYMBOLS USED AT FINDING LEVEL:

GRADE 1	= Minimal / very few / very small
GRADE 2	= Slight / few / small
GRADE 3	= Moderate / moderate number / moderate size
P	= Finding present, severity not scored

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NUMBER OF ANIMALS WITH NECROPSY FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, INCL. DEATHS
All animals

DOSE GROUP:	01		02		03		04	
SEX:	M	F	M	F	M	F	M	F
ORGAN/FINDING ANIM.EXAM.:	10	10	10	10	10	10	10	10
GENERAL OBSERVATIONS								
- emaciated	-	-	-	-	-	-	1	1
THYMUS								
- dark	1	-	-	-	1	-	2	-
- discolouration	-	1	-	-	-	-	-	1
- focus/foci	1	-	-	-	2	-	2	-
- red	1	1	-	-	1	-	2	-
STOMACH								
- discolouration	-	-	-	-	-	-	1	-
- irregular surface	-	-	-	-	-	-	1	-
- thickened	-	-	-	-	-	-	1	-
LIVER								
- accentuated lobular pattern	-	-	-	1	-	-	1	-
- discolouration, dark red	-	-	1	-	-	-	-	-
- enlarged	-	-	-	-	-	-	1	-
ADRENAL GLANDS								
- focus/foci	-	-	-	1	-	-	-	-
EPIDIDYMIDES								
- nodule(s)	-	-	-	-	-	-	4	-
CECUM								
- discolouration	-	-	-	-	-	-	1	-
CLITORAL GLANDS								
- focus/foci	-	-	-	-	-	1	-	-
DUODENUM								
- discolouration	-	-	-	-	-	-	1	-
KIDNEYS								
- pelvic dilation	-	-	-	-	2	-	2	1
LUNG								
- discolouration, dark red	-	-	-	-	-	-	1	-

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NUMBER OF ANIMALS WITH NECROPSY FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, INCL. DEATHS
All animals

DOSE GROUP:	01		02		03		04	
SEX:	M	F	M	F	M	F	M	F
ORGAN/FINDING ANIM.EXAM.:	10	10	10	10	10	10	10	10
MANDIB.LYMPH NODES :								
- discolouration, dark red :	-	1	-	2	-	2	1	1
MESENT. LYMPH NODE :								
- discolouration, dark red :	-	-	-	-	-	-	-	1
SKIN/SUBCUTIS :								
- areas of alopecia :	-	1	-	-	-	-	-	-
URINARY BLADDER :								
- dark :	-	-	-	-	-	-	1	-
- red :	-	-	-	-	-	-	1	-
UTERUS :								
- contains fluid :	-	-	-	-	-	-	-	2
- cyst(s) :	-	-	-	-	-	-	-	1

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NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, INCL. DEATHS
All animals

SEX :					MALE
DOSE GROUP:	01	02	03	04	
NO.ANIMALS:	10	10	10	10	
GENERAL OBSERVATIONS :	-	-	-	2	
- Autolysis :	-	-	-	2	
Grade 2:	-	-	-	1	
Grade 3:	-	-	-	1	
THYMUS :	7	5	7	8	
- Hemorrhage :	2	-	2	5	
Grade 1:	2	-	1	3	
Grade 2:	-	-	1	1	
Grade 3:	-	-	-	1	
- Atrophy :	-	-	-	1	
Grade 2:	-	-	-	1	
Grade 3:	-	-	-	-	
STOMACH :	6	5	5	7	
- Hyperplasia (LR) :	-	1	-	2	
Grade 1:	-	1	-	2	
- Hyperkeratosis :	-	-	-	1	
Grade 2:	-	-	-	1	
- Acanthosis :	-	-	-	1	
Grade 1:	-	-	-	-	
Grade 2:	-	-	-	1	
- Myositis :	-	1	-	-	
Grade 1:	-	1	-	-	

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NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, INCL. DEATHS
All animals

SEX :					MALE
DOSE GROUP:	01	02	03	04	
NO.ANIMALS:	10	10	10	10	
LIVER :	6	5	5	8	
- Inflamm cell foci :	5	4	4	4	
Grade 1:	5	3	2	4	
Grade 2:	-	1	2	-	
- Hepatocyte hypertrop:	-	-	-	6	
Grade 1:	-	-	-	5	
Grade 2:	-	-	-	1	
- Centrilob degenerat :	-	-	-	2	
Grade 1:	-	-	-	2	
- Congestion :	-	-	-	2	
Grade 2:	-	-	-	2	
- Focal necrosis :	-	-	1	-	
Grade 1:	-	-	1	-	
- Vacuolation (pp) :	-	1	-	-	
Grade 1:	-	1	-	-	
- Exmed hematopoiesis :	-	1	-	-	
Grade 1:	-	1	-	-	
SPLEEN :	6	5	5	7	
- Exmed hematopoiesis :	6	5	5	6	
Grade 1:	1	1	2	1	
Grade 2:	5	3	3	-	
Grade 3:	-	1	-	5	
- Hemosiderosis :	-	-	-	1	
Grade 1:	-	-	-	-	
Grade 2:	-	-	-	1	
ADRENAL GLANDS :	6	5	5	8	
- Cortical vacuolation:	2	2	3	4	
Grade 1:	1	2	3	2	
Grade 2:	1	-	-	2	

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NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, INCL. DEATHS
All animals

SEX :				MALE
DOSE GROUP:	01	02	03	04
NO.ANIMALS:	10	10	10	10
TESTES :	10	10	10	9
- Tubular atrophy :	1	-	-	1
Grade 1:	1	-	-	-
Grade 3:	-	-	-	1
- Tubular dilation :	-	1	-	2
Grade 1:	-	1	-	-
Grade 2:	-	-	-	2
- Giant cells :	-	-	-	1
Grade 1:	-	-	-	1
EPIDIDYMIDES :	10	10	10	9
- Reduced spermatozoa :	-	-	-	1
Grade 3:	-	-	-	1
- Cellular debris :	-	1	-	1
Grade 2:	-	1	-	-
Grade 3:	-	-	-	1
- Sperm granuloma :	-	1	-	5
Grade 2:	-	-	-	2
Grade 3:	-	1	-	3
DUODENUM :	5	-	-	7
- Congestion :	-	-	-	1
Grade 1:	-	-	-	1
ESOPHAGUS :	5	-	-	8
- Myositis :	-	-	-	1
Grade 1:	-	-	-	1
- Hyperkeratosis :	-	-	-	2
Grade 1:	-	-	-	2
Grade 2:	-	-	-	-
HEART :	5	-	-	8
- Myocarditis :	-	-	-	1
Grade 1:	-	-	-	1

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NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: KO, INCL. DEATHS
All animals

SEX :					MALE
DOSE GROUP:	01	02	03	04	
NO.ANIMALS:	10	10	10	10	
KIDNEYS :	5	-	2	9	
- Hydronephrosis :	-	-	2	2	
Grade 1:	-	-	1	1	
Grade 2:	-	-	1	-	
Grade 3:	-	-	-	1	
- Tubular basophilia :	2	-	-	2	
Grade 1:	2	-	-	1	
Grade 3:	-	-	-	1	
LUNG :	5	-	-	8	
- Alveolar macrophages:	1	-	-	1	
Grade 1:	1	-	-	-	
Grade 2:	-	-	-	1	
- Congestion :	-	-	-	2	
Grade 1:	-	-	-	1	
Grade 2:	-	-	-	1	
- Alveolar debris :	-	-	-	1	
Grade 2:	-	-	-	1	
MANDIB.LYMPH NODES :	5	-	-	8	
- Congestion :	-	-	-	2	
Grade 1:	-	-	-	-	
Grade 2:	-	-	-	2	
PEYER'S PATCHES :	5	-	-	6	
- Germinal centres :	5	-	-	6	
PREPUTIAL GLANDS :	5	1	2	9	
- Inflamm cell foci :	1	-	1	1	
Grade 1:	1	-	-	1	
Grade 2:	-	-	1	-	
- Dilated acini :	-	-	-	1	
Grade 2:	-	-	-	1	

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NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, INCL. DEATHS
All animals

SEX :					MALE
DOSE GROUP:	01	02	03	04	
NO.ANIMALS:	10	10	10	10	
PROSTATE GLAND :	5	1	2	9	
- Lymphoid cell foci :	2	1	-	2	
Grade 1:	1	1	-	2	
Grade 2:	1	-	-	-	
SEMINAL VESICLES :	5	1	2	9	
- Reduced contents :	-	-	-	1	
Grade 1:	-	-	-	1	
TESTES (STAGING) :	5	-	-	5	
- Stage I :	5	-	-	4	
- Stage VIII :	5	-	-	4	
- Stage XI :	5	-	-	4	
- Stage XIV :	5	-	-	4	
THYROID GLAND :	5	-	-	8	
- Hyperpl/hypert foll :	1	-	-	-	
Grade 1:	1	-	-	-	
URINARY BLADDER :	5	-	-	8	
- Hemorrhage :	-	-	-	1	
Grade 3:	-	-	-	1	

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NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, INCL. DEATHS
All animals

SEX :				FEMALE
DOSE GROUP:	01	02	03	04
NO.ANIMALS:	10	10	10	10
GENERAL OBSERVATIONS :	-	-	-	1
- Autolysis :	-	-	-	1
Grade 2:	-	-	-	1
Grade 3:	-	-	-	-
THYMUS :	5	5	6	7
- Hemorrhage :	1	-	1	1
Grade 1:	-	-	1	1
Grade 2:	1	-	-	-
Grade 3:	-	-	-	-
- Atrophy :	-	-	-	1
Grade 2:	-	-	-	-
Grade 3:	-	-	-	1
STOMACH :	5	5	6	7
- Dilated glands :	-	1	2	-
Grade 1:	-	1	2	-
- Hyperplasia (LR) :	-	-	2	1
Grade 1:	-	-	2	1
- Hyperkeratosis :	-	-	-	1
Grade 2:	-	-	-	1
- Acanthosis :	-	-	-	1
Grade 1:	-	-	-	1
Grade 2:	-	-	-	-
- Cyst :	-	-	1	-
Grade 1:	-	-	1	-
- Ectopic squamous ep :	-	1	-	-

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NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, INCL. DEATHS
All animals

SEX :				FEMALE
DOSE GROUP:	01	02	03	04
NO.ANIMALS:	10	10	10	10
LIVER :	5	5	6	7
- Inflamm cell foci :	5	2	5	6
Grade 1:	5	2	5	5
Grade 2:	-	-	-	1
- Hepatocyte hypertrop:	-	-	-	6
Grade 1:	-	-	-	6
Grade 2:	-	-	-	-
- Focal necrosis :	-	-	1	-
Grade 1:	-	-	1	-
- Vacuolation (pp) :	4	4	3	-
Grade 1:	4	4	3	-
- Exmed hematopoiesis :	-	-	-	1
Grade 1:	-	-	-	1
SPLEEN :	5	5	6	7
- Exmed hematopoiesis :	5	5	6	7
Grade 1:	1	2	2	3
Grade 2:	2	3	3	3
Grade 3:	2	-	1	1
- Hemosiderosis :	-	-	2	5
Grade 1:	-	-	1	1
Grade 2:	-	-	1	4
- Development anomaly :	-	-	1	-
ADRENAL GLANDS :	5	5	6	7
- Cortical vacuolation:	-	-	-	1
Grade 1:	-	-	-	1
Grade 2:	-	-	-	-
BRAIN :	5	5	6	7
- Meningitis :	-	-	-	2
Grade 3:	-	-	-	2

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NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: KO, INCL. DEATHS
All animals

SEX :				FEMALE
DOSE GROUP:	01	02	03	04
NO.ANIMALS:	10	10	10	10
SPINAL CORD :	5	5	6	7
- Degenerate fibres :	-	-	1	-
Grade 1:	-	-	1	-
- Meningitis :	-	-	-	2
Grade 1:	-	-	-	2
CLITORAL GLANDS :	5	1	4	10
- Inflamm cell foci :	1	-	2	1
Grade 1:	1	-	1	1
Grade 2:	-	-	1	-
- Dilated lumen :	1	-	1	-
Grade 1:	1	-	-	-
Grade 2:	-	-	1	-
ESOPHAGUS :	5	-	1	7
- Myositis :	-	-	-	1
Grade 1:	-	-	-	1
- Hyperkeratosis :	-	-	-	1
Grade 1:	-	-	-	-
Grade 2:	-	-	-	1
EYES :	-	1	-	-
- Hemorrhage :	-	1	-	-
Grade 3:	-	1	-	-
HEART :	5	-	1	7
- Ventricular dilation:	-	-	1	-
Grade 3:	-	-	1	-
KIDNEYS :	5	-	1	7
- Hydronephrosis :	-	-	-	1
Grade 1:	-	-	-	1
Grade 2:	-	-	-	-
Grade 3:	-	-	-	-
- Tubular basophilia :	2	-	1	3
Grade 1:	2	-	1	3
Grade 3:	-	-	-	-

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TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, INCL. DEATHS
All animals

SEX :				FEMALE
DOSE GROUP:	01	02	03	04
NO.ANIMALS:	10	10	10	10
LUNG :	5	-	1	7
- Alveolar macrophages:	2	-	-	3
Grade 1:	2	-	-	3
Grade 2:	-	-	-	-
- Hemorrhage :	-	-	1	-
Grade 1:	-	-	1	-
- Congestion :	-	-	-	1
Grade 1:	-	-	-	-
Grade 2:	-	-	-	1
- Alveolar debris :	-	-	-	1
Grade 2:	-	-	-	1
LYMPH NODES :	-	-	-	1
- Erythrophagocytosis :	-	-	-	1
Grade 3:	-	-	-	1
MANDIB.LYMPH NODES :	5	2	3	8
- Hemorrhage :	1	2	2	-
Grade 1:	1	1	1	-
Grade 2:	-	1	1	-
- Congestion :	-	-	-	2
Grade 1:	-	-	-	2
Grade 2:	-	-	-	-
PANCREAS :	5	-	1	7
- Exocr atrophy (foc) :	-	-	1	1
Grade 1:	-	-	1	-
Grade 2:	-	-	-	1
- Exocr atrophy (dif) :	-	-	-	1
Grade 2:	-	-	-	1
PEYER'S PATCHES :	4	-	1	6
- Germinal centres :	4	-	1	6

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, INCL. DEATHS
All animals

SEX :				FEMALE
DOSE GROUP:	01	02	03	04
NO.ANIMALS:	10	10	10	10
UTERUS :	5	1	3	10
- Implantation site(s):	5	-	1	4
- Cyclical change :	-	-	-	2
- Uterine prolapse :	-	-	1	-
- Cyst :	-	-	-	1
Grade 3:	-	-	-	1

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

ANIMAL HEADING DATA
DOSE GROUP : 01, CONTROL

ANIMAL NUMBER	SEX M/F	DEFINED AND FINAL STATE OF NECROPSY		TEST DAYS	FIRST AND LAST DAY UNDER TEST		DATE OF NECROPSY
1	M	KO	KO	28	21-JUL-03	17-AUG-03	18-AUG-03
2	M	KO	KO	28	21-JUL-03	17-AUG-03	18-AUG-03
3	M	KO	KO	28	21-JUL-03	17-AUG-03	18-AUG-03
4	M	KO	KO	28	21-JUL-03	17-AUG-03	18-AUG-03
5	M	KO	KO	28	21-JUL-03	17-AUG-03	18-AUG-03
6	M	KO	KO	28	21-JUL-03	17-AUG-03	18-AUG-03
7	M	KO	KO	28	21-JUL-03	17-AUG-03	18-AUG-03
8	M	KO	KO	28	21-JUL-03	17-AUG-03	18-AUG-03
9	M	KO	KO	28	21-JUL-03	17-AUG-03	18-AUG-03
10	M	KO	KO	28	21-JUL-03	17-AUG-03	18-AUG-03
41	F	KO	KO	42	21-JUL-03	31-AUG-03	01-SEP-03
42	F	KO	KO	45	21-JUL-03	03-SEP-03	04-SEP-03
43	F	KO	KO	45	21-JUL-03	03-SEP-03	04-SEP-03
44	F	KO	KO	42	21-JUL-03	31-AUG-03	01-SEP-03
45	F	KO	KO	43	21-JUL-03	01-SEP-03	02-SEP-03
46	F	KO	KO	42	21-JUL-03	31-AUG-03	01-SEP-03
47	F	KO	KO	43	21-JUL-03	01-SEP-03	02-SEP-03
48	F	KO	KO	42	21-JUL-03	31-AUG-03	01-SEP-03
49	F	KO	KO	43	21-JUL-03	01-SEP-03	02-SEP-03
50	F	KO	KO	45	21-JUL-03	03-SEP-03	04-SEP-03

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, CONTROL MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 1

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2
ADRENAL GLANDS:
-Cortical vacuolation, bilateral, grade 2
PARATHYROID GLANDS:
Only one of paired organs examined/present
PEYER'S PATCHES:
-Germinal centres
TESTES (STAGING):
-Stage I spermatogenesis, bilateral
-Stage VIII spermatogenesis, bilateral
-Stage XI spermatogenesis, bilateral
-Stage XIV spermatogenesis, bilateral
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, CONTROL
MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28
* ANIMAL NO. : 2

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

SPLEEN:
-Extramedullary hematopoiesis, grade 2
ADRENAL MEDULLAS:
Only one of paired organs examined/present
PARATHYROID GLANDS:
Only one of paired organs examined/present
PEYER'S PATCHES:
-Germinal centres
PREPUTIAL GLANDS (INGUINAL GLANDS):
-Inflammatory cell foci, unilateral, grade 1
PROSTATE GLAND:
-Lymphoid cell foci, grade 2
TESTES (STAGING):
-Stage I spermatogenesis, bilateral
-Stage VIII spermatogenesis, bilateral
-Stage XI spermatogenesis, bilateral
-Stage XIV spermatogenesis, bilateral
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, CONTROL
MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28
* ANIMAL NO. : 3

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2
ADRENAL GLANDS:
Only one of paired organs examined/present
ADRENAL MEDULLAS:
Only one of paired organs examined/present
TESTES:
-Tubular atrophy, unilateral, grade 1
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
PEYER'S PATCHES:
-Germinal centres
TESTES (STAGING):
-Stage I spermatogenesis, bilateral
-Stage VIII spermatogenesis, bilateral
-Stage XI spermatogenesis, bilateral
-Stage XIV spermatogenesis, bilateral
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, CONTROL
MALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 28
* ANIMAL NO. : 4

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
LUNG:
-Alveolar macrophages, grade 1
PEYER'S PATCHES:
-Germinal centres
TESTES (STAGING):
-Stage I spermatogenesis, bilateral
-Stage VIII spermatogenesis, bilateral
-Stage XI spermatogenesis, bilateral
-Stage XIV spermatogenesis, bilateral
THYROID GLAND (BOTH LOBES):
-Hyperplastic/hypertrophic follicles, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, CONTROL MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 5

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 1
PEYER'S PATCHES:
-Germinal centres
PROSTATE GLAND:
-Lymphoid cell foci, grade 1
TESTES (STAGING):
-Stage I spermatogenesis, bilateral
-Stage VIII spermatogenesis, bilateral
-Stage XI spermatogenesis, bilateral
-Stage XIV spermatogenesis, bilateral
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 6

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, CONTROL
MALE

CONT./FF. ANIMAL NO. : 6

* MICROSCOPIC FINDINGS

THYMUS:
-Hemorrhage, grade 1
LIVER:
-Inflammatory cell foci, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2
ADRENAL GLANDS:
-Cortical vacuolation, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28
* ANIMAL NO. : 7

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO MICROSCOPIC FINDINGS NOTED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, CONTROL
MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28
* ANIMAL NO. : 8

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO MICROSCOPIC FINDINGS NOTED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28
* ANIMAL NO. : 9

* NECROPSY FINDINGS

THYMUS:
01: FOCUS/FOCI, MANY, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:
-Hemorrhage, grade 1
This finding corresponds to necropsy observation no: 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, CONTROL
MALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 28
* ANIMAL NO. : 10

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO MICROSCOPIC FINDINGS NOTED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, CONTROL
FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 42
* ANIMAL NO. : 41

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Periportal vacuolation, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 3
CLITORAL GLANDS:
-Inflammatory cell foci, bilateral, grade 1
PEYER'S PATCHES:
-Germinal centres
UTERUS:
-Implantation site(s)
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 45
* ANIMAL NO. : 42

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, CONTROL
FEMALE

CONT./FF. ANIMAL NO. : 42

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 45
* ANIMAL NO. : 43

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 42
* ANIMAL NO. : 44

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, CONTROL
FEMALE

CONT./FF. ANIMAL NO. : 44

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Periportal vacuolation, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
PEYER'S PATCHES:
Tissue not present for histologic examination
UTERUS:
-Implantation site(s)
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 43
* ANIMAL NO. : 45

* NECROPSY FINDINGS

MANDIBULAR LYMPH NODES:
01: RIGHT SIDE: DISCOLOURATION, DARK RED.
SKIN/SUBCUTIS:
01: THROAT REGION: ALOPECIA.
NO OTHER NECROPSY OBSERVATIONS NOTED

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, CONTROL FEMALE

CONT./FF. ANIMAL NO. : 45

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 3
MANDIBULAR LYMPH NODES:
-Hemorrhage, unilateral, grade 1
This finding corresponds to necropsy observation no: 01.
PARATHYROID GLANDS:
Only one of paired organs examined/present
PEYER'S PATCHES:
-Germinal centres
SKIN/SUBCUTIS:
Nothing abnormal discovered corresponding to necropsy observation no.01.
UTERUS:
-Implantation site(s)
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: KO
DAYS ON TEST : 42 * ANIMAL NO. : 46

* NECROPSY FINDINGS

THYMUS:
01: DISCOLOURATION, LIGHT RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, CONTROL
FEMALE

CONT./FF. ANIMAL NO. : 46

* MICROSCOPIC FINDINGS

THYMUS:
-Hemorrhage, grade 2
This finding corresponds to necropsy observation no: 01.
LIVER:
-Inflammatory cell foci, grade 1
-Periportal vacuolation, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2
LUNG:
-Alveolar macrophages, grade 1
PARATHYROID GLANDS:
Tissue not present for histologic examination
PEYER'S PATCHES:
-Germinal centres
UTERUS:
-Implantation site(s)
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: KO
DAYS ON TEST : 43
* ANIMAL NO. : 47

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, CONTROL
FEMALE

CONT./FF. ANIMAL NO. : 47

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 42
* ANIMAL NO. : 48

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Periportal vacuolation, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 1
CLITORAL GLANDS:
-Dilated lumen, bilateral, grade 1
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
LUNG:
-Alveolar macrophages, grade 1
PARATHYROID GLANDS:
Only one of paired organs examined/present
PEYER'S PATCHES:
-Germinal centres
UTERUS:
-Implantation site(s)

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, CONTROL FEMALE

CONT./FF. ANIMAL NO. : 48

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 43 * ANIMAL NO. : 49

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 45 * ANIMAL NO. : 50

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

ANIMAL HEADING DATA
DOSE GROUP : 02, 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-JUL-03	17-AUG-03	18-AUG-03
12	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
13	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
14	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
15	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
16	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
17	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
18	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
19	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
20	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
51	F	K0	K0	43	21-JUL-03	01-SEP-03	02-SEP-03
52	F	K0	K0	42	21-JUL-03	31-AUG-03	01-SEP-03
53	F	K0	K0	42	21-JUL-03	31-AUG-03	01-SEP-03
54	F	K0	K0	43	21-JUL-03	01-SEP-03	02-SEP-03
55	F	K0	K0	43	21-JUL-03	01-SEP-03	02-SEP-03
56	F	K0	K0	44	21-JUL-03	02-SEP-03	03-SEP-03
57	F	K0	K0	46	21-JUL-03	04-SEP-03	05-SEP-03
58	F	K0	K0	45	21-JUL-03	03-SEP-03	04-SEP-03
59	F	K0	K0	42	21-JUL-03	31-AUG-03	01-SEP-03
60	F	K0	K0	45	21-JUL-03	03-SEP-03	04-SEP-03

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 50 MG/KG
MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28
* ANIMAL NO. : 11

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

STOMACH:
-Hyperplasia (Limiting ridge), grade 1
LIVER:
-Inflammatory cell foci, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2
TESTES:
-Tubular dilation, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28
* ANIMAL NO. : 12

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Extramedullary hematopoiesis, grade 1

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 50 MG/KG
MALE

CONT./FF. ANIMAL NO. : 12

SPLEEN:
-Extramedullary hematopoiesis, grade 3
ADRENAL GLANDS:
-Cortical vacuolation, bilateral, grade 1
EPIDIDYMIDES:
-Sperm granuloma, unilateral, grade 3
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

LIVER:
-Inflammatory cell foci, grade 2
SPLEEN:
-Extramedullary hematopoiesis, grade 2
EPIDIDYMIDES:
-Cellular debris, bilateral, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 50 MG/KG MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 14

* NECROPSY FINDINGS

LIVER:
01: DISCOLOURATION, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
No microscopic finding corresponding to necropsy observation no. 01.
-Inflammatory cell foci, grade 1
-Periportal vacuolation, grade 1
SPLEEN:
-Extramedullary hematopoiesis, 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

STOMACH:
-Myositis, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 50 MG/KG MALE

CONT./FF. ANIMAL NO. : 15

ADRENAL GLANDS:
-Cortical vacuolation, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 16

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO MICROSCOPIC FINDINGS NOTED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 17

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 50 MG/KG MALE

CONT./FF. ANIMAL NO. : 17

* MICROSCOPIC FINDINGS

PROSTATE GLAND:
-Lymphoid cell foci, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 18

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO MICROSCOPIC FINDINGS NOTED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 19

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 50 MG/KG MALE

CONT./FF. ANIMAL NO. : 19

* MICROSCOPIC FINDINGS

NO MICROSCOPIC FINDINGS NOTED.

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 20

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO MICROSCOPIC FINDINGS NOTED.

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 50 MG/KG FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 43 * ANIMAL NO. : 51

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 42 * ANIMAL NO. : 52

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

STOMACH:
-Ectopic squamous epithelium
LIVER:
-Inflammatory cell foci, grade 1
-Periportal vacuolation, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 50 MG/KG
FEMALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 42
* ANIMAL NO. : 53

* NECROPSY FINDINGS

LIVER:
01: ACCENTUATED LOBULAR PATTERN.
ADRENAL GLANDS:
01: LEFT SIDE: FOCUS/FOCI, ISOLATED, GRAY-WHITE.
02: RIGHT SIDE: FOCUS/FOCI, SEVERAL, GRAY-WHITE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Periportal vacuolation, grade 1
This finding corresponds to necropsy observation no: 01.
SPLEEN:
-Extramedullary hematopoiesis, grade 2
ADRENAL GLANDS:
No microscopic finding corresponding to necropsy observation no. 01,02.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 50 MG/KG
FEMALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 43
* ANIMAL NO. : 54

* NECROPSY FINDINGS

MANDIBULAR LYMPH NODES:
01: RIGHT SIDE: DISCOLOURATION, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Periportal vacuolation, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 1
MANDIBULAR LYMPH NODES:
-Hemorrhage, unilateral, grade 1
This finding corresponds to necropsy observation no: 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: KO
DAYS ON TEST : 43
* ANIMAL NO. : 55

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 50 MG/KG
FEMALE

CONT./FF. ANIMAL NO. : 55

* MICROSCOPIC FINDINGS

STOMACH:
-Dilated glands, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 44
* ANIMAL NO. : 56

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 50 MG/KG
FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 46
* ANIMAL NO. : 57

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO MICROSCOPIC FINDINGS NOTED.

* STATE AT NECROPSY: K0
DAYS ON TEST : 45
* ANIMAL NO. : 58

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 50 MG/KG
FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 42
* ANIMAL NO. : 59

* NECROPSY FINDINGS

EYES:
01: RIGHT SIDE : EXOPHTALMUS.
MANDIBULAR LYMPH NODES:
01: RIGHT SIDE: DISCOLOURATION, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Periportal vacuolation, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2
EYES:
Only one of paired organs examined/present
-Hemorrhage, unilateral, grade 3
This finding corresponds to necropsy observation no: 01.
MANDIBULAR LYMPH NODES:
Only one of paired organs examined/present
-Hemorrhage, unilateral, grade 2
This finding corresponds to necropsy observation no: 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 50 MG/KG
FEMALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 45
* ANIMAL NO. : 60

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

ANIMAL HEADING DATA
DOSE GROUP : 03, 150 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-JUL-03	17-AUG-03	18-AUG-03
22	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
23	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
24	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
25	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
26	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
27	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
28	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
29	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
30	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
61	F	K0	K0	42	21-JUL-03	31-AUG-03	01-SEP-03
62	F	K0	K0	45	21-JUL-03	03-SEP-03	04-SEP-03
63	F	K0	K0	42	21-JUL-03	31-AUG-03	01-SEP-03
64	F	K0	K0	43	21-JUL-03	01-SEP-03	02-SEP-03
65	F	K0	+2	42	21-JUL-03	31-AUG-03	01-SEP-03
66	F	K0	K0	42	21-JUL-03	31-AUG-03	01-SEP-03
67	F	K0	K0	45	21-JUL-03	03-SEP-03	04-SEP-03
68	F	K0	K0	46	21-JUL-03	04-SEP-03	05-SEP-03
69	F	K0	K0	43	21-JUL-03	01-SEP-03	02-SEP-03
70	F	K0	K0	46	21-JUL-03	04-SEP-03	05-SEP-03

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 150 MG/KG
MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28
* ANIMAL NO. : 21

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

SPLEEN:
-Extramedullary hematopoiesis, grade 2
ADRENAL GLANDS:
-Cortical vacuolation, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28
* ANIMAL NO. : 22

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 2
SPLEEN:
-Extramedullary hematopoiesis, grade 1
ADRENAL GLANDS:
-Cortical vacuolation, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 150 MG/KG
MALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 28
* ANIMAL NO. : 23

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2
ADRENAL GLANDS:
-Cortical vacuolation, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: KO
DAYS ON TEST : 28
* ANIMAL NO. : 24

* NECROPSY FINDINGS

KIDNEYS:
01: RIGHT SIDE: PELVIC DILATION.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 150 MG/KG
MALE

CONT./FF. ANIMAL NO. : 24

KIDNEYS:
-Hydronephrosis, unilateral, grade 2
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. : 25

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 2
-Focal necrosis, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 150 MG/KG
MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28
* ANIMAL NO. : 26

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO MICROSCOPIC FINDINGS NOTED.

* STATE AT NECROPSY: K0
DAYS ON TEST : 28
* ANIMAL NO. : 27

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO MICROSCOPIC FINDINGS NOTED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 150 MG/KG
MALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 28
* ANIMAL NO. : 28

* NECROPSY FINDINGS

THYMUS:
01: BOTH SIDES: FOCUS/FOCI, MANY, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:
-Hemorrhage, grade 2
This finding corresponds to necropsy observation no: 01.
PREPUTIAL GLANDS (INGUINAL GLANDS):
-Inflammatory cell foci, unilateral, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: KO
DAYS ON TEST : 28
* ANIMAL NO. : 29

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO MICROSCOPIC FINDINGS NOTED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 150 MG/KG
MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28
* ANIMAL NO. : 30

* NECROPSY FINDINGS

THYMUS:
01: RIGHT SIDE: FOCUS/FOCI, SEVERAL, REDDISH.
KIDNEYS:
01: RIGHT SIDE: PELVIC DILATION.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:
-Hemorrhage, grade 1
This finding corresponds to necropsy observation no: 01.
KIDNEYS:
-Hydronephrosis, unilateral, grade 1
This finding corresponds to necropsy observation no: 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 150 MG/KG FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 42 * ANIMAL NO. : 61

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Periportal vacuolation, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 45 * ANIMAL NO. : 62

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 150 MG/KG
FEMALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 42
* ANIMAL NO. : 63

* NECROPSY FINDINGS

SPLEEN:
01: CONSTRICTED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2
-Developmental anomaly
This finding corresponds to necropsy observation no: 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: KO
DAYS ON TEST : 43
* ANIMAL NO. : 64

* NECROPSY FINDINGS

MANDIBULAR LYMPH NODES:
01: RIGHT SIDE: DISCOLOURATION, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 150 MG/KG FEMALE

CONT./FF. ANIMAL NO. : 64

* MICROSCOPIC FINDINGS

STOMACH:
-Dilated glands, grade 1
-Hyperplasia (Limiting ridge), grade 1
LIVER:
-Inflammatory cell foci, grade 1
-Periportal vacuolation, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2
-Hemosiderosis, grade 1
MANDIBULAR LYMPH NODES:
-Hemorrhage, unilateral, grade 2
This finding corresponds to necropsy observation no: 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0/+2
DAYS ON TEST : 42 * ANIMAL NO. : 65

* CAUSE OF DEATH / MORBIDITY

UTERUS:
-Uterine prolapse

* NECROPSY FINDINGS

UTERUS:
01: PROLAPSE OF THE UTERUS.
NO OTHER NECROPSY OBSERVATIONS NOTED

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 150 MG/KG
FEMALE

CONT./FF. ANIMAL NO. : 65

* MICROSCOPIC FINDINGS

LIVER:
-Focal necrosis, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 3
-Hemosiderosis, grade 2
CLITORAL GLANDS:
-Inflammatory cell foci, bilateral, grade 2
HEART:
-Ventricular dilation, grade 3
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
LUNG:
-Hemorrhage, grade 1
PANCREAS:
-Exocrine atrophy (focal), grade 1
PEYER'S PATCHES:
-Germinal centres
UTERUS:
-Implantation site(s)
-Uterine prolapse
This finding corresponds to necropsy observation no: 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 150 MG/KG
FEMALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 42
* ANIMAL NO. : 66

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

THYMUS:
-Hemorrhage, grade 1
STOMACH:
-Dilated glands, grade 1
-Cyst, grade 1
LIVER:
-Inflammatory cell foci, grade 1
-Periportal vacuolation, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2
SPINAL CORD:
-Degenerate fibres, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: KO
DAYS ON TEST : 45
* ANIMAL NO. : 67

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 150 MG/KG
FEMALE

CONT./FF. ANIMAL NO. : 67

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 46
* ANIMAL NO. : 68

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

CLITORAL GLANDS:
-Inflammatory cell foci, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 43
* ANIMAL NO. : 69

* NECROPSY FINDINGS

CLITORAL GLANDS:
01: BOTH SIDES: FOCUS/FOCI, SEVERAL, TAN.
MANDIBULAR LYMPH NODES:
01: RIGHT SIDE: DISCOLOURATION, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 150 MG/KG
FEMALE

CONT./FF. ANIMAL NO. : 69

* MICROSCOPIC FINDINGS

STOMACH:
-Hyperplasia (Limiting ridge), grade 1
LIVER:
-Inflammatory cell foci, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 1
CLITORAL GLANDS:
-Dilated lumen, bilateral, grade 2
This finding corresponds to necropsy observation no: 01.
MANDIBULAR LYMPH NODES:
-Hemorrhage, unilateral, grade 1
This finding corresponds to necropsy observation no: 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 46
* ANIMAL NO. : 70

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO MICROSCOPIC FINDINGS NOTED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

ANIMAL HEADING DATA
DOSE GROUP : 04, 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
31	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
32	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
33	M	K0	+1	12	21-JUL-03	01-AUG-03	01-AUG-03
34	M	K0	+1	6	21-JUL-03	26-JUL-03	27-JUL-03
35	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
36	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
37	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
38	M	K0	+2	24	21-JUL-03	13-AUG-03	13-AUG-03
39	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
40	M	K0	K0	28	21-JUL-03	17-AUG-03	18-AUG-03
71	F	K0	K0	46	21-JUL-03	04-SEP-03	05-SEP-03
72	F	K0	K0	46	21-JUL-03	04-SEP-03	05-SEP-03
73	F	K0	K0	46	21-JUL-03	04-SEP-03	05-SEP-03
74	F	K0	K0	42	21-JUL-03	31-AUG-03	01-SEP-03
75	F	K0	K0	46	21-JUL-03	04-SEP-03	05-SEP-03
76	F	K0	K0	46	21-JUL-03	04-SEP-03	05-SEP-03
77	F	K0	+2	14	21-JUL-03	03-AUG-03	03-AUG-03
78	F	K0	+1	28	21-JUL-03	17-AUG-03	18-AUG-03
79	F	K0	K0	46	21-JUL-03	04-SEP-03	05-SEP-03
80	F	K0	K0	46	21-JUL-03	04-SEP-03	05-SEP-03

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG
MALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 28
* ANIMAL NO. : 31

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

THYMUS:
-Hemorrhage, grade 1
LIVER:
-Inflammatory cell foci, grade 1
-Hepatocyte hypertrophy, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 3
ADRENAL GLANDS:
-Cortical vacuolation, bilateral, grade 2
TESTES:
-Tubular atrophy, bilateral, grade 3
EPIDIDYMIDES:
-Reduced spermatozoa, bilateral, grade 3
-Cellular debris, bilateral, grade 3
-Sperm granuloma, unilateral, grade 3
PEYER'S PATCHES:
-Germinal centres
TESTES (STAGING):
Staging not possible.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG
MALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 28
* ANIMAL NO. : 32

* NECROPSY FINDINGS

EPIDIDYMIDES:
01: LEFT SIDE, HEAD: NODULE(S), YELLOWISH.
02: RIGHT SIDE, TAIL: NODULE(S), YELLOWISH.
KIDNEYS:
01: RIGHT SIDE: PELVIC DILATION.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Hepatocyte hypertrophy, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 3
TESTES:
-Giant cells, unilateral, grade 1
EPIDIDYMIDES:
-Sperm granuloma, bilateral, grade 3
This finding corresponds to necropsy observations nos: 01,02.
KIDNEYS:
-Hydronephrosis, unilateral, grade 1
This finding corresponds to necropsy observation no: 01.
PEYER'S PATCHES:
-Germinal centres
PREPUTIAL GLANDS (INGUINAL GLANDS):
-Dilated acini, bilateral, grade 2
TESTES (STAGING):
-Stage I spermatogenesis, bilateral
-Stage VIII spermatogenesis, bilateral
-Stage XI spermatogenesis, bilateral
Reduction in numbers of pachytene spermatocytes.
-Stage XIV spermatogenesis, bilateral

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG MALE

CONT./FF. ANIMAL NO. : 32

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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* STATE AT NECROPSY: K0/+1
DAYS ON TEST : 12 * ANIMAL NO. : 33

* CAUSE OF DEATH / MORBIDITY

SYSTEMIC:
-Gavage error

* NECROPSY FINDINGS

GENERAL OBSERVATIONS:
01: CANNIBALISM:ORGAN MISSING PARTLY G.I.TRACTUS PARTLY GENITAL REGION.
THYMUS:
01: FOCUS/FOCI, ISOLATED, DARK RED.
LUNG:
01: DISCOLOURATION, DARK RED.
MANDIBULAR LYMPH NODES:
01: DISCOLOURATION, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG MALE

CONT./FF. ANIMAL NO. : 33

* MICROSCOPIC FINDINGS

GENERAL OBSERVATIONS:
Tissue with necropsy observation no.01 not submitted for microscopic examination.
-Autolysis, grade 2
THYMUS:
-Hemorrhage, grade 2
This finding corresponds to necropsy observation no: 01.
LIVER:
-Centrilobular degeneration, grade 1
-Congestion, grade 2
SPLEEN:
-Extramedullary hematopoiesis, grade 3
TESTES:
Only one of paired organs examined/present
EPIDIDYMIDES:
Only one of paired organs examined/present
CECUM:
Tissue not present for histologic examination
ESOPHAGUS:
-Hyperkeratosis, grade 1
ILEUM:
Tissue not present for histologic examination
JEJUNUM:
Tissue not present for histologic examination
LUNG:
-Congestion, grade 2
This finding corresponds to necropsy observation no: 01.
-Alveolar debris, grade 2
MANDIBULAR LYMPH NODES:
-Congestion, bilateral, grade 2
This finding corresponds to necropsy observation no: 01.
MESENTERIC LYMPH NODE:
Tissue not present for histologic examination

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG MALE

CONT./FF. ANIMAL NO. : 33

PANCREAS:
Tissue not present for histologic examination
PEYER'S PATCHES:
Tissue not present for histologic examination
RECTUM:
Tissue not present for histologic examination
SEMINAL VESICLES:
Only one of paired organs examined/present
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0/+1
DAYS ON TEST : 6 * ANIMAL NO. : 34

* CAUSE OF DEATH / MORBIDITY

SYSTEMIC:
-Not evident

* NECROPSY FINDINGS

GENERAL OBSERVATIONS:
01: BEGINNING AUTOLYSIS.
02: CANNIBALISM:ORGAN MISSING PARTLY GENITAL REGION PARTLY G.I.TRACTUS AND EYES.
THYMUS:
01: BOTH SIDES: FOCUS/FOCI, MANY, DARK RED.
STOMACH:
01: DISCOLOURATION, REDDISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG
MALE

CONT./FF. ANIMAL NO. : 34

* MICROSCOPIC FINDINGS

GENERAL OBSERVATIONS:
Tissue with necropsy observation no.02 not submitted for microscopic examination.
-Autolysis, grade 3
This finding corresponds to necropsy observation no: 01.
THYMUS:
-Hemorrhage, grade 3
This finding corresponds to necropsy observation no: 01.
STOMACH:
Severe autolysis, evaluation not possible
No microscopic finding corresponding to necropsy observation no. 01.
LIVER:
-Centrilobular degeneration, grade 1
-Congestion, grade 2
SPLEEN:
Severe autolysis, evaluation not possible
TESTES:
Tissue not present for histologic examination
EPIDIDYMIDES:
Tissue not present for histologic examination
CECUM:
Tissue not present for histologic examination
COLON:
Tissue not present for histologic examination
DUODENUM:
Severe autolysis, evaluation not possible
ESOPHAGUS:
-Hyperkeratosis, grade 1
ILEUM:
Tissue not present for histologic examination
JEJUNUM:
Severe autolysis, evaluation not possible
LUNG:
-Congestion, grade 1

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG MALE

CONT./FF. ANIMAL NO. : 34

MANDIBULAR LYMPH NODES:
-Congestion, bilateral, grade 2
MESENTERIC LYMPH NODE:
Severe autolysis, evaluation not possible
PANCREAS:
Severe autolysis, evaluation not possible
PARATHYROID GLANDS:
Only one of paired organs examined/present
PEYER'S PATCHES:
Tissue not present for histologic examination
RECTUM:
Severe autolysis, evaluation not possible
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 35

* NECROPSY FINDINGS

EPIDIDYMIDES:
01: RIGHT SIDE, TAIL: NODULE(S), SEVERAL, YELLOWISH, HARD.
DUODENUM:
01: DISCOLOURATION, REDDISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:
-Atrophy, grade 2
LIVER:
-Inflammatory cell foci, grade 1
-Hepatocyte hypertrophy, grade 1

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG
MALE

CONT./FF. ANIMAL NO. : 35

SPLEEN:
-Hemosiderosis, grade 2
ADRENAL GLANDS:
-Cortical vacuolation, bilateral, grade 1
TESTES:
-Tubular dilation, unilateral, grade 2
EPIDIDYMIDES:
-Sperm granuloma, unilateral, grade 3
This finding corresponds to necropsy observation no: 01.
DUODENUM:
-Congestion, grade 1
This finding corresponds to necropsy observation no: 01.
PEYER'S PATCHES:
-Germinal centres
PROSTATE GLAND:
-Lymphoid cell foci, grade 1
TESTES (STAGING):
-Stage I spermatogenesis, bilateral
-Stage VIII spermatogenesis, bilateral
-Stage XI spermatogenesis, bilateral
-Stage XIV spermatogenesis, bilateral
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 28
* ANIMAL NO. : 36

* NECROPSY FINDINGS

EPIDIDYMIDES:
01: LEFT SIDE, TAIL: NODULE(S), YELLOWISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG
MALE

CONT./FF. ANIMAL NO. : 36

* MICROSCOPIC FINDINGS

THYMUS:
-Hemorrhage, grade 1
STOMACH:
-Hyperplasia (Limiting ridge), grade 1
LIVER:
-Inflammatory cell foci, grade 1
-Hepatocyte hypertrophy, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 3
EPIDIDYMIDES:
-Sperm granuloma, unilateral, grade 2
This finding corresponds to necropsy observation no: 01.
PEYER'S PATCHES:
-Germinal centres
TESTES (STAGING):
-Stage I spermatogenesis, bilateral
-Stage VIII spermatogenesis, bilateral
-Stage XI spermatogenesis, bilateral
-Stage XIV spermatogenesis, bilateral
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 28
* ANIMAL NO. : 37

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG
MALE

CONT./FF. ANIMAL NO. : 37

* MICROSCOPIC FINDINGS

THYMUS:
-Hemorrhage, grade 1
LIVER:
-Hepatocyte hypertrophy, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 3
ADRENAL GLANDS:
-Cortical vacuolation, bilateral, grade 2
HEART:
-Myocarditis, grade 1
PEYER'S PATCHES:
-Germinal centres
PROSTATE GLAND:
-Lymphoid cell foci, grade 1
TESTES (STAGING):
-Stage I spermatogenesis, bilateral
-Stage VIII spermatogenesis, bilateral
-Stage XI spermatogenesis, bilateral
-Stage XIV spermatogenesis, bilateral
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0/+2
DAYS ON TEST : 24
* ANIMAL NO. : 38

* CAUSE OF DEATH / MORBIDITY

SYSTEMIC:

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG
MALE

CONT./FF. ANIMAL NO. : 38

-Not evident

* NECROPSY FINDINGS

GENERAL OBSERVATIONS:
01: EMACIATED.
STOMACH:
01: FORESTOMACH: IRREGULAR SURFACE.
02: LIMITING RIDGE: THICKENED.
LIVER:
01: ENLARGED.
02: ACCENTUATED LOBULAR PATTERN.
CECUM:
01: DISCOLOURATION, REDDISH.
URINARY BLADDER:
01: CONTENTS: DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

GENERAL OBSERVATIONS:
No microscopic finding corresponding to necropsy observation no. 01.
STOMACH:
-Hyperplasia (Limiting ridge), grade 1
This finding corresponds to necropsy observation no: 02.
-Hyperkeratosis, grade 2
This finding corresponds to necropsy observation no: 01.
-Acanthosis, grade 2
LIVER:
-Hepatocyte hypertrophy, grade 2
This finding corresponds to necropsy observations nos: 01,02.
SPLEEN:
-Extramedullary hematopoiesis, grade 1

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG
MALE

CONT./FF. ANIMAL NO. : 38

ADRENAL GLANDS:
-Cortical vacuolation, unilateral, grade 1
CECUM:
No microscopic finding corresponding to necropsy observation no. 01.
ESOPHAGUS:
-Myositis, grade 1
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
LUNG:
-Alveolar macrophages, grade 2
PEYER'S PATCHES:
-Germinal centres
PREPUTIAL GLANDS (INGUINAL GLANDS):
-Inflammatory cell foci, unilateral, grade 1
SEMINAL VESICLES:
-Reduced contents, bilateral, grade 1
URINARY BLADDER:
-Hemorrhage, grade 3
This finding corresponds to necropsy observation no: 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: KO
DAYS ON TEST : 28
* ANIMAL NO. : 39

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG
MALE

CONT./FF. ANIMAL NO. : 39

* MICROSCOPIC FINDINGS

NO MICROSCOPIC FINDINGS NOTED.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 28
* ANIMAL NO. : 40

* NECROPSY FINDINGS

EPIDIDYMIDES:
01: LEFT SIDE, TAIL: NODULE(S), YELLOWISH, SOFT.
KIDNEYS:
01: RIGHT SIDE: PELVIC DILATION.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

TESTES:
-Tubular dilation, bilateral, grade 2
EPIDIDYMIDES:
-Sperm granuloma, unilateral, grade 2
This finding corresponds to necropsy observation no: 01.
KIDNEYS:
-Hydronephrosis, unilateral, grade 3
This finding corresponds to necropsy observation no: 01.
-Tubular basophilia, unilateral, grade 3
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG
FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 46
* ANIMAL NO. : 71

* NECROPSY FINDINGS

UTERUS:
01: CONTAINS FLUID.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Hepatocyte hypertrophy, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 1
-Hemosiderosis, grade 2
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
PARATHYROID GLANDS:
Only one of paired organs examined/present
PEYER'S PATCHES:
-Germinal centres
UTERUS:
-Cyclical change
This finding corresponds to necropsy observation no: 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG
FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 46
* ANIMAL NO. : 72

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Hepatocyte hypertrophy, grade 1
-Extramedullary hematopoiesis, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2
-Hemosiderosis, grade 2
PARATHYROID GLANDS:
Only one of paired organs examined/present
PEYER'S PATCHES:
-Germinal centres
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 46
* ANIMAL NO. : 73

* NECROPSY FINDINGS

UTERUS:
01: RIGHT HORN: CYST(S), WATERY-CLEAR.
NO OTHER NECROPSY OBSERVATIONS NOTED

TEST ARTICLE : T-7601
TEST SYSTEM : RAT, 28 day + repro, gavage
SPONSOR : 3M Corporate Toxicology
PATHOL. NO.: 03019 RHA
DATE : 04-FEB-04
PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG
FEMALE

CONT./FF. ANIMAL NO. : 73

* MICROSCOPIC FINDINGS

UTERUS:
-Cyst, grade 3
This finding corresponds to necropsy observation no: 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 42
* ANIMAL NO. : 74

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Inflammatory cell foci, grade 1
-Hepatocyte hypertrophy, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2
KIDNEYS:
-Tubular basophilia, unilateral, grade 1
LUNG:
-Alveolar macrophages, grade 1
PEYER'S PATCHES:
-Germinal centres
UTERUS:
-Implantation site(s)
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 46 * ANIMAL NO. : 75

* NECROPSY FINDINGS

THYMUS:
01: RIGHT SIDE: DISCOLOURATION, REDDISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:
-Hemorrhage, grade 1
This finding corresponds to necropsy observation no: 01.
LIVER:
-Hepatocyte hypertrophy, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 3
-Hemosiderosis, grade 2
LYMPH NODES:
PANCREATIC
-Erythrophagocytosis, grade 3
PANCREAS:
-Exocrine atrophy (focal), grade 2
ORGAN/FINDING PRESENT ON SLIDE NUMBER:
5
PEYER'S PATCHES:
-Germinal centres
UTERUS:
-Implantation site(s)
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 46 * ANIMAL NO. : 76

* NECROPSY FINDINGS

MANDIBULAR LYMPH NODES:
01: RIGHT SIDE: DISCOLOURATION, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

MANDIBULAR LYMPH NODES:
No microscopic finding corresponding to necropsy observation no. 01.
NO MICROSCOPIC FINDINGS NOTED.

---

* STATE AT NECROPSY: K0/+2
DAYS ON TEST : 14 * ANIMAL NO. : 77

* CAUSE OF DEATH / MORBIDITY

BRAIN:
-Meningitis, grade 3

* NECROPSY FINDINGS

GENERAL OBSERVATIONS:
01: EMACIATED.
STOMACH:
01: FORESTOMACH: CRATERIFORM RETRACTION, MANY.
NO OTHER NECROPSY OBSERVATIONS NOTED

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG FEMALE

CONT./FF. ANIMAL NO. : 77

* MICROSCOPIC FINDINGS

GENERAL OBSERVATIONS:
For diagnosis of necropsy observation no. 01 see under: PANCREAS.
THYMUS:
-Atrophy, grade 3
STOMACH:
No microscopic finding corresponding to necropsy observation no. 01.
LIVER:
-Inflammatory cell foci, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 1
ADRENAL GLANDS:
-Cortical vacuolation, bilateral, grade 1
BRAIN:
-Meningitis, grade 3
(purulent)
SPINAL CORD:
-Meningitis, grade 1
CLITORAL GLANDS:
-Inflammatory cell foci, unilateral, grade 1
ESOPHAGUS:
-Hyperkeratosis, grade 2
LUNG:
-Alveolar macrophages, grade 1
PANCREAS:
-Exocrine atrophy (diffuse), grade 2
This finding corresponds to necropsy observation no.: 01
in the GENERAL OBSERVATIONS.
PARATHYROID GLANDS:
Only one of paired organs examined/present
PEYER'S PATCHES:
-Germinal centres
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG FEMALE

* STATE AT NECROPSY: K0/+1
DAYS ON TEST : 28 * ANIMAL NO. : 78

* CAUSE OF DEATH / MORBIDITY

BRAIN:
-Meningitis, grade 3

* NECROPSY FINDINGS

ADRENAL GLANDS:
01: LEFT SIDE: GROWN TOGETHER WITH: KIDNEYS.
MESENTERIC LYMPH NODE:
01: DISCOLOURATION, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

GENERAL OBSERVATIONS:
-Autolysis, grade 2
LIVER:
-Inflammatory cell foci, grade 1
-Hepatocyte hypertrophy, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 1
-Hemosiderosis, grade 2
ADRENAL GLANDS:
No microscopic finding corresponding to necropsy observation no. 01.
BRAIN:
-Meningitis, grade 3
(purulent)
SPINAL CORD:
-Meningitis, grade 1

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG FEMALE

CONT./FF. ANIMAL NO. : 78

LUNG:
-Congestion, grade 2
-Alveolar debris, grade 2
MANDIBULAR LYMPH NODES:
-Congestion, bilateral, grade 1
MESENTERIC LYMPH NODE:
No microscopic finding corresponding to necropsy observation no. 01.
PEYER'S PATCHES:
Tissue not present for histologic examination
UTERUS:
-Implantation site(s)
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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* STATE AT NECROPSY: K0
DAYS ON TEST : 46 * ANIMAL NO. : 79

* NECROPSY FINDINGS

UTERUS:
01: CONTAINS FLUID.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

UTERUS:
-Cyclical change
This finding corresponds to necropsy observation no: 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ARTICLE : T-7601 PATHOL. NO.: 03019 RHA
TEST SYSTEM : RAT, 28 day + repro, gavage DATE : 04-FEB-04
SPONSOR : 3M Corporate Toxicology PathData© System V6.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 1000 MG/KG FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 46 * ANIMAL NO. : 80

* NECROPSY FINDINGS

KIDNEYS:
01: PELVIC DILATION.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

STOMACH:
-Hyperplasia (Limiting ridge), grade 1
-Hyperkeratosis, grade 2
-Acanthosis, grade 1
LIVER:
-Inflammatory cell foci, grade 2
-Hepatocyte hypertrophy, grade 1
SPLEEN:
-Extramedullary hematopoiesis, grade 2
-Hemosiderosis, grade 1
ESOPHAGUS:
-Myositis, grade 1
KIDNEYS:
-Hydronephrosis, unilateral, grade 1
This finding corresponds to necropsy observation no: 01.
-Tubular basophilia, unilateral, grade 1
LUNG:
-Alveolar macrophages, grade 1
MANDIBULAR LYMPH NODES:
-Congestion, bilateral, grade 1
PEYER'S PATCHES:
-Germinal centres
UTERUS:
-Implantation site(s)
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

APPENDIX 5 DOSE RANGE FINDING STUDY

GENERAL

NOTOX Project	385717
NOTOX Project (Range Finding)	385728
NOTOX Test Substance Number	113769
Test Substance Name	T-7601

MATERIALS AND METHODS

If not mentioned otherwise, test system, procedures and techniques were identical to those used during the main study.

Number of rats/sex/group	3 (allocated at random, identified by ear- and tailmark)
Age	Approximately 6 weeks
Duration of treatment	5 days (30 June to 04 July 2003)
Dose levels *	150 and 1000 mg/kg body weight/day
Dose volume	5 ml/kg body weight/day
Vehicle	Propylene glycol, specific gravity 1.036

* Dose levels were based on the results of the acute oral toxicity study (NOTOX project 332178)

Observations	Clinical signs:	At least once daily.
	Mortality:	At least twice daily.
	Body weights:	On days 1 and 5.
	Food consumption:	Over days 1-5.
Pathology	Necropsy:	On day 5 (scheduled necropsy): all animals. No organs were fixed.
	Organ weights:	Terminal body weight, kidney, and liver weight.

RESULTS

Parameter	**150 mg/kg/day**	**1000 mg/kg/day**
Mortality	No mortality.	No mortality.
Clinical appearance	No clinical signs noted.	Salivation from days 3-5 in all males and females.
Body weight	Normal.	Normal.
Food consumption	Normal.	Slightly reduced absolute and relative food intake for males, but within normal range. Normal for females.
Macroscopic examination	Fluid in the uterus (one female).	Diaphragmatic hernia of the liver and accessory liver on the papillary process (one male).
Organ weights	Liver and kidney weights considered to be normal.	Liver and kidney weights considered to be normal.

CONCLUSION

Based on the results of this range finding study, dose levels selected for the main study (combined repeated dose toxicity study with reproduction/developmental toxicity screening test) are: 50, 150 and 1000 mg/kg body weight/day.