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TOXICOLOGY STUDY REPORT

PT02-0222

T-7758

**RAT REPEAT DOSE 28-DAY ORAL TOXICITY
+ 14-DAYS RECOVERY**

Original report for the sponsor

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Author:	Dr. G. Ehling	3M study number:	T-7758.1
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1 SUMMARY

STUDY NUMBER: PT02-0222

TITLE: T-7758
Rat repeat dose 28-day oral toxicity + 14-days recovery

AUTHOR(S): Dr. G. Ehling

1.1 OBSERVATIONS AND MEASUREMENTS

Groups of male and female rats received T-7758 by oral gavage at dose levels of 0, 0*, 0.3*, 3, 15, 60 or 240 mg/kg body weight per day for a period of 28 days. On day 29 five males and five females from each group were killed and necropsied. Five males and five females from the control and high dose group were killed and necropsied after a recovery period of 14 days.

* Another control- and low dose group was added at the end of the in-life phase of the other groups in order to confirm a NOEL.

Behavior and state of health were observed daily in all groups. Body weights and food consumption were recorded twice weekly.

Once before the first treatment and once a week thereafter, detailed clinical observations were performed in all animals outside the home cage in a standard arena ('open field'). Additionally, the animals were examined for opacity of the refracting media of the eyes and damage to the oral mucosa.

Neurotoxicological measurements including assessment of sensory function, motor activity, forelimb and hindlimb grip strength, were conducted at the end of the treatment period.

Hematological examinations, clinical chemistry and urine analyses were carried out at the end of the treatment period and after the recovery period.

During necropsy the animals were examined for macroscopically visible abnormalities, the main organs were weighed and the organ to body weight ratios calculated. Organs and tissues were processed for histopathological examination and checked for microscopically visible changes.

Body weights, hematological and clinical chemistry data, urine data (volume, specific weight), absolute and relative organ weights and neurotoxicological measurements (motor activity, forelimb and hindlimb grip strength) were analyzed with the aid of a statistical program to show differences compared to the controls.

1.2 RESULTS

T-7758 induced late-occurring mortality in one male and signs of poor general health condition at 240 mg/kg, as well as clinical findings such as squatting posture, stilted and uncoordinated gait, drawn in flanks and swollen abdomen, from 60 mg/kg onwards. These signs increased in incidence and severity during the treatment and recovery periods. A threshold dose for clinical observations was identified at 3 mg/kg. In addition, the male animal, which was found dead on study day 42, exhibited histopathological signs of severe immune-functional deficiency.

Associated with these clinical observations were impairments of neurobehavior (reduced fore- and hindlimb grip strength) and body weight development from 60 mg/kg onwards as compared to the controls (M/F up to -18/-12% at the end of treatment, and -40%/-16% after recovery, at 240 mg/kg). The males were slightly more sensitive than the females. Food consumption remained unaffected except of high dose males during recovery.

Major clinical pathology findings at 240 mg/kg comprised lower white blood cell (WBC) counts (in particular for recovery males), decreased triglycerides, increased liver enzyme activity (ALAT, gamma-GT), changes in the albumin/globulin ratio and the mineral household (sodium, potassium, calcium/phosphorus), as well as increased urinary volume. A threshold dose for clinical pathology findings was identified at 60mg/kg body weight.

Anatomic pathology findings at 240 mg/kg body weight included increased liver, kidney [females, only] and adrenal [males only] weights, as well as decreased spleen and thymus weight, generally indicating a threshold dose at 60 mg/kg body weight. Histopathological correlates of these findings were hepatocellular hypertrophy (240 mg/kg), tubular changes in the kidneys (from 60 mg/kg onwards), one nephroblastoma (at 240 mg/kg), lymphocyte depletion in spleen and thymus atrophy (at 240 mg/kg), with generally increasing severity during the recovery period. As a secondary result of general toxic stress, functional atrophy of primary and secondary sexual organs was noted for a few males at 240 mg/kg.

1.3 CONCLUSION

In conclusion, repeated administration of 240 mg T-7758/kg body weight induced severe clinical signs (and mortality), including changes in neurobehavior, marked impairment of body weight development, as well as clinical pathology findings, which were associated with liver enzyme induction/toxicity, kidney toxicity, and immunological disfunction. A threshold dose of 60 mg/kg body weight was identified for these severe findings. First general clinical signs at 15 and 3.0mg/kg body weight did not show any clinical- and/or anatomic pathology correlates. With regard to the present study the 'No Observed Effect Level' (NOEL) is 0.3mg/kg body weight/day.

Based on these results, T-7758 should be classified as 'harmful' "Xn", with risk phrase R48/22, "Danger of serious damage to health by prolonged (oral) exposure", according to the EU-Directive 2001/59/EC.

2 STATEMENTS

T-7758

Rat repeat dose 28-day oral toxicity + 14-days recovery

2.1 SCHEDULING

Date of protocol approval 11-Oct-2002

Date of initiation 17-Oct-2002

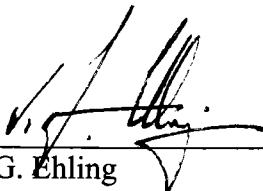
Date of termination 25-Feb-2003

THIS STUDY WAS CONDUCTED IN ACCORDANCE WITH GOOD LABORATORY PRACTICE REGULATIONS.

No unforeseen circumstances were observed which might have affected the quality or integrity of the study.

2.2 APPROVALS

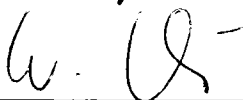
STUDY DIRECTOR



Dr. G. Ehling

18-Aug-2003
Date

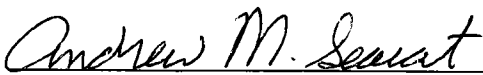
APPROVED BY



Dr. W. Mueller
Testing Facility Management
Head of ProTox – Germany

Aug. 31, 2003
Date

STUDY MONITOR



Dr. A. M. Seacat

Aug. 13, 2003
Date

2.3 STATEMENT OF GOOD LABORATORY PRACTICE

STUDY NUMBER: PT02-0222

TITLE: T-7758

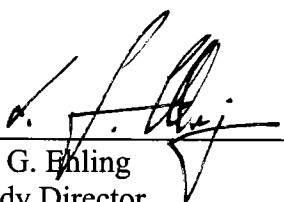
Rat repeat dose 28-day oral toxicity + 14-days recovery

This study was conducted under my direction and in accordance with the Principles of Good Laboratory Practice (GLP) as described under § 19, German Chemical Law (ChemG), Annex 1, in the version of May 8th, 2001, published in Bundesgesetzblatt Jahrgang 2001 Teil I Nr. 21, in Bonn, on May 14th, 2001, aforementioned law is the implementation of the OECD Principles of Good Laboratory Practice as published on March 23rd, 1999 (as revised in Principle 1999/11/EU of March 8th, 1999) Official Journal of the European Union L77/9. No unforeseen circumstances were observed which might have affected the quality or integrity of the study.

All raw data, specimens and other study documents pertaining to this study are stored in the respective department archives.

The following data are archived: Test-article reference sample, protocol, report, all raw data and specimens of laboratory investigation.

THIS STUDY WAS CONDUCTED IN ACCORDANCE WITH THE PROCEDURES HEREIN DESCRIBED AND THIS REPORT FULLY AND ACCURATELY REFLECTS THE RAW DATA GENERATED IN THE STUDY.



Dr. G. Ehling
Study Director

18-Aug-2003

Date

2.4 QUALITY ASSURANCE STATEMENT

STUDY NUMBER: PT02-0222

TITLE: T-7758

Rat repeat dose 28-day oral toxicity + 14-days recovery

This study was periodically inspected and properly signed records of these inspections were submitted to the testing facility management and the study director as shown below. This report has been audited by the quality assurance unit. The reported results accurately reflect the original data of the study.

<u>Dates of Inspection</u>	<u>Study Phase</u>	<u>Dates of Report to Study Director and Management</u>
14-Oct-2002	study plan	14-Oct-2002
17-Oct-2002	study conduct	17-Oct-2002
18-Oct-2002	study conduct	18-Oct-2002
22-Oct-2002	study conduct	22-Oct-2002
07-Nov-2002	study conduct	07-Nov-2002
14-Nov-2002	study conduct	14-Nov-2002
18-Nov-2002	study conduct	18-Nov-2002
06-Jan-2003	study conduct	06-Jan-2003
28-Jan-2003	study conduct	28-Jan-2003
25-Feb-2003	study conduct	25-Feb-2003
22-May-2003	contributor report	22-May-2003
22-May-2003	contributor report	22-May-2003
22-May-2003 – 03-Jun-2003	draft report	03-Jun-2003
26-May-2003	contributor report	26-May-2003
27-May-2003	contributor report	27-May-2003
08-Aug-2003	final report	08-Aug-2003

C. Ehrlich
C. Ehrlich
Quality Assurance (GLP)

08-Aug-2003
Date

3 PROFESSIONAL AND SUPERVISORY STAFF

Study director	: Dr. G. Ehling
Study Investigator	: L. Warzecha
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Sponsor	: 3M Corporate Toxicology 3M Center, Building 220-2E-02 Saint Paul, MN 55133-3220, USA
Monitor	: Dr. Andrew M. Seacat
Clinical Pathology	: Dr. A. Bube
Data Management	: DI H. Press
Lab Animal Science & Welfare	: Dr. R. Hack
Analytical toxicology / Test substance administration	: Dr. H.-M. Kauffmann
Quality Assurance (GLP)	: M. Michel
Histotechnique	: Dr. G. Ehling
Histopathology (P.I.) / QAU GLP: H. Kuhn	: Dr. B. Hein ProTox Emil v. Behringstrasse 76 Gebäude H6 D - 35041 Marburg
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Further testing facility Sponsor	: Dave Ehresman C/O Andrew Seacat 3M Center, 236-1B-22 Saint Paul MN, 55144, USA

4 INTRODUCTION

4.1 OBJECTIVE

The present 28-day toxicity study was conducted in order to characterize the toxicological profile of T-7758 after repeated oral exposure, including endpoints in neurobehavior, immune function and reproductive target organs. Additionally, the results of this study can be used as a dose-range finding for subchronic and chronic toxicity studies. The study should also provide a no-observed-adverse-effect level (NOAEL).

Rationale for species selection

The rat has proved to be a suitable species for subacute oral toxicity testing with many different substances and is the species of choice according to the international guidelines.

Rationale for the route of exposure

The oral route is considered to be a potential exposure route in man.

4.2 GUIDELINES

The present study was conducted in compliance with the requirements of

Commission Directive 96/54/EC
Annex IV D
Method B.7. "Subacute Oral Toxicity"
Adopted July 30 1996

and

OECD Guidelines for Testing of Chemicals
Section 4 Health Effects
407 Subacute Oral Toxicity
Adopted July 27, 1995

and

U.S. EPA: OPPTS 870.3050, Health Effects Test Guidelines:
Repeated dose 28-day oral toxicity study in rodents, July 2000

Principles of Good Laboratory Practice (GLP) as described under § 19, German Chemical Law (ChemG), Annex 1, in the version of May 08th, 2001, published in Bundesgesetzblatt Jahrgang 2001 Teil I Nr. 21, in Bonn, on May 14th, 2001, aforementioned law is the implementation of the OECD Principles of Good Laboratory Practice as published on March 23rd, 1999 (as revised in Principle 1999/11/EU of March 8th, 1999) Official Journal of the European Union L77/9.

5 MATERIALS AND METHODS

5.1 TEST COMPOUND

Name of compound	: T-7758
Synonym	: MV4S
CAS-Number	: 88190-28-7
Molecular formula	: C ₆ F ₁₂ O ₃ S
Molecular weight	: 380 g/mol
Batch number	: Lot 1
Certificate of analysis	: NMR dated 09-Apr-2002 and GCMS dated 04-Dec-2001 (3M)
Date of expiry	: 31-Dec-2003
Date of production	: 16-Oct-2001
Date of receiving	: 16-May-2002
Appearance	: clear, colourless liquid
Purity	: 96.5 %
Density	: 1.74 g/cm ³
Storage conditions	: at approximately 5 °C in a refrigerator in a stainless steel vessel inerted with nitrogen
Dose suspension analysis	: Once at start of the study samples were taken by Analytical Toxicology. Three samples were taken per dose group (top, middle and bottom) and analyzed for concentration of test substance by GC (Dr. H-M. Kauffmann, Analytical Toxicology, ProTox).
Stability and homogeneity in the vehicle	: is guaranteed for 4 hours in sesame oil by GC analysis. (Report Dr. H.-M. Kauffmann, Aventis Pharma Deutschland GmbH, Protox – Analytik, dated 15-Aug-2002 and 21-Jan-2003 archived with the raw data)

5.2 TEST SYSTEM

Species of animals	: Rat
Strain of animals	: Hsd:Sprague Dawley (SD)
Origin (supplier) of animals	: Harlan Winkelmann GmbH Gartenstrasse 27 D-33178 Borcheln
Animal identification	: Tattoo number on tail, fur marking and cage numbering
Age at start of study	: approximately 6 weeks
Randomization procedure	: Computer generated algorithm (archived with raw data)

5.3 HOUSING AND CARE OF ANIMALS

Animal maintenance	: In transparent macrolon [®] cages (type IV) on soft wood granulate* in an air-conditioned rooms, 5 animals per cage, separated according to sex
Room temperature	: 22 ± 3 °C (except short lasting deviations due to disturbances of air condition)
Relative humidity	: 50 ± 20 % (except short lasting deviations due to disturbances of air condition)
Lighting times	: 12 hours light / dark cycle
Acclimatization	: at least five days
Food	: ssniff [®] R/M-H (V 1534)* ad libitum, except for the period in which the animals were kept in diuresis cages * (Composition see page 370)
Water	: Tap water* in plastic bottles ad libitum, except for the period in which the animals were kept in diuresis cages *

* Results of routine analyzes are available on request (data storage in archive).

5.4 RATIONALE FOR DOSE SELECTION

In a dose range finding study 3 male and 3 female rats received T-7758 at doses of 200 and 400 mg/kg body weight per day over a period of 14 days and were necropsied on day 15. There were no deaths throughout the study. From day 1 up to day 10 of the study the animals in both dose groups exhibited stilted and uncoordinated gait, squatting posture, and irregular respiration and discolored feces. Diarrhea was noted in one animal of the 200 mg/kg dose group. Stilted and uncoordinated gait was observed up to the end of the study in the 400 mg/kg dose group. An initial loss of body weight was noted up to study day 4. There were no macroscopically visible changes at final necropsy.

Based on these results, dose levels of 0, 15, 60 and 240 mg/kg body weight per day were selected for the present study in the first instance. However, following slightly emerging general clinical signs at 15 mg/kg bw, another low-dose group with 3 mg/kg body weight per day was selected for this study. As this low dose group also exhibited very slight clinical signs at the end of the observation period another low-dose group with 0.3 mg/kg, as well as another corresponding control group, was placed in this study.

5.5 EXPERIMENTAL DESIGN

Route of administration	: Oral by gavage
Application volume	: 5 mL/kg bw.
Vehicle	: Sesame oil
Frequency of administrations	: once daily
Duration of the study	: 29 days, 28 applications
Duration of recovery period	: 14 days

Table 1: Dose levels and number of animals

Group	Dose levels (mg/kg/bw./d)	Number of animals main groups		Nubmer of animals recovery groups	
		male	female	male	female
1	0.0	5	5	5	5
2	15.0	5	5	-	-
3	60.0	5	5	-	-
4	240.0	5	5	5	5
5*	3.0	5	5	-	-
6**	0.0	5	5	-	-
7**	0.3	5	5	-	-
* = 1 st additional dose group (group 5)					
** = 2 nd d additional dose group (group 7) and corresponding 2 nd control group (group 6)					

5.6 TEST GROUPS

At the beginning of the acclimatization period, the test animals were randomized and assigned to the following groups:

Table 2: Number of animals / Animal numbers

Group	Dose (mg/kg bw.)	Number of Animals		Animal number	
		males	females	males	females
1	0.0	10	10	1 – 10	31 – 40
2	15.0	5	5	11 – 15	41 – 45
3	60.0	5	5	16 – 20	46 – 50
4	240.0	10	10	21 - 30	51 - 60
5	3.0	5	5	61 - 65	66 - 70
6	0.0	5	5	71 - 75	81 - 85
7	0.3	5	5	76 - 80	86 - 90

Table 3: Cage numbers / Animal numbers

Group	Cage number	Animal number males	Cage number	Animal number females
1	1	1 - 5	7	31 – 35
	2	6 - 10	8	36 – 40
2	3	11 – 15	9	41 – 45
3	4	16 – 20	10	46 – 50
4	5	21 – 25	11	51 – 55
	6	26 - 30	12	56 - 60
5	13	61 - 65	14	65 - 70
6	15	71 - 75	17	81 - 85
7	16	76 - 80	18	86 - 90

5.7 PREPARATION OF THE TEST COMPOUND

Table 4: Formulation of the test compound

Group	Dose (mg / kg bw.)	Concentration in mg / mL	Volume applied (mL / kg bw.)	Vehicle
1	0.0	0.00	5	sesame oil
2	15.0	3.00	5	sesame oil
3	60.0	12.00	5	sesame oil
4	240.0	48.00	5	sesame oil
5	3.0	0.60	5	sesame oil
6	0.0	0.00	5	sesame oil
7	0.3	0.06	5	sesame oil

T-7758 was dissolved in the stated concentrations in sesame oil daily.

After each measurement of the body weight, the calculation of the application volume was repeated.

5.8 IN-LIFE OBSERVATIONS

5.8.1 Mortality

Survival control of the animals was examined twice daily (on weekends and public holidays once daily).

5.8.2 Clinical observations

Individual clinical observations were observed once daily.

5.8.3 Neurological examinations

Once before the first treatment and thereafter once a week detailed clinical observations were performed in all animals outside the home cage in a standard arena ('open field'). Each animal was assessed for changes in skin, fur, eyes, mucous membranes, occurrence of secretions and excretions and autonomic activity such as lacrimation, salivation, nasal discharge, piloerection, pupil size, and unusual respiratory pattern. Changes in gait, posture, and response to handling as well as the presence of clonic or tonic movements, tremor, and any other abnormal motor movements (such as excessive grooming, repetitive circling or other stereotypes) or bizarre behavior (e.g. self-mutilation, walking backwards) were also recorded. In addition, defecation and urination were evaluated.

At the termination of the study sensory reactivity to stimuli of different types (auditory, visual, and proprioceptive) was evaluated including startle reflex (click response), response to approach with the finger to the nose of the animal, and righting reflex. The presence and absence of pupillary constriction was assessed using a pen flashlight directed into the eye. Assessments of motor function were performed including measurement of motor activity, and forelimb and hindlimb grip strength. The animals were evaluated for motor activity during a 60-minute period in a 16-station automated motor activity-monitoring device (FMI, Föhr Medical Instruments GmbH). Activity counts were recorded by the interruption of photocells in 3-minute-intervals to give a total of 20 intervals. A strain gauge device (FMI, Föhr Medical Instruments GmbH) measured fore- and hindlimb grip strength.

5.8.4 Body weight

The body weights of all animals were determined before the start of the study and then twice weekly throughout the study.

5.8.5 Food consumption

Food consumption was determined continuously (two times per week).

5.9 CLINICAL PATHOLOGY

5.9.1 Hematological investigations

At the termination of the study and after the recovery period, hematological examinations were performed on all animals without previous withdrawal of food. Blood samples were taken from the retrobulbar venous plexus in narcosis (intraperitoneal injection of 67 + 6.7 mg/kg body weight Ketamine-Hydrochloride + Xylazine). In order to prevent systematic errors, blood sampling was conducted in a randomized order.

The abbreviations, units, instrumentation, and methodologies used for these tests are presented in the tables, page 37.

Hematology parameters evaluated consisted of the following:

Table 5: Red Cell Counts parameters evaluated

Erythrocyte counts (RBC)	Mean corpuscular hemoglobin (MCH)	Mean corpuscular volume (MCV)
Heinz Body Counts*		Reticulocyte counts
Hematocrit (packed cell volume)	Mean corpuscular hemoglobin concentration (MCHC)	
Hemoglobin		

* This parameter was only evaluated in the animals from the control and high dose group, as well as for the amended additional control, 3.0 and 0.3 mg/kg body weight groups.

Table 6: White Cell Counts parameters evaluated

Differential leukocyte counts	Leukocyte counts (WBC)

Table 7: Coagulation parameters evaluated

Coagulation time (clotting time)	Thrombocyte counts (platelets)

5.9.2 Clinical Chemistry

After blood sampling for hematological testing, the animals were killed by section of the vena cava cranialis in deep narcosis and exsanguinated. In order to prevent systematic errors, exsanguination was conducted in a randomized order.

The abbreviations, units, instrumentation, and methodologies used for these tests are presented in the tables, page 38.

Clinical chemistry parameters evaluated consisted of the following:

Table 8: Clinical Chemistry parameters evaluated

γ-Glutamyltranspeptidase	Bilirubin total	Potassium (K⁺)
Alanine Aminotransferase (ALAT)	Calcium	Sodium (Na⁺)
Albumin	Chloride (Cl⁻)	Total Protein
Albumin / Globulin ratio (calculated)	Cholesterol	Triglycerides
Alkaline Phosphatase	Creatinine	Urea
Aspartate Aminotransferase (ASAT)	Globulin (calculated)	Uric Acid
	Glucose	
	Inorganic Phosphorous	

Serum collection (as much as possible) for optional future analysis was amended by the Sponsor for optional further investigations. Spare serum was kept deep frozen in liquid nitrogen and sent on dry ice to the Sponsor's address, after necropsy. This is not part of the study.

5.9.3 Urinalysis

Urine analysis was performed in all animals a few days before termination of the study as well as before the end of the recovery period.

For this purpose, the urine was collected by using metabolism cages overnight. This was done from day 22 to day 23 for groups 1-4, from day 25 to day 26 for group 5, from day 23 to day 24 for groups 6 – 7, and from day 40 to day 41 for recovery groups 1 and 4. Food and water was withdrawn during this period.

The abbreviations, units, instrumentation, and methodologies used for these tests are presented in the tables, page 39.

Urinalysis consisted of the following:

Table 9: Urinalysis - Semiquantitative parameters evaluated

Appearance	Glucose	Protein
Bilirubin	Ketone bodies	Urobilinogen
Blood	Microscopic Examination	
Color	(Sediment)*	
	pH	

* This parameter was only evaluated in the animals from the control and high dose group, as well as for the amended additional control and 0.3 mg/kg groups.

Table 10: Urinalysis - Quantitative Parameters evaluated

Specific Weight	Volume

5.10 ANATOMIC PATHOLOGY

5.10.1 Necropsy and macroscopic examination

After exsanguination, all animals were necropsied and checked for macroscopically visible abnormalities. The autopsy included macroscopic examination of the skin, orifices, eyes, teeth, oral mucosa and internal organs. Also intercurrent died and moribund killed animals are necropsied and checked for macroscopically visible abnormalities.

All abnormal findings were recorded.

Endotracheal fixation of the lungs: The lungs, including part of the trachea, were removed. The lungs were then fixed endotracheally with a 4% neutral buffered formaldehyde (equals 10% formalin) solution using a needle inserted into the trachea. The instillation pressure was between 20 and 30cm water column. Following completion of the endotracheal fixation the lungs were fixed, together with the other organs, in formalin solution.

5.10.2 Organ weights

The following organs were weighed:

Table 11: List of weighed organs

Adrenals	Heart	Spleen
Brain	Kidneys	Testes
Epidymides	Liver	Thymus

Organs from animals found dead are not weighed, these organs were removed and preserved in a suitable fixative (4% neutral buffered formaldehyde).

5.10.3 Macroscopic and microscopic observations

The following tissues or organs (or pieces of them) were preserved in a suitable fixative (4% neutral buffered formaldehyde (equals 10% formalin solution) and processed for histopathological investigations:

Table 12: List of tissues fixed and submitted for histological examinations

Adrenals	Lungs	Stomach
Bone marrow / sternum	Lymph nodes 1 mandibular	Testes
Brain with medulla oblongata	Lymph nodes 2 iliac	Thymus
Epididymides	Nerve sciatic nerve	Thyroid gland with parathyroids
Heart	Ovaries with oviducts	Trachea
Small Intestine 2 jejunum	Prostate	Urinary bladder
Large Intestine 2 colon	Seminal vesicle	Uterus
Kidneys	Spinal cord 1 cervical	All other gross lesions
Liver	Spleen	

Organs and tissues intended for microscopic examination were embedded by conventional histological technique in Paraplast, and stained with Hematoxylin-Eosin.

Histopathological examinations were carried out from all control and high dose group animals, as well as from the 2nd additionally placed dose group 7 (0.3 mg/kg) and its corresponding control group 6. The latter results were reported in a separate addendum to the pathology report.

In addition, histopathological evaluation was performed on all macroscopic findings, on all organs of intercurrently died animals, and also on target organs such as kidneys, liver, spleen and thymus of all animals, due to histopathologic findings in the high dose group.

Extra liver tissues (> 5 grams, cut into 0.5-1.0g pieces) were requested by the sponsor and were kept deep frozen in liquid nitrogen and send to the Sponsor's address on dry ice for possible future analysis. This was not part of the study.

6 RESULTS

6.1 DOSE SOLUTION ANALYSIS

Table 13: Results of dose suspension analysis

Dose level (mg/kg/day)	0	0	0.3	3	15	60	240
Concentration (mg/ml)	0	0	0.06	0.6	3	12	48
	Analysed content (mean %)						
Day 1	n.d.	n.d.	99	95	107	114	108

n.d. = not detected

The anticipated concentrations were satisfactorily confirmed.

(Analytical report archived with the raw data)

6.2 IN-LIFE OBSERVATIONS

6.2.1 Designation of dose groups (pathology designation in brackets*)

The designated groups 1-7 had to be re-allocated for statistical analyses in Provantis/Aventox:

Table 14: Designation of the dose groups (1 - 5) for individual data

	Group 1 (Co*)	Group 2 (D1*)	Group 3 (D2*)	Group 4 (D3*)	Group 5 (D4*)
mg / kg bw. / d	0	15	60	240	3

Table 15: Designation of the dose groups (1 - 5) for statistical evaluation and figures

	Group 1 (Co*)	Group 2 (D4*)	Group 3 (D1*)	Group 4 (D2*)	Group 5 (D3*)
mg / kg bw. / d	0	3	15	60	240

Table 16: Designation of the dose groups (6 - 7) for individual data

	Group 6 (C1 / 06*)	Group 7 (D5 / 07*)
mg / kg bw. / d	0	0.3

Table 17: Designation of the dose groups (6 - 7) for statistical evaluation and figures

	Group 1 (C1 / 06*)	Group 2 (D5 / 07*)
mg / kg bw. / d	0	0.3

6.2.2 Behavior, state of health and mortality

One male (animal No. 30*) at 240 mg/kg was found dead on study day 42 (recovery period). This animal, which was in a bad general health condition, exhibited histopathological signs of severe immune-functional deficiency. This finding was considered the cause of death, and was considered compound-related.

* animal no. 30 was excluded from summaries on body weight and food consumption, as well as from final clinical pathology evaluation (day 43), however, was evaluated for urine analysis and neurobehavior, which were carried out during study week 3.

6.2.3 Clinical observation

Behavior and state of health remained unaffected by the administration of the test compound in the at 0.3 mg/kg and generally at 3 mg/kg body weight/day throughout the study. No opacity of the refracting media of the eyes, changes of the oral mucosa, or impairment of dental growth was observed in these groups.

Main clinical signs, considered compound-related, comprised the following:

At 0.3 mg/kg: No abnormalities

At 3,0 mg/kg: generally no abnormalities, apart from squatting posture and stilted gait from day 22 up to the end of study (day 29).

At 15 mg/kg: squatting postures, stilted and uncoordinated gait from day 15 up to the end of study (day 29)

At 60 mg/kg: Squatting postures, stilted and uncoordinated gait, drawn in flanks, swollen abdomen, within the 1st 10 days; feces and tray bedding discolored yellowish from day 4 up to the end of study.

At 240 mg/kg: Squatting postures, stilted and uncoordinated gait, drawn in flanks, swollen abdomen, within the 1st 10 days. Feces and tray bedding discolored yellowish from day 4 up to the end of study. Additionally: swollen snout (No. 27, 30), blood-colored encrusted snout (No. 27, 30) and lower or upper incisors broken-off (No. 28, 30, 59), stupor and coat bristling (No. 30).

Group incidence tables see page 63

6.2.4 Neurobehavioral examinations

Motoractivity was not influenced by administration of the test compound in all groups. However, forelimb and hindlimb grip strength was statistically significantly decreased for males at 60 and 240 mg/kg and for females at 240 mg/kg body weight/day.

(Figures page 53, Summary tables and Statistics page 195, Individual data page 351)

6.2.5 Body weight

Mean body weights were statistically significantly decreased from 60 mg/kg onwards from study day 5 until onwards, reaching minus 18/12% for males/females, respectively, at 240 mg/kg body weight/day as compared to the control at study day 29. This finding got worse in particular for the males during the recovery period (M/F: -40/-16%), i.e., there was no evidence of recovery. Accordingly, overall mean body weight gains were markedly lower in these groups as compared to the control.

Table 18: Mean body weight gains [g] throughout the study (Groups 1 - 5)

Treatment group [mg/kg bw.]	Control		3 mg/kg		15 mg/kg		60 mg/kg		240 mg/kg	
	males	females	males	females	males	females	males	females	males	females
day 1 to day 29	141.2	82.6	145.8	74.4	125.6	74.8	117.8	66.6	84.4	59.4
day 29 to day 43	34.8	12.6	-	-	-	-	-	-	-36.0	2.0

Table 19: Mean body weight gains [g] throughout the study (Groups 6 - 7)

Treatment group [mg/kg bw.]	Control		0.3 mg/kg	
	males	females	males	females
day 1 to day 29	156.4	66.0	165.6	73.8

(Figures page 41, Summary tables and Statistics page 105, Individual data page 203)

6.2.6 Food consumption

Food consumption remained unaffected by the administration of the test compound throughout the study in all dose groups, except for recovery males (240 mg/kg), which exhibited moderately lower food intake during the recovery period as compared to the controls.

Table 20: Mean food consumption [g/kg bw./day] throughout the study (Group 1 - 5)

Treatment group [mg/kg bw.]	Control		3 mg/kg		15 mg/kg		60 mg/kg		240 mg/kg	
	males	females	males	females	males	females	males	females	males	females
day 1 to day 29	82.02	78.14	82.14	74.62	76.22	76.37	78.38	74.31	74.61	78.91
day 29 to day 43	65.81	68.39	-	-	-	-	-	-	50.98	72.40

Table 21: Mean food consumption [g/kg bw./day] throughout the study (Group 6 - 7)

Treatment group [mg/kg bw.]	Control		0.3 mg/kg	
	males	females	males	females
day 1 to day 29	86.78	76.42	84.06	75.86

(Figures page 47, Summary tables page 117, Individual data page 218)

6.3 CLINICAL PATHOLOGY

6.3.1 Hematology

Final hematology revealed the following changes of statistical and/or possible toxicological significance:

- reduced blood coagulation time (for females from 15 mg/kg onwards; finding was slightly outside the range of the historical control data, however, was not dose-related, was not observed in males, and hence, considered equivocal.
- slightly lower white blood cell (WBC) counts (for males at 240 mg/kg, not statistically significant)

Hematology at the end of the recovery period revealed the following changes of statistical and/or possible toxicological significance:

- increased red blood cell (RBC) counts (for recovery males, tendency also for females, both at 240 mg/kg)
- decreased reticulocytes (for recovery males, tendency also for females, both at 240 mg/kg)
- markedly lower WBC counts (for recovery males, at 240 mg/kg)

(Summary tables and Statistics page 125, Individual data page 233, Historical control data page 372).

6.3.2 Clinical chemistry

Final clinical chemistry revealed the following changes of statistical and/or possible toxicological significance:

- decreased triglycerides (males, 240 mg/kg; outside the range of historical control (HC) data)
- increased alanine aminotransferase (ALAT) activity (for males from 60 mg/kg, and for both genders at 240 mg/kg)
- increased gamma-glutamyltransferase (gGT) activity (for females, tendency also for males, both at 240 mg/kg)
- increased sodium (for females from 60 mg/kg onwards, outside the range of historical control data)
- increased albumin/globulin ratio (for females from 60 mg/kg onwards, tendency also for males at 240 mg/kg)

Clinical chemistry at the end of the recovery period revealed the following changes of statistical and/or possible toxicological significance:

- increased sodium and chloride (recovery males at 240 mg/kg)
- decreased potassium at 240 mg/kg for recovery males, increased for recovery females, hence, considered equivocal
- increased protein, albumin and globulin at 240 mg/kg for recovery males, decreased/or no finding for females, hence considered equivocal
- decreased alkaline phosphatase at 240 mg/kg for recovery males
- decreased calcium, increased phosphorus at 240 mg/kg for recovery females, not seen in males, considered equivocal
- distinctly decreased triglycerides at 240 mg/kg for recovery females, outside the range of HC-data, also decreased for recovery males (statistical evaluation not possible)
- distinctly decreased glucose at 240 mg/kg for recovery males, outside the range of HC-data

In addition, sporadic statistically significant changes were noted at 0.3 mg/kg body weight/day as compared to the respective control group, regarding sodium, potassium, phosphorus, total protein, albumin, alkaline phosphatase activity. All these changes were marginal and all within the range of the in-house historical control data. Moreover, no corresponding changes were seen at 3.0 or 15 mg/kg body weight/day. Hence, they were considered incidental.

(Summary tables and Statistics page 145, Individual data page 280, Historical control data page 372).

6.3.3 Urinalysis

Urinalyses revealed statistically significantly increased urine volume for males at 240 mg/kg. This finding was also observed for the females of this group, however, without being statistically significant due to high standard deviation. Apart from this finding urinalysis remained unaffected by administration of the test compound in all groups.

The urine sediment was generally unobtrusive in control- and 240 mg/kg-dosed animals. As an exception, the male No. 25 and female Nos. 51 and 59 (at 240 mg/kg) exhibited slightly higher leucocyte counts (degree 6-10), which in the absence of other clinical correlates was considered not toxicologically relevant.

(Summary tables and Statistics page 165, Individual data (including legende) page 310, Historical control data page 372).

6.4 ANATOMIC PATHOLOGY

6.4.1 Organ weights

Evaluation of mean absolute organ weights revealed the following changes of statistical and/or possible toxicological significance:

- increased liver weight (from 60 mg/kg body weight/day onwards, both genders)
- decreased spleen weight (at 15 mg/kg [males], and from 60 mg/kg onwards [both genders], also recovery males)
- decreased thymus weight (at 240 mg/kg, both genders), also recovery males
- increased kidney weight (for females from 60 mg/kg onwards)
- increased adrenal weight (for males at 240 mg/kg, outside the HC range, not observed for females, relevance considered equivocal)

Further mean absolute organ weight changes of statistical significance, i.e. for heart, brain, liver [recovery males], epididymis and kidneys [recovery], were considered due to the markedly decreased terminal body weight at 60 and 240 mg/kg body weight/day, and hence considered not toxicologically significant.

6.4.2 Relative organ weights

Evaluation of mean organ weights relative to terminal body weight revealed the following changes of statistical and/or possible toxicological significance:

- increased liver weight (from 60 mg/kg onwards, both genders, (M/F up to 49/87%))
- increased testes and brain weight (males at 240 mg/kg, testes also at 60 mg/kg, both findings possibly due to reduced terminal body weight as these organ weight changes do not go with body weight, of minor relevance)
- decreased thymus weight at 240 mg/kg for males, tendency also in females
- increased kidney weight (for females from 60 mg/kg onwards)
- decreased spleen weight (dose-related, for females from 60 mg/kg onwards)
- increased adrenal weight (males at 240 mg/kg, outside the HC-data range, also for recovery males, not observed in females)

Further mean relative organ weight changes of statistical significance at recovery, i.e. for testes and epididymis and brain were considered due to terminal body weight changes at recovery necropsy, and hence considered not toxicologically significant.

(Summary tables and Statistics page 173, Individual data page 336, Historical control data page 372).

6.4.3 Macroscopic observations

Relevant macroscopic changes were recorded for male or female animals of the following groups:

Group 4 (D3, 240 mg/kg):

K0/K0 animals:

Discoloured kidneys in three females (no. 52, 54, 55) and all 5 males, one *enlarged stomach* (male no. 24), two *enlarged livers* (females no. 51, 54), and one *opaque eye* in female no. 55.

R1/R1 animals:

Small accessory genital glands (prostate and/ or seminal vesicle) in no. 26, 27 and 28. Additionally, male no. 28 exhibited a *small thymus* and *enlarged adrenal glands*. An *irregular surface* could be observed on the *kidney* of male no. 28 as well as female no. 59.

R1/+1 animal (was found dead):

Small accessory genital glands (prostate and seminal vesicle) in combination with *small testes* and *epididymides*.

Group 3 (D2, 60 mg/kg):

K0/K0 animals:

Discoloured kidneys in four males (no. 17-20), and four females (no. 46, 47, 49, 50), and a *discoloured duodenum* in female no. 46.

Group 2 (D1,15 mg/kg):

K0/K0 animals:

Discoloured kidneys in three males (no. 11, 14 and 15), and female no. 45.

Group 5 (D4, 3 mg/kg):

K0/K0 animals:

Transparent margins in the *liver* of female animal no. 68.

Group 7 (D5, 0.3 mg/kg) as compared to control group 6 (C1):

There were no gross pathology findings, which could be related to administration of the test compound in the low dose group.

6.4.4 Microscopic observations

Animal no. 30 (group 4; 240 mg/kg, recovery) was found dead one day before termination of the recovery period (study day 42). Although autolysis was evident, microscopic examination indicated severe lymphocyte depletion in spleen, thymus and lymph nodes as cause of death. This finding was considered test-article related.

Relevant histopathological findings at scheduled necropsy (terminal and/or recovery) were seen in the following organs:

Liver: *Hypertrophy of hepatocytes* in nearly all animals at 240 mg/kg body weight/day (D3) at terminal necropsy.

Spleen: *Lymphocyte depletion* in the animals at 240 mg/kg (D3): one male at terminal necropsy, and two male at recovery necropsy.

Thymus: *Atrophy* in three males at 240 mg/kg (D3) at recovery necropsy.

Iliac lymph node: *Lymphoid cell depletion* in one animal at 240 mg/kg (D3), which died during the recovery.

Testes/ Epididymides: *Atrophy* in animal no. 30 (unscheduled death).

Prostate/ Seminal Vesicles: *Atrophy* in three animals (240 mg/kg, D3, recovery necropsy).

Findings in the **kidneys** were also noted and included *tubular changes*. These findings were sporadically seen in males and females with special focus at 240 mg/kg (D3) and at 60 mg/kg (D2) at the terminal sacrifice. A *nephroblastoma* could be detected in one female at 240 mg/kg (D3).

One male and one female at 240 mg/kg (D3) exhibited a *chronic nephropathy* at recovery necropsy.

The other findings should be discussed as spontaneous, they occurred in the control group, too, or could relatively often be observed in historical controls.

Sporadic changes in form of *cellular infiltrates / inflammatory foci* were observed in the **lungs** and **liver** of single animals of different groups. At 240 mg/kg (D3) (terminal sacrifice) a *submucosal edema* in the **forestomach**, a *dilatation* of the **uterus**, and an *enlarged epithelium* of the **cornea**, could be observed in different animals.

There were no histopathological findings at 0.3 mg/kg body weight/day (D5 /07), which could be related to administration of the test compound as compared to the respective control (C1 /06).

Sporadic changes in form of *dilatation* and *cellular infiltration* could be observed in the **uterus** of animal no. 89 (group D5/07). Single control animals (group C1/06) exhibited *tubular dilatation* in the **kidney** (no. 71), or *cellular infiltrations* in the **lungs** (no. 83) or glandular **stomach** (no. 75)

(Pathology report, page 375)

7 DISCUSSION

T-7758 induced late-occurring mortality in one male (240 mg/kg) and signs of poor general health condition at 240 mg/kg, and clinical findings such as squatting posture, stilted and uncoordinated gait, drawn in flanks and swollen abdomen, from 60 mg/kg body weight/day onwards. These signs increased in incidence and severity during both, the treatment and recovery periods. A threshold dose for clinical observations was identified at 3 mg/kg. In addition, the male, which was found dead on study day 42, exhibited histopathological signs of severe immune-functional deficiency.

Associated with these clinical observations were impairments of neurobehavior (reduced fore- and hindlimb grip strength) and body weight development from 60 mg/kg onwards as compared to the controls (M/F up to -18/-12% at the end of treatment, and -40%/-16% after recovery, at 240 mg/kg). The males were slightly more affected than the females. Food consumption remained unaffected, except of the high dose males, during recovery.

Major clinical pathology findings at 240 mg/kg comprised lower white blood cell (WBC) counts (in particular for recovery males), decreased triglycerides, increased liver enzyme activity (ALAT, gamma-GT), changes in the albumin/globulin ratio and the mineral household (sodium, potassium, calcium/phosphorus), as well as increased urinary volume. A threshold dose for clinical pathology findings was identified at 60mg/kg body weight.

Anatomic pathology: The 4-week oral gavage administration of T-7758 caused severe alterations in the target organs and unscheduled death at 240 mg/kg body weight/day one day before the end of the experiment.

One of the central organ systems involved in the toxicity of the test article were the “manufacturing plants” of white blood cells, particularly the thymus, but also spleen and lymph nodes, which exhibited a loss of white blood cells in the animals at 240 mg/kg. This effect could only be observed in some males at 240 mg/kg. A comparable effect (tubular atrophy) could be observed in the testes of one recovery group animal (240 mg/kg), which was found dead on study day 42. Both kinds of tissue demonstrate this reaction during the recovery period, following loss of their mature cells.

At terminal sacrifice hepatocellular hypertrophy was observed at 240 mg/kg, which had reversed after the 14-day recovery period.

The kidney was identified as another target organ of the test compound. Although it showed a more or less diffuse picture regarding incidence and evidence of its tubular alterations - which is not uncommon in particular for the male Sprague Dawley rat – the severity grades of these findings were distinctly higher at 60 and 240 mg/kg body weight/day (D2 and D3).

8 CONCLUSION

In conclusion, repeated administration of 240 mg T-7758/kg body weight induced severe clinical signs (and mortality) incl. changes in neurobehavior, marked impairment of body weight development, as well as clinical pathology findings, which were associated with liver enzyme induction/toxicity, kidney toxicity, and immunological disfunction. A threshold dose of 60 mg/kg body weight was identified for these severe findings. First general clinical signs at 15 and 3.0 mg/kg body weight did not show any clinical- and/or anatomic pathology correlates.

With regard to the present study the 'No Observed Effect Level' (NOEL) is 0.3mg/kg body weight per day.

Based on the results of this study, T-7758 should be classified as 'harmful' "Xn", with risk phrase R48/22, "Danger of serious damage to health by prolonged (oral) exposure", according to the EU-Directive 2001/59/EC.

9 REFERENCES

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Heinz Bodies

Microscopic, brilliant cresyl blue staining, Merck, Klin. Labor, p. 28 (1974)

9.2 CLINICAL CHEMISTRY METHODS

Bilirubin total

JENDRASSIK L., Grof P., Biochem J 297, 81-89 (1938)

PRELLWITZ W., Klinisch-chemische Diagnostik, 2. Aufl., Thieme, 18 (1976)

RICHTERLICH R., COLOMBO J.P., Klinische Chemie, 4. Aufl., karger, Basel, 485-486 (1978)

Examinations using Vitros 950 Analyzer

SONNTAG O., analytical element, coated on a support, Trockenchemie, Thieme Verlag, Stuttgart (1988)

9.3 URINALYSIS

Clinitek Atlas: Reagenzienpackung, Bayer Diagnostics GmbH, München

Sediment

Microscopic examination (without staining) HALLMANN, Klinische Chemie u. Mikroskopie, 189-202, Stuttgart (1980)

9.4 STATISTICAL EVALUATION

All Parameters

The assumption of a monotonic dose-response relationship for all parameters justifies the restriction of the significance level to 5 percent (per parameter and sex), using the method of: HOTHORN L, LEHMACHER W.: A Simple Testing Procedure "Control versus k Treatments" for One-sided Ordered Alternatives, with Application in Toxicology, Biom. J. 33, 179-189, Akademie Verlag

Bodyweights: The changes of parameter values compared to the treatment-free baseline values are analyzed. The baseline values themselves are not statistically evaluated, since by definition no treatment effect can be present at this stage. Method used:

t-Test:

HARTUNG J., ELPERT B., KLÖSENER K. H., Lehr- und Handbuch der angewandten Statistik (1989), R. Oldenbourg Verlag, München

Clinical Pathology Data: In dog studies, the changes of parameter values compared to the treatment-free preliminary values are analyzed. The preliminary values themselves are not statistically evaluated, since by definition no treatment effect can be present at this stage. In rat studies, the absolute values are analyzed.

Wilcoxon's Test:

HOLLANDER M., WOLFE, D. A.: Nonparametric statistical methods; Wiley Series in Probability and Mathematical Statistics (1973), John Wiley & Sons Inc., New York, with the exact distribution after

STEITBERG B, RÖHMEL J.: Exakte Verteilung für Rang- und Randomisierungstests im allgemeinen Stichprobenproblem, EDV in Medizin und Biologie 18, 12-19 (1987), Verlag Eugen Ulmer GmbH & Co., Stuttgart; Gustav Fisher Verlag KG, Stuttgart

Organ weights (absolute): t-Test

(HARTUNG J., ELPERT B., KLÖSENER K.H., Lehr- und Handbuch der angewandten Statistik (1989), R. Oldenbourg Verlag, München

Organ weights (relative to bodyweight): Wilcoxon's Test

HOLLANDER M., WOLFE, D.A.: Nonparametric statistical methods; Wiley Series in Probability and Mathematical Statistics (1973), John Wiley & Sons Inc., New York, with the exact distribution after

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10 TABLES

10.1 ABBREVIATIONS, UNITS AND METHODOLOGY

10.1.1 Hematology

10.1.1.1 Red cell count

Abbreviation	Parameter	Units	Methodology/Instrumentation	Ref. see page
Hemato-crit	Hematocrit	Unity	Advia 120 Bayer Diagnostics GmbH	35
Hemo-globin	Hemoglobin	g/l	Advia 120 Bayer Diagnostics GmbH	35
MCH	Mean Corpuscular Hemoglobin	10 ⁻¹² g (pg)	Advia 120 Bayer Diagnostics GmbH	35
MCHC	Mean Corpuscular Hemoglobin Concentration	g/l	Advia 120 Bayer Diagnostics GmbH	35
MCV	Mean Corpuscular Volume	10 ⁻¹⁵ l (fl)	Advia 120 Bayer Diagnostics GmbH	35
Red cell count	Red blood cell count (Erythrocyte count)	x10 ¹² /l	Advia 120 Bayer Diagnostics GmbH	35
Reticulo-cytes	Reticulocyte count	Unity	Advia 120 Bayer Diagnostics GmbH	35
Heinz Bodies	Heinz body count	Unity	Microscopic	35

10.1.1.2 White cell count

Abbreviation	Parameter	Units	Methodology/Instrumentation	Ref. see page
	Relative Differential Leukocyte Count	Unity	Advia 120 Bayer Diagnostics GmbH	35
White cell count	White blood cell count (Leucocyte count)	10 ⁹ /l	Advia 120 Bayer Diagnostics GmbH	35

10.1.1.3 Blood coagulation

Abbreviation	Parameter	Units	Methodology/Instrumentation	Ref. see page
Plate-lets	Platelet Count (Thrombocytes count)	10 ⁹ /l	Advia 120 Bayer Diagnostics GmbH	35
Coagul. time	Coagulation time (Clotting time)	s	Watch glass method	35

10.1.2 Clinical chemistry

Abbreviation	Parameter	Units	Methodology/Instrumentation	Ref. see page
G-Gluta. Transf. (γ-GT)	γ-Glutamyltranspeptidase	U/l	Vitros 950 Ortho Clinical Diagnostics	35
ALAT	Alanine Aminotransferase	U/l	Vitros 950 Ortho Clinical Diagnostics	35
Albumin	Albumin	g/l	Vitros 950 Ortho Clinical Diagnostics	35
Alb/Glob Ratio	Albumin Globulin Ratio		Calculated: (Albumin / Globulin)	
AP	Alkaline Phosphatase	U/l	Vitros 950 Ortho Clinical Diagnostics	35
ASAT	Aspartate Aminotransferase	U/l	Vitros 950 Ortho Clinical Diagnostics	35
Total Biliru.	Bilirubin, total	μmol/l	Cobas Mira Centrifugal Analyzer ABX Diagnostics	35
Calcium (Ca)	Calcium	mmol/l	Vitros 950 Ortho Clinical Diagnostics	35
Chloride (Cl)	Chloride	mmol/l	Vitros 950 Ortho Clinical Diagnostics	35
Chole- sterol	Cholesterol	mmol/l	Vitros 950 Ortho Clinical Diagnostics	35
Creati- nine	Creatinine	μmol/l	Vitros 950 Ortho Clinical Diagnostics	35
Globulin	Globulin	g/l	Calculated: (Total Protein - Albumin)	
Glucose	Glucose	mmol/l	Vitros 950 Ortho Clinical Diagnostics	35
Phos- phorus	Inorganic Phosphorus	mmol/l	Vitros 950 Ortho Clinical Diagnostics	35
Potas- sium (K)	Potassium	mmol/l	Vitros 950 Ortho Clinical Diagnostics	35
Sodium (Na)	Sodium	mmol/l	Vitros 950 Ortho Clinical Diagnostics	35
Total Protein	Total Protein	g/l	Vitros 950 Ortho Clinical Diagnostics	35
Triglyce- rides	Triglycerides	mmol/l	Vitros 950 Ortho Clinical Diagnostics	35
Urea Nitrogen	Urea Nitrogen	mmol/l	Vitros 950 Ortho Clinical Diagnostics	35
Uric Acid	Uric Acid	μmol/l	Vitros 950 Ortho Clinical Diagnostics	35

10.1.3 Urinalysis (semiquantitative parameters evaluated)

Abbreviation	Parameter	Units	Methodology/Instrumentation	Ref. see page
Urine Color	Urine Color		Clinitek Atlas Bayer Diagnostics GmbH	35
Appearance	Appearance of Urine		Clinitek Atlas Bayer Diagnostics GmbH	35
pH Value	pH Value (sq)		Clinitek Atlas Bayer Diagnostics GmbH	35
Protein	Protein (Albumine) (sq)		Clinitek Atlas Bayer Diagnostics GmbH	35
Glucose	Glucose (sq)		Clinitek Atlas Bayer Diagnostics GmbH	35
Ketone Bodies	Ketone Bodies (sq)		Clinitek Atlas Bayer Diagnostics GmbH	35
Bilirubin	Bilirubin (sq)		Clinitek Atlas Bayer Diagnostics GmbH	35
Blood (RBCs)	Blood (RBCs) (sq)		Clinitek Atlas Bayer Diagnostics GmbH	35
Urobilinogen	Urobilinogen (sq)		Clinitek Atlas Bayer Diagnostics GmbH	35
Microscopy of Sediment			Microscope, without staining	35

10.1.4 Urinalysis (quantitative parameters evaluated)

Abbreviation	Parameter	Units	Methodology/Instrumentation	Ref. see page
Volume	Volume	ml	Graduated Tube	
Specific Weight	Specific Weight	g/l	Clinitek Atlas Bayer Diagnostics GmbH	35

10.2 LIST OF ABBREVIATIONS USED IN THE REPORT

approx.	: Approximately
bw.; bdwt	: Body weight
d	: Day
M (m)	: Male
F (f)	: Female
GLP	: Good Laboratory Practice
GC	: Gas Chromatograph
ID	: Identification
incl.	: Includes
LASW	: Life Animal Safety Welfare
max.	: Maximum
min.	: Minimum
N (n)	: Number of animals
Rpm	: Rotation per minute
S.D.	: Standard deviation
STATS	: Statistical evaluations
K0/K0 animals	: Terminal sacrifice group
R1/R1 animals	: Recovery / post-treatment group
R1/+1 animal	: Recovery / post-treatment group / Found death

11 FIGURES

11.1 BODY WEIGHT (GROUPS 1 - 5)

Toxicology Study Report - PT02-0222

ATOX 10.2

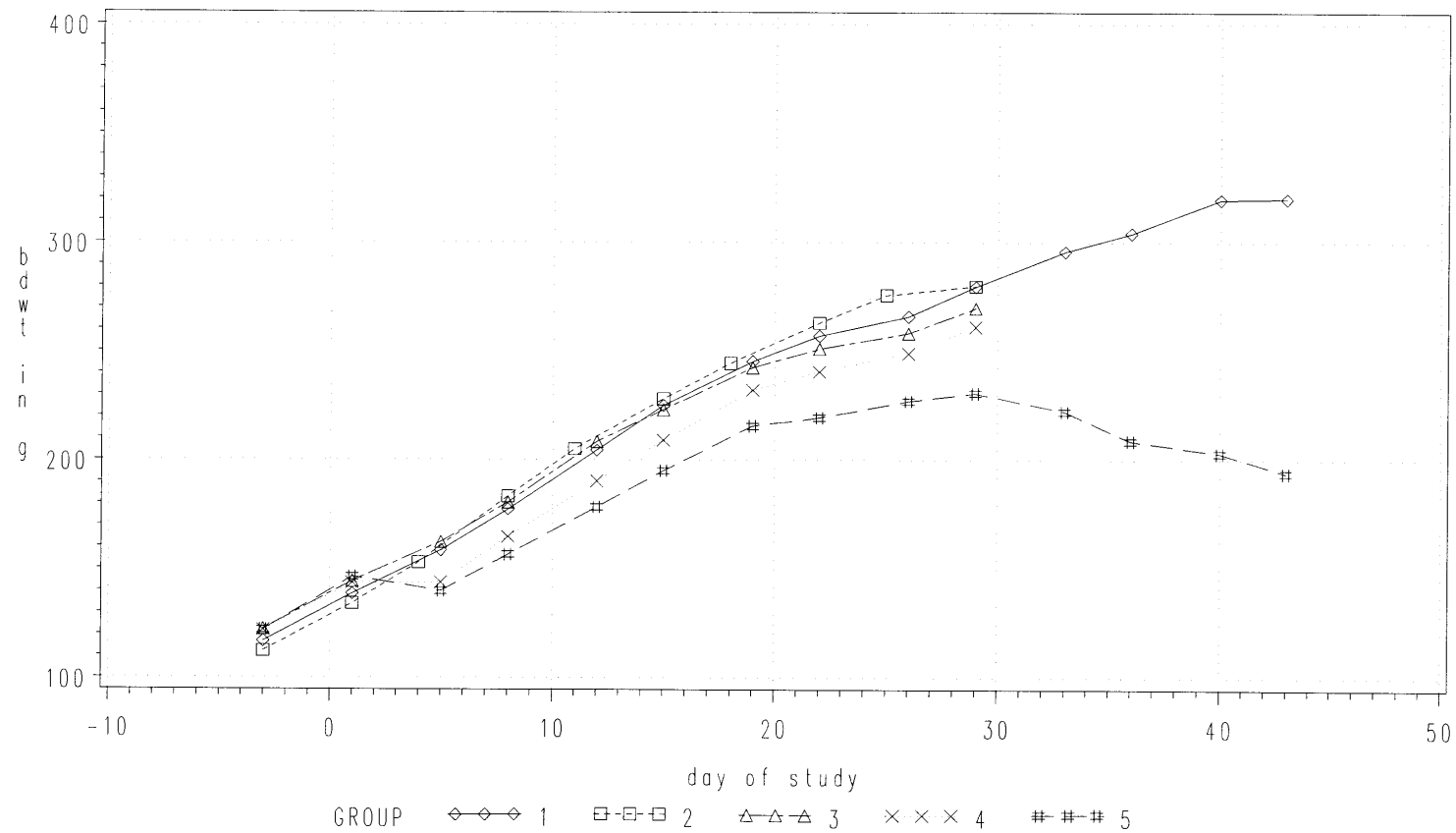
PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

BODYWEIGHT (MALE ANIMALS)



ATOX 10.2

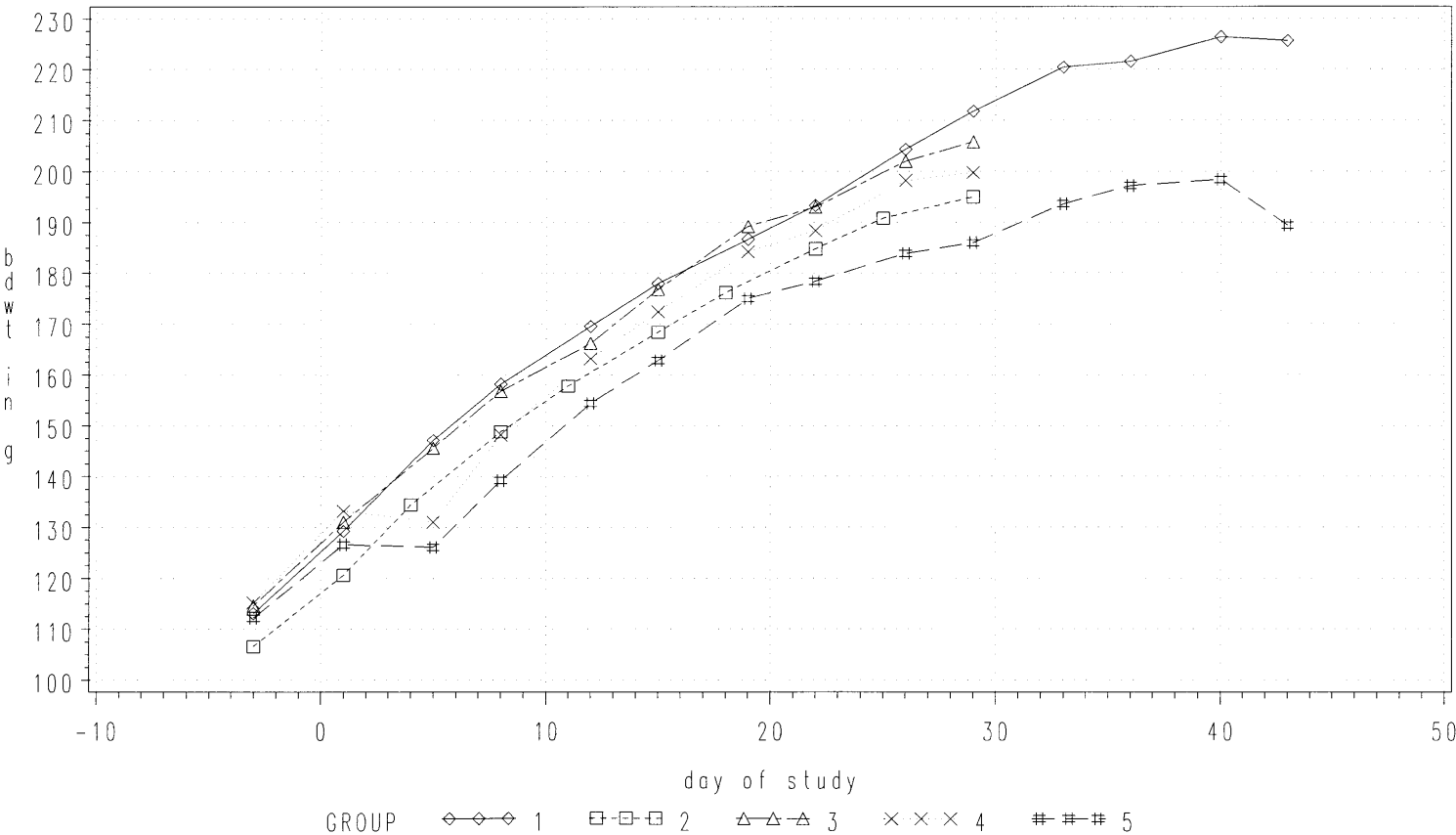
PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

BODYWEIGHT (FEMALE ANIMALS)



11.2 BODY WEIGHT (GROUPS 6 - 7)

ATOX 10.2

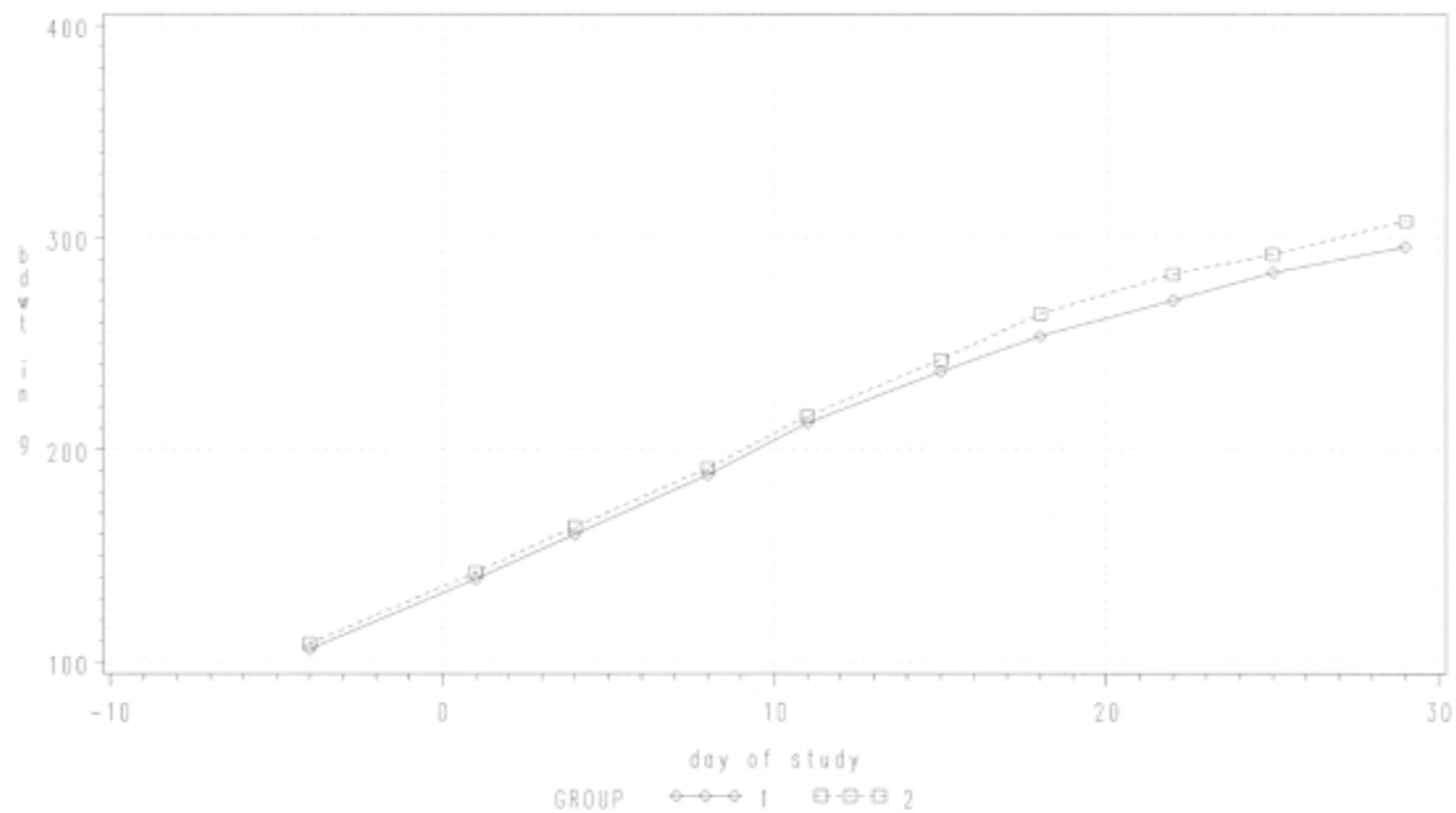
PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

BODYWEIGHT (MALE ANIMALS)



ATOX 10.2

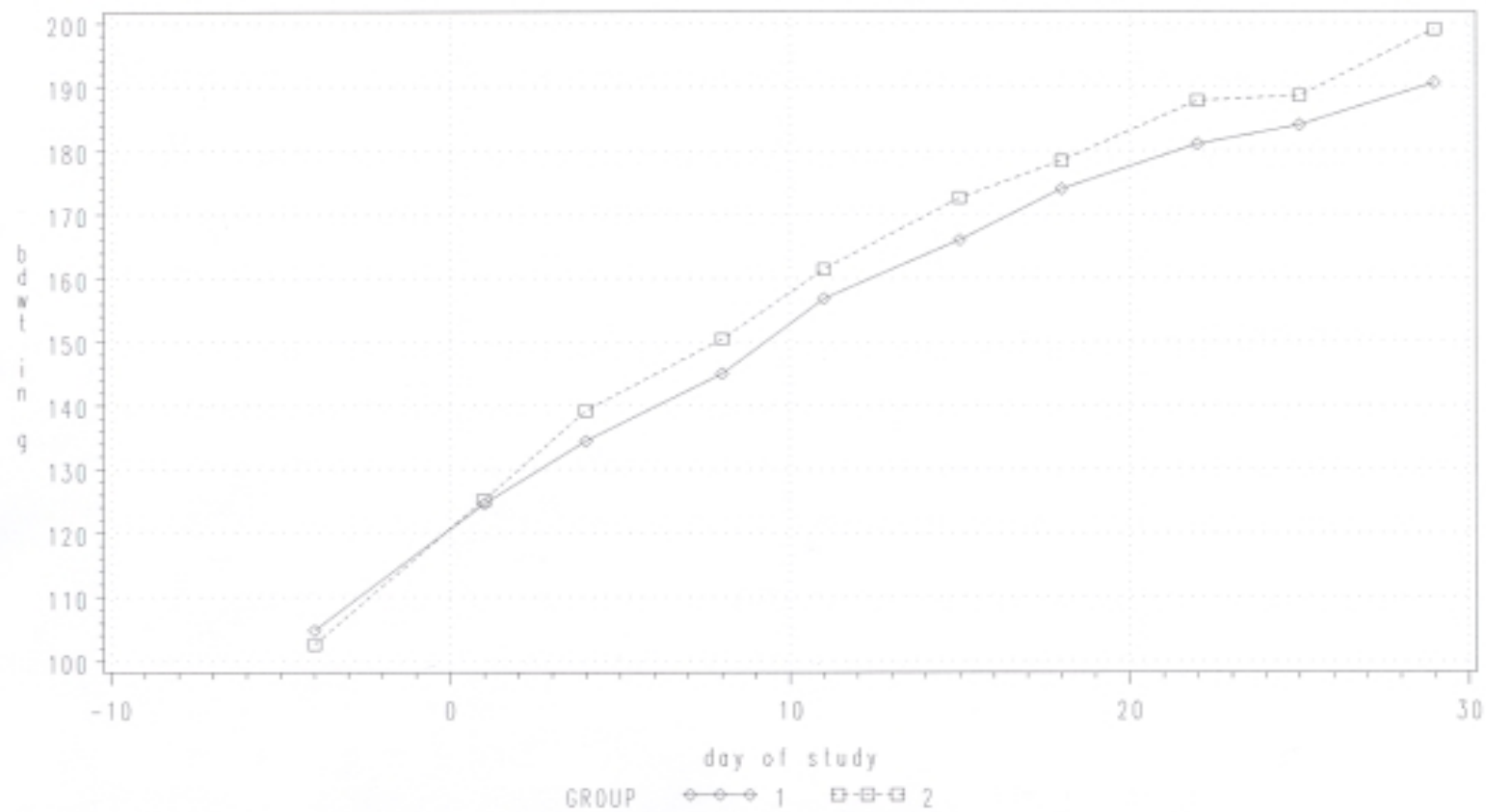
PROVANTIS

RUN DATE: 05-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

BODYWEIGHT (FEMALE ANIMALS)



11.3 FOOD CONSUMPTION (GROUPS 1 - 5)

ATOX 10.2

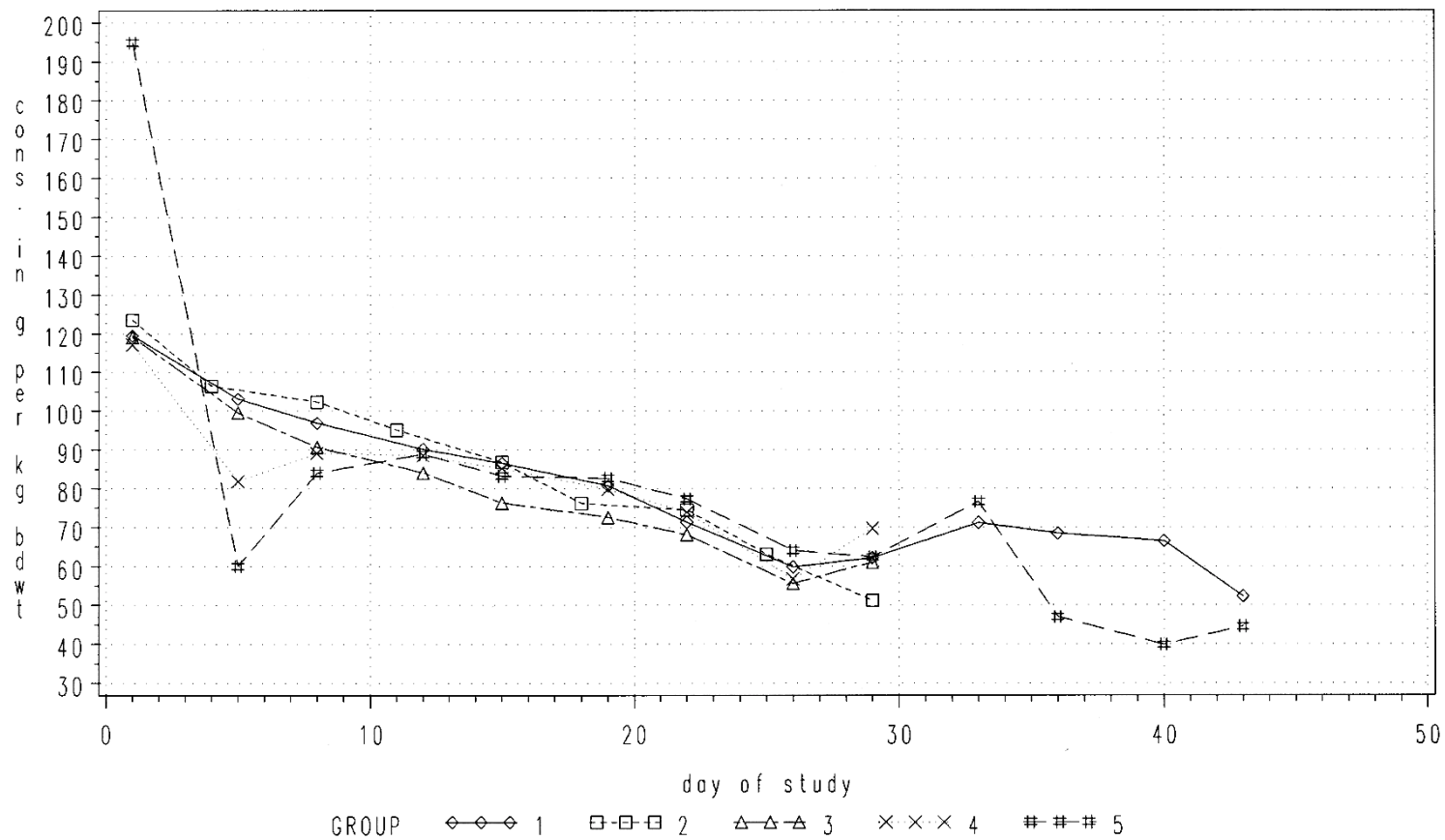
PROVANTIS

RUN DATE: 28-MAY-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FOOD CONSUMPTION (MALE ANIMALS)



ATOX 10.2

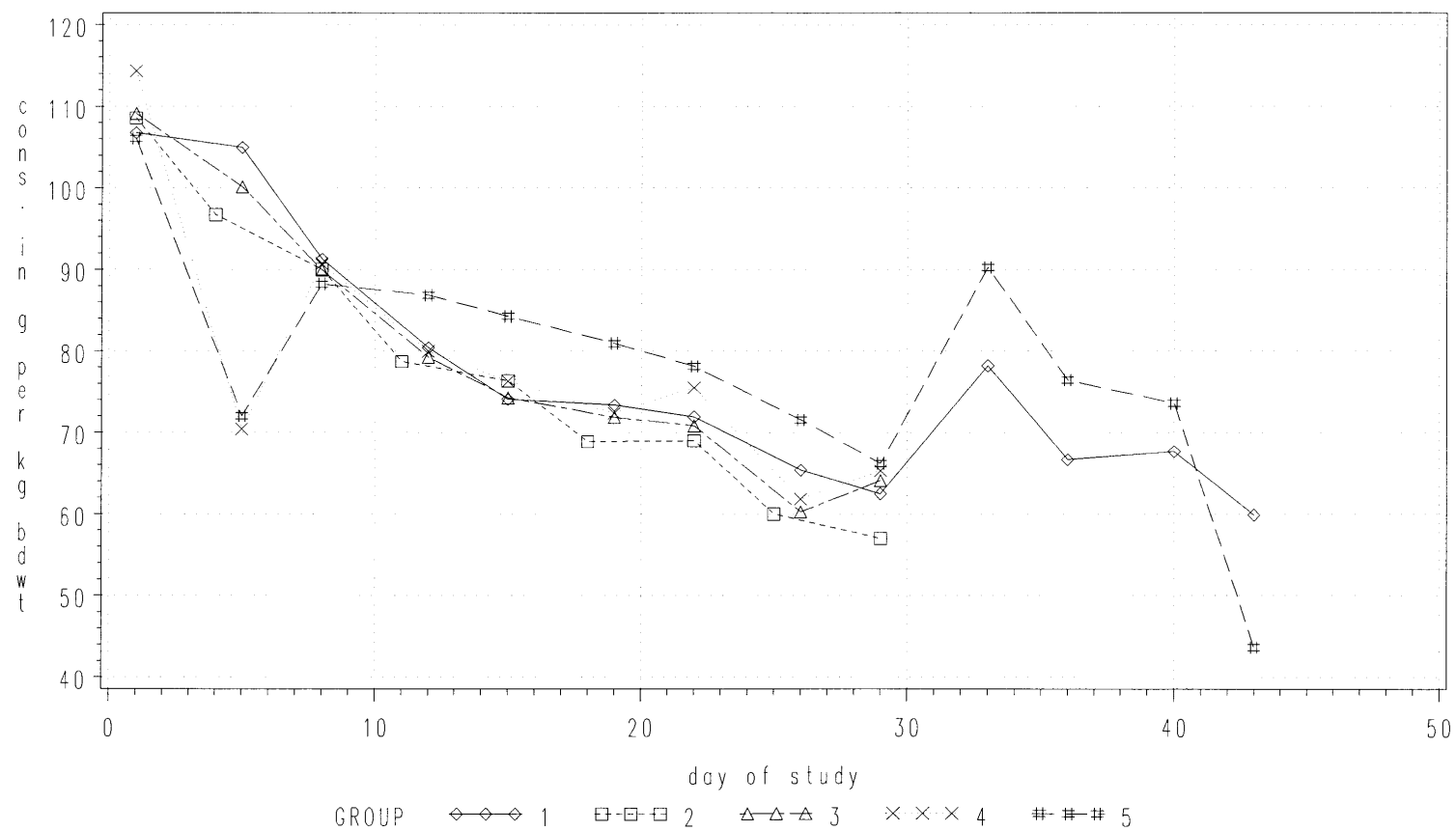
PROVANTIS

RUN DATE: 17-DEC-2002

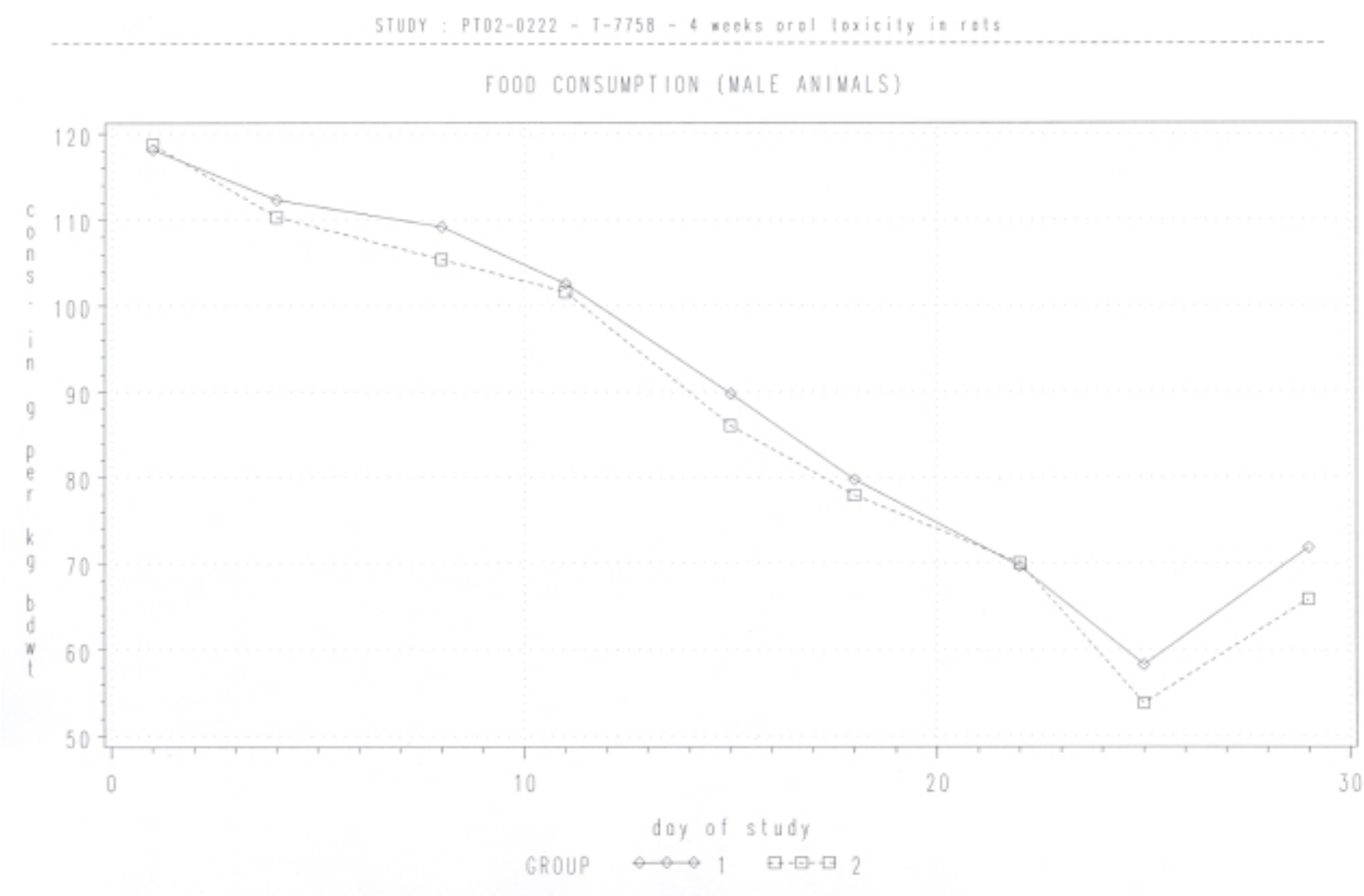
SUMMARY AND STATISTICAL EVALUATION

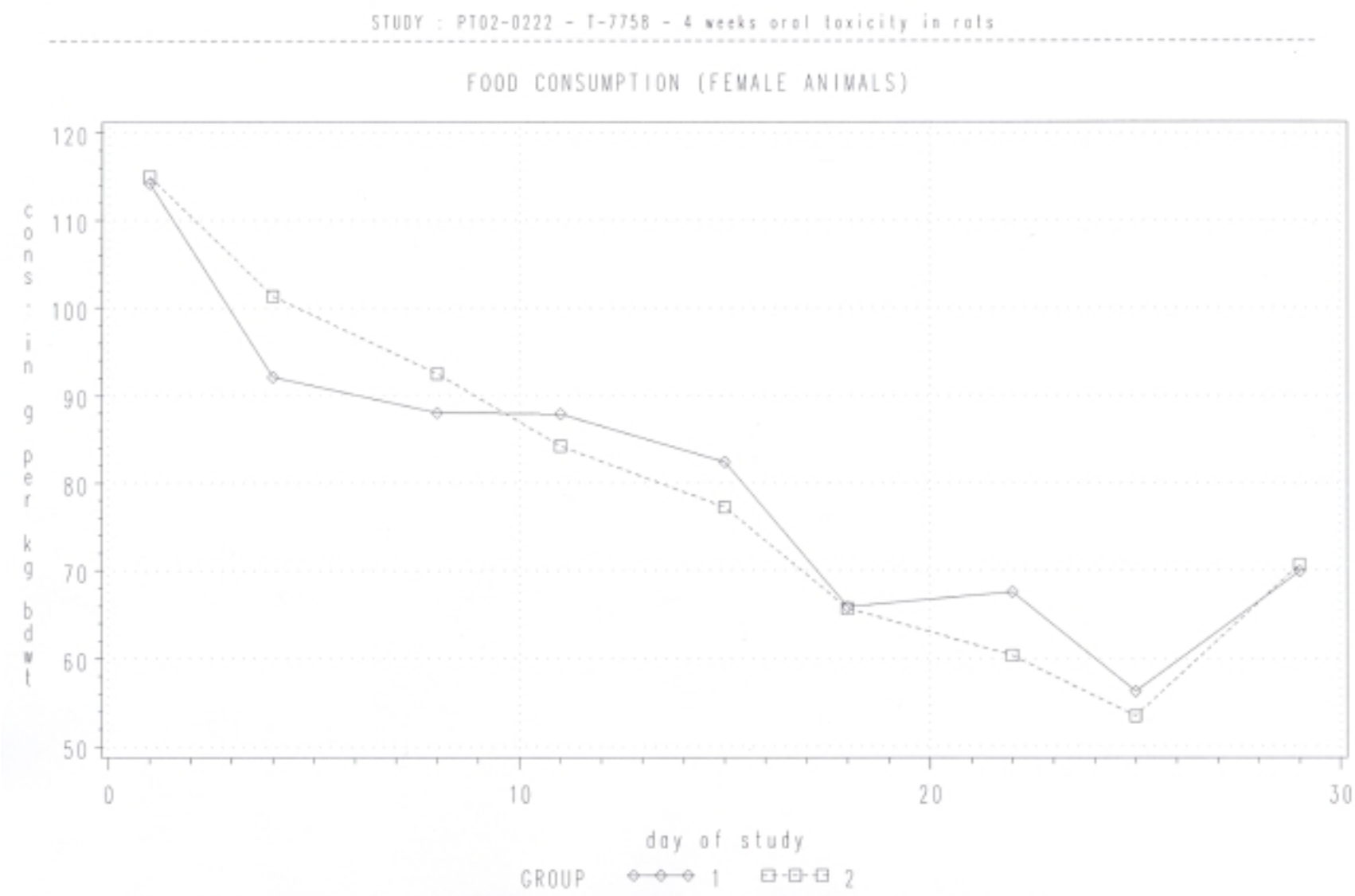
STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FOOD CONSUMPTION (FEMALE ANIMALS)



11.4 FOOD CONSUMPTION (GROUPS 6 - 7)





11.5 NEUROTOXICOLOGICAL EXAMINATIONS (GROUPS 1 - 5)

Toxicology Study Report - PT02-0222

ATOX 10.2

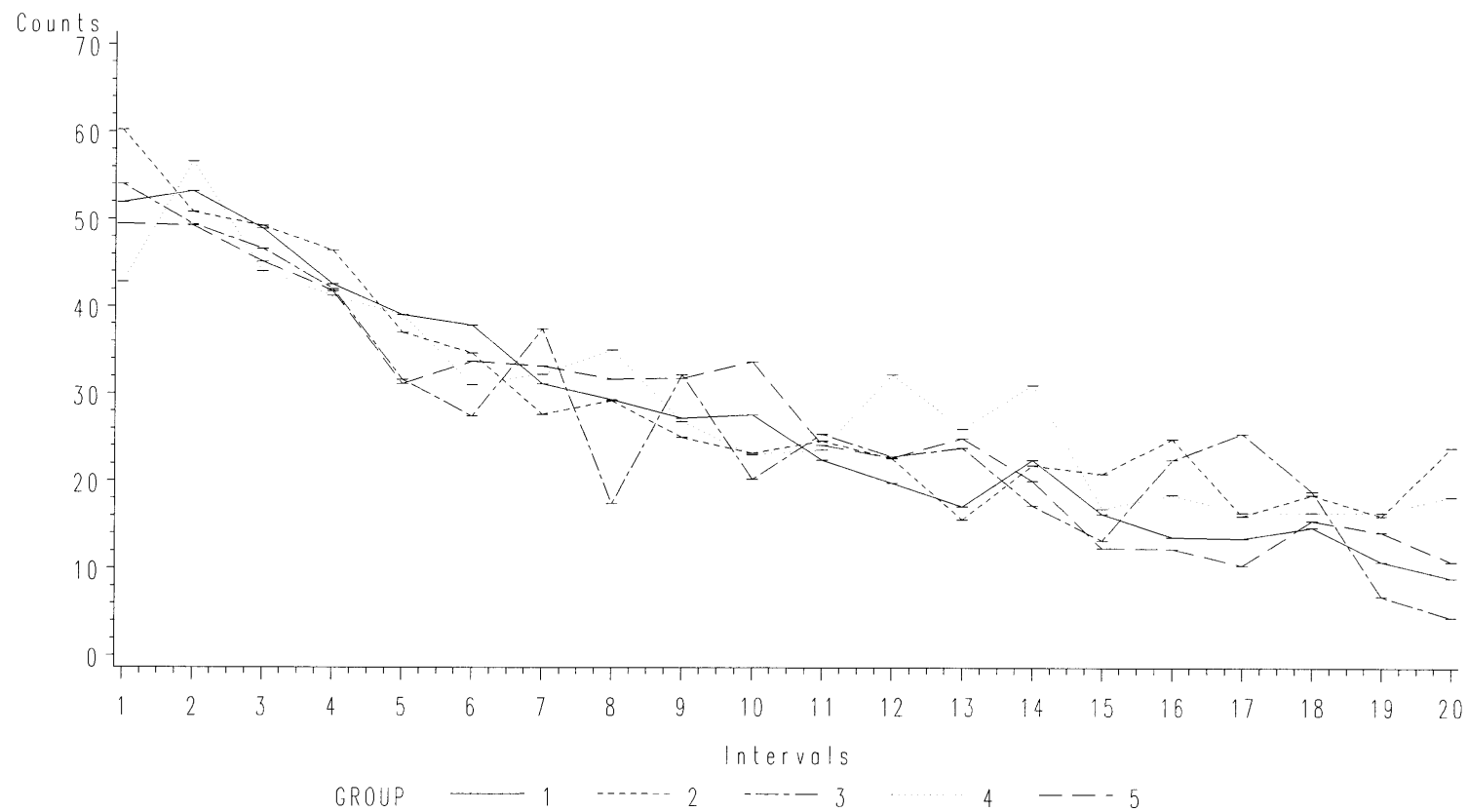
PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

MOTOR ACTIVITY/COUNTS PER 3-MINUTE-INTERVALS
MEASUREMENT=1 SEX=M



Toxicology Study Report - PT02-0222

ATOX 10.2

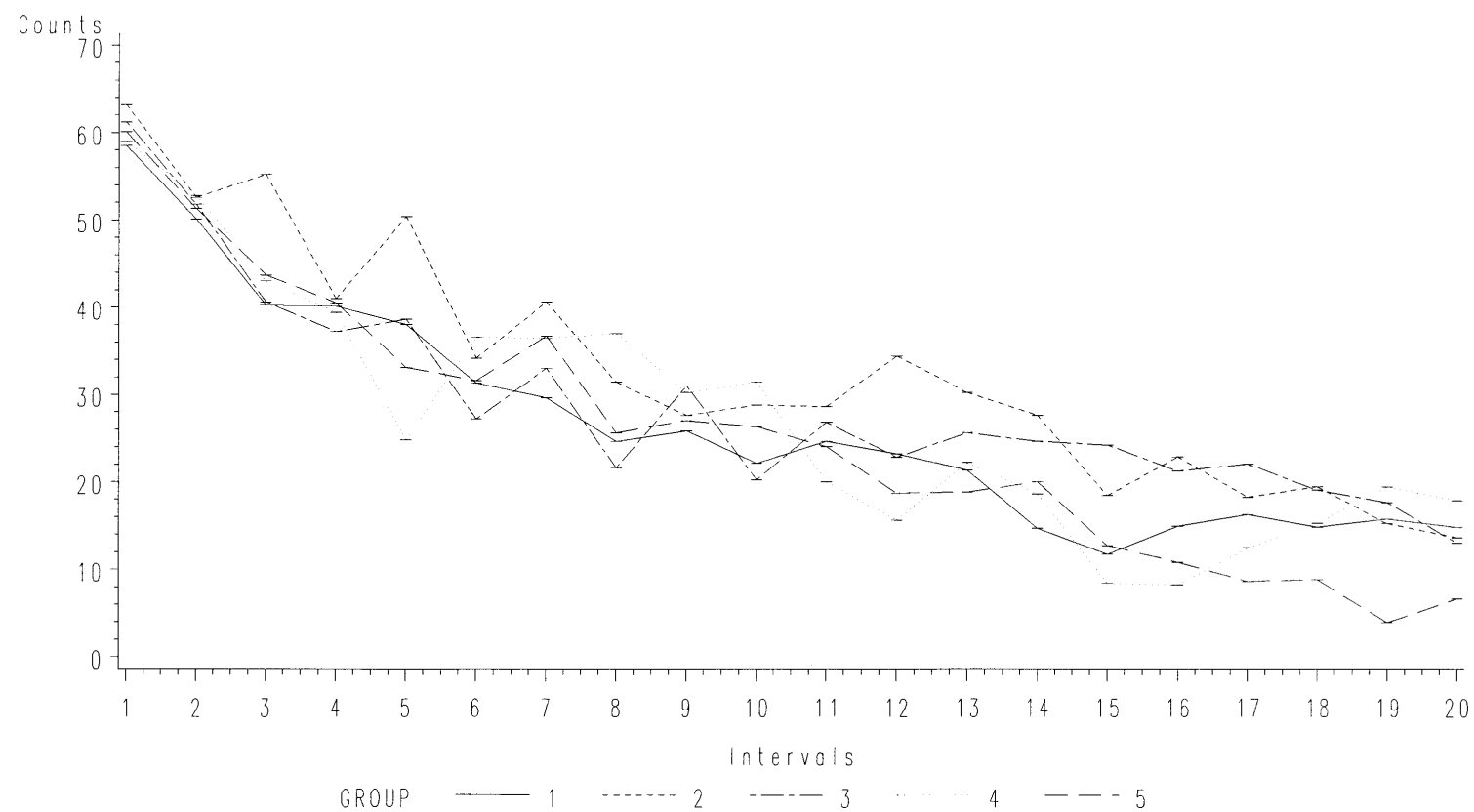
PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

MOTOR ACTIVITY/COUNTS PER 3-MINUTE-INTERVALS
MEASUREMENT=1 SEX=F



Toxicology Study Report - PT02-0222

ATOX 10.2

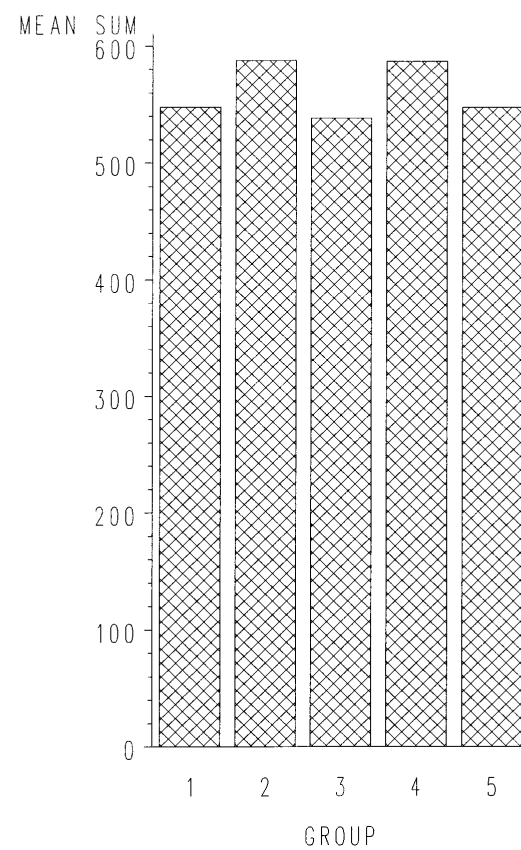
PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

MOTOR ACTIVITY/COUNTS PER 60-MINUTE-SESSION
MEASUREMENT=1 SEX=M



Toxicology Study Report - PT02-0222

ATOX 10.2

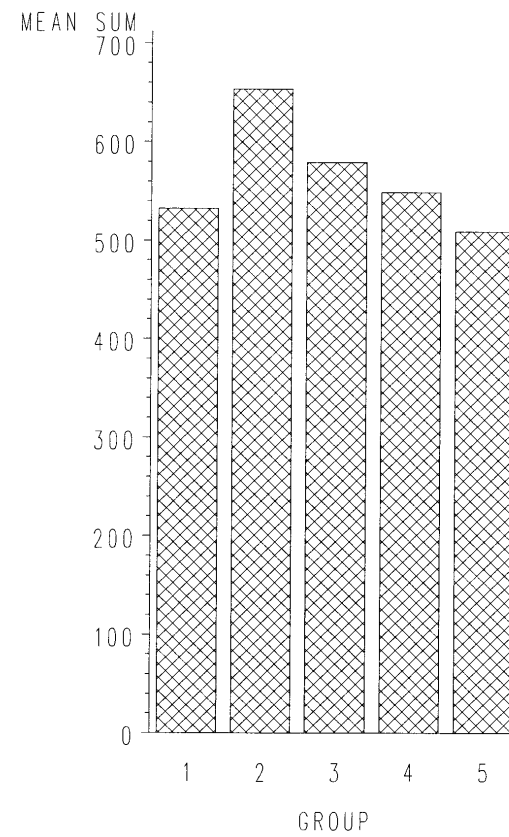
PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

MOTOR ACTIVITY/COUNTS PER 60-MINUTE-SESSION
MEASUREMENT=1 SEX=F



11.6 NEUROTOXICOLOGICAL EXAMINATIONS (GROUPS 6 - 7)

ATOX 10.2

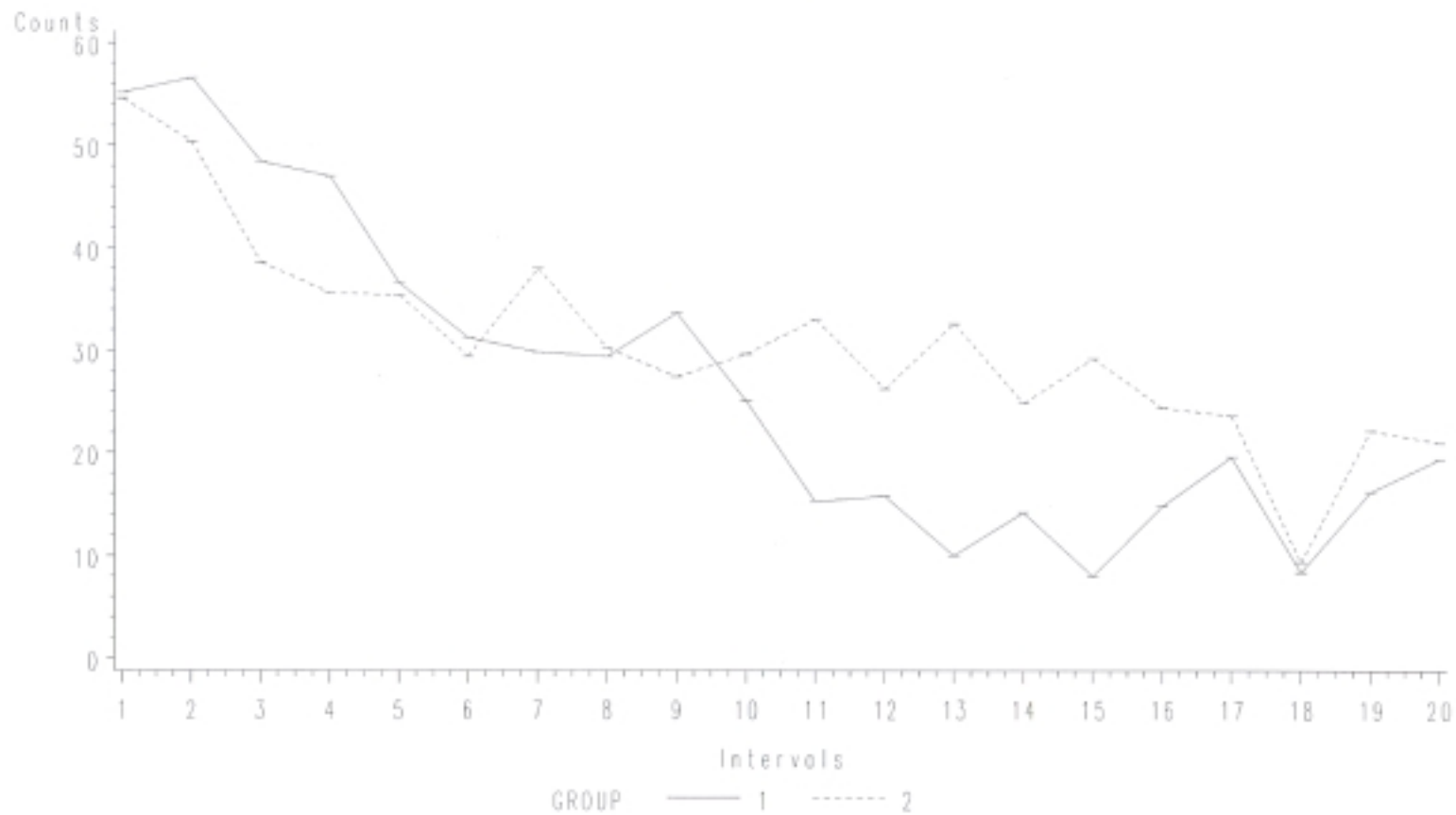
PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

MOTOR ACTIVITY/COUNTS PER 3-MINUTE-INTERVALS
MEASUREMENT=1 SEX=M



ATOX 10.2

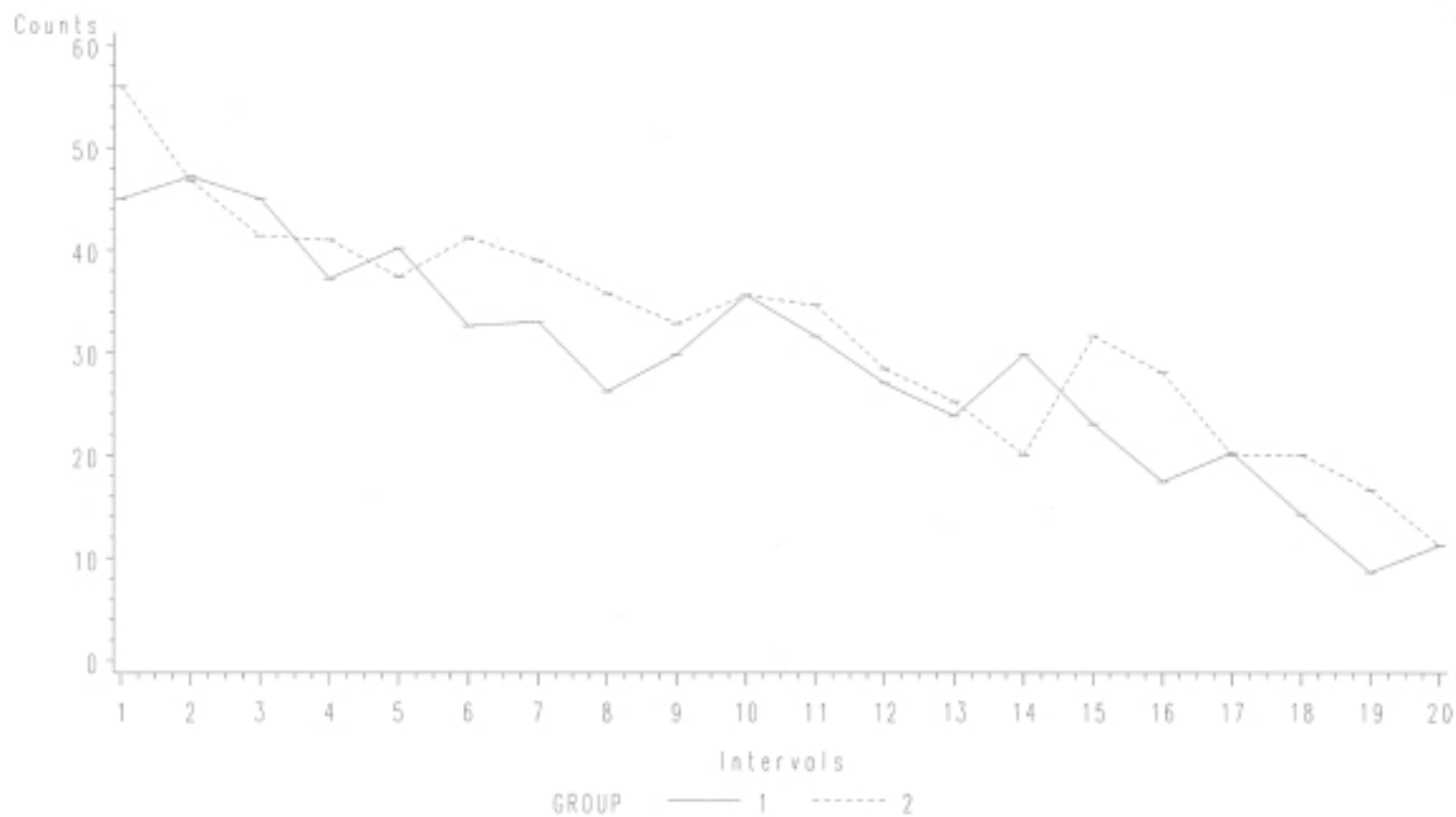
PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

MOTOR ACTIVITY/COUNTS PER 3-MINUTE-INTERVALS
MEASUREMENT=1 SEX=F



ATOX 10.2

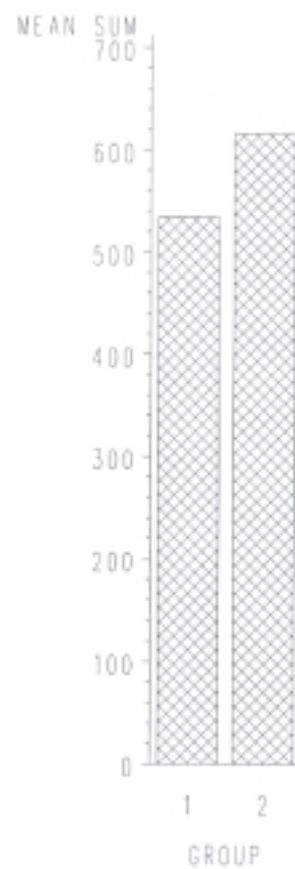
PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

MOTOR ACTIVITY/COUNTS PER 60-MINUTE-SESSION
MEASUREMENT=1 SEX=M



ATOX 10.2

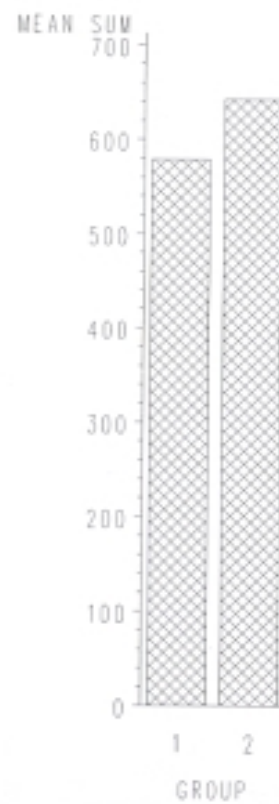
PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

MOTOR ACTIVITY/COUNTS PER 60-MINUTE-SESSION
MEASUREMENT=1 SEX=F



12 SUMMARY TABLES AND STATISTICS

All tables in this section are with statistics. The statistical markers are placed on the right side of the mean values of each parameter.

12.1 CLINICAL OBSERVATIONS - GROUPS 1 - 5 (INDIVIDUAL VALUES, WITHOUT STATS)

Toxicology Study Report - PT02-0222

RTA001-01/04

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Date: 16-Dec-2002 Page: 1

Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Clinical Sign	Day numbers relative to Start Date																					
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
1m	1	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	2	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	3	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	4	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	5	No Abnormalities Detected	X	X	X	X	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Respiratory sounds	.	.	.	.	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	6	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	7	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	.	.	X	X	X	X	X	X	X	X	X	X	X
		Respiratory sounds	.	.	.	.	.	.	.	.	.	X	X	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	8	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	9	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	10	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	2 3	2 4	2 5	2 6	2 7	2 8	2 9	3 0	3 1	3 2	3 3	3 4	3 5	3 6	3 7	3 8	3 9	4 0	4 1	4 2	4 3
1m	1	No Abnormalities Detected	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	2	No Abnormalities Detected	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	3	No Abnormalities Detected	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	4	No Abnormalities Detected	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	5	No Abnormalities Detected	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Respiratory sounds	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	6	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	7	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Respiratory sounds	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	8	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	9	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	10	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Clinical Sign	Day numbers relative to Start Date																					
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
1f	31	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	32	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	33	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	34	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	35	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	36	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	37	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	38	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	39	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	40	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																				
(continued)																							
Group	Animal		2	2	2	2	2	2	2	3	3	3	3	3	3	3	3	3	3	4	4	4	4
Sex	Number	Clinical Sign	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3
1f	31	No Abnormalities Detected	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	32	No Abnormalities Detected	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	33	No Abnormalities Detected	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	34	No Abnormalities Detected	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	35	No Abnormalities Detected	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	36	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	37	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	38	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	39	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	40	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Toxicology Study Report - PT02-0222

RTA001-01/04

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Date: 16-Dec-2002 Page: 5

Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																					
Group	Animal	Clinical Sign	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Sex	Number																							
2m	11	No Abnormalities Detected	X	X	X	X	X	X	X	.	.	.	.	X	X	X	X	.	.	.	.	.	.	.
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X
		Respiratory sounds	.	.	.	.	.	.	.	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	12	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.
		Gait uncoordinated	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	13	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	.	.	.
		Gait uncoordinated	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	14	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.
		Gait uncoordinated	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	15	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.
		Gait uncoordinated	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Toxicology Study Report - PT02-0222

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																				
(continued)																							
Group	Animal	Clinical Sign	2	2	2	2	2	2	2	3	3	3	3	3	3	3	3	3	3	4	4	4	4
Sex	Number		3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3
2m	11	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Respiratory sounds	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	12	Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	13	Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	14	Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	15	Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Toxicology Study Report - PT02-0222

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Date: 16-Dec-2002 Page: 7

Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Day numbers relative to Start Date																						
Group	Animal	Clinical Sign																						
Sex	Number		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
2f	41	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X
		Gait uncoordinated	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	42	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X
		Gait uncoordinated	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	43	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.
		Gait uncoordinated	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	44	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.
		Gait uncoordinated	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	45	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.
		Gait uncoordinated	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																				
(continued)																							
Group	Animal		2	2	2	2	2	2	2	3	3	3	3	3	3	3	3	3	3	4	4	4	4
Sex	Number	Clinical Sign	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3
2f	41	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	.	.	.	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	42	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	43	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	44	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	45	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
 X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																						
Group Sex	Animal Number	Clinical Sign	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	
3m	16	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	17	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.
	18	Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	.	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X
	19	Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces discolored	.	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces discolored	.	.	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																				
(continued)																							
Group	Animal	Clinical Sign	2	2	2	2	2	2	2	3	3	3	3	3	3	3	3	3	3	4	4	4	4
Sex	Number		3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3
3m	16	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	17	Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	18	Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	19	Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	19	Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	19	Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	19	Tray / bedding discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
 X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

* = result to left has an associated comment or marker
X = Present Y = yellowish

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

(continued)

			Day numbers relative to Start Date																				
Group	Animal		2	2	2	2	2	2	2	3	3	3	3	3	3	3	3	3	3	4	4	4	4
Sex	Number	Clinical Sign	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3
3m	20	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	.	.	.	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																					
Group Sex	Animal Number	Clinical Sign	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
3f	46	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	.	.	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.
	47	Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X
		Squatting posture	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	X	X	X	X
	48	Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X
		Gait uncoordinated	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X
	49	Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Flanks drawn in	.	.	.	.	.	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	X	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	X	X
		Gait uncoordinated	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X
		Squatting posture	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Feces discolored	.	.	.	.	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	2 3	2 4	2 5	2 6	2 7	2 8	2 9	3 0	3 1	3 2	3 3	3 4	3 5	3 6	3 7	3 8	3 9	4 0	4 1	4 2	4 3
3f	46	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	47	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	48	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	49	Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Flanks drawn in	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																					
Group Sex	Animal Number	Clinical Sign	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
3f	50	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish
Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																				
(continued)																							
Group	Animal		2	2	2	2	2	2	2	3	3	3	3	3	3	3	3	3	4	4	4	4	
Sex	Number	Clinical Sign	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3
3f	50	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																					
Group Sex	Animal Number	Clinical Sign	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
4m	21	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X
		Gait uncoordinated	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Feces discolored	.	.	.	.	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	22	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X
		Gait uncoordinated	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces discolored	.	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	23	Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X
		Gait uncoordinated	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X
		Feces discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																				
(continued)																							
Group	Animal		2	2	2	2	2	2	2	3	3	3	3	3	3	3	3	3	3	4	4	4	4
Sex	Number	Clinical Sign	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3
4m	21	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	22	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	23	Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
 X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Day numbers relative to Start Date																							
Group Sex	Animal Number	Clinical Sign	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	
4m	24	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Gait uncoordinated	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Abdomen swollen	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Squatting posture	.	.	.	.	X	X	X	X	X	.	.	.	.	.	.	.	.	.	X	X	X	X	X
		Feces discolored	.	.	.	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
	25	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	
		Gait uncoordinated	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Abdomen swollen	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Squatting posture	.	.	.	.	X	X	X	X	X	X	X	.	.	.	X	X	X	X	X	X	X	X	
		Feces discolored	.	.	.	.	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
	26	Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Gait uncoordinated	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Abdomen swollen	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	
		Feces discolored	.	.	.	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																				
(continued)																							
Group	Animal		2	2	2	2	2	2	2	3	3	3	3	3	3	3	3	3	3	4	4	4	4
Sex	Number	Clinical Sign	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3
4m	24	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	25	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	26	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X
		Gait uncoordinated	X	X	X	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	X	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Toxicology Study Report - PT02-0222

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Day numbers relative to Start Date																							
Group	Animal	Clinical Sign	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	
Sex	Number																								
4m	27	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Flanks drawn in	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Gait stilted	.	.	.	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Gait uncoordinated	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Abdomen swollen	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Squatting posture	.	.	.	.	X	X	X	X	X	X	X	X	X	.	X	X	X	X	X	X	X	X	
		Feces discolored	.	.	.	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
		Snout encrusted blood-colored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Snout swollen	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
	28	Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Flanks drawn in	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Gait uncoordinated	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Abdomen swollen	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	
		Feces discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
		Lower incisor(s) broken off	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Upper incisor(s) broken off	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	2 3	2 4	2 5	2 6	2 7	2 8	2 9	3 0	3 1	3 2	3 3	3 4	3 5	3 6	3 7	3 8	3 9	4 0	4 1	4 2	4 3
4m	27	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Flanks drawn in	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X
		Gait uncoordinated	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.
		Snout encrusted blood-colored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	.	.
		Snout swollen	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	.	.
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	28	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Flanks drawn in	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X
		Gait stilted	.	.	.	X	X	X	X	X	.	.	X	X	X	X	X	X	X	X	X	X	X
		Gait uncoordinated	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.
		Lower incisor(s) broken off	.	.	.	.	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Upper incisor(s) broken off	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Day numbers relative to Start Date																							
Group Sex	Animal Number	Clinical Sign	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	
4m	29	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Gait stilted	.	.	.	.	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	
		Gait uncoordinated	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Abdomen swollen	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Squatting posture	.	.	.	.	X	X	X	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	
		Feces discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		30	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
			Flanks drawn in	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	Gait stilted		.	.	.	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	X	X	
	Gait uncoordinated		.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
	Abdomen swollen		.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	
	Squatting posture		.	.	.	X	X	X	X	X	X	X	X	.	.	.	X	X	X	X	X	X	X	X	
	Stupor		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
	Coat bristling		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
	Feces discolored		.	.	.	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
	Tray / bedding discolored		.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Date: 16-Dec-2002 Page: 24

Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	2 3	2 4	2 5	2 6	2 7	2 8	2 9	3 0	3 1	3 2	3 3	3 4	3 5	3 6	3 7	3 8	3 9	4 0	4 1	4 2	4 3
4m	29	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	X	X	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	30	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Flanks drawn in	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	.	.
		Gait stilted	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	X	X	.	.
		Abdomen swollen	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	.	.
		Stupor	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	.	.
		Coat bristling	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	.	.
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.
		Snout encrusted blood-colored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	.
		Snout swollen	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	.
		Lower incisor(s) broken off	.	.	.	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Found dead	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Day numbers relative to Start Date																						
Group	Animal	Clinical Sign	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
4f	51	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X
		Gait uncoordinated	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X
		Feces discolored	.	.	.	Y	Y	Y	Y	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	52	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X
		Squatting posture	.	.	.	.	X	X	X	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X
		Feces discolored	.	.	.	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	53	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Squatting posture	.	.	.	.	.	.	X	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X
		Feces discolored	.	.	.	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	2 3	2 4	2 5	2 6	2 7	2 8	2 9	3 0	3 1	3 2	3 3	3 4	3 5	3 6	3 7	3 8	3 9	4 0	4 1	4 2	4 3
4f	51	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	52	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	53	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Day numbers relative to Start Date																						
Group	Animal	Clinical Sign	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
4f	54	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	X	X	X	X
		Gait uncoordinated	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	.	.	.	.	.	.	.	.	.	.	.	X	X	.	X	X	X	X	X	X	X	X
		Squatting posture	.	.	.	.	X	X	X	X	X	X	X	.	.	.	X	X	X	X	X	X	X	X
		Feces discolored	.	.	.	Y	Y	Y	Y	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	55	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	X	X	X	X	X	.	.	.	.	.	.	X	X	X	X	X	X	X	X
		Gait uncoordinated	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	.	.	.	.	.	.	.	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X
		Feces discolored	.	.	.	Y	Y	Y	Y	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	56	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X
		Gait uncoordinated	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X
		Feces discolored	.	.	.	Y	Y	Y	Y	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																				
(continued)																							
Group	Animal		2	2	2	2	2	2	2	3	3	3	3	3	3	3	3	3	3	4	4	4	4
Sex	Number	Clinical Sign	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3
4f	54	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	55	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	56	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	X	X	X	X	X	X	X	X	X
		Gait uncoordinated	X	X	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
 X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Day numbers relative to Start Date																								
Group Sex	Animal Number	Clinical Sign	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22		
4f	57	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Gait stilted	.	.	.	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	
		Gait uncoordinated	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Abdomen swollen	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	
		Squatting posture	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Feces discolored	.	.	.	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
	58	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Flanks drawn in	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Gait stilted	.	.	.	.	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	
		Gait uncoordinated	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Abdomen swollen	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	
		Squatting posture	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Feces discolored	.	.	.	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
	59	Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Flanks drawn in	.	.	.	.	.	.	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Gait stilted	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Gait uncoordinated	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Abdomen swollen	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X	X	X	
		Squatting posture	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Feces discolored	.	.	.	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
		Lower incisor(s) broken off	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Upper incisor(s) trimmed	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	2 3	2 4	2 5	2 6	2 7	2 8	2 9	3 0	3 1	3 2	3 3	3 4	3 5	3 6	3 7	3 8	3 9	4 0	4 1	4 2	4 3
4f	57	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Gait uncoordinated	X	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	58	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X
		Flanks drawn in	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	X
		Gait stilted	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Gait uncoordinated	X	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.
		Abdomen swollen	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.
	59	Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Flanks drawn in	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Gait uncoordinated	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.
		Lower incisor(s) broken off	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	.	.	.	.	.	.
		Upper incisor(s) trimmed	.	.	.	.	.	.	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Toxicology Study Report - PT02-0222

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																						
Group	Animal	Clinical Sign	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	
Sex	Number																								
4f	60	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Squatting posture	.	.	.	.	X	X	X	.	.	.	.	.	.	.	X	X	X	X	X	X	X	X	X
		Feces discolored	.	.	.	Y	Y	Y	Y	Y	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	.	.	.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Toxicology Study Report - PT02-0222

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																				
(continued)																							
Group	Animal		2	2	2	2	2	2	2	3	3	3	3	3	3	3	3	3	4	4	4	4	
Sex	Number	Clinical Sign	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3
4f	60	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait uncoordinated	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Abdomen swollen	X	X	.	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Feces discolored	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Tray / bedding discolored	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	.	.	.	.
		Killed: end of recovery	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Toxicology Study Report - PT02-0222

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																					
Group	Animal																							
Sex	Number	Clinical Sign	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
5m	61	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	62	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	63	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	64	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	65	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	2 3	2 4	2 5	2 6	2 7	2 8	2 9	3 0	3 1	3 2	3 3	3 4	3 5	3 6	3 7	3 8	3 9	4 0	4 1	4 2	4 3
5m	61	No Abnormalities Detected	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	.	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	62	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	.	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	63	Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	.	.	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	64	Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	65	Squatting posture	.	.	.	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Toxicology Study Report - PT02-0222

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Day numbers relative to Start Date																							
Group	Animal	Clinical Sign																							
Sex	Number		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	
5f	66	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	67	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	68	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	69	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
70	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	.	
	Gait stilted	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	
	Squatting posture	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X	
	Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date

(continued)

Group Sex	Animal Number	Clinical Sign	2 3	2 4	2 5	2 6	2 7	2 8	2 9	3 0	3 1	3 2	3 3	3 4	3 5	3 6	3 7	3 8	3 9	4 0	4 1	4 2	4 3
5f	66	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	67	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	.	.	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	68	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	69	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	70	No Abnormalities Detected	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Gait stilted	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Squatting posture	X	X	X	X	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		Killed: end of study	.	.	.	.	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present Y = yellowish

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

12.2 CLINICAL OBSERVATIONS - GROUPS 6 - 7 (INDIVIDUAL VALUES, WITHOUT STATS)

Toxicology Study Report - PT02-0222

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Date: 28-May-2003 Page: 1

Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																													
Group	Animal																															
Sex	Number	Clinical Sign	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	
6m	71	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	72	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	73	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	74	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	75	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

Toxicology Study Report - PT02-0222

RTA001-01/04

PROVANTIS

Date: 28-May-2003 Page: 2

Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																													
Group	Animal																															
Sex	Number	Clinical Sign	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	
6f	81	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	82	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	83	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	84	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	85	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker

X = Present

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

Toxicology Study Report - PT02-0222

RTA001-01/04

PROVANTIS

Date: 28-May-2003 Page: 3

Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																													
Group	Animal	Clinical Sign	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	
7m	76	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	77	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	78	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	79	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	80	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X

* = result to left has an associated comment or marker

X = Present

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

Toxicology Study Report - PT02-0222

RTA001-01/04

PROVANTIS

Date: 28-May-2003 Page: 4

Clinical Observations - Clinical Signs by Animal

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date																												
Group	Animal	Clinical Sign	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
7f	86	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	87	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	88	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	89	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	90	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Killed: end of study	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

* = result to left has an associated comment or marker
X = Present

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

12.3 BODY WEIGHT (GROUPS 1 - 5)

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

BODY WEIGHT - MALE ANIMALS (g)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
STUDY DAY						
-0003	NE MEAN	116.7	112.2	122.2	121.8	121.9
	S.D.	5.4	2.9	3.7	7.9	4.9
	N	10	5	5	5	9
+0001	MEAN	138.4	134.0	144.2	143.4	146.2 +
	S.D.	7.3	3.5	5.1	8.6	5.2
	N	10	5	5	5	9
+0004	MEAN		152.8 M			
	S.D.		4.1			
	N		5			
+0005	MEAN	158.4		162.2	143.6 -	139.8 -
	S.D.	14.8		11.5	5.7	10.3
	N	10		5	5	9
+0008	MEAN	177.2	183.2	180.4	164.6 -	156.4 -
	S.D.	17.9	5.4	12.7	9.1	8.0
	N	10	5	5	5	9
+0011	MEAN		205.0 M			
	S.D.		9.1			
	N		5			
+0012	MEAN	204.3		208.4	190.2 -	178.3 -
	S.D.	20.2		13.8	11.2	8.6
	N	10		5	5	9

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES, IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL (STATISTICAL ANALYSIS BASED ON CHANGES VERSUS PRELIMINARY VALUES).
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

BODY WEIGHT - MALE ANIMALS (g)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
STUDY DAY						
+0015	MEAN	224.9	228.0	223.0	209.0 -	194.9 -
	S.D.	19.5	11.6	12.7	13.0	12.1
	N	10	5	5	5	9
+0018	MEAN		244.4 M			
	S.D.		14.6			
	N		5			
+0019	MEAN	245.2		242.4	232.0 -	215.6 -
	S.D.	23.5		13.7	15.4	12.5
	N	10		5	5	9
+0022	MEAN	257.0	263.0	251.0	240.6 -	219.3 -
	S.D.	26.5	16.8	12.4	17.4	12.5
	N	10	5	5	5	9
+0025	MEAN		275.8 M			
	S.D.		18.5			
	N		5			
+0026	MEAN	266.0		258.2	249.0 -	227.0 -
	S.D.	30.4		15.3	19.9	17.5
	N	10		5	5	9
+0029	MEAN	279.6	279.8	269.8	261.2 -	230.7 -
	S.D.	31.3	18.4	13.8	21.6	17.9
	N	10	5	5	5	9

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL (STATISTICAL ANALYSIS BASED ON CHANGES VERSUS PRELIMINARY VALUES).
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

BODY WEIGHT - MALE ANIMALS (g)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
STUDY DAY						
+0033	MEAN	295.8				222.3 -
	S.D.	43.7				18.8
	N	5				4
+0036	MEAN	304.2				208.8 -
	S.D.	44.4				24.6
	N	5				4
+0040	MEAN	319.6				203.0 -
	S.D.	48.4				30.7
	N	5				4
+0043	MEAN	320.0				194.0 -
	S.D.	50.8				35.9
	N	5				4

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL (STATISTICAL ANALYSIS BASED ON CHANGES VERSUS PRELIMINARY VALUES).
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

BODY WEIGHT - FEMALE ANIMALS (g)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
STUDY DAY						
-0003	NE MEAN	113.1	106.6	114.6	115.2	112.2
	S.D.	4.6	3.9	3.0	4.2	4.8
	N	10	5	5	5	10
+0001	MEAN	129.2	120.6	131.0	133.2	126.6
	S.D.	4.5	2.6	3.4	2.6	5.4
	N	10	5	5	5	10
+0004	MEAN		134.4 M			
	S.D.		3.4			
	N		5			
+0005	MEAN	147.1		145.6	131.0 -	126.1 -
	S.D.	5.9		3.9	13.9	8.0
	N	10		5	5	10
+0008	MEAN	158.2	148.8	156.8	148.2 -	139.2 -
	S.D.	8.1	2.6	5.4	12.1	12.3
	N	10	5	5	5	10
+0011	MEAN		157.8 M			
	S.D.		4.1			
	N		5			
+0012	MEAN	169.5		166.2	163.2 -	154.4 -
	S.D.	9.9		4.3	10.5	11.0
	N	10		5	5	10

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL (STATISTICAL ANALYSIS BASED ON CHANGES VERSUS PRELIMINARY VALUES).
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

BODY WEIGHT - FEMALE ANIMALS (g)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
STUDY DAY						
+0015	MEAN S.D. N	178.0 8.4 10	168.4 5.1 5	176.8 5.1 5	172.4 - 9.2 5	162.8 - 11.8 10
+0018	MEAN S.D. N		176.2 M 6.4 5			
+0019	MEAN S.D. N	186.7 8.6 10		189.2 4.1 5	184.2 9.4 5	175.0 - 12.6 10
+0022	MEAN S.D. N	193.3 9.6 10	184.8 4.3 5	193.0 4.6 5	188.4 11.0 5	178.4 - 12.2 10
+0025	MEAN S.D. N		190.8 M 4.0 5			
+0026	MEAN S.D. N	204.3 11.9 10		202.0 6.0 5	198.2 10.4 5	183.9 - 14.1 10
+0029	MEAN S.D. N	211.8 12.0 10	195.0 4.9 5	205.8 5.0 5	199.8 - 8.7 5	186.0 - 20.1 10

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL (STATISTICAL ANALYSIS BASED ON CHANGES VERSUS PRELIMINARY VALUES).
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

BODY WEIGHT - FEMALE ANIMALS (g)

		GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5
		0	3	15	60	240
		mg/kg	mg/kg	mg/kg	mg/kg	mg/kg
STUDY						
DAY						
+0033	MEAN	220.4				193.6
	S.D.	14.9				26.2
	N	5				5
+0036	MEAN	221.6				197.2
	S.D.	14.2				29.6
	N	5				5
+0040	MEAN	226.4				198.4
	S.D.	18.9				27.8
	N	5				5
+0043	MEAN	225.6				189.4 -
	S.D.	17.5				29.9
	N	5				5

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL (STATISTICAL ANALYSIS BASED ON CHANGES VERSUS PRELIMINARY VALUES).
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

12.4 BODY WEIGHT (GROUPS 6 - 7)

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 05-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

BODY WEIGHT - MALE ANIMALS (g)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d
STUDY DAY			
-0004	NE MEAN S.D. N	106.2 4.0 5	108.8 3.6 5
+0001	MEAN S.D. N	139.2 3.8 5	142.2 4.1 5
+0004	MEAN S.D. N	160.0 3.3 5	163.6 5.7 5
+0008	MEAN S.D. N	188.0 4.0 5	191.2 6.4 5
+0011	MEAN S.D. N	212.4 4.6 5	215.6 10.5 5
+0015	MEAN S.D. N	236.6 8.4 5	242.4 11.3 5
+0018	MEAN S.D. N	253.4 13.5 5	264.0 16.0 5

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL (STATISTICAL ANALYSIS BASED ON CHANGES VERSUS PRELIMINARY VALUES).
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 05-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

BODY WEIGHT - MALE ANIMALS (g)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d
STUDY DAY			
+0022	MEAN S.D. N	270.4 16.5 5	282.8 22.4 5
+0025	MEAN S.D. N	283.4 17.1 5	292.0 20.4 5
+0029	MEAN S.D. N	295.6 17.5 5	307.8 25.4 5

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL (STATISTICAL ANALYSIS BASED ON CHANGES VERSUS PRELIMINARY VALUES).
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 05-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

BODY WEIGHT - FEMALE ANIMALS (g)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d
STUDY DAY			
-0004	NE MEAN S.D. N	104.8 4.1 5	102.6 3.4 5
+0001	MEAN S.D. N	124.6 4.7 5	125.2 4.2 5
+0004	MEAN S.D. N	134.4 5.9 5	139.2 + 5.6 5
+0008	MEAN S.D. N	145.0 8.3 5	150.4 8.7 5
+0011	MEAN S.D. N	156.8 7.6 5	161.4 8.5 5
+0015	MEAN S.D. N	166.0 8.6 5	172.6 9.2 5
+0018	MEAN S.D. N	174.0 8.9 5	178.4 10.2 5

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL (STATISTICAL ANALYSIS BASED ON CHANGES VERSUS PRELIMINARY VALUES).
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 05-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

BODY WEIGHT - FEMALE ANIMALS (g)		GROUP 1	GROUP 2
		0	0.3
		mg/kg/d	mg/kg/d
STUDY DAY			
+0022	MEAN	181.0	187.8
	S.D.	8.2	10.3
	N	5	5
+0025	MEAN	184.0	188.6
	S.D.	9.3	9.9
	N	5	5
+0029	MEAN	190.6	199.0
	S.D.	9.8	11.7
	N	5	5

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL (STATISTICAL ANALYSIS BASED ON CHANGES VERSUS PRELIMINARY VALUES).
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

12.5 FOOD CONSUMPTION - GROUPS 1 - 5 (WITHOUT STATS)

Toxicology Study Report - PT02-0222

RTA075-01/00

PROVANTIS

Date: 16-Dec-2002 Page: 1

Food Consumption By Animal - Intergroup Food Consumption Relative To Bodyweight

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date															
Group	From:	-3	1	5	8	12	15	19	22	26	29	33	36	40	Mean
Sex	To:	1	5	8	12	15	19	22	26	29	33	36	40	43	-3
															43
1m	Mean	119.69	103.52	97.74	90.97	87.17	81.33	72.03	60.49	62.89	72.48	69.67	67.74	53.36	82.98
	S.D.	5.84	6.90	9.41	9.05	7.98	7.56	7.96	8.00	6.90	10.73	10.52	10.29	8.38	7.74
	N	10	10	10	10	10	10	10	10	10	5	5	5	5	10
2m	Mean	119.22	99.73	91.04	84.42	76.57	72.81	68.25	55.71	61.26	.	.	.	.	81.00
	S.D.	3.87	4.77	6.52	5.78	4.65	4.07	3.60	3.07	3.44	.	.	.	.	4.09
	N	5	5	5	5	5	5	5	5	5	.	.	.	.	5
3m	Mean	117.50	82.03	89.29	88.73	85.43	80.10	74.22	57.06	70.16	.	.	.	.	82.72
	S.D.	7.31	3.93	4.36	5.19	5.31	5.40	5.41	4.54	5.95	.	.	.	.	4.97
	N	5	5	5	5	5	5	5	5	5	.	.	.	.	5
4m	Mean	185.28	60.97	83.31	87.61	82.27	81.71	76.29	63.09	61.68	73.77	45.85	38.68	45.62	81.04
	S.D.	72.41	11.40	4.33	4.51	4.55	4.85	4.57	4.22	6.43	5.97	4.91	5.52	7.97	3.97
	N	9	9	9	9	9	9	9	9	9	4	4	4	4	9

Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

Toxicology Study Report - PT02-0222

RTA075-01/00

PROVANTIS

Date: 16-Dec-2002 Page: 2

Food Consumption By Animal - Intergroup Food Consumption Relative To Bodyweight

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date															
Group	From:	-3	1	5	8	12	15	19	22	26	29	33	36	40	Mean
Sex	To:	1	5	8	12	15	19	22	26	29	33	36	40	43	-3
															43
1f	Mean	106.88	105.09	91.44	80.62	74.24	73.49	72.05	65.54	62.67	78.52	66.90	67.94	60.21	79.24
	S.D.	3.83	3.86	4.45	4.77	3.94	3.59	4.99	3.84	3.54	5.51	4.47	5.23	5.09	3.97
	N	10	10	10	10	10	10	10	10	10	5	5	5	5	10
2f	Mean	109.17	100.20	90.01	79.31	74.29	71.89	70.84	60.29	64.12	.	.	.	.	80.01
	S.D.	2.66	2.57	2.65	2.36	1.97	1.76	1.55	1.64	1.76	.	.	.	.	1.84
	N	5	5	5	5	5	5	5	5	5	.	.	.	.	5
3f	Mean	114.39	70.58	91.44	80.33	76.50	72.50	75.68	61.98	65.45	.	.	.	.	78.76
	S.D.	2.98	4.08	9.55	6.35	4.81	3.89	4.25	3.62	3.25	.	.	.	.	4.41
	N	5	5	5	5	5	5	5	5	5	.	.	.	.	5
4f	Mean	106.26	72.17	88.67	87.40	84.68	81.33	78.45	71.88	66.72	92.02	77.93	75.08	44.55	80.39
	S.D.	4.58	3.96	7.08	7.80	7.50	6.47	5.71	7.94	8.25	15.44	13.29	13.17	7.60	6.60
	N	10	10	10	10	10	10	10	10	10	5	5	5	5	10

Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

Food Consumption By Animal - Intergroup Food Consumption Relative To Bodyweight

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date											
Group	From:	-3	1	4	8	11	15	18	22	25	Mean
Sex	To:	1	4	8	11	15	18	22	25	29	-3
5m											29
	Mean	123.54	106.52	102.44	95.24	86.99	76.39	74.72	63.32	51.47	86.74
	S.D.	3.04	2.88	2.77	3.54	4.16	4.18	4.58	4.17	3.41	3.31
	N	5	5	5	5	5	5	5	5	5	5

Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 5 - 3 mg/kg

Toxicology Study Report - PT02-0222

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PROVANTIS

Date: 16-Dec-2002 Page: 2

Food Consumption By Animal - Intergroup Food Consumption Relative To Bodyweight

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date											
Group	From:	-3	1	4	8	11	15	18	22	25	Mean
Sex	To:	1	4	8	11	15	18	22	25	29	-3
5f	Mean	108.64	96.77	90.07	78.73	76.38	68.93	69.01	60.02	57.05	78.40
	S.D.	3.10	2.26	1.81	1.48	2.16	2.21	1.85	1.30	1.30	1.75
	N	5	5	5	5	5	5	5	5	5	5

Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 5 - 3 mg/kg

12.6 FOOD CONSUMPTION - GROUPS 6 - 7 (WITHOUT STATS)

Toxicology Study Report - PT02-0222

RTA075-01/00

PROVANTIS

Date: 03-Mar-2003 Page: 1

Food Consumption By Animal - Intergroup Food Consumption Relative To Bodyweight

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date											
Group	From:	-4	1	4	8	11	15	18	22	25	Mean
Sex	To:	1	4	8	11	15	18	22	25	29	-4 29
6m	Mean	118.26	112.34	109.23	102.60	89.81	79.86	69.87	58.44	72.06	90.28
	S.D.	3.67	2.56	2.15	2.18	2.51	3.72	4.15	3.68	4.52	2.14
	N	5	5	5	5	5	5	5	5	5	5
7m	Mean	118.79	110.40	105.51	101.75	86.17	78.12	70.33	54.06	66.18	87.92
	S.D.	3.21	3.43	3.60	4.22	4.00	4.27	5.15	4.22	5.32	3.60
	N	5	5	5	5	5	5	5	5	5	5

Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

Toxicology Study Report - PT02-0222

RTA075-01/00

PROVANTIS

Date: 03-Mar-2003 Page: 2

Food Consumption By Animal - Intergroup Food Consumption Relative To Bodyweight

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date											
Group	From:	-4	1	4	8	11	15	18	22	25	Mean
Sex	To:	1	4	8	11	15	18	22	25	29	-4 29
6f	Mean	114.35	92.26	88.23	88.12	82.58	66.02	67.73	56.36	70.08	80.64
	S.D.	4.42	3.69	4.60	4.76	4.26	3.38	3.26	2.68	3.53	3.67
	N	5	5	5	5	5	5	5	5	5	5
7f	Mean	115.11	101.47	92.73	84.45	77.42	65.88	60.49	53.61	70.86	80.22
	S.D.	3.85	3.76	4.74	4.79	4.25	3.67	3.30	2.86	3.89	3.73
	N	5	5	5	5	5	5	5	5	5	5

Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

12.7 CLINICAL PATHOLOGY

12.7.1 Hematology (Groups 1 - 5)

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

HEMATOLOGY - RED CELL COUNT (MALE)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg

Red blood cell count (10E12/L)	MEAN	7.76	7.91	7.83	7.80	7.56
	S.D.	0.26	0.15	0.35	0.37	0.43
	N	5	5	5	5	5
Hemoglobin (g/L)	MEAN	150	156	150	148	149
	S.D.	4	4	3	5	8
	N	5	5	5	5	5
Hematocrit (unity)	MEAN	0.45	0.46	0.45	0.45	0.44
	S.D.	0.01	0.01	0.02	0.02	0.02
	N	5	5	5	5	5
MCV (10E-15 L)	MEAN	57	58	58	58	58
	S.D.	1	1	1	1	1
	N	5	5	5	5	5
MCH (10E-12 g)	NE MEAN	20	20	19	19	20
	S.D.	1	1	1	0	0
	N	5	5	5	5	5
MCHC (g/L)	NE MEAN	339	342	334	326	338
	S.D.	8	3	9	4	4
	N	5	5	5	5	5
Reticulocytes (unity)	MEAN	0.029	0.029	0.026	0.029	0.026
	S.D.	0.001	0.003	0.002	0.002	0.005
	N	5	5	5	5	5
Heinz Bodies (unity)	NE MEAN	0.000	0.000			0.000
	S.D.	0.000	0.000			0.000
	N	5	5			5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

HEMATOLOGY - RED CELL COUNT (FEMALE)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
Red blood cell count (10E12/L)	MEAN	7.19	7.51	7.45	7.40	6.98
	S.D.	0.31	0.30	0.63	0.40	0.25
	N	5	5	4	5	4
Hemoglobin (g/L)	MEAN	138	149	141	143	130
	S.D.	6	4	10	5	4
	N	5	5	4	5	4
Hematocrit (unity)	MEAN	0.41	0.43	0.42	0.42	0.39
	S.D.	0.02	0.02	0.03	0.02	0.02
	N	5	5	4	5	4
MCV (10E-15 L)	MEAN	56	57	56	57	56
	S.D.	1	1	1	1	2
	N	5	5	4	5	4
MCH (10E-12 g)	NE MEAN	19	20	19	20	19
	S.D.	0	0	0	1	1
	N	5	5	4	5	4
MCHC (g/L)	NE MEAN	340	349	341	340	333
	S.D.	5	6	3	10	5
	N	5	5	4	5	4
Reticulocytes (unity)	MEAN	0.029	0.033	0.026	0.029	0.029
	S.D.	0.004	0.005	0.005	0.006	0.005
	N	5	5	4	5	4
Heinz Bodies (unity)	NE MEAN	0.000	0.000			0.000
	S.D.	0.000	0.000			0.000
	N	5	5			4

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

HEMATOLOGY - RED CELL COUNT (MALE)

		GROUP 1 0 mg/kg	GROUP 5 240 mg/kg
Red blood cell count (10E12/L)	MEAN S.D. N	8.68 0.27 5	9.22 + 0.31 4
Hemoglobin (g/L)	MEAN S.D. N	160 7 5	167 3 4
Hematocrit (unity)	MEAN S.D. N	0.48 0.02 5	0.50 0.01 4
MCV (10E-15 L)	MEAN S.D. N	55 2 5	54 2 4
MCH (10E-12 g)	NE MEAN S.D. N	18 1 5	18 1 4
MCHC (g/L)	NE MEAN S.D. N	334 4 5	335 5 4
Reticulocytes (unity)	MEAN S.D. N	0.024 0.010 5	0.008 - 0.005 4
Heinz Bodies (unity)	NE MEAN S.D. N	0.000 0.000 5	0.000 0.000 4

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

HEMATOLOGY - RED CELL COUNT (FEMALE)

		GROUP 1 0 mg/kg	GROUP 5 240 mg/kg
Red blood cell count (10E12/L)	MEAN S.D. N	8.07 0.09 5	8.45 0.43 5
Hemoglobin (g/L)	MEAN S.D. N	149 4 5	156 7 5
Hematocrit (unity)	MEAN S.D. N	0.44 0.01 5	0.46 0.02 5
MCV (10E-15 L)	MEAN S.D. N	54 1 5	54 1 5
MCH (10E-12 g)	NE MEAN S.D. N	19 1 5	18 1 5
MCHC (g/L)	NE MEAN S.D. N	344 5 5	341 3 5
Reticulocytes (unity)	MEAN S.D. N	0.020 0.003 5	0.015 0.004 5
Heinz Bodies (unity)	NE MEAN S.D. N	0.000 0.000 5	0.000 0.000 5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

HEMATOLOGY - WHITE CELL COUNT (MALE)

			GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
White blood cell count (10E9/L)							
	MEAN		10.8	13.5	13.1	11.4	9.4
	MEDIAN		11.4	13.8	12.9	11.1	9.1
	S.D.		1.6	1.8	2.0	1.9	1.8
	XMAX		12.6	16.2	15.3	13.4	12.4
	XMIN		8.2	11.3	11.0	9.0	7.8
	N		5	5	5	5	5
Neutrophils (unity)							
NE	MEDIAN		0.10	0.10	0.08	0.11	0.12
	XMIN		0.08	0.08	0.06	0.08	0.09
	XMAX		0.12	0.11	0.08	0.12	0.15
	N		5	5	5	5	5
Eosinophils (unity)							
NE	MEDIAN		0.00	0.01	0.00	0.00	0.00
	XMIN		0.00	0.00	0.00	0.00	0.00
	XMAX		0.02	0.02	0.01	0.01	0.01
	N		5	5	5	5	5
Basophils (unity)							
NE	MEDIAN		0.01	0.01	0.00	0.00	0.00
	XMIN		0.01	0.01	0.00	0.00	0.00
	XMAX		0.02	0.01	0.01	0.00	0.01
	N		5	5	5	5	5
Lymphocytes (unity)							
NE	MEDIAN		0.87	0.85	0.89	0.87	0.85
	XMIN		0.85	0.84	0.89	0.84	0.81
	XMAX		0.88	0.88	0.92	0.89	0.87
	N		5	5	5	5	5
Monocytes (unity)							
NE	MEDIAN		0.02	0.02	0.01	0.01	0.02
	XMIN		0.01	0.01	0.01	0.01	0.02
	XMAX		0.02	0.03	0.02	0.03	0.02
	N		5	5	5	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

HEMATOLOGY - WHITE CELL COUNT (FEMALE)

		GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5
		0	3	15	60	240
		mg/kg	mg/kg	mg/kg	mg/kg	mg/kg
White blood cell count (10E9/L)	MEAN	7.9	11.1	9.8	8.5	7.9
	MEDIAN	7.6	11.2	10.1	8.0	7.9
	S.D.	1.3	0.8	0.8	1.6	1.3
	XMAX	10.0	12.2	10.4	11.3	9.4
	XMIN	6.4	10.1	8.6	7.4	6.5
	N	5	5	4	5	4
Neutrophils (unity)	NE					
	MEDIAN	0.08	0.09	0.07	0.09	0.08
	XMIN	0.06	0.07	0.05	0.07	0.06
	XMAX	0.10	0.14	0.07	0.11	0.09
	N	5	5	4	5	4
Eosinophils (unity)	NE					
	MEDIAN	0.00	0.01	0.01	0.00	0.01
	XMIN	0.00	0.01	0.00	0.00	0.01
	XMAX	0.01	0.02	0.01	0.01	0.01
	N	5	5	4	5	4
Basophils (unity)	NE					
	MEDIAN	0.00	0.00	0.00	0.00	0.00
	XMIN	0.00	0.00	0.00	0.00	0.00
	XMAX	0.01	0.01	0.00	0.00	0.00
	N	5	5	4	5	4
Lymphocytes (unity)	NE					
	MEDIAN	0.90	0.88	0.92	0.89	0.90
	XMIN	0.87	0.82	0.90	0.87	0.89
	XMAX	0.92	0.89	0.94	0.91	0.91
	N	5	5	4	5	4
Monocytes (unity)	NE					
	MEDIAN	0.01	0.02	0.01	0.01	0.01
	XMIN	0.01	0.01	0.01	0.01	0.01
	XMAX	0.01	0.04	0.01	0.02	0.02
	N	5	5	4	5	4

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

HEMATOLOGY - WHITE CELL COUNT (MALE)

		GROUP 1	GROUP 5
		0	240
		mg/kg	mg/kg
White blood cell count (10E9/L)	MEAN	9.1	5.4 -
	MEDIAN	9.7	5.4
	S.D.	1.9	1.2
	XMAX	11.1	6.4
	XMIN	7.0	4.2
	N	5	4
Neutrophils (unity)	NE		
	MEDIAN	0.11	0.11
	XMIN	0.09	0.08
	XMAX	0.14	0.38
Eosinophils (unity)	NE		
	MEDIAN	0.01	0.01
	XMIN	0.00	0.01
	XMAX	0.01	0.01
Basophils (unity)	NE		
	MEDIAN	0.00	0.00
	XMIN	0.00	0.00
	XMAX	0.01	0.00
Lymphocytes (unity)	NE		
	MEDIAN	0.86	0.87
	XMIN	0.84	0.59
	XMAX	0.87	0.91
Monocytes (unity)	NE		
	MEDIAN	0.02	0.01
	XMIN	0.02	0.01
	XMAX	0.03	0.02
	N	5	4

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

HEMATOLOGY - WHITE CELL COUNT (FEMALE)

		GROUP 1	GROUP 5
		0	240
		mg/kg	mg/kg
White blood cell count (10E9/L)	MEAN	7.5	7.7
	MEDIAN	7.4	8.0
	S.D.	0.9	1.7
	XMAX	8.9	9.3
	XMIN	6.6	5.3
	N	5	5
Neutrophils (unity)	NE MEDIAN	0.07	0.08
	XMIN	0.06	0.06
	XMAX	0.10	0.13
	N	5	5
Eosinophils (unity)	NE MEDIAN	0.01	0.01
	XMIN	0.01	0.01
	XMAX	0.01	0.01
	N	5	5
Basophils (unity)	NE MEDIAN	0.00	0.00
	XMIN	0.00	0.00
	XMAX	0.00	0.00
	N	5	5
Lymphocytes (unity)	NE MEDIAN	0.90	0.89
	XMIN	0.87	0.83
	XMAX	0.92	0.92
	N	5	5
Monocytes (unity)	NE MEDIAN	0.01	0.02
	XMIN	0.01	0.01
	XMAX	0.02	0.02
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

HEMATOLOGY - BLOOD COAGULATION (MALE)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
Platelets (10E9/L)	MEAN	1030	1070	1111	1085	998
	S.D.	134	127	42	57	77
	N	5	5	5	5	5
Coagulation Time (Seconds)	MEAN	101	158	111	111	104
	S.D.	4	13	9	8	13
	N	5	5	5	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

HEMATOLOGY - BLOOD COAGULATION (FEMALE)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
Platelets (10E9/L)		MEAN 1060	1128	1085	1120	1100
	S.D.	167	274	59	124	138
	N	5	5	4	5	4
Coagulation Time (Seconds)		MEAN 131	160	99 -	105 -	104 -
	S.D.	10	11	7	21	6
	N	5	5	5	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

HEMATOLOGY - BLOOD COAGULATION (MALE)

		GROUP 1 0 mg/kg	GROUP 5 240 mg/kg
Platelets (10E9/L)	MEAN	1051	935
	S.D.	125	238
	N	5	4
Coagulation Time (Seconds)	MEAN	139	127
	S.D.	13	19
	N	5	4

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

HEMATOLOGY - BLOOD COAGULATION (FEMALE)

		GROUP 1 0 mg/kg	GROUP 5 240 mg/kg
Platelets (10E9/L)	MEAN S.D. N	1050 42 5	1280 205 5
Coagulation Time (Seconds)	MEAN S.D. N	151 15 5	135 17 5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

12.7.2 Hematology (Groups 6 - 7)

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

HEMATOLOGY - RED CELL COUNT (MALE)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d

Red blood cell count (10E12/L)	MEAN	7.99	7.93
	S.D.	0.29	0.27
	N	5	5
Hemoglobin (g/L)	MEAN	156	154
	S.D.	8	2
	N	5	5
Hematocrit (unity)	MEAN	0.46	0.45
	S.D.	0.02	0.00
	N	5	5
MCV (10E-15 L)	MEAN	58	57
	S.D.	1	2
	N	5	5
MCH (10E-12 g)	NE MEAN	19	19
	S.D.	1	1
	N	5	5
MCHC (g/L)	NE MEAN	337	338
	S.D.	4	3
	N	5	5
Reticulocytes (unity)	MEAN	0.032	0.033
	S.D.	0.003	0.005
	N	5	5
Heinz Bodies (unity)	NE MEAN	0.000	0.000
	S.D.	0.000	0.000
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

HEMATOLOGY - RED CELL COUNT (FEMALE)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d

Red blood cell count (10E12/L)	MEAN	7.82	7.65
	S.D.	0.26	0.17
	N	5	5
Hemoglobin (g/L)	MEAN	149	147
	S.D.	3	3
	N	5	5
Hematocrit (unity)	MEAN	0.44	0.43
	S.D.	0.01	0.01
	N	5	5
MCV (10E-15 L)	MEAN	56	56
	S.D.	1	1
	N	5	5
MCH (10E-12 g)	NE MEAN	19	19
	S.D.	0	0
	N	5	5
MCHC (g/L)	NE MEAN	342	344
	S.D.	3	7
	N	5	5
Reticulocytes (unity)	MEAN	0.026	0.033
	S.D.	0.003	0.008
	N	5	5
Heinz Bodies (unity)	NE MEAN	0.000	0.000
	S.D.	0.000	0.000
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

HEMATOLOGY - WHITE CELL COUNT (MALE)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d

White blood cell count (10E9/L)	MEAN	13.0	11.2
	MEDIAN	12.5	11.9
	S.D.	2.8	2.1
	XMAX	17.5	13.3
	XMIN	10.1	7.8
	N	5	5
Neutrophils (unity)	NE MEDIAN	0.12	0.10
	XMIN	0.10	0.09
	XMAX	0.15	0.11
	N	5	5
Eosinophils (unity)	NE MEDIAN	0.01	0.01
	XMIN	0.01	0.01
	XMAX	0.01	0.01
	N	5	5
Basophils (unity)	NE MEDIAN	0.00	0.00
	XMIN	0.00	0.00
	XMAX	0.00	0.00
	N	5	5
Lymphocytes (unity)	NE MEDIAN	0.84	0.86
	XMIN	0.82	0.84
	XMAX	0.86	0.88
	N	5	5
Monocytes (unity)	NE MEDIAN	0.02	0.02
	XMIN	0.01	0.02
	XMAX	0.03	0.03
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

HEMATOLOGY - WHITE CELL COUNT (FEMALE)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d

White blood cell count (10E9/L)	MEAN	10.8	7.9
	MEDIAN	11.5	8.2
	S.D.	1.9	1.2
	XMAX	12.6	8.8
	XMIN	7.7	6.0
	N	5	5
Neutrophils (unity)	NE MEDIAN	0.08	0.09
	XMIN	0.06	0.08
	XMAX	0.10	0.12
	N	5	5
Eosinophils (unity)	NE MEDIAN	0.02	0.01
	XMIN	0.01	0.01
	XMAX	0.02	0.02
	N	5	5
Basophils (unity)	NE MEDIAN	0.00	0.00
	XMIN	0.00	0.00
	XMAX	0.00	0.00
	N	5	5
Lymphocytes (unity)	NE MEDIAN	0.88	0.88
	XMIN	0.87	0.84
	XMAX	0.90	0.89
	N	5	5
Monocytes (unity)	NE MEDIAN	0.02	0.01
	XMIN	0.01	0.01
	XMAX	0.02	0.02
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

HEMATOLOGY - BLOOD COAGULATION (MALE)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d

Platelets (10E9/L)	MEAN	1151	1147
	S.D.	132	44
	N	5	5
Coagulation Time (Seconds)	MEAN	142	157
	S.D.	11	21
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

HEMATOLOGY - BLOOD COAGULATION (FEMALE)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d

Platelets (10E9/L)	MEAN	1134	1079
	S.D.	109	78
	N	5	5
Coagulation Time (Seconds)	MEAN	126	131
	S.D.	6	11
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

12.7.3 Clinical chemistry (Groups 1 - 5)

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ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

CLINICAL CHEMISTRY (MALE)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
Sodium (mmol/L)	MEAN S.D. N	141 2 5	138 2 5	140 1 5	141 1 5	142 1 5
Potassium (mmol/L)	MEAN S.D. N	6.07 0.33 5	5.92 0.40 5	6.12 0.24 5	5.58 0.25 5	5.91 0.51 5
Calcium (mmol/L)	MEAN S.D. N	2.42 0.03 5	2.43 0.04 5	2.31 0.07 5	2.33 0.06 5	2.34 0.08 5
Chloride (mmol/L)	MEAN S.D. N	103 1 5	102 2 5	101 1 5	101 2 5	102 1 5
Phosphorus (mmol/L)	MEAN S.D. N	3.05 0.17 5	3.11 0.21 5	3.21 0.13 5	2.87 0.23 5	2.98 0.14 5
Total Bilirubin (umol/L)	MEAN S.D. N	5.1 0.3 5	4.5 0.3 5	5.8 0.5 5	6.2 1.2 5	5.5 0.5 5
Glucose (mmol/L)	MEAN S.D. N	19.48 2.85 5	17.18 0.71 5	19.86 1.55 5	16.64 1.70 5	16.10 2.92 5
Uric Acid (umol/L)	MEAN S.D. N	33 7 5	27 3 5	52 10 5	63 20 5	51 18 5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

CLINICAL CHEMISTRY (MALE)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
Creatinine (umol/L)	MEAN S.D. N	47 2 5	46 3 5	52 5 5	47 4 5	43 5 5
Urea Nitrogen (mmol/L)	MEAN S.D. N	6.10 0.87 5	6.36 0.68 5	5.78 0.52 5	5.56 0.44 5	7.08 0.96 5
Cholesterol (mmol/L)	MEAN S.D. N	2.00 0.07 5	2.00 0.12 5	1.96 0.21 5	1.98 0.19 5	1.86 0.19 5
Triglycerides (mmol/L)	MEAN S.D. N	0.51 0.09 5	0.46 0.04 5	0.40 0.17 5	0.47 0.08 5	0.37 - 0.12 5
Total Protein (g/L)	MEAN S.D. N	52 2 5	50 2 5	53 2 5	54 1 5	52 1 5
Albumin (g/L)	MEAN S.D. N	26.0 1.0 5	24.0 1.4 5	26.2 0.8 5	26.4 0.5 5	26.6 1.1 5
ASAT (IU/L)	MEAN S.D. N	81 19 5	81 11 5	103 12 5	108 17 5	102 16 5
ALAT (IU/L)	MEAN S.D. N	42 4 5	44 10 5	45 3 5	59 + 4 5	64 + 10 5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

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ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

CLINICAL CHEMISTRY (MALE)

			GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
G-Gluta.Transf. (IU/L)	NE	MEAN	3	3	3	3	4
		S.D.	0	0	0	0	1
		N	5	5	5	5	5
Alkaline Phosphatase (IU/L)		MEAN	496	368	474	580	424
		S.D.	75	54	74	67	123
		N	5	5	5	5	5
Albumin/Globulin Ratio		MEAN	0.99	0.91	0.98	0.96	1.05
		S.D.	0.03	0.07	0.04	0.05	0.05
		N	5	5	5	5	5
Globulin (g/L)		MEAN	26	26	27	27	25
		S.D.	1	2	2	1	1
		N	5	5	5	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

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Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

CLINICAL CHEMISTRY (FEMALE)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
Sodium (mmol/L)	MEAN S.D. N	141 2 5	140 2 5	140 2 5	147 + 2 5	145 + 2 5
Potassium (mmol/L)	MEAN S.D. N	5.19 0.39 5	5.76 0.27 5	6.08 0.37 5	5.40 0.17 5	5.86 0.77 5
Calcium (mmol/L)	MEAN S.D. N	2.31 0.02 5	2.43 0.07 5	2.36 0.05 5	2.23 0.02 5	2.25 0.13 5
Chloride (mmol/L)	MEAN S.D. N	104 2 5	105 1 5	104 1 5	109 2 5	105 1 5
Phosphorus (mmol/L)	MEAN S.D. N	2.74 0.22 5	2.85 0.38 5	3.18 0.13 5	2.82 0.07 5	3.13 0.31 5
Total Bilirubin (umol/L)	MEAN S.D. N	6.0 0.4 5	5.0 0.3 5	6.3 0.4 5	6.9 1.4 5	5.9 0.7 5
Glucose (mmol/L)	MEAN S.D. N	13.36 2.01 5	13.36 1.62 5	16.38 1.67 5	13.94 1.83 5	14.54 1.42 5
Uric Acid (umol/L)	MEAN S.D. N	49 10 5	69 26 5	62 15 5	83 16 5	128 110 5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

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Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

CLINICAL CHEMISTRY (FEMALE)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
Creatinine (umol/L)	MEAN S.D. N	48 2 5	53 5 5	51 5 5	47 4 5	46 6 5
Urea Nitrogen (mmol/L)	MEAN S.D. N	5.84 0.27 5	5.82 0.69 5	6.02 0.61 5	5.72 1.33 5	5.82 0.84 5
Cholesterol (mmol/L)	MEAN S.D. N	1.90 0.26 5	2.18 0.27 5	2.28 0.04 5	2.74 0.25 5	2.38 0.46 5
Triglycerides (mmol/L)	MEAN S.D. N	0.49 0.08 5	0.35 0.04 5	0.36 0.05 5	0.39 0.06 5	0.42 0.13 5
Total Protein (g/L)	MEAN S.D. N	54 2 5	55 3 5	52 2 5	61 2 5	56 3 5
Albumin (g/L)	MEAN S.D. N	27.0 1.6 5	27.4 1.1 5	25.4 1.5 5	32.0 1.2 5	30.0 3.5 5
ASAT (IU/L)	MEAN S.D. N	101 13 5	105 18 5	110 22 5	103 8 5	96 15 5
ALAT (IU/L)	MEAN S.D. N	41 4 5	41 4 5	48 7 5	46 5 5	53 + 6 5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

CLINICAL CHEMISTRY (FEMALE)

			GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5
			0	3	15	60	240
			mg/kg	mg/kg	mg/kg	mg/kg	mg/kg
G-Gluta.Transf. (IU/L)	NE	MEAN	3	3	3	3	6 +
		S.D.	0	0	0	0	1
		N	5	5	5	5	5
Alkaline Phosphatase (IU/L)		MEAN	403	393	320	377	458
		S.D.	29	53	68	44	89
		N	5	5	5	5	5
Albumin/Globulin Ratio		MEAN	0.99	1.01	0.97	1.11 +	1.16 +
		S.D.	0.05	0.04	0.05	0.04	0.16
		N	5	5	5	5	5
Globulin (g/L)		MEAN	27	27	26	29	26
		S.D.	1	2	1	1	1
		N	5	5	5	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

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Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

CLINICAL CHEMISTRY (MALE)

		GROUP 1 0 mg/kg	GROUP 5 240 mg/kg
Sodium (mmol/L)	MEAN	139	144 +
	S.D.	1	1
	N	5	4
Potassium (mmol/L)	MEAN	6.01	4.90 -
	S.D.	0.28	0.22
	N	5	4
Calcium (mmol/L)	MEAN	2.29	2.31
	S.D.	0.11	0.09
	N	5	4
Chloride (mmol/L)	MEAN	102	107 +
	S.D.	1	2
	N	5	4
Phosphorus (mmol/L)	MEAN	2.94	2.77
	S.D.	0.24	0.14
	N	5	4
Total Bilirubin (umol/L)	MEAN	5.4	6.4
	S.D.	0.7	1.0
	N	5	4
Glucose (mmol/L)	MEAN	20.18	6.23 -
	S.D.	3.68	1.04
	N	5	4
Uric Acid (umol/L)	MEAN	41	55
	S.D.	14	14
	N	5	4

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

CLINICAL CHEMISTRY (MALE)

		GROUP 1 0 mg/kg	GROUP 5 240 mg/kg
Creatinine (umol/L)	MEAN	47	55
	S.D.	5	4
	N	5	4
Urea Nitrogen (mmol/L)	MEAN	6.98	11.53
	S.D.	0.90	5.15
	N	5	4
Cholesterol (mmol/L)	MEAN	1.84	1.95
	S.D.	0.11	0.10
	N	5	4
Triglycerides (mmol/L)	MEAN	0.48	0.26 M
	S.D.	0.10	0.10
	N	5	3
Total Protein (g/L)	MEAN	50	58 +
	S.D.	3	4
	N	5	4
Albumin (g/L)	MEAN	23.4	27.8 +
	S.D.	1.1	1.9
	N	5	4
ASAT (IU/L)	MEAN	104	108
	S.D.	16	19
	N	5	4
ALAT (IU/L)	MEAN	49	38
	S.D.	9	6
	N	5	4

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

CLINICAL CHEMISTRY (MALE)

			GROUP 1 0 mg/kg	GROUP 5 240 mg/kg
G-Gluta.Transf. (IU/L)	NE	MEAN	3	3
		S.D.	0	0
		N	5	4
Alkaline Phosphatase (IU/L)		MEAN	323	214 -
		S.D.	32	61
		N	5	4
Albumin/Globulin Ratio		MEAN	0.87	0.91
		S.D.	0.05	0.05
		N	5	4
Globulin (g/L)		MEAN	27	31 +
		S.D.	2	2
		N	5	4

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

CLINICAL CHEMISTRY (FEMALE)

		GROUP 1 0 mg/kg	GROUP 5 240 mg/kg
Sodium (mmol/L)	MEAN	143	142
	S.D.	0	2
	N	5	5
Potassium (mmol/L)	MEAN	4.76	5.69 +
	S.D.	0.26	0.35
	N	5	5
Calcium (mmol/L)	MEAN	2.38	2.30 -
	S.D.	0.03	0.05
	N	5	5
Chloride (mmol/L)	MEAN	105	107
	S.D.	1	1
	N	5	5
Phosphorus (mmol/L)	MEAN	2.44	3.06 +
	S.D.	0.19	0.22
	N	5	5
Total Bilirubin (umol/L)	MEAN	5.2	5.5
	S.D.	0.6	0.5
	N	5	5
Glucose (mmol/L)	MEAN	12.70	12.66
	S.D.	1.62	4.20
	N	5	5
Uric Acid (umol/L)	MEAN	61	67
	S.D.	21	20
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

CLINICAL CHEMISTRY (FEMALE)

		GROUP 1 0 mg/kg	GROUP 5 240 mg/kg
Creatinine (umol/L)	MEAN	55	56
	S.D.	4	8
	N	5	5
Urea Nitrogen (mmol/L)	MEAN	5.72	8.54
	S.D.	0.40	4.16
	N	5	5
Cholesterol (mmol/L)	MEAN	1.84	1.88
	S.D.	0.34	0.22
	N	5	5
Triglycerides (mmol/L)	MEAN	0.45	0.29 -
	S.D.	0.11	0.10
	N	5	5
Total Protein (g/L)	MEAN	58	52 -
	S.D.	2	2
	N	5	5
Albumin (g/L)	MEAN	28.4	24.2 -
	S.D.	1.1	0.8
	N	5	5
ASAT (IU/L)	MEAN	96	100
	S.D.	20	34
	N	5	5
ALAT (IU/L)	MEAN	35	43
	S.D.	4	21
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 27-JAN-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

CLINICAL CHEMISTRY (FEMALE)

			GROUP 1	GROUP 5
			0	240
			mg/kg	mg/kg
G-Gluta.Transf. (IU/L)	NE	MEAN	3	3
		S.D.	0	0
		N	5	5
Alkaline Phosphatase (IU/L)		MEAN	226	185
		S.D.	50	72
		N	5	5
Albumin/Globulin Ratio		MEAN	0.98	0.86 -
		S.D.	0.05	0.03
		N	5	5
Globulin (g/L)		MEAN	29	28
		S.D.	2	1
		N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

12.7.4 Clinical chemistry (Groups 6 - 7)

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

CLINICAL CHEMISTRY (MALE)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d

Sodium (mmol/L)	MEAN	138	140 +
	S.D.	1	1
	N	5	5
Potassium (mmol/L)	MEAN	5.67	5.09 -
	S.D.	0.11	0.21
	N	5	5
Calcium (mmol/L)	MEAN	2.49	2.45
	S.D.	0.05	0.06
	N	5	5
Chloride (mmol/L)	MEAN	102	102
	S.D.	1	1
	N	5	5
Phosphorus (mmol/L)	MEAN	3.10	2.78 -
	S.D.	0.10	0.13
	N	5	5
Total Bilirubin (umol/L)	MEAN	4.8	5.0
	S.D.	0.3	0.2
	N	5	5
Glucose (mmol/L)	MEAN	19.32	15.72
	S.D.	1.12	2.21
	N	5	5
Uric Acid (umol/L)	MEAN	24	33
	S.D.	7	15
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

CLINICAL CHEMISTRY (MALE)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d

Creatinine (umol/L)	MEAN	47	47
	S.D.	3	3
	N	5	5
Urea Nitrogen (mmol/L)	MEAN	5.98	5.54
	S.D.	0.92	0.79
	N	5	5
Cholesterol (mmol/L)	MEAN	2.00	2.18
	S.D.	0.12	0.13
	N	5	5
Triglycerides (mmol/L)	MEAN	0.55	0.60
	S.D.	0.07	0.15
	N	5	5
Total Protein (g/L)	MEAN	52	55 +
	S.D.	1	2
	N	5	5
Albumin (g/L)	MEAN	24.8	27.6 +
	S.D.	0.8	0.5
	N	5	5
ASAT (IU/L)	MEAN	90	78
	S.D.	8	14
	N	5	5
ALAT (IU/L)	MEAN	44	40
	S.D.	8	6
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

CLINICAL CHEMISTRY (MALE)

			GROUP 1	GROUP 2
			0	0.3
			mg/kg/d	mg/kg/d
G-Gluta.Transf. (IU/L)	NE	MEAN	4	4
		S.D.	0	0
		N	5	5
Alkaline Phosphatase (IU/L)		MEAN	365	448 +
		S.D.	30	28
		N	5	5
Albumin/Globulin Ratio		MEAN	0.93	1.00
		S.D.	0.05	0.07
		N	5	5
Globulin (g/L)		MEAN	27	28
		S.D.	1	2
		N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

CLINICAL CHEMISTRY (FEMALE)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d

Sodium (mmol/L)	MEAN	141	141
	S.D.	2	1
	N	5	5
Potassium (mmol/L)	MEAN	5.62	5.19
	S.D.	0.43	0.13
	N	5	5
Calcium (mmol/L)	MEAN	2.41	2.42
	S.D.	0.11	0.05
	N	5	5
Chloride (mmol/L)	MEAN	106	106
	S.D.	2	2
	N	5	5
Phosphorus (mmol/L)	MEAN	3.02	2.68 -
	S.D.	0.16	0.05
	N	5	5
Total Bilirubin (umol/L)	MEAN	5.3	5.2
	S.D.	0.5	0.8
	N	5	5
Glucose (mmol/L)	MEAN	15.12	14.12
	S.D.	2.56	2.06
	N	5	5
Uric Acid (umol/L)	MEAN	60	62
	S.D.	6	22
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

CLINICAL CHEMISTRY (FEMALE)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d

Creatinine (umol/L)	MEAN	49	52
	S.D.	4	5
	N	5	5
Urea Nitrogen (mmol/L)	MEAN	5.02	5.16
	S.D.	0.65	0.74
	N	5	5
Cholesterol (mmol/L)	MEAN	2.36	2.28
	S.D.	0.21	0.22
	N	5	5
Triglycerides (mmol/L)	MEAN	0.40	0.37
	S.D.	0.08	0.07
	N	5	5
Total Protein (g/L)	MEAN	55	59
	S.D.	3	1
	N	5	5
Albumin (g/L)	MEAN	27.0	28.8
	S.D.	1.4	1.1
	N	5	5
ASAT (IU/L)	MEAN	118	113
	S.D.	24	18
	N	5	5
ALAT (IU/L)	MEAN	43	43
	S.D.	3	4
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

CLINICAL CHEMISTRY (FEMALE)

			GROUP 1	GROUP 2
			0	0.3
			mg/kg/d	mg/kg/d
G-Gluta.Transf. (IU/L)	NE	MEAN	4	4
		S.D.	0	0
		N	5	5
Alkaline Phosphatase (IU/L)		MEAN	307	328
		S.D.	67	106
		N	5	5
Albumin/Globulin Ratio		MEAN	0.95	0.97
		S.D.	0.04	0.05
		N	5	5
Globulin (g/L)		MEAN	28	30
		S.D.	2	1
		N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

12.7.5 Urinalysis (Groups 1 - 5)

Toxicology Study Report - PT02-0222

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

URINALYSIS (MALE)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
Volume (mL)	MEAN	2.9	2.9	2.5	4.0	5.3 +
	S.D.	1.1	1.0	0.8	1.4	1.2
	N	5	5	5	5	5
pH Value (sq)	NE MEDIAN	7	7	7	6	7
	XMIN	7	6	6	6	6
	XMAX	7	7	7	7	7
Specific Weight (g/L)	MEAN	1059	1062	1061	1050	1038
	S.D.	14	10	11	7	9
	N	5	5	5	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

URINALYSIS (FEMALE)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
Volume (mL)		MEAN 3.1 S.D. 1.5 N 5	MEAN 3.1 S.D. 0.8 N 5	MEAN 4.8 S.D. 0.3 N 5	MEAN 3.7 S.D. 1.2 N 5	MEAN 6.2 S.D. 3.6 N 5
pH Value (sq)		NE MEDIAN 7 XMIN 6 XMAX 8	NE MEDIAN 7 XMIN 7 XMAX 7	NE MEDIAN 7 XMIN 7 XMAX 7	NE MEDIAN 7 XMIN 6 XMAX 8	NE MEDIAN 6 XMIN 6 XMAX 6
Specific Weight (g/L)		MEAN 1039 S.D. 10 N 4	MEAN 1047 S.D. 10 N 5	MEAN 1032 S.D. 7 N 5	MEAN 1036 S.D. 2 N 5	MEAN 1034 S.D. 13 N 5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

URINALYSIS (MALE)

		GROUP 1	GROUP 5
		0	240
		mg/kg	mg/kg
Volume (mL)	MEAN	4.9	4.2
	S.D.	3.7	2.9
	N	5	4
pH Value (sq)	NE MEDIAN	7	8
	XMIN	7	8
	XMAX	8	8
Specific Weight (g/L)	MEAN	1049	1041 M
	S.D.	20	18
	N	5	3

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE
URINALYSIS (FEMALE)

		GROUP 1	GROUP 5
		0	240
		mg/kg	mg/kg
-----		-----	
Volume (mL)	MEAN	5.9	4.7
	S.D.	2.2	2.3
	N	5	5
pH Value (sq)	NE MEDIAN	7	7
	XMIN	7	6
	XMAX	8	7
Specific Weight (g/L)	MEAN	1033	1041
	S.D.	9	10
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

12.7.6 Urinalysis (Groups 6 - 7)

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE			
URINALYSIS (MALE)			

		GROUP 1	GROUP 2
		0	0.3
		mg/kg/d	mg/kg/d

Volume	MEAN	3.7	5.9
(mL)	S.D.	0.8	2.3
	N	5	5
pH Value (sq)	NE MEDIAN	7	7
	XMIN	6	6
	XMAX	7	7
Specific Weight	MEAN	1044	1035
(g/L)	S.D.	7	12
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES, IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

URINALYSIS (FEMALE)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d

Volume (mL)	MEAN	4.0	3.9
	S.D.	1.7	0.5
	N	5	5
pH Value (sq)	NE MEDIAN	6	6
	XMIN	6	6
	XMAX	7	7
Specific Weight (g/L)	MEAN	1038	1037
	S.D.	10	6
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

12.8 ORGAN WEIGHTS (GROUPS 1 - 5)

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

ORGAN WEIGHTS (MALE)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
BODY WEIGHT (g) NE	MEAN	274.0	279.8	269.8	261.2	231.2
	S.D.	23.2	18.4	13.8	21.6	19.9
	N	5	5	5	5	5
Heart Weight (g)	MEAN	1.005	1.129	0.871	0.939	0.809 -
	S.D.	0.120	0.124	0.094	0.098	0.089
	N	5	5	5	5	5
Liver Weight (g)	MEAN	11.238	10.792	11.084	12.904 +	14.118 +
	S.D.	1.106	0.920	1.019	1.465	1.372
	N	5	5	5	5	5
Kidneys Weight (g)	MEAN	2.097	2.049	2.105	2.229	1.964
	S.D.	0.279	0.185	0.092	0.251	0.098
	N	5	5	5	5	5
Spleen Weight (g)	MEAN	0.817	0.753	0.676 -	0.641 -	0.583 -
	S.D.	0.145	0.108	0.070	0.091	0.090
	N	5	5	5	5	5
Testes Weight (g)	MEAN	3.216	3.543	3.297	3.481	3.463
	S.D.	0.277	0.335	0.256	0.333	0.076
	N	5	5	5	5	5
Epididymis Weight (g)	MEAN	0.824	0.861	0.826	0.813	0.780
	S.D.	0.076	0.062	0.067	0.050	0.090
	N	5	5	5	5	5
Adrenals Weight (g)	MEAN	0.0456	0.0452	0.0426	0.0470	0.0558 +
	S.D.	0.0022	0.0054	0.0044	0.0040	0.0057
	N	5	5	5	5	5

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE						
ORGAN WEIGHTS (MALE)						

		GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5
		0	3	15	60	240
		mg/kg	mg/kg	mg/kg	mg/kg	mg/kg

Brain Weight (g)	MEAN	1.836	1.850	1.746	1.774	1.767
	S.D.	0.093	0.068	0.076	0.089	0.060
	N	5	5	5	5	5
Thymus Weight (g)	MEAN	0.479	0.511	0.409	0.445	0.346 -
	S.D.	0.044	0.036	0.067	0.079	0.053
	N	5	5	5	5	5

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

ORGAN WEIGHTS (FEMALE)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
BODY WEIGHT (g) NE	MEAN S.D. N	210.6 9.4 5	195.0 4.9 5	205.8 5.0 5	199.8 8.7 5	184.6 11.7 5
Heart Weight (g)	MEAN S.D. N	0.776 0.060 5	0.828 0.079 5	0.754 0.070 5	0.710 - 0.032 5	0.667 - 0.048 5
Liver Weight (g)	MEAN S.D. N	8.408 0.576 5	7.294 0.436 5	8.346 0.507 5	9.804 + 0.666 5	13.792 + 1.814 5
Kidneys Weight (g)	MEAN S.D. N	1.461 0.103 5	1.304 0.059 5	1.513 0.111 5	1.929 + 0.142 5	1.642 + 0.146 5
Spleen Weight (g)	MEAN S.D. N	0.649 0.040 5	0.641 0.073 5	0.713 0.056 5	0.581 - 0.051 5	0.456 - 0.038 5
Adrenals Weight (g)	MEAN S.D. N	0.0604 0.0095 5	0.0548 0.0033 5	0.0590 0.0070 5	0.0590 0.0038 5	0.0596 0.0086 5
Brain Weight (g)	MEAN S.D. N	1.781 0.054 5	1.709 0.093 5	1.726 0.093 5	1.684 - 0.053 5	1.659 - 0.105 5
Thymus Weight (g)	MEAN S.D. N	0.407 0.076 5	0.399 0.054 5	0.430 0.070 5	0.354 0.022 5	0.309 - 0.067 5

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

ORGAN WEIGHTS (MALE)

		GROUP 1 0 mg/kg	GROUP 5 240 mg/kg

BODY WEIGHT (g) NE	MEAN	320.0	194.0
	S.D.	50.8	35.9
	N	5	4
Heart Weight (g)	MEAN	1.188	0.758 -
	S.D.	0.252	0.121
	N	5	4
Liver Weight (g)	MEAN	10.446	5.748 -
	S.D.	2.238	1.373
	N	5	4
Kidneys Weight (g)	MEAN	2.303	1.496 -
	S.D.	0.401	0.348
	N	5	4
Spleen Weight (g)	MEAN	0.772	0.428 -
	S.D.	0.125	0.125
	N	5	4
Testes Weight (g)	MEAN	3.510	3.332
	S.D.	0.464	0.294
	N	5	4
Epididymis Weight (g)	MEAN	1.143	0.910 -
	S.D.	0.120	0.130
	N	5	4
Adrenals Weight (g)	MEAN	0.0486	0.0450
	S.D.	0.0066	0.0042
	N	5	4

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

ORGAN WEIGHTS (MALE)

		GROUP 1 0 mg/kg	GROUP 5 240 mg/kg
-----		-----	
Brain Weight (g)	MEAN	1.939	1.730
	S.D.	0.140	0.127
	N	5	4
Thymus Weight (g)	MEAN	0.385	0.202 -
	S.D.	0.072	0.117
	N	5	4
-----		-----	

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

ORGAN WEIGHTS (FEMALE)

		GROUP 1 0 mg/kg	GROUP 5 240 mg/kg

BODY WEIGHT (g) NE	MEAN	225.6	189.4
	S.D.	17.5	29.9
	N	5	5
Heart Weight (g)	MEAN	0.816	0.710
	S.D.	0.064	0.101
	N	5	5
Liver Weight (g)	MEAN	7.556	6.502
	S.D.	0.864	1.373
	N	5	5
Kidneys Weight (g)	MEAN	1.572	1.412
	S.D.	0.072	0.187
	N	5	5
Spleen Weight (g)	MEAN	0.674	0.537
	S.D.	0.123	0.111
	N	5	5
Adrenals Weight (g)	MEAN	0.0636	0.0514
	S.D.	0.0075	0.0099
	N	5	5
Brain Weight (g)	MEAN	1.837	1.774
	S.D.	0.072	0.066
	N	5	5
Thymus Weight (g)	MEAN	0.350	0.311
	S.D.	0.050	0.064
	N	5	5

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

12.9 ORGAN WEIGHTS (GROUPS 6 - 7)

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 05-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

ORGAN WEIGHTS (MALE)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d

BODY WEIGHT (g) NE	MEAN	295.6	307.8
	S.D.	17.5	25.4
	N	5	5
Heart Weight (g)	MEAN	1.171	1.188
	S.D.	0.199	0.115
	N	5	5
Liver Weight (g)	MEAN	12.222	12.174
	S.D.	1.301	1.883
	N	5	5
Kidneys Weight (g)	MEAN	2.411	2.430
	S.D.	0.208	0.324
	N	5	5
Spleen Weight (g)	MEAN	0.801	0.802
	S.D.	0.094	0.052
	N	5	5
Testes Weight (g)	MEAN	3.598	3.579
	S.D.	0.194	0.283
	N	5	5
Epididymis Weight (g)	MEAN	0.888	0.848
	S.D.	0.056	0.045
	N	5	5
Adrenals Weight (g)	MEAN	0.0512	0.0466
	S.D.	0.0070	0.0061
	N	5	5

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 05-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

ORGAN WEIGHTS (MALE)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d

Brain Weight (g)	MEAN	1.883	1.900
	S.D.	0.075	0.076
	N	5	5
Thymus Weight (g)	MEAN	0.570	0.584
	S.D.	0.116	0.110
	N	5	5

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 05-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

ORGAN WEIGHTS (FEMALE)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d

BODY WEIGHT (g) NE	MEAN	190.6	199.0
	S.D.	9.8	11.7
	N	5	5
Heart Weight (g)	MEAN	0.778	0.793
	S.D.	0.074	0.068
	N	5	5
Liver Weight (g)	MEAN	6.948	7.480
	S.D.	0.637	0.961
	N	5	5
Kidneys Weight (g)	MEAN	1.332	1.417
	S.D.	0.075	0.121
	N	5	5
Spleen Weight (g)	MEAN	0.613	0.679
	S.D.	0.060	0.072
	N	5	5
Adrenals Weight (g)	MEAN	0.0580	0.0554
	S.D.	0.0087	0.0072
	N	5	5
Brain Weight (g)	MEAN	1.720	1.757
	S.D.	0.113	0.093
	N	5	5
Thymus Weight (g)	MEAN	0.322	0.381
	S.D.	0.083	0.079
	N	5	5

T-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

12.10 RELATIVE ORGAN WEIGHTS (GROUPS 1 - 5)

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

RELATIVE ORGAN WEIGHTS MALES (g/kg bdwt)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
BODY WEIGHT (g) NE	MEAN	274.0	279.8	269.8	261.2	231.2
	S.D.	23.2	18.4	13.8	21.6	19.9
	N	5	5	5	5	5
Heart Weight	MEAN	3.663	4.027	3.230	3.589	3.495
	S.D.	0.189	0.244	0.337	0.114	0.186
	N	5	5	5	5	5
Liver Weight	MEAN	40.983	38.536	41.020	49.301 +	61.061 +
	S.D.	0.975	0.993	1.985	1.620	2.650
	N	5	5	5	5	5
Kidneys Weight	MEAN	7.639	7.318	7.819	8.532	8.523
	S.D.	0.594	0.284	0.526	0.670	0.451
	N	5	5	5	5	5
Spleen Weight	MEAN	2.973	2.696	2.507	2.451	2.520
	S.D.	0.390	0.375	0.241	0.249	0.283
	N	5	5	5	5	5
Testes Weight	MEAN	11.767	12.660	12.211	13.347 +	15.072 +
	S.D.	1.028	0.741	0.536	0.948	1.395
	N	5	5	5	5	5
Epididymis Weight	MEAN	3.023	3.085	3.067	3.117	3.394
	S.D.	0.355	0.264	0.271	0.105	0.487
	N	5	5	5	5	5
Adrenals Weight	MEAN	0.1676	0.1623	0.1583	0.1811	0.2413 +
	S.D.	0.0184	0.0245	0.0192	0.0244	0.0128
	N	5	5	5	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE						
RELATIVE ORGAN WEIGHTS MALES (g/kg bdwt)						

		GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5
		0	3	15	60	240
		mg/kg	mg/kg	mg/kg	mg/kg	mg/kg

Brain Weight	MEAN	6.727	6.625	6.485	6.814	7.688 +
	S.D.	0.477	0.258	0.461	0.443	0.715
	N	5	5	5	5	5
Thymus Weight	MEAN	1.750	1.834	1.523	1.712	1.496 -
	S.D.	0.071	0.176	0.295	0.336	0.171
	N	5	5	5	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL
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Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

RELATIVE ORGAN WEIGHTS FEMALES (g/kg bdwt)

		GROUP 1 0 mg/kg	GROUP 2 3 mg/kg	GROUP 3 15 mg/kg	GROUP 4 60 mg/kg	GROUP 5 240 mg/kg
BODY WEIGHT (g) NE	MEAN S.D. N	210.6 9.4 5	195.0 4.9 5	205.8 5.0 5	199.8 8.7 5	184.6 11.7 5
Heart Weight	MEAN S.D. N	3.685 0.261 5	4.254 0.502 5	3.668 0.360 5	3.560 0.260 5	3.616 0.141 5
Liver Weight	MEAN S.D. N	39.929 2.145 5	37.383 1.466 5	40.539 1.889 5	49.078 + 2.797 5	74.510 + 5.710 5
Kidneys Weight	MEAN S.D. N	6.952 0.645 5	6.688 0.330 5	7.344 0.381 5	9.659 + 0.671 5	8.902 + 0.717 5
Spleen Weight	MEAN S.D. N	3.081 0.109 5	3.291 0.402 5	3.463 0.266 5	2.906 - 0.183 5	2.467 - 0.096 5
Adrenals Weight	MEAN S.D. N	0.2882 0.0558 5	0.2813 0.0203 5	0.2872 0.0375 5	0.2961 0.0280 5	0.3221 0.0326 5
Brain Weight	MEAN S.D. N	8.471 0.521 5	8.778 0.685 5	8.386 0.364 5	8.438 0.319 5	8.995 0.366 5
Thymus Weight	MEAN S.D. N	1.931 0.366 5	2.042 0.252 5	2.089 0.313 5	1.773 0.074 5	1.677 0.347 5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

RELATIVE ORGAN WEIGHTS MALES (g/kg bdwt)

		GROUP 1 0 mg/kg	GROUP 5 240 mg/kg
BODY WEIGHT (g) NE	MEAN S.D. N	320.0 50.8 5	194.0 35.9 4
Heart Weight	MEAN S.D. N	3.693 0.248 5	3.934 0.362 4
Liver Weight	MEAN S.D. N	32.441 2.019 5	29.388 1.924 4
Kidneys Weight	MEAN S.D. N	7.194 0.344 5	7.658 0.579 4
Spleen Weight	MEAN S.D. N	2.423 0.244 5	2.172 0.267 4
Testes Weight	MEAN S.D. N	11.024 0.784 5	17.675 + 4.005 4
Epididymis Weight	MEAN S.D. N	3.605 0.332 5	4.731 + 0.426 4
Adrenals Weight	MEAN S.D. N	0.1531 0.0191 5	0.2355 + 0.0272 4

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

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Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE			
RELATIVE ORGAN WEIGHTS MALES (g/kg bdwt)			
		GROUP 1	GROUP 5
		0	240
		mg/kg	mg/kg
Brain Weight	MEAN	6.163	9.088 +
	S.D.	0.954	1.276
	N	5	4
Thymus Weight	MEAN	1.207	0.978
	S.D.	0.143	0.452
	N	5	4

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 17-DEC-2002

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

RECOVERY VALUE

RELATIVE ORGAN WEIGHTS FEMALES (g/kg bdwt)

		GROUP 1 0 mg/kg	GROUP 5 240 mg/kg
BODY WEIGHT (g) NE	MEAN S.D. N	225.6 17.5 5	189.4 29.9 5
Heart Weight	MEAN S.D. N	3.620 0.170 5	3.761 0.192 5
Liver Weight	MEAN S.D. N	33.510 3.125 5	34.229 3.310 5
Kidneys Weight	MEAN S.D. N	6.994 0.493 5	7.506 0.632 5
Spleen Weight	MEAN S.D. N	2.979 0.411 5	2.833 0.285 5
Adrenals Weight	MEAN S.D. N	0.2854 0.0570 5	0.2715 0.0360 5
Brain Weight	MEAN S.D. N	8.178 0.637 5	9.533 + 1.339 5
Thymus Weight	MEAN S.D. N	1.549 0.157 5	1.643 0.213 5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

12.11 RELATIVE ORGAN WEIGHTS (GROUPS 6 - 7)

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 05-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

RELATIVE ORGAN WEIGHTS MALES (g/kg bdwt)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d

BODY WEIGHT (g) NE	MEAN	295.6	307.8
	S.D.	17.5	25.4
	N	5	5
Heart Weight	MEAN	3.940	3.863
	S.D.	0.493	0.259
	N	5	5
Liver Weight	MEAN	41.264	39.383
	S.D.	2.444	3.539
	N	5	5
Kidneys Weight	MEAN	8.150	7.895
	S.D.	0.330	0.814
	N	5	5
Spleen Weight	MEAN	2.705	2.613
	S.D.	0.239	0.139
	N	5	5
Testes Weight	MEAN	12.185	11.656
	S.D.	0.490	0.834
	N	5	5
Epididymis Weight	MEAN	3.007	2.766
	S.D.	0.158	0.230
	N	5	5
Adrenals Weight	MEAN	0.1728	0.1522
	S.D.	0.0176	0.0231
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 05-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE			
RELATIVE ORGAN WEIGHTS MALES (g/kg bdwt)			

		GROUP 1	GROUP 2
		0	0.3
		mg/kg/d	mg/kg/d

Brain Weight	MEAN	6.385	6.199
	S.D.	0.377	0.470
	N	5	5
Thymus Weight	MEAN	1.924	1.891
	S.D.	0.339	0.277
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 05-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

RELATIVE ORGAN WEIGHTS FEMALES (g/kg bdwt)

		GROUP 1 0 mg/kg/d	GROUP 2 0.3 mg/kg/d

BODY WEIGHT (g) NE	MEAN	190.6	199.0
	S.D.	9.8	11.7
	N	5	5
Heart Weight	MEAN	4.077	3.981
	S.D.	0.257	0.207
	N	5	5
Liver Weight	MEAN	36.394	37.491
	S.D.	1.542	3.015
	N	5	5
Kidneys Weight	MEAN	6.987	7.114
	S.D.	0.225	0.366
	N	5	5
Spleen Weight	MEAN	3.222	3.405
	S.D.	0.318	0.229
	N	5	5
Adrenals Weight	MEAN	0.3037	0.2783
	S.D.	0.0382	0.0327
	N	5	5
Brain Weight	MEAN	9.022	8.850
	S.D.	0.297	0.656
	N	5	5
Thymus Weight	MEAN	1.683	1.916
	S.D.	0.366	0.392
	N	5	5

WILCOXON-TEST. TWO-TAILED TEST FOR THE HIGHEST DOSE AND ONE-TAILED TESTS FOR LOWER DOSES,
IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

12.12 NEUROTOXICOLOGICAL EXAMINATIONS

12.12.1 Griph strength - Groups 1 - 5

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 28-MAY-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

NEUROTOXICOLOGICAL EVALUATION

		GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5
		0	3	15	60	240
		mg/kg	mg/kg	mg/kg	mg/kg	mg/kg
FORELIMB GRIP STRENGTH (g) (MALES)	MEAN	807.0	750.0	788.0	726.0 -	683.0 -
	S.D.	38.6	55.2	37.7	68.4	51.4
	N	10	5	5	5	10
HINDLIMB GRIP STRENGTH (g) (MALES)	MEAN	298.0	283.0	279.0	282.0 -	253.0 -
	S.D.	15.7	24.1	15.2	8.4	11.4
	N	10	5	5	5	10
FORELIMB GRIP STRENGTH (g) (FEMALES)	MEAN	759.0	708.0	694.0	706.0	686.0 -
	S.D.	51.5	24.9	50.3	66.2	64.2
	N	10	5	5	5	10
HINDLIMB GRIP STRENGTH (g) (FEMALES)	MEAN	279.0	258.0	256.0	273.0	231.0 -
	S.D.	11.3	9.1	16.4	12.0	20.4
	N	10	5	5	5	10

WILCOXON-TEST. ONE-TAILED TESTS FOR ALL COMPARISONS

LOWER DOSES ARE ONLY TESTED IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

TESTS ARE PERFORMED ONLY WHEN SIGNIFICANCE IS FOUND ON PRELIMINARY EXAMINATION

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

12.12.2 Griph strength - Groups 6 - 7

Toxicology Study Report - PT02-0222

ATOK 18.2

PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

NEUROTOXICOLOGICAL EVALUATION

		GROUP 1	GROUP 2
		0	0.3
		mg/kg/d	mg/kg/d
-----		-----	-----
FORELIMB GRIP STRENGTH (g)	MEAN	796.0	804.0
(MALES)	S.D.	15.2	20.7
	N	5	5
HINDLIMB GRIP STRENGTH (g)	MEAN	290.0	286.0
(MALES)	S.D.	3.5	12.4
	N	5	5
FORELIMB GRIP STRENGTH (g)	MEAN	770.0	740.0
(FEMALES)	S.D.	36.7	40.0
	N	5	5
HINDLIMB GRIP STRENGTH (g)	MEAN	282.0	268.0
(FEMALES)	S.D.	7.6	14.4
	N	5	5
-----		-----	-----

WILCOXON-TEST, ONE-TAILED TESTS FOR ALL COMPARISONS

LOWER DOSES ARE ONLY TESTED IF ALL HIGHER DOSES ARE SIGNIFICANTLY DIFFERENT FROM CONTROL (P < 0.05).

TESTS ARE PERFORMED ONLY WHEN SIGNIFICANCE IS FOUND ON PRELIMINARY EXAMINATION

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL

NE : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

12.12.3 Motor activity (Groups 1 - 5)

Toxicology Study Report - PT02-0222

ATOX 10.2 PROVANTIS RUN DATE: 28-MAY-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE

NEUROTOXICOLOGICAL EVALUATION

		GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5
		0	3	15	60	240
		mg/kg	mg/kg	mg/kg	mg/kg	mg/kg

NUMBER OF MOVEMENTS (MALES)	MEAN	547.8	587.6	538.4	587.0	533.7
	S.D.	131.8	131.1	82.7	99.3	134.0
	N	10	5	5	5	10
NUMBER OF MOVEMENTS (FEMALES)		MEAN	653.4	579.2	548.4	508.8
		S.D.	78.0	84.6	69.9	103.4
		N	5	5	5	10

WILCOXON-TEST. SEQUENTIALLY REJECTIVE MULTIPLE COMPARISONS (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

12.12.4 Motor activity (Groups 6 - 7)

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 11-MAR-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

FINAL VALUE			
NEUROTOXICOLOGICAL EVALUATION			
		GROUP 1	GROUP 2
		0	0.3
		mg/kg/d	mg/kg/d
NUMBER OF MOVEMENTS (MALES)	MEAN	534.4	615.6
	S.D.	78.6	45.4
	N	5	5
NUMBER OF MOVEMENTS (FEMALES)	MEAN	578.6	642.6
	S.D.	89.0	129.0
	N	5	5

WILCOXON-TEST. SEQUENTIALLY REJECTIVE MULTIPLE COMPARISONS (P < 0.05).

+/- : SIGNIFICANTLY DIFFERENT FROM CONTROL
M : EVALUATION NOT POSSIBLE NE : NO STATISTICAL EVALUATION

13 APPENDICES

13.1 INDIVIDUAL TABLES

13.1.1 Body weights

Toxicology Study Report - PT02-0222

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PROVANTIS

Date: 16-Dec-2002 Page: 1

Bodyweights - Individual Bodyweights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Bodyweights (g)														

		Day numbers relative to Start Date														
Group	Animal	-3	1	5	8	12	15	19	22	26	29	33	36	40	42	43
Sex	Number															
1m	1	118	138	166	184	210	224	244	248	254	271	.	.	.	.	.
	2	111	128	149	165	191	210	229	236	239	255	.	.	.	.	.
	3	112	134	158	176	202	219	235	242	249	262	.	.	.	.	.
	4	118	143	171	191	221	246	270	286	299	314	.	.	.	.	.
	5	120	144	136	157	190	215	238	250	258	268	.	.	.	.	.
	6	119	142	173	192	219	241	265	279	293	304	324	333	356	.	353
	7	113	132	145	157	173	195	205	214	222	231	240	248	259	.	259
	8	109	130	142	158	184	209	228	245	251	266	266	273	289	.	284
	9	127	151	180	210	240	259	285	303	321	337	349	358	378	.	385
	10	120	142	164	182	213	231	253	267	274	288	300	309	316	.	319
Mean		116.7	138.4	158.4	177.2	204.3	224.9	245.2	257.0	266.0	279.6	295.8	304.2	319.6	.	320.0
S.D.		5.4	7.3	14.8	17.9	20.2	19.5	23.5	26.5	30.4	31.3	43.7	44.4	48.4	.	50.8
N		10	10	10	10	10	10	10	10	10	10	5	5	5	0	5

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

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Date: 16-Dec-2002 Page: 2

Bodyweights - Individual Bodyweights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Bodyweights (g)														

		Day numbers relative to Start Date														
Group	Animal	-3	1	5	8	12	15	19	22	26	29	33	36	40	42	43
Sex	Number															
1f	31	110	126	143	147	152	168	175	178	188	199	.	.	.	.	.
	32	119	133	149	158	173	177	183	188	201	210	.	.	.	.	.
	33	109	127	148	159	172	182	194	198	210	221	.	.	.	.	.
	34	117	135	155	170	180	188	197	202	214	219	.	.	.	.	.
	35	111	125	141	154	165	173	184	189	196	204	.	.	.	.	.
	36	111	127	141	155	167	174	186	194	202	204	212	214	218	.	213
	37	118	132	152	162	176	187	199	206	224	233	239	235	237	.	238
	38	110	123	139	146	155	163	173	179	187	193	200	201	197	.	201
	39	119	136	155	169	182	184	186	201	214	217	225	233	242	.	237
	40	107	128	148	162	173	184	190	198	207	218	226	225	238	.	239
Mean	113.1	129.2	147.1	158.2	169.5	178.0	186.7	193.3	204.3	211.8	220.4	221.6	226.4	.	225.6	
S.D.	4.6	4.5	5.9	8.1	9.9	8.4	8.6	9.6	11.9	12.0	14.9	14.2	18.9	.	17.5	
N	10	10	10	10	10	10	10	10	10	10	5	5	5	0	5	

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

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Date: 16-Dec-2002 Page: 3

Bodyweights - Individual Bodyweights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Bodyweights (g)														

		Day numbers relative to Start Date														
Group	Animal	-3	1	5	8	12	15	19	22	26	29	33	36	40	42	43
Sex	Number															
2m	11	122	143	146	162	190	210	233	243	251	264	.	.	.	.	.
	12	116	137	160	178	201	210	226	235	236	250	.	.	.	.	.
	13	125	151	176	197	227	239	261	267	276	287	.	.	.	.	.
	14	125	144	170	185	212	228	243	253	262	273	.	.	.	.	.
	15	123	146	159	180	212	228	249	257	266	275	.	.	.	.	.
	Mean	122.2	144.2	162.2	180.4	208.4	223.0	242.4	251.0	258.2	269.8	.	.	.	.	.
	S.D.	3.7	5.1	11.5	12.7	13.8	12.7	13.7	12.4	15.3	13.8	.	.	.	.	.
	N	5	5	5	5	5	5	5	5	5	5	0	0	0	0	0

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

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Date: 16-Dec-2002 Page: 4

Bodyweights - Individual Bodyweights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Bodyweights (g)														

		Day numbers relative to Start Date														
Group	Animal	-3	1	5	8	12	15	19	22	26	29	33	36	40	42	43
Sex	Number															
2f	41	118	131	146	160	166	175	191	194	202	207	.	.	.	.	.
	42	115	132	145	152	163	178	192	193	205	206	.	.	.	.	.
	43	117	136	151	161	171	182	191	193	203	206	.	.	.	.	.
	44	111	129	146	161	170	180	190	199	208	212	.	.	.	.	.
	45	112	127	140	150	161	169	182	186	192	198	.	.	.	.	.
Mean		114.6	131.0	145.6	156.8	166.2	176.8	189.2	193.0	202.0	205.8	.	.	.	.	.
S.D.		3.0	3.4	3.9	5.4	4.3	5.1	4.1	4.6	6.0	5.0	.	.	.	.	.
N		5	5	5	5	5	5	5	5	5	5	0	0	0	0	0

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

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PROVANTIS

Date: 16-Dec-2002 Page: 5

Bodyweights - Individual Bodyweights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Bodyweights (g)														

		Day numbers relative to Start Date														
Group	Animal	-3	1	5	8	12	15	19	22	26	29	33	36	40	42	43
Sex	Number															
3m	16	112	132	135	151	173	190	207	214	220	230	.	.	.	.	.
	17	122	141	144	163	187	201	227	233	238	249	.	.	.	.	.
	18	130	152	143	165	195	216	242	250	264	276	.	.	.	.	.
	19	116	140	145	168	193	218	241	258	268	283	.	.	.	.	.
	20	129	152	151	176	203	220	243	248	255	268	.	.	.	.	.
	Mean	121.8	143.4	143.6	164.6	190.2	209.0	232.0	240.6	249.0	261.2	.	.	.	.	.
	S.D.	7.9	8.6	5.7	9.1	11.2	13.0	15.4	17.4	19.9	21.6	.	.	.	.	.
	N	5	5	5	5	5	5	5	5	5	5	0	0	0	0	0

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

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Date: 16-Dec-2002 Page: 6

Bodyweights - Individual Bodyweights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Bodyweights (g)														

		Day numbers relative to Start Date														
Group	Animal	-3	1	5	8	12	15	19	22	26	29	33	36	40	42	43
Sex	Number															
3f	46	111	129	137	156	172	176	187	195	209	210	.	.	.	.	.
	47	113	134	133	150	166	178	183	195	202	200	.	.	.	.	.
	48	122	136	143	155	166	175	194	191	201	202	.	.	.	.	.
	49	114	133	107	127	145	156	169	169	181	186	.	.	.	.	.
	50	116	134	135	153	167	177	188	192	198	201	.	.	.	.	.
	Mean	115.2	133.2	131.0	148.2	163.2	172.4	184.2	188.4	198.2	199.8	.	.	.	.	.
	S.D.	4.2	2.6	13.9	12.1	10.5	9.2	9.4	11.0	10.4	8.7	.	.	.	.	.
	N	5	5	5	5	5	5	5	5	5	5	0	0	0	0	0

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

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Date: 16-Dec-2002 Page: 7

Bodyweights - Individual Bodyweights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Bodyweights (g)														

		Day numbers relative to Start Date														
Group	Animal	-3	1	5	8	12	15	19	22	26	29	33	36	40	42	43
Sex	Number															
4m	21	126	150	156	174	191	211	228	226	237	235	.	.	.	.	.
	22	118	143	141	155	176	196	214	210	218	228	.	.	.	.	.
	23	131	157	145	155	177	194	217	220	232	239	.	.	.	.	.
	24	116	142	145	158	186	208	234	240	251	254	.	.	.	.	.
	25	120	144	136	152	168	178	197	199	206	200	.	.	.	.	.
	26	125	148	144	156	181	199	220	226	241	243	235	226	222	.	216
	27	117	141	118	146	164	176	199	207	214	216	219	206	192	.	176
	28	120	142	135	150	177	190	208	218	202	213	197	175	165	.	153
	29	124	149	138	162	185	202	223	228	242	248	238	228	233	.	231
	30	111	134	124	131	156	162	188	185	168	173	184	174	144	133	.
	Mean	120.8	145.0	138.2	153.9	176.1	191.6	212.8	215.9	221.1	224.9	214.6	201.8	191.2	133.0	194.0
	S.D.	5.8	6.3	10.9	11.0	10.8	15.4	14.7	16.0	24.9	24.8	23.6	26.4	37.5	.	35.9
	N	10	10	10	10	10	10	10	10	10	10	5	5	5	1	4

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

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Bodyweights - Individual Bodyweights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Bodyweights (g)														
		Day numbers relative to Start Date														
Group	Animal	-3	1	5	8	12	15	19	22	26	29	33	36	40	42	43
Sex	Number															
4f	51	119	135	133	149	164	173	186	191	195	198	.	.	.	.	.
	52	116	129	127	139	158	168	184	183	191	195	.	.	.	.	.
	53	106	121	122	135	151	152	164	164	166	170	.	.	.	.	.
	54	107	120	112	130	150	153	164	169	178	182	.	.	.	.	.
	55	114	128	127	142	150	159	167	174	174	178	.	.	.	.	.
	56	111	127	138	154	171	179	192	198	204	209	217	221	221	.	218
	57	116	130	126	145	156	167	181	181	190	197	198	201	204	.	186
	58	115	131	130	146	158	172	185	189	198	203	207	212	207	.	184
	59	105	118	115	110	129	140	153	160	161	140	149	146	150	.	144
	60	113	127	131	142	157	165	174	175	182	188	197	206	210	.	215
Mean		112.2	126.6	126.1	139.2	154.4	162.8	175.0	178.4	183.9	186.0	193.6	197.2	198.4	.	189.4
S.D.		4.8	5.4	8.0	12.3	11.0	11.8	12.6	12.2	14.1	20.1	26.2	29.6	27.8	.	29.9
N		10	10	10	10	10	10	10	10	10	10	5	5	5	0	5

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

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Date: 16-Dec-2002 Page: 1

Bodyweights - Individual Bodyweights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Bodyweights (g)									
		Day numbers relative to Start Date									
Group	Animal	-3	1	4	8	11	15	18	22	25	29
Sex	Number										
5m	61	112	137	157	190	215	238	260	274	290	298
	62	108	128	146	177	195	213	232	250	262	272
	63	116	135	153	179	197	219	229	243	253	256
	64	113	134	155	183	205	231	242	264	277	274
	65	112	136	153	187	213	239	259	284	297	299
	Mean	112.2	134.0	152.8	183.2	205.0	228.0	244.4	263.0	275.8	279.8
	S.D.	2.9	3.5	4.1	5.4	9.1	11.6	14.6	16.8	18.5	18.4
	N	5	5	5	5	5	5	5	5	5	5

* = result to left has an associated comment or marker

Nominal Dose: Group 5 - 3 mg/kg

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Date: 16-Dec-2002 Page: 2

Bodyweights - Individual Bodyweights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

		Bodyweights (g)									
		Day numbers relative to Start Date									
Group	Animal	-3	1	4	8	11	15	18	22	25	29
Sex	Number										
5f	66	112	124	137	148	159	170	174	185	191	198
	67	107	122	137	151	163	175	181	189	196	200
	68	101	117	129	146	152	161	166	180	186	188
	69	107	120	133	147	159	169	179	189	193	197
	70	106	120	136	152	156	167	181	181	188	192
	Mean	106.6	120.6	134.4	148.8	157.8	168.4	176.2	184.8	190.8	195.0
	S.D.	3.9	2.6	3.4	2.6	4.1	5.1	6.4	4.3	4.0	4.9
	N	5	5	5	5	5	5	5	5	5	5

* = result to left has an associated comment or marker

Nominal Dose: Group 5 - 3 mg/kg

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Date: 03-Mar-2003 Page: 1

Bodyweights - Individual Bodyweights

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

		Bodyweights (g)									
		Day numbers relative to Start Date									
Group	Animal	-4	1	4	8	11	15	18	22	25	29
Sex	Number										
6m	71	107	139	161	189	214	245	267	286	296	307
	72	100	133	156	185	211	241	259	284	297	311
	73	111	141	159	183	205	223	231	245	256	268
	74	106	140	159	190	216	239	257	270	290	303
	75	107	143	165	193	216	235	253	267	278	289
	Mean	106.2	139.2	160.0	188.0	212.4	236.6	253.4	270.4	283.4	295.6
	S.D.	4.0	3.8	3.3	4.0	4.6	8.4	13.5	16.5	17.1	17.5
	N	5	5	5	5	5	5	5	5	5	5

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Bodyweights - Individual Bodyweights

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

		Bodyweights (g)									
		Day numbers relative to Start Date									
Group	Animal	-4	1	4	8	11	15	18	22	25	29
Sex	Number										
6f	81	106	127	138	151	161	171	173	182	184	191
	82	110	128	132	141	155	164	173	181	184	189
	83	99	117	125	133	145	153	162	169	172	176
	84	103	123	138	146	158	166	175	181	182	194
	85	106	128	139	154	165	176	187	192	198	203
	Mean	104.8	124.6	134.4	145.0	156.8	166.0	174.0	181.0	184.0	190.6
	S.D.	4.1	4.7	5.9	8.3	7.6	8.6	8.9	8.2	9.3	9.8
	N	5	5	5	5	5	5	5	5	5	5

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Date: 03-Mar-2003 Page: 3

Bodyweights - Individual Bodyweights

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

		Bodyweights (g)									
		Day numbers relative to Start Date									
Group	Animal	-4	1	4	8	11	15	18	22	25	29
Sex	Number										
7m	76	105	141	164	191	215	242	265	282	294	308
	77	105	137	155	183	204	237	260	288	288	312
	78	113	141	162	187	207	227	240	246	261	266
	79	110	148	167	197	223	250	272	292	300	319
	80	111	144	170	198	229	256	283	306	317	334
	Mean	108.8	142.2	163.6	191.2	215.6	242.4	264.0	282.8	292.0	307.8
	S.D.	3.6	4.1	5.7	6.4	10.5	11.3	16.0	22.4	20.4	25.4
	N	5	5	5	5	5	5	5	5	5	5

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Bodyweights - Individual Bodyweights

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

		Bodyweights (g)									
		Day numbers relative to Start Date									
Group	Animal	-4	1	4	8	11	15	18	22	25	29
Sex	Number										
7f	86	97	118	130	137	148	157	165	175	174	185
	87	105	125	142	156	163	179	186	191	193	201
	88	105	128	138	147	159	172	172	186	188	195
	89	104	128	142	153	168	176	179	184	187	197
	90	102	127	144	159	169	179	190	203	201	217
	Mean	102.6	125.2	139.2	150.4	161.4	172.6	178.4	187.8	188.6	199.0
	S.D.	3.4	4.2	5.6	8.7	8.5	9.2	10.2	10.3	9.9	11.7
	N	5	5	5	5	5	5	5	5	5	5

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

13.1.2 Food Consumption

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Food Consumption By Animal - Individual Food Consumption Relative To Bodyweight

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date																
Group	Animal	From:	-3	1	5	8	12	15	19	22	26	29	33	36	40	Mean
Sex	Number	To:	1	5	8	12	15	19	22	26	29	33	36	40	43	-3
1m	1		118.75	100.33	91.43	88.58	85.10	79.70	69.38	57.17	64.25	.	.	.	.	83.85
	2		127.20	110.11	101.91	98.03	92.10	84.97	73.41	60.42	68.29	.	.	.	.	90.72
	3		123.58	104.45	95.81	92.33	87.73	82.16	71.56	58.45	66.01	.	.	.	.	86.90
	4		116.48	97.13	88.40	84.71	79.09	72.29	61.39	49.06	55.03	.	.	.	.	78.18
	5		115.15	108.93	109.22	100.58	91.19	82.34	69.95	56.50	64.13	.	.	.	.	88.67
	6		116.99	97.46	90.59	82.48	81.16	76.28	69.12	59.44	57.17	65.92	62.51	60.23	47.20	74.35
	7		124.63	110.83	109.49	102.73	101.45	96.50	89.74	77.98	75.35	87.90	84.15	81.85	64.61	92.86
	8		127.75	112.87	110.22	99.12	95.00	88.33	79.49	68.55	66.02	77.82	76.19	73.84	58.41	87.20
	9		109.83	92.75	84.79	75.33	74.82	70.96	63.95	54.49	51.87	60.35	58.09	56.39	43.86	69.04
	10		116.54	100.33	95.57	85.82	84.08	79.75	72.31	62.85	60.74	70.41	67.43	66.40	52.70	78.07
-----			-----													
	Mean		119.69	103.52	97.74	90.97	87.17	81.33	72.03	60.49	62.89	72.48	69.67	67.74	53.36	82.98
	S.D.		5.84	6.90	9.41	9.05	7.98	7.56	7.96	8.00	6.90	10.73	10.52	10.29	8.38	7.74
	N		10	10	10	10	10	10	10	10	10	5	5	5	5	10
-----			-----													

* = result to left has an associated comment or marker
Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

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Food Consumption By Animal - Individual Food Consumption Relative To Bodyweight

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date																	
Group	Animal	From:	-3	1	5	8	12	15	19	22	26	29	33	36	40	Mean	
Sex	Number	To:	1	5	8	12	15	19	22	26	29	33	36	40	43	-3	
																43	
1f	31		110.17	108.18	94.25	85.95	80.00	79.01	73.28	68.58	66.84	.	.	.	.	85.14	
	32		103.17	103.19	89.03	77.64	73.14	75.28	69.72	64.52	62.94	.	.	.	.	79.85	
	33		110.17	105.82	89.03	77.64	72.32	72.07	65.99	61.52	60.02	.	.	.	.	79.40	
	34		103.17	100.34	84.10	73.43	69.57	70.39	64.83	60.34	59.74	.	.	.	.	76.21	
	35		110.17	109.40	92.66	80.56	75.74	75.91	69.35	65.19	64.67	.	.	.	.	82.63	
	36		108.12	107.84	95.95	83.85	75.86	73.33	75.79	67.93	64.37	81.49	69.17	70.14	62.80	79.74	
	37		102.93	101.76	90.45	79.88	71.26	68.39	71.11	62.56	57.18	71.82	62.17	64.19	56.98	73.90	
	38		110.44	110.31	99.65	89.70	81.34	78.57	81.82	73.50	68.77	86.26	73.48	76.13	68.01	84.46	
	39		100.92	99.31	87.65	76.92	70.67	71.35	74.42	64.82	60.63	76.70	64.34	63.79	56.51	74.46	
	40		109.50	104.71	91.61	80.60	72.46	70.59	74.23	66.42	61.49	76.35	65.34	65.44	56.74	76.58	
	-----		-----		-----		-----		-----		-----		-----		-----		
		Mean		106.88	105.09	91.44	80.62	74.24	73.49	72.05	65.54	62.67	78.52	66.90	67.94	60.21	79.24
		S.D.		3.83	3.86	4.45	4.77	3.94	3.59	4.99	3.84	3.54	5.51	4.47	5.23	5.09	3.97
	N		10	10	10	10	10	10	10	10	10	5	5	5	5	10	

* = result to left has an associated comment or marker
Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

Toxicology Study Report - PT02-0222

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Date: 16-Dec-2002 Page: 3

Food Consumption By Animal - Individual Food Consumption Relative To Bodyweight

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date																	
Group	Animal	From:	-3	1	5	8	12	15	19	22	26	29	33	36	40	Mean	
Sex	Number	To:	1	5	8	12	15	19	22	26	29	33	36	40	43	43	
2m	11		119.75	105.54	100.87	92.90	82.33	76.30	70.59	57.29	62.65	.	.	.	.	85.36	
	12		125.43	102.69	91.91	86.28	80.13	77.52	72.89	60.08	66.39	.	.	.	.	84.81	
	13		114.98	93.27	83.29	77.12	70.67	67.60	63.64	52.12	57.31	.	.	.	.	75.56	
	14		117.97	97.13	87.51	82.37	74.85	71.76	67.74	54.95	60.31	.	.	.	.	79.40	
	15		117.97	100.00	91.64	83.42	74.85	70.86	66.40	54.11	59.64	.	.	.	.	79.88	
	-----		-----														
		Mean		119.22	99.73	91.04	84.42	76.57	72.81	68.25	55.71	61.26	.	.	.	.	81.00
		S.D.		3.87	4.77	6.52	5.78	4.65	4.07	3.60	3.07	3.44	.	.	.	.	4.09
	N		5	5	5	5	5	5	5	5	5	.	.	.	.	5	

* = result to left has an associated comment or marker
Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

Toxicology Study Report - PT02-0222

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Date: 16-Dec-2002 Page: 4

Food Consumption By Animal - Individual Food Consumption Relative To Bodyweight

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date																
Group	Animal	From:	-3	1	5	8	12	15	19	22	26	29	33	36	40	Mean
Sex	Number	To:	1	5	8	12	15	19	22	26	29	33	36	40	43	-3
																43
2f	41		107.63	100.00	88.89	78.53	74.68	71.86	70.30	60.10	63.90	.	.	.	.	79.54
	42		108.50	100.00	91.58	81.27	74.68	71.08	70.30	59.80	63.58	.	.	.	.	80.09
	43		105.93	96.52	87.18	77.11	72.14	70.51	70.49	60.10	63.90	.	.	.	.	78.21
	44		111.67	100.73	88.60	77.34	72.76	71.08	69.58	58.48	62.22	.	.	.	.	79.16
	45		112.13	103.75	93.79	82.32	77.17	74.93	73.55	62.96	67.01	.	.	.	.	83.07
	-----		-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	
		Mean	109.17	100.20	90.01	79.31	74.29	71.89	70.84	60.29	64.12	.	.	.	.	80.01
		S.D.	2.66	2.57	2.65	2.36	1.97	1.76	1.55	1.64	1.76	.	.	.	.	1.84
		N	5	5	5	5	5	5	5	5	5	.	.	.	.	5

* = result to left has an associated comment or marker
Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

Toxicology Study Report - PT02-0222

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Food Consumption By Animal - Individual Food Consumption Relative To Bodyweight

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date																
Group	Animal	From:	-3	1	5	8	12	15	19	22	26	29	33	36	40	Mean
Sex	Number	To:	1	5	8	12	15	19	22	26	29	33	36	40	43	-3
																43
3m	16		127.32	88.01	96.04	96.91	93.66	88.66	82.98	64.06	79.11	.	.	.	.	90.75
	17		118.12	82.46	89.47	89.71	87.63	82.24	75.94	59.02	73.10	.	.	.	.	84.19
	18		110.17	79.66	89.18	87.22	82.73	76.86	71.00	54.09	65.93	.	.	.	.	79.65
	19		121.35	82.46	87.75	86.98	82.73	76.69	70.01	52.85	64.61	.	.	.	.	80.60
	20		110.56	77.56	84.00	82.85	80.38	76.03	71.15	55.27	68.07	.	.	.	.	78.43
			-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
	Mean		117.50	82.03	89.29	88.73	85.43	80.10	74.22	57.06	70.16	.	.	.	.	82.72
	S.D.		7.31	3.93	4.36	5.19	5.31	5.40	5.41	4.54	5.95	.	.	.	.	4.97
	N		5	5	5	5	5	5	5	5	5	.	.	.	.	5

* = result to left has an associated comment or marker
Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

Toxicology Study Report - PT02-0222

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Food Consumption By Animal - Individual Food Consumption Relative To Bodyweight

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date																
Group	Animal	From:	-3	1	5	8	12	15	19	22	26	29	33	36	40	Mean
Sex	Number	To:	1	5	8	12	15	19	22	26	29	33	36	40	43	43
3f	46		118.33	69.92	86.46	75.91	73.56	71.07	73.65	59.16	62.05	.	.	.	.	76.68
	47		114.98	69.66	89.52	78.80	74.42	71.47	74.43	60.20	64.68	.	.	.	.	77.57
	48		110.08	66.67	85.01	77.57	75.07	69.92	73.07	60.97	64.52	.	.	.	.	75.88
	49		114.98	77.50	108.26	91.54	85.05	79.38	83.23	68.29	70.84	.	.	.	.	86.56
	50		113.60	69.14	87.96	77.81	74.42	70.68	74.04	61.28	65.16	.	.	.	.	77.12
	-----		-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
		Mean	114.39	70.58	91.44	80.33	76.50	72.50	75.68	61.98	65.45	.	.	.	.	78.76
		S.D.	2.98	4.08	9.55	6.35	4.81	3.89	4.25	3.62	3.25	.	.	.	.	4.41
		N	5	5	5	5	5	5	5	5	5	.	.	.	.	5

* = result to left has an associated comment or marker
Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

Toxicology Study Report - PT02-0222

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Food Consumption By Animal - Individual Food Consumption Relative To Bodyweight

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date																
Group	Animal	From:	-3	1	5	8	12	15	19	22	26	29	33	36	40	Mean
Sex	Number	To:	1	5	8	12	15	19	22	26	29	33	36	40	43	-3 43
4m	21		121.26	66.99	76.77	79.45	76.62	76.77	71.95	61.56	63.28	.	.	.	.	77.18
	22		128.22	72.18	85.59	87.61	82.80	82.20	77.04	66.59	66.97	.	.	.	.	83.24
	23		116.20	67.88	84.44	87.35	83.02	82.00	74.75	63.05	63.41	.	.	.	.	80.23
	24		129.72	71.43	83.61	84.30	78.17	76.24	68.92	58.04	59.14	.	.	.	.	78.84
	25		126.77	73.21	87.96	90.63	89.02	89.87	82.49	70.37	73.56	.	.	.	.	87.10
	26		254.95	46.92	79.11	87.83	80.00	79.00	75.34	58.89	53.44	69.46	42.52	35.04	40.44	77.15
	27		269.77	52.90	89.90	95.48	89.41	88.27	82.76	65.32	60.16	76.32	46.12	39.45	48.14	84.92
	28		265.65	49.46	83.27	90.52	82.83	83.17	78.87	65.48	62.33	80.98	52.69	46.18	55.71	84.40
	29		254.95	47.74	79.11	85.30	78.55	77.88	74.50	58.51	52.79	68.31	42.06	34.06	38.18	76.30
	30		284.08	53.10	93.07	103.14	95.60	94.57	90.08	77.90	75.86	93.00	54.75	49.37	63.95	94.50
	Mean		195.16	60.18	84.28	89.16	83.60	83.00	77.67	64.57	63.09	77.61	47.63	40.82	49.28	82.39
	S.D.		75.08	11.03	5.11	6.49	6.01	6.12	6.13	6.14	7.54	10.03	5.82	6.76	10.71	5.66
	N		10	10	10	10	10	10	10	10	10	5	5	5	5	10

* = result to left has an associated comment or marker
Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

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Food Consumption By Animal - Individual Food Consumption Relative To Bodyweight

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date																
Group	Animal	From:	-3	1	5	8	12	15	19	22	26	29	33	36	40	Mean
Sex	Number	To:	1	5	8	12	15	19	22	26	29	33	36	40	43	43
4f	51		100.26	66.04	83.69	80.83	75.96	73.54	73.92	61.14	66.50	.	.	.	.	75.76
	52		103.95	69.14	88.72	85.19	78.53	75.00	75.93	63.10	67.70	.	.	.	.	78.58
	53		112.19	72.84	91.83	88.46	84.49	83.54	84.96	71.52	77.78	.	.	.	.	85.29
	54		112.19	76.29	97.52	90.36	84.49	83.28	83.68	68.01	72.59	.	.	.	.	85.38
	55		105.23	69.41	87.73	86.64	82.85	80.98	81.72	67.82	74.24	.	.	.	.	81.85
	56		105.88	70.57	79.45	79.08	79.62	76.28	70.09	70.40	55.21	80.75	68.19	65.84	38.57	72.30
	57		102.44	73.05	85.61	85.38	86.27	81.32	75.51	76.28	58.91	87.09	74.85	71.85	43.42	77.08
	58		102.44	71.65	84.06	84.54	84.44	79.27	73.08	73.13	56.86	83.90	71.28	69.45	43.31	75.19
	59		113.00	80.26	103.11	107.53	103.59	96.59	87.33	88.16	75.75	119.03	101.24	98.31	57.60	94.73
	60		105.00	72.48	84.98	85.95	86.54	83.48	78.32	79.27	61.62	89.35	74.11	69.95	39.84	77.76
	-----		-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
	Mean		106.26	72.17	88.67	87.40	84.68	81.33	78.45	71.88	66.72	92.02	77.93	75.08	44.55	80.39
	S.D.		4.58	3.96	7.08	7.80	7.50	6.47	5.71	7.94	8.25	15.44	13.29	13.17	7.60	6.60
	N		10	10	10	10	10	10	10	10	10	5	5	5	5	10

* = result to left has an associated comment or marker
Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg

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Food Consumption By Animal - Individual Food Consumption Relative To Bodyweight

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date												
Group	Animal	From:	-3	1	4	8	11	15	18	22	25	Mean
Sex	Number	To:	1	4	8	11	15	18	22	25	29	-3
												29
5m	61		122.09	103.85	99.14	91.19	83.00	72.29	70.79	60.28	48.47	83.46
	62		128.81	111.44	106.50	99.28	92.16	80.90	78.42	66.41	53.37	90.81
	63		121.12	106.02	103.61	98.23	90.38	80.36	80.08	68.55	55.99	89.37
	64		123.08	105.65	101.78	95.19	86.24	76.11	74.70	62.85	51.72	86.37
	65		122.58	105.65	101.18	92.33	83.19	72.29	69.61	58.52	47.82	83.69
	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
		Mean	123.54	106.52	102.44	95.24	86.99	76.39	74.72	63.32	51.47	86.74
		S.D.	3.04	2.88	2.77	3.54	4.16	4.18	4.58	4.17	3.41	3.31
		N	5	5	5	5	5	5	5	5	5	5
	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

* = result to left has an associated comment or marker
Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 5 - 3 mg/kg

Toxicology Study Report - PT02-0222

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Date: 16-Dec-2002 Page: 2

Food Consumption By Animal - Individual Food Consumption Relative To Bodyweight

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date													
Group	Animal	From:	-3	1	4	8	11	15	18	22	25	Mean	
Sex	Number	To:	1	4	8	11	15	18	22	25	29	-3	
5f	66		104.52	94.51	89.47	78.61	75.68	68.99	69.36	59.93	56.56	77.51	
	67		107.71	95.24	88.54	76.86	73.67	66.67	67.30	58.53	55.56	76.68	
	68		113.15	100.27	92.73	80.98	79.55	72.58	71.97	61.57	58.82	81.29	
	69		108.66	97.50	91.07	78.87	75.91	68.20	67.66	58.99	56.41	78.14	
	70		109.14	96.35	88.54	78.35	77.09	68.20	68.78	61.07	57.89	78.38	
		Mean	108.64	96.77	90.07	78.73	76.38	68.93	69.01	60.02	57.05	78.40	
		S.D.	3.10	2.26	1.81	1.48	2.16	2.21	1.85	1.30	1.30	1.75	
		N	5	5	5	5	5	5	5	5	5	5	

* = result to left has an associated comment or marker
Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 5 - 3 mg/kg

Toxicology Study Report - PT02-0222

RTA072-01/00

PROVANTIS

Date: 03-Mar-2003 Page: 1

Food Consumption By Animal - Individual Food Consumption Relative To Bodyweight

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date												
Group	Animal	From:	-4	1	4	8	11	15	18	22	25	Mean
Sex	Number	To:	1	4	8	11	15	18	22	25	29	-4
6m	71		117.89	112.00	108.57	101.90	87.80	76.30	66.00	55.44	68.99	88.32
	72		124.46	116.26	111.44	103.70	89.16	78.13	67.22	55.54	68.42	90.48
	73		115.08	112.00	111.11	105.84	94.16	86.05	76.68	64.40	79.39	93.86
	74		117.89	112.37	108.88	101.15	88.57	78.76	69.26	57.62	70.15	89.41
	75		116.00	109.09	106.15	100.41	89.36	80.05	70.19	59.20	73.37	89.31
		Mean	118.26	112.34	109.23	102.60	89.81	79.86	69.87	58.44	72.06	90.28
		S.D.	3.67	2.56	2.15	2.18	2.51	3.72	4.15	3.68	4.52	2.14
		N	5	5	5	5	5	5	5	5	5	5

* = result to left has an associated comment or marker
Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

Toxicology Study Report - PT02-0222

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Date: 03-Mar-2003 Page: 2

Food Consumption By Animal - Individual Food Consumption Relative To Bodyweight

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

			Day numbers relative to Start Date									
Group	Animal	From:	-4	1	4	8	11	15	18	22	25	Mean
Sex	Number	To:	1	4	8	11	15	18	22	25	29	-4 29
6f	81		112.45	90.06	85.12	85.04	80.12	65.12	67.61	56.10	69.87	79.05
	82		110.08	91.79	90.11	89.64	83.39	66.47	67.80	56.26	70.24	80.64
	83		121.30	98.62	95.35	95.44	89.26	71.11	72.51	60.22	75.29	86.57
	84		115.93	91.44	86.62	87.28	82.10	65.69	67.42	56.57	69.68	80.30
	85		111.97	89.39	83.96	83.18	78.01	61.71	63.32	52.65	65.34	76.61
		Mean	114.35	92.26	88.23	88.12	82.58	66.02	67.73	56.36	70.08	80.64
		S.D.	4.42	3.69	4.60	4.76	4.26	3.38	3.26	2.68	3.53	3.67
		N	5	5	5	5	5	5	5	5	5	5

* = result to left has an associated comment or marker
Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

Toxicology Study Report - PT02-0222

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Date: 03-Mar-2003 Page: 3

Food Consumption By Animal - Individual Food Consumption Relative To Bodyweight

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date												
Group	Animal	From:	-4	1	4	8	11	15	18	22	25	Mean
Sex	Number	To:	1	4	8	11	15	18	22	25	29	-4 29
7m	76		121.14	110.60	105.35	101.81	86.21	77.84	70.02	53.70	65.61	88.03
	77		123.14	115.53	110.65	106.80	89.34	79.41	69.89	53.70	65.83	90.48
	78		117.32	111.33	107.16	104.91	90.78	84.51	78.81	61.01	74.95	92.31
	79		115.50	107.09	102.75	98.41	83.30	75.61	67.91	52.25	63.81	85.18
	80		116.86	107.43	101.63	96.80	81.24	73.22	65.03	49.65	60.68	83.62
		-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
		Mean	118.79	110.40	105.51	101.75	86.17	78.12	70.33	54.06	66.18	87.92
		S.D.	3.21	3.43	3.60	4.22	4.00	4.27	5.15	4.22	5.32	3.60
		N	5	5	5	5	5	5	5	5	5	5
		-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

* = result to left has an associated comment or marker
Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Food Consumption By Animal - Individual Food Consumption Relative To Bodyweight

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Day numbers relative to Start Date												
Group	Animal	From:	-4	1	4	8	11	15	18	22	25	Mean
Sex	Number	To:	1	4	8	11	15	18	22	25	29	-4 29
7f	86		121.86	108.06	100.37	92.16	84.59	71.64	65.00	57.69	76.32	86.41
	87		113.91	100.37	89.93	82.34	75.44	63.20	58.62	52.43	69.54	78.42
	88		112.45	100.75	94.04	85.84	77.95	67.05	61.73	53.83	71.54	80.58
	89		112.93	99.26	90.85	81.83	75.00	64.98	60.88	54.27	71.35	79.04
	90		114.41	98.89	88.45	80.08	74.14	62.51	56.23	49.83	65.55	76.68
		Mean	115.11	101.47	92.73	84.45	77.42	65.88	60.49	53.61	70.86	80.22
		S.D.	3.85	3.76	4.74	4.79	4.25	3.67	3.30	2.86	3.89	3.73
		N	5	5	5	5	5	5	5	5	5	5

* = result to left has an associated comment or marker
Food consumption units are g/kg bodyweight/day

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

13.1.3 Clinical Pathology

13.1.3.1 Hematology

Legend of the plus signs in the red blood count (rat)

Anisocytosis: The variation in RBC Volume (Red Cell Distribution Width = RDW) is equal to or greater than 16,1 %.

- + : RDW $\geq$ 16,1 % - 18,29 %
- ++ : RDW > 18,29 % - 20,4 %
- +++ : RDW > 20,4 %

Hyperchromia: The percentage of cells with high cellular hemoglobin concentration [more than 41 g/dl] (% Hyper) is equal to or greater than 4 %.

- + : % Hyper $\geq$ 4,0 % - 7,9 %
- ++ : % Hyper > 8,0 % - 12,0 %
- +++ : % Hyper > 12,0 %

Hypochromia: The percentage of cells with low cellular hemoglobin concentration [less than 28 g/dl] (% Hypo) is equal to or greater than 4 %.

- + : % Hypo $\geq$ 4,0 % - 7,9 %
- ++ : % Hypo > 8,0 % - 12,0 %
- +++ : % Hypo > 12,0 %

Macrocytosis: The percentage of red blood cells with higher than normal cell volumes [$\geq$ 120 fl] (% Macro) is equal to or greater than 2,5 %.

- + : % Macro $\geq$ 2,5 % - 6,4 %
- ++ : % Macro > 6,5 % - 10,5 %
- +++ : % Macro > 10,5 %

Microcytosis: The percentage of red blood cells with lower than normal cell volumes [< 60 fl] (% Micro) is equal to or greater than 2,5 %.

- + : % Micro $\geq$ 2,5 % - 6,4 %
- ++ : % Micro > 6,5 % - 10,5 %
- +++ : % Micro > 10,5 %

Polychromasie: The hemoglobin distribution width (HDW) is equal to or greater than 3,4 %.

- + : HDW $\geq$ 3,4 % - 3,9 %
- ++ : HDW > 3,9 % - 4,6 %
- +++ : HDW > 4,6 %

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Red Cell Count

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Red cell count 10E12/L	Hemo globin g/L	Hemato crit unity	MCV 10E-15 L	MCH 10E-12 g	MCHC g/L	Reticulo cytes unity	Heinz Bodies unity	Hyper chromas.
1m	1	29	7.53	154	0.44	59	20	348	0.030	0.000	
	2	29	8.16	153	0.47	57	19	330	0.029	0.000	
	3	29	7.57	147	0.44	58	20	338	0.028	0.000	
	4	29	7.85	146	0.44	55	19	335	0.029	0.000	
	5	29	7.68	151	0.44	57	20	346	0.030	0.000	
	6	43	8.63	155	0.47	54	18	332	0.023	0.000	
	7	43	8.35	158	0.48	58	19	328	0.041	0.000	
	8	43	8.85	167	0.49	56	19	337	0.019	0.000	
	9	43	9.04	167	0.50	55	18	336	0.019	0.000	
	10	43	8.54	152	0.45	53	18	336	0.016	0.000	+

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Date: 27-Jan-2003 Page: 2

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Red Cell Count

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Red cell count 10E12/L	Hemo globin g/L	Hemato crit unity	MCV 10E-15 L	MCH 10E-12 g	MCHC g/L	Reticulo cytes unity	Heinz Bodies unity	Hyper chromas.
1f	31	29	7.32	140	0.42	57	19	337	0.033	0.000	
	32	29	7.56	146	0.43	56	19	343	0.030	0.000	
	33	29	7.28	136	0.41	56	19	335	0.028	0.000	
	34	29	7.07	137	0.40	56	19	346	0.022	0.000	
	35	29	6.74	130	0.39	57	19	338	0.030	0.000	
	36	43	8.05	143	0.42	52	18	338	0.022	0.000	
	37	43	8.10	149	0.44	54	18	341	0.019	0.000	
	38	43	8.16	153	0.45	55	19	344	0.022	0.000	
	39	43	7.93	150	0.43	54	19	351	0.021	0.000	
	40	43	8.11	151	0.44	54	19	345	0.016	0.000	

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Red Cell Count

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Red cell count 10E12/L	Hemo globin g/L	Hemato crit unity	MCV 10E-15 L	MCH 10E-12 g	MCHC g/L	Reticulo cytes unity	Heinz Bodies unity	Hyper chromas.
2m	11	29	7.33	148	0.43	59	20	344	0.029		
	12	29	7.84	150	0.45	58	19	331	0.027		
	13	29	8.11	148	0.46	56	18	323	0.023		
	14	29	7.66	150	0.44	57	20	343	0.025		
	15	29	8.19	155	0.47	58	19	328	0.024		

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Red Cell Count

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Red cell count 10E12/L	Hemo globin g/L	Hemato crit unity	MCV 10E-15 L	MCH 10E-12 g	MCHC g/L	Reticulo cytes unity	Heinz Bodies unity	Hyper chromas.
2f	41	29	. *	. *	. *	. *	. *	. *	. *		
	42	29	8.12	153	0.45	56	19	339	0.028		
	43	29	7.76	143	0.43	55	19	338	0.018		
	44	29	6.67	128	0.37	56	19	344	0.028		
	45	29	7.23	140	0.41	57	19	343	0.029		

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Red Cell Count

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Red cell count 10E12/L	Hemo globin g/L	Hemato crit unity	MCV 10E-15 L	MCH 10E-12 g	MCHC g/L	Reticulo cytes unity	Heinz Bodies unity	Hyper chromas.
3m	16	29	8.26	151	0.47	57	18	323	0.027		
	17	29	8.12	154	0.48	59	19	323	0.030		
	18	29	7.53	143	0.44	59	19	324	0.030		
	19	29	7.63	146	0.44	58	19	332	0.031		
	20	29	7.44	144	0.44	59	19	329	0.027		

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Red Cell Count

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Red cell count 10E12/L	Hemo globin g/L	Hemato crit unity	MCV 10E-15 L	MCH 10E-12 g	MCHC g/L	Reticulo cytes unity	Heinz Bodies unity	Hyper chromas.
3f	46	29	7.15	140	0.40	56	20	347	0.035		
	47	29	7.60	142	0.44	57	19	326	0.030		
	48	29	8.00	149	0.44	56	19	335	0.019		
	49	29	7.21	145	0.42	58	20	345	0.028		
	50	29	7.03	137	0.39	56	20	349	0.031		

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Red Cell Count

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Red cell count 10E12/L	Hemo globin g/L	Hemato crit unity	MCV 10E-15 L	MCH 10E-12 g	MCHC g/L	Reticulo cytes unity	Heinz Bodies unity	Hyper chromas.
4m	21	29	8.25	160	0.47	58	19	337	0.025	0.000	
	22	29	7.16	140	0.41	57	20	343	0.031	0.000	
	23	29	7.61	151	0.45	59	20	338	0.031	0.000	
	24	29	7.28	144	0.43	59	20	333	0.026	0.000	
	25	29	7.48	148	0.44	58	20	340	0.019	0.000	
	26	43	9.04	165	0.50	56	18	328	0.010	0.000	
	27	43	9.16	164	0.49	53	18	337	0.003	0.000	
	28	43	9.68	171	0.50	52	18	339	0.005	0.000	+
	29	43	9.00	167	0.50	55	19	337	0.013	0.000	

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Red Cell Count

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Red cell count 10E12/L	Hemo globin g/L	Hemato crit unity	MCV 10E-15 L	MCH 10E-12 g	MCHC g/L	Reticulo cytes unity	Heinz Bodies unity	Hyper chromas.
4f	51	29	. *	. *	. *	. *	. *	. *	. *		
	52	29	7.02	135	0.41	59	19	326	0.032	0.000	
	53	29	7.32	131	0.40	54	18	332	0.023	0.000	
	54	29	6.73	125	0.37	55	19	338	0.034	0.000	
	55	29	6.86	127	0.38	56	19	334	0.025	0.000	
	56	43	8.16	153	0.45	55	19	339	0.014	0.000	
	57	43	8.30	155	0.45	55	19	342	0.019	0.000	
	58	43	9.07	167	0.48	53	18	346	0.010	0.000	+
	59	43	8.71	157	0.46	53	18	342	0.011	0.000	+
	60	43	8.02	147	0.44	54	18	338	0.019	0.000	

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Red Cell Count

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Red cell count 10E12/L	Hemo globin g/L	Hemato crit unity	MCV 10E-15 L	MCH 10E-12 g	MCHC g/L	Reticulo cytes unity	Heinz Bodies unity	Hyper chromas.
5m	61	29	8.03	155	0.45	57	19	341	0.028	0.000	
	62	29	7.88	152	0.45	57	19	339	0.030	0.000	
	63	29	7.87	156	0.46	58	20	340	0.031	0.000	
	64	29	8.07	162	0.47	58	20	346	0.025	0.000	
	65	29	7.69	156	0.45	59	20	346	0.032	0.000	

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Red Cell Count

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Red cell count 10E12/L	Hemo globin g/L	Hemato crit unity	MCV 10E-15 L	MCH 10E-12 g	MCHC g/L	Reticulo cytes unity	Heinz Bodies unity	Hyper chromas.
5f	66	29	7.14	144	0.40	57	20	358	0.030	0.000	
	67	29	7.75	153	0.45	58	20	343	0.032	0.000	
	68	29	7.28	145	0.42	58	20	346	0.034	0.000	
	69	29	7.84	152	0.44	56	19	349	0.029	0.000	
	70	29	7.54	150	0.43	57	20	351	0.041	0.000	

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Red Cell Count

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Comments and Markers

Group Sex	Animal Number	Day Number	Measurement	Marker	Comment
2f	41	29	Red blood cell count		Sample coagulated
			Hemoglobin		Sample coagulated
			Hematocrit		Sample coagulated
			MCV		Sample coagulated
			MCH		Sample coagulated
			MCHC		Sample coagulated
			Reticulocytes		Sample coagulated
4f	51	29	Red blood cell count		Sample coagulated
			Hemoglobin		Sample coagulated
			Hematocrit		Sample coagulated
			MCV		Sample coagulated
			MCH		Sample coagulated
			MCHC		Sample coagulated
			Reticulocytes		Sample coagulated

Marker = E implies value excluded from means

Toxicology Study Report - PT02-0222

RTA053-01/04

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Date: 11-Mar-2003 Page: 1

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Red Cell Count

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Red cell count 10E12/L	Hemo globin g/L	Hemato crit unity	MCV 10E-15 L	MCH 10E-12 g	MCHC g/L	Reticulo cytes unity	Heinz Bodies unity	Hyper chromas.
6m	71	29	8.30	166	0.49	59	20	337	0.030	0.000	
	72	29	7.58	146	0.44	58	19	334	0.028	0.000	
	73	29	7.82	151	0.44	56	19	344	0.030	0.000	
	74	29	8.16	161	0.48	59	20	335	0.036	0.000	
	75	29	8.08	156	0.47	58	19	335	0.035	0.000	

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

Toxicology Study Report - PT02-0222

RTA053-01/04

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Date: 11-Mar-2003 Page: 2

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Red Cell Count

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Red cell count 10E12/L	Hemo globin g/L	Hemato crit unity	MCV 10E-15 L	MCH 10E-12 g	MCHC g/L	Reticulo cytes unity	Heinz Bodies unity	Hyper chromas.
6f	81	29	7.52	150	0.44	58	20	344	0.023	0.000	
	82	29	7.68	148	0.44	57	19	338	0.030	0.000	
	83	29	8.21	153	0.45	55	19	342	0.022	0.000	
	84	29	7.92	149	0.43	55	19	344	0.027	0.000	
	85	29	7.75	144	0.42	55	19	340	0.026	0.000	

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

Toxicology Study Report - PT02-0222

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PROVANTIS

Date: 11-Mar-2003 Page: 3

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Red Cell Count

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Red cell count 10E12/L	Hemo globin g/L	Hemato crit unity	MCV 10E-15 L	MCH 10E-12 g	MCHC g/L	Reticulo cytes unity	Heinz Bodies unity	Hyper chromas.
7m	76	29	8.20	155	0.46	56	19	336	0.036	0.000	
	77	29	7.73	152	0.45	59	20	335	0.038	0.000	
	78	29	8.22	154	0.45	55	19	340	0.026	0.000	
	79	29	7.84	152	0.45	57	19	338	0.033	0.000	
	80	29	7.65	156	0.45	59	20	343	0.032	0.000	

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

Toxicology Study Report - PT02-0222

RTA053-01/04

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Date: 11-Mar-2003 Page: 4

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Red Cell Count

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Red cell count 10E12/L	Hemo globin g/L	Hemato crit unity	MCV 10E-15 L	MCH 10E-12 g	MCHC g/L	Reticulo cytes unity	Heinz Bodies unity	Hyper chromas.
7f	86	29	7.67	144	0.43	55	19	339	0.028	0.000	
	87	29	7.80	149	0.43	55	19	349	0.029	0.000	
	88	29	7.50	148	0.42	56	20	353	0.025	0.000	+
	89	29	7.46	143	0.41	56	19	345	0.045	0.000	
	90	29	7.84	151	0.45	57	19	336	0.038	0.000	

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Date: 27-Jan-2003 Page: 1

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - White Cell Count (rel. values)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	White cell cnt 10E9/L	Neutro phils unity	Lympho cytes unity	Mono cytes unity	Eosino phils unity	Baso phils unity
1m	1	29	12.55	0.08	0.88	0.02	0.00	0.02
	2	29	8.24	0.12	0.85	0.01	0.00	0.01
	3	29	11.41	0.10	0.87	0.02	0.00	0.01
	4	29	10.40	0.11	0.86	0.02	0.00	0.01
	5	29	11.48	0.08	0.88	0.01	0.02	0.01
	6	43	9.70	0.09	0.87	0.02	0.00	0.01
	7	43	6.99	0.14	0.84	0.02	0.00	0.00
	8	43	11.14	0.09	0.87	0.02	0.01	0.00
	9	43	10.37	0.11	0.86	0.02	0.01	0.00
	10	43	7.25	0.11	0.84	0.03	0.01	0.00

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Date: 27-Jan-2003 Page: 2

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - White Cell Count (rel. values)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	White cell cnt 10E9/L	Neutro phils unity	Lympho cytes unity	Mono cytes unity	Eosino phils unity	Baso phils unity
1f	31	29	6.41	0.08	0.90	0.01	0.00	0.00
	32	29	7.95	0.06	0.92	0.01	0.00	0.01
	33	29	7.41	0.10	0.87	0.01	0.01	0.00
	34	29	9.99	0.08	0.90	0.01	0.00	0.01
	35	29	7.55	0.09	0.88	0.01	0.01	0.00
	36	43	6.95	0.08	0.89	0.01	0.01	0.00
	37	43	7.74	0.10	0.87	0.02	0.01	0.00
	38	43	7.37	0.07	0.91	0.01	0.01	0.00
	39	43	6.58	0.07	0.90	0.02	0.01	0.00
	40	43	8.85	0.06	0.92	0.01	0.01	0.00

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Date: 27-Jan-2003 Page: 3

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - White Cell Count (rel. values)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	White cell cnt 10E9/L	Neutro phils unity	Lympho cytes unity	Mono cytes unity	Eosino phils unity	Baso phils unity
2m	11	29	15.31	0.08	0.89	0.01	0.01	0.01
	-----	-----	-----	-----	-----	-----	-----	-----
	12	29	11.50	0.06	0.92	0.01	0.00	0.00
	-----	-----	-----	-----	-----	-----	-----	-----
	13	29	14.99	0.06	0.92	0.01	0.00	0.00
	-----	-----	-----	-----	-----	-----	-----	-----
	14	29	10.99	0.08	0.89	0.02	0.00	0.00
	-----	-----	-----	-----	-----	-----	-----	-----
	15	29	12.87	0.08	0.89	0.02	0.00	0.00

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - White Cell Count (rel. values)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	White cell cnt 10E9/L	Neutro phils unity	Lympho cytes unity	Mono cytes unity	Eosino phils unity	Baso phils unity
2f	41	29	. *	. *	. *	. *	. *	. *
	42	29	10.35	0.06	0.92	0.01	0.01	0.00
	43	29	8.55	0.07	0.91	0.01	0.01	0.00
	44	29	9.97	0.05	0.94	0.01	0.00	0.00
	45	29	10.23	0.07	0.90	0.01	0.01	0.00

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Date: 27-Jan-2003 Page: 5

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - White Cell Count (rel. values)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	White cell cnt 10E9/L	Neutro phils unity	Lympho cytes unity	Mono cytes unity	Eosino phils unity	Baso phils unity
3m	16	29	10.49	0.11	0.86	0.02	0.00	0.00
	-----	----	-----	-----	-----	-----	-----	-----
	17	29	11.05	0.12	0.84	0.03	0.00	0.00
	-----	----	-----	-----	-----	-----	-----	-----
	18	29	8.98	0.09	0.88	0.01	0.01	0.00
	-----	----	-----	-----	-----	-----	-----	-----
	19	29	13.41	0.08	0.89	0.01	0.01	0.00
	-----	----	-----	-----	-----	-----	-----	-----
	20	29	13.20	0.11	0.87	0.01	0.00	0.00

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - White Cell Count (rel. values)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	White cell cnt 10E9/L	Neutro phils unity	Lympho cytes unity	Mono cytes unity	Eosino phils unity	Baso phils unity
3f	46	29	8.24	0.07	0.91	0.01	0.00	0.00
	47	29	11.30	0.08	0.90	0.01	0.01	0.00
	48	29	8.04	0.09	0.88	0.02	0.00	0.00
	49	29	7.76	0.09	0.89	0.02	0.00	0.00
	50	29	7.36	0.11	0.87	0.01	0.01	0.00

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Date: 27-Jan-2003 Page: 7

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - White Cell Count (rel. values)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	White cell cnt 10E9/L	Neutro phils unity	Lympho cytes unity	Mono cytes unity	Eosino phils unity	Baso phils unity
4m	21	29	7.99	0.13	0.85	0.02	0.00	0.01
	-----	-----	-----	-----	-----	-----	-----	-----
	22	29	9.83	0.09	0.87	0.02	0.01	0.00
	-----	-----	-----	-----	-----	-----	-----	-----
	23	29	9.05	0.12	0.85	0.02	0.00	0.01
	-----	-----	-----	-----	-----	-----	-----	-----
	24	29	7.82	0.11	0.86	0.02	0.00	0.00
	-----	-----	-----	-----	-----	-----	-----	-----
	25	29	12.36	0.15	0.81	0.02	0.01	0.00
	-----	-----	-----	-----	-----	-----	-----	-----
	26	43	4.42	0.14	0.84	0.01	0.01	0.00
	-----	-----	-----	-----	-----	-----	-----	-----
	27	43	6.44	0.08	0.91	0.01	0.01	0.00
	-----	-----	-----	-----	-----	-----	-----	-----
	28	43	4.24	0.38	0.59	0.02	0.01	0.00
	-----	-----	-----	-----	-----	-----	-----	-----
	29	43	6.44	0.08	0.89	0.01	0.01	0.00

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - White Cell Count (rel. values)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	White cell cnt 10E9/L	Neutro phils unity	Lympho cytes unity	Mono cytes unity	Eosino phils unity	Baso phils unity
4f	51	29	. *	. *	. *	. *	. *	. *
	52	29	7.27	0.09	0.89	0.01	0.01	0.00
	53	29	6.48	0.07	0.91	0.01	0.01	0.00
	54	29	8.58	0.08	0.89	0.02	0.01	0.00
	55	29	9.40	0.06	0.91	0.01	0.01	0.00
	56	43	8.98	0.06	0.92	0.01	0.01	0.00
	57	43	5.29	0.09	0.88	0.02	0.01	0.00
	58	43	9.31	0.13	0.83	0.02	0.01	0.00
	59	43	6.76	0.07	0.91	0.01	0.01	0.00
	60	43	7.99	0.08	0.89	0.02	0.01	0.00

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - White Cell Count (rel. values)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	White cell cnt 10E9/L	Neutro phils unity	Lympho cytes unity	Mono cytes unity	Eosino phils unity	Baso phils unity
5m	61	29	13.80	0.11	0.84	0.03	0.01	0.01
	62	29	11.31	0.08	0.88	0.02	0.00	0.01
	63	29	13.77	0.10	0.86	0.01	0.01	0.01
	64	29	12.51	0.11	0.84	0.02	0.02	0.01
	65	29	16.22	0.10	0.85	0.03	0.01	0.01

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - White Cell Count (rel. values)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	White cell cnt 10E9/L	Neutro phils unity	Lympho cytes unity	Mono cytes unity	Eosino phils unity	Baso phils unity
5f	66	29	11.22	0.09	0.89	0.01	0.01	0.00
	67	29	10.56	0.11	0.82	0.04	0.01	0.01
	68	29	12.18	0.08	0.88	0.02	0.01	0.00
	69	29	11.30	0.14	0.82	0.02	0.02	0.01
	70	29	10.12	0.07	0.89	0.02	0.01	0.00

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Generalised Results By Animal - Animals Against Parameters - Multiple Times
Activity : - White Cell Count (rel. values)
Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Comments and Markers					

Group	Animal	Day	Measurement	Marker	Comment
Sex	Number	Number			

2f	41	29	White blood cell count		Sample coagulated
			Neutrophils (%)		Sample coagulated
			Lymphocytes (%)		Sample coagulated
			Monocytes (%)		Sample coagulated
			Eosinophils (%)		Sample coagulated
			Basophils (%)		Sample coagulated
4f	51	29	White blood cell count		Sample coagulated
			Neutrophils (%)		Sample coagulated
			Lymphocytes (%)		Sample coagulated
			Monocytes (%)		Sample coagulated
			Eosinophils (%)		Sample coagulated
			Basophils (%)		Sample coagulated

Marker = E implies value excluded from means

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Date: 11-Mar-2003 Page: 1

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - White Cell Count (rel. values)

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	White cell cnt 10E9/L	Neutro phils unity	Lympho cytes unity	Mono cytes unity	Eosino phils unity	Baso phils unity
6m	71	29	12.54	0.13	0.82	0.03	0.01	0.00
	72	29	10.07	0.12	0.84	0.03	0.01	0.00
	73	29	17.52	0.15	0.82	0.01	0.01	0.00
	74	29	13.10	0.11	0.86	0.02	0.01	0.00
	75	29	11.84	0.10	0.86	0.02	0.01	0.00

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Date: 11-Mar-2003 Page: 2

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - White Cell Count (rel. values)

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	White cell cnt 10E9/L	Neutro phils unity	Lympho cytes unity	Mono cytes unity	Eosino phils unity	Baso phils unity
6f	81	29	12.63	0.10	0.87	0.02	0.01	0.00
	82	29	11.49	0.09	0.87	0.02	0.02	0.00
	83	29	10.34	0.08	0.88	0.01	0.02	0.00
	84	29	7.73	0.08	0.88	0.02	0.02	0.00
	85	29	11.85	0.06	0.90	0.02	0.01	0.00

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Date: 11-Mar-2003 Page: 3

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - White Cell Count (rel. values)

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	White cell cnt 10E9/L	Neutro phils unity	Lympho cytes unity	Mono cytes unity	Eosino phils unity	Baso phils unity
7m	76	29	12.31	0.11	0.86	0.02	0.01	0.00
	-----	-----	-----	-----	-----	-----	-----	-----
	77	29	11.00	0.11	0.84	0.03	0.01	0.00
	-----	-----	-----	-----	-----	-----	-----	-----
	78	29	7.75	0.09	0.88	0.02	0.01	0.00
	-----	-----	-----	-----	-----	-----	-----	-----
	79	29	13.26	0.09	0.86	0.03	0.01	0.00
	-----	-----	-----	-----	-----	-----	-----	-----
	80	29	11.88	0.10	0.86	0.02	0.01	0.00

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Date: 11-Mar-2003 Page: 4

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - White Cell Count (rel. values)

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	White cell cnt 10E9/L	Neutro phils unity	Lympho cytes unity	Mono cytes unity	Eosino phils unity	Baso phils unity
7f	86	29	5.96	0.09	0.88	0.01	0.01	0.00
	87	29	8.80	0.08	0.89	0.01	0.01	0.00
	88	29	8.19	0.09	0.88	0.01	0.01	0.00
	89	29	8.81	0.08	0.88	0.01	0.02	0.00
	90	29	7.68	0.12	0.84	0.02	0.01	0.00

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Date: 27-Jan-2003 Page: 1

Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Blood Coagulation
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Coagul. Time sec	Plate lets 10E9/L
1m	1	29	100	1119
	2	29	96	1049
	3	29	99	1021
	4	29	102	1153
	5	29	106	810
	6	43	129	1179
	7	43	126	844
	8	43	137	1077
	9	43	144	1101
	10	43	159	1056

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Date: 27-Jan-2003 Page: 2

Generalised Results By Animal - Animals Against Parameters - Multiple Times
Activity : - Blood Coagulation
Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Coagul. Time sec	Plate lets 10E9/L
1f	31	29	135	849
	32	29	115	1006
	33	29	133	1184
	34	29	142	992
	35	29	132	1270
	36	43	151	1065
	37	43	145	1076
	38	43	176	978
	39	43	138	1051
	40	43	147	1081

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Blood Coagulation
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Coagul. Time sec	Plate lets 10E9/L
2m	11	29	102	1132
	12	29	106	1098
	13	29	111	1066
	14	29	126	1087
	15	29	112	1173

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Blood Coagulation
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Coagul. Time sec	Plate lets 10E9/L
2f	41	29	105	. *
	42	29	96	1095
	43	29	88	1087
	44	29	105	1007
	45	29	102	1149

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Date: 27-Jan-2003 Page: 5

Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Blood Coagulation
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Coagul. Time sec	Plate lets 10E9/L
3m	16	29	124	1103
	-----	----	-----	-----
	17	29	105	1177
	-----	----	-----	-----
	18	29	108	1042
	-----	----	-----	-----
	19	29	115	1060
	-----	----	-----	-----
	20	29	104	1042

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Blood Coagulation
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Coagul. Time sec	Plate lets 10E9/L
3f	46	29	68	1093
	47	29	106	1029
	48	29	112	1324
	49	29	120	1016
	50	29	119	1136

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Blood Coagulation
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Coagul. Time sec	Plate lets 10E9/L
4m	21	29	124	960
	22	29	101	942
	23	29	97	1050
	24	29	90	930
	25	29	106	1108
	26	43	148	904
	27	43	132	1012
	28	43	125	627
	29	43	102	1195

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Generalised Results By Animal - Animals Against Parameters - Multiple Times
Activity : - Blood Coagulation
Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Coagul. Time sec	Plate lets 10E9/L
4f	51	29	96	. *
	52	29	108	1258
	53	29	98	1173
	54	29	111	988
	55	29	105	982
	56	43	153	1206
	57	43	122	1316
	58	43	153	1443
	59	43	125	967
	60	43	121	1470

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Blood Coagulation
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Coagul. Time sec	Plate lets 10E9/L
5m	61	29	179	1141
	62	29	157	1229
	63	29	157	1088
	64	29	150	980
	65	29	145	910

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Blood Coagulation
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Coagul. Time sec	Plate lets 10E9/L
5f	66	29	173	1299
	67	29	153	1503
	68	29	164	815
	69	29	146	957
	70	29	164	1066

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Generalised Results By Animal - Animals Against Parameters - Multiple Times
Activity : - Blood Coagulation
Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Comments and Markers					

Group	Animal	Day	Measurement	Marker	Comment
Sex	Number	Number			

2f	41	29	Platelets		Sample coagulated
4f	51	29	Platelets		Sample coagulated

Marker = E implies value excluded from means

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Blood Coagulation

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

```

-----
Group  Animal  Day  Coagul.  Plate
Sex    Number   Number Time    lets
                                sec    10E9/L

   6m      71      29      133      966
-----
          72      29      132     1170
-----
          73      29      159     1322
-----
          74      29      147     1093
-----
          75      29      139     1204

```

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Blood Coagulation

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Coagul. Time sec	Plate lets 10E9/L
6f	81	29	126	1122
	82	29	129	1104
	83	29	118	996
	84	29	134	1147
	85	29	122	1300

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Date: 11-Mar-2003 Page: 3

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Blood Coagulation

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

```

-----
Group  Animal  Day  Coagul.  Plate
Sex    Number   Number Time    lets
                                sec    10E9/L

7m      76      29      167      1088
-----
       77      29      168      1158
-----
       78      29      181      1143
-----
       79      29      132      1211
-----
       80      29      137      1133

```

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Blood Coagulation
 Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Coagul. Time sec	Plate lets 10E9/L
7f	86	29	135	1143
	87	29	123	1088
	88	29	148	1166
	89	29	119	1001
	90	29	131	998

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

13.1.3.2 *Clinical chemistry*

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Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Clinical Chemistry
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Sodium mmol/L	Potas sium mmol/L	Calcium mmol/L	Chloride mmol/L	Phos phorus mmol/L	Glucose mmol/L	Uric Acid umol/L	Creati nine umol/L	Urea Nitrogen mmol/L	ALAT IU/L	ASAT IU/L
1m	1	29	142	5.74	2.39	105	2.90	18.5	37	44	5.5	38	67
	2	29	142	5.89	2.46	104	2.86	18.8	21	47	5.4	46	69
	3	29	139	5.85	2.42	102	3.05	18.1	36	50	5.5	45	105
	4	29	139	6.39	2.45	102	3.18	24.5	34	47	6.9	38	66
	5	29	141	6.46	2.40	104	3.25	17.5	38	45	7.2	45	98
	6	43	139	5.80	2.21	102	2.53	17.0	38	54	6.9	42	111
	7	43	137	6.20	2.18	102	3.01	19.8	60	46	5.9	49	116
	8	43	139	6.40	2.27	103	3.12	21.6	49	51	8.3	60	116
	9	43	141	5.90	2.42	103	3.08	25.7	24	42	6.5	56	80
	10	43	139	5.75	2.39	101	2.96	16.8	35	42	7.3	39	95

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Clinical Chemistry
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

 (continued)

Group Sex	Animal Number	Day Number	Alk.Phos phatase IU/L	G-Gluta. Transf. IU/L	Total Protein g/L	Chole sterol mmol/L	Triglyce rides mmol/L	Albumin g/L	Globulin g/L	Alb/Glob Ratio	Total Biliru. umol/L
1m	1	29	515	3	51	1.9	0.53	25	26	0.96	4.7
	2	29	450	3	54	2.1	0.35	27	27	1.00	5.4
	3	29	396	3	50	2.0	0.53	25	25	1.00	5.3
	4	29	532	3	53	2.0	0.56	26	27	0.96	4.9
	5	29	588	3	53	2.0	0.59	27	26	1.04	5.0
	6	43	364	3	49	1.7	0.57	22	27	0.81	6.0
	7	43	307	3	48	1.8	0.38	23	25	0.92	6.1
	8	43	327	3	51	1.9	0.55	24	27	0.89	5.6
	9	43	337	3	55	2.0	0.54	25	30	0.83	4.4
	10	43	279	4	49	1.8	0.38	23	26	0.88	5.0

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times
Activity : - Clinical Chemistry
Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Sodium mmol/L	Potas sium mmol/L	Calcium mmol/L	Chloride mmol/L	Phos phorus mmol/L	Glucose mmol/L	Uric Acid umol/L	Creati nine umol/L	Urea Nitrogen mmol/L	ALAT IU/L	ASAT IU/L
1f	31	29	142	4.65	2.30	104	2.54	12.2	47	51	5.6	43	114
	32	29	142	5.05	2.29	105	2.76	15.5	59	49	5.5	35	97
	33	29	138	5.35	2.31	101	3.05	14.7	33	46	6.0	39	87
	34	29	140	5.18	2.30	106	2.51	10.5	54	45	6.1	42	91
	35	29	141	5.71	2.34	103	2.83	13.9	51	48	6.0	46	115
	36	43	144	4.84	2.37	106	2.42	10.5	90	58	5.7	38	124
	37	43	143	4.41	2.39	106	2.44	12.2	33	48	5.3	29	71
	38	43	143	4.66	2.41	106	2.26	12.2	52	54	5.4	36	98
	39	43	143	4.75	2.40	104	2.35	14.3	58	58	5.9	33	85
	40	43	143	5.12	2.34	105	2.75	14.3	72	58	6.3	38	102

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times
Activity : - Clinical Chemistry
Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

(continued)

Group Sex	Animal Number	Day Number	Alk.Phos phatase IU/L	G-Gluta. Transf. IU/L	Total Protein g/L	Chole sterol mmol/L	Triglyce rides mmol/L	Albumin g/L	Globulin g/L	Alb/Glob Ratio	Total Biliru. umol/L
1f	31	29	419	3	56	2.0	0.49	28	28	1.00	6.5
	32	29	380	3	53	2.0	0.49	26	27	0.96	5.8
	33	29	442	3	51	1.5	0.44	25	26	0.96	5.5
	34	29	404	3	55	1.8	0.63	27	28	0.96	6.4
	35	29	372	3	56	2.2	0.42	29	27	1.07	5.9
	36	43	201	3	61	2.4	0.27	30	31	0.97	5.3
	37	43	306	3	59	1.5	0.49	29	30	0.97	6.3
	38	43	241	3	55	1.8	0.41	28	27	1.04	4.9
	39	43	209	3	56	1.7	0.55	28	28	1.00	5.0
	40	43	175	4	57	1.8	0.52	27	30	0.90	4.7

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Clinical Chemistry

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Sodium mmol/L	Potas sium mmol/L	Calcium mmol/L	Chloride mmol/L	Phos phorus mmol/L	Glucose mmol/L	Uric Acid umol/L	Creati nine umol/L	Urea Nitrogen mmol/L	ALAT IU/L	ASAT IU/L
2m	11	29	140	6.20	2.40	101	3.27	17.4	58	50	6.6	47	110
	12	29	140	6.35	2.23	102	3.35	19.5	51	55	5.8	40	98
	13	29	139	5.88	2.26	102	3.06	21.1	46	47	5.5	48	97
	14	29	141	6.32	2.32	101	3.29	21.2	64	59	5.8	46	119
	15	29	139	5.85	2.32	101	3.08	20.1	39	47	5.2	43	90

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Clinical Chemistry
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

(continued)

Group Sex	Animal Number	Day Number	Alk.Phos phatase IU/L	G-Gluta. Transf. IU/L	Total Protein g/L	Chole sterol mmol/L	Triglyce rides mmol/L	Albumin g/L	Globulin g/L	Alb/Glob Ratio	Total Biliru. umol/L
2m	11	29	516	3	51	1.7	0.48	26	25	1.04	5.9
	12	29	380	3	54	1.8	0.18	26	28	0.93	5.2
	13	29	553	3	50	2.1	0.62	25	25	1.00	6.3
	14	29	412	3	55	2.0	0.37	27	28	0.96	6.4
	15	29	507	3	55	2.2	0.33	27	28	0.96	5.4

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Clinical Chemistry

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Sodium mmol/L	Potas sium mmol/L	Calcium mmol/L	Chloride mmol/L	Phos phorus mmol/L	Glucose mmol/L	Uric Acid umol/L	Creati nine umol/L	Urea Nitrogen mmol/L	ALAT IU/L	ASAT IU/L
2f	41	29	142	5.67	2.41	106	3.33	15.7	57	47	6.3	47	98
	42	29	141	6.15	2.30	104	3.12	15.3	67	53	6.7	44	112
	43	29	141	6.64	2.40	104	3.30	14.6	82	57	6.3	60	148
	44	29	140	5.84	2.31	104	3.04	18.4	40	46	5.2	45	91
	45	29	138	6.09	2.38	103	3.11	17.9	66	52	5.6	43	102

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Clinical Chemistry
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

(continued)

Group Sex	Animal Number	Day Number	Alk.Phos phatase IU/L	G-Gluta. Transf. IU/L	Total Protein g/L	Chole sterol mmol/L	Triglyce rides mmol/L	Albumin g/L	Globulin g/L	Alb/Glob Ratio	Total Biliru. umol/L
2f	41	29	307	3	53	2.3	0.34	26	27	0.96	6.5
	42	29	296	3	54	2.2	0.35	27	27	1.00	6.8
	43	29	243	3	52	2.3	0.30	26	26	1.00	6.1
	44	29	428	3	50	2.3	0.42	25	25	1.00	5.7
	45	29	325	3	49	2.3	0.41	23	26	0.88	6.3

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Clinical Chemistry

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Sodium mmol/L	Potas sium mmol/L	Calcium mmol/L	Chloride mmol/L	Phos phorus mmol/L	Glucose mmol/L	Uric Acid umol/L	Creati nine umol/L	Urea Nitrogen mmol/L	ALAT IU/L	ASAT IU/L
3m	16	29	140	5.75	2.31	102	3.05	14.9	87	49	5.7	58	127
	17	29	142	5.76	2.25	102	2.82	16.9	76	41	6.2	64	102
	18	29	141	5.25	2.41	103	2.48	16.2	36	46	5.1	58	83
	19	29	141	5.36	2.34	99	3.00	15.8	58	50	5.2	53	111
	20	29	142	5.78	2.35	101	3.00	19.4	56	48	5.6	60	119

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Clinical Chemistry
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

(continued)

Group Sex	Animal Number	Day Number	Alk.Phos phatase IU/L	G-Gluta. Transf. IU/L	Total Protein g/L	Chole sterol mmol/L	Triglyce rides mmol/L	Albumin g/L	Globulin g/L	Alb/Glob Ratio	Total Biliru. umol/L
3m	16	29	608	3	54	2.0	0.44	26	28	0.93	6.0
	17	29	533	3	53	1.9	0.36	27	26	1.04	7.6
	18	29	606	3	53	2.1	0.49	26	27	0.96	4.9
	19	29	661	3	54	2.2	0.51	26	28	0.93	7.3
	20	29	491	3	55	1.7	0.56	27	28	0.96	5.4

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Clinical Chemistry

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Sodium mmol/L	Potas sium mmol/L	Calcium mmol/L	Chloride mmol/L	Phos phorus mmol/L	Glucose mmol/L	Uric Acid umol/L	Creati nine umol/L	Urea Nitrogen mmol/L	ALAT IU/L	ASAT IU/L
3f	46	29	145	5.11	2.20	109	2.77	12.3	107	45	4.3	43	95
	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
	47	29	146	5.56	2.25	108	2.81	13.5	66	46	6.9	49	99
	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
	48	29	147	5.46	2.25	106	2.81	15.5	74	53	7.1	45	104
	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
	49	29	149	5.43	2.24	109	2.79	12.2	89	49	5.9	53	115
	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
	50	29	146	5.42	2.23	111	2.94	16.2	78	44	4.4	42	100

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Clinical Chemistry

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

(continued)

Group Sex	Animal Number	Day Number	Alk.Phos phatase IU/L	G-Gluta. Transf. IU/L	Total Protein g/L	Chole sterol mmol/L	Triglyce rides mmol/L	Albumin g/L	Globulin g/L	Alb/Glob Ratio	Total Biliru. umol/L
3f	46	29	377	3	62	2.9	0.30	32	30	1.07	6.4
	47	29	409	3	62	3.1	0.46	33	29	1.14	8.6
	48	29	382	3	62	2.5	0.40	33	29	1.14	5.5
	49	29	412	3	60	2.6	0.37	32	28	1.14	8.0
	50	29	304	3	58	2.6	0.40	30	28	1.07	5.9

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times
Activity : - Clinical Chemistry
Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Sodium mmol/L	Potas sium mmol/L	Calcium mmol/L	Chloride mmol/L	Phos phorus mmol/L	Glucose mmol/L	Uric Acid umol/L	Creati nine umol/L	Urea Nitrogen mmol/L	ALAT IU/L	ASAT IU/L
4m	21	29	143	5.50	2.24	101	2.86	15.2	59	40	7.3	66	87
	22	29	144	5.71	2.37	102	2.86	18.5	36	38	5.8	77	107
	23	29	141	6.66	2.45	102	3.20	12.4	50	50	7.8	68	127
	24	29	141	5.46	2.35	100	2.99	14.8	33	42	6.4	59	88
	25	29	141	6.20	2.27	104	2.97	19.6	77	47	8.1	51	100
	26	43	144	5.18	2.34	106	2.88	7.3	52	54	8.1	42	111
	27	43	145	4.80	2.31	107	2.65	5.6	73	59	11.8	44	108
	28	43	144	4.94	2.18	109	2.64	5.1	55	55	18.7	32	130
	29	43	144	4.67	2.40	105	2.90	6.9	38	50	7.5	32	84

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Clinical Chemistry
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

 (continued)

Group Sex	Animal Number	Day Number	Alk.Phos phatase IU/L	G-Gluta. Transf. IU/L	Total Protein g/L	Chole sterol mmol/L	Triglyce rides mmol/L	Albumin g/L	Globulin g/L	Alb/Glob Ratio	Total Biliru. umol/L
4m	21	29	382	4	51	1.6	0.20	26	25	1.04	5.5
	22	29	469	4	54	2.0	0.50	28	26	1.08	5.0
	23	29	303	3	52	1.8	0.33	27	25	1.08	5.2
	24	29	615	3	52	1.8	0.48	27	25	1.08	5.5
	25	29	351	4	51	2.1	0.36	25	26	0.96	6.4
	26	43	266	3	59	2.0	0.31	29	30	0.97	7.4
	27	43	243	3	61	2.0	0.15	28	33	0.85	6.5
	28	43	127	3	53	1.8	*	25	28	0.89	6.6
	29	43	219	3	60	2.0	0.33	29	31	0.94	5.1

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Clinical Chemistry

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Sodium mmol/L	Potas sium mmol/L	Calcium mmol/L	Chloride mmol/L	Phos phorus mmol/L	Glucose mmol/L	Uric Acid umol/L	Creati nine umol/L	Urea Nitrogen mmol/L	ALAT IU/L	ASAT IU/L
4f	51	29	148	6.10	2.45	105	3.38	16.0	322	54	6.8	53	82
	52	29	144	5.55	2.22	107	2.86	12.2	80	50	4.9	49	119
	53	29	145	7.07	2.32	105	3.55	14.5	100	38	6.0	60	101
	54	29	143	5.51	2.15	105	2.95	14.8	49	42	5.0	47	82
	55	29	143	5.07	2.12	103	2.91	15.2	89	45	6.4	58	94
	56	43	141	5.23	2.37	106	2.83	16.1	39	45	6.4	31	68
	57	43	143	6.11	2.27	109	3.07	11.2	85	64	7.3	29	97
	58	43	142	5.55	2.24	106	2.88	12.3	86	61	8.8	80	152
	59	43	144	5.96	2.28	106	3.13	6.6	69	61	15.5	43	111
	60	43	140	5.62	2.34	106	3.38	17.1	57	50	4.7	32	71

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times
Activity : - Clinical Chemistry
Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

(continued)

Group Sex	Animal Number	Day Number	Alk.Phos phatase IU/L	G-Gluta. Transf. IU/L	Total Protein g/L	Chole sterol mmol/L	Triglyce rides mmol/L	Albumin g/L	Globulin g/L	Alb/Glob Ratio	Total Biliru. umol/L
4f	51	29	437	5	61	3.1	0.60	36	25	1.44	7.2
	52	29	328	5	56	2.3	0.48	29	27	1.07	5.5
	53	29	556	8	56	2.1	0.36	29	27	1.07	5.8
	54	29	443	7	55	2.5	0.39	29	26	1.12	5.4
	55	29	524	6	52	1.9	0.25	27	25	1.08	5.8
	56	43	229	3	53	2.1	0.39	25	28	0.89	4.9
	57	43	111	3	51	2.1	0.19	24	27	0.89	5.4
	58	43	112	3	50	1.8	0.24	23	27	0.85	5.3
	59	43	199	3	54	1.6	0.25	25	29	0.86	6.3
	60	43	274	3	53	1.8	0.40	24	29	0.83	5.4

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Clinical Chemistry

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Sodium mmol/L	Potas sium mmol/L	Calcium mmol/L	Chloride mmol/L	Phos phorus mmol/L	Glucose mmol/L	Uric Acid umol/L	Creati nine umol/L	Urea Nitrogen mmol/L	ALAT IU/L	ASAT IU/L
5m	61	29	136	6.33	2.39	99	3.43	17.8	25	48	7.3	33	67
	62	29	137	6.08	2.39	101	2.91	16.4	31	46	6.4	42	81
	63	29	138	6.20	2.42	103	3.17	16.6	25	50	6.7	41	98
	64	29	139	5.52	2.45	104	2.95	18.0	30	44	5.7	45	79
	65	29	140	5.47	2.48	104	3.11	17.1	26	44	5.7	61	82

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Clinical Chemistry
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

(continued)

Group Sex	Animal Number	Day Number	Alk.Phos phatase IU/L	G-Gluta. Transf. IU/L	Total Protein g/L	Chole sterol mmol/L	Triglyce rides mmol/L	Albumin g/L	Globulin g/L	Alb/Glob Ratio	Total Biliru. umol/L
5m	61	29	347	3	53	1.9	0.54	25	28	0.89	4.3
	62	29	390	3	47	1.9	0.44	22	25	0.88	4.5
	63	29	371	3	50	2.0	0.44	25	25	1.00	5.0
	64	29	292	3	51	2.0	0.43	25	26	0.96	4.4
	65	29	438	3	51	2.2	0.46	23	28	0.82	4.5

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Clinical Chemistry

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Sodium mmol/L	Potas sium mmol/L	Calcium mmol/L	Chloride mmol/L	Phos phorus mmol/L	Glucose mmol/L	Uric Acid umol/L	Creati nine umol/L	Urea Nitrogen mmol/L	ALAT IU/L	ASAT IU/L
5f	66	29	139	5.36	2.39	104	2.39	11.2	78	48	6.2	46	104
	67	29	142	5.67	2.42	106	2.53	12.5	90	61	5.0	42	100
	68	29	138	5.77	2.55	104	3.28	13.4	91	54	5.6	42	129
	69	29	141	5.97	2.44	107	2.98	14.3	58	54	5.5	43	113
	70	29	140	6.05	2.37	105	3.09	15.4	29	49	6.8	34	81

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Clinical Chemistry
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

(continued)

Group Sex	Animal Number	Day Number	Alk.Phos phatase IU/L	G-Gluta. Transf. IU/L	Total Protein g/L	Chole sterol mmol/L	Triglyce rides mmol/L	Albumin g/L	Globulin g/L	Alb/Glob Ratio	Total Biliru. umol/L
5f	66	29	411	3	54	2.2	0.30	27	27	1.00	4.7
	67	29	387	3	54	2.2	0.30	28	26	1.08	4.9
	68	29	435	3	54	2.0	0.39	27	27	1.00	5.6
	69	29	304	3	59	2.6	0.38	29	30	0.97	5.0
	70	29	427	3	52	1.9	0.37	26	26	1.00	5.0

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Activity : - Clinical Chemistry

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Comments and Markers

Group Animal Day
Sex Number Number Measurement

Marker Comment

4m 28 43 Triglycerides

Result lies below the detection limit

Marker = E implies value excluded from means

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Clinical Chemistry

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Sodium mmol/L	Potas sium mmol/L	Calcium mmol/L	Chloride mmol/L	Phos phorus mmol/L	Glucose mmol/L	Uric Acid umol/L	Creati nine umol/L	Urea Nitrogen mmol/L	ALAT IU/L	ASAT IU/L
6m	71	29	138	5.51	2.44	102	3.14	18.4	21	48	7.5	46	97
	72	29	139	5.80	2.51	101	3.09	18.5	23	46	5.1	40	93
	73	29	137	5.67	2.43	101	2.95	20.1	30	51	5.6	38	95
	74	29	139	5.62	2.56	102	3.12	18.7	15	47	6.1	57	82
	75	29	137	5.75	2.50	102	3.21	20.9	32	44	5.6	41	81

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Clinical Chemistry

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

(continued)

Group Sex	Animal Number	Day Number	Alk.Phos phatase IU/L	G-Gluta. Transf. IU/L	Total Protein g/L	Chole sterol mmol/L	Triglyce rides mmol/L	Albumin g/L	Globulin g/L	Alb/Glob Ratio	Total Biliru. umol/L
6m	71	29	338	4	52	1.9	0.52	24	28	0.86	4.3
	72	29	412	4	53	1.9	0.57	26	27	0.96	5.1
	73	29	341	4	51	2.0	0.47	25	26	0.96	5.0
	74	29	366	4	51	2.2	0.52	24	27	0.89	4.6
	75	29	369	4	51	2.0	0.65	25	26	0.96	4.9

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Clinical Chemistry

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Sodium mmol/L	Potas sium mmol/L	Calcium mmol/L	Chloride mmol/L	Phos phorus mmol/L	Glucose mmol/L	Uric Acid umol/L	Creati nine umol/L	Urea Nitrogen mmol/L	ALAT IU/L	ASAT IU/L
6f	81	29	138	5.69	2.29	104	3.15	16.1	57	54	5.7	45	134
	82	29	141	5.63	2.42	106	2.96	18.0	60	50	5.3	41	128
	83	29	140	6.12	2.31	108	2.96	16.2	65	49	4.8	46	141
	84	29	143	5.73	2.48	108	2.82	11.3	51	46	4.0	38	101
	85	29	141	4.93	2.56	105	3.21	14.0	65	44	5.3	44	85

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Clinical Chemistry

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

(continued)

Group Sex	Animal Number	Day Number	Alk.Phos phatase IU/L	G-Gluta. Transf. IU/L	Total Protein g/L	Chole sterol mmol/L	Triglyce rides mmol/L	Albumin g/L	Globulin g/L	Alb/Glob Ratio	Total Biliru. umol/L
6f	81	29	312	4	54	2.4	0.34	26	28	0.93	5.3
	82	29	275	4	55	2.1	0.37	26	29	0.90	4.6
	83	29	370	4	52	2.2	0.34	26	26	1.00	5.8
	84	29	209	4	57	2.5	0.39	28	29	0.97	5.6
	85	29	367	4	59	2.6	0.54	29	30	0.97	5.1

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Clinical Chemistry

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Sodium mmol/L	Potas sium mmol/L	Calcium mmol/L	Chloride mmol/L	Phos phorus mmol/L	Glucose mmol/L	Uric Acid umol/L	Creati nine umol/L	Urea Nitrogen mmol/L	ALAT IU/L	ASAT IU/L
7m	76	29	140	5.45	2.47	103	2.80	13.9	57	46	6.2	34	79
	77	29	141	4.97	2.48	102	2.97	14.5	34	46	5.7	45	78
	78	29	139	5.03	2.34	103	2.82	14.2	31	48	4.2	41	90
	79	29	139	4.95	2.47	102	2.65	17.0	27	52	5.6	47	88
	80	29	142	5.05	2.50	102	2.67	19.0	16	43	6.0	35	55

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Clinical Chemistry

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

(continued)

Group Sex	Animal Number	Day Number	Alk.Phos phatase IU/L	G-Gluta. Transf. IU/L	Total Protein g/L	Chole sterol mmol/L	Triglyce rides mmol/L	Albumin g/L	Globulin g/L	Alb/Glob Ratio	Total Biliru. umol/L
7m	76	29	428	4	54	2.2	0.60	28	26	1.08	5.1
	77	29	442	4	57	2.1	0.60	27	30	0.90	5.2
	78	29	484	4	53	2.1	0.50	27	26	1.04	4.7
	79	29	416	4	57	2.4	0.47	28	29	0.97	5.0
	80	29	468	4	56	2.1	0.84	28	28	1.00	5.1

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Clinical Chemistry

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Sodium mmol/L	Potas sium mmol/L	Calcium mmol/L	Chloride mmol/L	Phos phorus mmol/L	Glucose mmol/L	Uric Acid umol/L	Creati nine umol/L	Urea Nitrogen mmol/L	ALAT IU/L	ASAT IU/L
7f	86	29	141	5.35	2.36	107	2.64	13.9	67	52	5.3	40	114
	87	29	140	5.25	2.45	104	2.64	11.8	91	58	5.6	45	127
	88	29	142	5.13	2.48	105	2.68	12.7	72	50	6.0	46	123
	89	29	140	5.22	2.40	107	2.77	17.0	40	45	4.1	36	83
	90	29	143	5.00	2.39	108	2.67	15.2	40	54	4.8	46	119

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - Clinical Chemistry
 Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

(continued)

Group Sex	Animal Number	Day Number	Alk.Phos phatase IU/L	G-Gluta. Transf. IU/L	Total Protein g/L	Chole sterol mmol/L	Triglyce rides mmol/L	Albumin g/L	Globulin g/L	Alb/Glob Ratio	Total Biliru. umol/L
7f	86	29	227	4	57	2.1	0.30	28	29	0.97	6.5
	87	29	486	4	60	2.4	0.36	30	30	1.00	5.6
	88	29	283	4	59	2.1	0.33	30	29	1.03	5.0
	89	29	260	4	58	2.6	0.40	28	30	0.93	4.5
	90	29	382	4	59	2.2	0.48	28	31	0.90	4.6

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

13.1.3.3 Urinalysis (including legend)

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urinalysis (semiquant. Params)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Appear ence	Urine Color	Volume mL	pH Value	Specific Weight g/L	Protein (Album.)	Bili rubin	Urobili nogen	Ketone Bodies	Glucose	Blood (RBCs)
1m	1	23	CLEAR	DK YELL	3.0	6.5	1061	3+	NEGATIV	TRACE	1+	NEGATIV	NEGATIV
	2	23	CLEAR	DK YELL	1.8	6.5	1068	2+	NEGATIV	TRACE	1+	NEGATIV	NEGATIV
	3	23	CLEAR	YELLOW	3.2	6.5	1056	2+	NEGATIV	TRACE	1+	NEGATIV	NEGATIV
	4	23	CLEAR	YELLOW	4.5	7.0	1036	1+	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV
	5	23	CLOUDY	DK YELL	1.9	6.5	1072	2+	NEGATIV	TRACE	1+	NEGATIV	NEGATIV
	6	41	CLEAR	YELLOW	7.6	7.5	1031	1+	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV
	7	41	CLEAR	DK YELL	1.7	6.5	1069	3+	NEGATIV	TRACE	1+	NEGATIV	NEGATIV
	8	41	CLOUDY	DK YELL	1.3	6.5	1071	4+	NEGATIV	TRACE	2+	NEGATIV	NEGATIV
	9	41	CLEAR	YELLOW	9.8	7.5	1029	2+	NEGATIV	NEGATIV	1+	NEGATIV	NEGATIV
	10	41	CLEAR	YELLOW	3.9	7.0	1047	1+	NEGATIV	NEGATIV	1+	NEGATIV	NEGATIV

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urinalysis (semiquant. Params)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Appearance	Urine Color	Volume mL	pH Value	Specific Weight g/L	Protein (Album.)	Bili rubin	Urobilinogen	Ketone Bodies	Glucose	Blood (RBCs)
1f	31	23	CLEAR	DK YELL	2.1	6.0	1054	1+	NEGATIV	TRACE	TRACE	NEGATIV	NEGATIV
	32	23	CLEAR	YELLOW	3.5	7.5	1034	1+	NEGATIV	TRACE	TRACE	NEGATIV	NEGATIV
	33	23	*	*	1.2	.	.	*	*	*	*	*	*
	34	23	CLEAR	YELLOW	3.9	6.5	1034	1+	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	35	23	CLEAR	YELLOW	5.0	6.5	1034	TRACE	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	36	41	CLEAR	YELLOW	5.0	7.0	1031	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	37	41	CLEAR	YELLOW	5.2	7.0	1036	1+	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	38	41	CLEAR	YELLOW	2.9	6.5	1048	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	39	41	CLEAR	YELLOW	8.0	7.0	1027	1+	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	40	41	CLEAR	YELLOW	8.2	7.5	1024	TRACE	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urinalysis (Semiquant. Params)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Appear ence	Urine Color	Volume mL	pH Value	Specific Weight g/L	Protein (Album.)	Bili rubin	Urobili nogen	Ketone Bodies	Glucose	Blood (RBCs)
2m	11	23	CLEAR	DK YELL	1.8	6.0	1079	2+	NEGATIV	TRACE	TRACE	NEGATIV	NEGATIV
	12	23	CLOUDY	DK YELL	2.2	6.5	1065	2+	NEGATIV	TRACE	1+	NEGATIV	NEGATIV
	13	23	CLEAR	DK YELL	3.5	6.5	1053	3+	NEGATIV	TRACE	1+	NEGATIV	NEGATIV
	14	23	CLOUDY	DK YELL	1.9	6.5	1053	2+	NEGATIV	TRACE	1+	NEGATIV	NEGATIV
	15	23	CLEAR	DK YELL	3.3	6.5	1054	1+	NEGATIV	TRACE	TRACE	NEGATIV	NEGATIV

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urinalysis (Semiquant. Params)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Appear ence	Urine Color	Volume mL	pH Value	Specific Weight g/L	Protein (Album.)	Bili rubin	Urobili nogen	Ketone Bodies	Glucose	Blood (RBCs)
2f	41	23	CLEAR	YELLOW	5.0	7.0	1027	1+	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV
	42	23	CLEAR	YELLOW	4.8	6.5	1041	1+	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV
	43	23	CLEAR	YELLOW	4.3	7.0	1024	TRACE	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV
	44	23	CLEAR	YELLOW	4.7	6.5	1038	1+	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV
	45	23	CLEAR	YELLOW	5.0	7.0	1030	1+	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urinalysis (Semiquant. Params)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Appear ence	Urine Color	Volume mL	pH Value	Specific Weight g/L	Protein (Album.)	Bili rubin	Urobili nogen	Ketone Bodies	Glucose	Blood (RBCs)
3m	16	23	CLEAR	YELLOW	2.9	6.0	1051	2+	NEGATIV	TRACE	TRACE	NEGATIV	NEGATIV
	17	23	CLOUDY	YELLOW	4.5	6.0	1044	1+	NEGATIV	TRACE	1+	NEGATIV	NEGATIV
	18	23	CLEAR	DK YELL	3.4	6.5	1058	2+	NEGATIV	TRACE	1+	NEGATIV	NEGATIV
	19	23	CLEAR	YELLOW	6.2	6.0	1042	1+	NEGATIV	NEGATIV	1+	NEGATIV	NEGATIV
	20	23	CLOUDY	DK YELL	3.0	6.0	1057	2+	NEGATIV	TRACE	TRACE	NEGATIV	NEGATIV

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urinalysis (Semiquant. Params)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Appear ence	Urine Color	Volume mL	pH Value	Specific Weight g/L	Protein (Album.)	Bili rubin	Urobili nogen	Ketone Bodies	Glucose	Blood (RBCs)
3f	46	23	CLEAR	YELLOW	4.6	7.0	1035	2+	NEGATIV	NEGATIV	1+	NEGATIV	NEGATIV
	47	23	CLEAR	YELLOW	5.3	6.5	1036	1+	NEGATIV	NEGATIV	1+	NEGATIV	NEGATIV
	48	23	CLOUDY	DK YELL	2.8	6.5	1039	1+	NEGATIV	NEGATIV	1+	NEGATIV	NEGATIV
	49	23	CLEAR	DK YELL	3.0	8.0	1036	1+	NEGATIV	NEGATIV	1+	NEGATIV	NEGATIV
	50	23	CLOUDY	DK YELL	2.6	6.0	1035	2+	NEGATIV	NEGATIV	1+	NEGATIV	NEGATIV

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urinalysis (semiquant. Params)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Appear ence	Urine Color	Volume mL	pH Value	Specific Weight g/L	Protein (Album.)	Bili rubin	Urobili nogen	Ketone Bodies	Glucose	Blood (RBCs)
4m	21	23	CLEAR	YELLOW	5.7	7.0	1029	1+	NEGATIV	NEGATIV	1+	NEGATIV	NEGATIV
	22	23	CLOUDY	YELLOW	5.1	6.0	1039	1+	NEGATIV	TRACE	1+	NEGATIV	NEGATIV
	23	23	CLOUDY	YELLOW	7.1	6.5	1028	1+	NEGATIV	NEGATIV	1+	NEGATIV	NEGATIV
	24	23	CLEAR	DK YELL	4.9	6.5	1044	1+	NEGATIV	TRACE	1+	NEGATIV	NEGATIV
	25	23	CLEAR	YELLOW	3.8	6.5	1048	1+	NEGATIV	TRACE	1+	NEGATIV	NEGATIV
	26	41	CLEAR	YELLOW	7.8	7.5	1022	1+	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	27	41	CLEAR	DK YELL	3.0	7.5	1058	1+	NEGATIV	TRACE	TRACE	NEGATIV	NEGATIV
	28	41	*	*	1.1	.	.	*	*	*	*	*	*
	29	41	CLEAR	YELLOW	4.8	7.5	1044	TRACE	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV
	30	41	CLEAR	YELLOW	2.4	6.0	1066	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urinalysis (semiquant. Params)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Appearance	Urine Color	Volume mL	pH Value	Specific Weight g/L	Protein (Album.)	Bilirubin	Urobilinogen	Ketone Bodies	Glucose	Blood (RBCs)
4f	51	23	CLEAR	DK YELL	4.4	6.0	1044	1+	NEGATIV	TRACE	1+	NEGATIV	NEGATIV
	52	23	TURBID	DK YELL	3.7	6.0	1045	1+	NEGATIV	NEGATIV	1+	NEGATIV	2+
	53	23	CLOUDY	YELLOW	4.9	6.0	1035	TRACE	NEGATIV	NEGATIV	2+	NEGATIV	NEGATIV
	54	23	CLEAR	YELLOW	12.5	6.0	1013	NEGATIV	NEGATIV	NEGATIV	1+	NEGATIV	NEGATIV
	55	23	CLEAR	YELLOW	5.4	6.0	1034	TRACE	NEGATIV	NEGATIV	1+	NEGATIV	NEGATIV
	56	41	CLEAR	YELLOW	8.4	6.5	1028	1+	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	57	41	CLEAR	YELLOW	4.5	6.5	1039	TRACE	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	58	41	CLEAR	YELLOW	3.7	7.0	1035	1+	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	59	41	CLEAR	YELLOW	2.3	6.0	1053	2+	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	60	41	CLEAR	YELLOW	4.8	7.0	1048	1+	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urinalysis (Semiquant. Params)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Appear ence	Urine Color	Volume mL	pH Value	Specific Weight g/L	Protein (Album.)	Bili rubin	Urobili nogen	Ketone Bodies	Glucose	Blood (RBCs)
5m	61	26	CLEAR	DK YELL	3.1	6.5	1064	2+	NEGATIV	TRACE	TRACE	NEGATIV	NEGATIV
	62	26	CLEAR	DK YELL	1.5	6.0	1075	2+	NEGATIV	TRACE	TRACE	NEGATIV	NEGATIV
	63	26	CLEAR	DK YELL	2.6	6.5	1055	2+	NEGATIV	TRACE	1+	NEGATIV	NEGATIV
	64	26	CLEAR	DK YELL	3.2	6.0	1069	2+	NEGATIV	TRACE	TRACE	NEGATIV	NEGATIV
	65	26	CLOUDY	DK YELL	4.1	6.5	1049	1+	NEGATIV	TRACE	1+	NEGATIV	NEGATIV

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urinalysis (Semiquant. Params)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Appear ence	Urine Color	Volume mL	pH Value	Specific Weight g/L	Protein (Album.)	Bili rubin	Urobili nogen	Ketone Bodies	Glucose	Blood (RBCs)
5f	66	26	CLEAR	YELLOW	2.7	6.5	1057	2+	NEGATIV	TRACE	TRACE	NEGATIV	NEGATIV
	67	26	CLEAR	YELLOW	3.0	6.5	1042	1+	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	68	26	CLEAR	YELLOW	3.4	6.5	1043	1+	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV
	69	26	CLEAR	YELLOW	4.2	6.5	1035	1+	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV
	70	26	CLEAR	YELLOW	2.0	7.0	1057	1+	NEGATIV	TRACE	TRACE	NEGATIV	NEGATIV

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urinalysis (semiquant. Params)

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Comments and Markers

Group Sex	Animal Number	Day Number	Measurement	Marker	Comment
1f	33	23	Appearance of Urine	Sample	too small - not examined
			Urine Color	Sample	too small - not examined
			pH Value (sq)	Sample	too small - not examined
			Specific Weight	Sample	too small - not examined
			Protein (Albumine)(sq)	Sample	too small - not examined
			Bilirubin (sq)	Sample	too small - not examined
			Urobilinogen (sq)	Sample	too small - not examined
			Ketone Bodies (sq)	Sample	too small - not examined
			Glucose (sq)	Sample	too small - not examined
			Blood (RBCs)(sq)	Sample	too small - not examined
4m	28	41	Appearance of Urine	Sample	too small - not examined
			Urine Color	Sample	too small - not examined
			pH Value (sq)	Sample	too small - not examined
			Specific Weight	Sample	too small - not examined
			Protein (Albumine)(sq)	Sample	too small - not examined
			Bilirubin (sq)	Sample	too small - not examined
			Urobilinogen (sq)	Sample	too small - not examined
			Ketone Bodies (sq)	Sample	too small - not examined
			Glucose (sq)	Sample	too small - not examined
			Blood (RBCs)(sq)	Sample	too small - not examined

Marker = E implies value excluded from means

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urinalysis (Semiquant. Params)

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Appear ence	Urine Color	Volume mL	pH Value	Specific Weight g/L	Protein (Album.)	Bili rubin	Urobili nogen	Ketone Bodies	Glucose	Blood (RBCs)
6m	71	24	CLOUDY	YELLOW	3.0	6.0	1052	4+	NEGATIV	TRACE	TRACE	NEGATIV	TRACE
	72	24	CLEAR	YELLOW	4.7	6.5	1039	1+	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV
	73	24	CLEAR	YELLOW	3.3	6.5	1040	3+	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV
	74	24	CLEAR	YELLOW	3.0	6.5	1051	4+	NEGATIV	TRACE	TRACE	NEGATIV	NEGATIV
	75	24	CLEAR	YELLOW	4.5	6.5	1036	1+	NEGATIV	NEGATIV	1+	NEGATIV	NEGATIV

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urinalysis (Semiquant. Params)

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Appear ence	Urine Color	Volume mL	pH Value	Specific Weight g/L	Protein (Album.)	Bili rubin	Urobili nogen	Ketone Bodies	Glucose	Blood (RBCs)
6f	81	24	CLEAR	YELLOW	3.8	6.0	1037	1+	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	82	24	CLEAR	YELLOW	3.1	6.0	1046	1+	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	83	24	CLEAR	YELLOW	1.9	6.0	1049	1+	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV
	84	24	CLEAR	YELLOW	4.9	7.0	1029	TRACE	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	85	24	CLEAR	YELLOW	6.4	6.5	1027	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urinalysis (Semiquant. Params)

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Appear ence	Urine Color	Volume mL	pH Value	Specific Weight g/L	Protein (Album.)	Bili rubin	Urobili nogen	Ketone Bodies	Glucose	Blood (RBCs)
7m	76	24	CLEAR	YELLOW	7.1	6.5	1028	1+	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV
	77	24	CLEAR	YELLOW	4.8	6.0	1038	1+	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV
	78	24	CLOUDY	DK YELL	2.4	6.5	1055	2+	NEGATIV	TRACE	1+	NEGATIV	NEGATIV
	79	24	CLEAR	YELLOW	7.2	6.5	1027	2+	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV
	80	24	CLEAR	YELLOW	8.0	6.5	1029	1+	NEGATIV	NEGATIV	TRACE	NEGATIV	NEGATIV

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urinalysis (Semiquant. Params)

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Appear ence	Urine Color	Volume mL	pH Value	Specific Weight g/L	Protein (Album.)	Bili rubin	Urobili nogen	Ketone Bodies	Glucose	Blood (RBCs)
7f	86	24	CLEAR	YELLOW	3.7	6.5	1034	TRACE	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	87	24	CLEAR	YELLOW	3.8	6.0	1036	1+	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	88	24	CLEAR	YELLOW	3.3	6.0	1046	1+	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	89	24	CLEAR	YELLOW	4.4	6.5	1029	TRACE	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV
	90	24	CLEAR	YELLOW	4.4	6.0	1038	1+	NEGATIV	NEGATIV	NEGATIV	NEGATIV	NEGATIV

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urine Sediment

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Erythro cytes	Leuco cytes	Squamous E.Cells	Other Ep.Cells	Triple Phosphat	Calcium Oxalate	Sperms	Bacteria
1m	1	23			1-5		x			several
	2	23			1-5		x			several
	3	23		1-5	1-5		x		several	several
	4	23		1-5	1-5		x			several
	5	23	1-5	1-5	1-5		x		several	several
	6	41			1-5		x		several	several
	7	41		1-5	1-5		x		several	several
	8	41			1-5		x		several	several
	9	41		1-5	1-5		x		several	several
	10	41			1-5		x		several	several

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urine Sediment

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Erythro cytes	Leuco cytes	Squamous E.Cells	Other Ep.Cells	Triple Phosphat	Calcium Oxalate	Sperms	Bacteria
1f	31	23		1-5	1-5		x			several
	32	23		1-5	1-5		x			several
	33	23		1-5	1-5		x			several
	34	23		1-5	1-5		x			several
	35	23		1-5	1-5		x			several
	36	41			1-5		x			several
	37	41		1-5	1-5		x			several
	38	41			1-5		x			several
	39	41		1-5	1-5		x			several
	40	41		1-5	1-5		x			several

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urine Sediment

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Erythro cytes	Leuco cytes	Squamous E.Cells	Other Ep.Cells	Triple Phosphat	Calcium Oxalate	Sperms	Bacteria
4m	21	23		1-5	1-5		x		several	several
	22	23		1-5	1-5	<5 grn				several
	23	23		1-5	1-5	<5 grn				several
	24	23		1-5	1-5				several	several
	25	23		6-10	1-5				several	several
	26	41		1-5	1-5		x		several	several
	27	41			1-5		x		several	several
	28	41			1-5		x			several
	29	41			1-5		x	x	several	several
	30	41			1-5		x		several	numers.

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urine Sediment

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Erythro cytes	Leuco cytes	Squamous E.Cells	Other Ep.Cells	Triple Phosphat	Calcium Oxalate	Sperms	Bacteria
4f	51	23		6-10	1-5					several
	52	23	31-50	1-5	1-5					numers.
	53	23		1-5	1-5					several
	54	23		1-5	1-5		x			several
	55	23		1-5	1-5					several
	56	41		1-5	1-5		x			several
	57	41			1-5		x			several
	58	41		1-5	1-5		x			several
	59	41		6-10	1-5		x			several
	60	41		1-5	1-5		x			several

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urine Sediment

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Erythro cytes	Leuco cytes	Squamous E.Cells	Triple Phosphat	Calcium Oxalate	Sperms	Bacteria
6m	71	24	6-10	1-5	1-5	x		several	several
	72	24		1-5	1-5	x		several	several
	73	24		1-5	1-5	x		several	several
	74	24	1-5	1-5	1-5	x			several
	75	24		1-5	1-5	x		several	several

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urine Sediment

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Erythro cytes	Leuco cytes	Squamous E.Cells	Triple Phosphat	Calcium Oxalate	Sperms	Bacteria
6f	81	24		1-5	1-5	x			several
	82	24		1-5	1-5	x			several
	83	24		1-5	1-5				several
	84	24		1-5	1-5	x			several
	85	24		1-5	1-5	x			several

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urine Sediment

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Erythro cytes	Leuco cytes	Squamous E.Cells	Triple Phosphat	Calcium Oxalate	Sperms	Bacteria
7m	76	24		1-5	1-5	x		several	several
	77	24			1-5	x		several	several
	78	24		1-5	1-5	x		several	several
	79	24		1-5	1-5	x		several	several
	80	24		1-5	1-5	x		several	several

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Urine Sediment

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Erythro cytes	Leuco cytes	Squamous E.Cells	Triple Phosphat	Calcium Oxalate	Sperms	Bacteria
7f	86	24		1-5	1-5	x			several
	87	24			1-5				several
	88	24		1-5	1-5	x			several
	89	24		1-5	1-5	x	x		several
	90	24			1-5	x			several

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

EXPLANATION OF URINALYSIS SYMBOLS
Semiquantitative Parameters

Protein (Albumin) NEGATIVE = negative TRACE = trace 1+ = approx. 0.3 g/L 2+ = approx. 1.0 g/L 3+ = approx. 3.0 g/L 4+ >= 10.0 g/L	Blood (Erythrocytes) NEGATIVE = negative TRACE = trace 1+ = small 2+ = moderate 3+ = large	Glucose NEGATIVE TRACE = approx. 5.5 mmol/L 1+ = approx. 14.0 mmol/L 2+ = approx. 28.0 mmol/L 3+ => 55.0 mmol/L	Ketone Bodies NEGATIVE = negative TRACE = trace 1+ = 1.5 mmol/L 2+ = 3.9 mmol/L 3+ = 7.8 mmol/L 4+ >= 15.6 mmol/L
Bilirubin NEGATIVE = negative 1+ = small 2+ = moderate 3+ = large	Urobilinogen NEGATIVE <= 3 µmol/L TRACE = 16 µmol/L 1+ = 33 µmol/L 2+ = 66 µmol/L 3+ >= 131 µmol/L	Nitrite NEGATIVE = negative POSITIVE = positive	
Appearance CLEAR = clear CLOUDY = cloudy SL CLOUDY = slightly cloudy TURBID = turbid	Colour AMBER = amber DK YELLOW = Dark yellow GREEN = green ORANGE = orange	OTHER OTHER = other RED = red STRAW = straw YELLOW = yellow	

E X P L A N A T I O N O F U R I N A L Y S I S S Y M B O L S S e d i m e n t

Erythrocytes	Leucocytes	Squamous Epithelial Cells	Round Epithelial Cells	Round Epith. Cells with large Nuclei	Other Epithelial Cells
per visual field	per visual field	per visual field	per visual field	No. per visual field	No. per visual field
1 - 5	1 - 5	1 - 5	1 - 5	1 - 5	< 5 tld = 1 - 5 tailed epithelial cells
6 - 10	6 - 10	6 - 10	6 - 10	6 - 10	< 10 tld = 6 - 10 tailed epithelial cells
11 - 20	11 - 20	11 - 20	11 - 20	11 - 20	> 10 tld = > 10 tailed epithelial cells
21 - 30	21 - 30	21 - 30	21 - 30	21 - 30	
31 - 50	31 - 50	31 - 50	31 - 50	31 - 50	< 5 grn = 1 - 5 irregular forms, extreme granulated
51 - 100	51 - 100	31 - 50	31 - 50	31 - 50	< 10 grn = 6 - 10 irregular forms, extreme granulated
> 100	> 100	> 50	> 50	> 50	> 10 grn = > 10 irregular forms, extreme granulated

Crystals		
TriplePhos	=	Triple Phosphate
Uric Acid	=	Uric Acid
Urates	=	Urates
Ca Oxalate	=	Calcium Oxalate
AmorphSalt	=	Amorphous Salt

Miscellaneous					
2CaPhos	=	Dicalcium Phosphate	Cystine	=	Cystine
2MgPhos	=	Dimagnesium Phosphate	Cystein	=	Cystein
AmmonCl	=	Ammonium Chloride	Cholest	=	Cholesterol
CaSulf	=	Calcium Sulfate	Carbte	=	Carbonate
HipAcid	=	Hippuric Acid	CPrecpt	=	Compound Precipitate
Hemtdin	=	Hematoidin	YstCell	=	Yeast Cells
Leucine	=	Leucine	SqEpCCl	=	Squamous Epithelial Cell Clusters
Tyrosn	=	Tyrosine	MucThrd	=	Mucous-Thread

Casts		
hyaline	=	hyaline
erythr.	=	erythrocytic
leucoc.	=	leucocytic
epithel.	=	epithelial
granul.	=	granular
waxy	=	waxy
cylind.	=	cylindrical
fatty	=	fatty

Sperms		
per visual field		
several	=	several
numers.	=	numerous

Bacteria		
per visual field		
several	=	several
numers.	=	numerous

Eggs		
per visual field		
Oxyuris	=	Oxyuris
Trichus	=	Trichuris

13.1.4 Organ weights

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Organ Weights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Heart Weight g	Liver Weight g	Kidneys Weight g	Adrenals Weight g	Spleen Weight g	Thymus Weight g	Brain Weight g	Testes Weight g	Epidi dymis Wt g
1m	1	29	0.998	11.01	1.927	0.045	0.682	0.471	1.792	3.021	0.897
	2	29	0.912	10.06	1.888	0.046	0.878	0.475	1.804	2.879	0.707
	3	29	1.005	10.97	1.888	0.045	0.726	0.439	1.725	3.217	0.854
	4	29	1.204	13.07	2.495	0.043	1.040	0.554	1.906	3.391	0.792
	5	29	0.908	11.08	2.286	0.049	0.757	0.458	1.955	3.570	0.871
	6	43	1.231	11.68	2.356	0.051	0.794	0.481	1.958	3.605	1.115
	7	43	0.910	7.95	1.896	0.047	0.727	0.333	2.020	2.977	1.047
	8	43	1.050	9.22	2.024	0.038	0.631	0.354	1.719	3.082	1.032
	9	43	1.581	13.65	2.933	0.055	0.970	0.441	2.089	4.019	1.324
	10	43	1.168	9.73	2.307	0.052	0.740	0.317	1.911	3.867	1.197

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Toxicology Study Report - PT02-0222

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Organ Weights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Heart Weight g	Liver Weight g	Kidneys Weight g	Adrenals Weight g	Spleen Weight g	Thymus Weight g	Brain Weight g	Testes Weight g	Epidi dymis Wt g
2m	11	29	0.857	11.15	1.944	0.050	0.565	0.513	1.628	2.986	0.868
	12	29	0.796	9.49	2.167	0.040	0.667	0.424	1.789	3.070	0.784
	13	29	0.843	12.30	2.124	0.041	0.688	0.375	1.709	3.572	0.832
	14	29	1.034	11.44	2.130	0.043	0.708	0.335	1.792	3.476	0.908
	15	29	0.824	11.04	2.161	0.039	0.752	0.396	1.810	3.379	0.739

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Organ Weights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Heart Weight g	Liver Weight g	Kidneys Weight g	Adrenals Weight g	Spleen Weight g	Thymus Weight g	Brain Weight g	Testes Weight g	Epidi dymis Wt g
3m	16	29	0.798	10.93	1.822	0.051	0.535	0.504	1.714	3.235	0.759
	17	29	0.902	11.96	2.395	0.043	0.672	0.336	1.746	3.401	0.768
	18	29	1.024	13.93	2.300	0.051	0.627	0.407	1.800	3.544	0.840
	19	29	1.040	14.54	2.456	0.047	0.776	0.534	1.916	4.025	0.878
	20	29	0.930	13.16	2.173	0.043	0.594	0.444	1.692	3.202	0.818

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Organ Weights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Heart Weight g	Liver Weight g	Kidneys Weight g	Adrenals Weight g	Spleen Weight g	Thymus Weight g	Brain Weight g	Testes Weight g	Epidi dymis Wt g
4m	21	29	0.841	13.98	1.904	0.062	0.590	0.311	1.731	3.479	0.829
	22	29	0.754	14.79	1.993	0.054	0.596	0.305	1.729	3.491	0.904
	23	29	0.903	13.87	1.980	0.057	0.494	0.355	1.724	3.337	0.670
	24	29	0.863	15.84	2.102	0.059	0.722	0.435	1.863	3.541	0.758
	25	29	0.683	12.11	1.842	0.047	0.513	0.324	1.789	3.468	0.738
	26	43	0.893	6.73	1.791	0.050	0.494	0.268	1.898	2.973	1.032
	27	43	0.647	5.16	1.378	0.044	0.385	0.162	1.713	3.215	0.784
	28	43	0.664	4.09	1.056	0.040	0.275	0.056	1.589	3.520	0.813
	29	43	0.828	7.01	1.758	0.046	0.558	0.320	1.720	3.618	1.011

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Organ Weights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Heart Weight g	Liver Weight g	Kidneys Weight g	Adrenals Weight g	Spleen Weight g	Thymus Weight g	Brain Weight g	Testes Weight g	Epidi dymis Wt g
5m	61	29	1.296	11.86	2.141	0.040	0.619	0.467	1.903	3.611	0.867
	62	29	0.997	10.57	1.909	0.043	0.805	0.555	1.835	3.427	0.777
	63	29	1.028	9.72	1.879	0.051	0.701	0.482	1.738	3.345	0.901
	64	29	1.119	10.19	1.992	0.041	0.735	0.521	1.888	3.242	0.826
	65	29	1.203	11.62	2.326	0.051	0.904	0.532	1.888	4.091	0.934

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Organ Weights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Heart Weight g	Liver Weight g	Kidneys Weight g	Adrenals Weight g	Spleen Weight g	Thymus Weight g	Brain Weight g
1f	31	29	0.743	8.17	1.472	0.077	0.623	0.300	1.846
	32	29	0.687	7.64	1.307	0.055	0.669	0.400	1.703
	33	29	0.831	9.20	1.466	0.060	0.690	0.387	1.769
	34	29	0.804	8.64	1.463	0.055	0.671	0.437	1.812
	35	29	0.814	8.39	1.596	0.055	0.592	0.509	1.773
	36	43	0.741	6.19	1.553	0.070	0.600	0.348	1.718
	37	43	0.865	8.13	1.696	0.061	0.678	0.328	1.887
	38	43	0.769	7.46	1.521	0.073	0.581	0.281	1.868
	39	43	0.811	7.56	1.569	0.056	0.627	0.413	1.825
	40	43	0.894	8.44	1.521	0.058	0.883	0.380	1.889

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Organ Weights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Heart Weight g	Liver Weight g	Kidneys Weight g	Adrenals Weight g	Spleen Weight g	Thymus Weight g	Brain Weight g
2f	41	29	0.703	8.13	1.529	0.061	0.734	0.418	1.719
	42	29	0.703	7.97	1.547	0.068	0.790	0.363	1.607
	43	29	0.872	8.86	1.556	0.053	0.640	0.392	1.777
	44	29	0.737	8.92	1.610	0.051	0.712	0.546	1.850
	45	29	0.757	7.85	1.322	0.062	0.687	0.433	1.677

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Organ Weights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Heart Weight g	Liver Weight g	Kidneys Weight g	Adrenals Weight g	Spleen Weight g	Thymus Weight g	Brain Weight g
3f	46	29	0.740	9.73	2.094	0.054	0.652	0.355	1.760
	47	29	0.695	10.65	2.055	0.056	0.577	0.357	1.644
	48	29	0.695	9.62	1.857	0.061	0.531	0.372	1.719
	49	29	0.746	8.86	1.885	0.061	0.535	0.317	1.664
	50	29	0.673	10.16	1.753	0.063	0.610	0.371	1.635

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Organ Weights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Heart Weight g	Liver Weight g	Kidneys Weight g	Adrenals Weight g	Spleen Weight g	Thymus Weight g	Brain Weight g
4f	51	29	0.743	16.47	1.713	0.073	0.495	0.384	1.730
	52	29	0.686	14.87	1.645	0.063	0.478	0.270	1.742
	53	29	0.643	12.62	1.510	0.057	0.395	0.323	1.559
	54	29	0.632	12.74	1.845	0.052	0.450	0.353	1.734
	55	29	0.633	12.26	1.496	0.053	0.461	0.217	1.532
	56	43	0.842	7.98	1.568	0.058	0.715	0.409	1.869
	57	43	0.664	5.46	1.264	0.053	0.514	0.299	1.747
	58	43	0.691	5.94	1.362	0.060	0.478	0.328	1.763
	59	43	0.580	5.16	1.222	0.035	0.422	0.235	1.691
	60	43	0.772	7.97	1.646	0.051	0.558	0.283	1.800

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Organ Weights

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Heart Weight g	Liver Weight g	Kidneys Weight g	Adrenals Weight g	Spleen Weight g	Thymus Weight g	Brain Weight g
5f	66	29	0.790	7.77	1.398	0.055	0.600	0.483	1.659
	67	29	0.795	7.59	1.271	0.054	0.632	0.392	1.687
	68	29	0.910	6.63	1.282	0.054	0.589	0.380	1.843
	69	29	0.734	7.26	1.246	0.051	0.616	0.403	1.602
	70	29	0.910	7.22	1.321	0.060	0.769	0.335	1.755

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Organ Weights

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Heart Weight g	Liver Weight g	Kidneys Weight g	Adrenals Weight g	Spleen Weight g	Thymus Weight g	Brain Weight g	Testes Weight g	Epidi dymis Wt g
6m	71	29	1.248	13.38	2.439	0.054	0.772	0.586	1.890	3.899	0.951
	72	29	1.340	13.01	2.670	0.052	0.845	0.528	1.904	3.619	0.903
	73	29	0.826	10.04	2.089	0.039	0.648	0.445	1.792	3.406	0.857
	74	29	1.219	12.25	2.432	0.056	0.880	0.758	1.839	3.620	0.920
	75	29	1.220	12.43	2.427	0.055	0.858	0.535	1.992	3.448	0.809

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Organ Weights

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Heart Weight g	Liver Weight g	Kidneys Weight g	Adrenals Weight g	Spleen Weight g	Thymus Weight g	Brain Weight g	Testes Weight g	Epidi dymis Wt g
7m	76	29	1.096	11.88	2.236	0.047	0.798	0.702	1.803	3.393	0.788
	77	29	1.258	13.67	2.888	0.056	0.848	0.486	1.897	3.826	0.868
	78	29	1.083	9.25	2.080	0.045	0.737	0.456	1.869	3.349	0.837
	79	29	1.149	12.08	2.320	0.039	0.770	0.604	1.919	3.382	0.835
	80	29	1.353	13.99	2.627	0.046	0.859	0.672	2.011	3.944	0.910

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Organ Weights

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Heart Weight g	Liver Weight g	Kidneys Weight g	Adrenals Weight g	Spleen Weight g	Thymus Weight g	Brain Weight g
6f	81	29	0.736	7.05	1.393	0.049	0.708	0.350	1.625
	82	29	0.712	6.87	1.353	0.066	0.608	0.309	1.740
	83	29	0.727	6.02	1.209	0.048	0.576	0.259	1.588
	84	29	0.836	6.99	1.316	0.063	0.551	0.244	1.784
	85	29	0.878	7.81	1.387	0.064	0.624	0.450	1.863

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - Organ Weights

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Heart Weight g	Liver Weight g	Kidneys Weight g	Adrenals Weight g	Spleen Weight g	Thymus Weight g	Brain Weight g
7f	86	29	0.709	6.28	1.213	0.045	0.571	0.339	1.641
	87	29	0.830	6.98	1.440	0.063	0.675	0.509	1.812
	88	29	0.824	7.66	1.475	0.061	0.658	0.313	1.875
	89	29	0.733	7.60	1.426	0.052	0.733	0.401	1.763
	90	29	0.867	8.88	1.529	0.056	0.756	0.342	1.693

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

13.1.5 Neurotoxicological examinations

13.1.5.1 Grip strength

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Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - FOB - Clinical Part

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Str. of F.limbs1 g	Str. of F.limbs2 g	Str. of H.limbs1 g	Str. of H.limbs2 g
1m	1	26	900	840	350	310
	2	26	700	800	300	280
	3	26	740	800	320	280
	4	26	800	840	300	300
	5	26	800	820	270	290
	6	26	800	800	320	300
	7	26	780	800	300	260
	8	26	780	760	280	290
	9	26	800	900	300	320
	10	26	800	880	290	300

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

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Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - FOB - Clinical Part
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Str. of F.limbs1 g	Str. of F.limbs2 g	Str. of H.limbs1 g	Str. of H.limbs2 g
1f	31	22	740	680	300	280
	-----	-----	-----	-----	-----	-----
	32	22	800	820	290	270
	-----	-----	-----	-----	-----	-----
	33	22	700	720	270	270
	-----	-----	-----	-----	-----	-----
	34	22	700	660	260	280
	-----	-----	-----	-----	-----	-----
	35	22	800	800	280	270
	-----	-----	-----	-----	-----	-----
	36	22	800	820	290	270
	-----	-----	-----	-----	-----	-----
	37	22	800	820	250	270
	-----	-----	-----	-----	-----	-----
	38	22	720	740	270	290
	-----	-----	-----	-----	-----	-----
	39	22	700	760	300	300
	-----	-----	-----	-----	-----	-----
	40	22	800	800	270	300

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Toxicology Study Report - PT02-0222

RTA053-01/04

PROVANTIS

Date: 17-Dec-2002 Page: 3

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - FOB - Clinical Part

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Str. of F.limbs1 g	Str. of F.limbs2 g	Str. of H.limbs1 g	Str. of H.limbs2 g
2m	11	26	800	780	280	300
	-----	-----	-----	-----	-----	-----
	12	26	700	800	300	300
	-----	-----	-----	-----	-----	-----
	13	26	800	860	260	270
	-----	-----	-----	-----	-----	-----
	14	26	800	840	260	280
	-----	-----	-----	-----	-----	-----
	15	26	800	700	280	260

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

RTA053-01/04

PROVANTIS

Date: 17-Dec-2002 Page: 4

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - FOB - Clinical Part

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Str. of F.limbs1 g	Str. of F.limbs2 g	Str. of H.limbs1 g	Str. of H.limbs2 g
2f	41	22	640	640	260	240
	-----	-----	-----	-----	-----	-----
	42	22	780	760	280	250
	-----	-----	-----	-----	-----	-----
	43	22	700	680	290	270
	-----	-----	-----	-----	-----	-----
	44	22	700	720	240	240
	-----	-----	-----	-----	-----	-----
	45	22	640	680	250	240

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - FOB - Clinical Part
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Str. of F.limbs1 g	Str. of F.limbs2 g	Str. of H.limbs1 g	Str. of H.limbs2 g
3m	16	26	800	760	290	300
	----- 17	----- 26	----- 600	----- 700	----- 300	----- 250
	----- 18	----- 26	----- 700	----- 780	----- 260	----- 300
	----- 19	----- 26	----- 640	----- 680	----- 280	----- 290
	----- 20	----- 26	----- 800	----- 800	----- 300	----- 250

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

RTA053-01/04

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Date: 17-Dec-2002 Page: 6

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - FOB - Clinical Part

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Str. of F.limbs1 g	Str. of F.limbs2 g	Str. of H.limbs1 g	Str. of H.limbs2 g
3f	46	22	600	680	280	300
	-----	-----	-----	-----	-----	-----
	47	22	600	700	270	290
	-----	-----	-----	-----	-----	-----
	48	22	760	720	260	270
	-----	-----	-----	-----	-----	-----
	49	22	800	800	260	280
	-----	-----	-----	-----	-----	-----
	50	22	700	700	270	250

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Toxicology Study Report - PT02-0222

RTA053-01/04

PROVANTIS

Date: 17-Dec-2002 Page: 7

Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - FOB - Clinical Part
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Str. of F.limbs1 g	Str. of F.limbs2 g	Str. of H.limbs1 g	Str. of H.limbs2 g
4m	21	26	700	680	240	250
	22	26	600	680	240	260
	23	26	620	700	250	260
	24	26	700	800	250	270
	25	26	780	700	280	270
	26	26	740	800	270	250
	27	26	600	660	260	250
	28	26	620	680	240	240
	29	26	620	680	240	270
	30	26	700	600	220	250

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - FOB - Clinical Part

Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Str. of F.limbs1 g	Str. of F.limbs2 g	Str. of H.limbs1 g	Str. of H.limbs2 g
4f	51	22	620	700	240	210
	52	22	600	700	270	240
	53	22	680	600	200	220
	54	22	640	700	220	240
	55	22	600	640	230	210
	56	22	780	780	270	240
	57	22	740	780	240	210
	58	22	700	740	260	250
	59	22	600	600	250	230
	60	22	740	780	200	190

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - FOB - Clinical Part
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Str. of F.limbs1 g	Str. of F.limbs2 g	Str. of H.limbs1 g	Str. of H.limbs2 g
5m	61	23	800	820	300	320
	-----	-----	-----	-----	-----	-----
	62	23	680	720	240	250
	-----	-----	-----	-----	-----	-----
	63	23	700	680	280	280
	-----	-----	-----	-----	-----	-----
	64	23	780	820	270	300
	-----	-----	-----	-----	-----	-----
	65	23	700	800	290	300

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Toxicology Study Report - PT02-0222

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Date: 17-Dec-2002 Page: 10

Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - FOB - Clinical Part
 Study : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Str. of F.limbs1 g	Str. of F.limbs2 g	Str. of H.limbs1 g	Str. of H.limbs2 g
5f	66	23	660	720	250	270
	67	23	700	680	230	260
	68	23	700	700	250	260
	69	23	680	740	240	280
	70	23	720	780	290	250

* = result to left has an associated comment or marker

Nominal Dose: Group 1 - 0 mg/kg Group 2 - 15 mg/kg Group 3 - 60 mg/kg Group 4 - 240 mg/kg Group 5 - 3 mg/kg

Toxicology Study Report - PT02-0222

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Date: 03-Mar-2003 Page: 1

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - FOB - Clinical Part

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Str. of F.limbs1 g	Str. of F.limbs2 g	Str. of H.limbs1 g	Str. of H.limbs2 g
6m	71	22	760	800	270	310
	72	22	800	800	290	280
	73	22	800	840	280	300
	74	22	780	800	300	290
	75	22	800	780	300	280

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - FOB - Clinical Part

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Str. of F.limbs1 g	Str. of F.limbs2 g	Str. of H.limbs1 g	Str. of H.limbs2 g
6f	81	22	720	760	270	280
	82	22	800	820	260	300
	83	22	800	820	280	300
	84	22	720	760	260	290
	85	22	700	800	300	280

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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PROVANTIS

Date: 03-Mar-2003 Page: 3

Generalised Results By Animal - Animals Against Parameters - Multiple Times

Activity : - FOB - Clinical Part

Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Str. of F.limbs1 g	Str. of F.limbs2 g	Str. of H.limbs1 g	Str. of H.limbs2 g
7m	76	22	760	820	310	280
	77	22	780	820	300	290
	78	22	780	780	270	280
	79	22	860	800	250	290
	80	22	800	840	290	300

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

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PROVANTIS

Date: 03-Mar-2003 Page: 4

Generalised Results By Animal - Animals Against Parameters - Multiple Times
 Activity : - FOB - Clinical Part
 Study : PT02-0222 /1 - T-7758 - 4 weeks oral toxicity in rats

Group Sex	Animal Number	Day Number	Str. of F.limbs1 g	Str. of F.limbs2 g	Str. of H.limbs1 g	Str. of H.limbs2 g
7f	86	22	660	700	280	250
	87	22	780	800	250	270
	88	22	700	800	270	300
	89	22	680	780	250	250
	90	22	780	720	300	260

* = result to left has an associated comment or marker

Nominal Dose: Group 6 - 0 mg/kg/d Group 7 - 0.3 mg/kg/d

13.1.5.2 Motor activity (movements per 60 minutes)

ATOX 10.2

PROVANTIS

RUN DATE: 28-MAY-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

MOTOR ACTIVITY/INDIVIDUAL VALUES
(NUMBER OF COUNTS PER 60-MINUTE-SESSION)

----- MEASUREMENT=1 GROUP=1 SEX=F -----

ANIMAL	VALUE
31	405
32	477
33	406
34	679
35	451
36	648
37	169
38	751
39	607
40	729

----- MEASUREMENT=1 GROUP=1 SEX=M -----

ANIMAL	VALUE
1	604
2	453
3	370
4	638
5	609
6	728
7	372
8	629
9	414
10	661

----- MEASUREMENT=1 GROUP=2 SEX=F -----

ANIMAL	VALUE
66	621
67	561
68	684
69	769
70	632

----- MEASUREMENT=1 GROUP=2 SEX=M -----

ANIMAL	VALUE
61	581
62	657
63	501
64	432
65	767

----- MEASUREMENT=1 GROUP=3 SEX=F -----

ANIMAL	VALUE
41	496
42	672
43	669
44	523
45	536

Toxicology Study Report - PT02-0222

ATOX 10.2

PROVANTIS

RUN DATE: 28-MAY-2003

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

MOTOR ACTIVITY/INDIVIDUAL VALUES (NUMBER OF COUNTS PER 60-MINUTE-SESSION)

----- MEASUREMENT=1 GROUP=3 SEX=M -----

ANIMAL	VALUE
11	480
12	649
13	520
14	448
15	595

----- MEASUREMENT=1 GROUP=4 SEX=F -----

ANIMAL	VALUE
46	509
47	474
48	594
49	519
50	646

----- MEASUREMENT=1 GROUP=4 SEX=M -----

ANIMAL	VALUE
16	441
17	558
18	706
19	587
20	643

----- MEASUREMENT=1 GROUP=5 SEX=F -----

ANIMAL	VALUE
51	527
52	414
53	432
54	632
55	487
56	418
57	590
58	686
59	372
60	530

----- MEASUREMENT=1 GROUP=5 SEX=M -----

ANIMAL	VALUE
21	314
22	545
23	632
24	481
25	420
26	777
27	561
28	644
29	553
30	410

ATOX 10.1 PROXANTIS RUN DATE: 11-MAR-10

SUMMARY AND STATISTICAL EVALUATION

STUDY : PT02-0222 - T-7758 - 4 weeks oral toxicity in rats

MOTOR ACTIVITY/INDIVIDUAL VALUES
(NUMBER OF COUNTS PER 60-MINUTE-SESSION)

----- MEASUREMENT=1 GROUP=1 SEX=F -----

ANIMAL	VALUE
81	493
82	513
83	690
84	540
85	657

----- MEASUREMENT=1 GROUP=1 SEX=M -----

ANIMAL	VALUE
71	514
72	428
73	645
74	515
75	562

----- MEASUREMENT=1 GROUP=2 SEX=F -----

ANIMAL	VALUE
86	829
87	527
88	636
89	781
90	520

----- MEASUREMENT=1 GROUP=2 SEX=M -----

ANIMAL	VALUE
76	576
77	691
78	623
79	593
80	595

13.2 ADDITIONAL DATA

13.2.1 Composition of diet

SSNIFF® R/M-H: SOLE DIET FOR RATS AND MICE - MAINTENANCE

Ingredients		Amino Acids		Vitamins		Trace elements	
[average % content in the diet]		[average % content in the diet]		[per kg diet]		[per kg diet]	
Crude protein	19.00	Lysine	1.00	Vitamin A	10 000 IU	Managanese	75.0 mg
Crude fat	3.00	Methionine	0.30	Vitamin D2	1 280 IU	Copper	12.0 mg
Crude fiber	5.20	Cystine	0.25	Vitamin E	120 mg	Zinc	70.0 mg
Ash	6.70	Glycine	0.90	Vitamin C	500 mg	Iodine	1.5 mg
		Leucine	1.50	Vitamin B1	15 mg	Iron	220.0 mg
Calcium	1.10	Isoleucine	0.90	Vitamin B2	25 mg	Fluorine	10.0 mg
Phosphorous	0.80	Arginine	1.20	Vitamin B6	12 mg		
Sodium	0.25	Phenylalanine	0.90	Vitamin B12	50 µg		
Magnesium	0.20	Tryptophane	0.25	Biotin	200 µg	Metabolizable energy	
Potassium	1.00	Histidine	0.45	Pantothenic acid	40 mg	[per kg diet]	
		Alanine	0.70	Choline	1 600 mg		
		Tyrosine	0.60	Folic acid	4 mg	ME	12.1 MJ
		Asparagine acid	1.40	Nicotinic acid	100 mg		
		Glutamine acide	2.20	Vitamin K3	5 mg		
		Valine	0.90	Inosit	50 mg		

13.2.2 Historical control data

Species: Rat

Strain: Hsd:SD

Male animals (Age: 10 - 16 weeks) Version from 26-Nov-2002

Parameter	Unity	Min	Max	Mean	SD	Number of studies
Red blood cell count	10 ¹² /l	7,44	8,27	7,84	0,22	32
Hemoglobin	g/l	145	160	152,59	3,57	32
Hematocrit		0,43	0,5	0,46	0,02	32
MCV	10 ⁻¹⁵ l	55	63	58,47	1,68	32
MCH	10 ⁻¹² g	18	20	19,47	0,57	32
MCHC	g/l	307	354	333,97	10,16	32
Reticulocytes		0,007	0,045	0,03	0,01	32
Heinz Bodies		0	0	0,00	0,00	29
White blood cell count	10 ⁹ /l	9	12,7	10,53	1,05	32
Platelets	10 ⁹ /l	783	1121	957,97	78,29	31
Coagulation Time	Seconds	99	151	128,42	13,79	31
Sodium	mmol/l	135	144	140,16	2,03	32
Potassium	mmol/l	4,55	7,17	5,57	0,48	32
Calcium	mmol/l	2,27	2,51	2,40	0,06	32
Chloride	mmol/l	99	104	101,09	1,17	32
Phosphorus	mmol/l	2,53	3,6	2,89	0,21	32
Total Bilirubin	umol/l	2,4	10,6	4,87	2,32	32
Direct Bilirubin	umol/l	0	1,4	0,14	0,35	30
Glucose	mmol/l	9,24	23,66	15,14	2,58	32
Uric Acid	umol/l	35	146	65,29	21,39	31
Creatinine	umol/l	37	67	51,28	7,34	32
Urea Nitrogen	mmol/l	3,54	7,74	6,21	0,82	32
Cholesterol	mmol/l	1,57	2,5	2,06	0,19	32
Triglycerides	mmol/l	0,48	1,08	0,79	0,14	32
Total Protein	g/l	49	59	53,69	2,32	32
Albumin	g/l	21,8	29,4	25,60	2,08	23
ASAT	IU/l	42	131	90,34	24,07	32
ALAT	IU/l	30	82	41,09	10,49	32
G-Gluta.Transf.	IU/l	2	4	3,00	0,82	22
Alkaline Phosphatase	IU/l	294	471	354,47	43,64	32
Volume	ml	1,6	6,9	4,56	1,45	23
pH Value		6	8	7,12	0,52	31
Specific Weight	g/l	1027	1076	1041,39	12,18	23
Body weight	g	249	309,2	278,57	14,45	32
Heart Weight	g	0,937	1,141	1,03	0,05	32
Liver Weight	g	9,336	12,125	11,00	0,77	32
Kidneys Weight	g	1,764	2,329	2,04	0,17	32
Spleen Weight	g	0,594	0,857	0,72	0,06	32
Testes Weight	g	2,972	3,631	3,35	0,14	32
Epididymis Weight	g	0,735	0,906	0,85	0,05	22
Adrenals Weight	g	0,0334	0,5	0,05	0,08	32
Brain Weight	g	1,676	1,897	1,81	0,05	32
Thymus Weight	g	0,404	0,553	0,46	0,04	23
Lung Weight	g	1,195	1,725	1,48	0,17	9
Thyroid Gland Weight	g	0,0127	0,016	0,01	0,00	10
Pituitary Gland Weight	g	0,0068	0,0096	0,01	0,00	10
g/kg						
Heart Weight		3,371	4,104	3,71	0,20	32
Liver Weight		35,964	43,486	39,44	1,84	32
Kidneys Weight		6,437	8,464	7,31	0,49	32
Spleen Weight		2,294	3,074	2,60	0,19	32
Testes Weight		10,923	13,077	12,06	0,56	32
Epididymis Weight		2,832	3,466	3,10	0,19	22
Adrenals Weight		0,1225	0,1845	0,15	0,01	32
Brain Weight		6,07	7,121	6,53	0,29	32
Thymus Weight		1,432	1,985	1,66	0,15	23
Lung Weight		4,334	5,928	5,17	0,49	9
Thyroid Gland Weight		0,042	0,0542	0,05	0,00	10
Pituitary Gland Weight		0,025	0,033	0,03	0,00	10

Species: Rat

Strain: Hsd:SD

Female animals (Age: 10 - 16 weeks) Version from 26-Nov-2002

Parameter	Unity	Min	Max	Mean	SD	Number of studies
Red blood cell count	10 ¹² /l	6,96	8,03	7,43	0,26	32
Hemoglobin	g/l	132,00	154,00	143,88	5,53	32
Hematocrit		0,40	0,46	0,43	0,02	32
MCV	10 ⁻¹⁵ l	55,00	61,00	57,19	1,67	32
MCH	10 ⁻¹² g	18,00	21,00	19,50	0,62	32
MCHC	g/l	320,00	358,00	339,09	9,43	32
Reticulocytes		0,01	0,08	0,03	0,01	32
Heinz Bodies		0,00	0,00	0,00	0,00	29
White blood cell count	10 ⁹ /l	5,30	11,40	8,06	1,35	32
Platelets	10 ⁹ /l	818,00	1187,00	990,81	93,59	31
Coagulation Time	Seconds	107,00	171,00	127,03	13,15	31
Sodium	mmol/l	137,00	144,00	140,50	1,93	32
Potassium	mmol/l	4,32	6,60	5,33	0,49	32
Calcium	mmol/l	2,28	2,53	2,39	0,07	32
Chloride	mmol/l	101,00	107,00	103,38	1,48	32
Phosphorus	mmol/l	2,31	3,46	2,78	0,27	32
Total Bilirubin	umol/l	2,10	9,90	5,03	2,35	32
Direct Bilirubin	umol/l	0,00	1,10	0,15	0,29	30
Glucose	mmol/l	7,70	18,04	13,01	1,94	32
Uric Acid	umol/l	56,00	160,00	78,74	22,33	31
Creatinine	umol/l	38,00	73,00	53,13	7,16	32
Urea Nitrogen	mmol/l	4,80	6,76	5,86	0,50	32
Cholesterol	mmol/l	1,63	2,69	2,10	0,25	32
Triglycerides	mmol/l	0,40	1,09	0,60	0,12	32
Total Protein	g/l	48,00	60,00	54,41	2,73	32
Albumin	g/l	22,20	30,20	27,07	2,15	23
ASAT	IU/l	40,00	133,00	93,28	23,80	32
ALAT	IU/l	27,00	57,00	37,06	6,22	32
G-Gluta.Transf.	IU/l	2,00	4,00	3,05	0,72	22
Alkaline Phosphatase	IU/l	189,00	380,00	269,75	42,61	32
Volume	ml	1,40	6,40	4,03	1,23	23
pH Value		6,00	8,00	6,85	0,50	31
Specific Weight	g/l	1024,00	1054,00	1036,35	8,14	22
Body weight	g	173,60	210,40	197,50	8,74	32
Heart Weight	g	0,69	0,91	0,78	0,05	32
Liver Weight	g	6,22	8,29	7,38	0,57	32
Kidneys Weight	g	1,23	1,61	1,36	0,10	32
Spleen Weight	g	0,46	0,70	0,62	0,06	32
Adrenals Weight	g	0,04	0,06	0,05	0,00	32
Brain Weight	g	1,60	1,80	1,71	0,06	30
Thymus Weight	g	0,27	0,43	0,34	0,04	23
Ovaries Weight	g	0,11	0,14	0,13	0,01	12
Lung Weight	g	0,95	1,39	1,21	0,13	9
Thyroid Gland Weight	g	0,01	0,11	0,02	0,03	10
Pituitary Gland Weight	g	0,01	0,01	0,01	0,00	10
g/kg						
Heart Weight		3,45	4,62	3,97	0,24	32
Liver Weight		33,56	41,09	37,32	1,99	32
Kidneys Weight		6,17	8,04	6,89	0,43	32
Spleen Weight		2,41	3,43	3,14	0,23	32
Adrenals Weight		0,23	0,31	0,27	0,02	32
Brain Weight		8,22	9,51	8,71	0,34	32
Thymus Weight		1,36	2,02	1,73	0,15	23
Ovaries Weight		0,55	0,73	0,63	0,05	12
Lung Weight		4,94	6,64	6,01	0,58	9
Thyroid Gland Weight		0,06	0,08	0,07	0,01	10
Pituitary Gland Weight		0,04	0,06	0,05	0,01	10

13.3 REPORTS INCLUDING

13.3.1 Pathology report

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PATHOLOGY REPORT
Study-No.: PT02-0222
T-7758

prepared by: DR. BERNDT HEIN
Pathologist

SUMMARY

Mortality:

One recovery high-dose animal was found dead at study day 42. The cause of death was related to treatment with the test article.

Necropsy Findings:

Group 4 (D3; high dose, 240 mg/kg):

K0/K0 animals:

Discoloured kidneys in three females and all 5 males, one *enlarged stomach*, two *enlarged livers*, and one *opaque eye*.

R1/R1 animals:

Small accessory genital glands (prostate and/ or seminal vesicle) in three animals. Additionally, one male exhibited a *small thymus* and *enlarged adrenal glands*. An *irregular surface* could be observed on the **kidney** of one male as well as one female.

R1/+1 animal (died):

Small accessory genital glands (prostate and seminal vesicle) in combination with *small testes* and *epididymides*.

Group 3 (D2; mid-high dose, 60 mg/kg):

K0/K0 animals:

Discoloured kidneys in four males, and four females, and a *discoloured duodenum* in one female.

Group 2 (D1; mid dose. 15 mg/kg):

K0/K0 animals:

Discoloured kidneys in three males, and one female.

Group 5 (D4; low-mid dose, 3 mg/kg):

K0/K0 animals:

Transparent margins in the **liver** of female animal no. 68.

Microscopical Findings:

Relevant histopathological findings were seen in the following organs:

Liver: *Hypertrophy of hepatocytes* in nearly all animals of the high dose group D3 at terminal necropsy.

Spleen: *Lymphocyte depletion* in the animals of the high dose group D3: one male at terminal necropsy, and two male at recovery necropsy.

Thymus: *Atrophy* in three males of group D3 at recovery necropsy.

Iliac lymph node: *Lymphoid cell depletion* in animal no. 30 (group D3), which died during the recovery.

Testes/ Epididymides: *Atrophy* in animal no. 30 (unscheduled death).

Prostate/ Seminal Vesicles: *Atrophy* in three animals of group D3/ recovery necropsy.

Findings in the **kidneys** were also noted and included *tubular changes*. These findings were sporadically seen in males and females with special focus on group D3 and D2 at the terminal sacrifice. A *nephroblastoma* could be detected in one female (no. 51).

One male and one female of group D3 exhibited a *chronic nephropathy* at recovery necropsy.

Sporadic changes in form of *cellular infiltrates / inflammatory foci* were observed in the **lungs** and **liver** of some animals of different groups. In group D3 (terminal sacrifice) could be observed a *submucosal edema* in the **forestomach**, a *dilatation* of the **uterus**, and an *enlarged epithelium* of the **cornea**, in different animals.

Conclusion:

The 4-week oral gavage administration of the test article caused severe alterations in the target organs and unscheduled death in one high-dose male one day before the end of the experiment.

One of the central organ systems involved in the toxicity of the test article were the “manufacturing plants” of white blood cells, particularly the thymus, but also spleen and lymph nodes, which exhibited a loss of white blood cells in the animals of the high dose group. This effect could only be observed in single males of the high dose group D3. A comparable effect (tubular atrophy) could be observed in the testes of one animal of the high dose group. Both kinds of tissue demonstrate this reaction during the recovery period.

At terminal sacrifice the animals of the high dose group exhibited an increase of hepatocellular activity (hypertrophy caused by enzyme induction), which had returned to normal after the 14-day recovery period.

The kidney was identified as another target organ of the test article. Although it showed a more or less diffuse picture regarding incidence and evidence of its tubular alterations - which is not uncommon in particular for the male Sprague Dawley rat - severity grades of these findings were distinctly higher in the dose groups D2 (60 mg/kg) and D3 (240 mg/kg).

The other findings should be discussed as spontaneous, they occurred in the control group, too, or could relatively often be observed in historical controls.

MATERIAL AND METHODS

GROUP DESIGN FOR PATHOLOGIC EVALUATION:

Group No.		Dose	Animal-No.: (male)		Animal-No.: (female)	
			mg/kg bw.	K0-Group	R1-Group	K0-Group
1 / Co	control	0	1 - 5	6 - 10	31 - 35	36 - 40
2 / D1	mid	15	11 - 15	-	41 - 45	-
3 / D2	mid-high	60	16 - 20	-	46 - 50	-
4 / D3	high	240	21 - 25	26 - 30	51 - 55	56 - 60
5 / D4	mid-low*	3	61 - 65	-	66 - 70	-

* the **low dose D5** (0.3 mg/kg) is added in an addendum (no. **90222**) to this report against another control group.

ADMINISTRATION OF THE TEST ARTICLE

The test article was orally administrated by means of a pharyngeal tube, 28 administrations for four weeks.

NECROPSY AND HISTOPATHOLOGY

All animals were killed by exsanguination (dissection of the V. cava cran.) after intraperitoneal anaesthesia with Ketamin-Hydrochloride and Xylazin at termination (K0-subgroup on day 29; R1-subgroup on day 43) and were subjected to necropsy.

Sections of the following organs / tissues were examined microscopically from all male and female rats of terminal sacrifice (K0) group 1 (control), and group 4 (high dose) according to the protocol:

Heart, lungs (incl. bronchi) and trachea, liver, kidneys, spleen, brain (cerebrum, cerebellum, stem, medulla oblongata), spinal cord (cervical), testes, epididymis, prostate, seminal vesicles, ovaries, uterus, urinary bladder, stomach, jejunum, colon, adrenals, thymus, bone marrow (sternum), sciatic nerve, thyroid and parathyroid gland; iliac and mandibular lymphnode;

additionally all macroscopically visible changes in organs, and all organs of intercurrently died animals; also kidneys, liver, spleen and thymus of all animals, due to histopathological changes in the high dose group (K0 or R1).

All tissue specimen subjected to histopathology were fixed in formalin, embedded in Paraffin, and stained with hematoxylin and eosin (HE). The lungs were additionally instilled with 4 % formaldehyde prior to embedding.

DATA COMPILATION

The animal data as well as the necropsy data were recorded in Provantis, during the section at ProTox Kastengrund Testing Facility, entered into the PATHDATA computer system and transferred via electronic mail to the Test Site ProTox Marburg.

The microscopic findings were recorded by the undersigned pathologist using on-line input into the PATHDATA computer system.

All macroscopic and microscopic findings are given for each animal in text form under TEXT OF GROSS AND MICROSCOPIC FINDINGS.

Histopathologic changes were described, wherever possible, according to their distribution, severity, and morphologic character. Severity scores were assigned as given under EXPLANATION OF CODES AND SYMBOLS.

In paired organs non-neoplastic lesions of different severity were scored as follows:

- grade 1/2 or grade 1/3 = grade 2
- grade 1/4 or grade 2/3 or grade 2/4 = grade 3
- grade 1/5 or grade 2/5 or grade 3/4 or grade 3/5 = grade 4
- grade 4/5 = grade 5

All incidence tables were created by the PATHDATA computer system.

RESULTS

MORTALITY

Animal no. 30 (group 4: high dose, recovery) was found dead one day before termination of the recovery period (study day 42). Although autolysis was evident, microscopic examination indicated severe lymphocytes depletion in spleen, thymus and lymph nodes as cause of death. This finding was considered test-article related

NECROPSY FINDINGS

Group 4 (D3; high dose, 240 mg/kg):

K0/K0 animals:

Discoloured kidneys in three females (no. 52, 54, 55) and all 5 males, one *enlarged stomach* (male no. 24), two *enlarged livers* (females no. 51, 54), and one *opaque eye* in female no. 55.

R1/R1 animals:

Small accessory genital glands (prostate and/ or seminal vesicle) in no. 26, 27 and 28. Additionally, male no. 28 exhibited a *small thymus* and *enlarged adrenal glands*. An *irregular surface* could be observed on the *kidney* of male no. 28 as well as female no. 59.

R1/+1 animal (died):

Small accessory genital glands (prostate and seminal vesicle) in combination with *small testes* and *epididymides*.

Group 3 (D2; mid-high dose, 60 mg/kg):

K0/K0 animals:

Discoloured kidneys in four males (no. 17-20), and four females (no. 46, 47, 49, 50), and a *discoloured duodenum* in female no. 46.

Group 2 (D1; mid dose ,15 mg/kg):

K0/K0 animals:

Discoloured kidneys in three males (no. 11, 14 and 15), and female no. 45.

Group 5 (D4; low-mid dose, 3 mg/kg):

K0/K0 animals:

Transparent margins in the *liver* of female animal no. 68.

For details see also TEXT OF GROSS AND MICROSCOPIC FINDINGS.

HISTOPATHOLOGY FINDINGS

Relevant histopathological findings were seen in the following organs:

Liver: *Hypertrophy of hepatocytes* in nearly all animals of the high dose group D3 at terminal necropsy.

Spleen: *Lymphocyte depletion* in the animals of the high dose group D3: one male at terminal necropsy, and two male at recovery necropsy.

Thymus: *Atrophy* in three males of high dose group D3 at recovery necropsy.

Iliac lymph node: *Lymphoid cell depletion* in one animal (high dose group D3), which died during the recovery.

Testes/ Epididymides: *Atrophy* in animal no. 30 (unscheduled death).

Prostate/ Seminal Vesicles: *Atrophy* in three animals of group D3/ recovery necropsy.

Findings in the **kidneys** were also noted and included *tubular changes*. These findings were sporadically seen in males and females with special focus on high dose group D3 and mid-high dose group D2 at the terminal sacrifice. A *nephroblastoma* could be detected in one high dose (D3) female.

One male and one female of group D3 exhibited a *chronic nephropathy* at recovery necropsy.

Sporadic changes in form of *cellular infiltrates / inflammatory foci* were observed in the **lungs** and **liver** of some animals of different groups. In group D3 (terminal sacrifice) could be observed a *submucosal edema* in the **forestomach**, a *dilatation* of the **uterus**, and an *enlarged epithelium* of the **cornea**, in different animals.

CONCLUSIONS

The 4-week oral gavage administration of the test article caused severe alterations in the target organs and unscheduled death in one high-dose male (D3) one day before the end of the experiment.

One of the central organ systems involved in the toxicity of the test article were the “manufacturing plants” of white blood cells, particularly the thymus, but also spleen and lymph nodes, which exhibited a loss of white blood cells in the animals of the high dose group. This effect could only be observed in single males of the high dose group D3. A comparable effect (tubular atrophy) could be observed in the testes of one animal of the high dose recovery group which was found dead on study day 42. Both kinds of tissue demonstrate this reaction during the recovery period.

At terminal sacrifice the animals of the high dose group exhibited an increase of hepatocellular activity (hypertrophy caused by enzyme induction), which had returned to normal after the 14-day recovery period.

The kidney was identified as another target organ of the test article. Although it showed a more or less diffuse picture regarding incidence and evidence of its tubular alterations - which is not uncommon in particular for the male Sprague Dawley rat - severity grades of these findings were distinctly higher in the high dose groups (D2 and D3).

The other findings should be discussed as spontaneous, they occurred in the control group, too, or could relatively often be observed in historical controls.

 16.17.07

Signature
(Dr. B. Hein)

Veterinary Pathologist
Principal Investigator

END OF REPORT SECTION

□

PATHOLOGY REPORT

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TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

AUTHENTICATION

I, the undersigned hereby declares that the histopathology data in this report were compiled by me, and that they reflect accurately the primary data records.

ProTox Marburg


Dr. Berndt Hein
ProTox Marburg
Aventis Pharma Deutschland GmbH
Marburg

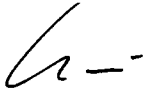
PATHOLOGY REPORT

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PT02-0222

TEST ARTICLE : T-7758 *PATHOL. NO.:* 02222 HE
TEST SYSTEM : Rat, 1 month, Oral Gavage *DATE* : 16-JUL-03
SPONSOR : 3M Corporate Toxicology *PathData© System V5.1b*

STATEMENT OF COMPLIANCE

The undersigned hereby declares that this study was performed
according to the regulations of Good Laboratory Practice (GLP).


(Study Pathologist)

Date: 16.17.07

ProTox Marburg

PATHOLOGY REPORT

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PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

EXPLANATION OF CODES AND SYMBOLS

CODES AND SYMBOLS USED AT ANIMAL LEVEL:

M = Male animal
F = Female animal
K0 = Terminal sacrifice group
R1...R9 = Recovery / post-treatment group 1...9
+ = Intercurrent death/sacrificed moribund
+1 = Found dead

CODES AND SYMBOLS USED AT ORGAN LEVEL:

A = Severe autolysis, evaluation not possible
G = Gross observation checked off histologically
! = Gross observat.not checked off histologically
0 = Tissue not present for histologic examination
' = Histologic examination not required
+ = Organ examined, findings present
- = Organ examined, no pathologic findings noted (AOFT only)
(= Only one of paired organs examined/present

CODES AND SYMBOLS USED AT FINDING LEVEL:

GRADE 2 = Slight / few / small
GRADE 3 = Moderate / moderate number / moderate size
GRADE 4 = Marked / many / large
N0 = Malignant neoplasm
(= Finding unilateral in paired organs
* = Comment in text of individual animal data

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TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

 NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
 STATUS AT NECROPSY: K0

SEX :						MALE
DOSE GROUP:	C0	D1	D2	D3	D4	
NO.ANIMALS:	5	5	5	5	5	

KIDNEYS	:	5	5	5	5	5
- Atrophy:Tubular	:	-	-	3	1	-
- Dilation:Tubular	:	-	-	-	2	-
- Tubular Necrosis	:	-	-	1	-	-

LIVER	:	5	5	5	5	5
- Hypertrophy	:	-	-	-	4	-
- Inflammatory Foci	:	1	-	2	-	2
- Mixed Cell Infiltrat:	:	-	-	-	-	1

LUNGS	:	5	-	-	5	-
- Interstit.Infiltrat.:	:	1	-	-	-	-

SPLEEN	:	5	5	5	5	5
- Lymphocyte Depletion:	:	-	-	-	1	-

PATHOLOGY REPORT
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TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

 NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
 STATUS AT NECROPSY: K0

SEX :						FEMALE
DOSE GROUP:	C0	D1	D2	D3	D4	
NO.ANIMALS:	5	5	5	5	5	

KIDNEYS	:	5	5	5	5	5
- Atrophy:Tubular	:	-	-	1	-	-
- Dilatation:Tubular	:	1	-	-	-	-
- Tubular Degeneration:	:	-	-	-	1	-
- Tubular Necrosis	:	-	-	1	-	-
- Tubular Hyaline	:	-	-	-	1	-
- Nephroblastoma	:	-	-	-	1	-

LIVER	:	5	5	5	5	5
- Hypertrophy	:	-	-	-	5	-
- Inflammatory Foci	:	-	-	-	1	-

FORESTOMACH	:	5	-	-	5	-
- Edema, submucosal	:	-	-	-	1	-

UTERUS	:	5	-	-	5	-
- Dilatation	:	-	-	-	1	-

EYES	:	-	-	-	1	-
- Epithelization	:	-	-	-	1	-

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TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData©	System V5.1b

 NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
 STATUS AT NECROPSY: R1, INCL. DEATHS

	SEX :						MALE
	DOSE GROUP:	C0	D1	D2	D3	D4	
	NO.ANIMALS:	5	-	-	5	-	
KIDNEYS	:	5	-	-	4	-	
- Chronic Nephropathy:		-	-	-	1	-	
- Dilation:Tubular	:	3	-	-	-	-	
LIVER	:	5	-	-	4	-	
- Inflammatory Foci	:	-	-	-	1	-	
SPLEEN	:	5	-	-	5	-	
- Lymphocyte Depletion:		-	-	-	2	-	
THYMUS	:	5	-	-	5	-	
- Atrophy	:	-	-	-	3	-	
ILIAC LYMPH NODE	:	-	-	-	1	-	
- Lymphocyte Depletion:		-	-	-	1	-	
PROSTATE	:	-	-	-	3	-	
- Atrophy	:	-	-	-	3	-	
SEMINAL VESICLES	:	-	-	-	4	-	
- Atrophy	:	-	-	-	3	-	
TESTES	:	-	-	-	1	-	
- Atrophy:Tubular	:	-	-	-	1	-	
EPIDIDYMIDES	:	-	-	-	1	-	
- Atrophy	:	-	-	-	1	-	

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TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1, INCL. DEATHS

SEX	:						FEMALE
DOSE GROUP:		C0	D1	D2	D3	D4	
NO.ANIMALS:		5	-	-	5	-	

KIDNEYS	:	5	-	-	5	-	
- Chronic Nephropathy:		1	-	-	1	-	

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TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

 SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX
 STATUS AT NECROPSY: K0

SEX :						MALE
DOSE GROUP:	C0	D1	D2	D3	D4	
NO. ANIMALS:	5	5	5	5	5	

KIDNEYS	:	5	5	5	5	5
- Atrophy:Tubular						
GRADE 2 :	-	-	3	1	-	
TOTAL AFFECTED :	-	-	3	1	-	
MEAN SEVERITY :	-	-	2.0	2.0	-	

- Dilation:Tubular						
GRADE 2 :	-	-	-	2	-	
TOTAL AFFECTED :	-	-	-	2	-	
MEAN SEVERITY :	-	-	-	2.0	-	

- Tubular Necrosis						
GRADE 2 :	-	-	1	-	-	
TOTAL AFFECTED :	-	-	1	-	-	
MEAN SEVERITY :	-	-	2.0	-	-	

LIVER	:	5	5	5	5	5
- Hypertrophy						
GRADE 2 :	-	-	-	4	-	
TOTAL AFFECTED :	-	-	-	4	-	
MEAN SEVERITY :	-	-	-	2.0	-	

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TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

 SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX
 STATUS AT NECROPSY: K0

		SEX :	FEMALE				
		DOSE GROUP:	C0	D1	D2	D3	D4
		NO. ANIMALS:	5	5	5	5	5
KIDNEYS		:	5	5	5	5	5
- Atrophy:Tubular							
	GRADE 2 :		-	-	1	-	-
	TOTAL AFFECTED :		-	-	1	-	-
	MEAN SEVERITY :		-	-	2.0	-	-
.....							
- Dilation:Tubular							
	GRADE 2 :		1	-	-	-	-
	TOTAL AFFECTED :		1	-	-	-	-
	MEAN SEVERITY :		2.0	-	-	-	-
.....							
- Tubular Degeneration							
	GRADE 2 :		-	-	-	1	-
	TOTAL AFFECTED :		-	-	-	1	-
	MEAN SEVERITY :		-	-	-	2.0	-
.....							
- Tubular Necrosis							
	GRADE 2 :		-	-	1	-	-
	TOTAL AFFECTED :		-	-	1	-	-
	MEAN SEVERITY :		-	-	2.0	-	-
.....							
- Tubular Hyaline							
	GRADE 2 :		-	-	-	1	-
	TOTAL AFFECTED :		-	-	-	1	-
	MEAN SEVERITY :		-	-	-	2.0	-
.....							
LIVER		:	5	5	5	5	5
- Hypertrophy							
	GRADE 2 :		-	-	-	3	-
	GRADE 3 :		-	-	-	2	-
	TOTAL AFFECTED :		-	-	-	5	-
	MEAN SEVERITY :		-	-	-	2.4	-

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TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

 SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX
 STATUS AT NECROPSY: R1, INCL. DEATHS

SEX	:						MALE
DOSE GROUP:		C0	D1	D2	D3	D4	
NO. ANIMALS:		5	-	-	5	-	

KIDNEYS	:	5	-	-	4	-	
- Chronic Nephropathy							
GRADE 3	:	-	-	-	1	-	
TOTAL AFFECTED	:	-	-	-	1	-	
MEAN SEVERITY	:	-	-	-	3.0	-	

- Dilation: Tubular							
GRADE 2	:	3	-	-	-	-	
TOTAL AFFECTED	:	3	-	-	-	-	
MEAN SEVERITY	:	2.0	-	-	-	-	

THYMUS	:	5	-	-	5	-	
- Atrophy							
GRADE 2	:	-	-	-	1	-	
GRADE 3	:	-	-	-	1	-	
GRADE 4	:	-	-	-	1	-	
TOTAL AFFECTED	:	-	-	-	3	-	
MEAN SEVERITY	:	-	-	-	3.0	-	

PROSTATE	:	-	-	-	3	-	
- Atrophy							
GRADE 3	:	-	-	-	3	-	
TOTAL AFFECTED	:	-	-	-	3	-	
MEAN SEVERITY	:	-	-	-	3.0	-	

SEMINAL VESICLES	:	-	-	-	4	-	
- Atrophy							
GRADE 3	:	-	-	-	3	-	
TOTAL AFFECTED	:	-	-	-	3	-	
MEAN SEVERITY	:	-	-	-	3.0	-	

PATHOLOGY REPORT

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TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX

STATUS AT NECROPSY: R1, INCL. DEATHS

SEX	:						MALE
DOSE GROUP:		C0	D1	D2	D3	D4	
NO.ANIMALS:		5	-	-	5	-	

TESTES	:	-	-	-	1	-	
- Atrophy:Tubular							
GRADE 3	:	-	-	-	1	-	
TOTAL AFFECTED	:	-	-	-	1	-	
MEAN SEVERITY	:	-	-	-	3.0	-	

PATHOLOGY REPORT
SUMMARY TABLESPAGE : 12/ 58
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TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1, INCL. DEATHS

SEX	:						FEMALE
DOSE GROUP:		C0	D1	D2	D3	D4	
NO. ANIMALS:		5	-	-	5	-	

KIDNEYS	:	5	-	-	5	-	
- Chronic Nephropathy							
GRADE 2	:	1	-	-	-	-	
GRADE 4	:	-	-	-	1	-	

TOTAL AFFECTED	:	1	-	-	1	-	
MEAN SEVERITY	:	2.0	-	-	4.0	-	

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

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TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS
 DOSE GROUP : C0, control

ANIMAL NUMBER :

	1	2	3	4	5	6	7	8	9	10
	MK0	MK0	MK0	MK0	MK0	MR1	MR1	MR1	MR1	MR1
HEART	-	-	-	-	-	'	'	'	'	'
KIDNEYS	-	-	-	-	-	-	+	+	+	-
- Dilation:Tubular	.	.	.	.	.	.	2.	2.	2.	.
LIVER	-	-	+	-	-	-	-	-	-	-
- Inflammatory Foci	.	.	2.	.	.	.	.	.	.	.
LUNGS	-	-	+	-	-	'	'	'	'	'
- Interstit.Infiltrat.	.	.	2.	.	.	.	.	.	.	.
SPLEEN	-	-	-	-	-	-	-	-	-	-
THYMUS	-	-	-	-	-	-	-	-	-	-
TRACHEA	-	-	-	-	-	'	'	'	'	'
ILIAC LYMPH NODE	-	-	-	-	-	'	'	'	'	'
MANDIBULAR LYMPH NO.	-	-	-	-	-	'	'	'	'	'
FORESTOMACH	-	-	-	-	-	'	'	'	'	'
GLANDULAR STOMACH	-	-	-	-	-	'	'	'	'	'
JEJUNUM	-	-	-	-	-	'	'	'	'	'
COLON	-	-	-	-	-	'	'	'	'	'
CEREBRUM	-	-	-	-	-	'	'	'	'	'
CEREBELLUM	-	-	-	-	-	'	'	'	'	'
MEDULLA OBLONGATA	-	-	-	-	-	'	'	'	'	'
SPINAL CORD, CERVIC.	-	-	-	-	-	'	'	'	'	'
SCIATIC NERVE	-	-	-	-	-	'	'	'	'	'

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INDIVIDUAL ANIMAL DATA

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TEST ARTICLE : T-7758	PATHOL. NO.: 02222 HE
TEST SYSTEM : Rat, 1 month, Oral Gavage	DATE : 16-JUL-03
SPONSOR : 3M Corporate Toxicology	PathData© System V5.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS
 DOSE GROUP : C0, control

ANIMAL NUMBER :

	1	2	3	4	5	6	7	8	9	10
	MK0	MK0	MK0	MK0	MK0	MR1	MR1	MR1	MR1	MR1
ADRENAL CORTEX	-	-	-	-	-	'	'	'	'	'
ADRENAL MEDULLA	-	-	-	-	-	'	'	'	'	'
THYROID GLAND	-	-	-	-	-	'	'	'	'	'
PARATHYROID GLANDS	-	-	-	-	-	'	'	'	'	'
URINARY BLADDER	-	-	-	-	-	'	'	'	'	'
PROSTATE	-	-	-	-	-	'	'	'	'	'
SEMINAL VESICLES	-	-	-	-	-	'	'	'	'	'
TESTES	-	-	-	-	-	'	'	'	'	'
EPIDIDYMIDES	-	-	-	-	-	'	'	'	'	'
BONE MARROW	-	-	-	-	-	'	'	'	'	'

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TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS
 DOSE GROUP : C0, control

ANIMAL NUMBER :

	31	32	33	34	35	36	37	38	39	40
	FK0	FK0	FK0	FK0	FK0	FR1	FR1	FR1	FR1	FR1
HEART	-	-	-	-	-	'	'	'	'	'
KIDNEYS	-	-	+	-	-	-	-	-	-	+
- Chronic Nephropathy	.	.	.	.	.	.	.	.	.	2.
- Dilatation:Tubular	.	.	2.	.	.	.	.	.	.	.
LIVER	-	-	-	-	-	-	-	-	-	-
LUNGS	-	-	-	-	-	'	'	'	'	'
SPLEEN	-	-	-	-	-	-	-	-	-	-
THYMUS	-	-	-	-	-	-	-	-	-	-
TRACHEA	-	-	-	-	0	'	'	'	'	'
ILIAC LYMPH NODE	-	-	-	-	-	'	'	'	'	'
MANDIBULAR LYMPH NO.	-	-	-	-	-	'	'	'	'	'
FORESTOMACH	-	-	-	-	-	'	'	'	'	'
GLANDULAR STOMACH	-	-	-	-	-	'	'	'	'	'
JEJUNUM	-	-	-	-	-	'	'	'	'	'
COLON	-	-	-	-	-	'	'	'	'	'
CEREBRUM	-	-	-	-	-	'	'	'	'	'
CEREBELLUM	-	-	-	-	-	'	'	'	'	'
MEDULLA OBLONGATA	-	-	-	-	-	'	'	'	'	'
SPINAL CORD, CERVIC.	-	-	-	-	0	'	'	'	'	'
SCIATIC NERVE	-	-	-	-	-	'	'	'	'	'
ADRENAL CORTEX	-	-	-	-	-	'	'	'	'	'

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INDIVIDUAL ANIMAL DATA

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TEST ARTICLE : T-7758
TEST SYSTEM : Rat, 1 month, Oral Gavage
SPONSOR : 3M Corporate Toxicology

PATHOL. NO.: 02222 HE
DATE : 16-JUL-03
PathData© System V5.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS

DOSE GROUP : C0, control

ANIMAL NUMBER :

	31	32	33	34	35	36	37	38	39	40
	FK0	FK0	FK0	FK0	FK0	FR1	FR1	FR1	FR1	FR1
ADRENAL MEDULLA	-	-	-	-	-	'	'	'	'	'
THYROID GLAND	-	-	-	-	-	'	'	'	'	'
PARATHYROID GLANDS	-	-	-	-	-	'	'	'	'	'
URINARY BLADDER	0	-	-	-	-	'	'	'	'	'
OVARIES	-	-	-	-	-	'	'	'	'	'
UTERUS	-	-	-	-	-	'	'	'	'	'
BONE MARROW	-	-	-	-	-	'	'	'	'	'

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TEST ARTICLE : T-7758
TEST SYSTEM : Rat, 1 month, Oral Gavage
SPONSOR : 3M Corporate Toxicology

PATHOL. NO.: 02222 HE
DATE : 16-JUL-03
PathData© System V5.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS

DOSE GROUP : D1, mid dose

ANIMAL NUMBER :

[illegible]

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TEST ARTICLE : T-7758
TEST SYSTEM : Rat, 1 month, Oral Gavage
SPONSOR : 3M Corporate Toxicology

PATHOL. NO.: 02222 HE
DATE : 16-JUL-03
PathData© System V5.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS
DOSE GROUP : D2, mid-high dose

ANIMAL NUMBER :

	16	17	18	19	20	46	47	48	49	50
	MKO	MKO	MKO	MKO	MKO	FKO	FKO	FKO	FKO	FKO
KIDNEYS	+	-G	+G	+G	+G	-G	-G	-	+G	+G
- Atrophy:Tubular	.	.	2.	2.	2.	.	.	.	2.	.
- Tubular Necrosis	2.	.	.	.	.	.	.	.	.	2.
LIVER	-	-	-	+	+	-	-	-	-	-
- Inflammatory Foci	.	.	.	2.	2.	.	.	.	.	.
SPLEEN	-	-	-	-	-	-	-	-	-	-
THYMUS	-	-	-	-	-	-	-	-	-	-
SMALL INTESTINE	'	'	'	'	'	-G	'	'	'	'

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TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS
 DOSE GROUP : D3, high dose

ANIMAL NUMBER :

	21	22	23	24	25	26	27	28	29	30
	MK0	MK0	MK0	MK0	MK0	MR1	MR1	MR1	MR1	MR1+
HEART	-	-	-	-	-	'	'	'	'	-
KIDNEYS	+G	-G	+G	-G	-G	-	-	+G	-	A
- Chronic Nephropathy	.	.	.	.	.	.	.	3*	.	.
- Atrophy:Tubular	.	.	2.	.	.	.	.	.	.	.
- Dilatation:Tubular	2.	.	2.	.	.	.	.	.	.	.
LIVER	-	+	+	+	+	-	-	-	+	A
- Hypertrophy	.	2*	2*	2*	2*	.	.	.	.	.
- Inflammatory Foci	.	.	.	.	.	.	.	.	2.	.
LUNGS	-	-	-	-	-	'	'	'	'	-
SPLEEN	-	-	-	-	+	-	-	+	-	+
- Lymphocyte Depletion	.	.	.	.	3.	.	.	3.	.	4.
THYMUS	-	-	-	-	-	-	+	+G	-	+
- Atrophy	.	.	.	.	.	.	2.	4.	.	3.
TRACHEA	-	-	-	-	-	'	'	'	'	-
ILIAC LYMPH NODE	-	-	-	-	-	'	'	'	'	+
- Lymphocyte Depletion	.	.	.	.	.	.	.	.	.	3.
MANDIBULAR LYMPH NO.	-	-	-	-	-	'	'	'	'	-
STOMACH	'	'	'	'G	'	'	'	'	'	'
FORESTOMACH	-	-	-	-	-	'	'	'	'	A
GLANDULAR STOMACH	-	-	-	-	-	'	'	'	'	A
JEJUNUM	-	-	-	-	-	'	'	'	'	A
COLON	-	-	-	-	-	'	'	'	'	A
CEREBRUM	-	-	-	-	-	'	'	'	'	-
CEREBELLUM	-	-	-	-	-	'	'	'	'	-

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TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS
 DOSE GROUP : D3, high dose

ANIMAL NUMBER :

	21	22	23	24	25	26	27	28	29	30
	MK0	MK0	MK0	MK0	MK0	MR1	MR1	MR1	MR1	MR1+
MEDULLA OBLONGATA	-	-	-	-	-	'	'	'	'	-
SPINAL CORD, CERVIC.	-	-	-	-	-	'	'	'	'	-
SCIATIC NERVE	-	-	-	-	-	'	'	'	'	-
ADRENAL GLANDS	'	'	'	'	'	'	'	'G	'	'
ADRENAL CORTEX	-	-	-	-	-	'	'	-	'	-
ADRENAL MEDULLA	-	-	-	-	-	'	'	-	'	-
THYROID GLAND	-	-	(-	-	-	'	'	'	'	-
PARATHYROID GLANDS	-	-	(-	-	-	'	'	'	'	-
URINARY BLADDER	-	-	-	-	-	'	'	'	'	0
PROSTATE	-	-	-	-	-	'	+G	+G	'	+G
- Atrophy	.	.	.	.	.	.	3.	3.	.	3.
SEMINAL VESICLES	-	-	-	-	-	-G	+G	+G	'	+G
- Atrophy	.	.	.	.	.	.	3.	3.	.	3.
TESTES	-	-	-	-	-	'	'	'	'	+G
- Atrophy:Tubular	.	.	.	.	.	.	.	.	.	3.
EPIDIDYMIDES	-	-	-	-	-	'	'	'	'	+G
- Atrophy	.	.	.	.	.	.	.	.	.	3.
BONE MARROW	-	-	-	-	-	'	'	'	'	-

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TEST ARTICLE : T-7758	PATHOL. NO.: 02222 HE
TEST SYSTEM : Rat, 1 month, Oral Gavage	DATE : 16-JUL-03
SPONSOR : 3M Corporate Toxicology	PathData© System V5.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS
 DOSE GROUP : D3, high dose

ANIMAL NUMBER :

	51	52	53	54	55	56	57	58	59	60
	FK0	FK0	FK0	FK0	FK0	FR1	FR1	FR1	FR1	FR1
HEART	-	-	-	-	-	'	'	'	'	'
KIDNEYS	+	-G	+	+G	-G	-	-	-	+G	-
- Chronic Nephropathy	.	.	.	.	.	.	.	.	4*	.
- Tubular Degeneration	.	.	.	2.	.	.	.	.	.	.
- Tubular Hyaline	.	.	2.	.	.	.	.	.	.	.
- Nephroblastoma (NO.	.	.	.	.	.	.	.	.	.	.
LIVER	+G	+	+	+G	+	-	-	-	-	-
- Hypertrophy	3*	2*	2*	2*	3*	.	.	.	.	.
- Inflammatory Foci	.	2.	.	.	.	.	.	.	.	.
LUNGS	-	-	-	-	-	'	'	'	'	'
SPLEEN	-	-	-	-	-	-	-	-	-	-
THYMUS	-	-	-	-	-	-	-	-	-	-
TRACHEA	-	-	-	-	-	'	'	'	'	'
ILIAC LYMPH NODE	-	-	-	-	-	'	'	'	'	'
MANDIBULAR LYMPH NO.	-	-	-	-	-	'	'	'	'	'
FORESTOMACH	-	-	+	-	-	'	'	'	'	'
- Edema, submucosal	.	.	2.	.	.	.	.	.	.	.
GLANDULAR STOMACH	-	-	-	-	-	'	'	'	'	'
JEJUNUM	-	-	-	-	-	'	'	'	'	'
COLON	-	-	-	-	-	'	'	'	'	'
CEREBRUM	-	-	-	-	-	'	'	'	'	'
CEREBELLUM	-	-	-	-	-	'	'	'	'	'
MEDULLA OBLONGATA	-	-	-	-	-	'	'	'	'	'

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

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TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS
 DOSE GROUP : D3, high dose

ANIMAL NUMBER :

	51	52	53	54	55	56	57	58	59	60
	FK0	FK0	FK0	FK0	FK0	FR1	FR1	FR1	FR1	FR1
SPINAL CORD, CERVIC.	-	-	-	-	-	'	'	'	'	'
SCIATIC NERVE	-	-	-	-	-	'	'	'	'	'
ADRENAL CORTEX	-	-	-	-	-	'	'	'	'	'
ADRENAL MEDULLA	-	-	-	-	-	'	'	'	'	'
THYROID GLAND	-	-	-	-	-	'	'	'	'	'
PARATHYROID GLANDS	-	-	(-	-	(-	'	'	'	'	'
URINARY BLADDER	-	-	-	-	-	'	'	'	'	'
OVARIES	-	-	-	-	-	'	'	'	'	'
UTERUS	+	-	-	-	-	'	'	'	'	'
- Dilatation	2.	.	.	.	.					
BONE MARROW	-	-	-	-	-	'	'	'	'	'
EYES	'	'	'	'	+G	'	'	'	'	'
- Epithelization					2.					

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INDIVIDUAL ANIMAL DATA

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TEST ARTICLE : T-7758
TEST SYSTEM : Rat, 1 month, Oral Gavage
SPONSOR : 3M Corporate Toxicology

PATHOL. NO.: 02222 HE
DATE : 16-JUL-03
PathData© System V5.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS

DOSE GROUP : D4, mid-low dose

ANIMAL NUMBER :

[illegible]

PATHOLOGY REPORT
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TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

ANIMAL HEADING DATA
DOSE GROUP : C0, 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	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
2	M	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
3	M	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
4	M	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
5	M	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
6	M	R1	R1	43	17-OCT-02 28-NOV-02	28-NOV-02
7	M	R1	R1	43	17-OCT-02 28-NOV-02	28-NOV-02
8	M	R1	R1	43	17-OCT-02 28-NOV-02	28-NOV-02
9	M	R1	R1	43	17-OCT-02 28-NOV-02	28-NOV-02
10	M	R1	R1	43	17-OCT-02 28-NOV-02	28-NOV-02
31	F	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
32	F	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
33	F	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
34	F	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
35	F	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
36	F	R1	R1	43	17-OCT-02 28-NOV-02	28-NOV-02
37	F	R1	R1	43	17-OCT-02 28-NOV-02	28-NOV-02
38	F	R1	R1	43	17-OCT-02 28-NOV-02	28-NOV-02
39	F	R1	R1	43	17-OCT-02 28-NOV-02	28-NOV-02
40	F	R1	R1	43	17-OCT-02 28-NOV-02	28-NOV-02

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TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : C0, control

MALE

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	3

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:

-Microgranuloma, focal/multifocal (inflammatory foci), grade 2

LUNGS:

-Interstitial infiltration (mononuclear)/ pneumonia, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY:	R1		
DAYS ON TEST	: 43	* ANIMAL NO. :	7

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:

-Tubular dilation, multifocal, bilateral, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 26/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : C0, control

MALE

* STATE AT NECROPSY:	R1		
DAYS ON TEST	: 43	* ANIMAL NO. :	8

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:

-Tubular dilation, multifocal, bilateral, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY:	R1		
DAYS ON TEST	: 43	* ANIMAL NO. :	9

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:

-Tubular dilation, multifocal, bilateral, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

**PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA**PAGE : 27/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : C0, control FEMALE

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	31

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

URINARY BLADDER:

Tissue not present for histologic examination

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	33

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:

-Tubular dilation, multifocal, bilateral, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 28/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : C0, control FEMALE

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	35

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TRACHEA:

Tissue not present for histologic examination

SPINAL CORD (CERVICAL SEGMENT):

Tissue not present for histologic examination

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY:	R1		
DAYS ON TEST	: 43	* ANIMAL NO. :	40

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:

-Chronic nephropathic foci, bilateral, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

PAGE : 29/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : C0, control FEMALE

- ALL OTHER ANIMALS IN DOSE GROUP WITHOUT PATHOLOGICAL FINDINGS -

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 30/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

ANIMAL HEADING DATA

DOSE GROUP : D1, mid dose

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	29	17-OCT-02 14-NOV-02	14-NOV-02
12	M	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
13	M	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
14	M	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
15	M	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
41	F	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
42	F	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
43	F	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
44	F	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02
45	F	K0	K0	29	17-OCT-02 14-NOV-02	14-NOV-02

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 31/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D1, mid dose

MALE

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	11

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

NO MICROSCOPIC FINDINGS NOTED.

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	14

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

NO MICROSCOPIC FINDINGS NOTED.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 32/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D1, mid dose MALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 29

* ANIMAL NO. : 15

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

NO MICROSCOPIC FINDINGS NOTED.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 33/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D1, mid dose FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 29

* ANIMAL NO. : 45

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

NO MICROSCOPIC FINDINGS NOTED.

- ALL OTHER ANIMALS IN DOSE GROUP WITHOUT PATHOLOGICAL FINDINGS -

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 34/ 58
PT02-0222TEST ARTICLE : T-7758
TEST SYSTEM : Rat, 1 month, Oral Gavage
SPONSOR : 3M Corporate ToxicologyPATHOL. NO.: 02222 HE
DATE : 16-JUL-03
PathData© System V5.1b

ANIMAL HEADING DATA

DOSE GROUP : D2, mid-high dose

ANIMAL NUMBER	SEX M/F	DEFINED AND FINAL STATE OF NECROPSY	TEST DAYS	FIRST AND LAST DAY UNDER TEST	DATE OF NECROPSY
16	M	K0 K0	29	17-OCT-02 14-NOV-02	14-NOV-02
17	M	K0 K0	29	17-OCT-02 14-NOV-02	14-NOV-02
18	M	K0 K0	29	17-OCT-02 14-NOV-02	14-NOV-02
19	M	K0 K0	29	17-OCT-02 14-NOV-02	14-NOV-02
20	M	K0 K0	29	17-OCT-02 14-NOV-02	14-NOV-02
46	F	K0 K0	29	17-OCT-02 14-NOV-02	14-NOV-02
47	F	K0 K0	29	17-OCT-02 14-NOV-02	14-NOV-02
48	F	K0 K0	29	17-OCT-02 14-NOV-02	14-NOV-02
49	F	K0 K0	29	17-OCT-02 14-NOV-02	14-NOV-02
50	F	K0 K0	29	17-OCT-02 14-NOV-02	14-NOV-02

**PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA**PAGE : 35/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData@ System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : D2, mid-high dose

MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 29

* ANIMAL NO. : 16

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:
-Tubular necrosis, multifocal, bilateral, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0
DAYS ON TEST : 29

* ANIMAL NO. : 17

* NECROPSY FINDINGS

KIDNEYS:
01: Discolored, light brown.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:
No microscopic finding corresponding to necropsy observation no. 01.
NO MICROSCOPIC FINDINGS NOTED.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 36/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D2, mid-high dose MALE

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	18

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

-Tubular atrophy, focal/multifocal, bilateral, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	19

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

-Tubular atrophy, focal/multifocal, bilateral, grade 2

LIVER:

-Microgranuloma, focal/multifocal (inflammatory foci), grade 2

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 37/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : D2, mid-high dose MALE

CONT./FF. ANIMAL NO. : 19

.....
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	20

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.
-Tubular atrophy, focal/multifocal, bilateral, grade 2

LIVER:

-Microgranuloma, focal/multifocal (inflammatory foci), grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

**PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA**PAGE : 38/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D2, mid-high dose FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 29

* ANIMAL NO. : 46

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.

SMALL INTESTINE:

01: Duodenum, Mucous Membrane: Discolored, white.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

SMALL INTESTINE:

No microscopic finding corresponding to necropsy observation no. 01.

NO MICROSCOPIC FINDINGS NOTED.

* STATE AT NECROPSY: K0

DAYS ON TEST : 29

* ANIMAL NO. : 47

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.

NO OTHER NECROPSY OBSERVATIONS NOTED

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 39/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D2, mid-high dose FEMALE

CONT./FF. ANIMAL NO. : 47

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.
NO MICROSCOPIC FINDINGS NOTED.

* STATE AT NECROPSY: K0

DAYS ON TEST : 29

* ANIMAL NO. : 49

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.
-Tubular atrophy, focal/multifocal, bilateral, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 40/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D2, mid-high dose FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 29

* ANIMAL NO. : 50

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

-Tubular necrosis, multifocal, bilateral, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

- ALL OTHER ANIMALS IN DOSE GROUP WITHOUT PATHOLOGICAL FINDINGS -

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

 PAGE : 41/ 58
 PT02-0222

<i>TEST ARTICLE</i> : T-7758	<i>PATHOL. NO.:</i> 02222 HE
<i>TEST SYSTEM</i> : Rat, 1 month, Oral Gavage	<i>DATE</i> : 16-JUL-03
<i>SPONSOR</i> : 3M Corporate Toxicology	<i>PathData© System V5.1b</i>

ANIMAL HEADING DATA

 DOSE GROUP : D3, high dose

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	29	17-OCT-02 14-NOV-02
22	M	K0	K0	29	17-OCT-02 14-NOV-02
23	M	K0	K0	29	17-OCT-02 14-NOV-02
24	M	K0	K0	29	17-OCT-02 14-NOV-02
25	M	K0	K0	29	17-OCT-02 14-NOV-02
26	M	R1	R1	43	17-OCT-02 28-NOV-02
27	M	R1	R1	43	17-OCT-02 28-NOV-02
28	M	R1	R1	43	17-OCT-02 28-NOV-02
29	M	R1	R1	43	17-OCT-02 28-NOV-02
30	M	R1	+1	42	17-OCT-02 27-NOV-02
51	F	K0	K0	29	17-OCT-02 14-NOV-02
52	F	K0	K0	29	17-OCT-02 14-NOV-02
53	F	K0	K0	29	17-OCT-02 14-NOV-02
54	F	K0	K0	29	17-OCT-02 14-NOV-02
55	F	K0	K0	29	17-OCT-02 14-NOV-02
56	F	R1	R1	43	17-OCT-02 28-NOV-02
57	F	R1	R1	43	17-OCT-02 28-NOV-02
58	F	R1	R1	43	17-OCT-02 28-NOV-02
59	F	R1	R1	43	17-OCT-02 28-NOV-02
60	F	R1	R1	43	17-OCT-02 28-NOV-02

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 42/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D3, high dose MALE

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	21

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

-Tubular dilation, multifocal, bilateral, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	22

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

LIVER:

-Hypertrophy, centrilobular, grade 2

(= hepatocytes with pale, mostly fine granulated cytoplasm)

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 43/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : D3, high dose MALE

CONT./FF. ANIMAL NO. : 22

.....
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	23

* NECROPSY FINDINGS

KIDNEYS:
01: Discolored, light brown.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:
No microscopic finding corresponding to necropsy observation no. 01.
-Tubular atrophy, focal/multifocal, bilateral, grade 2
-Tubular dilation, multifocal, bilateral, grade 2
LIVER:
-Hypertrophy, diffuse, grade 2
(= hepatocytes with pale, mostly fine granulated cytoplasm)
THYROID GLAND:
Only one of paired organs examined/present
PARATHYROID GLANDS:
Only one of paired organs examined/present
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 44/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D3, high dose

MALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 29

* ANIMAL NO. : 24

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.

STOMACH:

01: Large.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

LIVER:

-Hypertrophy, diffuse, grade 2

(= hepatocytes with pale, mostly fine granulated cytoplasm)

STOMACH:

No microscopic finding corresponding to necropsy observation no. 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0

DAYS ON TEST : 29

* ANIMAL NO. : 25

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.

NO OTHER NECROPSY OBSERVATIONS NOTED

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 45/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D3, high dose

MALE

CONT./FF. ANIMAL NO. : 25

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

LIVER:

-Hypertrophy, centrilobular, grade 2
(= hepatocytes with pale, mostly fine granulated
cytoplasm)

SPLEEN:

-Lymphocyte depletion, grade 3

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1

DAYS ON TEST : 43

* ANIMAL NO. : 26

* NECROPSY FINDINGS

SEMINAL VESICLES:

01: Small.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

SEMINAL VESICLES:

No microscopic finding corresponding to necropsy observation no. 01.
NO MICROSCOPIC FINDINGS NOTED.

**PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA**PAGE : 46/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D3, high dose MALE

* STATE AT NECROPSY:	R1		
DAYS ON TEST	: 43	* ANIMAL NO. :	27

* NECROPSY FINDINGS

PROSTATE:

01: Small.

SEMINAL VESICLES:

01: Small.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:

-Atrophy, grade 2

PROSTATE:

-Atrophy, grade 3

This finding corresponds to necropsy observation no: 01.

SEMINAL VESICLES:

-Atrophy, bilateral, grade 3

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY:	R1		
DAYS ON TEST	: 43	* ANIMAL NO. :	28

* NECROPSY FINDINGS

KIDNEYS:

01: Surface changed, irregular.

THYMUS:

01: Small.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 47/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D3, high dose MALE

CONT./FF. ANIMAL NO. : 28

ADRENAL GLANDS:

01: Large.

PROSTATE:

01: Small.

SEMINAL VESICLES:

01: Small.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

-Chronic nephropathic foci, bilateral, grade 3
(degenerative alterations mainly in the tubuli, with
round cellular infiltrations in the interstitium)
This finding corresponds to necropsy observation no: 01.

SPLEEN:

-Lymphocyte depletion, grade 3

THYMUS:

-Atrophy, grade 4

This finding corresponds to necropsy observation no: 01.

ADRENAL GLANDS:

No microscopic finding corresponding to necropsy observation no. 01.

PROSTATE:

-Atrophy, grade 3

This finding corresponds to necropsy observation no: 01.

SEMINAL VESICLES:

-Atrophy, bilateral, grade 3

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 48/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D3, high dose MALE

CONT./FF. ANIMAL NO. : 28

* REMARKS

THYMUS: Thymus submitted in large capsule

* STATE AT NECROPSY: R1

DAYS ON TEST : 43

* ANIMAL NO. : 29

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:

-Microgranuloma, focal/multifocal (inflammatory foci), grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: R1/+1

DAYS ON TEST : 42

* ANIMAL NO. : 30

* NECROPSY FINDINGS

PROSTATE:

01: Small.

SEMINAL VESICLES:

01: Small.

TESTES:

01: Small.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 49/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D3, high dose MALE

CONT./FF. ANIMAL NO. : 30

EPIDIDYMIDES:

01: Small.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

Severe autolysis, evaluation not possible

LIVER:

Severe autolysis, evaluation not possible

SPLEEN:

-Lymphocyte depletion, grade 4

THYMUS:

-Atrophy, grade 3

ILIAC LYMPH NODE:

-Depletion of lymphocytes, grade 3

FORESTOMACH:

Severe autolysis, evaluation not possible

GLANDULAR STOMACH:

Severe autolysis, evaluation not possible

JEJUNUM:

Severe autolysis, evaluation not possible

COLON:

Severe autolysis, evaluation not possible

URINARY BLADDER:

Tissue not present for histologic examination

PROSTATE:

-Atrophy, grade 3

This finding corresponds to necropsy observation no: 01.

SEMINAL VESICLES:

-Atrophy, bilateral, grade 3

This finding corresponds to necropsy observation no: 01.

TESTES:

-Tubular atrophy, multifocal, bilateral, grade 3

This finding corresponds to necropsy observation no: 01.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 50/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D3, high dose

MALE

CONT./FF. ANIMAL NO. : 30

EPIDIDYIMIDES:

-Atrophy, bilateral, grade 3

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* REMARKS

THYMUS: Thymus submitted in capsule 1

URINARY BLADDER: submitted in capsule 1

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 51/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D3, high dose FEMALE

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	51

* NECROPSY FINDINGS

LIVER:

01: Large.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

-Nephroblastoma, unilateral (malignant neoplasm)

LIVER:

-Hypertrophy, diffuse, grade 3

(= hepatocytes with pale, mostly fine granulated cytoplasm)

This finding corresponds to necropsy observation no: 01.

UTERUS:

-Dilatation, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	52

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.

NO OTHER NECROPSY OBSERVATIONS NOTED

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 52/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D3, high dose FEMALE

CONT./FF. ANIMAL NO. : 52

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

LIVER:

-Hypertrophy, diffuse, grade 2

(= hepatocytes with pale, mostly fine granulated cytoplasm)

-Microgranuloma, focal/multifocal (inflammatory foci), grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: KO

DAYS ON TEST : 29

* ANIMAL NO. : 53

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:

-Hyaline resorption bodies, tubular, focal, bilateral, grade 2

LIVER:

-Hypertrophy, diffuse, grade 2

(= hepatocytes with pale, mostly fine granulated cytoplasm)

FORESTOMACH:

-Submucosal inflammatory edema, focal, grade 2

PARATHYROID GLANDS:

Only one of paired organs examined/present

**PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA**PAGE : 53/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D3, high dose FEMALE

CONT./FF. ANIMAL NO. : 53

.....
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0

DAYS ON TEST : 29

* ANIMAL NO. : 54

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.

LIVER:

01: Large.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

-Tubular degeneration, multifocal, bilateral, grade 2

LIVER:

-Hypertrophy, centrilobular, grade 2

(= hepatocytes with pale, mostly fine granulated cytoplasm)

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 54/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D3, high dose FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 29

* ANIMAL NO. : 55

* NECROPSY FINDINGS

KIDNEYS:

01: Discolored, light brown.

EYES:

01: RIGHT, Opaque, Both eyes submittet in large Capsule.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

LIVER:

-Hypertrophy, centrolobular, grade 3

(= hepatocytes with pale, mostly fine granulated cytoplasm)

PARATHYROID GLANDS:

Only one of paired organs examined/present

EYES:

-Epithelium of the cornea enlarged (4 layers), bilateral, grade 2

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

**PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA**PAGE : 55/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D3, high dose FEMALE

* STATE AT NECROPSY:	R1		
DAYS ON TEST	: 43	* ANIMAL NO. :	59

* NECROPSY FINDINGS

KIDNEYS:

01: Surface changed, irregular.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:

-Chronic nephropathic foci, bilateral, grade 4
(degenerative alterations mainly in the tubuli, with round
cellular infiltrations in the interstitium)
This finding corresponds to necropsy observation no: 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

- ALL OTHER ANIMALS IN DOSE GROUP WITHOUT PATHOLOGICAL FINDINGS -

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 56/ 58
PT02-0222

TEST ARTICLE : T-7758
TEST SYSTEM : Rat, 1 month, Oral Gavage
SPONSOR : 3M Corporate Toxicology

PATHOL. NO.: 02222 HE
DATE : 16-JUL-03
PathData© System V5.1b

ANIMAL HEADING DATA

DOSE GROUP : D4, mid-low dose

ANIMAL NUMBER	SEX M/F	DEFINED AND FINAL STATE OF NECROPSY	TEST DAYS	FIRST AND LAST DAY UNDER TEST	DATE OF NECROPSY	
61	M	K0	K0	29	18-NOV-02 16-DEC-02	16-DEC-02
62	M	K0	K0	29	18-NOV-02 16-DEC-02	16-DEC-02
63	M	K0	K0	29	18-NOV-02 16-DEC-02	16-DEC-02
64	M	K0	K0	29	18-NOV-02 16-DEC-02	16-DEC-02
65	M	K0	K0	29	18-NOV-02 16-DEC-02	16-DEC-02
66	F	K0	K0	29	18-NOV-02 16-DEC-02	16-DEC-02
67	F	K0	K0	29	18-NOV-02 16-DEC-02	16-DEC-02
68	F	K0	K0	29	18-NOV-02 16-DEC-02	16-DEC-02
69	F	K0	K0	29	18-NOV-02 16-DEC-02	16-DEC-02
70	F	K0	K0	29	18-NOV-02 16-DEC-02	16-DEC-02

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 57/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D4, mid-low dose

MALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 29

* ANIMAL NO. : 61

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:

-Microgranuloma, focal/multifocal (inflammatory foci), grade 2
with necrotic hepatocytes.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0

DAYS ON TEST : 29

* ANIMAL NO. : 64

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:

-Microgranuloma, focal/multifocal (inflammatory foci), grade 2
+ single cell necrosis

-Mixed cell infiltration, in the portal area, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 58/ 58
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	02222 HE
TEST SYSTEM	: Rat, 1 month, Oral Gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporate Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D4, mid-low dose FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 29

* ANIMAL NO. : 68

* NECROPSY FINDINGS

LIVER:

01: Margins changed, partly, transparent.

BRAIN:

01: DAMAGED.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:

No microscopic finding corresponding to necropsy observation no. 01.
NO MICROSCOPIC FINDINGS NOTED.

- ALL OTHER ANIMALS IN DOSE GROUP WITHOUT PATHOLOGICAL FINDINGS -

PATHOLOGY REPORT
Study-No.: PT02-0222
T-7758
PathData-No. 90222

prepared by: DR. BERNDT HEIN
Pathologist

SUMMARY

Mortality:

There were no unscheduled deaths during the course of the experiment.

Necropsy Findings:

There were no gross pathology findings, which could be related to administration of the test compound in all dose groups.

Microscopical Findings:

There were no histopathological findings, which could be related to administration of the test compound in all animals investigated.

Conclusion:

All the observed findings could sporadically be observed in **various organs** of animals from different groups. They occurred at an incidence and severity historically seen at the testing facility for rats of their age and strain. Therefore, they were *not considered related to treatment*.

MATERIAL AND METHODS

GROUP DESIGN FOR PATHOLOGIC EVALUATION:

Group No. *	Animal-No.:	Animal-No.:	Dose (mg/kg)
	male	female	
C1 / 06 Control	71-75	81-85	0
D5 / 07 Low Dose	76-80	86-90	0.3

* the dose groups D1 to D4 (15 – 60 – 240 –3 mg/kg) incl. a control group are reported in no. **02222**)

ADMINISTRATION OF THE TEST ARTICLE

The test article was orally administrated by means of a pharyngeal tube, 28 administrations for four weeks.

NECROPSY AND HISTOPATHOLOGY

All animals were killed by exsanguination (dissection of the V. cava cran.) after intraperitoneal anaesthesia with Ketamin-Hydrochloride and Xylazin at termination and were subjected to necropsy.

Sections of the following organs / tissues were examined microscopically from all male and female rats according to the protocol and its changes:

Heart, lungs (incl. bronchi) and trachea, liver, kidneys, spleen, brain (cerebrum, cerebellum, stem, medulla oblongata), spinal cord (cervical), testes, epididymis, prostate, seminal vesicles, ovaries, uterus, urinary bladder, stomach, small (jejunum) and large intestine (colon), adrenals, thymus, bone marrow (sternum), sciatic nerve, thyroid and parathyroid gland, iliac and mandibular lymphnode; additionally all macroscopically changes organs.

All tissue specimen subjected to histopathology were fixed in formaline, embedded in Paraffin, and stained with hematoxylin and eosin (HE). The lungs were additionally instilled with 4% formaldehyde prior to embedding.

DATA COMPILATION

The animal data as well as the necropsy data were recorded in Provantis, during the section at ProTox Kastengrund Testing Facility, entered into the PATHDATA computer system and transferred via electronic mail to the Test Site ProTox Marburg.

The microscopic findings were recorded by the undersigned pathologist using on-line input into the PATHDATA computer system.

All macroscopic and microscopic findings are given for each animal in text form under TEXT OF GROSS AND MICROSCOPIC FINDINGS.

Histopathologic changes were described, wherever possible, according to their distribution, severity, and morphologic character. Severity scores were assigned as given under EXPLANATION OF CODES AND SYMBOLS.

In paired organs non-neoplastic lesions of different severity were scored as follows:

- grade 1/2 or grade 1/3 = grade 2
- grade 1/4 or grade 2/3 or grade 2/4 = grade 3
- grade 1/5 or grade 2/5 or grade 3/4 or grade 3/5 = grade 4
- grade 4/5 = grade 5

All incidence tables were created by the PATHDATA computer system.

RESULTS

MORTALITY

There were no unscheduled deaths during the course of the experiment.

NECROPSY FINDINGS

There were no gross pathology findings, which could be related to administration of the test compound in all dose groups.

HISTOPATHOLOGY FINDINGS

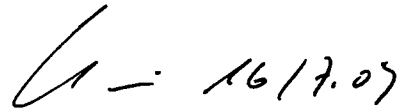
There were no histopathological findings, which could be related to administration of the test compound in all animals investigated.

Sporadic changes in form of *dilatation* and *cellular infiltration* could be observed in the **uterus** of animal no. 89 (group D5/07). Single control animals (group C1/06) exhibited *tubular dilatation* in the **kidney** (no. 71), or *cellular infiltrations* in the **lungs** (no. 83) or glandular **stomach** (no. 75)

For further details see also NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS, TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS, and TEXT OF GROSS AND MICROSCOPIC FINDINGS.

CONCLUSIONS

All the observed findings could sporadically be observed in **various organs** of animals from different groups. They occurred at an incidence and severity historically seen at the testing facility for rats of their age and strain. Therefore, they were *not considered related to treatment*.



Signature
(Dr. B. Hein)

Veterinary Pathologist
Principal Investigator

END OF REPORT SECTION

PATHOLOGY REPORT

PAGE : 1/ 17
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	90222 HE
TEST SYSTEM	: Rat, 1 month, Oral gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporated Toxicology	PathData© System	V5.1b

AUTHENTICATION

I, the undersigned hereby declares that the histopathology data in this report were compiled by me, and that they reflect accurately the primary data records.

ProTox Marburg

 1617.07
Dr. Berndt Hein
ProTox Marburg
Aventis Pharma Deutschland GmbH
Marburg

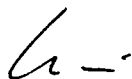
PATHOLOGY REPORT

PAGE : 2/ 17
PT02-0222

TEST ARTICLE : T-7758 PATHOL. NO.: 90222 HE
TEST SYSTEM : Rat, 1 month, Oral gavage DATE : 16-JUL-03
SPONSOR : 3M Corporated Toxicology PathData© System V5.1b

STATEMENT OF COMPLIANCE

The undersigned hereby declares that this study was performed
according to the regulations of Good Laboratory Practice (GLP).



(Study Pathologist)

Date: 16.07.03

ProTox Marburg

PATHOLOGY REPORT

PAGE : 3/ 17
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	90222 HE
TEST SYSTEM	: Rat, 1 month, Oral gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporated Toxicology	PathData© System	V5.1b

EXPLANATION OF CODES AND SYMBOLS

CODES AND SYMBOLS USED AT ANIMAL LEVEL:

M = Male animal
F = Female animal
K0 = Terminal sacrifice group

CODES AND SYMBOLS USED AT ORGAN LEVEL:

' = Histologic examination not required
+ = Organ examined, findings present
- = Organ examined, no pathologic findings noted (AOFT only)
(= Only one of paired organs examined/present

CODES AND SYMBOLS USED AT FINDING LEVEL:

GRADE 2 = Slight / few / small

PATHOLOGY REPORT
SUMMARY TABLESPAGE : 4/ 17
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	90222 HE
TEST SYSTEM	: Rat, 1 month, Oral gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporated Toxicology	PathData© System	V5.1b

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

	DOSE GROUP:	C1		D5	
	SEX :	M	F	M	F
	NO.ANIMALS:	5	5	5	5
KIDNEYS	:	5	5	5	5
- Dilation:Tubular	:	1	-	-	-
LUNGS	:	5	5	5	5
- Interstit.Infiltrat.:	:	-	1	-	-
GLANDULAR STOMACH	:	5	5	5	5
- Mixed cell.infiltrat:	:	1	-	-	-
UTERUS	:	-	5	-	5
- Dilatation	:	-	-	-	1
- PMN cell.infiltrat. :	:	-	-	-	1

PAGE : 5/ 17
PT02-0222

PATHOL. NO.: 90222 HE
DATE : 16-JUL-03
PathData© System V5.1b

ANIMAL NUMBER :

[illegible]

PATHOLOGY REPORT

INDIVIDUAL ANIMAL DATA

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PT02-0222

TEST ARTICLE : T-7758
TEST SYSTEM : Rat, 1 month, Oral gavage
SPONSOR : 3M Corporated Toxicology

PATHOL. NO.: 90222 HE
DATE : 16-JUL-03
PathData© System V5.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS
DOSE GROUP : C1, Sixth group

ANIMAL NUMBER :

71	72	73	74	75	81	82	83	84	85
MK0	MK0	MK0	MK0	MK0	FK0	FK0	FK0	FK0	FK0

[illegible]

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

PAGE : 7/ 17
PT02-0222

TEST ARTICLE : T-7758
TEST SYSTEM : Rat, 1 month, Oral gavage
SPONSOR : 3M Corporated Toxicology

PATHOL. NO.: 90222 HE
DATE : 16-JUL-03
PathData© System V5.1b

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS
DOSE GROUP : D5, Seventh group

ANIMAL NUMBER :

76	77	78	79	80	86	87	88	89	90
MKO	MKO	MKO	MKO	MKO	FKO	FKO	FKO	FKO	FKO

[illegible]

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 9/ 17
PT02-0222

TEST ARTICLE : T-7758
TEST SYSTEM : Rat, 1 month, Oral gavage
SPONSOR : 3M Corporated Toxicology

PATHOL. NO.: 90222 HE
DATE : 16-JUL-03
PathData© System V5.1b

ANIMAL HEADING DATA

DOSE GROUP : C1, Sixth group

ANIMAL NUMBER	SEX M/F	DEFINED AND FINAL STATE OF NECROPSY	TEST DAYS	FIRST AND LAST DAY UNDER TEST	DATE OF NECROPSY
71	M	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
72	M	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
73	M	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
74	M	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
75	M	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
81	F	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
82	F	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
83	F	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
84	F	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
85	F	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 10/ 17
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	90222 HE
TEST SYSTEM	: Rat, 1 month, Oral gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporated Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : C1, Sixth group MALE

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	71

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:

-Tubular dilation, multifocal, bilateral, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	75

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

GLANDULAR STOMACH:

-Mixed cellular infiltration, in the submucosal area, grade 2

PARATHYROID GLANDS:

Only one of paired organs examined/present

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 11/ 17
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	90222 HE
TEST SYSTEM	: Rat, 1 month, Oral gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporated Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : C1, Sixth group FEMALE

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	81

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PARATHYROID GLANDS:

Only one of paired organs examined/present

NO MICROSCOPIC FINDINGS NOTED.

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	83

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LUNGS:

-Interstitial infiltration (mononuclear)/ pneumonia, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 12/ 17
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	90222 HE
TEST SYSTEM	: Rat, 1 month, Oral gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporated Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : C1, Sixth group FEMALE

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	84

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

THYROID GLAND:

Only one of paired organs examined/present

PARATHYROID GLANDS:

Only one of paired organs examined/present

NO MICROSCOPIC FINDINGS NOTED.

- ALL OTHER ANIMALS IN DOSE GROUP WITHOUT PATHOLOGICAL FINDINGS -

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 13/ 17
PT02-0222

TEST ARTICLE : T-7758 PATHOL. NO.: 90222 HE
TEST SYSTEM : Rat, 1 month, Oral gavage DATE : 16-JUL-03
SPONSOR : 3M Corporated Toxicology PathData© System V5.1b

ANIMAL HEADING DATA

DOSE GROUP : D5, Seventh group

ANIMAL NUMBER	SEX M/F	DEFINED AND FINAL STATE OF NECROPSY	TEST DAYS	FIRST AND LAST DAY UNDER TEST	DATE OF NECROPSY
76	M	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
77	M	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
78	M	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
79	M	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
80	M	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
86	F	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
87	F	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
88	F	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
89	F	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03
90	F	K0 K0	29	28-JAN-03 25-FEB-03	25-FEB-03

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 14/ 17
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	90222 HE
TEST SYSTEM	: Rat, 1 month, Oral gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporated Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D5, Seventh group

MALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 29

* ANIMAL NO. : 76

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PARATHYROID GLANDS:

Only one of paired organs examined/present

NO MICROSCOPIC FINDINGS NOTED.

* STATE AT NECROPSY: K0

DAYS ON TEST : 29

* ANIMAL NO. : 79

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PARATHYROID GLANDS:

Only one of paired organs examined/present

NO MICROSCOPIC FINDINGS NOTED.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 15/ 17
PT02-0222

TEST ARTICLE	: T-7758	PATHOL. NO.:	90222 HE
TEST SYSTEM	: Rat, 1 month, Oral gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporated Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D5, Seventh group MALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 29

* ANIMAL NO. : 80

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PARATHYROID GLANDS:

Only one of paired organs examined/present

NO MICROSCOPIC FINDINGS NOTED.

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATAPAGE : 16/ 17
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TEST ARTICLE	: T-7758	PATHOL. NO.:	90222 HE
TEST SYSTEM	: Rat, 1 month, Oral gavage	DATE	: 16-JUL-03
SPONSOR	: 3M Corporated Toxicology	PathData© System	V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : D5, Seventh group FEMALE

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	89

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

UTERUS:

- Dilatation, grade 2
- Infiltration with polymorphnuclear cells, endometrial, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY:	K0		
DAYS ON TEST	: 29	* ANIMAL NO. :	90

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PARATHYROID GLANDS:

- Only one of paired organs examined/present

NO MICROSCOPIC FINDINGS NOTED.

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PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

PAGE : 17/ 17
PT02-0222

TEST ARTICLE : T-7758 PATHOL. NO.: 90222 HE
TEST SYSTEM : Rat, 1 month, Oral gavage DATE : 16-JUL-03
SPONSOR : 3M Corporated Toxicology PathData© System V5.1b

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : D5, Seventh group FEMALE

- ALL OTHER ANIMALS IN DOSE GROUP WITHOUT PATHOLOGICAL FINDINGS -
