

**Electronic Submission**

March 6, 2017

NO CBI

Document Processing Center
EPA East – Room 6428 Attn: Section 8(e)
Office of Pollution Prevention and Toxics, U.S. EPA
1200 Pennsylvania Avenue NW
Washington, DC 20460-0001

Re: TSCA 8(e) Substantial Risk Notice on 2-Propenoic acid, 2-[methyl [(nonafluorobutyl)sulfonyl]amino]ethyl ester, CASRN 67584-55-8; Docket #8EHQ-16-20454

To whom it may concern:

In July of 2016, the EPA was informed of draft results from a Repeat Dose 90-Day Oral Toxicity Study in rats by oral gavage on 2-Propenoic acid, 2-[methyl [(nonafluorobutyl)sulfonyl]amino]ethyl ester, CASRN 67584-55-8.

Groups of male and female SPF-bred Wistar rats were subject to oral gavage doses of 0 (vehicle control-arachis oil), 100, 300 or 1,000/600 mg/kg/day for a 90-day period. Animals at the initial dose of 1000 mg/kg were not dosed from Day 31 up to and including Day 34 based upon adverse health effects observed in both male and females whereupon the dose for this group was reduced from 1,000 to 600 mg/kg/day on test day 35. Secondary groups from the 0 and 1,000/600 mg/kg/day were subsequently held for a 28-day recovery period to determine the reversibility of any adverse effects observed following the dosing period. The study we performed following the OECD 408, Repeated Dose 90-Day Oral Toxicity Study in Rodents testing guideline.

Postmortem examination of the animals revealed test substance-related adverse findings in the liver, kidney and urinary bladder. In the liver, a dose-dependent incidence and severity of hepatocellular necrosis of the centrilobular area and focal/multifocal coagulative necrosis were observed in both male and females dosed with 300 and 1,000/600 mg/kg/day. Macroscopic correlates that were noted in these animals were discoloration, enlargement and accentuated lobular pattern of the liver. These microscopic findings correlated with increased serum liver enzymes, total bilirubin, bile acids and decreased total protein, glucose and cholesterol at 300 and 1000/600mg/kg test substance. In the kidney vacuolar degeneration/necrosis and granular casts were observed in males and in females a high severity of tubular basophilia was observed at 1000/600 mg/kg. These renal findings were accompanied by higher kidney weights and increased serum urea and creatinine levels in males at this dose level. The hypertrophy/hyperplasia of the urothelium of the urinary bladder in male and female rats dosed with 300 or 1000/600 mg/kg, while present at a low incidence, demonstrated a dose-response relationship in severity and demonstrated no recovery.

Therefore, based upon the results presented in this report a No Observed Adverse Effect Level (NOAEL) for test substance of 100 mg/kg was established.

These histopathological observations in the liver, kidney and urinary bladder are reportable findings per EPA's TSCA 8(e) reporting criteria.

The final report is enclosed.

If you have any questions or would like any additional information, please contact 3M TSCA 8(e) Program Managers, Cher Sanchez at (651)733-7841, csanchez2@mmm.com or Jon Gerber at (651)-733-0226, jmgerber1@mmm.com

Sincerely,

Handwritten signature of Carol A. Ley (KCS) in cursive script.

Carol A. Ley, MD, MPH
Vice President and Corporate Medical Director, 3M Medical Department

Enclosure (1)

FINAL REPORT

Test Facility Study No. 511505

Sponsor Reference No.

3M MTDID Number 7831
3M Study ID Number 15-236

**Repeated Dose 90-Day Oral Toxicity Study with
MTDID 7831
by Daily Gavage in the Rat followed by a 28-Day Recovery Period**

SPONSOR:

3M Belgium BVBA
Canadastraat 11
B-2070 Zwijndrecht
Belgium

TEST FACILITY:

Charles River Laboratories Den Bosch B.V.
Hambakenwetering 7
5231 DD 's-Hertogenbosch
The Netherlands

Charles River Laboratories Den Bosch B.V.
Nistelrooisebaan 3
5374 RE Schaijk
The Netherlands

03 February 2017

TABLE OF CONTENTS

LIST OF APPENDICES	3
1. STATEMENT OF GLP COMPLIANCE.....	4
2. TEST FACILITY QUALITY ASSURANCE STATEMENT	5
3. SUMMARY	7
4. INTRODUCTION	11
4.1. Study Schedule.....	11
4.2. Purpose.....	11
4.3. Guidelines	12
4.4. Retention of Records and Materials.....	12
4.5. Responsible Personnel	13
4.5.1. Test Facility	13
4.5.2. Sponsor Representative.....	13
4.5.3. Data Collection	13
5. MATERIALS AND METHODS	14
5.1. Test Item	14
5.1.1. Test Item Information	14
5.1.2. Study Specific Item Information.....	14
5.2. Vehicle Information	14
5.3. Test Item Preparation.....	15
5.4. Chemical Analysis of Dose Preparations.....	15
5.5. Test System.....	16
5.6. Allocation.....	16
5.7. Animal Husbandry	17
5.8. Treatment	18
5.9. Observations	18
5.10. Clinical Laboratory Investigations.....	20
5.11. Pathology	22
5.11.1. Necropsy	22
5.11.2. Organ Weights	23
5.11.3. Histotechnology	23
5.11.4. Histopathology	23
5.12. Interpretation.....	24
5.13. List of Deviations.....	24
5.13.1. List of Study Plan Deviations	24
5.13.2. List of Standard Operating Procedures Deviations.....	25
6. ELECTRONIC SYSTEMS FOR DATA ACQUISITION.....	26
7. RESULTS.....	27
7.1. Analysis of Dose Preparations	27
7.2. Observations	27
7.2.1. Mortality	27
7.2.2. Clinical Signs	28
7.2.3. Functional Observations	28
7.2.4. Body Weights.....	28
7.2.5. Food Consumption.....	28
7.2.6. Ophthalmoscopic Examination.....	29
7.3. Clinical Laboratory Investigations.....	29

7.3.1.	Haematology	29
7.3.2.	Clinical Biochemistry	29
7.4.	Pathology	30
7.4.1.	Macroscopic Examination	30
7.4.2.	Organ Weights	31
7.4.3.	Microscopic Examination	32
8.	DISCUSSION AND CONCLUSION	39
9.	REFERENCES	42

LIST OF APPENDICES

APPENDIX 1 FIGURES AND SUMMARY TABLES

APPENDIX 2 INDIVIDUAL DATA TABLES

APPENDIX 3 PHASE REPORT FORMULATION ANALYSIS

APPENDIX 4 PHASE REPORT HISTOPATHOLOGY

1. STATEMENT OF GLP COMPLIANCE

Charles River Den Bosch, 's-Hertogenbosch, The Netherlands

All phases of this study performed by the test facility were conducted in compliance with:

- OECD Principles of Good Laboratory Practice.
- EC Council Directive 2004 (2004/10/EC, February 11, 2004, Official Journal of February 20, 2004).

Except for the following:

- The test item characterisation information supplied by the sponsor was produced under the sponsor's quality system.
- Trial formulation preparation (for optimal vehicle selection) had a non-GLP status but was carried out in the quality assured environment of Charles River Den Bosch GLP test facility.

The data generated and reported are considered to be valid.

Charles River Den Bosch

Signature:



Name: C.G.M. Beerens-Heijnen, PhD.

Title: Study Director

Date:

03 February 2017

2. TEST FACILITY QUALITY ASSURANCE STATEMENT

Charles River Den Bosch, 's-Hertogenbosch, The Netherlands.

Study title: Repeated dose 90-Day oral toxicity study with MTDID 7831 by daily gavage in the rat followed by a 28-Day recovery period

This report was inspected by the Charles River Den Bosch Quality Assurance Unit (QAU) according to the Standard Operating Procedure(s).

The reported method and procedures were found to describe those used and the report reflects the raw data.

During the on-site process inspections, procedures applicable to this type of study were inspected.

The dates of Quality Assurance inspections are given below.

Project 511505

Type of Inspections	Phase/Process	Start Inspection date	End Inspection date	Reporting date to TFM and SD*
Study	Study Plan	17-Feb-2016	17-Feb-2016	17-Feb-2016
	Exposure	25-Feb-2016	25-Feb-2016	26-Feb-2016
	Study Plan Amendment 01	30-Mar-2016	30-Mar-2016	30-Mar-2016
	Study Plan Amendment 02	31-Mar-2016	31-Mar-2016	31-Mar-2016
	Study Plan Amendment 03	25-May-2016	25-May-2016	25-May-2016
	Necropsy	31-May-2016	31-May-2016	31-May-2016
	Specimen processing	31-May-2016	31-May-2016	31-May-2016
	Specimen receipt	31-May-2016	31-May-2016	31-May-2016
	Specimen sampling	31-May-2016	31-May-2016	31-May-2016
	Study Plan Amendment 05	02-Jun-2016	02-Jun-2016	02-Jun-2016
	Study Plan Amendment 06	02-Jun-2016	02-Jun-2016	02-Jun-2016
	Report	17-Jan-2017	27-Jan-2017	27-Jan-2017
	Study Plan Amendment 04	17-Jan-2017	17-Jan-2017	17-Jan-2017
	Study Plan Amendment 07	17-Jan-2017	17-Jan-2017	17-Jan-2017
	Process	Test Substance Receipt Test Substance Handling	08-Feb-2016	29-Feb-2016
Test Substance Formulation Test Substance Handling Test Substance Handling		25-Feb-2016	15-Mar-2016	15-Mar-2016
Analytical and physical chemistry Test Substance Handling Exposure		01-Mar-2016	11-Mar-2016	14-Mar-2016

TEST FACILITY QUALITY ASSURANCE STATEMENT (continued)

Type of Inspections	Phase/Process	Start Inspection date	End Inspection date	Reporting date to TFM and SD*
	Necropsy Observations/Measurements Specimen Handling	01-Mar-2016	11-Mar-2016	14-Mar-2016
	Histology Specimen Handling	14-Mar-2016	22-Mar-2016	22-Mar-2016
	Animal Facilities Test Substance Handling Exposure Observations/Measurements Specimen Handling	04-Apr-2016	15-Apr-2016	15-Apr-2016
	Clinical pathology Observations/Measurements Specimen Handling	17-May-2016	31-May-2016	31-May-2016
	Histology Specimen Handling	06-Jun-2016	17-Jun-2016	17-Jun-2016
	Necropsy Observations/Measurements Specimen Handling	06-Jun-2016	17-Jun-2016	17-Jun-2016

*TFM=Test Facility Management SD = Study Director
The review of the final report was completed on the date of signing this QA statement.
The facility inspection program is conducted in accordance with Standard Operating Procedure.

Charles River Den Bosch

Signature: 

Name: **ALI BOUHUIJZEN, MSc.**
Manager Regulatory Compliance

Date: 03-Feb-2017

3. SUMMARY

Title

Repeated dose 90-day oral toxicity study with MTDID 7831 by daily gavage in the rat, followed by a 28-day recovery period.

Guidelines

The study was based on the following guidelines:

- EC No 440/2008, B.26 Repeated Dose (90 days) Toxicity (oral), 2008.
- OECD 408, Repeated Dose 90-day Oral Toxicity Study in Rodents, 1998.
- OPPTS 870.3100, EPA 712-C-98-199, 90-Day Oral Toxicity in Rodents, 1998.
- Japanese Chemical Substances Control Law 1973, Notification of Mar. 31 2011 by MHLW (0331 No.7), METI (H23.03.29 SeiKyoku No. 5) and MOE (No. 110331009).

Rationale for dose levels

Based on the results of a 14-day range finding study (Test Facility Study No. 511506), the dose levels for this 90-day oral gavage study were selected to be 0, 100, 300 and 1000 mg/kg. Animals at the initial dose of 1000 mg/kg were not dosed from Day 31 up to and including Day 34 based upon adverse health effects observed in both male and females. Treatment of Group 4 was subsequently recommenced on Day 35 (and onwards) at a dose level of 600 mg/kg.

Study outline

The test item, formulated in Arachis oil, was administered daily for 88-92 days (males) or 97 days (females) by oral gavage to SPF-bred Wistar rats. One control group and three treated groups were tested, each consisting of 10 males and 10 females. An extra 5 animals per sex in the control and high dose group were allowed 28 days of recovery.

Evaluated parameters

Chemical analyses of formulations were conducted three times during the study to assess accuracy, homogeneity and stability over 6 hours and over 8 days.

The following animal parameters were evaluated: daily clinical signs of toxicity; functional observation tests in Week 12-13; weekly body weight and food consumption; ophthalmoscopy at pretest and in Week 13; clinical pathology (at end of treatment and end of recovery period) and macroscopy at termination; organ weights and histopathology on selected tissues.

Results

Chemical analyses confirmed that formulations of test item in arachis oil were prepared accurately and homogeneously, and were stable when stored at room temperature under normal laboratory light conditions for at least 6 hours and in a refrigerator protected from light for at least 8 days.

There were twelve premature/unexpected decedents in the study:

- Five males and two females in the 1000/600 mg/kg MTDID 7831 group were euthanized for ethical reasons during the treatment period. These animals demonstrated body weight loss and/or moribundity prior to death. The main cause of morbidity was hepatocellular necrosis of the centrilobular area of the liver and/or degenerative findings in the kidney.

- Single females at 100, 300 and 1000 mg/kg were found dead during treatment period. Although one female dosed with 100 mg/kg and one female dosed with 300 mg/kg test item demonstrated body weight losses, no cause of death could be determined for all three animals from the clinical and microscopic pathology evaluations.
- One male and one female at 1000 mg/kg were found dead during the treatment period. Cause of death for these animals was determined to be a gavage accident. No body weight loss was noted and rales, swelling of abdomen and lean appearance were noted among these animals on the days prior to death.

Notable clinical signs of toxicity noted in surviving males and females dosed with 1000/600 mg/kg MTDID 7831 were rales, swelling of the abdomen, hunched posture, labored or deep respiration and lean appearance at a higher incidence when compared to control group animals. At 300 mg/kg rales and swelling of abdomen were also noted at a higher incidence when compared to the control group.

Male rats dosed with 1000/600 mg/kg MTDID 7831 began demonstrating a statistically significant reduction in mean body weight when compared with the control group on Day 8 which persisted throughout the dosing period with the mean body weight being 15% less than the control group by Day 91 of the study. Males dosed with 300 mg/kg demonstrated statistically significant reductions in mean body weights on Days 57 through 71 (-8 to -9%) and on Day 91 (-8%) while males dosed with 100 mg/kg demonstrated no differences in body weight over the course of the study. Female rats dosed with 1000/600 mg/kg demonstrated statistically significant reductions in mean body weight on test days 33 and 34 (-6 to -7%) when compared to the control group; however, these slight reductions were not considered adverse due to the sporadic and minimal nature of the change. No treatment related body weight changes were noted in females at 100 mg/kg and females at 300 mg/kg. Following the 4-week recovery period, males dosed with 600/1000 mg/kg no longer demonstrated significant differences in body weight when compared to the control group, indicating reversibility of this effect.

Minimal effects were observed in the food consumption data in males, with animals in the 600/1000 mg/kg group demonstrating a statistical reduction on Days 1-8 and an elevation on Days 85-91. In conjunction with the body weight data, the relative food consumption in male rats dosed with 600/1000 mg/kg were statistically reduced on Days 1-8 and elevated on Days 8-15, 29-57, 64-78 and 85-91. No alterations were in food consumption parameters were noted in males dosed with 100 or 300 mg/kg MTDID 7831. Female rats dosed with 600/1000 mg/kg demonstrated a statistically reduce food consumption on Days 1-8 and a statistical increased on Days 22-36, 43-57 and 78-85 which correlated with a significant reduction in relative food consumption on Days 1-8 and increased relative food consumption on Days 8-15, 22-57 and 67-91. Sporadic statistical increases in absolute and relative food consumption were noted in females from the 300 mg/kg dose group which were considered minimal in nature and non-adverse; females dosed with 100 mg/kg demonstrated no changes in food consumption parameters.

No effects were seen in the functional observations nor in the ophthalmoscopy.

Postmortem examination of the animals revealed MTDID 7831-related findings in the liver (hepatocellular necrosis of the centrilobular area and focal/multifocal coagulative necrosis and hepatocellular hypertrophy), kidney (vacuolar degeneration/necrosis and the granular casts in males and tubular basophilia in females), urinary bladder (hypertrophy/hyperplasia of the urothelium), thyroid gland (follicular cell hypertrophy), sternal bone marrow (increased number of adipocytes), stomach (lymphogranulocytic inflammation, hyperplasia of squamous

cells, erosions/ulcerations and edema) in both male and female rats as well as changes in the thymus (lymphocytolysis), adrenal gland (vacuolation of the zona glomerulosa) and spleen (extramedullary hematopoiesis) of females.

In the liver the hepatocellular necrosis of the centrilobular area and focal/multifocal coagulative necrosis were degenerative findings and therefore considered adverse in nature. The brown pigmentation of the liver in some recovery animals at 1000/600 mg/kg was probably digested remnants of necrotic cellular material, resulting from the hepatocellular necrosis observed at the end of the treatment period. The minimal or slight hepatocellular hypertrophy of the liver observed in the males and females at 100 mg/kg, in the absence of any degenerative findings or changes in absolute liver weight was considered to be a non-adverse finding (Kerlin et. al., 2016).

Macroscopic correlates that were noted in these animals were discolouration, enlargement and accentuated lobular pattern of the liver. These microscopic findings correlated with increased serum liver enzymes, total bilirubine, bile acids and decreased total protein, glucose and cholesterol at 300 and 1000/600mg/kg MTDID 7831.

In the kidney the vacuolar degeneration/necrosis and the granular casts recorded in males and the high severity of tubular basophilia observed in females were degenerative in nature and therefore considered to be adverse microscopic findings at 1000/600 mg/kg. These renal findings were accompanied by higher kidney weights and increased serum urea and creatinine levels in males at this dose level.

The hypertrophy/hyperplasia of the urothelium of the urinary bladder in male and female rats dosed with 300 or 1000/600 mg/kg, were present at a low incidence, but demonstrated a dose-response relationship in severity and demonstrated no recovery and was, therefore, considered to be an adverse microscopic finding (Sahota et. al., 2013).

Thyroid gland hypertrophy in rats is usually an adaptive response to induction of hepatic enzymes. This results in increase in the hepatic/biliary clearance of T3/T4 leading to increase in TSH and compensatory follicular cell hypertrophy and/or hyperplasia (Wu and Farrelly, 2006) and is therefore, considered to be a secondary result of MTDID 7831 hepatic toxicity.

The findings reported in the sternal bone marrow, as well as thymus and adrenal observations in the female rats were considered to be spontaneous background findings as they demonstrated no dose-response relationship, were not accompanied by any degenerative findings and showed complete or partial recovery. Therefore these findings are considered to be non-adverse (Kerlin et. al., 2016).

Macroscopic and microscopic findings were recorded for the stomach of all dose groups including controls. There was no dose response relationship and therefore these findings were considered to be due to the gavage treatment procedure with Arachis Oil as vehicle and not related to the treatment with MTDID 7831.

The differences in severity of extramedullary hematopoiesis noticed in the spleen of females of all test item-treated dose groups compared to the control females at the end of the treatment period were considered to be related to the blood sampling procedure: Blood samples were collected from the females of the Main Control group after 92 days of treatment and these animals (except animal 51) were subsequently necropsied after 96 days of treatment on Day 97. No blood samples were collected of the remaining females on Day 92. The differences in the red blood cell parameters (decreased red blood cell counts and increased reticulocytes), increased organ weight of the spleen and microscopic finding

(increased extramedullary hematopoiesis) in the spleen of the Main Control females after the treatment period, represent a physiological response after the blood sampling procedure and these differences between the control and test item treated groups are therefore regarded to be unrelated to the test item.

Conclusion

Adverse MTDID 7831-related morphologic alterations in Wistar (Han) rats subjected to 90-Day oral gavage toxicity study, followed by a 4-week recovery period up to a dose of 1000/600 mg/kg were present in liver (hepatocellular necrosis of the centrilobular area, coagulative necrosis), kidney (vacuolar degeneration/necrosis, granular casts, increased severity of tubular basophilia) and urinary bladder (hypertrophy/hyperplasia of the urothelium) of both sexes starting at 300 mg/kg. These microscopic histopathology findings correlated with concurrent and expected changes in serum clinical chemistry parameters and the severity of toxicity also reflected dose-related reductions in animal body weights over the dosing phase of this study.

There were no adverse test item-related morphologic alterations at 100 mg/kg. The death of one female at 100 mg/kg was considered not test item related in the absence of, a cause of death, other mortalities in this group and of any other adverse findings or comparable morphological changes at this dose level.

Therefore, based upon the results presented in this report a No Observed Adverse Effect Level (NOAEL) for MTDID 7831 of 100 mg/kg was established.

4. INTRODUCTION

Due to the acquisition of WIL Research by Charles River, the name of the WIL Research facility in Den Bosch, has been changed to Charles River Laboratories Den Bosch BV, Hambakenwetering 7, 5231 DD Den Bosch, The Netherlands. Study documents may contain both names and both names are considered equivalent and may be used as the name of WIL Research transitions to Charles River.

4.1. Study Schedule

Experimental starting date	:	18 February 2016 (allocation)
Start treatment	:	25 February 2016
Start Recovery	:	26 May 2016 (males) 31 May 2016 (females)
Clinical Pathology	:	26 May 2016 (All males) 27 May 2016 (Females Group 1) 31 May 2016 (All females) 23 June 2016 (All Recovery group males) 28 June 2016 (All Recovery group females)
Necropsy	:	26 May 2016 (All Main group males) 31 May 2016 (All Main group females) ¹ 23 June 2016 (All Recovery group males) 28 June 2016 (All Recovery group females)
Experimental completion date	:	28 June 2016 (end of in-life phase)

Test item formulations, all animal activities and necropsy were performed at the Schaijk location, all other activities were performed at the 's-Hertogenbosch location.

4.2. Purpose

The nature and purpose of this toxicity study was to assess the toxic potential of the test item when administered to rats by daily oral gavage for a period of 13 weeks, followed by a 28-day recovery period. A No Observed Adverse Effect Level (NOAEL) was evaluated.

This study should provide a rational basis for toxicological risk assessment in man. The oral route was selected as it is a possible route of human exposure during manufacture, handling or use of the test item.

¹ With the exception of Female no. 51 (Group 1); necropsy performed on 27 May 2016

4.3. Guidelines

This type of study plan was reviewed and agreed by the Laboratory Animal Welfare Officer and the Ethical Committee (DEC 14-59) as required by the Dutch Act on Animal Experimentation (February 1997).

The study procedures described in this report were in compliance with the following guidelines:

1. Commission regulation (EC) No 440/2008 Part B: Methods for the Determination of Toxicity and other Health Effects; B.26: "Sub-chronic Oral Toxicity Test: Repeated dose 90-day toxicity study in rodents". Official Journal of the European Union No. L142, May 2008.
2. OECD "Guidelines for Testing of Chemicals", Section 4, Health Effects, No. 408, "Repeated Dose 90-day Oral Toxicity Study in Rodents", Paris Cedex, September 1998.
3. United States Environmental Protection Agency Prevention, Pesticides and Toxic Substances (7101) EPA 712-C-98-199 "Health Effects Test Guidelines" OPPTS 870.3100 "90-Day Oral Toxicity in Rodents", August 1998.
4. Japanese Chemical Substances Control Law 1973, Notification of Mar. 31 2011 by MHLW (0331 No.7), METI (H23.03.29 SeiKyoku No. 5) and MOE (No. 110331009).

4.4. Retention of Records and Materials

Records and material pertaining to the study, which include study plan and amendments, raw data, specimens, except perishable specimens, and a copy of the final report will be retained in the archives of the test facility for a minimum of 5 years after the finalization of the report. The final report will be sent to the Sponsor. After this period, the sponsor will be contacted to determine how the records and materials should be handled. The test facility will retain information concerning decisions made.

Perishable specimens (e.g. requiring refrigeration or freezing) will be discarded following evaluation in the study without further notice to the study sponsor.

A sample of the test item will be retained until expiry date or applicable retest date. After this period the sample(s) will be destroyed.

4.5. Responsible Personnel

4.5.1. Test Facility

Study Director	C.G.M. Beerens-Heijnen, PhD. Email: chantal.beerens@crl.com
Coordinating Biotechnician	M.M.A. Rijkers (Charles River Den Bosch)
Clinical Pathology	C.W. Koot, BSc. (Charles River Den Bosch)
Analytical Chemistry	M.C.J. Brekelmans. MSc. (Principal Scientist, Charles River Den Bosch)
Necropsy	M. Schelling (Charles River Den Bosch)
Histotechnology	W. Verhoef (Charles River Den Bosch)
Histopathology	J.H. van den Brink – Knol, DVM, CRP/TP (Principal Scientist, Charles River Den Bosch)
QA	C.J. Mitchell, BSc. (Charles River Den Bosch) Email: christine.mitchell@crl.com
Test facility Management Representative	H.H. Emmen, MSc. (Charles River Den Bosch) Email: harry.emmen@crl.com

4.5.2. Sponsor Representative

Study Monitor Michael DeLorme

4.5.3. Data Collection

Three Test Facility Study numbers were used to collect online data. All data are reported under Test Facility Study No. 511505.

Test Facility Study No.	Online data
514129	Clinical signs, body weights and food consumption for females from Day 93 up to scheduled day of necropsy
511765	Clinical signs in arena observations
511505	All other data

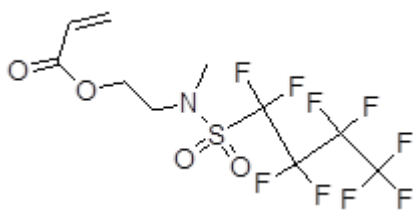
5. MATERIALS AND METHODS

5.1. Test Item

5.1.1. Test Item Information

Test Item	203613/B
Identification	MTDID 7831
Appearance	Off white to white waxy solid
Batch	Lot 40265 / lot 40267 20/80 ratio
Purity/Composition	95.6 w%
Test item storage	At room temperature
Stable under storage conditions until	01 May 2017 (expiry date)

5.1.2. Study Specific Item Information

Purity/composition	No correction factor required
correction factor	
Stability at higher temperatures	Yes, maximum temperature: approximately 55°C, maximum duration: >60 minutes
Chemical name (IUPAC), synonym or trade name	2-Propenoic Acid, 2-[Methyl[(Nonafluorobutyl)Sulfonyl]Amino]Ethyl Ester
CAS Number	67584-55-8
Molecular structure	

Molecular formula	C ₁₀ F ₉ H ₁₀ SO ₄ N
Molecular weight	411

Analysis of stability, homogeneity and concentration of the test item under test conditions were performed as part of this study.

5.2. Vehicle Information

Vehicle	Arachis Oil, Specific gravity 0.885 (Fagron, Capelle aan de IJssel, The Netherlands).
Rationale for vehicle	Based on trial formulations performed at Charles River Den Bosch and on information from the sponsor.

5.3. Test Item Preparation

Method of formulation

Day 1-64 Formulations (w/w) were prepared daily within 6 hours prior to dosing.

Day 65- 91²/96³ Formulations (w/w) were prepared daily within 6 hours up to 4 days prior to dosing,

Formulations (w/w) were homogenized to visually acceptable levels. The formulations were heated to a maximum of 50±5°C for a maximum of 60 minutes to obtain visual homogeneity. Formulations were allowed to cool down below 40°C before dosing. No correction was made for purity/composition of the test item.

Storage conditions At ambient temperature at the day of dosing or in the refrigerator in the dark (when not dosed on day of preparation).

Appearance of preparation Clear liquid (Group 2)
Cloudy liquid (Groups 3 and 4).

5.4. Chemical Analysis of Dose Preparations

Samples of formulations were analyzed for homogeneity (highest and lowest concentration) and accuracy of preparation (all concentrations, in Weeks 1, 6 and 13). Stability in vehicle over 6 hours at room temperature under normal laboratory light conditions and over 8 days in the refrigerator under protection from light were also determined (highest and lowest concentration, in Week 1).

The accuracy of preparation was considered acceptable if the mean measured concentrations were 90-110% of the target concentration for solutions, or 85-115% for suspensions. Homogeneity was demonstrated if the coefficient of variation was ≤ 10%. Formulations were considered stable if the relative difference before and after storage was maximally 10%.

² Males

³ Females

5.5. Test System

Test system	Rat: Crl:WI(Han) (outbred, SPF-Quality).
Rationale	Recognized by international guidelines as the recommended test system (e.g. EPA, FDA, OECD and EC).
Source	Charles River Deutschland, Sulzfeld, Germany.
Total number of animals	50 males, 50 females. Females were nulliparous and non-pregnant).
Age at start of treatment	Approximately 6 weeks.
Identification	Earmark and tattoo.
Randomization	By computer-generated random algorithm according to body weight, with all animals within $\pm 20\%$ of the sex mean.
Acclimatization period	At least 5 days before the start of treatment under laboratory conditions.
Health inspection	Upon receipt of the animals.

5.6. Allocation

Treatment phase:

Group	Dose level ¹ mg/kg	Dose volume mL/kg	Number of animals		Animal numbers	
			Males	Females	Males	Females
1 Main	0 (Arachis oil)	5	10	10	1-10	51-60
1 Recovery	0 (Arachis oil)	5	5	5	11-15	61-65
2 Main	100	5	10	10	16-25	66-75
3 Main	300	5	10	10	26-35	76-85
4 Main ²	1000 – 600	5	10	10	36-45	86-95
4 Recovery ²	1000 – 600	5	5	5	45-50	96-100

¹ The dose levels were selected on the basis of a 14-day dose range finding study (Test Facility Study No.511506).

² Group 4 was not dosed from Day 31 onwards based on health status of the animals. The animals were weighed on Day 33 to evaluate if dosing could be re-started. Treatment of Group 4 was recommenced on Day 35 (and onwards) at a dose level of 600 mg/kg.

Recovery phase:

Due to mortality of Group 4 animals the animals of Group 4 were re-allocated to have sufficient information at the end of recovery period. The animals remained in their home cage.

Group	Dose level mg/kg	Dose volume mL/kg	Number of animals		Animal numbers	
			Males	Females	Males	Females
1 Main	0 (Arachis oil)	5	10	10	1-10	51-60
1 Recovery	0 (Arachis oil)	5	5	5	11-15	61-65
4 Main ¹	1000 – 600	5	7	8	36-42	86-93
4 Recovery ¹	1000 – 600	5	8	7	43-50	94-100

¹ Group 4 was not dosed from Day 31 onwards based on health status of the animals. The animals were weighed on Day 33 to evaluate if dosing could be re-started. Treatment of Group 4 was recommenced on Day 35 (and onwards) at a dose level of 600 mg/kg.

5.7. Animal Husbandry

Room number	MR1218 (MR1221B for motor activity measurements).
Conditions	Environmental controls for the animal room are set to maintain 18 to 24°C, a relative humidity of 40 to 70% and at least 10 air changes/hour, and a 12-hour light/12-hour dark cycle (actual daily mean ranges: 18-24°C and 25-70%). Any variations to these conditions were evaluated and maintained in the raw data.
Accommodation	Group housing of 5 animals per sex in Macrolon cages (MIV type, height 18 cm) with sterilized sawdust as bedding material (Lignocel S 8-15, JRS - J.Rettenmaier & Söhne GmbH + CO. KG, Rosenberg, Germany) and paper as cage-enrichment (Enviro-dri, Wm. Lilico & Son (Wonham Mill Ltd), Surrey, United Kingdom). During locomotor activity monitoring, animals were housed individually in a Hi-temp polycarbonate cage (Ancare corp., USA; dimensions: 48.3 x 26.7 x 20.3 cm) without cage-enrichment, bedding material, food and water.
Diet	Free access to pelleted rodent diet (SM R/M-Z from SSNIFF® Spezialdiäten GmbH, Soest, Germany).
Water	Free access to tap water.

Diet, water, bedding and cage enrichment evaluation for contaminants and/or nutrients was performed according to facility standard procedures. There were no findings that could interfere with the study.

5.8. Treatment

Method	Oral gavage, using a plastic feeding tube. Formulations were placed on a magnetic stirrer during dosing. A dose control system (DCS) was used to verify the dosing procedure.
Frequency	Once daily, 7 days per week, approximately the same time each day with a maximum of 6 hours difference between the earliest and latest dose.
Dose volume	5 mL/kg body weight. Actual dose volumes were calculated weekly according to the latest body weight.
Duration of treatment	At least 13 weeks. Main animals were dosed up to the day prior to necropsy, and Recovery animals were dosed up to the day prior to start of the recovery period. Group 4 was not dosed from Day 31 onwards based on health status of the animals. The animals were weighed on Day 33 to evaluate if dosing could be re-started. Treatment of Group 4 was recommenced on Day 35 (and onwards) at a dose level of 600 mg/kg.
Duration of recovery	At least 28 days.

5.9. Observations

Mortality / Viability	At least twice daily. Animals showing pain, distress or discomfort, which was considered not transient in nature or was likely to become more severe, were sacrificed for humane reasons based on OECD guidance document on humane endpoints (ENV/JM/MONO/ 2000/7). The time of death was recorded as precisely as possible.
Clinical signs	At least once daily from start of treatment onwards, detailed clinical observations were made in all animals after dosing (no peak effect of occurrence of clinical signs was observed in the dose range finding study (Test Facility Study No. 511506)). Once prior to start of treatment and at weekly intervals, this was also performed outside the home cage in a standard arena. The time of onset, grade and duration of any observed signs were recorded. Signs were graded for severity and the maximum grade was predefined at 3 or 4. Grades were coded as slight (grade 1), moderate (grade 2), severe (grade 3) and very severe (grade 4). For certain signs, only its presence (grade 1) or absence (grade 0) was scored. In the data tables, the scored grades are reported, as well as the percentage of animals affected in summary tables.

Functional Observations During Week 12-13 of treatment, the following tests were performed in all 5 Recovery Group 1 animals/sex and 5 Group 4 animals/sex (i.e. the surviving recovery animals completed with the first Main animals up to a total of 5 animals/sex) and the first 5 animals/sex/group for Group 2 and 3. These test were performed after dosing at no specific time point, but within a similar time period after dosing for the respective animals (based on the absence of a peak effect in occurrence of clinical signs in the dose range finding study (Test Facility Study No. 511506)) (abbreviations mentioned in the respective tables indicated between brackets):

- hearing ability (HEARING), pupillary reflex (PUPIL L/R), static righting reflex (STATIC R) (Score 0 = normal/present, score 1 = abnormal/absent).
- fore- and hind-limb grip strength, recorded as the mean of three measurements per animal (Series M4-10, Mark-10 Corporation, J.J. Bos, Gouda, The Netherlands).
- locomotor activity (recording period: 1-hour under normal laboratory light conditions, using a computerized monitoring system, Kinder Scientific LLC, Poway, USA). Total movements and ambulations are reported. Ambulations represent movements characterized by a relocation of the entire body position like walking, whereas total movements represent all movements made by the animals, including ambulations but also smaller or more fine movements like grooming, weaving or movements of the head.

Since the abovementioned measurements did not reveal treatment-related effects, the functional observation tests were not performed at the end of the recovery phase.

Ophthalmoscopic
Examination (direct)

Following instillation of tropicamide solution (5 mg/mL, Minims[®] Tropicamide 0.5% w/v, Bausch&Lomb Pharma, Brussel, Belgium) both eyes were examined by means of an ophthalmoscope (Heine Beta 200S):

at pretest : All animals
at Week 13 : Groups 1 and 4 (Main group animals)

Since no treatment-related ophthalmologic findings were noted in Week 13, the eyes of the rats of Groups 2 and 3 were not examined, and no ophthalmoscopic examination was performed at the end of the recovery period.

Body weights

Weekly.

Food consumption

Weekly.

Water consumption

Subjective appraisal was maintained during the study, but no quantitative investigation introduced as no effect was suspected.

5.10. Clinical Laboratory Investigations

Clinical laboratory investigations were conducted at the end of treatment (Main and Recovery animals) and at the end of recovery (Recovery animals).

Blood samples were collected under anaesthesia using isoflurane (Abbott B.V., Hoofddorp, The Netherlands), between 7.00 and 10.30 a.m. The animals were deprived of food overnight (with a maximum of 24 hours) before blood sampling, but water was available. Blood samples of the main control females (no 52-60)⁴ were collected as part of the necropsy procedure.

Blood samples were drawn from the retro-orbital sinus of all rats/sex/group at the end of treatment and recovery period, and collected into

- tubes prepared with K3-EDTA for haematological parameters (0.5 mL),
- tubes prepared with citrate for clotting tests (0.45 mL)
- tubes treated with Li-heparin for clinical biochemistry parameters (0.5 mL)
- serum tubes (Greiner Bio-One GmbH, Kremsmünster, Austria) for determination of bile acids (0.25 mL)
- serum tubes (Greiner Bio-One GmbH, Kremsmünster, Austria) for further analysis under responsibility of the Sponsor and not included in this study (0.4 mL). After clotting and centrifugation, serum was stored in a labelled polypropylene tube (Greiner Bio-One GmbH, Frickenhausen, Germany) at $\leq -75^{\circ}\text{C}$ until shipment on dry ice to the Sponsor for further analysis under responsibility of the Sponsor and not included in this study (Ryan Krisko, 3M Center, US)

The following parameters were determined:

Parameter	Abbreviation	Unit
<i>Haematology</i> ^a		
White blood cells	WBC	10 ⁹ /L
Differential leucocyte count neutrophils, lymphocytes, monocytes, eosinophils, basophils		%WBC
Red blood cells		10 ¹² /L
Reticulocytes		%RBC
Red blood cell distribution width	RDW	%
Haemoglobin		mmol/L
Haematocrit		L/L
Mean corpuscular volume	MCV	fL
Mean corpuscular haemoglobin	MCH	fmol
Mean corpuscular haemoglobin concentration	MCHC	mmol/L
Platelets		10 ⁹ /L
<i>Clotting Potential</i> ^b		
Prothrombin time	PT	s
Activated Partial thromboplastin time	APTT	s

^a Instrumentation: ADVIA® 2120i (Siemens Healthcare Diagnostics B.V., Den Haag, The Netherlands).

^b Instrumentation: STA Compact (Diagnostica Stago S.A.S., Asnières, France).

⁴ Due to the non-fasted blood sampling at 27-May 2016 (see deviation), the control animals will be sampled as part of the necropsy procedure.

Parameter	Abbreviation	Unit
<i>Clinical Biochemistry</i> [°]		
Alanine aminotransferase	ALAT	U/L
Aspartate aminotransferase	ASAT	U/L
Alkaline phosphatase	ALP	U/L
Total Protein		g/L
Albumin		g/L
Total Bilirubin		µmol/L
Urea		mmol/L
Creatinine		µmol/L
Glucose		mmol/L
Cholesterol		mmol/L
Sodium		mmol/L
Potassium		mmol/L
Chloride		mmol/L
Calcium		mmol/L
Inorganic Phosphate	Inorg. Phos	mmol/L
Bile acids		µmol/L

[°] Instrumentation: Olympus AU400 (Beckman Coulter Nederland B.V., Woerden, The Netherlands).

5.11. Pathology

5.11.1. Necropsy

Animals surviving to the scheduled day of necropsy and all moribund animals were deeply anaesthetized using isoflurane (Abbott B.V., Hoofddorp, The Netherlands) and subsequently exsanguinated and subjected to a full *post mortem* examination. Animals were deprived of food overnight (with a maximum of 24 hours) prior to scheduled necropsy.

Blood samples of main control females were collected immediately prior to sacrifice as part of the necropsy procedure, based on the health status of these animals.

All animals assigned to the study were necropsied and descriptions of all macroscopic abnormalities recorded. Rats found dead were subjected to a full *post mortem* examination as soon as possible after death and always within 24 hours. Samples of the following tissues and organs were collected from all animals at necropsy and fixed in 10% buffered formalin (neutral phosphate buffered 4% formaldehyde solution, Klinipath, Duiven, The Netherlands):

Identification marks: not processed	Ovaries
Adrenal glands	Pancreas
Aorta	Peyer's patches [jejunum, ileum] if detectable
Brain [cerebellum, mid-brain, cortex] (7 levels)	Pituitary gland
Caecum	(Preputial gland)
Cervix (Clitoral gland)	Prostate gland
Colon	Rectum
Duodenum	Salivary glands - mandibular, sublingual
Epididymides *	Sciatic nerve
Eyes with optic nerve [if detectable] and Harderian gland *	Seminal vesicles (Skeletal muscle)
Female mammary gland area (Femur including joint)	Skin
Heart	Spinal cord -cervical, midthoracic, lumbar
Ileum	Spleen
Jejunum	Sternum with bone marrow
Kidneys	Stomach
Larynx (Lacrimal gland, exorbital)	Testes *
Liver	Thymus
Lung, infused with formalin	Thyroid including parathyroid [if detectable] (Tongue)
Lymph nodes - mandibular, mesenteric (Nasopharynx)	Trachea
Oesophagus	Urinary bladder
	Uterus
	Vagina
	All gross lesions

* Fixed in modified Davidson's solution, prepared at Charles River Den Bosch using Formaldehyde 37-40%, Ethanol, Acetic acid - glacial (all Merck, Darmstadt, Germany) and Milli-Ro water (Millipore Corporation, Bedford, USA). Tissues were transferred to formalin after fixation for at least 24 hours.

Tissues/organs mentioned in parentheses were not examined by the pathologist, since no signs of toxicity were noted at macroscopic examination.

5.11.2. Organ Weights

The following organ weights and terminal body weight were recorded from the surviving animals on the scheduled day of necropsy:

Adrenal glands	Spleen
Brain	Testes
Epididymides	Thymus
Heart	Uterus (including cervix)
Kidneys	Prostate
Liver	Seminal vesicles including coagulating glands
Ovaries	Thyroid including parathyroid

After weighing of the liver, a small piece of left lateral lobe of the liver (approximately 0.5 g) was placed in labeled bags, frozen in liquid nitrogen, stored in freezer (at $\leq -75^{\circ}\text{C}$) and shipped on dry ice to the Sponsor (Ryan Krisko, 3M Center, US). Further analysis will be performed under responsibility of the Sponsor and will not be included in this study.

5.11.3. Histotechnology

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

5.11.4. Histopathology

The following slides were examined by a pathologist:

- all tissues collected at the scheduled sacrifice from all Main group 1 and 4 animals,
- all tissues from all animals of all dose groups which died spontaneously or were terminated in extremis,
- Thymus, spleen and adrenal glands at the scheduled sacrifice from all Main group 2 and 3 and all Recovery Group 1 and 4 females,
- Thyroid gland, stomach, liver, kidneys, urinary bladder and bone marrow (sternum) at the scheduled sacrifice from all Main group 2 and 3 and all Recovery Group 1 and 4 animals,
- all gross lesions.

All abnormalities were described and included in the report. An attempt was made to correlate gross observations with microscopic findings.

Histopathology was subjected to a peer review.

5.12. Interpretation

The following statistical methods were used to analyze the data:

- If the variables could be assumed to follow a normal distribution, the Dunnett-test (Ref. 1; many-to-one t-test) based on a pooled variance estimate was applied for the comparison of the treated groups and the control groups for each sex.
- The Steel-test (Ref. 2; many-to-one rank test) was applied if the data could not be assumed to follow a normal distribution.
- The Fisher Exact-test (Ref. 3) was applied to frequency data.
- The Kruskal-Wallis nonparametric ANOVA test (Ref. 4) was applied to motor activity data to determine intergroup differences.

All tests were two-sided and in all cases $p < 0.05$ was accepted as the lowest level of significance. Group means were calculated for continuous data and medians were calculated for discrete data (scores) in the summary tables. Test statistics were calculated on the basis of exact values for means and pooled variances. Individual values, means and standard deviations may have been rounded off before printing. Therefore, two groups may display the same printed means for a given parameter, yet display different test statistics values.

5.13. List of Deviations

5.13.1. List of Study Plan Deviations

1. Temporary deviations from the daily mean relative humidity occurred on two days.
Evaluation: Laboratory historical data do not indicate an effect of the deviations.
2. On several days the DCS system could not be used for verification or the dosing procedures.
Evaluation: As DCS is an additional tool to check the dosing procedure and the other checking procedures (according to SOPs) remain intact, it was therefore concluded that the right formulations were dosed.
3. Main females were not deprived of food before the intended necropsy date. Blood was sampled from 10 control females (no. 51-60) and one of these animals was necropsied (no. 51).
Evaluation: Necropsy was cancelled and treatment of females was extended with 5 days until rescheduled necropsy. The non-fasted blood samples were analyzed and kept in the raw data but were not reported. At the rescheduled necropsy the blood was sampled in fasted rats. The slightly longer dosing period was considered not to affect the study integrity. The repeat of blood sampling within 5 days did influence the red blood cell parameters (decreased red blood cell counts and increased reticulocytes), organ weight of the spleen and microscopic finding (increased extramedullary hematopoiesis) in the spleen of the Main Control females. These effects were considered to represent a physiological response after the blood sampling procedure and these differences between the control and test item treated groups are therefore regarded to be unrelated to the test item. Sufficient data was available to evaluate the test item treated groups.

4. No food consumption was determined for the females during the second week of recovery.
Evaluation: Sufficient data is available for evaluation of the food consumption during the 28-day recovery period
5. On Day 3 of the Recovery period of females, body weights were determined from female nos. 63, 64, 65, 94 and 95. On Day 18 of the Recovery period of males, body weights were determined from all males.
Evaluation: The additional information did not influence the outcome of the study.
6. On Day 22 of treatment arena observations were performed twice (once before dosing and once after dosing).
Evaluation: Sufficient information if available for evaluation of the results. Incidental additional handling did not affect the outcome of the study.
7. Inadvertently, a few tissues were not available for histopathology. Reasons for missing a few tissues included that these tissues were not discernable at necropsy or trimming, or were erroneously not collected at necropsy. Missing tissues are listed in raw data and pathology report.
Evaluation: Sufficient data was available for evaluation.
8. On three occasions clinical signs could not immediately be recorded electronically due to a technical error.
Evaluation: The raw data was recorded manually and recorded electronically when the system was available again. The original raw data of one of these time points was not available therefore this observation was excluded from interpretation and will not be reported. Sufficient data was available for evaluation.

5.13.2. List of Standard Operating Procedures Deviations

Any deviations from standard operating procedures were evaluated and filed in the study file. There were no deviations from standard operating procedures that affected the integrity of the study.

6. ELECTRONIC SYSTEMS FOR DATA ACQUISITION

Observations/measurements in the study were recorded electronically using the following programme(s):

- REES Centron Environmental Monitoring system version SQL 2.0 (REES Scientific, Trenton, NJ, USA): Environmental monitoring.
- TOXDATA version 8.0 (WIL Research Europe B.V., The Netherlands): Mortality / Clinical signs (except on Days 12 and 21 of the main study) / Functional Observations (hearing ability, pupillary reflex and static righting reflex) / Body weights (Body weight for health monitoring purposes may be recorded manually) / Food consumption / Organ weights.
- MotorMonitor II version 15251-16GLP_(Kinder Scientific LLC, Poway, USA): Motor activity measurement.
- ADVIA® 2120i Hematology System Version V.3.1.8.0.MS (Siemens Healthcare Diagnostics B.V., Den Haag, The Netherlands): Haematology.
- STA Compact® version 107.07 (Diagnostica Stago S.A.S., Asnières, France): Clotting parameters.
- AU400 version 9.1 (Beckman Coulter Nederland B.V., Woerden, The Netherlands): Clinical biochemistry.
- Pathdata version 6.2e2 (Pathology Data Systems, Basel, Switzerland): Histopathology
- DCS Client application version 1.0.6, Server application version 1.0.6. and DCS Smart client version 1.0.6 (OCS Consulting , 's-Hertogenbosch, The Netherlands): dosing control.

Any upgrades were approved by the Study Director (or Principal Scientist/Investigator) in the study files.

7. RESULTS

For further detail on summary data, see [APPENDIX 1](#) and on individual data, see [APPENDIX 2](#).

7.1. Analysis of Dose Preparations

Accuracy of preparation

The concentrations analysed in the formulations of Group 2, Group 3 and Group 4 were in agreement with target concentrations (i.e. mean accuracies between 85% and 115%).

No test item was detected in the Group 1 formulations.

Homogeneity

The formulations of Group 2 and Group 4 were homogeneous (i.e. coefficient of variation $\leq 10\%$).

Stability

Group 2 and Group 4 formulations were stable when stored at room temperature under normal laboratory light conditions for at least 6 hours and in a refrigerator protected from light for at least 8 days.

For further detail on formulation analysis see also [APPENDIX 3](#).

7.2. Observations

7.2.1. Mortality

There were twelve premature decedents in the study: 1/10 at 100 mg/kg, 1/10 at 300 mg/kg and 10/30 at 1000 mg/kg. Rales, swelling of abdomen and lean appearance were noted among these animals on the days prior to death.

Males at 1000/600 mg/kg (no. 36, 40, 47, 48, 50) and females at 1000/600 mg/kg (no. 88 and 100) were euthanized for ethical reasons after respectively 70, 19, 30, 62, 84, 22 and 63 days of treatment. Most of these animals showed body weight loss prior to death. Main cause of morbidity was hepatocellular necrosis of the centrilobular area of the liver and/or degenerative findings in the kidney.

Single female at 100, 300 and 1000 mg/kg (no. 74, 77 and 93) were found dead after respectively 91, 77 and 19 days of treatment. Although animals 74 and 77 showed body weight loss, no cause of death could be determined for all three animals from the sections examined.

One male and one female at 1000 mg/kg (no 44 and 96) were found dead after respectively 26 and 30 days of treatment. Cause of death for these animals was a gavage accident. No body weight loss was noted in these animals.

For further detail on the histopathology of these premature decedents see also [APPENDIX 4](#).

7.2.2. Clinical Signs

Animals showed rales and swelling of the abdomen among all groups, showing higher incidence compared to controls at 300 and 1000/600 mg/kg in both sexes.

Additional clinical signs at 1000/600 mg/kg included: hunched posture, labored or deep respiration and lean appearance.

No clinical signs were noted during the recovery period and no additional findings were noted during the arena observations in this study.

Salivation seen after dosing among all animals was not considered toxicologically relevant, taking into account the nature and minor severity of the effect and its time of occurrence (i.e. after dosing). This sign was considered to be a physiological response related to taste of the vehicle and formulations rather than a sign of systemic toxicity.

Any other clinical signs noted during the treatment period occurred within the range of background findings to be expected for rats of this age and strain which are housed and treated under the conditions in this study and did not show any apparent dose-related trend. At the incidence observed, these were considered to be unrelated to treatment.

7.2.3. Functional Observations

Hearing ability, pupillary reflex and static righting reflex were normal in all examined animals. Grip strength and motor activity was similar between control and high dose animals.

All groups showed a similar motor activity habituation profile with a decreasing trend in activity over the duration of the test period.

7.2.4. Body Weights

Male rats dosed with 1000/600 mg/kg MTDID 7831 began demonstrating a statistically significant reduction in mean body weight when compared with the control group on Day 8 which persisted throughout the dosing period with the mean body weight being 15% less than the control group by Day 91 of the study. Males dosed with 300 mg/kg demonstrated statistically significant reductions in mean body weights on Days 57 through 71 (-8 to -9%) and on Day 91 (-8%) while males dosed with 100 mg/kg demonstrated no differences in body weight over the course of the study. Female rats dosed with 1000/600 mg/kg demonstrated statistically significant reductions in mean body weight on test days 33 and 34 (-6 to -7%) when compared to the control group; however, these slight reductions were not considered adverse due to the sporadic and minimal nature of the change. No treatment related body weight changes were noted in females at 100 mg/kg and females at 300 mg/kg.

Following the 4-week recovery period, males dosed with 600/1000 mg/kg no longer demonstrated significant differences in body weight when compared to the control group, indicating reversibility of this effect.

7.2.5. Food Consumption

Minimal effects were observed in the food consumption data in males, with animals in the 600/1000 mg/kg group demonstrating a statistical reduction on Days 1-8 and an elevation on Days 85-91. In conjunction with the body weight data, the relative food consumption in male rats dosed with 600/1000 mg/kg were statistically reduced on Days 1-8 and elevated on Days 8-15, 29-57, 64-78 and 85-91. No alterations were in food consumption parameters were noted in males dosed with 100 or 300 mg/kg MTDID 7831. Female rats dosed with 600/1000 mg/kg demonstrated a statistically reduce food consumption on Days 1-8 and a statistical increased on Days 22-36, 43-57 and 78-85 which correlated with a significant reduction in relative food consumption on Days 1-8 and increased relative food consumption

on Days 8-15, 22-57 and 67-91. Sporadic statistical increases in absolute and relative food consumption were noted in females from the 300 mg/kg dose group which were considered minimal in nature and non-adverse; females dosed with 100 mg/kg demonstrated no changes in food consumption parameters.

7.2.6. Ophthalmoscopic Examination

No ophthalmology findings were noted that were considered to be related to treatment.

The nature and incidence of ophthalmology findings noted during pretest and in Week 13 was similar among the groups, and occurred within the range considered normal for rats of this age and strain. These findings were therefore considered to be unrelated to treatment with the test item.

7.3. Clinical Laboratory Investigations

7.3.1. Haematology

The following (statistically significant) changes in haematology parameters distinguished treated from control animals:

- Lower lymphocytes level in females at 300 and 1000/600 mg/kg,
- Higher white blood cell count in females at 1000/600 mg/kg,

All effects recovered after a 28-day treatment-free period.

The slightly lower red blood cells, higher reticulocytes and red blood cell distribution width (RDW), lower mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH) in control females is only seen in the first 10 females which were sampled twice within a week. Therefore these findings were considered to be a result of recovery after blood sampling and not related to the test item.

Any other statistically significant changes in haematology parameters were considered to be unrelated to treatment as these occurred in the absence of a dose-related trend.

7.3.2. Clinical Biochemistry

The following (statistically significant) changes in clinical biochemistry parameters distinguished treated from control animals:

- Higher alanine aminotransferase (ALAT) in males and females at 300 and 1000/600 mg/kg,
- Higher aspartate aminotransferase (ASAT) in females at 1000/600mg/kg
- Higher alkaline phosphatase (ALP) in males and females at 300 and 1000/600 mg/kg,
- Higher total bilirubine in males and females at 300 and 1000/600 mg/kg,
- Higher bile acids in males at 1000/600mg/kg
- Higher urea and creatinine levels in males at 300 and 1000/600mg/kg
- Lower total protein in males and females at 300 and 1000/600 mg/kg,
- Lower glucose in males and females at 300 and 1000/600 mg/kg,
- Lower cholesterol level in males and females at 300 and 1000/600 mg/kg.

All effects recovered after a 28-day treatment-free period.

Any other statistically significant changes in clinical biochemistry parameters were considered to be unrelated to treatment as these occurred in the absence of a dose-related trend.

7.4. Pathology

7.4.1. Macroscopic Examination

Test item-related macroscopic findings in the surviving rats were present in the following organs:

Liver: An enlarged liver at the end of the treatment period was recorded in 2/10 males at 100 mg/kg, in 10/10 males and 3/9 females at 300 mg/kg and in 5/5 males and 6/6 females at 1000/600 mg/kg. After a 28-day treatment-free recovery period enlargement of the liver was not recorded. Discoloration (red-brown or black-brown) at the end of the treatment period was recorded 4/10 males and 3/9 females at 300 mg/kg and in 5/5 males and 6/6 females at 1000/600 mg/kg. After a 28 day treatment-free recovery period red-brown discoloration for the liver was recorded in 2/4 males and 2/5 females at 1000/600 mg/kg (microscopic correlate: brown pigment deposition). An accentuated lobular pattern in the liver was recorded in 1/10 males and 3/9 females at 300 mg/kg. This finding was not recorded after a 28-day treatment-free recovery period.

Kidney: Discolouration (red-brown or greenish) was recorded 1/10 males at 100 mg/kg, 3/10 males and 1/9 females at 300 mg/kg and 5/5 males and 5/6 females at 1000/600 mg/kg. After a 28 day treatment-free recovery period discoloration of the kidneys was recorded in 2/5 females at 1000/600 mg/kg.

Thyroid gland: An enlarged thyroid gland, was recorded in 2/10 males and 2/9 females at 300 mg/kg, in 1/6 main females at 1000/600 mg/kg and in the recovery group in 1/5 males of the control and 1/4 males of the 1000/600 mg/kg treated group. After a 28-day treatment-free recovery period enlarged thyroid glands were recorded at comparable incidences in control and treated rats.

Stomach: Macroscopic findings were recorded in all dose groups including controls. These findings consisted of dark red/reddish/black-brown foci in the glandular mucosa of the stomach in 1/10 males of Main Group 1, 1/5 males of the Recovery Group 1, 1/10 males and 2/9 females at 100 mg/kg, 1/5 males at 1000/600 mg/kg, reddish/black foci in the forestomach in 1/9 females at 100 mg/kg, 1/9 females at 300 mg/kg and 3/6 females at 1000/600 mg/kg and an irregular surface of the forestomach in 1/10 males at 100 mg/kg and 2/5 males at 1000/600 mg/kg. There was complete recovery for the stomach findings after a 28 day treatment-free recovery period. The macroscopic findings recorded at the end of the treatment period were considered to be related to the gavage treatment procedure with Arachis Oil with or without test item.

The remainder of the recorded macroscopic findings were within the range of background gross observations encountered in rats of this age and strain.

7.4.2. Organ Weights

Statistically significant organ weight changes were noted in liver and kidney of both sexes, thyroid gland and adrenal gland of males and thymus and spleen of females.

Mean Percent Organ Weight Differences from Control Groups - Males

Dose level (mg/kg):	Main			Recovery 1000/600
	100	300	1000/600	
LIVER				
Absolute	+12	+30**	+61**	0
Relative to body weight	+11*	+43**	+101**	+7
KIDNEY				
Absolute	+14**	+14**	+11*	+15
Relative to body weight	+12*	24**	+38**	+25**
THYROID GLAND				
Absolute	+13	+20*	+7	+19
Relative to body weight	0	+25**	+25**	+25
ADRENAL GLAND				
Absolute	-6	-6	+17*	-4
Relative to body weight	-7	0	+40**	0

*: P<0.05, **: P<0.01

Mean Percent Organ Weight Differences from Control Groups - Females

Dose level (mg/kg):	Main			Recovery 1000/600
	100	300	1000/600	
LIVER				
Absolute	-3	+15**	+41**	-3
Relative to body weight	0	+26**	+53**	+4
KIDNEYS				
Absolute	+6	+13*	+24**	+3
Relative to body weight	+10*	+23**	+35**	+9
THYMUS				
Absolute	-2	-23*	-20	+30*
Relative to body weight	+1	-16	-13	+40*
SPLEEN				
Absolute	-17**	-24**	-23**	-9
Relative to body weight	-14*	-18**	-16*	-2

*: P<0.05, **: P<0.01

Liver: At the end of the 90-day treatment period statistically significant higher absolute liver weights were noted in both sexes starting at 300 mg/kg and relative to body weight was noted in males starting at 100 mg/kg and in females starting at 300 mg/kg.

There was complete recovery in males and females after the 28-day recovery period.

Kidney: At the end of the 90-day treatment period statistically significant higher kidney weights (absolute and relative to body weights) were noted in males starting at 100 mg/kg. In females the relative to body weight was increased starting at 100 mg/kg and in the absolute kidney weight was increased starting at 300 mg/kg. There was partial recovery for this increase in males (significant relative to body weight) and complete recovery in females at 1000/600 mg/kg after the 28-day recovery period.

Thyroid gland (males): At the end of the 90-day treatment period an apparent increase in thyroid gland weight (relative to body weights) was noted starting at 300 mg/kg (only statistically significant increase of absolute thyroid gland weight at 300 mg/kg). There was partial recovery for this increase (apparent increase, not statistically significant) at 1000/600 mg/kg after the 28-day recovery period.

Adrenal gland (males): At the end of the 90-day treatment period statistically significant higher adrenal gland weights (absolute and relative to body weights) were noted at 1000/600 mg/kg. There was complete recovery after the 28-day recovery period.

Thymus (females): At the end of the 90-day treatment period an apparent decrease in thymus weight was noted starting at 300 mg/kg (only statistically significant decrease of absolute thymus weight at 300 mg/kg). There was complete recovery for this decrease at 1000/600 mg/kg after the 28-day recovery period, the thymus weight of the recovery females at 1000/600 mg/kg was statistically higher compared to the control recovery females.

Spleen (females): At the end of the 90-day treatment period a statistically significant decrease in spleen weight (absolute and relative to body weights) was noted starting at 100 mg/kg. There was complete recovery for this decrease at 1000/600 mg/kg after the 28-day recovery period.

The remaining (statistically significant) organ weight differences compared to the control group were considered to be the result of a test item-related decrease in final body weight.

7.4.3. Microscopic Examination

Treatment-related microscopic findings after treatment with MTDID 7831 were noted in the thyroid gland, stomach, liver, kidney, urinary bladder and bone marrow (sternum) of both sexes and thymus, adrenal gland and spleen of females.

THYROID GLAND:

Summary Test Item-Related Microscopic Thyroid Gland Findings – Scheduled Euthanasia Animals

Dose level (mg/kg):	MAIN				RECOVERY	
	0	100	300	1000/600	0	1000/600
THYROID GLAND MALES ^a <i>Hypertrophy follicular cell</i>	10	10	10	5	5	4
Minimal	3	3	4	-	2	1
Slight	2	3	4	4	-	1
Moderate	-	2	-	1	-	-
THYROID GLAND FEMALES ^a <i>Hypertrophy follicular cell</i>	10	9	9	6	5	5
Minimal	1	2	3	3	1	1
Slight	-	-	-	3	-	-

^a = Number of tissues examined from each group.

An increased incidence and severity of *hypertrophy of the follicular cells* of the thyroid gland was recorded in males starting at 100 mg/kg and females at 1000/600 mg/kg. There was complete recovery for this finding after a 28 day treatment-free recovery period. The incidences and severities recorded for females at 100 and 300 mg/kg and the males and females of the recovery groups were within background pathology for rats of this age and strain.

STOMACH:

Summary Test Item-Related Microscopic Stomach Findings – Scheduled Euthanasia Animals

Dose level (mg/kg):	MAIN				RECOVERY	
	0	100	300	1000/600	0	1000/600
STOMACH MALES ^a	10	10	10	5	5	4
<i>Inflammation forestomach</i>						
Minimal	6	2	3	1	-	-
Slight	2	-	2	-	-	-
<i>Hyperplasia squamous cell</i>						
Minimal	3	2	3	2	-	-
Slight	5	2	4	1	-	-
Moderate	-	-	-	1	-	-
<i>Erosion/ulceration</i>						
Minimal	-	-	1	1	-	-
Slight	1	-	-	-	-	-
<i>Edema</i>						
Minimal	1	4	-	-	-	-
Slight	2	1	2	-	-	-
Moderate	1	-	-	-	-	-

Dose level (mg/kg):	MAIN				RECOVERY	
	0	100	300	1000/600	0	1000/600
STOMACH FEMALES ^a	10	9	9	6	5	5
<i>Inflammation forestomach</i>						
Minimal	1	1	1	1	-	1
Slight	2	2	1	2	-	-
Moderate	-	1	-	-	-	-
<i>Hyperplasia squamous cell</i>						
Minimal	1	2	2	3	-	1
Slight	3	2	-	-	-	-
Moderate	-	1	2	2	-	-
<i>Erosion/ulceration</i>						
Minimal	-	1	-	1	-	-
Slight	1	1	1	1	-	-
<i>Edema</i>						
Minimal	1	3	-	-	-	-
Slight	2	1	1	1	-	-

^a = Number of tissues examined from each group.

Microscopic findings above background incidences and severities were recorded for the stomach (forestomach) of all dose groups including controls. These microscopic findings consisted of *lymphogranulocytic inflammation*, *hyperplasia of squamous cells*, *erosions/ulcerations* and *edema*. There was complete recovery for these findings in males and almost complete recovery in females after the 28-day treatment-free recovery period.

LIVER:

Summary Test Item-Related Microscopic Liver Findings – Scheduled Euthanasia Animals

Dose level (mg/kg):	MAIN				RECOVERY	
	0	100	300	1000/600	0	1000/600
LIVER MALES ^a	10	10	10	5	5	4
<i>Hypertrophy, centrilobular/diffuse</i>						
Minimal	-	10	2	-	-	-
Slight	-	-	7	1	-	-
Moderate	-	-	1	4	-	-
<i>Necrosis hepatocellular, centrilobular</i>						
Minimal	-	-	-	1	-	-
Slight	-	-	-	4	-	-
<i>Necrosis coagulative</i>						
Minimal	-	-	1	1	-	-
Slight	-	-	-	1	-	-
<i>Pigment deposition yellow-brown</i>						
Slight	-	-	-	-	-	1

Dose level (mg/kg):	MAIN				RECOVERY	
	0	100	300	1000/600	0	1000/600
LIVER FEMALES ^a	10	9	9	6	5	5
<i>Hypertrophy, centrilobular/diffuse</i>						
Minimal	-	2	6	-	-	-
Slight	-	-	3	-	-	-
Moderate	-	-	-	6	-	-
<i>Necrosis hepatocellular, centrilobular</i>						
Minimal	-	-	1	2	-	1
Slight	-	-	-	3	-	-
Moderate	-	-	-	1	-	-
<i>Necrosis coagulative</i>						
Minimal	-	-	-	1	1	-
Slight	-	-	-	-	-	-
<i>Pigment deposition yellow-brown</i>						
Minimal	-	-	-	-	-	1
Slight	-	-	-	-	1	1

^a = Number of tissues examined from each group.

A combination of findings was recorded for the liver of males and females:

Centrilobular/diffuse hepatocellular hypertrophy with eosinophilic cytoplasm was recorded starting at 100 mg/kg. There was complete recovery for this finding after a 28-day treatment-free recovery period.

Hepatocellular necrosis of the centrilobular area (in some instances with additional brown pigmentation) was recorded in females starting at 300 mg/kg and in males at 1000/600 mg/kg. There was complete recovery this finding in males and partial recovery in females.

Focal/multifocal coagulative necrosis was recorded at an increased incidence and severity in males at 1000/600 mg/kg. There was complete recovery for this finding after a 28 day treatment-free recovery period. The single incidences of minimal coagulative necrosis recorded in the remaining dose groups including the control recovery females is considered to be within background pathology of rats of this age and strain.

Yellow-brown pigment deposition was recorded in a single male and a few females at 1000/600 mg/kg of the recovery group.

KIDNEY:

Summary Test Item-Related Microscopic Kidney Findings – Scheduled Euthanasia Animals

Dose level (mg/kg):	MAIN				RECOVERY	
	0	100	300	1000/600	0	1000/600
KIDNEY MALES ^a	10	10	10	5	5	4
<i>Basophilia tubule</i>						
Minimal	3	-	1	1	1	-
Slight	-	-	-	1	-	-
<i>Vacuolar degeneration/necrosis</i>						
Minimal	-	-	-	1	-	-
<i>Granular cast</i>						
Slight	-	-	-	1	-	-
<i>Eosinophilic content tubular</i>						
Minimal	1	1	-	3	-	-
Slight	-	-	-	2	-	-
<i>Papil hyperplasia epithelium</i>						
Minimal	-	-	-	2	-	-
<i>Pigment yellow-brown</i>						
Minimal	-	-	-	-	-	3
KIDNEY FEMALES ^a	10	9	9	6	5	5
<i>Basophilia tubule</i>						
Minimal	2	-	1	-	-	1
Slight	-	-	-	-	-	-
Moderate	-	-	-	1	-	-
<i>Eosinophilic content tubular</i>						
Minimal	-	-	-	2	-	-
<i>Papil hyperplasia epithelium</i>						
Slight	-	-	-	2	-	-
<i>Papil eosinophilic content</i>						
Minimal	-	-	3	-	-	-
Slight	-	-	-	1	-	-
<i>Calculus</i>						
Slight	-	-	-	1	-	-
Moderate	-	-	-	1	-	-

^a = Number of tissues examined from each group.

A combination of findings was recorded for the kidney of males and females:

Tubular basophilia was recorded at an increased severity in both sexes at 1000/600 mg/kg. There was complete recovery for this finding after a 28-day treatment-free recovery period. The incidences and severities recorded for the males and females of the remaining dose groups including controls were considered to be within background pathology for rats of this age and strain.

Vacuolar degeneration/necrosis was recorded in one male surviving the 90-day treatment period. There was complete recovery for this finding after a 28-day treatment-free recovery period.

Granular casts were recorded in one male at 1000/600 mg/kg. There was complete recovery for this finding after a 28-day treatment-free recovery period.

Eosinophilic content of the tubuli was recorded at an increased incidence and severity in males and females at 1000/600 mg/kg. There was complete recovery for this finding after a 28-day treatment-free recovery period.

Eosinophilic content of the papil was recorded in a few females starting at 300 mg/kg. There was complete recovery for this finding after a 28-day treatment-free recovery period.

Hyperplasia of the epithelium of the papil with cellular debris/casts was recorded in a few males and females at 1000/600 mg/kg. There was complete recovery for this finding after a 28 day treatment-free recovery period.

A calculus in the papil or pelvis was recorded in a few females at 1000/600 mg/kg. There was complete recovery for this finding after a 28 day treatment-free recovery period.

After a 28 day treatment-free recovery period *yellow-brown tubular pigment* was recorded in a few males at 1000/600 mg/kg.

URINARY BLADDER:

Text Table 7.

Summary Test Item-Related Microscopic Urinary Bladder Findings – Scheduled Euthanasia Animals

Dose level (mg/kg):	MAIN				RECOVERY	
	0	100	300	1000/600	0	1000/600
URINARY BLADDER MALES ^a <i>Hyperplasia/hypertrophy urothelium</i>	10	10	10	5	5	4
Minimal	-	-	2	2	-	1
Slight	-	-	2	1	-	2
Moderate	-	-	-	1	-	-
URINARY BLADDER FEMALES ^a <i>Hyperplasia/hypertrophy urothelium</i>	10	9	9	6	5	5
Minimal	-	-	2	3	-	3
Slight	-	-	-	-	-	1

^a = Number of tissues examined from each group.

Hypertrophy/hyperplasia of the urothelium of the urinary bladder was recorded in both sexes starting at 300 mg/kg. There was no recovery for this finding after a 28 day treatment-free recovery period.

BONE MARROW (STERNUM):

Summary Test Item-Related Microscopic Bone Marrow (sternum) findings – Scheduled Euthanasia Animals

Dose level (mg/kg):	MAIN				RECOVERY	
	0	100	300	1000/600	0	1000/600
BONE MARROW MALES ^a	10	10	10	5	5	4
<i>Increased adipocytes</i>						
Minimal	-	2	3	-	-	1
Slight	-	-	1	-	-	1
Moderate	-	-	-	1	-	-
BONE MARROW FEMALES ^a	10	9	9	6	5	5
<i>Increased adipocytes</i>						
Minimal	-	1	2	2	-	1

^a = Number of tissues examined from each group.

An increased number of adipocytes (incidence and/or severity) in the bone marrow (sternum) was recorded in a few males and females starting at 100 mg/kg. There was partial recovery for this finding after a 28-day treatment-free recovery period.

THYMUS (FEMALES):

Summary Test Item-Related Microscopic Thymus Findings – Scheduled Euthanasia Animals

Dose level (mg/kg):	MAIN				RECOVERY	
	0	100	300	1000/600	0	1000/600
THYMUS ^a	10	9	9	6	5	5
<i>Lymphocytolysis increased</i>						
Minimal	-	1	1	2	-	-

^a = Number of tissues examined from each group.

A minor increase in incidence and severity of lymphocytolysis in the thymus was recorded in females starting at 100 mg/kg. There was complete recovery for this finding after a 28-day treatment-free recovery period.

ADRENAL GLAND (FEMALES):

Summary Test Item-Related Microscopic Adrenal Gland Findings – Scheduled Euthanasia Animals

Dose level (mg/kg):	MAIN				RECOVERY	
	0	100	300	1000/600	0	1000/600
ADRENAL GLAND FEMALES ^a	10	9	9	6	5	5
<i>Vacuolation zona glomerulosa</i>						
Minimal	1	2	4	2	2	1
Slight	-	-	-	2	-	-

^a = Number of tissues examined from each group.

A minor increase in incidence and severity of vacuolation of the zona glomerulosa of the adrenal gland was recorded in females at 1000/600 mg/kg. There was complete recovery for this finding after a 28-day treatment-free recovery period. The incidences and severities recorded for females at 100 and 300 mg/kg and the recovery groups were within background pathology for female rats of this age and strain.

SPLEEN (FEMALES):

Text Table 11.
 Summary Treatment-Related Microscopic Spleen Findings – Scheduled Euthanasia Animals

Dose level (mg/kg):	MAIN				RECOVERY	
	0	100	300	1000/600	0	1000/600
SPLEEN FEMALES ^a	10	9	9	6	5	5
<i>Hematopoiesis extramedullary</i>						
Minimal	2	5	3	4	-	-
Slight	5	-	-	-	-	-
Moderate	3	-	-	-	-	-

^a = Number of tissues examined from each group.

A high incidence and severity of extramedullary hematopoiesis was recorded for the spleen of females of the Control group after the 90-day treatment period, compared to the test item-treated dose groups. There was no extramedullary hematopoiesis in the spleen after the 28 day treatment-free recovery period in females of the control and 1000/600 mg/kg treated females, suggesting complete recovery.

Remaining histologic changes were considered to be incidental. There was no test item-related alteration in the prevalence, severity, or histologic character of those incidental tissue alterations.

For further detail on histopathology see also [APPENDIX 4](#).

8. DISCUSSION AND CONCLUSION

Wistar rats were treated with MTDID 7831 for 13 weeks by daily oral gavage at dose levels of 100, 300 and 1000/600 mg/kg followed by a 28-day treatment-free recovery period. Based on the clinical signs and general health of the animals treated at 1000 mg/kg, the dose level was reduced to 600 mg/kg from Day 35 and onwards.

Chemical analyses confirmed that formulations of test item in arachis oil were prepared accurately and homogeneously, and were stable when stored at room temperature under normal laboratory light conditions for at least 6 hours and in a refrigerator protected from light for at least 8 days.

There were twelve premature/unexpected decedents in the study:

- Five males and two females in the 1000/600 mg/kg MTDID 7831 group were euthanized for ethical reasons during the treatment period. These animals demonstrated body weight loss and/or moribundity prior to death. The main cause of morbidity was hepatocellular necrosis of the centrilobular area of the liver and/or degenerative findings in the kidney.
- Single females at 100, 300 and 1000 mg/kg were found dead during treatment period. Although one female dosed with 100 mg/kg and one female dosed with 300 mg/kg test item demonstrated body weight losses, no cause of death could be determined for all three animals from the clinical and microscopic pathology evaluations.
- One male and one female at 1000 mg/kg were found dead during the treatment period. Cause of death for these animals was determined to be a gavage accident. No body weight loss was noted and rales, swelling of abdomen and lean appearance were noted among these animals on the days prior to death.

Notable clinical signs of toxicity noted in surviving males and females dosed with 1000/600 mg/kg MTDID 7831 were rales, swelling of the abdomen, hunched posture, labored or deep respiration and lean appearance at a higher incidence when compared to control group animals. At 300 mg/kg rales and swelling of abdomen were also noted at a higher incidence when compared to the control group.

Male rats dosed with 1000/600 mg/kg MTDID 7831 began demonstrating a statistically significant reduction in mean body weight when compared with the control group on Day 8 which persisted throughout the dosing period with the mean body weight being 15% less than the control group by Day 91 of the study. Males dosed with 300 mg/kg demonstrated statistically significant reductions in mean body weights on Days 57 through 71 (-8 to -9%) and on Day 91 (-8%) while males dosed with 100 mg/kg demonstrated no differences in body weight over the course of the study. Female rats dosed with 1000/600 mg/kg demonstrated statistically significant reductions in mean body weight on test days 33 and 34 (-6 to -7%) when compared to the control group; however, these slight reductions were not considered adverse due to the sporadic and minimal nature of the change. No treatment related body weight changes were noted in females at 100 mg/kg and females at 300 mg/kg.

Following the 4-week recovery period, males dosed with 600/1000 mg/kg no longer demonstrated significant differences in body weight when compared to the control group, indicating reversibility of this effect.

Minimal effects were observed in the food consumption data in males, with animals in the 600/1000 mg/kg group demonstrating a statistical reduction on Days 1-8 and an elevation on Days 85-91. In conjunction with the body weight data, the relative food consumption in male rats dosed with 600/1000 mg/kg were statistically reduced on Days 1-8 and elevated on Days 8-15, 29-57, 64-78 and 85-91. No alterations were in food consumption parameters were

noted in males dosed with 100 or 300 mg/kg MTDID 7831. Female rats dosed with 600/1000 mg/kg demonstrated a statistically reduce food consumption on Days 1-8 and a statistical increased on Days 22-36, 43-57 and 78-85 which correlated with a significant reduction in relative food consumption on Days 1-8 and increased relative food consumption on Days 8-15, 22-57 and 67-91. Sporadic statistical increases in absolute and relative food consumption were noted in females from the 300 mg/kg dose group which were considered minimal in nature and non-adverse; females dosed with 100 mg/kg demonstrated no changes in food consumption parameters.

No effects were seen in the functional observations nor in the ophthalmoscopy.

Postmortem examination of the animals revealed MTDID 7831-related findings in the liver (hepatocellular necrosis of the centrilobular area and focal/multifocal coagulative necrosis and hepatocellular hypertrophy), kidney (vacuolar degeneration/necrosis and the granular casts in males and tubular basophilia in females), urinary bladder (hypertrophy/hyperplasia of the urothelium), thyroid gland (follicular cell hypertrophy), sternal bone marrow (increased number of adipocytes), stomach (lymphogranulocytic inflammation, hyperplasia of squamous cells, erosions/ulcerations and edema) in both male and female rats as well as changes in the thymus (lymphocytolysis), adrenal gland (vacuolation of the zona glomerulosa) and spleen (extramedullary hematopoiesis) of females.

In the liver the hepatocellular necrosis of the centrilobular area and focal/multifocal coagulative necrosis were degenerative findings and therefore considered adverse in nature. The brown pigmentation of the liver in some recovery animals at 1000/600 mg/kg was probably digested remnants of necrotic cellular material, resulting from the hepatocellular necrosis observed at the end of the treatment period. The minimal or slight hepatocellular hypertrophy of the liver observed in the males and females at 100 mg/kg, in the absence of any degenerative findings or changes in absolute liver weight was considered to be a non-adverse finding (Kerlin et. al., 2016).

Macroscopic correlates that were noted in these animals were discolouration, enlargement and accentuated lobular pattern of the liver. These microscopic findings correlated with increased serum liver enzymes, total bilirubine, bile acids and decreased total protein, glucose and cholesterol at 300 and 1000/600mg/kg MTDID 7831.

In the kidney the vacuolar degeneration/necrosis and the granular casts recorded in males and the high severity of tubular basophilia observed in females were degenerative in nature and therefore considered to be adverse microscopic findings at 1000/600 mg/kg. These renal findings were accompanied by higher kidney weights and increased serum urea and creatinine levels in males at this dose level.

The hypertrophy/hyperplasia of the urothelium of the urinary bladder in male and female rats dosed with 300 or 1000/600 mg/kg, where present at a low incidence, but demonstrated a dose-response relationship in severity and demonstrated no recovery and was, therefore, considered to be an adverse microscopic finding (Sahota et. al., 2013).

Thyroid gland hypertrophy in rats is usually an adaptive response to induction of hepatic enzymes. This results in increase in the hepatic/biliary clearance of T3/T4 leading to increase in TSH and compensatory follicular cell hypertrophy and/or hyperplasia (Wu and Farrelly, 2006) and is therefore, considered to be a secondary result of MTDID 7831 hepatic toxicity.

The findings reported in the sternal bone marrow, as well as thymus and adrenal observations in the female rats were considered to be spontaneous background findings as they demonstrated no dose-response relationship, were not accompanied by any degenerative findings and showed complete or partial recovery. Therefore these findings are considered to be non-adverse (Kerlin et. al., 2016).

Macroscopic and microscopic findings were recorded for the stomach of all dose groups including controls. There was no dose response relationship and therefore these findings were considered to be due to the gavage treatment procedure with Arachis Oil as vehicle and not related to the treatment with MTDID 7831.

The differences in severity of extramedullary hematopoiesis noticed in the spleen of females of all test item-treated dose groups compared to the control females at the end of the treatment period were considered to be related to the blood sampling procedure: Blood samples were collected from the females of the Main Control group after 92 days of treatment and these animals (except animal 51) were subsequently necropsied after 96 days of treatment on Day 97. No blood samples were collected of the remaining females on Day 92. The differences in the red blood cell parameters (decreased red blood cell counts and increased reticulocytes), increased organ weight of the spleen and microscopic finding (increased extramedullary hematopoiesis) in the spleen of the Main Control females after the treatment period, represent a physiological response after the blood sampling procedure and these differences between the control and test item treated groups are therefore regarded to be unrelated to the test item.

Conclusion

Adverse MTDID 7831-related morphologic alterations in Wistar (Han) rats subjected to 90-Day oral gavage toxicity study, followed by a 4-week recovery period up to a dose of 1000/600 mg/kg were present in liver (hepatocellular necrosis of the centrilobular area, coagulative necrosis), kidney (vacuolar degeneration/necrosis, granular casts, increased severity of tubular basophilia) and urinary bladder (hypertrophy/hyperplasia of the urothelium) of both sexes starting at 300 mg/kg. These microscopic histopathology findings correlated with concurrent and expected changes in serum clinical chemistry parameters and the severity of toxicity also reflected dose-related reductions in animal body weights over the dosing phase of this study.

There were no adverse test item-related morphologic alterations at 100 mg/kg. The death of one female at 100 mg/kg was considered not test item related in the absence of, a cause of death, other mortalities in this group and of any other adverse findings or comparable morphological changes at this dose level.

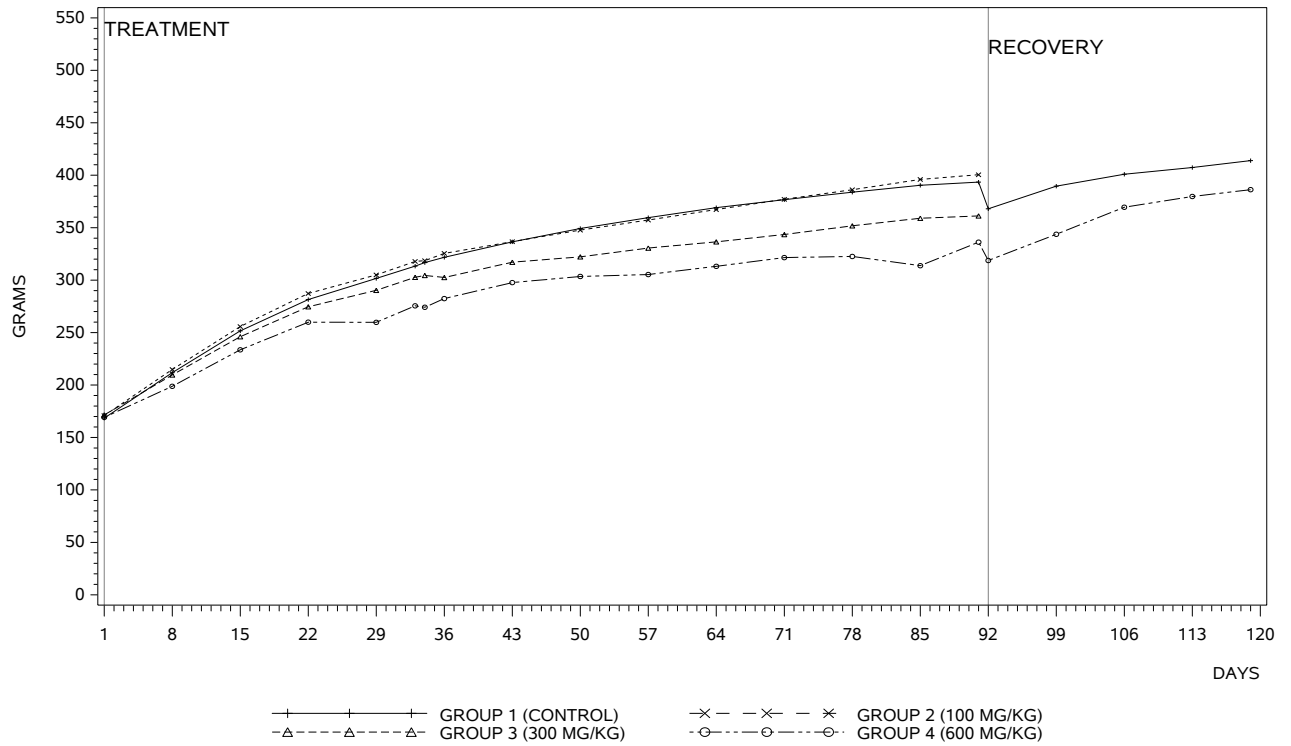
Therefore, based upon the results presented in this report a No Observed Adverse Effect Level (NOAEL) for MTDID 7831 of 100 mg/kg was established.

9. REFERENCES

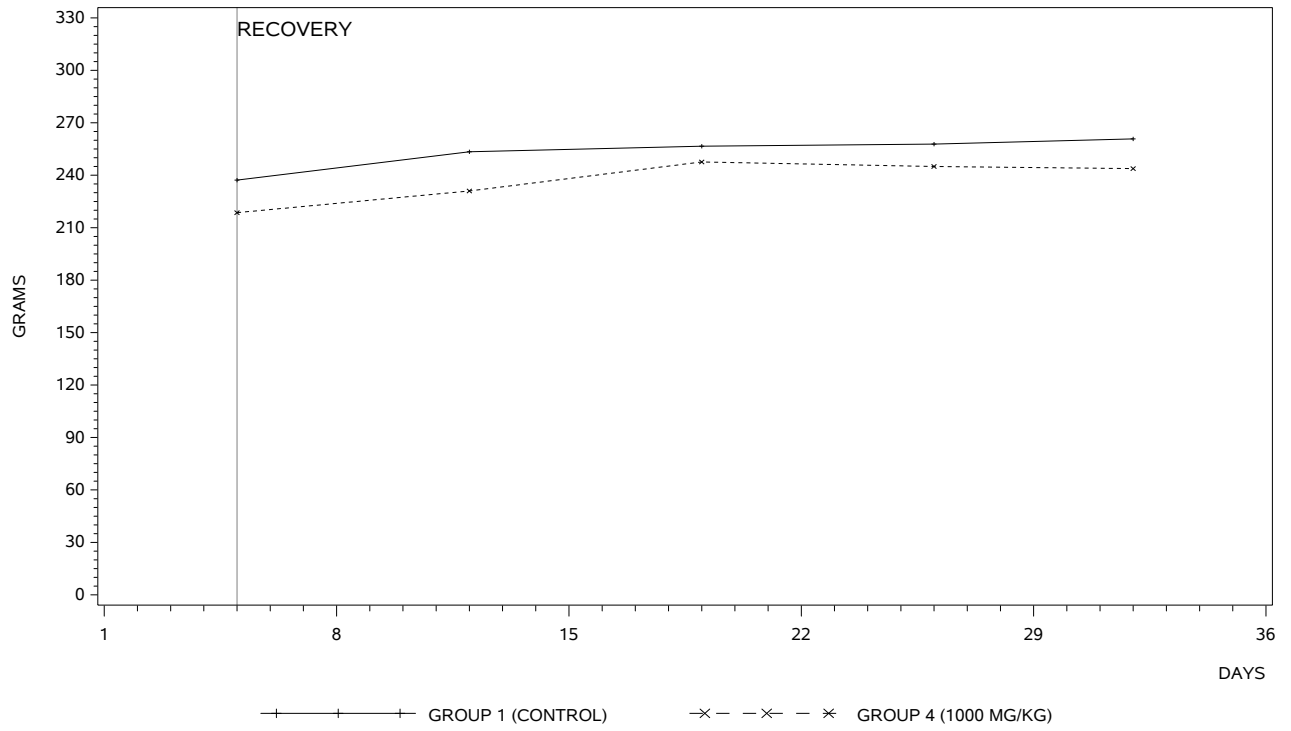
- Ref. 1 C.W. Dunnett, A Multiple Comparison Procedure for Comparing Several Treatments with a Control, J. Amer. Stat. Assoc. 50, 1096-1121 (1955).
- Ref. 2 R.G. Miller, Simultaneous Statistical Inference, Springer Verlag, New York (1981).
- Ref. 3 R.A. Fisher, Statistical Methods for Research Workers, Oliver and Boyd, Edinburgh (1950).
- Ref. 4 Kruskal W.H. and Wallis W.A.. Use of ranks in one-criterion variance analysis. Journal of the American Statistical Association 47 (260): 583-621, December (1952).
- Ref. 5 Wilcoxon, F. Individual comparisons by ranking methods. Biometrics, 1, 80-83 (1945).

APPENDIX 1
FIGURES AND SUMMARY TABLES

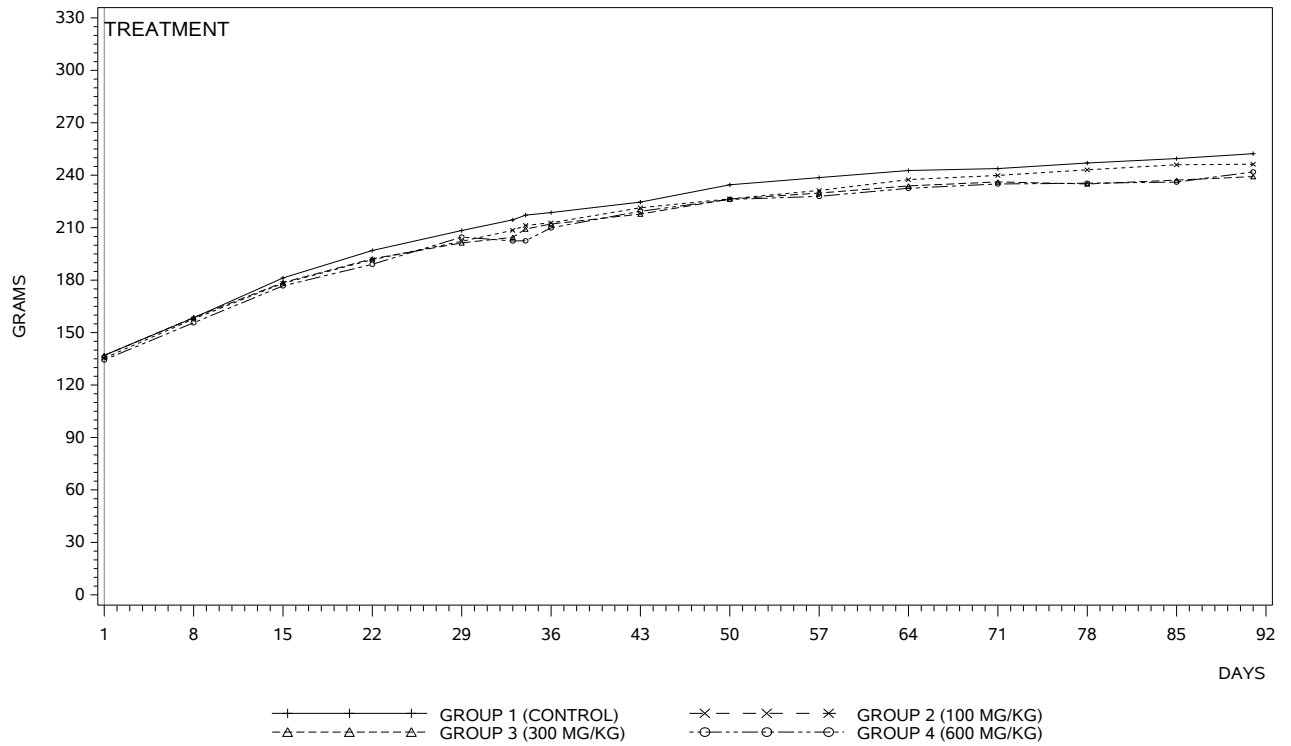
1.1 BODY WEIGHTS (GRAM) MALES



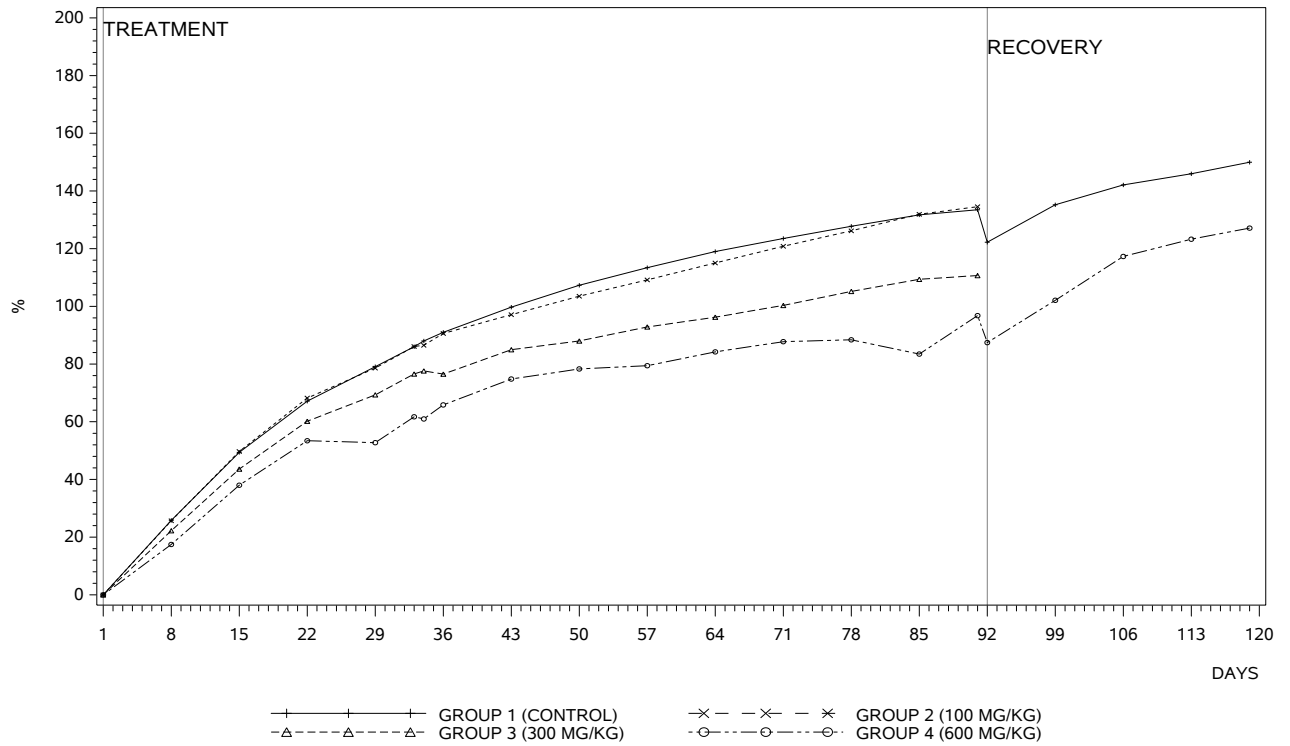
1.1 BODY WEIGHTS (GRAM) FEMALES



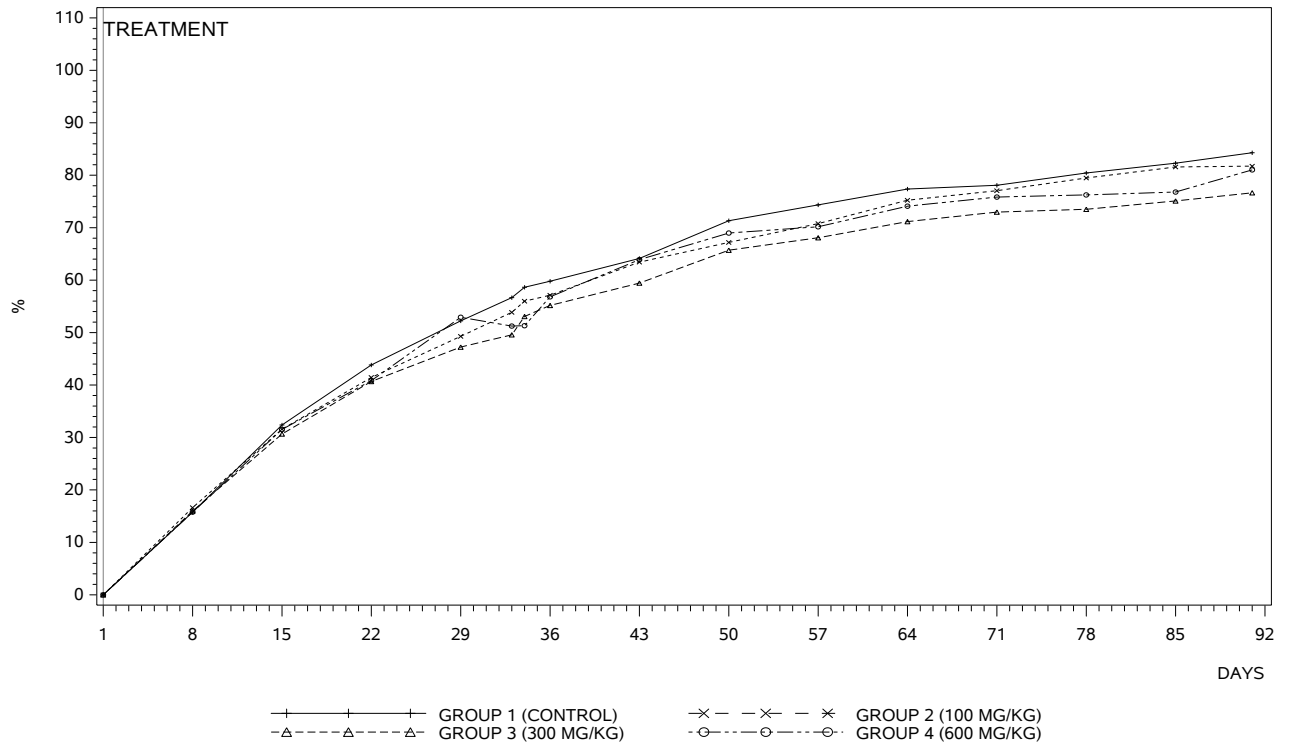
1.1 BODY WEIGHTS (GRAM) FEMALES



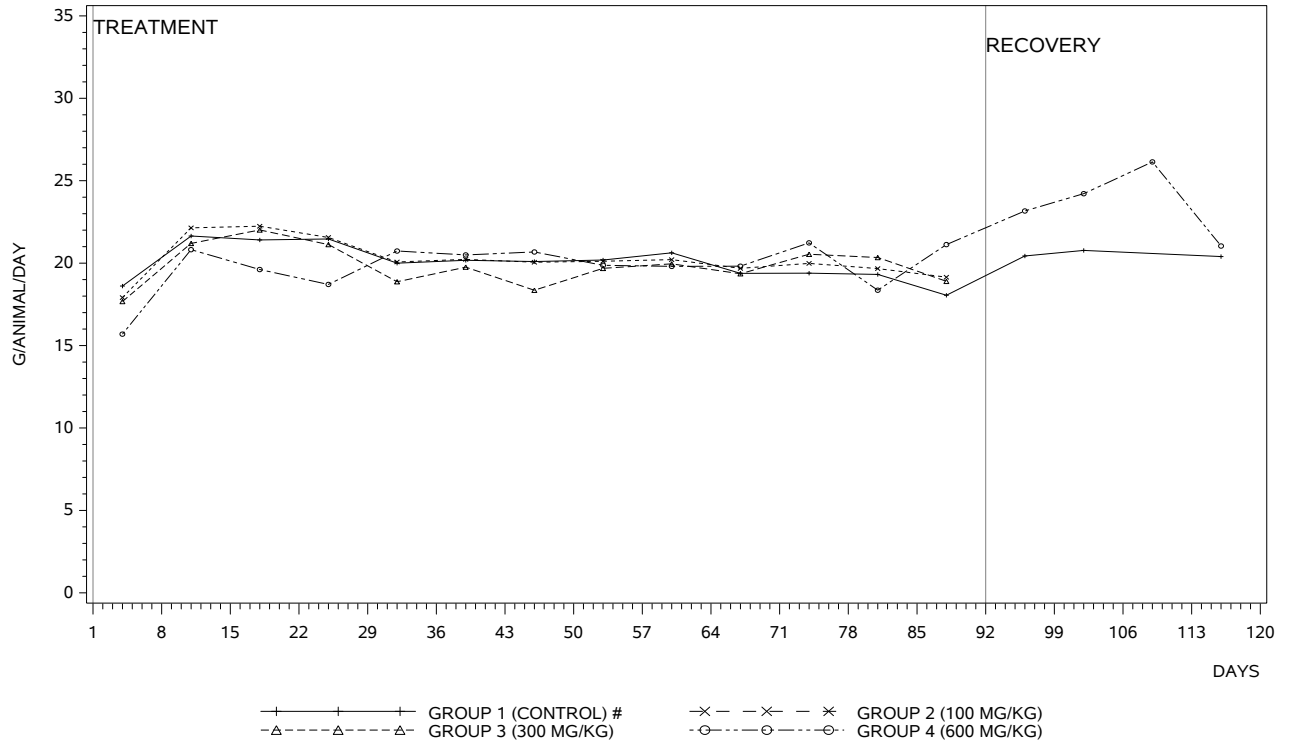
1.2 BODY WEIGHT GAIN (%) MALES



1.2 BODY WEIGHT GAIN (%) FEMALES

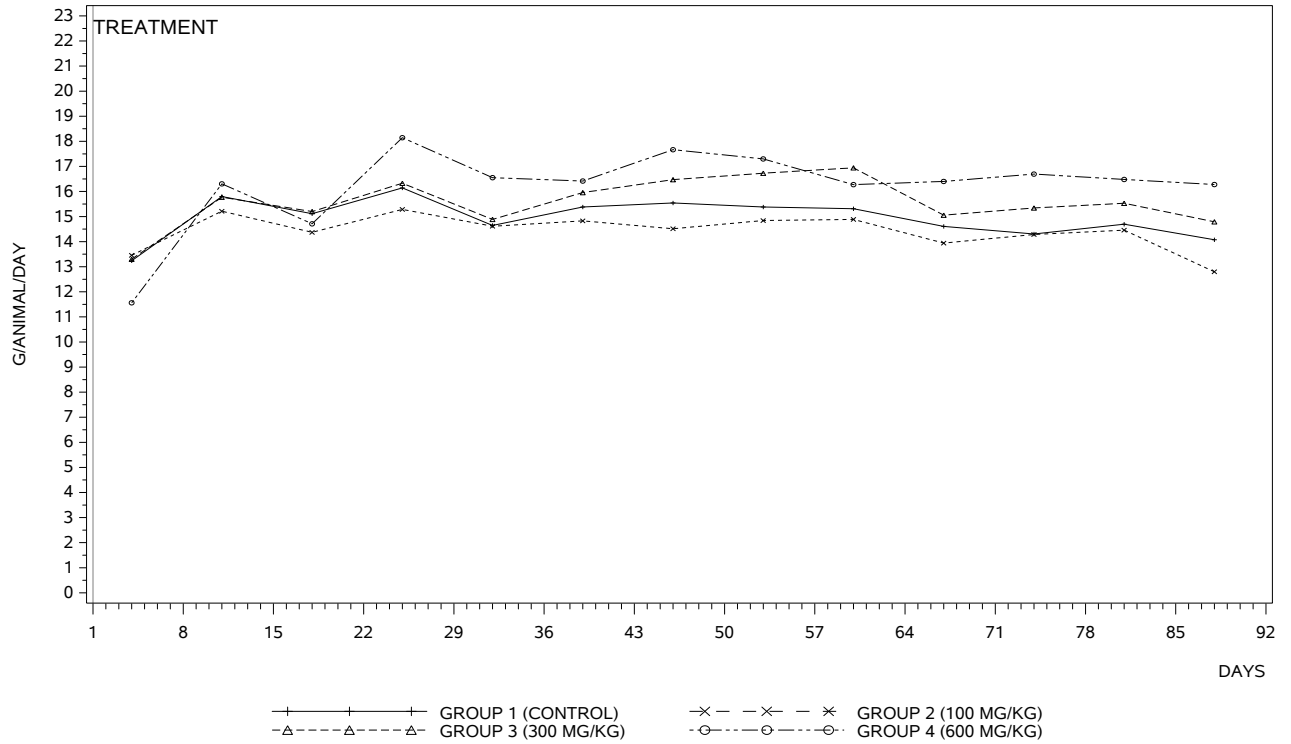


1.3 FOOD CONSUMPTION (G/ANIMAL/DAY) MALES

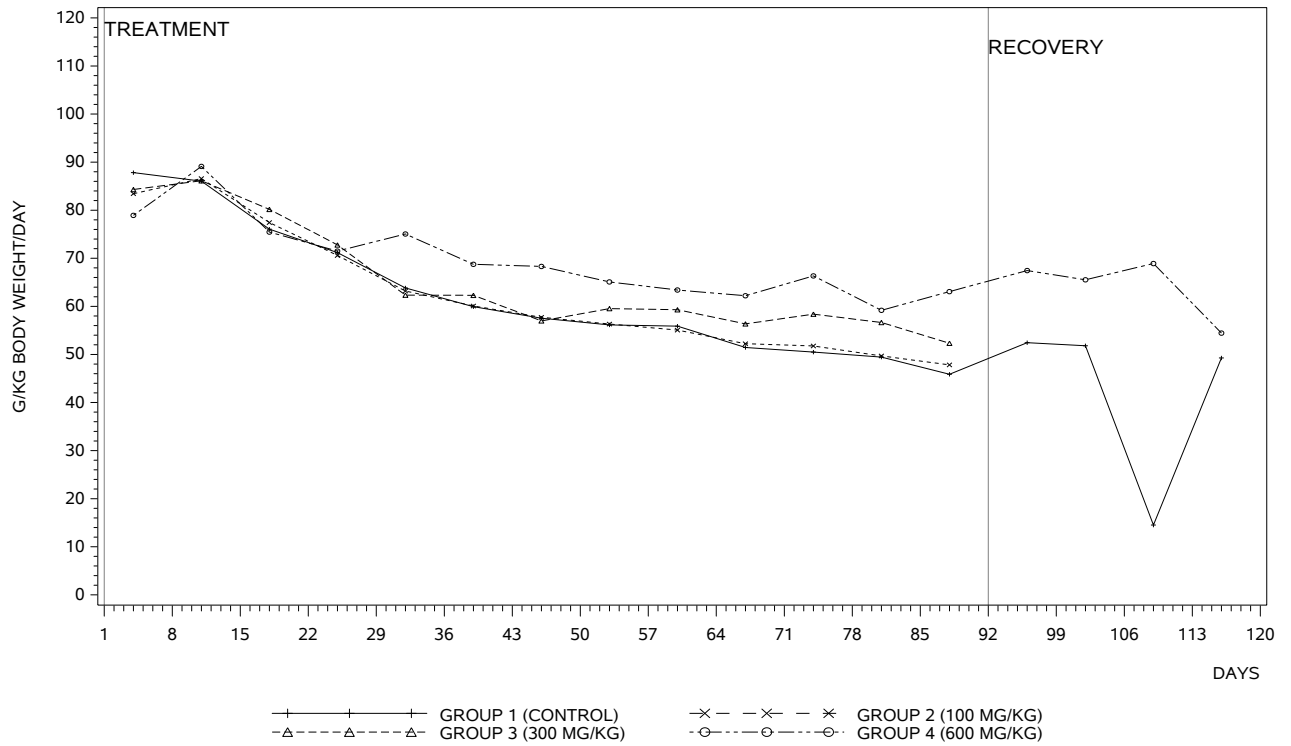


Explanations for excluded data are listed in the tables of individual values

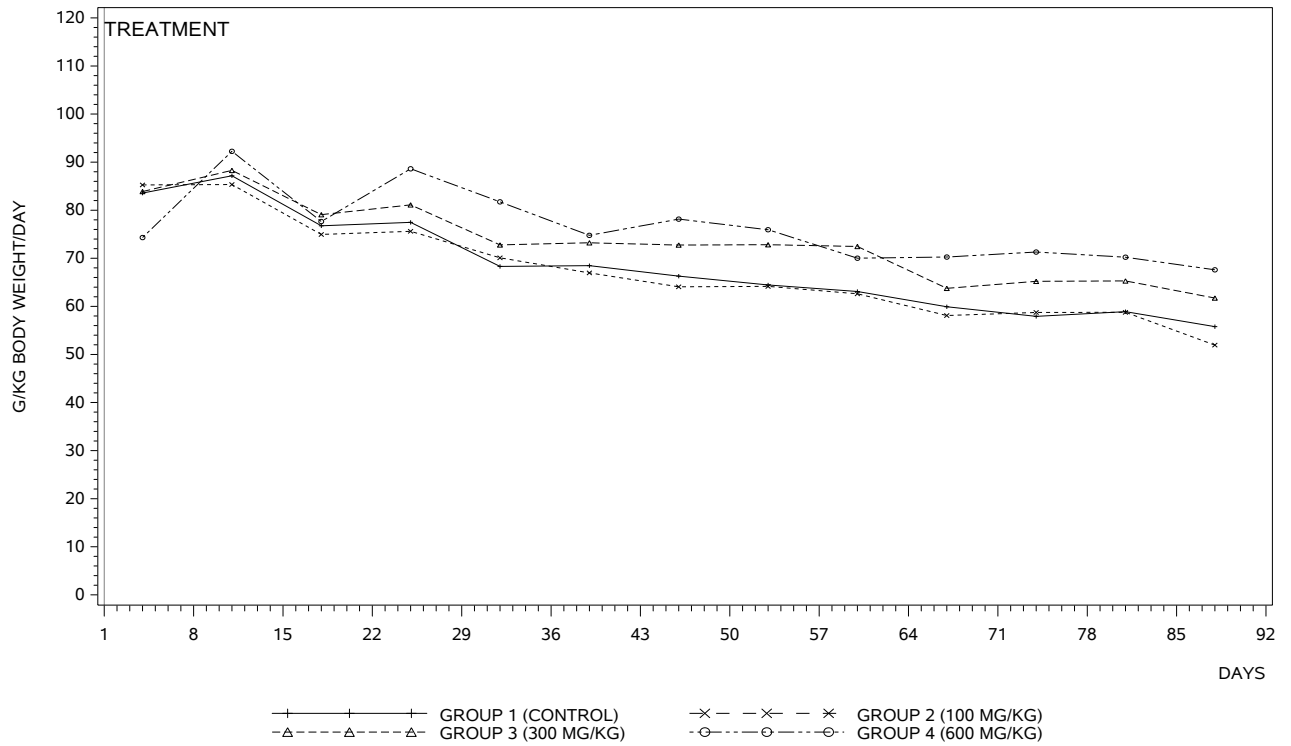
1.3 FOOD CONSUMPTION (G/ANIMAL/DAY) FEMALES



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



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



Final Report

MTDID 7831
APPENDIX 1

Project 511505

1.5 CLINICAL SIGNS SUMMARY MALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT							
	WEEK: 1	2	3	4	5	6	7	8
GROUP 1 (CONTROL)								
Breathing								
Rales (3)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
Skin / fur								
Swelling (4) (Abdomen)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
Secretion / excretion								
Salivation (3)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
GROUP 2 (100 MG/KG)								
Breathing								
Rales (3)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
Skin / fur								
Swelling (4) (Abdomen)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
Piloerection (1)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
Secretion / excretion								
Salivation (3)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
GROUP 3 (300 MG/KG)								
Breathing								
Rales (3)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
Skin / fur								
Swelling (4) (Abdomen)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
Secretion / excretion								
Salivation (3)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
Chromodacryorrhoea (3) (Neck)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
GROUP 4 (600 MG/KG)								
Posture								
Hunched posture (1)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
Breathing								
Laboured respiration (3)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
Deep respiration (1)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
Rales (3)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
Skin / fur								
Swelling (4) (Abdomen)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
Piloerection (1)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
Secretion / excretion								
Salivation (3)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
Various								
Lean (1)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
Exophthalmos (1)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11
Exophthalmos (1)	G:	11	11	11	11	11	11	11
	%:	11	11	11	11	11	11	11

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

Final Report

MTDID 7831
APPENDIX 1

Project 511505

1.5 CLINICAL SIGNS SUMMARY MALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT								
	WEEK:	1	2	3	4	5	6	7	8
	DAY:	1234567	1234567	1234567	1234567	1234567	1234567	1234567	1234567
GROUP 4 (600 MG/KG)									
(Eye right)	%:								
Opacity (1)	G:								
(Eye right)	%:								
Red (1)	G:				1				
(Snout)	%:				1				

MALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT				RECOVERY				
	WEEK:	1	2	3	4	1	2	3	4
	DAY:	71234567	1234567	1234567	1234567	1234567	1234567	1234567	1234567
GROUP 1 (CONTROL)									
Breathing									
Rales (3)	G:		11		1				
	%:		11		1				
Skin / fur									
Swelling (4)	G:		1111111111						
(Abdomen)	%:		1111111111						
Secretion / excretion									
Salivation (3)	G:		1111111111111111111111111111						
	%:		AAAAAAAAAAAAAAAAAAAAAAAAAAAA						
GROUP 2 (100 MG/KG)									
Breathing									
Rales (3)	G:								
	%:								
Skin / fur									
Swelling (4)	G:		1111111111111111111111111111						
(Abdomen)	%:		2222222222222222222222222222						
Piloerection (1)	G:								
	%:								
Secretion / excretion									
Salivation (3)	G:		1111111111111111111111111111						
	%:		AAAAAAAAAAAAAAAAAAAAAAAAAAAA						
GROUP 3 (300 MG/KG)									
Breathing									
Rales (3)	G:		1111111112111111111111111111						
	%:		122222222112332221111111112						
Skin / fur									
Swelling (4)	G:		1111111111111111111111111111						
(Abdomen)	%:		2444444444444444333333333333						
Secretion / excretion									
Salivation (3)	G:		1111111111111111111111111111						
	%:		AAAAAAAAAAAAAAAAAAAAAAAAAAAA						
Chromodacryorrhoea (3)	G:		11111						
(Neck)	%:		11111						
GROUP 4 (600 MG/KG)									
Posture									
Hunched posture (1)	G:		1	11111111111111111111111111					
	%:		1	111121111111111111112211111					
Breathing									
Laboured respiration (3)	G:								11
	%:								11
Deep respiration (1)	G:								111
	%:								111
Rales (3)	G:								11111111111111111111111111
	%:								2344433333332223333344344344

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

Final Report

MTDID 7831
APPENDIX 1

Project 511505

1.5 CLINICAL SIGNS SUMMARY MALES

SIGN (MAX. GRADE) (LOCATION)	WEEK: DAY:	TREATMENT	RECOVERY
	 12.....	1..... 4.....
		71234567123456712345671234567	1234567123456712345671234567
GROUP 4 (600 MG/KG)			
Skin / fur			
Swelling (4)	G:	11111111111111111111111111111111	1.....
(Abdomen)	%:	566777778888888888888888888888	8.....
Piloerection (1)	G:
	%:
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111
	%:	AAAAAAAAAAAAAAAAAAAAAAAAAAAAA
Various			
Lean (1)	G:	111111111111111111111111.....
	%:	111111121111111111111111.....
Exophthalmos (1)	G:	1.....
	%:	3.....
Exophthalmos (1)	G:	111111111.....
(Eye right)	%:	333333333.....
Opacity (1)	G:	11111111111111111111111111111111
(Eye right)	%:	33333333333333333333333333333333
Red (1)	G:
(Snout)	%:

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

Final Report

MTDID 7831
APPENDIX 1

Project 511505

1.5 CLINICAL SIGNS SUMMARY FEMALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT							
	WEEK: 1	2	3	4	5	6	7	8
	DAY: 12345671234567123456712345671234567123456712345671234567							
GROUP 4 (600 MG/KG)								
Various								
Dehydrated (3)	G:			1				
	%:			1				
Lean (1)	G:			111111				11
	%:			111111				12

FEMALES vrouwen

SIGN (MAX. GRADE) (LOCATION)	TREATMENT				RECOVERY			
	WEEK: 1	2	3	4	1	2	3	4
	DAY: 71234567123456712345671234567 12345671234567123456712345672							
GROUP 1 (CONTROL)								
Posture								
Hunched posture (1)	G:							
	%:							
Breathing								
Rales (3)	G:	1		1	11			
	%:	1		1	11			
Skin / fur								
Swelling (4) (Abdomen)	G:	11111111111111111111111111111111			1			
	%:	23333333333333333333333333333311			1			
Scabs (3) (Neck)	G:							
	%:							
Secretion / excretion								
Salivation (3)	G:	11111111111111111111111111111111			1			
	%:	AAAAAAAAAAAAAAAAAAAAAAAAAAAAA			A			
GROUP 2 (100 MG/KG)								
Breathing								
Rales (3)	G:				122111		1	
	%:				111111		1	
Skin / fur								
Swelling (4) (Abdomen)	G:	11111111111111111111111111111111			1			
	%:	222222222222222222222222222222			2			
Secretion / excretion								
Salivation (3)	G:	11111111111111111111111111111111			1			
	%:	AAAAAAAAAAAAAAAAAAAAAAAAAAAAA			9			
Various								
Lean (1)	G:				1			
	%:				1			
GROUP 3 (300 MG/KG)								
Breathing								
Rales (3)	G:		11111		1		1	
	%:		11221		1		1	
Skin / fur								
Swelling (4) (Abdomen)	G:	11111111111111111111111111111111			1			
	%:	233333333333333333222222222222			2			
Secretion / excretion								
Salivation (3)	G:	11111111111111111111111111111111			1			
	%:	AAAAAAAAAAAAA9AAAAAAAAAAAAA			A			
Various								
Lean (1)	G:				1			
	%:				1			
GROUP 4 (600 MG/KG)								
Posture								
Hunched posture (1)	G:	1						
	%:	1						

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

Final Report

MTDID 7831
APPENDIX 1

Project 511505

1.5 CLINICAL SIGNS SUMMARY FEMALES

SIGN (MAX. GRADE) (LOCATION)	WEEK: DAY:	TREATMENT	RECOVERY
	 12.....	1..... 4.....
		71234567123456712345671234567	12345671234567123456712345672
GROUP 4 (600 MG/KG)			
Breathing			
Laboured respiration (3)	G:
	%:
Rales (3)	G:	11111111112211111111111111111111	1.....
	%:	333331111111111111111111122333333	3.....
Skin / fur			
Swelling (4) (Abdomen)	G:	11111111111111111111111111111111	1.....
	%:	6666688888888888888888888888888888	8.....
Piloerection (1)	G:	1.....
	%:	1.....
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	1.....
	%:	AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA	A.....
Various			
Dehydrated (3)	G:
	%:
Lean (1)	G:	1.....
	%:	2.....

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

Final Report

MTDID 7831
APPENDIX 1

Project 511505

1.5 CLINICAL SIGNS SUMMARY FEMALES

SIGN (MAX. GRADE) (LOCATION)	WEEK: DAY:	TREATMENT	RECOVERY
		1 . . . 1234	1 4 12345671234567123456712345671
GROUP 1 (CONTROL)			
Breathing			
Rales (3)	G: . . 11 %: . . 11		
Secretion / excretion			
Salivation (3)	G: 1111 %: 9999		
GROUP 2 (100 MG/KG)			
Secretion / excretion			
Salivation (3)	G: 1111 %: 9AAA		
GROUP 3 (300 MG/KG)			
Secretion / excretion			
Salivation (3)	G: 1111 %: 9AAA		
GROUP 4 (1000 MG/KG)			
Breathing			
Rales (3)	G: . . 11 %: . . 11		
Skin / fur			
Swelling (4) (Abdomen)	G: 1111 %: 1111		
Alopecia (3)	G: %: 1111111111 2222222222
Secretion / excretion			
Salivation (3)	G: 1111 %: 7AAA		

Note: From Day 93 up to scheduled day of necropsy clinical signs were recorded in Project 514129
 G: Median value of the highest individual daily grades
 %: Percent of affected animals (0=less than 5%, 1=between 5% and 15%,..., A=more than 95%) .:
 Observation performed, sign not present

**1.6 FUNCTIONAL OBSERVATIONS SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
WEEK 13					
HEARING SCORE 0/1	MEDIAN	0	0	0	0
	N	5	5	5	5
PUPIL L SCORE 0/1	MEDIAN	0	0	0	0
	N	5	5	5	5
PUPIL R SCORE 0/1	MEDIAN	0	0	0	0
	N	5	5	5	5
STATIC R SCORE 0/1	MEDIAN	0	0	0	0
	N	5	5	5	5
GRIP FORE GRAM	MEAN	997	825	860	938
	ST.DEV	241	193	153	200
	N	5	5	5	5
GRIP HIND GRAM	MEAN	518	417	406	412
	ST.DEV	152	73	51	52
	N	5	5	5	5

FEMALES

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
WEEK 13					
HEARING SCORE 0/1	MEDIAN	0	0	0	0
	N	5	5	5	5
PUPIL L SCORE 0/1	MEDIAN	0	0	0	0
	N	5	5	5	5
PUPIL R SCORE 0/1	MEDIAN	0	0	0	0
	N	5	5	5	5
STATIC R SCORE 0/1	MEDIAN	0	0	0	0
	N	5	5	5	5
GRIP FORE GRAM	MEAN	1082	874	882	1037
	ST.DEV	286	205	164	239
	N	5	5	5	5
GRIP HIND GRAM	MEAN	431	411	427	472
	ST.DEV	45	27	33	61
	N	5	5	5	5

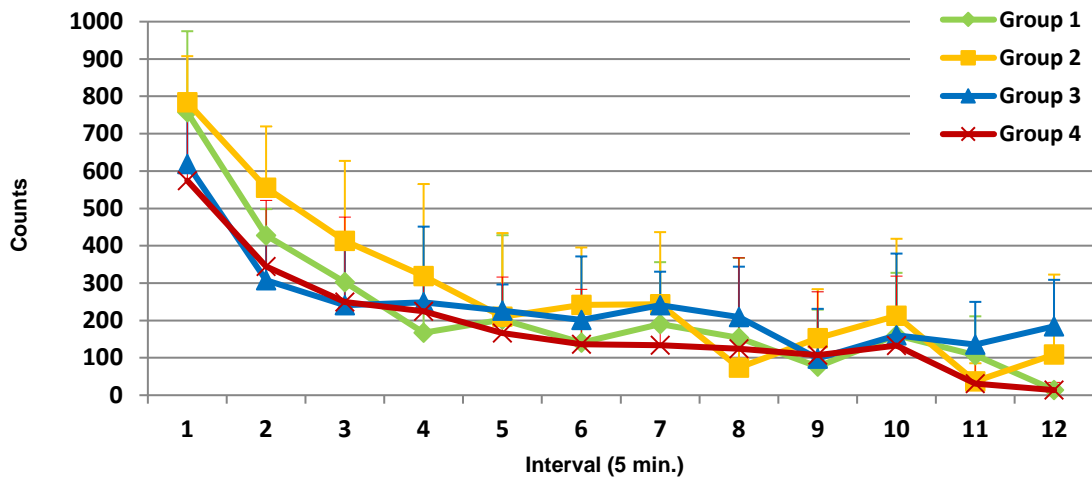
*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level
+/** Steel-test significant at 5% (+) or 1% (++) level

1.7 MOTOR ACTIVITY TEST SUMMARY
 MALES

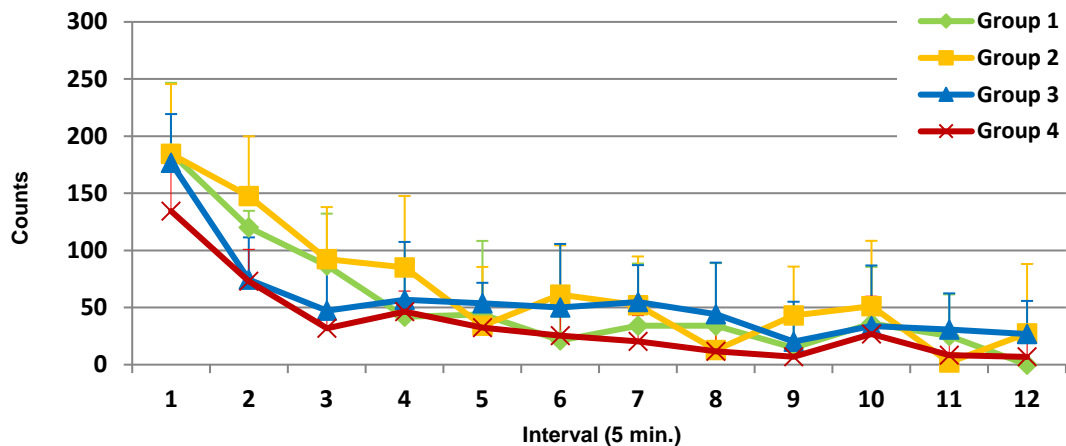
AT WEEK 12-13

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
Total Movements	MEAN ¹	2700	3352	2874	2238
	ST.DEV	968	835	634	1383
	N	5	5	5	5
Ambulations	MEAN ¹	643	793	669	424
	ST.DEV	250	321	152	111
	N	5	5	5	5

Total Movements Males²



Ambulations Males²



** Wilcoxon test significant at 5% (*) or 1% (**) level

¹ Group mean of all intervals combined

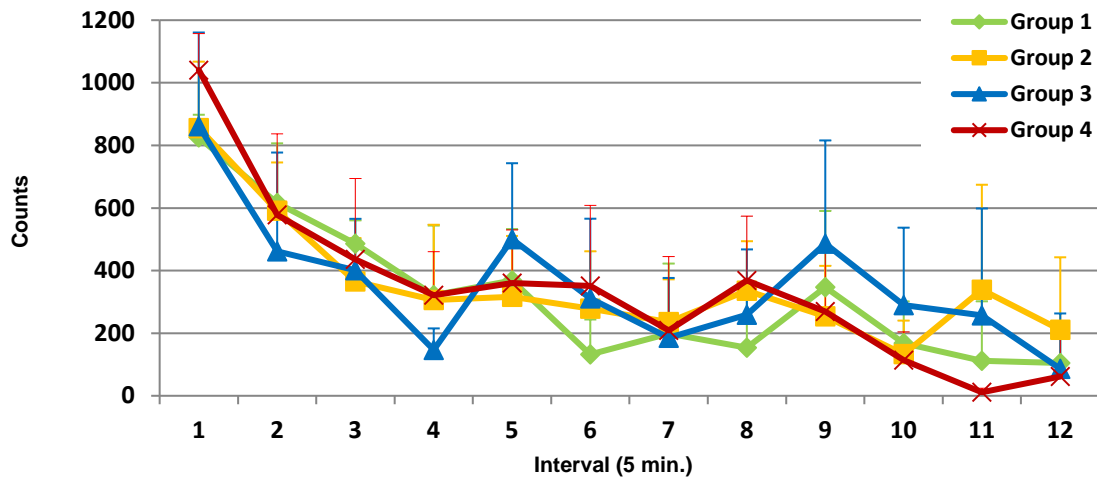
² Mean counts per interval.

1.7 MOTOR ACTIVITY TEST SUMMARY
 FEMALES

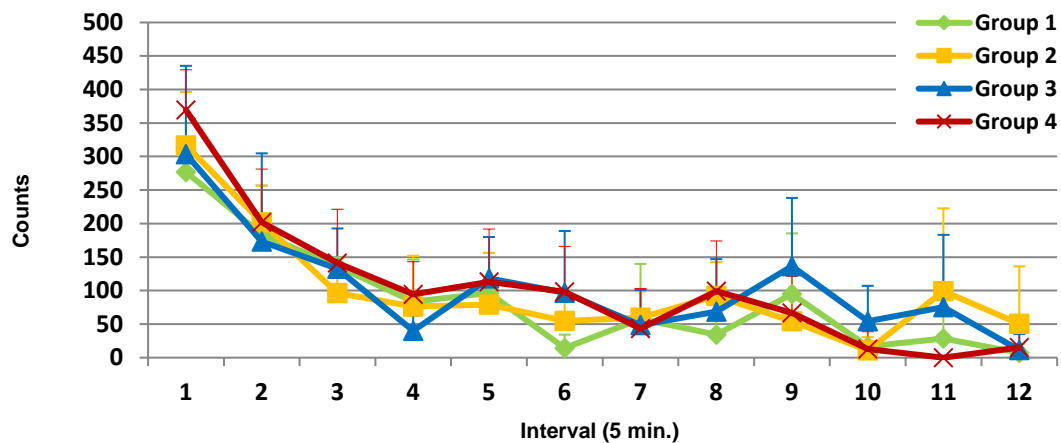
AT WEEK 12-13

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
Total Movements	MEAN ¹	3833	4221	4246	4121
	ST.DEV	969	897	2005	1004
	N	5	5	5	5
Ambulations	MEAN ¹	1030	1192	1260	1256
	ST.DEV	303	325	637	318
	N	5	5	5	5

Total Movements Females²



Ambulations Females²



*/** Wilcoxon test significant at 5% (*) or 1% (**) level

¹ Group mean of all intervals combined

² Mean counts per interval.

Final Report

MTDID 7831
APPENDIX 1

Project 511505

1.8 OPHTHALMOSCOPIC EXAMINATIONS SUMMARY MALES

	GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
PRETEST				
No Findings	7/15	5/10	5/10	8/15
Corneal Edema	1/15	0/10	1/10	4/15
Focal Corneal Edema	4/15	1/10	2/10	3/15
Focal Corneal Opacity	7/15	4/10	4/10	2/15
Haemorrhage In Retina	0/15	1/10	0/10	0/15
Pinpoint Corneal Opacities	0/15	2/10	0/10	0/15
AT WEEK 13				
No Findings	5/15			3/9
Focal Corneal Edema	3/15			1/9
Focal Corneal Opacity	10/15			6/9
Pinpoint Corneal Opacities	0/15			2/9

FEMALES

	GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
PRETEST				
No Findings	8/15	4/10	5/10	9/15
Corneal Edema	1/15	1/10	2/10	0/15
Focal Corneal Edema	2/15	2/10	3/10	2/15
Focal Corneal Opacity	6/15	5/10	3/10	4/15
Pinpoint Corneal Opacities	0/15	0/10	0/10	1/15
AT WEEK 13				
No Findings	3/15			2/11
Focal Corneal Edema	4/15			1/11
Focal Corneal Opacity	11/15			9/11

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

**1.9 BODY WEIGHTS (GRAM) SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
TREATMENT					
DAY 1	MEAN	168	171	172	169
WEEK 1	ST.DEV	5.6	10.7	4.6	7.7
	N	15	10	10	15
DAY 8	MEAN	212	215	210	199 **
WEEK 2	ST.DEV	8.2	14.1	7.8	13.2
	N	15	10	10	15
DAY 15	MEAN	252	256	246	234 **
WEEK 3	ST.DEV	12.8	17.9	10.4	16.3
	N	15	10	10	15
DAY 22	MEAN	282	287	275	260 **
WEEK 4	ST.DEV	15.9	18.2	12.3	16.4
	N	15	10	10	14
DAY 29	MEAN	302	305	290	260 **
WEEK 5	ST.DEV	19.0	22.5	16.7	28.5
	N	15	10	10	13
DAY 33	MEAN	313	318	303	276 **
WEEK 5	ST.DEV	21.6	22.4	17.7	22.5
	N	15	10	10	12
DAY 34	MEAN	317	319	305	274 **
WEEK 5	ST.DEV	21.9	22.8	17.0	26.6
	N	15	10	10	12
DAY 36	MEAN	322	326	303	282 **
WEEK 6	ST.DEV	23.1	22.4	22.0	27.1
	N	15	10	10	12
DAY 43	MEAN	336	337	317	298 **
WEEK 7	ST.DEV	24.3	24.3	19.3	29.2
	N	15	10	10	12
DAY 50	MEAN	349	348	322	304 **
WEEK 8	ST.DEV	26.3	25.5	19.8	36.2
	N	15	10	10	12
DAY 57	MEAN	360	357	331 *	305 **
WEEK 9	ST.DEV	28.2	25.5	19.4	37.2
	N	15	10	10	12
DAY 64	MEAN	369	367	337 *	313 **
WEEK 10	ST.DEV	30.3	25.9	20.4	34.4
	N	15	10	10	11
DAY 71	MEAN	377	377	344 *	322 **
WEEK 11	ST.DEV	30.9	25.7	22.8	41.2
	N	15	10	10	10
DAY 78	MEAN	384	386	352	323 **
WEEK 12	ST.DEV	34.1	25.9	24.8	43.4
	N	15	10	10	10
DAY 85	MEAN	390	396	359	314 **
WEEK 13	ST.DEV	35.6	27.2	27.1	48.4
	N	15	10	10	10

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

**1.9 BODY WEIGHTS (GRAM) SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
TREATMENT					
DAY 91	MEAN	393	401	361 *	336 **
WEEK 13	ST.DEV	36.4	27.8	24.9	27.6
	N	15	10	10	9
RECOVERY					
DAY 1	MEAN	368			319 *
WEEK 1	ST.DEV	26.1			33.3
	N	5			4
DAY 8	MEAN	390			344
WEEK 2	ST.DEV	31.9			37.2
	N	5			4
DAY 15	MEAN	401			370
WEEK 3	ST.DEV	32.4			37.8
	N	5			4
DAY 22	MEAN	407			380
WEEK 4	ST.DEV	31.3			40.8
	N	5			4
DAY 28	MEAN	414			386
WEEK 4	ST.DEV	31.2			43.1
	N	5			4

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

**1.9 BODY WEIGHTS (GRAM) SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
TREATMENT					
DAY 1	MEAN	137	135	137	134
WEEK 1	ST.DEV	6.2	6.7	8.3	8.1
	N	15	10	10	15
DAY 8	MEAN	158	158	159	156
WEEK 2	ST.DEV	5.5	5.8	6.9	10.2
	N	15	10	10	15
DAY 15	MEAN	181	178	179	177
WEEK 3	ST.DEV	7.8	10.7	7.5	11.9
	N	15	10	10	15
DAY 22	MEAN	197	192	192	189
WEEK 4	ST.DEV	9.0	14.8	6.4	16.9
	N	15	10	10	14
DAY 29	MEAN	208	202	201	205
WEEK 5	ST.DEV	9.3	12.1	8.6	15.4
	N	15	10	10	13
DAY 33	MEAN	214	209	205	202 *
WEEK 5	ST.DEV	9.7	14.7	10.1	15.4
	N	15	10	10	12
DAY 34	MEAN	217	211	209	203 *
WEEK 5	ST.DEV	11.0	13.6	8.4	15.1
	N	15	10	10	12
DAY 36	MEAN	219	213	212	210
WEEK 6	ST.DEV	10.3	15.4	9.4	18.0
	N	15	10	10	12
DAY 43	MEAN	225	221	218	219
WEEK 7	ST.DEV	10.6	14.9	11.1	18.2
	N	15	10	10	12
DAY 50	MEAN	235	227	226	226
WEEK 8	ST.DEV	13.3	15.3	12.3	17.7
	N	15	10	10	12
DAY 57	MEAN	239	231	230	228
WEEK 9	ST.DEV	14.3	14.0	12.1	21.8
	N	15	10	10	12
DAY 64	MEAN	243	238	234	233
WEEK 10	ST.DEV	11.9	18.9	13.1	20.1
	N	15	10	10	11
DAY 71	MEAN	244	240	236	235
WEEK 11	ST.DEV	11.8	17.6	10.5	22.3
	N	15	10	10	11
DAY 78	MEAN	247	243	235	235
WEEK 12	ST.DEV	13.4	16.4	12.7	20.6
	N	15	10	9	11
DAY 85	MEAN	250	246	237	236
WEEK 13	ST.DEV	13.1	17.4	15.7	18.8
	N	15	10	9	11

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

**1.9 BODY WEIGHTS (GRAM) SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
TREATMENT					
DAY 91	MEAN	252	246	239	242
WEEK 13	ST.DEV	12.9	21.0	11.9	22.8
	N	15	10	9	11

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

**1.9 BODY WEIGHTS (GRAM) SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 4 1000 MG/KG
RECOVERY			
DAY 1	MEAN	237	219
WEEK 1	ST.DEV	12.2	26.8
	N	5	5
DAY 8	MEAN	253	231
WEEK 2	ST.DEV	12.1	28.3
	N	5	5
DAY 15	MEAN	257	248
WEEK 3	ST.DEV	11.5	25.3
	N	5	5
DAY 22	MEAN	258	245
WEEK 4	ST.DEV	14.3	23.9
	N	5	5
DAY 28	MEAN	261	244
WEEK 4	ST.DEV	11.4	26.0
	N	5	5

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

**1.10 BODY WEIGHT GAIN (%) SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
TREATMENT					
DAY 1	MEAN	0	0	0	0
WEEK 1	ST.DEV	0.0	0.0	0.0	0.0
	N	15	10	10	15
DAY 8	MEAN	26	26	22	17 **
WEEK 2	ST.DEV	2.6	2.8	3.5	5.1
	N	15	10	10	15
DAY 15	MEAN	49	50	44	38 **
WEEK 3	ST.DEV	5.1	5.5	7.1	6.2
	N	15	10	10	15
DAY 22	MEAN	67	68	60	53 **
WEEK 4	ST.DEV	6.4	6.6	7.7	8.2
	N	15	10	10	14
DAY 29	MEAN	79	79	69	53 **
WEEK 5	ST.DEV	8.4	9.8	9.7	13.7
	N	15	10	10	13
DAY 33	MEAN	86	86	77	62 **
WEEK 5	ST.DEV	9.8	9.0	10.6	10.2
	N	15	10	10	12
DAY 34	MEAN	88	87	78	61 **
WEEK 5	ST.DEV	10.2	8.8	10.2	13.6
	N	15	10	10	12
DAY 36	MEAN	91	91	77 *	66 **
WEEK 6	ST.DEV	10.6	9.1	13.8	14.0
	N	15	10	10	12
DAY 43	MEAN	100	97	85 *	75 **
WEEK 7	ST.DEV	11.2	9.4	11.5	15.2
	N	15	10	10	12
DAY 50	MEAN	107	104	88 **	78 **
WEEK 8	ST.DEV	12.0	9.4	12.8	20.2
	N	15	10	10	12
DAY 57	MEAN	113	109	93 **	79 **
WEEK 9	ST.DEV	12.8	10.0	11.7	21.3
	N	15	10	10	12
DAY 64	MEAN	119	115	96 **	84 **
WEEK 10	ST.DEV	13.7	10.5	11.5	18.7
	N	15	10	10	11
DAY 71	MEAN	124	121	100 **	88 **
WEEK 11	ST.DEV	14.5	10.9	12.9	23.7
	N	15	10	10	10
DAY 78	MEAN	128	126	105 **	88 **
WEEK 12	ST.DEV	16.5	11.4	14.1	25.0
	N	15	10	10	10
DAY 85	MEAN	132	132	109 *	83 **
WEEK 13	ST.DEV	17.4	12.1	15.6	29.1
	N	15	10	10	10

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

**1.10 BODY WEIGHT GAIN (%) SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
TREATMENT					
DAY 91	MEAN	133	135	111 **	97 **
WEEK 13	ST.DEV	17.4	12.3	14.6	15.3
	N	15	10	10	9
RECOVERY					
DAY 1	MEAN	122			87 **
WEEK 1	ST.DEV	14.9			11.3
	N	5			4
DAY 8	MEAN	135			102 *
WEEK 2	ST.DEV	17.6			12.8
	N	5			4
DAY 15	MEAN	142			117
WEEK 3	ST.DEV	18.0			12.6
	N	5			4
DAY 22	MEAN	146			123
WEEK 4	ST.DEV	17.3			14.1
	N	5			4
DAY 28	MEAN	150			127
WEEK 4	ST.DEV	17.1			16.3
	N	5			4

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

**1.10 BODY WEIGHT GAIN (%) SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
TREATMENT					
DAY 1	MEAN	0	0	0	0
WEEK 1	ST.DEV	0.0	0.0	0.0	0.0
	N	15	10	10	15
DAY 8	MEAN	16	17	16	16
WEEK 2	ST.DEV	3.5	2.8	3.1	3.2
	N	15	10	10	15
DAY 15	MEAN	32	32	31	32
WEEK 3	ST.DEV	4.2	3.4	4.9	5.1
	N	15	10	10	15
DAY 22	MEAN	44	41	41	41
WEEK 4	ST.DEV	5.0	5.4	6.4	10.7
	N	15	10	10	14
DAY 29	MEAN	52	49	47	53
WEEK 5	ST.DEV	5.9	3.1	5.1	7.6
	N	15	10	10	13
DAY 33	MEAN	57	54	50 *	51
WEEK 5	ST.DEV	6.2	4.3	6.0	5.9
	N	15	10	10	12
DAY 34	MEAN	59	56	53	51 **
WEEK 5	ST.DEV	6.7	4.2	6.7	5.5
	N	15	10	10	12
DAY 36	MEAN	60	57	55	57
WEEK 6	ST.DEV	8.1	7.2	6.5	7.9
	N	15	10	10	12
DAY 43	MEAN	64	63	59	64
WEEK 7	ST.DEV	7.4	5.2	9.8	7.5
	N	15	10	10	12
DAY 50	MEAN	71	67	66	69
WEEK 8	ST.DEV	9.0	5.4	10.2	7.0
	N	15	10	10	12
DAY 57	MEAN	74	71	68	70
WEEK 9	ST.DEV	9.9	4.2	7.4	9.7
	N	15	10	10	12
DAY 64	MEAN	77	75	71	74
WEEK 10	ST.DEV	9.1	7.3	10.1	8.4
	N	15	10	10	11
DAY 71	MEAN	78	77	73	76
WEEK 11	ST.DEV	7.7	6.7	10.9	9.1
	N	15	10	10	11
DAY 78	MEAN	80	79	74	76
WEEK 12	ST.DEV	9.0	6.2	12.4	8.3
	N	15	10	9	11
DAY 85	MEAN	82	82	75	77
WEEK 13	ST.DEV	9.1	6.5	13.4	7.6
	N	15	10	9	11

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

**1.10 BODY WEIGHT GAIN (%) SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
TREATMENT					
DAY 91	MEAN	84	82	77	81
WEEK 13	ST.DEV	8.0	9.6	12.6	9.2
	N	15	10	9	11

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

**1.11 FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
TREATMENT					
DAYS 1-8	MEAN	19	18	18	16 **
WEEKS 1-2	ST.DEV	0.6	0.2	0.4	0.7
	N (CAGE)	3	2	2	3
DAYS 8-15	MEAN	22	22	21	21
WEEKS 2-3	ST.DEV	0.7	0.8	0.8	0.9
	N (CAGE)	3	2	2	3
DAYS 15-22	MEAN	21	22	22	20
WEEKS 3-4	ST.DEV	0.7	0.8	0.4	2.8
	N (CAGE)	3	2	2	3
DAYS 22-29	MEAN	21	22	21	19
WEEKS 4-5	ST.DEV	0.4	2.2	0.2	2.4
	N (CAGE)	3	2	2	3
DAYS 29-36	MEAN	20	20	19	21
WEEKS 5-6	ST.DEV	0.8	0.6	0.5	2.8
	N (CAGE)	3	2	2	3
DAYS 36-43	MEAN	20	20	20	21
WEEKS 6-7	ST.DEV	0.8	0.8	0.6	2.3
	N (CAGE)	3	2	2	3
DAYS 43-50	MEAN	20	20	18	21
WEEKS 7-8	ST.DEV	0.6	0.2	0.1	1.4
	N (CAGE)	3	2	2	3
DAYS 50-57	MEAN	20	20	20	20
WEEKS 8-9	ST.DEV	0.8	0.5	1.3	1.7
	N (CAGE)	3	2	2	3
DAYS 57-64	MEAN	21	20	20	20
WEEKS 9-10	ST.DEV	0.8	0.3	0.6	2.8
	N (CAGE)	3	2	2	3
DAYS 64-71	MEAN	19	20	19	20
WEEKS 10-11	ST.DEV	0.8	1.1	0.0	1.6
	N (CAGE)	3	2	2	3
DAYS 71-78	MEAN	19	20	21	21
WEEKS 11-12	ST.DEV	1.2	0.5	1.1	1.2
	N (CAGE)	3	2	2	3
DAYS 78-85	MEAN	19	20	20	18
WEEKS 12-13	ST.DEV	0.7	0.0	1.4	2.0
	N (CAGE)	3	2	2	3
DAYS 85-91	MEAN	18	19	19	21 *
WEEK 13	ST.DEV	1.2	0.0	0.5	1.0
	N (CAGE)	3	2	2	3
MEAN OF MEANS OVER TREATMENT	MEAN	20	20	20	20
RECOVERY					
DAYS 2-8	MEAN	20			23
WEEKS 1-2	ST.DEV	---			1.2
	N (CAGE)	1			2

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

**1.11 FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
RECOVERY					
DAYS 8-15	MEAN	21			24
WEEKS 2-3	ST.DEV	---			1.7
	N (CAGE)	1			2
DAYS 15-22	MEAN	---			26
WEEKS 3-4	ST.DEV	---			0.9
	N (CAGE)	0 x			2
DAYS 22-28	MEAN	20			21
WEEK 4	ST.DEV	---			1.7
	N (CAGE)	1			2
MEAN OF MEANS OVER RECOVERY	MEAN	21			24

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

**1.11 FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
TREATMENT					
DAYS 1-8	MEAN	13	13	13	12 **
WEEKS 1-2	ST.DEV	0.3	0.6	0.0	0.5
	N (CAGE)	3	2	2	3
DAYS 8-15	MEAN	16	15	16	16
WEEKS 2-3	ST.DEV	0.1	0.9	0.7	0.4
	N (CAGE)	3	2	2	3
DAYS 15-22	MEAN	15	14	15	15
WEEKS 3-4	ST.DEV	0.3	0.4	0.4	1.7
	N (CAGE)	3	2	2	3
DAYS 22-29	MEAN	16	15	16	18 **
WEEKS 4-5	ST.DEV	0.0	0.2	0.6	0.8
	N (CAGE)	3	2	2	3
DAYS 29-36	MEAN	15	15	15	17 *
WEEKS 5-6	ST.DEV	0.3	0.3	0.5	1.1
	N (CAGE)	3	2	2	3
DAYS 36-43	MEAN	15	15	16	16
WEEKS 6-7	ST.DEV	0.0	0.6	1.1	1.1
	N (CAGE)	3	2	2	3
DAYS 43-50	MEAN	16	15	16	18 **
WEEKS 7-8	ST.DEV	0.1	0.6	0.6	0.3
	N (CAGE)	3	2	2	3
DAYS 50-57	MEAN	15	15	17 *	17 **
WEEKS 8-9	ST.DEV	0.3	0.7	0.5	0.3
	N (CAGE)	3	2	2	3
DAYS 57-64	MEAN	15	15	17	16
WEEKS 9-10	ST.DEV	0.1	1.4	0.6	3.1
	N (CAGE)	3	2	2	3
DAYS 64-71	MEAN	15	14	15	16
WEEKS 10-11	ST.DEV	0.1	0.8	0.4	1.3
	N (CAGE)	3	2	2	3
DAYS 71-78	MEAN	14	14	15	17
WEEKS 11-12	ST.DEV	0.1	1.0	0.9	1.3
	N (CAGE)	3	2	2	3
DAYS 78-85	MEAN	15	14	16	16 **
WEEKS 12-13	ST.DEV	0.2	0.6	0.0	0.6
	N (CAGE)	3	2	2	3
DAYS 85-91	MEAN	14	13	15	16
WEEK 13	ST.DEV	0.2	0.8	0.3	1.7
	N (CAGE)	3	2	2	3
MEAN OF MEANS OVER TREATMENT	MEAN	15	14	16	16

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

**1.11 FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 4 1000 MG/KG
RECOVERY			
DAYS 1-8	MEAN	17	17
WEEKS 1-2	ST.DEV	---	0.8
	N (CAGE)	1	2
DAYS 8-15	MEAN	---	---
WEEKS 2-3	ST.DEV	---	---
	N (CAGE)	0	0
DAYS 15-22	MEAN	12	11
WEEKS 3-4	ST.DEV	---	---
	N (CAGE)	1	1
DAYS 22-28	MEAN	16	16
WEEK 4	ST.DEV	---	2.2
	N (CAGE)	1	2
MEAN OF MEANS OVER RECOVERY	MEAN	15	15

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

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

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
TREATMENT					
DAYS 1-8	MEAN	88	83	84	79 **
WEEKS 1-2	ST.DEV	0.9	3.1	1.3	2.4
	N (CAGE)	3	2	2	3
DAYS 8-15	MEAN	86	87	86	89 *
WEEKS 2-3	ST.DEV	0.6	0.6	1.5	1.2
	N (CAGE)	3	2	2	3
DAYS 15-22	MEAN	76	77	80	75
WEEKS 3-4	ST.DEV	1.6	0.6	2.1	9.1
	N (CAGE)	3	2	2	3
DAYS 22-29	MEAN	71	71	73	71
WEEKS 4-5	ST.DEV	2.0	2.9	1.5	6.5
	N (CAGE)	3	2	2	3
DAYS 29-36	MEAN	64	63	62	75 *
WEEKS 5-6	ST.DEV	1.8	1.4	1.2	5.8
	N (CAGE)	3	2	2	3
DAYS 36-43	MEAN	60	60	62	69 **
WEEKS 6-7	ST.DEV	1.0	0.2	1.4	2.9
	N (CAGE)	3	2	2	3
DAYS 43-50	MEAN	58	58	57	68 **
WEEKS 7-8	ST.DEV	0.7	2.5	0.3	4.6
	N (CAGE)	3	2	2	3
DAYS 50-57	MEAN	56	56	60	65 **
WEEKS 8-9	ST.DEV	1.1	2.7	3.5	0.3
	N (CAGE)	3	2	2	3
DAYS 57-64	MEAN	56	55	59	63
WEEKS 9-10	ST.DEV	1.4	2.5	1.4	5.8
	N (CAGE)	3	2	2	3
DAYS 64-71	MEAN	51	52	56	62 *
WEEKS 10-11	ST.DEV	1.8	3.8	0.1	6.0
	N (CAGE)	3	2	2	3
DAYS 71-78	MEAN	50	52	58 *	66 **
WEEKS 11-12	ST.DEV	2.5	2.1	2.7	2.8
	N (CAGE)	3	2	2	3
DAYS 78-85	MEAN	49	50	57	59
WEEKS 12-13	ST.DEV	0.8	1.3	3.1	6.9
	N (CAGE)	3	2	2	3
DAYS 85-91	MEAN	46	48	52 *	63 **
WEEK 13	ST.DEV	2.3	1.1	1.3	1.7
	N (CAGE)	3	2	2	3
MEAN OF MEANS OVER TREATMENT	MEAN	62	62	65	70
RECOVERY					
DAYS 2-8	MEAN	52			67
WEEKS 1-2	ST.DEV	---			1.5
	N (CAGE)	1			2

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

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

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
RECOVERY					
DAYS 8-15	MEAN	52			66 *
WEEKS 2-3	ST.DEV	---			0.4
	N (CAGE)	1			2
DAYS 15-22	MEAN	---			69
WEEKS 3-4	ST.DEV	---			2.0
	N (CAGE)	0 x			2
DAYS 22-28	MEAN	49			54
WEEK 4	ST.DEV	---			1.0
	N (CAGE)	1			2
MEAN OF MEANS OVER RECOVERY	MEAN	51			64

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

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

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
TREATMENT					
DAYS 1-8	MEAN	84	85	84	74 *
WEEKS 1-2	ST.DEV	3.3	2.8	1.8	3.4
	N (CAGE)	3	2	2	3
DAYS 8-15	MEAN	87	85	88	92 *
WEEKS 2-3	ST.DEV	0.8	3.6	1.5	0.9
	N (CAGE)	3	2	2	3
DAYS 15-22	MEAN	77	75	79	78
WEEKS 3-4	ST.DEV	0.6	0.7	1.6	9.1
	N (CAGE)	3	2	2	3
DAYS 22-29	MEAN	77	76	81	89 **
WEEKS 4-5	ST.DEV	1.3	1.0	0.7	3.5
	N (CAGE)	3	2	2	3
DAYS 29-36	MEAN	68	70	73	82 **
WEEKS 5-6	ST.DEV	1.7	0.3	0.2	2.9
	N (CAGE)	3	2	2	3
DAYS 36-43	MEAN	68	67	73 *	75 **
WEEKS 6-7	ST.DEV	0.7	1.0	2.4	1.9
	N (CAGE)	3	2	2	3
DAYS 43-50	MEAN	66	64	73 **	78 **
WEEKS 7-8	ST.DEV	0.9	0.9	0.1	1.5
	N (CAGE)	3	2	2	3
DAYS 50-57	MEAN	64	64	73 **	76 **
WEEKS 8-9	ST.DEV	0.8	0.9	1.3	2.0
	N (CAGE)	3	2	2	3
DAYS 57-64	MEAN	63	63	72	70
WEEKS 9-10	ST.DEV	1.1	3.7	0.9	10.6
	N (CAGE)	3	2	2	3
DAYS 64-71	MEAN	60	58	64	70 **
WEEKS 10-11	ST.DEV	0.6	1.5	0.0	2.0
	N (CAGE)	3	2	2	3
DAYS 71-78	MEAN	58	59	65	71 **
WEEKS 11-12	ST.DEV	0.8	1.5	6.9	2.4
	N (CAGE)	3	2	2	3
DAYS 78-85	MEAN	59	59	65	70 **
WEEKS 12-13	ST.DEV	1.1	0.1	3.4	3.4
	N (CAGE)	3	2	2	3
DAYS 85-91	MEAN	56	52	62	68 **
WEEK 13	ST.DEV	0.2	1.9	3.3	2.5
	N (CAGE)	3	2	2	3
MEAN OF MEANS OVER TREATMENT	MEAN	68	67	73	76

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

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

		GROUP 1 CONTROL	GROUP 4 1000 MG/KG
RECOVERY			
DAYS 1-8	MEAN	68	74
WEEKS 1-2	ST.DEV	---	5.1
	N (CAGE)	1	2
DAYS 8-15	MEAN	---	---
WEEKS 2-3	ST.DEV	---	---
	N (CAGE)	0	0
DAYS 15-22	MEAN	46	47
WEEKS 3-4	ST.DEV	---	---
	N (CAGE)	1	1
DAYS 22-28	MEAN	63	64
WEEK 4	ST.DEV	---	1.9
	N (CAGE)	1	2
MEAN OF MEANS OVER RECOVERY	MEAN	59	62

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

**1.13 HAEMATOLOGY SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
END OF TREATMENT					
WBC	MEAN	8.1	7.8	7.6	8.0
10E9/L	ST.DEV	2.0	1.8	1.8	2.4
	N	12	10	9	8
Neutrophils	MEAN	16.3	15.4	15.3	20.8
%WBC	ST.DEV	3.5	3.6	4.4	6.9
	N	12	10	9	8
Lymphocytes	MEAN	80.2	81.8	80.5	76.1
%WBC	ST.DEV	3.7	4.1	4.3	7.3
	N	12	10	9	8
Monocytes	MEAN	1.7	1.4	2.3	1.7
%WBC	ST.DEV	0.4	0.3	1.2	0.6
	N	12	10	9	8
Eosinophils	MEAN	1.7	1.3	1.8	1.3
%WBC	ST.DEV	0.8	0.4	0.6	0.4
	N	12	10	9	8
Basophils	MEAN	0.1	0.1	0.1	0.1
%WBC	ST.DEV	0.1	0.1	0.1	0.0
	N	12	10	9	8
Red blood cells	MEAN	9.67	9.36	8.78 **	9.16 *
10E12/L	ST.DEV	0.42	0.35	0.35	0.63
	N	12	10	9	8
Reticulocytes	MEAN	2.3	2.1	2.1 +	2.6
%RBC	ST.DEV	0.4	0.3	0.5	0.7
	N	12	10	9	8
RDW	MEAN	12.6	12.4	13.9	13.3
%	ST.DEV	0.4	0.6	3.1	0.6
	N	12	10	9	8
Haemoglobin	MEAN	10.0	9.9	9.3 **	9.6 *
mmol/L	ST.DEV	0.2	0.4	0.3	0.5
	N	12	10	9	8
Haematocrit	MEAN	0.492	0.486	0.453 **	0.469 *
L/L	ST.DEV	0.013	0.021	0.019	0.026
	N	12	10	9	8
MCV	MEAN	50.9	52.0	51.7	51.3
fL	ST.DEV	1.3	1.1	1.1	1.6
	N	12	10	9	8
MCH	MEAN	1.04	1.06	1.06	1.04
fmol	ST.DEV	0.04	0.03	0.02	0.04
	N	12	10	9	8
MCHC	MEAN	20.41	20.29	20.49	20.35
mmol/L	ST.DEV	0.39	0.39	0.60	0.39
	N	12	10	9	8
Platelets	MEAN	766	768	802	735
10E9/L	ST.DEV	94	69	98	111
	N	12	10	9	8

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

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

**1.13 HAEMATOLOGY SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
END OF TREATMENT					
PT s	MEAN	16.7	16.3	16.2	16.6
	ST.DEV	0.9	0.6	1.1	1.5
	N	12	10	9	8
APTT s	MEAN	19.0	19.9	19.3	18.3
	ST.DEV	2.1	1.7	2.1	1.7
	N	12	10	9	8

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

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

**1.13 HAEMATOLOGY SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
END OF RECOVERY					
WBC	MEAN	7.0			7.4
10E9/L	ST.DEV	1.4			0.9
	N	5			4
Neutrophils	MEAN	17.6			15.3
%WBC	ST.DEV	1.7			4.7
	N	5			4
Lymphocytes	MEAN	79.2			82.2
%WBC	ST.DEV	1.9			4.7
	N	5			4
Monocytes	MEAN	1.5			1.3
%WBC	ST.DEV	0.4			0.2
	N	5			4
Eosinophils	MEAN	1.6			1.1
%WBC	ST.DEV	0.3			0.4
	N	5			4
Basophils	MEAN	0.2			0.2
%WBC	ST.DEV	0.1			0.1
	N	5			4
Red blood cells	MEAN	9.32			9.00
10E12/L	ST.DEV	0.32			0.34
	N	5			4
Reticulocytes	MEAN	2.0			1.9
%RBC	ST.DEV	0.3			0.2
	N	5			4
RDW	MEAN	12.6			12.7
%	ST.DEV	0.3			0.3
	N	5			4
Haemoglobin	MEAN	10.1			9.7
mmol/L	ST.DEV	0.4			0.2
	N	5			4
Haematocrit	MEAN	0.490			0.470
L/L	ST.DEV	0.016			0.009
	N	5			4
MCV	MEAN	52.6			52.2
fL	ST.DEV	0.7			1.5
	N	5			4
MCH	MEAN	1.08			1.07
fmol	ST.DEV	0.02			0.03
	N	5			4
MCHC	MEAN	20.55			20.54
mmol/L	ST.DEV	0.45			0.20
	N	5			4
Platelets	MEAN	743			784
10E9/L	ST.DEV	83			103
	N	5			4

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

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

**1.13 HAEMATOLOGY SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
END OF RECOVERY					
PT	MEAN	17.3			18.7
s	ST.DEV	1.9			0.9
	N	5			4
APTT	MEAN	17.7			18.7
s	ST.DEV	1.9			1.4
	N	5			4

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

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

**1.13 HAEMATOLOGY SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
END OF TREATMENT					
WBC	MEAN	5.1	6.0	6.1	8.2 **
10E9/L	ST.DEV	1.6	1.1	1.3	2.0
	N	13	9	9	11
Neutrophils	MEAN	14.4	16.1	19.0	19.2
%WBC	ST.DEV	4.4	4.8	5.3	5.2
	N	13	9	9	11
Lymphocytes	MEAN	82.7	79.9	76.9 +	76.7 +
%WBC	ST.DEV	4.6	5.2	6.0	5.8
	N	13	9	9	11
Monocytes	MEAN	1.8	2.3	2.5	2.4
%WBC	ST.DEV	0.6	0.6	1.4	1.3
	N	13	9	9	11
Eosinophils	MEAN	1.0	1.6	1.5	1.6
%WBC	ST.DEV	0.6	0.5	1.0	0.7
	N	13	9	9	11
Basophils	MEAN	0.1	0.1	0.1	0.1
%WBC	ST.DEV	0.1	0.1	0.1	0.1
	N	13	9	9	11
Red blood cells	MEAN	7.87	8.33	8.31	8.72 **
10E12/L	ST.DEV	0.93	0.46	0.45	0.58
	N	13	9	9	11
Reticulocytes	MEAN	6.2	2.7 +	2.5 ++	2.5 +
%RBC	ST.DEV	3.5	0.3	0.6	0.9
	N	13	9	9	11
RDW	MEAN	14.0	11.3 **	11.9 *	12.5
%	ST.DEV	2.7	0.3	0.7	0.6
	N	13	9	9	11
Haemoglobin	MEAN	8.9	9.3	9.2	9.4
mmol/L	ST.DEV	0.8	0.4	0.3	0.5
	N	13	9	9	11
Haematocrit	MEAN	0.427	0.450	0.443	0.452
L/L	ST.DEV	0.036	0.022	0.018	0.021
	N	13	9	9	11
MCV	MEAN	54.5	54.0	53.3	51.9 **
fL	ST.DEV	2.2	0.7	1.7	1.5
	N	13	9	9	11
MCH	MEAN	1.13	1.11	1.11	1.07 **
fmol	ST.DEV	0.05	0.03	0.04	0.03
	N	13	9	9	11
MCHC	MEAN	20.73	20.58	20.86	20.71
mmol/L	ST.DEV	0.43	0.36	0.32	0.32
	N	13	9	9	11
Platelets	MEAN	782	720	670	696
10E9/L	ST.DEV	156	85	81	144
	N	13	9	9	11

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

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

**1.13 HAEMATOLOGY SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
END OF TREATMENT					
PT s	MEAN	15.9	16.0	15.9	16.1
	ST.DEV	0.3	0.5	0.4	0.4
	N	13	9	9	11
APTT s	MEAN	18.3	21.0 **	19.6	17.5
	ST.DEV	2.2	1.0	0.7	1.9
	N	13	9	9	11

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

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

**1.13 HAEMATOLOGY SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
END OF RECOVERY					
WBC	MEAN	4.0			5.1
10E9/L	ST.DEV	1.5			1.2
	N	5			5
Neutrophils	MEAN	14.1			13.5
%WBC	ST.DEV	3.5			5.4
	N	5			5
Lymphocytes	MEAN	82.3			82.5
%WBC	ST.DEV	3.9			6.6
	N	5			5
Monocytes	MEAN	2.0			2.1
%WBC	ST.DEV	0.7			0.8
	N	5			5
Eosinophils	MEAN	1.6			1.8
%WBC	ST.DEV	0.4			0.6
	N	5			5
Basophils	MEAN	0.1			0.1
%WBC	ST.DEV	0.0			0.0
	N	5			5
Red blood cells	MEAN	8.74			8.87
10E12/L	ST.DEV	0.78			0.30
	N	5			5
Reticulocytes	MEAN	2.0			1.8
%RBC	ST.DEV	0.2			0.4
	N	5			5
RDW	MEAN	12.1			11.9
%	ST.DEV	1.0			0.7
	N	5			5
Haemoglobin	MEAN	9.8			9.9
mmol/L	ST.DEV	0.7			0.2
	N	5			5
Haematocrit	MEAN	0.469			0.479
L/L	ST.DEV	0.036			0.013
	N	5			5
MCV	MEAN	53.7			54.0
fL	ST.DEV	1.4			1.4
	N	5			5
MCH	MEAN	1.12			1.12
fmol	ST.DEV	0.06			0.03
	N	5			5
MCHC	MEAN	20.97			20.61
mmol/L	ST.DEV	0.67			0.17
	N	5			5
Platelets	MEAN	670			828
10E9/L	ST.DEV	165			156
	N	5			5

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

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

**1.13 HAEMATOLOGY SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
END OF RECOVERY					
PT	MEAN	17.9			16.8
s	ST.DEV	1.0			1.0
	N	4			5
APTT	MEAN	15.7			17.6 **
s	ST.DEV	0.5			0.8
	N	4			5

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

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

**1.14 CLINICAL BIOCHEMISTRY SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
END OF TREATMENT					
ALAT U/L	MEAN	45.9	50.5	79.5	130.5 **
	ST.DEV	8.5	8.4	46.8	102.8
	N	15	10	10	9
ASAT U/L	MEAN	92.6	74.2	91.5	105.0
	ST.DEV	26.6	6.2	22.5	38.7
	N	15	10	10	9
ALP U/L	MEAN	178	165	264 **	299 **
	ST.DEV	43	31	69	81
	N	15	10	10	9
Total protein g/L	MEAN	62.8	64.0	60.1 *	58.8 **
	ST.DEV	2.8	2.2	2.5	3.1
	N	15	10	10	9
Albumin g/L	MEAN	32.3	33.0	32.7	33.3
	ST.DEV	1.1	0.7	1.2	1.3
	N	15	10	10	9
Total bilirubin umol/L	MEAN	1.8	1.7	2.4 **	3.2 **
	ST.DEV	0.2	0.3	0.4	0.7
	N	15	10	10	9
Urea mmol/L	MEAN	7.4	7.4	7.8	9.5 **
	ST.DEV	1.2	1.1	1.2	2.2
	N	15	10	10	9
Creatinine umol/L	MEAN	41.8	45.8 *	49.4 **	47.0 **
	ST.DEV	3.9	3.6	5.0	2.7
	N	15	10	10	9
Glucose mmol/L	MEAN	8.97	8.67	7.67 *	6.19 **
	ST.DEV	1.31	0.97	1.11	0.65
	N	15	10	10	9
Cholesterol mmol/L	MEAN	1.60	1.41	0.98 **	0.81 **
	ST.DEV	0.45	0.35	0.23	0.11
	N	15	10	10	9
Bile Acids umol/L	MEAN	26.3	23.9	35.1	51.9 **
	ST.DEV	9.8	9.1	19.1	15.1
	N	15	10	10	9
Sodium mmol/L	MEAN	140.8	143.1 **	143.4 **	141.4
	ST.DEV	0.9	1.0	1.0	1.6
	N	15	10	10	9
Potassium mmol/L	MEAN	4.06	3.91	3.95	3.99
	ST.DEV	0.40	0.15	0.26	0.26
	N	15	10	10	9
Chloride mmol/L	MEAN	101	103	103	100
	ST.DEV	1	1	1	2
	N	15	10	10	9
Calcium mmol/L	MEAN	2.55	2.54	2.51	2.51
	ST.DEV	0.06	0.04	0.07	0.07
	N	15	10	10	9

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

**1.14 CLINICAL BIOCHEMISTRY SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
END OF TREATMENT					
Inorg.Phos	MEAN	1.83	1.72	1.88	2.34 **
mmol/L	ST.DEV	0.27	0.19	0.22	0.23
	N	15	10	10	9

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

**1.14 CLINICAL BIOCHEMISTRY SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
END OF RECOVERY					
ALAT	MEAN	47.2			42.5
U/L	ST.DEV	24.2			3.9
	N	5			4
ASAT	MEAN	93.3			69.3
U/L	ST.DEV	36.0			7.0
	N	5			4
ALP	MEAN	160			130
U/L	ST.DEV	33			13
	N	5			4
Total protein	MEAN	67.4			69.4
g/L	ST.DEV	3.7			3.5
	N	5			4
Albumin	MEAN	33.5			33.4
g/L	ST.DEV	1.8			1.8
	N	5			4
Total bilirubin	MEAN	2.0			1.8
umol/L	ST.DEV	0.5			0.5
	N	5			4
Urea	MEAN	7.8			7.4
mmol/L	ST.DEV	1.3			1.4
	N	5			4
Creatinine	MEAN	37.7			34.4
umol/L	ST.DEV	4.2			2.2
	N	5			4
Glucose	MEAN	10.01			8.67
mmol/L	ST.DEV	1.88			0.49
	N	5			4
Cholesterol	MEAN	2.23			2.16
mmol/L	ST.DEV	0.33			0.32
	N	5			4
Bile Acids	MEAN	25.6			49.5 *
umol/L	ST.DEV	7.5			20.3
	N	5			4
Sodium	MEAN	141.6			142.2
mmol/L	ST.DEV	0.7			0.5
	N	5			4
Potassium	MEAN	4.21			4.21
mmol/L	ST.DEV	0.09			0.14
	N	5			4
Chloride	MEAN	104			104
mmol/L	ST.DEV	2			1
	N	5			4
Calcium	MEAN	2.66			2.68
mmol/L	ST.DEV	0.04			0.05
	N	5			4

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

**1.14 CLINICAL BIOCHEMISTRY SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
END OF RECOVERY					
Inorg.Phos	MEAN	1.80			1.94
mmol/L	ST.DEV	0.23			0.07
	N	5			4

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

**1.14 CLINICAL BIOCHEMISTRY SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
END OF TREATMENT					
ALAT	MEAN	50.1	55.5	73.4 *	85.6 **
U/L	ST.DEV	10.2	15.0	23.5	28.9
	N	14	9	9	11
ASAT	MEAN	78.9	78.1	86.4	112.5 *
U/L	ST.DEV	11.1	13.5	11.5	53.3
	N	14	9	9	11
ALP	MEAN	83	84	97	189 **
U/L	ST.DEV	41	36	50	74
	N	14	9	9	11
Total protein	MEAN	66.7	68.2	68.3	62.6
g/L	ST.DEV	2.3	4.1	4.5	5.9
	N	14	9	9	11
Albumin	MEAN	34.1	35.9	36.2	34.4
g/L	ST.DEV	1.3	2.4	2.0	3.0
	N	14	9	9	11
Total bilirubin	MEAN	2.2	2.6	2.5	3.1 **
umol/L	ST.DEV	0.4	0.5	0.3	1.0
	N	14	9	9	11
Urea	MEAN	8.2	8.1	8.8	8.1
mmol/L	ST.DEV	1.0	1.6	1.4	1.7
	N	14	9	9	11
Creatinine	MEAN	45.1	45.6	48.4 *	46.2
umol/L	ST.DEV	1.4	3.4	3.0	3.7
	N	14	9	9	11
Glucose	MEAN	7.87	7.57	7.00	5.70 **
mmol/L	ST.DEV	1.08	1.11	1.38	1.15
	N	14	9	9	11
Cholesterol	MEAN	1.70	1.84	1.64	1.43
mmol/L	ST.DEV	0.43	0.30	0.29	0.37
	N	14	9	9	11
Bile Acids	MEAN	41.2	51.6	52.2	57.7
umol/L	ST.DEV	22.5	41.9	18.6	15.4
	N	14	9	9	11
Sodium	MEAN	139.1	140.0	139.4	138.8
mmol/L	ST.DEV	1.4	1.5	0.8	2.0
	N	14	9	9	11
Potassium	MEAN	3.63	3.66	3.52	3.43
mmol/L	ST.DEV	0.24	0.29	0.18	0.20
	N	14	9	9	11
Chloride	MEAN	102	103	101	99 *
mmol/L	ST.DEV	2	1	2	3
	N	14	9	9	11
Calcium	MEAN	2.59	2.60	2.59	2.54
mmol/L	ST.DEV	0.06	0.09	0.07	0.11
	N	14	9	9	11

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

**1.14 CLINICAL BIOCHEMISTRY SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
END OF TREATMENT					
Inorg.Phos	MEAN	1.68	1.50	1.63	1.89
mmol/L	ST.DEV	0.35	0.18	0.21	0.26
	N	14	9	9	11

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

**1.14 CLINICAL BIOCHEMISTRY SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
END OF RECOVERY					
ALAT U/L	MEAN	27.5			25.6
	ST.DEV	5.8			2.7
	N	5			5
ASAT U/L	MEAN	74.1			72.2
	ST.DEV	6.1			7.3
	N	5			5
ALP U/L	MEAN	52			69
	ST.DEV	15			32
	N	5			5
Total protein g/L	MEAN	67.4			65.6
	ST.DEV	1.7			1.2
	N	5			5
Albumin g/L	MEAN	34.8			33.5 *
	ST.DEV	0.8			0.5
	N	5			5
Total bilirubin umol/L	MEAN	1.9			1.8
	ST.DEV	0.1			0.3
	N	5			5
Urea mmol/L	MEAN	7.1			7.4
	ST.DEV	0.7			1.3
	N	5			5
Creatinine umol/L	MEAN	42.9			40.3
	ST.DEV	2.6			2.6
	N	5			5
Glucose mmol/L	MEAN	7.52			7.05
	ST.DEV	0.44			0.69
	N	5			5
Cholesterol mmol/L	MEAN	1.76			1.82
	ST.DEV	0.52			0.54
	N	5			5
Bile Acids umol/L	MEAN	32.9			23.6
	ST.DEV	20.6			16.6
	N	5			5
Sodium mmol/L	MEAN	140.7			141.1
	ST.DEV	1.0			1.1
	N	5			5
Potassium mmol/L	MEAN	3.64			3.76
	ST.DEV	0.29			0.13
	N	5			5
Chloride mmol/L	MEAN	104			105
	ST.DEV	2			1
	N	5			5
Calcium mmol/L	MEAN	2.62			2.59
	ST.DEV	0.05			0.03
	N	5			5

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

**1.14 CLINICAL BIOCHEMISTRY SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 600 MG/KG
END OF RECOVERY					
Inorg.Phos	MEAN	1.57			1.47
mmol/L	ST.DEV	0.25			0.17
	N	5			5

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

**1.15 MACROSCOPIC FINDINGS SUMMARY
MALES**

	GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 1000/600 MG/KG
INTERCURRENT DEATH				
Animals examined				6
Animals affected				6
General observations				
Gi-tractus: distended with gas.				3
Emaciated				4
Heart				
Reduced in size				1
Trachea				
Contains fluid				1
Perforation(s)				1
Lungs				
Focus/foci				1
Enlarged				1
Esophagus				
Discolouration				1
Stomach				
Focus/foci				4
Irregular surface				3
Liver				
Focus/foci				4
Enlarged				3
Discolouration				2
Kidneys				
Focus/foci				2
Enlarged				1
Discolouration				2
Prostate				
Reduced in size				4
Seminal vesicles				
Reduced in size				4
Preputial glands				
Reduced in size				2
Spleen				
Reduced in size				2
Thymus				
Reduced in size				5
Harderian glands				
Discolouration				1
Body cavities				
Contains blood/blood clots				1
END OF TREATMENT				
Animals examined	10	10	10	5
Animals without findings	7	2	0	0
Animals affected	3	8	10	5
Stomach				
Focus/foci	1	1	0	1
Irregular surface	0	1	0	2
Liver				
Right medial lobe: accessory lobe.	1	0	1	0
Accentuated lobular pattern	0	0	1	0
Enlarged	0	2	10 ##	5 ##
Discolouration	0	0	4	5 ##
Kidneys				
Enlarged	0	1	0	0
Discolouration	0	1	3	5 ##
Urinary bladder				
Contains gravel	0	0	0	1

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

**1.15 MACROSCOPIC FINDINGS SUMMARY
MALES**

	GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 1000/600 MG/KG
END OF TREATMENT				
Thickened Prostate	0	0	0	1
Seminal vesicles Reduced in size	0	0	1	1
Preputial glands Reduced in size	1	0	0	1
Thyroid gland Reduced in size	1	3	1	1
Spleen Enlarged	0	0	2	0
Thymus Reduced in size	0	0	0	1
Thymus Focus/foci	0	0	1	0
Thymus Enlarged	0	0	1	0
Thymus Reduced in size	0	0	1	2
Thymus Discolouration	0	0	1	0
Mesenteric lymph n Reduced in size	0	0	0	1
Mandibular lymph n Discolouration	0	1	0	0
Lacrimal glands Reduced in size	0	1	0	0
END OF RECOVERY				
Animals examined	5			4
Animals without findings	3			2
Animals affected	2			2
Stomach Focus/foci	1			0
Liver Discolouration	0			2
Thyroid gland Enlarged	1			1

FEMALES

	GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 1000/600 MG/KG
INTERCURRENT DEATH				
Animals examined		1	1	4
Animals affected		1	1	4
General observations				
Emaciated		1	0	2
Cannibalism:organ missing		0	1	1
Beginning autolysis		1	0	0
Advanced autolysis		0	1	1
Lungs				
Focus/foci		0	0	1
Stomach				
Focus/foci		0	1	1
Irregular surface		0	1	1
Liver				
Enlarged		0	1	2

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

**1.15 MACROSCOPIC FINDINGS SUMMARY
FEMALES**

	GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 1000/600 MG/KG
INTERCURRENT DEATH				
Kidneys				
Discolouration		0	0	1
Adrenal glands				
Enlarged		0	1	0
Spleen				
Reduced in size		1	0	1
Thymus				
Focus/foci		0	1	0
Reduced in size		0	0	2
Discolouration		1	0	2
Mesenteric lymph n				
Discolouration		1	0	0
Mandibular lymph n				
Discolouration		1	0	0
Renal lymph node				
Enlarged		0	1	1
Discolouration		0	0	1
Body cavities				
Contains fluid		0	1	0
Contents:		0	0	1
END OF TREATMENT				
Animals examined	10	9	9	6
Animals without findings	3	2	3	0
Animals affected	7	7	6	6
Lungs				
Discolouration	0	1	0	0
Stomach				
Focus/foci	0	3	1	3 #
Liver				
Accentuated lobular pattern	0	0	3	0
Diaphragmatic hernia	0	1	0	0
Focus/foci	1	0	0	0
Enlarged	1	0	3	6 ##
Discolouration	1	0	3	6 ##
Kidneys				
Pelvic dilation	0	0	1	0
Enlarged	0	0	1	0
Discolouration	0	0	1	5 ##
Ovaries				
Enlarged	0	0	1	0
Uterus				
Contains fluid	6	4	4	4
Thyroid gland				
Enlarged	0	0	2	1
Mandibular lymph n				
Discolouration	1	0	1	0
Parathyroid lymph n.				
Enlarged	0	1	0	0
Body cavities				
Nodule(s)	1	0	0	0
END OF RECOVERY				
Animals examined	5			5
Animals without findings	0			2
Animals affected	5			3
Liver				

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

**1.15 MACROSCOPIC FINDINGS SUMMARY
FEMALES**

	GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 1000/600 MG/KG
END OF RECOVERY				
Discolouration	0			2
Kidneys				
Discolouration	0			2
Uterus				
Contains fluid	5			2
Clitoral glands				
Focus/foci	0			1
Adrenal glands				
Enlarged	0			1
Thymus				
Focus/foci	0			1

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

**1.16 ORGAN WEIGHTS (GRAM) SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 1000/600 MG/KG
END OF TREATMENT					
BODY W. (GRAM)	MEAN	372	375	337 *	298 **
	ST.DEV	38	25	23	22
	N	10	10	10	5
BRAIN (GRAM)	MEAN	2.02	2.05	2.00	1.96
	ST.DEV	0.07	0.08	0.09	0.08
	N	10	10	10	5
HEART (GRAM)	MEAN	0.968	0.948	0.859 *	0.776 **
	ST.DEV	0.102	0.089	0.039	0.046
	N	10	10	10	5
LIVER (GRAM)	MEAN	11.00	12.31	14.25 **	17.66 **
	ST.DEV	1.11	1.11	1.29	1.81
	N	10	10	10	5
THYROIDS (GRAM)	MEAN	0.015	0.017	0.018 *	0.016
	ST.DEV	0.002	0.003	0.003	0.001
	N	10	10	10	5
THYMUS (GRAM)	MEAN	0.300	0.332	0.315	0.207 *
	ST.DEV	0.051	0.074	0.074	0.036
	N	10	10	10	5
KIDNEYS (GRAM)	MEAN	2.44	2.77 **	2.77 **	2.71 *
	ST.DEV	0.14	0.24	0.21	0.17
	N	10	10	10	5
ADRENALS (GRAM)	MEAN	0.054	0.051	0.051	0.063 *
	ST.DEV	0.005	0.006	0.008	0.006
	N	10	10	10	5
SPLEEN (GRAM)	MEAN	0.548	0.555	0.503	0.436 *
	ST.DEV	0.101	0.077	0.033	0.085
	N	10	10	10	5
TESTES (GRAM)	MEAN	3.58	3.55	3.52	3.57
	ST.DEV	0.28	0.37	0.29	0.25
	N	10	10	10	5
PROSTATE GLAND (GRAM)	MEAN	0.769	0.685	0.656	0.642
	ST.DEV	0.131	0.135	0.148	0.152
	N	10	9	10	5
EPIDIDYMIDES (GRAM)	MEAN	1.199	1.152	1.161	1.136
	ST.DEV	0.067	0.129	0.101	0.052
	N	10	10	10	5
SEMINAL VESICLES (GRAM)	MEAN	1.190	1.297	1.271	0.937
	ST.DEV	0.177	0.181	0.254	0.242
	N	10	10	10	5

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

**1.16 ORGAN WEIGHTS (GRAM) SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 1000/600 MG/KG
END OF RECOVERY					
BODY W. (GRAM)	MEAN	390			363
	ST.DEV	25			43
	N	5			4
BRAIN (GRAM)	MEAN	2.00			2.05
	ST.DEV	0.06			0.04
	N	5			4
HEART (GRAM)	MEAN	1.047			0.983
	ST.DEV	0.196			0.114
	N	5			4
LIVER (GRAM)	MEAN	8.96			8.98
	ST.DEV	0.74			1.25
	N	5			4
THYROIDS (GRAM)	MEAN	0.016			0.019
	ST.DEV	0.005			0.002
	N	5			4
THYMUS (GRAM)	MEAN	0.289			0.356
	ST.DEV	0.092			0.091
	N	5			4
KIDNEYS (GRAM)	MEAN	2.20			2.53
	ST.DEV	0.16			0.28
	N	5			4
ADRENALS (GRAM)	MEAN	0.050			0.048
	ST.DEV	0.006			0.003
	N	5			4
SPLEEN (GRAM)	MEAN	0.533			0.569
	ST.DEV	0.118			0.027
	N	5			4
TESTES (GRAM)	MEAN	3.59			3.76
	ST.DEV	0.25			0.35
	N	5			4
PROSTATE GLAND (GRAM)	MEAN	0.713			0.658
	ST.DEV	0.143			0.046
	N	5			4
EPIDIDYMIDES (GRAM)	MEAN	1.299			1.269
	ST.DEV	0.072			0.161
	N	5			4
SEMINAL VESICLES (GRAM)	MEAN	1.409			1.360
	ST.DEV	0.293			0.111
	N	5			4

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

**1.16 ORGAN/BODY WEIGHT RATIOS (%) SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 1000/600 MG/KG
END OF TREATMENT					
BODY W. (GRAM)	MEAN	372	375	337 *	298 **
	ST.DEV	38	25	23	22
	N	10	10	10	5
BRAIN (%)	MEAN	0.55	0.55	0.60 *	0.66 **
	ST.DEV	0.05	0.04	0.04	0.05
	N	10	10	10	5
HEART (%)	MEAN	0.260	0.253	0.256	0.261
	ST.DEV	0.014	0.017	0.018	0.010
	N	10	10	10	5
LIVER (%)	MEAN	2.96	3.28 *	4.23 **	5.94 **
	ST.DEV	0.11	0.16	0.25	0.50
	N	10	10	10	5
THYROIDS (%)	MEAN	0.004	0.004	0.005 **	0.005 **
	ST.DEV	0.000	0.001	0.001	0.001
	N	10	10	10	5
THYMUS (%)	MEAN	0.080	0.088	0.093	0.069
	ST.DEV	0.009	0.015	0.021	0.010
	N	10	10	10	5
KIDNEYS (%)	MEAN	0.66	0.74 *	0.82 **	0.91 **
	ST.DEV	0.05	0.07	0.05	0.08
	N	10	10	10	5
ADRENALS (%)	MEAN	0.015	0.014	0.015	0.021 **
	ST.DEV	0.002	0.001	0.002	0.003
	N	10	10	10	5
SPLEEN (%)	MEAN	0.147	0.148	0.150	0.146
	ST.DEV	0.022	0.015	0.014	0.026
	N	10	10	10	5
TESTES (%)	MEAN	0.97	0.95	1.05	1.20 **
	ST.DEV	0.09	0.07	0.10	0.08
	N	10	10	10	5
PROSTATE GLAND (%)	MEAN	0.209	0.186	0.195	0.214
	ST.DEV	0.039	0.039	0.042	0.041
	N	10	9	10	5
EPIDIDYMIDES (%)	MEAN	0.325	0.308	0.346	0.383 **
	ST.DEV	0.031	0.029	0.038	0.028
	N	10	10	10	5
SEMINAL VESICLES (%)	MEAN	0.324	0.346	0.379	0.313
	ST.DEV	0.060	0.047	0.080	0.075
	N	10	10	10	5

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

**1.16 ORGAN/BODY WEIGHT RATIOS (%) SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 1000/600 MG/KG
END OF RECOVERY					
BODY W. (GRAM)	MEAN	390			363
	ST.DEV	25			43
	N	5			4
BRAIN (%)	MEAN	0.51			0.57
	ST.DEV	0.04			0.08
	N	5			4
HEART (%)	MEAN	0.267			0.270
	ST.DEV	0.035			0.006
	N	5			4
LIVER (%)	MEAN	2.30			2.47
	ST.DEV	0.15			0.09
	N	5			4
THYROIDS (%)	MEAN	0.004			0.005
	ST.DEV	0.001			0.000
	N	5			4
THYMUS (%)	MEAN	0.074			0.097
	ST.DEV	0.023			0.017
	N	5			4
KIDNEYS (%)	MEAN	0.56			0.70 **
	ST.DEV	0.02			0.01
	N	5			4
ADRENALS (%)	MEAN	0.013			0.013
	ST.DEV	0.001			0.001
	N	5			4
SPLEEN (%)	MEAN	0.136			0.159
	ST.DEV	0.022			0.028
	N	5			4
TESTES (%)	MEAN	0.92			1.04 **
	ST.DEV	0.04			0.04
	N	5			4
PROSTATE GLAND (%)	MEAN	0.182			0.182
	ST.DEV	0.030			0.011
	N	5			4
EPIDIDYMIDES (%)	MEAN	0.333			0.350
	ST.DEV	0.021			0.034
	N	5			4
SEMINAL VESICLES (%)	MEAN	0.361			0.382
	ST.DEV	0.075			0.084
	N	5			4

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

**1.16 ORGAN WEIGHTS (GRAM) SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 1000/600 MG/KG
END OF TREATMENT					
BODY W. (GRAM)	MEAN	242	235	222 *	224
	ST.DEV	16	19	15	10
	N	10	9	9	6
BRAIN (GRAM)	MEAN	1.93	1.86 *	1.92	1.88
	ST.DEV	0.06	0.05	0.05	0.07
	N	10	9	9	6
HEART (GRAM)	MEAN	0.744	0.739	0.697	0.676 *
	ST.DEV	0.039	0.055	0.050	0.039
	N	10	9	9	6
LIVER (GRAM)	MEAN	8.95	8.66	10.27 **	12.60 **
	ST.DEV	0.90	0.75	0.64	0.97
	N	10	9	9	6
THYROIDS (GRAM)	MEAN	0.016	0.015	0.018	0.017
	ST.DEV	0.003	0.002	0.004	0.004
	N	10	9	9	6
THYMUS (GRAM)	MEAN	0.306	0.301	0.236 *	0.245
	ST.DEV	0.078	0.049	0.027	0.052
	N	10	9	9	6
KIDNEYS (GRAM)	MEAN	1.68	1.78	1.89 *	2.08 **
	ST.DEV	0.15	0.14	0.18	0.13
	N	10	9	9	6
ADRENALS (GRAM)	MEAN	0.076	0.070	0.076	0.075
	ST.DEV	0.016	0.013	0.009	0.008
	N	10	9	9	6
SPLEEN (GRAM)	MEAN	0.559	0.466 **	0.423 **	0.433 **
	ST.DEV	0.066	0.030	0.057	0.072
	N	10	9	9	6
OVARIES (GRAM)	MEAN	0.166	0.157	0.143 *	0.153
	ST.DEV	0.019	0.022	0.020	0.017
	N	10	9	9	6
UTERUS (GRAM)	MEAN	1.138	0.945	0.988	1.358
	ST.DEV	0.521	0.495	0.624	1.330
	N	10	9	9	6

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

**1.16 ORGAN WEIGHTS (GRAM) SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 1000/600 MG/KG
END OF RECOVERY					
BODY W. (GRAM)	MEAN	241			226
	ST.DEV	10			24
	N	5			5
BRAIN (GRAM)	MEAN	1.93			1.88
	ST.DEV	0.02			0.06
	N	5			5
HEART (GRAM)	MEAN	0.751			0.692
	ST.DEV	0.080			0.066
	N	5			5
LIVER (GRAM)	MEAN	5.98			5.82
	ST.DEV	0.39			0.66
	N	5			5
THYROIDS (GRAM)	MEAN	0.016			0.016
	ST.DEV	0.001			0.002
	N	5			5
THYMUS (GRAM)	MEAN	0.291			0.377 *
	ST.DEV	0.067			0.046
	N	5			5
KIDNEYS (GRAM)	MEAN	1.65			1.70
	ST.DEV	0.13			0.20
	N	5			5
ADRENALS (GRAM)	MEAN	0.066			0.068
	ST.DEV	0.012			0.020
	N	5			5
SPLEEN (GRAM)	MEAN	0.461			0.421
	ST.DEV	0.077			0.029
	N	5			5
OVARIES (GRAM)	MEAN	0.158			0.148
	ST.DEV	0.046			0.034
	N	5			5
UTERUS (GRAM)	MEAN	2.178			1.046
	ST.DEV	1.086			0.764
	N	5			5

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

**1.16 ORGAN/BODY WEIGHT RATIOS (%) SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 1000/600 MG/KG
END OF TREATMENT					
BODY W. (GRAM)	MEAN	242	235	222 *	224
	ST.DEV	16	19	15	10
	N	10	9	9	6
BRAIN (%)	MEAN	0.80	0.80	0.87 *	0.84
	ST.DEV	0.04	0.07	0.05	0.03
	N	10	9	9	6
HEART (%)	MEAN	0.308	0.316	0.314	0.302
	ST.DEV	0.018	0.016	0.018	0.013
	N	10	9	9	6
LIVER (%)	MEAN	3.69	3.70	4.64 **	5.63 **
	ST.DEV	0.20	0.27	0.43	0.39
	N	10	9	9	6
THYROIDS (%)	MEAN	0.007	0.007	0.008	0.008
	ST.DEV	0.001	0.001	0.001	0.002
	N	10	9	9	6
THYMUS (%)	MEAN	0.127	0.128	0.107	0.110
	ST.DEV	0.036	0.021	0.013	0.022
	N	10	9	9	6
KIDNEYS (%)	MEAN	0.69	0.76 *	0.85 **	0.93 **
	ST.DEV	0.05	0.04	0.07	0.05
	N	10	9	9	6
ADRENALS (%)	MEAN	0.031	0.030	0.034	0.033
	ST.DEV	0.006	0.003	0.004	0.002
	N	10	9	9	6
SPLEEN (%)	MEAN	0.232	0.200 *	0.190 **	0.194 *
	ST.DEV	0.036	0.021	0.016	0.034
	N	10	9	9	6
OVARIES (%)	MEAN	0.069	0.067	0.065	0.069
	ST.DEV	0.010	0.008	0.010	0.008
	N	10	9	9	6
UTERUS (%)	MEAN	0.474	0.407	0.449	0.613
	ST.DEV	0.218	0.220	0.293	0.602
	N	10	9	9	6

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

**1.16 ORGAN/BODY WEIGHT RATIOS (%) SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 100 MG/KG	GROUP 3 300 MG/KG	GROUP 4 1000/600 MG/KG
END OF RECOVERY					
BODY W. (GRAM)	MEAN	241			226
	ST.DEV	10			24
	N	5			5
BRAIN (%)	MEAN	0.80			0.84
	ST.DEV	0.02			0.08
	N	5			5
HEART (%)	MEAN	0.311			0.308
	ST.DEV	0.021			0.023
	N	5			5
LIVER (%)	MEAN	2.48			2.59
	ST.DEV	0.12			0.21
	N	5			5
THYROIDS (%)	MEAN	0.006			0.007
	ST.DEV	0.001			0.001
	N	5			5
THYMUS (%)	MEAN	0.121			0.169 *
	ST.DEV	0.026			0.032
	N	5			5
KIDNEYS (%)	MEAN	0.69			0.75
	ST.DEV	0.03			0.08
	N	5			5
ADRENALS (%)	MEAN	0.027			0.030
	ST.DEV	0.004			0.008
	N	5			5
SPLEEN (%)	MEAN	0.191			0.188
	ST.DEV	0.026			0.018
	N	5			5
OVARIES (%)	MEAN	0.065			0.065
	ST.DEV	0.016			0.010
	N	5			5
UTERUS (%)	MEAN	0.903			0.444
	ST.DEV	0.449			0.283
	N	5			5

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

APPENDIX 2
INDIVIDUAL DATA TABLES

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.1 MORTALITY DATA MALES

ANIMAL	SCHEDULED SACRIFICE	SPONTANEOUS DEATH	KILLED IN EXTREMIS	TREATMENT FROM	TO
GROUP 1 (CONTROL)					
1	26MAY16			25FEB16	25MAY16
2	26MAY16			25FEB16	25MAY16
3	26MAY16			25FEB16	25MAY16
4	26MAY16			25FEB16	25MAY16
5	26MAY16			25FEB16	25MAY16
6	26MAY16			25FEB16	25MAY16
7	26MAY16			25FEB16	25MAY16
8	26MAY16			25FEB16	25MAY16
9	26MAY16			25FEB16	25MAY16
10	26MAY16			25FEB16	25MAY16
11	23JUN16			25FEB16	26MAY16
12	23JUN16			25FEB16	26MAY16
13	23JUN16			25FEB16	26MAY16
14	23JUN16			25FEB16	26MAY16
15	23JUN16			25FEB16	26MAY16
GROUP 2 (100 MG/KG)					
16	26MAY16			25FEB16	25MAY16
17	26MAY16			25FEB16	25MAY16
18	26MAY16			25FEB16	25MAY16
19	26MAY16			25FEB16	25MAY16
20	26MAY16			25FEB16	25MAY16
21	26MAY16			25FEB16	25MAY16
22	26MAY16			25FEB16	25MAY16
23	26MAY16			25FEB16	25MAY16
24	26MAY16			25FEB16	25MAY16
25	26MAY16			25FEB16	25MAY16
GROUP 3 (300 MG/KG)					
26	26MAY16			25FEB16	25MAY16
27	26MAY16			25FEB16	25MAY16
28	26MAY16			25FEB16	25MAY16
29	26MAY16			25FEB16	25MAY16
30	26MAY16			25FEB16	25MAY16
31	26MAY16			25FEB16	25MAY16
32	26MAY16			25FEB16	25MAY16
33	26MAY16			25FEB16	25MAY16
34	26MAY16			25FEB16	25MAY16
35	26MAY16			25FEB16	25MAY16
GROUP 4 (1000/600 MG/KG)					
36			04MAY16	25FEB16	04MAY16
37	26MAY16			25FEB16	25MAY16
38	26MAY16			25FEB16	25MAY16
39	26MAY16			25FEB16	25MAY16
40			15MAR16	25FEB16	14MAR16
41	26MAY16			25FEB16	25MAY16
42	26MAY16			25FEB16	25MAY16
43	23JUN16			25FEB16	26MAY16
44		21MAR16		25FEB16	21MAR16
45	23JUN16			25FEB16	26MAY16
46	23JUN16			25FEB16	26MAY16
47			25MAR16	25FEB16	25MAR16
48			26APR16	25FEB16	26APR16
49	23JUN16			25FEB16	26MAY16
50			19MAY16	25FEB16	18MAY16

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.1 MORTALITY DATA FEMALES

ANIMAL	SCHEDULED SACRIFICE	SPONTANEOUS DEATH	KILLED IN EXTREMIS	TREATMENT FROM	TO
GROUP 1 (CONTROL)					
51	27MAY16			25FEB16	26MAY16
52	31MAY16			25FEB16	30MAY16
53	31MAY16			25FEB16	30MAY16
54	31MAY16			25FEB16	30MAY16
55	31MAY16			25FEB16	30MAY16
56	31MAY16			25FEB16	30MAY16
57	31MAY16			25FEB16	30MAY16
58	31MAY16			25FEB16	30MAY16
59	31MAY16			25FEB16	30MAY16
60	31MAY16			25FEB16	30MAY16
61	28JUN16			25FEB16	30MAY16
62	28JUN16			25FEB16	30MAY16
63	28JUN16			25FEB16	30MAY16
64	28JUN16			25FEB16	30MAY16
65	28JUN16			25FEB16	30MAY16
GROUP 2 (100 MG/KG)					
66	31MAY16			25FEB16	30MAY16
67	31MAY16			25FEB16	30MAY16
68	31MAY16			25FEB16	30MAY16
69	31MAY16			25FEB16	30MAY16
70	31MAY16			25FEB16	30MAY16
71	31MAY16			25FEB16	30MAY16
72	31MAY16			25FEB16	30MAY16
73	31MAY16			25FEB16	30MAY16
74		26MAY16		25FEB16	25MAY16
75	31MAY16			25FEB16	30MAY16
GROUP 3 (300 MG/KG)					
76	31MAY16			25FEB16	30MAY16
77		12MAY16		25FEB16	11MAY16
78	31MAY16			25FEB16	30MAY16
79	31MAY16			25FEB16	30MAY16
80	31MAY16			25FEB16	30MAY16
81	31MAY16			25FEB16	30MAY16
82	31MAY16			25FEB16	30MAY16
83	31MAY16			25FEB16	30MAY16
84	31MAY16			25FEB16	30MAY16
85	31MAY16			25FEB16	30MAY16
GROUP 4 (1000/600 MG/KG)					
86	31MAY16			25FEB16	30MAY16
87	31MAY16			25FEB16	30MAY16
88			18MAR16	25FEB16	17MAR16
89	31MAY16			25FEB16	30MAY16
90	31MAY16			25FEB16	30MAY16
91	31MAY16			25FEB16	30MAY16
92	31MAY16			25FEB16	30MAY16
93		15MAR16		25FEB16	14MAR16
94	28JUN16			25FEB16	30MAY16
95	28JUN16			25FEB16	30MAY16
96		25MAR16		25FEB16	25MAR16
97	28JUN16			25FEB16	30MAY16
98	28JUN16			25FEB16	30MAY16
99	28JUN16			25FEB16	30MAY16
100			27APR16	25FEB16	27APR16

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.2 CLINICAL SIGNS MALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT							
	WEEK: 1	2	3	4	5	6	7	8
	DAY: 1234567	1234567	1234567	1234567	1234567	1234567	1234567	1234567
GROUP 1 (CONTROL)								
ANIMAL 1								
Secretion / excretion	G:	1111111111	2211111111	1111111111	1111111111	1111111111	1111111111
Salivation (3)								
ANIMAL 2								
Skin / fur	G:	1111111111
Swelling (4) (Abdomen)								
Secretion / excretion	G:	1111111111	2211111111	1111111111	1111111111	1111111111	1111111111
Salivation (3)								
ANIMAL 3								
Secretion / excretion	G:	1111111111	2211111111	1111111111	1111111111	1111111111	1111111111
Salivation (3)								
ANIMAL 4								
Secretion / excretion	G:	1111111111	1111111111	1111111111	1111111111	1111111111	1111111111
Salivation (3)								
ANIMAL 5								
Secretion / excretion	G:	1111111111	2222111111	1111111111	1111111111	1111111111	1111111111
Salivation (3)								
ANIMAL 6								
Breathing	G:
Rales (3)								
Skin / fur	G:
Swelling (4) (Abdomen)								
Secretion / excretion	G:	1111111111	2211111111	1111111111	1111111111	1111111111	1111111111
Salivation (3)								
ANIMAL 7								
Breathing	G:
Rales (3)								
Secretion / excretion	G:	1111111111	2221121111	1111111111	1111111111	1111111111	1111111111
Salivation (3)								
ANIMAL 8								
Secretion / excretion	G:	1111111111	1111111111	1111111111	1111111111	1111111111	1111111111
Salivation (3)								
ANIMAL 9								
Secretion / excretion	G:	1111111111	1111111111	1111111111	1111111111	1111111111	1111111111
Salivation (3)								
ANIMAL 10								
Secretion / excretion	G:	1111111111	1111111111	1111111111	1111111111	1111111111	1111111111
Salivation (3)								
ANIMAL 11								
Secretion / excretion	G:	1111111111	2222111111	1111111111	1111111111	1111111111	1111111111
Salivation (3)								
ANIMAL 12								
Secretion / excretion	G:	1111111111	1111111111	1111111111	1111111111	1111111111	1111111111
Salivation (3)								
ANIMAL 13								
Secretion / excretion	G:	1111111111	2222111111	1111111111	1111111111	1111111111	1111111111
Salivation (3)								
ANIMAL 14								
Secretion / excretion	G:	1111111111	1111111111	1111111111	1111111111	1111111111
Salivation (3)								
ANIMAL 15								
Breathing	G:
Rales (3)								
Secretion / excretion	G:	1111111111	1111111111	1111111111	1111111111	1111111111	1111111111
Salivation (3)								
GROUP 2 (100 MG/KG)								
ANIMAL 16								
Skin / fur	G:

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

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.2 CLINICAL SIGNS MALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT							
	WEEK: 1	2	3	4	5	6	7	8
	DAY: 1234567	1234567	1234567	1234567	1234567	1234567	1234567	1234567
GROUP 2 (100 MG/KG)								
Swelling (4) (Abdomen)	G:			11111111111111111111				
Secretion / excretion Salivation (3)	G:	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111
ANIMAL 17								
Breathing Rales (3)	G:			111				
Skin / fur Piloerection (1)	G:			11111				
Secretion / excretion Salivation (3)	G:	11111111111111111111	22222111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111
ANIMAL 18								
Breathing Rales (3)	G:			11				
Secretion / excretion Salivation (3)	G:	11111111111111111111	11121111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111
ANIMAL 19								
Secretion / excretion Salivation (3)	G:	11111111111111111111	11122111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111
ANIMAL 20								
Secretion / excretion Salivation (3)	G:	11111111111111111111	22221121111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111
ANIMAL 21								
Secretion / excretion Salivation (3)	G:	11111111111111111111	22222112111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111
ANIMAL 22								
Skin / fur Swelling (4) (Abdomen)	G:						111111111111	
Secretion / excretion Salivation (3)	G:	11111111111111111111	22222111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111
ANIMAL 23								
Secretion / excretion Salivation (3)	G:	11111111111111111111	1111111121	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111
ANIMAL 24								
Secretion / excretion Salivation (3)	G:	11111111111111111111	22222111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111
ANIMAL 25								
Skin / fur Swelling (4) (Abdomen)	G:							1
Secretion / excretion Salivation (3)	G:	11111111111111111111	22222112111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111
GROUP 3 (300 MG/KG)								
ANIMAL 26								
Breathing Rales (3)	G:			111				
Skin / fur Swelling (4) (Abdomen)	G:							1
Secretion / excretion Salivation (3)	G:	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111
Chromodacryorrhoea (3) (Neck)	G:							
ANIMAL 27								
Secretion / excretion Salivation (3)	G:	11111111111111111111	11111112111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111
ANIMAL 28								
Secretion / excretion Salivation (3)	G:	11111111111111111111	22222111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111

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

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.2 CLINICAL SIGNS MALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT							
	WEEK: 1	2	3	4	5	6	7	8
GROUP 3 (300 MG/KG)								
ANIMAL 29								
Skin / fur								
Swelling (4) (Abdomen)	G:							1
Secretion / excretion								
Salivation (3)	G:	11111111111111111111	22222111111111111111	11111111111111111111	11111111111111111111	121111111111	
ANIMAL 30								
Secretion / excretion								
Salivation (3)	G:	11111111111111111111	11112111111111111111	11111111111111111111	11111111111111111111	121111111111	
ANIMAL 31								
Skin / fur								
Swelling (4) (Abdomen)	G:							
Secretion / excretion								
Salivation (3)	G:	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	121111111111	
ANIMAL 32								
Breathing								
Rales (3)	G:							1111. 1
Skin / fur								
Swelling (4) (Abdomen)	G:							
Secretion / excretion								
Salivation (3)	G:	11111111111111111111	11111212111111111111	11111111111111111111	11111111111111111111	121111111111	
ANIMAL 33								
Breathing								
Rales (3)	G:			1			11	1
Skin / fur								
Swelling (4) (Abdomen)	G:							
Secretion / excretion								
Salivation (3)	G:	11111111111111111111	11111111111111111111	11111111111111111111	11111111111111111111	121111111111	
ANIMAL 34								
Breathing								
Rales (3)	G:				1		11111111	1
Secretion / excretion								
Salivation (3)	G:	11111111111111111111	22222121111111111111	11111111111111111111	11111111111111111111	122111111111	
ANIMAL 35								
Breathing								
Rales (3)	G:			1		11		1
Skin / fur								
Swelling (4) (Abdomen)	G:						11111111111111111111	1
Secretion / excretion								
Salivation (3)	G:	11111111111111111111	11111121111111111111	11111111111111111111	11111111111111111111	121111111111	
GROUP 4 (600 MG/KG)								
ANIMAL 36								
Posture								
Hunched posture (1)	G:							
Skin / fur								
Swelling (4) (Abdomen)	G:				11111		111	
Secretion / excretion								
Salivation (3)	G:	...	11111111111111222222	11111221	...	11111111111111111111	121111111111	
Various								
Lean (1)	G:							
ANIMAL 37								
Posture								
Hunched posture (1)	G:							
Skin / fur								
Swelling (4)	G:					111111		

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

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.2 CLINICAL SIGNS
MALES

SIGN (MAX. GRADE) (LOCATION)	WEEK: 1.....4.....8..... DAY: 123456712345671234567123456712345671234567123456	TREATMENT	
GROUP 4 (600 MG/KG)			
(Abdomen)			
Secretion / excretion			
Salivation (3)	G:	. . . 11111111111122222211111221.	111111111111111111121111111111
ANIMAL 38			
Posture			
Hunched posture (1)	G:
Breathing			
Rales (3)	G: 11.....
Skin / fur			
Swelling (4)	G: 11111..... 111.....
(Abdomen)			
Secretion / excretion			
Salivation (3)	G:	. . . 11111111111122222211222221.	111111111111111111121111111111
ANIMAL 39			
Skin / fur			
Swelling (4)	G: 11111..... 11111.....
(Abdomen)			
Secretion / excretion			
Salivation (3)	G:	. . . 111111111111222222222222221.	111111111111111111121111111111
ANIMAL 40			
Posture			
Hunched posture (1)	G: 111.....
Skin / fur			
Swelling (4)	G: 11.....
(Abdomen)			
Secretion / excretion			
Salivation (3)	G:	. . . 111111111111222.....
Various			
Lean (1)	G: 11.....
Red (1)	G: 1.....
(Snout)			
ANIMAL 41			
Breathing			
Rales (3)	G: 111..... 21. 1. 1.....
Skin / fur			
Swelling (4)	G: 11
(Abdomen)			
Secretion / excretion			
Salivation (3)	G:	. . . 11111111111122222211111221.	111111111111111111121111111111
ANIMAL 42			
Breathing			
Rales (3)	G: 111. 1. 1111. 11.
Skin / fur			
Swelling (4)	G: 11
(Abdomen)			
Secretion / excretion			
Salivation (3)	G:	. . . 11111111111122222211112221.	111111111111111111121111111111
ANIMAL 43			
Skin / fur			
Swelling (4)	G: 11111..... 11111111111111111111111111
(Abdomen)			
Secretion / excretion			
Salivation (3)	G:	. . . 11111111111122222211112221.	111111111111111111121111111111
ANIMAL 44			
Secretion / excretion			
Salivation (3)	G:	. . . 111111111111222222111.....
ANIMAL 45			
Posture			
Hunched posture (1)	G: 111.....
Breathing			
Rales (3)	G: 111111..... 111111

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

Final Report

MTDID 7831
APPENDIX 2

Project 511505

**2.2 CLINICAL SIGNS
MALES**

SIGN (MAX. GRADE) (LOCATION)		TREATMENT	
		WEEK: 1.....4.....8.....	DAY: 1234567123456712345671234567123456712345671234567
GROUP 4 (600 MG/KG)			
Swelling (4) (Abdomen)	G: 11111..... 11	
Piloerection (1)	G: 1.....	
Secretion / excretion Salivation (3)	G:	... 11111111111111112222222222222222... 11	
Various Lean (1)	G: 111111111..... 111.....	

MALES

SIGN (MAX. GRADE) (LOCATION)		TREATMENT		RECOVERY	
		WEEK: 12.....	DAY: 71234567123456712345671234567	1.....4.....	DAY: 12345671234567123456712345672
GROUP 1 (CONTROL)					
ANIMAL 1					
Secretion / excretion Salivation (3)	G:	11			
ANIMAL 2					
Skin / fur					
Swelling (4) (Abdomen)	G:			
Secretion / excretion					
Salivation (3)	G:	11			
ANIMAL 3					
Secretion / excretion					
Salivation (3)	G:	11			
ANIMAL 4					
Secretion / excretion					
Salivation (3)	G:	11			
ANIMAL 5					
Secretion / excretion					
Salivation (3)	G:	11			
ANIMAL 6					
Breathing					
Rales (3)	G: 11.....			
Skin / fur					
Swelling (4) (Abdomen)	G:	1111111111.....			
Secretion / excretion					
Salivation (3)	G:	11			
ANIMAL 7					
Breathing					
Rales (3)	G: 1..			
Secretion / excretion					
Salivation (3)	G:	11			
ANIMAL 8					
Secretion / excretion					
Salivation (3)	G:	11			
ANIMAL 9					
Secretion / excretion					
Salivation (3)	G:	11			
ANIMAL 10					
Secretion / excretion					
Salivation (3)	G:	11			
ANIMAL 11					
Secretion / excretion					
Salivation (3)	G:	11.....			

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

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.2 CLINICAL SIGNS MALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT		RECOVERY
	WEEK:	12.....	1.....4.....
	DAY:	71234567123456712345671234567	12345671234567123456712345672
GROUP 3 (300 MG/KG)			
ANIMAL 26			
Breathing			
Rales (3)	G:	
Skin / fur			
Swelling (4) (Abdomen)	G:	
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	
Chromodacryorrhoea (3) (Neck)	G:11111.....	
ANIMAL 27			
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	
ANIMAL 28			
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	
ANIMAL 29			
Skin / fur			
Swelling (4) (Abdomen)	G:	11111111111111111111111111111111	
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	
ANIMAL 30			
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	
ANIMAL 31			
Skin / fur			
Swelling (4) (Abdomen)	G:	.11111111111111111111111111111111	
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	
ANIMAL 32			
Breathing			
Rales (3)	G:	11111111112.1111111.....	
Skin / fur			
Swelling (4) (Abdomen)	G:	.11111111111111111111111111111111	
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	
ANIMAL 33			
Breathing			
Rales (3)	G:	.111111111...1111111111111111	
Skin / fur			
Swelling (4) (Abdomen)	G:	.1111111111111111.....	
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	
ANIMAL 34			
Breathing			
Rales (3)	G:1111.....1	
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	
ANIMAL 35			
Breathing			
Rales (3)	G:	
Skin / fur			
Swelling (4) (Abdomen)	G:	1.....	
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	

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

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.2 CLINICAL SIGNS MALES

SIGN (MAX. GRADE) (LOCATION)	WEEK: DAY:	TREATMENT	RECOVERY
	 12.....	1..... 4.....
GROUP 4 (600 MG/KG)			
ANIMAL 36			
Posture			
Hunched posture (1)	G: 1	
Skin / fur			
Swelling (4) (Abdomen)	G:	
Secretion / excretion			
Salivation (3)	G:	11111111	
Various			
Lean (1)	G: 1	
ANIMAL 37			
Posture			
Hunched posture (1)	G: 11.....	
Skin / fur			
Swelling (4) (Abdomen)	G:	
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	
ANIMAL 38			
Posture			
Hunched posture (1)	G: 111111	
Breathing			
Rales (3)	G:	
Skin / fur			
Swelling (4) (Abdomen)	G:	... 1111111111111111111111111111	
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	
ANIMAL 39			
Skin / fur			
Swelling (4) (Abdomen)	G:	. 1111111111111111111111111111	
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	
ANIMAL 40			
Posture			
Hunched posture (1)	G:		
Skin / fur			
Swelling (4) (Abdomen)	G:		
Secretion / excretion			
Salivation (3)	G:		
Various			
Lean (1)	G:		
Red (1) (Snout)	G:		
ANIMAL 41			
Breathing			
Rales (3)	G:	.. 111..... 11111111. 11. 11	
Skin / fur			
Swelling (4) (Abdomen)	G:	11111111111111111111111111111111	
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	
ANIMAL 42			
Breathing			
Rales (3)	G: 1111111111111111	
Skin / fur			
Swelling (4) (Abdomen)	G:	11111111111111111111111111111111	
Secretion / excretion			

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

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.2 CLINICAL SIGNS MALES

SIGN (MAX. GRADE) (LOCATION)	WEEK: DAY:	TREATMENT	RECOVERY
	 12.....	1..... 4.....
		71234567123456712345671234567	12345671234567123456712345672
GROUP 4 (600 MG/KG)			
Salivation (3)	G:	11111111111111111111111111111111	
ANIMAL 43			
Skin / fur			
Swelling (4) (Abdomen)	G:	11111111111111111111111111111111	1.....
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111
ANIMAL 44			
Secretion / excretion			
Salivation (3)	G:		
ANIMAL 45			
Posture			
Hunched posture (1)	G:
Breathing			
Rales (3)	G:	. 11111111111111111111111111111111	1.....
Skin / fur			
Swelling (4) (Abdomen)	G:	11111111111111111111111111111111	1.....
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111
Various			
Exophthalmos (1)	G:	1.....
Exophthalmos (1) (Eye right)	G:	1111111111.....
Opacity (1) (Eye right)	G:	11111111111111111111111111111111.....
ANIMAL 46			
Breathing			
Rales (3)	G:
Skin / fur			
Swelling (4) (Abdomen)	G:	11111111111111111111111111111111	1.....
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111
ANIMAL 47			
Posture			
Hunched posture (1)	G:
Breathing			
Rales (3)	G:
Skin / fur			
Swelling (4) (Abdomen)	G:
Piloerection (1)	G:
Secretion / excretion			
Salivation (3)	G:
Various			
Lean (1)	G:
ANIMAL 48			
Posture			
Hunched posture (1)	G:
Breathing			
Laboured respiration (3)	G:
Rales (3)	G:
Skin / fur			
Swelling (4) (Abdomen)	G:
Secretion / excretion			
Salivation (3)	G:
Various			
Lean (1)	G:

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

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.2 CLINICAL SIGNS MALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT							RECOVERY												
	WEEK:	12							1	4										
	DAY:	7	12	34	56	71	23	45	67	12	34	56	71	23	45	67	12	34	56	72
GROUP 4 (600 MG/KG)																				
ANIMAL 49																				
Breathing																				
Rales (3)	G:	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Skin / fur																				
Swelling (4) (Abdomen)	G:																			
Secretion / excretion																				
Salivation (3)	G:	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
ANIMAL 50																				
Posture																				
Hunched posture (1)	G:	1																		
Breathing																				
Laboured respiration (3)	G:																			11
Deep respiration (1)	G:																			111
Rales (3)	G:	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Skin / fur																				
Swelling (4) (Abdomen)	G:	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Piloerection (1)	G:																			
Secretion / excretion																				
Salivation (3)	G:	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Various																				
Lean (1)	G:	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

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

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.2 CLINICAL SIGNS FEMALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT							
	WEEK: 1	2	3	4	5	6	7	8
GROUP 1 (CONTROL)								
ANIMAL 51								
Secretion / excretion								
Salivation (3)	G:	1111111111	1111111111	1111111111	1111111111	1111111111	1111111111
ANIMAL 52								
Secretion / excretion								
Salivation (3)	G:	1111111111	1111111111	1111111111	1111111111	1111111111	1111111111
ANIMAL 53								
Breathing								
Rales (3)	G:						
Secretion / excretion								
Salivation (3)	G:	1111111111	1111111111	1111111111	1111111111	1111111111	1111111111
ANIMAL 54								
Skin / fur								
Swelling (4) (Abdomen)	G:						
Secretion / excretion								
Salivation (3)	G:	1111111111	1111111111	1111111111	1111111111	1111111111
ANIMAL 55								
Secretion / excretion								
Salivation (3)	G:	1111111111	1111111111	1111111111	1111111111	1111111111	1111111111
ANIMAL 56								
Secretion / excretion								
Salivation (3)	G:	1111111111	1211111111	1111111111	1111111111	1111111111
ANIMAL 57								
Secretion / excretion								
Salivation (3)	G:	111. 1111111111	1111111111	1111111111	1111111111	1111111111	1111111111
ANIMAL 58								
Skin / fur								
Swelling (4) (Abdomen)	G:						
Secretion / excretion								
Salivation (3)	G:	1111111111	1211111111	1111111111	1111111111	1111111111	1111111111
ANIMAL 59								
Skin / fur								
Swelling (4) (Abdomen)	G:						
Secretion / excretion								
Salivation (3)	G:	1111111111	1111111111	1111111111	1111111111	1111111111	1111111111
ANIMAL 60								
Skin / fur								
Swelling (4) (Abdomen)	G:						
Secretion / excretion								
Salivation (3)	G:	1111111111	1111111111	1111111111	1111111111	1111111111	1111111111
ANIMAL 61								
Secretion / excretion								
Salivation (3)	G:	1111111111	12211111	12221111	11111111	11111111	11111111
ANIMAL 62								
Breathing								
Rales (3)	G:						
Secretion / excretion								
Salivation (3)	G:	1111111111	12221111	12221111	1112.	1111111111	1111111111
ANIMAL 63								
Skin / fur								
Scabs (3) (Neck)	G:					1111.
Secretion / excretion								
Salivation (3)	G:	1111111111	1111111111	1111111111	1111111111	1111111111	1111111111
ANIMAL 64								
Secretion / excretion								
Salivation (3)	G:	1111111111	1111111111	1211.	1111111111	1111111111	1111111111

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

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.2 CLINICAL SIGNS FEMALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT							
	WEEK: 1	2	3	4	5	6	7	8
	DAY:	1234567	1234567	1234567	1234567	1234567	1234567	1234567
GROUP 1 (CONTROL)								
ANIMAL 65								
Posture								
Hunched posture (1)	G:			11				
Breathing								
Rales (3)	G:							
Secretion / excretion								
Salivation (3)	G:	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111
GROUP 2 (100 MG/KG)								
ANIMAL 66								
Secretion / excretion								
Salivation (3)	G:	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111
ANIMAL 67								
Secretion / excretion								
Salivation (3)	G:	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111
ANIMAL 68								
Breathing								
Rales (3)	G:							
Secretion / excretion								
Salivation (3)	G:	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111
ANIMAL 69								
Secretion / excretion								
Salivation (3)	G:	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111
ANIMAL 70								
Skin / fur								
Swelling (4) (Abdomen)	G:							1
Secretion / excretion								
Salivation (3)	G:	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111
ANIMAL 71								
Skin / fur								
Swelling (4) (Abdomen)	G:							1
Secretion / excretion								
Salivation (3)	G:	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111
ANIMAL 72								
Secretion / excretion								
Salivation (3)	G:	1111111111111111	1111111111111111	2111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111
ANIMAL 73								
Secretion / excretion								
Salivation (3)	G:	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111
ANIMAL 74								
Secretion / excretion								
Salivation (3)	G:	1111111111111111	1111111111111111	1211111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111
Various								
Lean (1)	G:							
ANIMAL 75								
Secretion / excretion								
Salivation (3)	G:	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111	1111111111111111
GROUP 3 (300 MG/KG)								
ANIMAL 76								
Breathing								
Rales (3)	G:						1	
Skin / fur								
Swelling (4) (Abdomen)	G:							1
Secretion / excretion								
Salivation (3)	G:	111111111111122222	1111112211111111	1111111111111111	1111111111111111	1111111111111111	1211111111111111	1111111111111111
ANIMAL 77								
Skin / fur								

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

**2.2 CLINICAL SIGNS
FEMALES**

SIGN (MAX. GRADE) (LOCATION)	TREATMENT							
	WEEK: 1	2	3	4	5	6	7	8
GROUP 3 (300 MG/KG)								
Swelling (4) (Abdomen)	G:
Secretion / excretion Salivation (3)	G:	11111111111111111111	11112211112111111111111111111111111111	11112211112111111111111111111111111111
ANIMAL 78 Secretion / excretion Salivation (3)	G:	11111111112111111111	11112211111111111111111111111111111111	11112211111111111111111111111111111111
ANIMAL 79 Secretion / excretion Salivation (3)	G:	11111111111122211112	11112211112111111111111111111111111111	11112211111111111111111111111111111111
ANIMAL 80 Breathing Rales (3)	G:	11
Skin / fur Swelling (4) (Abdomen)	G:1
Secretion / excretion Salivation (3)	G:	11111111111111111111	11111121111111111111111111111111111111	11111121111111111111111111111111111111
ANIMAL 81 Secretion / excretion Salivation (3)	G:	11111111111111111111	11112211111111111111111111111111111111	11112211111111111111111111111111111111
ANIMAL 82 Secretion / excretion Salivation (3)	G:	111111111111112221	1111111111.....	11111111111111111111222111111111
ANIMAL 83 Skin / fur Swelling (4) (Abdomen)	G:1
Secretion / excretion Salivation (3)	G:	11111111111111111112	11111112111111111111111111111111111111	11111112111111111111111111111111111111
ANIMAL 84 Breathing Rales (3)	G:	1111111111
Secretion / excretion Salivation (3)	G:	11111111111111111111	11111211111111111111111111111111111111	11111112111111111111111111111111111111
ANIMAL 85 Breathing Rales (3)	G:	111	1
Secretion / excretion Salivation (3)	G:	11111111111111111111	11112211112211111111111111111111111111	11112211111111111111111111111111111111
Various Lean (1)	G:
GROUP 4 (600 MG/KG)								
ANIMAL 86 Skin / fur Swelling (4) (Abdomen)	G:	11111	1111
Secretion / excretion Salivation (3)	G:	111111111111112222	22111122221.....	11111111111111111111	1111111111111111
Various Lean (1)	G:1
ANIMAL 87 Breathing Rales (3)	G:	1111111111111111
Skin / fur Swelling (4) (Abdomen)	G:	1111
Secretion / excretion Salivation (3)	G:	111111111111112222	221222221.....	11111111111111111111	11111111111111

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

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.2 CLINICAL SIGNS FEMALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT							
	WEEK: 1	2	3	4	5	6	7	8
	DAY:	1234567	1234567	1234567	1234567	1234567	1234567	1234567
GROUP 4 (600 MG/KG)								
ANIMAL 88								
Posture								
Hunched posture (1)	G:			1				
Breathing								
Rales (3)	G:			1111				
Secretion / excretion								
Salivation (3)	G:			111111111111222222				
Various								
Dehydrated (3)	G:			1				
Lean (1)	G:			111111				
ANIMAL 89								
Posture								
Hunched posture (1)	G:			111111				
Breathing								
Rales (3)	G:			11				1111111111
Skin / fur								
Swelling (4) (Abdomen)	G:			1111				
Secretion / excretion								
Salivation (3)	G:			11111111111122222212222222				1111111111111111222111111111
ANIMAL 90								
Breathing								
Rales (3)	G:			1				
Skin / fur								
Swelling (4) (Abdomen)	G:			1111				111111
Secretion / excretion								
Salivation (3)	G:			11111111111122222212222222				1111111111111111222111111111
ANIMAL 91								
Skin / fur								
Swelling (4) (Abdomen)	G:			111111				1111
Secretion / excretion								
Salivation (3)	G:			11111111111122222212222222				1111111111111111222111111111
ANIMAL 92								
Skin / fur								
Swelling (4) (Abdomen)	G:			11111111111112111111111111111111111111111111111111111				
Secretion / excretion								
Salivation (3)	G:			11111111111122222212222222				1111111111111111222111111111
ANIMAL 93								
Posture								
Hunched posture (1)	G:			111				
Breathing								
Laboured respiration (3)	G:			111				
Skin / fur								
Swelling (4) (Abdomen)	G:			11				
Secretion / excretion								
Salivation (3)	G:			111111111111222				
Various								
Lean (1)	G:			11				
ANIMAL 94								
Breathing								
Rales (3)	G:							1
Skin / fur								
Swelling (4) (Abdomen)	G:			111				1111111111111111111111111111111111
Secretion / excretion								
Salivation (3)	G:			11111111111122222212222221				111111111111111122221111111111

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

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.2 CLINICAL SIGNS FEMALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT							
	WEEK: 1	2	3	4	5	6	7	8
	DAY: 1234567123456712345671234567123456712345671234567123456							
GROUP 4 (600 MG/KG)								
ANIMAL 95								
Skin / fur								
Swelling (4) (Abdomen)	G:			111				111111111
Secretion / excretion								
Salivation (3)	G:	...	11111111111112222222	12222222	...	1111111111111111	122221111111	
ANIMAL 96								
Skin / fur								
Swelling (4) (Abdomen)	G:			11111111				
Secretion / excretion								
Salivation (3)	G:	...	11111111111122222221	12222222	...			
ANIMAL 97								
Skin / fur								
Swelling (4) (Abdomen)	G:			111				11111
Secretion / excretion								
Salivation (3)	G:	...	11111111111122222221222222	...	1111111111111111	122211111111		
ANIMAL 98								
Skin / fur								
Swelling (4) (Abdomen)	G:			11				
Secretion / excretion								
Salivation (3)	G:	...	111111111111222222211222222	...	1111111111111111	122211111111		
ANIMAL 99								
Breathing								
Rales (3)	G:							11111
Skin / fur								
Swelling (4) (Abdomen)	G:			1111				
Secretion / excretion								
Salivation (3)	G:	...	11111111111122222221222222	...	1111111111111111	122211111111		
ANIMAL 100								
Posture								
Hunched posture (1)	G:							11
Skin / fur								
Swelling (4) (Abdomen)	G:			1111				111111111111
Piloerection (1)	G:							11111
Secretion / excretion								
Salivation (3)	G:	...	111111111111222222211222222	...	1111111111111111	122221111111		
Various								
Lean (1)	G:							11

FEMALES

SIGN (MAX. GRADE) (LOCATION)	TREATMENT				RECOVERY
	WEEK: 1	2	3	12	1
	DAY: 71234567123456712345671234567 123456				
GROUP 1 (CONTROL)					
ANIMAL 51					
Secretion / excretion					
Salivation (3)	G:	1111111111111111111111111111	1		
ANIMAL 52					
Secretion / excretion					
Salivation (3)	G:	1111111111111111111111111111	1	...	
ANIMAL 53					
Breathing					

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

Final Report

MTDID 7831
APPENDIX 2

Project 511505

**2.2 CLINICAL SIGNS
FEMALES**

SIGN (MAX. GRADE) (LOCATION)	TREATMENT		RECOVERY
	WEEK: DAY: 12.....	1..... 123456
GROUP 4 (600 MG/KG)			
ANIMAL 89			
Posture			
Hunched posture (1)	G:	
Breathing			
Rales (3)	G:	
Skin / fur			
Swelling (4) (Abdomen)	G:	. 11111111111111111111111111111111	1.....
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	1.....
ANIMAL 90			
Breathing			
Rales (3)	G: 11111111	1.....
Skin / fur			
Swelling (4) (Abdomen)	G:	11111111111111111111111111111111	1.....
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	1.....
ANIMAL 91			
Skin / fur			
Swelling (4) (Abdomen)	G:	
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	1.....
ANIMAL 92			
Skin / fur			
Swelling (4) (Abdomen)	G:	11111111111111111111111111111111	1.....
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	1.....
ANIMAL 93			
Posture			
Hunched posture (1)	G:		
Breathing			
Laboured respiration (3)	G:		
Skin / fur			
Swelling (4) (Abdomen)	G:		
Secretion / excretion			
Salivation (3)	G:		
Various			
Lean (1)	G:		
ANIMAL 94			
Breathing			
Rales (3)	G:	11111..... 111111	1.....
Skin / fur			
Swelling (4) (Abdomen)	G:	11111111111111111111111111111111	1.....
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	1.....
ANIMAL 95			
Skin / fur			
Swelling (4) (Abdomen)	G:	11111111111111111111111111111111	1.....
Secretion / excretion			
Salivation (3)	G:	11111111111111111111111111111111	1.....
ANIMAL 96			
Skin / fur			
Swelling (4) (Abdomen)	G:		
Secretion / excretion			

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

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.2 CLINICAL SIGNS FEMALES

SIGN (MAX. GRADE) (LOCATION)	WEEK: DAY:	TREATMENT	RECOVERY
		1... 1234	1.....4..... 12345671234567123456712345671
GROUP 1 (CONTROL)			
ANIMAL 51			
No clinical signs noted			
ANIMAL 52			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 53			
Breathing			
Rales (3)	G:	.. 11	
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 54			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 55			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 56			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 57			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 58			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 59			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 60			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 61			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 62			
Breathing			
Rales (3)	G:	.. 11	
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 63			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 64			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 65			
Secretion / excretion			
Salivation (3)	G:	1111	
GROUP 2 (100 MG/KG)			
ANIMAL 66			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 67			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 68			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 69			
Secretion / excretion			

Note: From Day 93 up to scheduled day of necropsy clinical signs were recorded in Project 514129
G: Highest daily grades
.: Observation performed, sign not present

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.2 CLINICAL SIGNS FEMALES

SIGN (MAX. GRADE) (LOCATION)	WEEK: DAY:	TREATMENT	RECOVERY
		1... 1234	1.....4..... 12345671234567123456712345671
GROUP 2 (100 MG/KG)			
Salivation (3)	G:	1111	
ANIMAL 70			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 71			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 72			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 73			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 74			
No clinical signs noted			
ANIMAL 75			
Secretion / excretion			
Salivation (3)	G:	1111	
GROUP 3 (300 MG/KG)			
ANIMAL 76			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 77			
No clinical signs noted			
ANIMAL 78			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 79			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 80			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 81			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 82			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 83			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 84			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 85			
Secretion / excretion			
Salivation (3)	G:	1111	
GROUP 4 (1000 MG/KG)			
ANIMAL 86			
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 87			
Breathing			
Rales (3)	G:	. . 11	
Secretion / excretion			
Salivation (3)	G:	1111	
ANIMAL 88			
No clinical signs noted			

Note: From Day 93 up to scheduled day of necropsy clinical signs were recorded in Project 514129
G: Highest daily grades
.: Observation performed, sign not present

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.2 CLINICAL SIGNS FEMALES

SIGN (MAX. GRADE) (LOCATION)	WEEK: DAY:	TREATMENT	RECOVERY
		1... 1234	1.....4..... 12345671234567123456712345671
GROUP 4 (1000 MG/KG)			
ANIMAL 89			
Secretion / excretion			
Salivation (3)	G: 1111		
ANIMAL 90			
Secretion / excretion			
Salivation (3)	G: 1111		
ANIMAL 91			
Secretion / excretion			
Salivation (3)	G: 1111		
ANIMAL 92			
Skin / fur			
Swelling (4) (Abdomen)	G: 1111		
Secretion / excretion			
Salivation (3)	G: 1111		
ANIMAL 93			
No clinical signs noted			
ANIMAL 94			
Skin / fur			
Alopecia (3)	G: 1111111111.	
Secretion / excretion			
Salivation (3)	G: 1111		
ANIMAL 95			
Secretion / excretion			
Salivation (3)	G: 1111		
ANIMAL 96			
No clinical signs noted			
ANIMAL 97			
Secretion / excretion			
Salivation (3)	G: 1111		
ANIMAL 98			
Secretion / excretion			
Salivation (3)	G: 1111		
ANIMAL 99			
Secretion / excretion			
Salivation (3)	G: 1111		
ANIMAL 100			
No clinical signs noted			

Note: From Day 93 up to scheduled day of necropsy clinical signs were recorded in Project 514129
G: Highest daily grades
.: Observation performed, sign not present

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.3 FUNCTIONAL OBSERVATIONS MALES

WEEK 13

ANIMAL	HEARING SCORE 0/1	PUPIL L SCORE 0/1	PUPIL R SCORE 0/1	STATIC R SCORE 0/1	GRIP FORE GRAM	GRIP HIND GRAM
GROUP 1 (CONTROL)						
11	0	0	0	0	1170	722
12	0	0	0	0	767	399
13	0	0	0	0	1239	640
14	0	0	0	0	1095	396
15	0	0	0	0	712	433
GROUP 2 (100 MG/KG)						
16	0	0	0	0	878	335
17	0	0	0	0	782	419
18	0	0	0	0	805	498
19	0	0	0	0	561	352
20	0	0	0	0	1098	479
GROUP 3 (300 MG/KG)						
26	0	0	0	0	887	362
27	0	0	0	0	615	371
28	0	0	0	0	944	491
29	0	0	0	0	1018	395
30	0	0	0	0	835	411
GROUP 4 (600 MG/KG)						
37	0	0	0	0	937	377
38	0	0	0	0	673	395
39	0	0	0	0	1114	401
46	0	0	0	0	1148	503
49	0	0	0	0	816	383

FEMALES

WEEK 13

ANIMAL	HEARING SCORE 0/1	PUPIL L SCORE 0/1	PUPIL R SCORE 0/1	STATIC R SCORE 0/1	GRIP FORE GRAM	GRIP HIND GRAM
GROUP 1 (CONTROL)						
61	0	0	0	0	911	377
62	0	0	0	0	1315	410
63	0	0	0	0	675	419
64	0	0	0	0	1155	451
65	0	0	0	0	1353	497
GROUP 2 (100 MG/KG)						
66	0	0	0	0	1011	418
67	0	0	0	0	696	377
68	0	0	0	0	967	411
69	0	0	0	0	617	398
70	0	0	0	0	1081	450
GROUP 3 (300 MG/KG)						
76	0	0	0	0	1006	449
78	0	0	0	0	871	425
79	0	0	0	0	1059	400
80	0	0	0	0	834	469
81	0	0	0	0	640	391
GROUP 4 (600 MG/KG)						
86	0	0	0	0	883	412
87	0	0	0	0	1361	523
97	0	0	0	0	897	401
98	0	0	0	0	823	495

**2.3 FUNCTIONAL OBSERVATIONS
FEMALES**

WEEK 13

ANIMAL	HEARING SCORE 0/1	PUPIL L SCORE 0/1	PUPIL R SCORE 0/1	STATIC R SCORE 0/1	GRIP FORE GRAM	GRIP HIND GRAM
GROUP 4 (600 MG/KG)						
99	0	0	0	0	1221	527

2.4 MOTOR ACTIVITY TEST - TOTAL MOVEMENTS

MALES

AT WEEK 12-13

ANIMAL	Interval (5 min.)												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
GROUP 1 (CONTROL)													
11	610	394	121	33	29	191	221	472	349	297	60	6	2783
12	537	341	312	100	273	4	26	5	1	106	178	39	1922
13	819	439	341	204	101	63	400	279	2	6	3	6	2663
14	727	434	249	56	43	245	20	3	23	19	44	7	1870
15	1094	532	489	444	567	200	285	7	8	375	252	11	4264
GROUP 2 (100 MG/KG)													
16	984	830	563	469	30	178	535	98	35	2	5	0	3729
17	789	547	296	296	404	425	101	2	10	84	0	0	2954
18	651	437	239	178	6	326	328	1	152	431	56	3	2808
19	765	420	252	10	119	20	57	113	271	437	114	50	2628
20	733	542	715	642	493	261	195	154	296	111	11	490	4643
GROUP 3 (300 MG/KG)													
26	632	421	363	122	161	219	138	270	43	541	156	121	3187
27	837	336	407	510	315	85	148	384	62	123	204	69	3480
28	468	305	229	398	171	239	303	149	334	107	278	341	3322
29	682	377	171	199	287	10	313	24	13	25	26	98	2225
30	476	99	36	13	197	454	303	221	39	7	14	295	2154
GROUP 4 (600 MG/KG)													
37	461	241	189	213	94	285	97	50	26	7	1	6	1670
38	462	174	173	188	4	20	24	6	37	186	1	10	1285
39	912	623	622	313	408	69	247	558	409	437	1	0	4599
46	535	404	255	290	158	305	301	3	54	6	5	2	2318
49	503	282	7	118	167	1	1	5	10	29	146	50	1319

2.4 MOTOR ACTIVITY TEST - AMBULATIONS

MALES

AT WEEK 12-13

ANIMAL	Interval (5 min.)												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
GROUP 1 (CONTROL)													
11	122	128	17	0	0	4	1	126	73	38	0	0	509
12	116	113	109	21	74	0	0	0	0	22	47	0	502
13	242	135	101	52	2	15	126	44	0	0	0	0	717
14	212	98	71	14	0	42	2	0	1	0	0	0	440
15	234	126	136	123	144	45	42	0	0	120	79	0	1049
GROUP 2 (100 MG/KG)													
16	157	182	102	103	2	34	97	2	2	0	0	0	681
17	258	157	68	93	47	102	24	0	0	0	0	0	749
18	103	122	48	58	0	95	96	0	53	130	9	1	715
19	174	72	78	1	3	0	3	6	58	89	1	0	485
20	230	205	166	171	119	75	40	56	102	37	0	136	1337
GROUP 3 (300 MG/KG)													
26	194	86	80	24	33	58	16	96	10	127	25	22	771
27	132	60	61	111	70	1	36	87	9	23	54	2	646
28	156	94	81	109	64	55	71	33	82	17	72	31	865
29	242	114	13	40	66	0	100	0	0	2	1	5	583
30	159	18	1	0	35	136	51	5	0	0	1	74	480
GROUP 4 (600 MG/KG)													
37	104	66	36	65	27	66	12	0	0	0	0	0	376
38	137	37	39	32	0	0	1	0	2	47	0	0	295
39	165	90	45	24	49	0	46	58	33	75	0	0	585
46	83	62	39	62	36	61	43	0	0	0	0	0	386
49	183	110	0	49	50	0	0	0	0	12	42	34	480

**2.4 MOTOR ACTIVITY TEST - TOTAL MOVEMENTS
 FEMALES**

AT WEEK 12-13

ANIMAL	Interval (5 min.)												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
GROUP 1 (CONTROL)													
61	775	590	415	386	428	41	572	208	497	283	4	36	4235
62	949	384	537	620	572	104	9	33	654	216	69	12	4159
63	776	572	395	28	131	39	50	66	19	35	38	180	2329
64	830	620	528	376	298	306	150	431	328	290	448	296	4901
65	796	914	554	198	412	172	213	29	238	14	0	0	3540
GROUP 2 (100 MG/KG)													
66	1115	808	211	167	181	377	327	390	431	66	228	85	4386
67	880	621	505	118	594	254	304	279	353	316	897	602	5723
68	786	529	257	344	392	160	0	315	312	137	334	173	3739
69	953	615	510	190	321	67	237	131	130	52	237	193	3636
70	543	386	346	709	91	534	311	563	45	93	0	0	3621
GROUP 3 (300 MG/KG)													
76	1068	814	531	137	899	689	64	127	754	464	722	9	6278
78	748	265	488	246	422	179	439	244	605	33	0	0	3669
79	397	33	142	59	244	2	68	24	30	49	23	0	1071
80	952	510	510	169	501	308	17	567	784	591	15	21	4945
81	1142	685	335	124	438	376	341	335	257	310	524	402	5269
GROUP 4 (600 MG/KG)													
86	1034	607	514	131	89	88	14	393	51	164	29	1	3115
87	918	433	448	265	394	285	80	246	432	33	4	30	3568
97	1039	633	346	299	542	413	58	580	389	167	1	2	4469
98	1230	956	791	449	330	760	572	538	62	0	1	1	5690
99	982	262	80	465	444	209	322	86	414	203	21	274	3762

**2.4 MOTOR ACTIVITY TEST - AMBULATIONS
 FEMALES**

AT WEEK 12-13

ANIMAL	Interval (5 min.)												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
GROUP 1 (CONTROL)													
61	299	183	134	98	145	14	199	54	142	70	1	2	1341
62	331	139	153	172	145	1	0	0	227	8	0	0	1176
63	271	153	126	0	2	0	0	0	0	0	0	3	555
64	238	134	146	92	75	49	50	118	69	4	142	31	1148
65	246	310	124	55	114	6	39	0	36	0	0	0	930
GROUP 2 (100 MG/KG)													
66	402	255	48	29	23	70	48	105	78	1	13	0	1072
67	274	227	176	20	197	53	105	53	94	46	306	198	1749
68	335	201	59	119	102	50	0	119	66	4	108	0	1163
69	370	216	117	23	74	2	80	30	32	3	69	54	1070
70	202	111	81	190	0	100	64	154	2	0	0	0	904
GROUP 3 (300 MG/KG)													
76	410	313	171	22	224	230	1	7	263	80	237	0	1958
78	242	95	183	75	94	21	107	52	157	1	0	0	1027
79	120	0	34	21	66	0	33	1	1	15	0	0	291
80	299	170	155	50	115	108	1	193	188	132	2	3	1416
81	447	289	121	32	93	126	101	90	74	43	137	54	1607
GROUP 4 (600 MG/KG)													
86	294	213	129	25	26	27	0	117	15	3	0	0	849
87	378	155	208	80	130	69	0	34	90	3	0	0	1147
97	384	269	138	124	229	181	0	193	120	0	0	0	1638
98	455	281	215	89	55	159	118	139	1	0	0	0	1512
99	336	92	16	154	125	56	99	12	107	59	0	77	1133

**2.5 OPHTHALMOSCOPIC EXAMINATIONS
MALES****PRETEST**

ANIMAL	EYES	OBSERVATION
GROUP 1 (CONTROL)		
1	Left	Focal Corneal Edema
1	Both	Focal Corneal Opacity
2	Left	Focal Corneal Edema
2	Right	Focal Corneal Opacity
3	Right	Focal Corneal Opacity
4	Both	No Findings
5	Both	Corneal Edema
6	Both	No Findings
7	Both	No Findings
8	Both	Focal Corneal Edema
8	Both	Focal Corneal Opacity
9	Right	Focal Corneal Edema
9	Right	Focal Corneal Opacity
10	Both	No Findings
11	Both	No Findings
12	Both	No Findings
13	Right	Focal Corneal Opacity
14	Both	No Findings
15	Right	Focal Corneal Opacity
GROUP 2 (100 MG/KG)		
16	Both	No Findings
17	Right	Focal Corneal Opacity
18	Both	Pinpoint Corneal Opacities
19	Both	No Findings
20	Both	No Findings
21	Left	Haemorrhage In Retina
21	Right	Focal Corneal Edema
21	Right	Focal Corneal Opacity
22	Right	Focal Corneal Opacity
23	Both	No Findings
24	Both	No Findings
25	Left	Pinpoint Corneal Opacities
25	Right	Focal Corneal Opacity
GROUP 3 (300 MG/KG)		
26	Right	Focal Corneal Opacity
27	Left	Focal Corneal Edema
27	Both	Focal Corneal Opacity
28	Right	Focal Corneal Opacity
29	Both	Focal Corneal Edema
29	Both	Focal Corneal Opacity
30	Both	No Findings
31	Both	No Findings
32	Both	No Findings
33	Both	Corneal Edema
34	Both	No Findings
35	Both	No Findings
GROUP 4 (600 MG/KG)		
36	Both	No Findings
37	Right	Focal Corneal Edema
38	Both	No Findings
39	Both	No Findings
40	Right	Focal Corneal Edema
40	Both	Focal Corneal Opacity
41	Both	Corneal Edema
42	Right	Focal Corneal Edema
42	Right	Focal Corneal Opacity
43	Both	No Findings
44	Both	No Findings
45	Both	No Findings
46	Both	No Findings

**2.5 OPHTHALMOSCOPIC EXAMINATIONS
MALES****PRETEST**

ANIMAL	EYES	OBSERVATION
GROUP 4 (600 MG/KG)		
47	Both	Corneal Edema
48	Both	No Findings
49	Both	Corneal Edema
50	Both	Corneal Edema

MALES**AT WEEK 13**

ANIMAL	EYES	OBSERVATION
GROUP 1 (CONTROL)		
1	Both	No Findings
2	Both	Focal Corneal Edema
2	Both	Focal Corneal Opacity
3	Both	No Findings
4	Right	Focal Corneal Opacity
5	Both	Focal Corneal Edema
5	Both	Focal Corneal Opacity
6	Right	Focal Corneal Opacity
7	Right	Focal Corneal Opacity
8	Both	No Findings
9	Both	No Findings
10	Right	Focal Corneal Opacity
11	Both	No Findings
12	Left	Focal Corneal Edema
12	Both	Focal Corneal Opacity
13	Right	Focal Corneal Opacity
14	Left	Focal Corneal Opacity
15	Right	Focal Corneal Opacity
GROUP 4 (600 MG/KG)		
37	Both	No Findings
38	Right	Focal Corneal Opacity
39	Both	No Findings
41	Both	Pinpoint Corneal Opacities
41	Both	Focal Corneal Opacity
42	Both	No Findings
43	Right	Pinpoint Corneal Opacities
43	Both	Focal Corneal Opacity
45	Left	Focal Corneal Opacity
46	Left	Focal Corneal Edema
46	Both	Focal Corneal Opacity
49	Left	Focal Corneal Opacity

FEMALES**PRETEST**

ANIMAL	EYES	OBSERVATION
GROUP 1 (CONTROL)		
51	Right	Focal Corneal Opacity
52	Both	No Findings
53	Both	No Findings
54	Both	No Findings
55	Right	Focal Corneal Opacity
56	Right	Focal Corneal Edema
56	Both	Focal Corneal Opacity

**2.5 OPHTHALMOSCOPIC EXAMINATIONS
FEMALES****PRETEST**

ANIMAL	EYES	OBSERVATION
GROUP 1 (CONTROL)		
57	Right	Focal Corneal Opacity
57	Both	Corneal Edema
58	Both	No Findings
59	Right	Focal Corneal Opacity
60	Right	Focal Corneal Edema
61	Both	No Findings
62	Both	No Findings
63	Both	No Findings
64	Both	No Findings
65	Right	Focal Corneal Opacity
GROUP 2 (100 MG/KG)		
66	Both	No Findings
67	Both	No Findings
68	Both	Corneal Edema
69	Both	No Findings
70	Both	Focal Corneal Opacity
71	Left	Focal Corneal Opacity
72	Both	No Findings
73	Right	Focal Corneal Edema
73	Both	Focal Corneal Opacity
74	Right	Focal Corneal Edema
74	Right	Focal Corneal Opacity
75	Right	Focal Corneal Opacity
GROUP 3 (300 MG/KG)		
76	Both	No Findings
77	Right	Focal Corneal Edema
77	Right	Focal Corneal Opacity
78	Both	No Findings
79	Both	No Findings
80	Right	Focal Corneal Opacity
80	Both	Focal Corneal Edema
81	Right	Corneal Edema
82	Both	No Findings
83	Both	Focal Corneal Edema
83	Both	Focal Corneal Opacity
84	Both	Corneal Edema
85	Both	No Findings
GROUP 4 (600 MG/KG)		
86	Both	No Findings
87	Both	No Findings
88	Right	Focal Corneal Opacity
89	Right	Focal Corneal Edema
90	Both	No Findings
91	Both	No Findings
92	Both	No Findings
93	Right	Focal Corneal Opacity
94	Both	No Findings
95	Right	Pinpoint Corneal Opacities
96	Both	No Findings
97	Both	No Findings
98	Both	Focal Corneal Edema
98	Both	Focal Corneal Opacity
99	Left	Focal Corneal Opacity
100	Both	No Findings

**2.5 OPHTHALMOSCOPIC EXAMINATIONS
FEMALES****AT WEEK 13**

ANIMAL	EYES	OBSERVATION
GROUP 1 (CONTROL)		
51	Right	Focal Corneal Edema
51	Right	Focal Corneal Opacity
52	Both	Focal Corneal Opacity
53	Right	Focal Corneal Opacity
54	Both	No Findings
55	Right	Focal Corneal Opacity
56	Left	Focal Corneal Edema
57	Both	Focal Corneal Opacity
58	Right	Focal Corneal Opacity
59	Left	Focal Corneal Edema
59	Both	Focal Corneal Opacity
60	Both	No Findings
61	Left	Focal Corneal Opacity
62	Right	Focal Corneal Edema
62	Right	Focal Corneal Opacity
63	Both	No Findings
64	Right	Focal Corneal Opacity
65	Both	Focal Corneal Opacity
GROUP 4 (600 MG/KG)		
86	Right	Focal Corneal Opacity
87	Right	Focal Corneal Opacity
89	Left	Focal Corneal Opacity
90	Right	Focal Corneal Opacity
91	Left	Focal Corneal Edema
91	Left	Focal Corneal Opacity
92	Right	Focal Corneal Opacity
94	Both	No Findings
95	Right	Focal Corneal Opacity
97	Both	No Findings
98	Both	Focal Corneal Opacity
99	Right	Focal Corneal Opacity

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.6 BODY WEIGHTS (GRAM) MALES

DAYS WEEKS ANIMAL	TREATMENT														RECOVERY					
	1	8	15	22	29	33	34	36	43	50	57	64	71	78	85	91	1	2	8	15
	1	2	3	4	5	5	5	6	7	8	9	10	11	12	13	13	1	1	2	3
GROUP 1 (CONTROL)																				
1	167	208	244	270	286	293	293	294	311	325	335	345	348	346	358	366	---	---	---	
2	170	220	268	305	326	341	347	348	365	381	390	402	416	426	431	435	---	---	---	
3	170	212	245	274	289	298	299	303	315	326	336	342	348	352	360	361	---	---	---	
4	158	204	243	273	295	309	313	315	328	337	346	351	360	363	371	362	---	---	---	
5	170	207	248	281	303	315	320	327	344	359	370	382	394	399	411	406	---	---	---	
6	180	230	283	318	349	367	369	380	397	416	433	446	449	461	474	484	---	---	---	
7	169	209	253	285	289	303	306	312	331	341	348	354	361	363	364	365	---	---	---	
8	177	227	260	293	315	332	336	340	353	364	378	390	398	406	414	416	---	---	---	
9	169	212	252	279	298	308	312	318	332	345	357	364	370	378	386	388	---	---	---	
10	168	205	248	275	295	300	308	310	325	334	339	345	345	351	357	362	---	---	---	
11	161	201	228	252	272	283	284	292	306	318	328	335	342	351	358	363	340	351	359	
12	166	208	242	269	292	303	309	313	323	338	344	355	361	367	371	380	355	378	390	
13	168	215	262	293	321	334	335	344	364	380	391	405	411	429	437	437	408	438	447	
14	171	211	249	281	296	304	305	310	322	335	347	361	372	380	371	377	359	383	395	
15	162	209	249	275	299	310	315	321	331	340	352	359	375	385	394	400	378	398	414	
GROUP 2 (100 MG/KG)																				
16	184	231	271	297	316	334	338	343	361	375	385	392	404	413	421	430	---	---	---	
17	163	201	241	272	273	290	290	298	308	325	337	347	362	370	378	385	---	---	---	
18	158	196	233	264	281	295	298	306	318	327	346	354	370	382	389	389	---	---	---	
19	159	205	239	270	289	301	301	308	317	329	336	344	356	361	369	378	---	---	---	
20	182	223	257	288	298	312	314	319	326	340	356	362	373	381	389	390	---	---	---	
21	171	208	244	274	294	305	304	311	323	334	337	348	350	357	365	369	---	---	---	
22	184	236	288	318	347	364	366	373	386	397	404	414	424	433	446	450	---	---	---	
23	169	219	266	297	323	321	323	330	349	370	382	396	399	408	422	427	---	---	---	
24	160	202	247	282	306	320	318	326	328	324	328	339	346	359	372	373	---	---	---	
25	179	227	272	311	323	336	334	341	351	356	362	377	387	398	409	414	---	---	---	
GROUP 3 (300 MG/KG)																				
26	166	200	240	277	290	305	307	308	317	322	330	329	335	348	354	351	---	---	---	
27	172	210	249	276	294	308	309	312	321	331	336	337	348	355	364	365	---	---	---	
28	175	212	252	285	305	317	321	328	339	351	351	360	368	382	393	390	---	---	---	
29	179	207	229	271	289	306	306	297	323	300	337	349	354	360	365	359	---	---	---	
30	174	214	244	271	284	287	288	287	295	307	309	316	317	325	336	344	---	---	---	
31	171	219	267	299	325	340	340	346	356	359	370	377	389	403	417	419	---	---	---	
32	170	211	245	264	281	285	290	284	304	311	311	313	317	327	333	342	---	---	---	
33	167	206	236	252	260	278	281	282	295	305	312	319	324	331	342	343	---	---	---	
34	176	221	253	276	287	299	302	277	305	312	319	330	341	345	341	346	---	---	---	
35	165	196	246	275	288	302	301	304	316	324	331	335	342	342	345	353	---	---	---	
GROUP 4 (600 MG/KG)																				
36	157	189	220	238	233	246	249	261	267	269	277	270	---	---	---	---	---	---	---	
37	169	207	233	255	264	270	267	276	289	297	300	309	310	315	313	322	---	---	---	
38	182	218	245	246	278	284	285	295	304	311	303	303	314	322	270	293	---	---	---	
39	175	215	251	278	299	306	305	315	333	333	338	339	347	352	333	355	---	---	---	
40	165	173	205	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
41	173	197	242	270	283	294	295	303	321	333	340	336	350	342	337	344	---	---	---	
42	161	195	229	259	268	281	282	287	295	304	305	304	296	307	303	321	---	---	---	
43	179	215	258	279	299	307	308	316	331	342	336	345	352	350	348	359	331	359	384	
44	164	197	235	268	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
45	172	205	249	277	254	282	287	300	328	342	349	355	364	363	366	362	338	364	389	
46	172	205	242	276	280	287	287	285	312	330	338	342	349	356	361	368	337	364	392	
47	165	197	232	260	204	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
48	173	190	230	249	240	257	263	276	277	262	233	---	---	---	---	---	---	---	---	
49	156	176	198	224	231	241	241	251	275	292	293	298	308	304	302	302	269	288	313	
50	175	203	235	260	244	251	221	224	240	227	252	244	225	215	205	---	---	---	---	

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.6 BODY WEIGHTS (GRAM) MALES

	RECOVERY	
DAYS	22	28
WEEKS	4	4
ANIMAL		

GROUP 1 (CONTROL)

1	---	---
2	---	---
3	---	---
4	---	---
5	---	---
6	---	---
7	---	---
8	---	---
9	---	---
10	---	---
11	368	374
12	393	402
13	452	459
14	404	410
15	420	425

GROUP 2 (100 MG/KG)

16
17
18
19
20
21
22
23
24
25

GROUP 3 (300 MG/KG)

26
27
28
29
30
31
32
33
34
35

GROUP 4 (600 MG/KG)

36	---	---
37	---	---
38	---	---
39	---	---
40	---	---
41	---	---
42	---	---
43	395	395
44	---	---
45	399	412
46	406	415
47	---	---
48	---	---
49	319	323
50	---	---

**2.6 BODY WEIGHTS (GRAM)
FEMALES**

		TREATMENT															
DAYS	1	8	15	22	29	33	34	36	43	50	57	64	71	78	85	91	
WEEKS	1	2	3	4	5	5	5	6	7	8	9	10	11	12	13	13	
ANIMAL																	
GROUP 1 (CONTROL)																	
51	137	164	188	208	211	218	229	235	238	239	255	262	256	256	269	272	
52	140	165	184	206	222	225	228	230	235	247	251	255	255	260	263	261	
53	140	157	177	192	202	203	205	205	206	215	221	224	223	225	228	234	
54	141	165	184	207	222	227	227	231	230	248	255	253	252	259	262	261	
55	137	154	174	193	201	208	214	210	224	232	233	237	236	245	246	251	
56	136	152	183	199	211	221	223	218	228	251	239	240	251	253	249	258	
57	127	150	171	181	189	195	196	196	204	208	207	222	225	217	226	229	
58	144	159	191	198	217	225	229	223	233	244	251	259	259	259	257	267	
59	149	165	187	201	208	214	216	214	223	229	227	234	245	245	247	252	
60	131	156	178	184	203	211	203	219	222	221	239	241	241	236	247	248	
61	137	161	183	196	205	213	218	223	227	231	235	240	240	241	240	247	
62	130	151	165	186	201	205	207	213	213	232	239	235	234	248	247	241	
63	144	165	195	212	219	227	231	226	240	254	260	254	261	267	271	272	
64	131	155	180	197	214	218	221	215	223	238	238	245	237	248	247	242	
65	131	158	179	194	201	207	213	222	224	229	230	240	242	246	244	250	
GROUP 2 (100 MG/KG)																	
66	131	156	176	191	198	204	206	215	224	231	233	242	243	248	251	257	
67	124	146	164	168	183	186	195	195	201	204	206	212	217	219	220	220	
68	137	157	181	192	201	212	211	195	218	225	227	229	231	233	236	237	
69	133	162	181	194	200	201	211	213	220	226	226	231	234	235	233	243	
70	137	161	176	199	212	219	220	223	224	226	237	245	247	242	253	248	
71	144	162	195	214	215	226	229	221	237	245	242	256	254	256	263	260	
72	142	164	188	199	216	225	219	231	238	242	251	259	261	264	270	277	
73	144	163	188	208	216	224	231	237	243	245	249	265	268	271	268	274	
74	129	151	161	171	189	192	191	196	204	202	218	213	219	230	230	216	
75	133	156	172	181	192	196	200	202	205	219	224	223	225	233	236	231	
GROUP 3 (300 MG/KG)																	
76	149	167	189	203	213	217	224	227	228	241	244	245	246	245	255	255	
77	147	165	189	196	214	220	215	226	234	236	248	256	251	---	---	---	
78	128	149	172	183	190	193	198	202	214	217	225	229	230	236	233	235	
79	142	165	186	197	204	206	209	215	223	227	228	236	237	240	240	243	
80	140	160	174	188	205	210	215	217	216	240	243	243	237	253	259	249	
81	133	156	180	198	204	211	213	207	223	234	234	234	245	242	249	245	
82	135	154	169	185	190	190	196	198	195	204	213	208	217	212	221	224	
83	122	149	171	187	192	195	203	209	215	223	216	230	237	235	238	245	
84	134	155	175	191	200	202	210	210	223	230	226	236	239	233	229	239	
85	139	166	181	194	201	201	209	210	207	212	221	222	223	219	211	218	
GROUP 4 (600 MG/KG)																	
86	139	160	181	193	207	201	208	218	221	222	226	230	230	233	236	234	
87	138	165	178	190	198	201	204	219	227	230	217	233	243	239	243	243	
88	141	156	177	155	---	---	---	---	---	---	---	---	---	---	---	---	
89	123	138	160	168	187	190	187	193	209	211	212	223	226	228	230	234	
90	134	151	173	190	209	208	210	218	231	238	236	241	250	248	242	252	
91	122	147	170	179	197	190	191	194	203	208	207	212	216	216	215	223	
92	144	166	191	212	222	228	231	242	248	255	264	269	270	269	267	275	
93	135	153	166	---	---	---	---	---	---	---	---	---	---	---	---	---	
94	151	177	200	209	221	223	219	216	237	245	251	254	266	263	256	281	
95	131	151	176	196	207	207	206	208	219	229	231	241	237	239	241	247	
96	134	164	189	212	225	---	---	---	---	---	---	---	---	---	---	---	
97	124	144	164	176	176	176	178	185	189	197	195	201	200	200	205	204	
98	127	144	158	174	184	184	185	182	192	207	203	211	207	214	214	220	
99	136	159	182	195	213	211	201	218	222	228	239	243	240	241	248	248	
100	137	159	186	198	214	210	210	226	235	244	254	---	---	---	---	---	

**2.6 BODY WEIGHTS (GRAM)
FEMALES**

	RECOVERY				
DAYS	1	8	15	22	28
WEEKS	1	2	3	4	4
ANIMAL					

GROUP 1 (CONTROL)

51	---	---	---	---	---
52	---	---	---	---	---
53	---	---	---	---	---
54	---	---	---	---	---
55	---	---	---	---	---
56	---	---	---	---	---
57	---	---	---	---	---
58	---	---	---	---	---
59	---	---	---	---	---
60	---	---	---	---	---
61	232	248	250	251	255
62	235	247	250	248	254
63	258	275	277	283	281
64	226	249	253	254	257
65	235	248	253	253	257

GROUP 4 (1000 MG/KG)

86	---	---	---	---	---
87	---	---	---	---	---
88	---	---	---	---	---
89	---	---	---	---	---
90	---	---	---	---	---
91	---	---	---	---	---
92	---	---	---	---	---
93	---	---	---	---	---
94	260	272	277	275	274
95	210	236	251	254	258
96	---	---	---	---	---
97	192	200	207	219	216
98	202	209	252	222	217
99	229	238	251	255	254
100	---	---	---	---	---

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.7 BODY WEIGHT GAIN (%) MALES

DAYS WEEKS ANIMAL	TREATMENT															RECOVERY			
	1	8	15	22	29	33	34	36	43	50	57	64	71	78	85	91	1	2	8
	1	2	3	4	5	5	5	6	7	8	9	10	11	12	13	13	1	1	2
GROUP 1 (CONTROL)																			
1	0	25	46	62	71	75	75	76	86	95	101	107	108	107	114	119	---	---	---
2	0	29	58	79	92	101	104	105	115	124	129	136	145	151	154	156	---	---	---
3	0	25	44	61	70	75	76	78	85	92	98	101	105	107	112	112	---	---	---
4	0	29	54	73	87	96	98	99	108	113	119	122	128	130	135	129	---	---	---
5	0	22	46	65	78	85	88	92	102	111	118	125	132	135	142	139	---	---	---
6	0	28	57	77	94	104	105	111	121	131	141	148	149	156	163	169	---	---	---
7	0	24	50	69	71	79	81	85	96	102	106	109	114	115	115	116	---	---	---
8	0	28	47	66	78	88	90	92	99	106	114	120	125	129	134	135	---	---	---
9	0	25	49	65	76	82	85	88	96	104	111	115	119	124	128	130	---	---	---
10	0	22	48	64	76	79	83	85	93	99	102	105	105	109	113	115	---	---	---
11	0	25	42	57	69	76	76	81	90	98	104	108	112	118	122	125	111	---	118
12	0	25	46	62	76	83	86	89	95	104	107	114	117	121	123	129	114	---	128
13	0	28	56	74	91	99	99	105	117	126	133	141	145	155	160	160	143	---	161
14	0	23	46	64	73	78	78	81	88	96	103	111	118	122	117	120	110	---	124
15	0	29	54	70	85	91	94	98	104	110	117	122	131	138	143	147	133	---	146
GROUP 2 (100 MG/KG)																			
16	0	26	47	61	72	82	84	86	96	104	109	113	120	124	129	134	---	---	---
17	0	23	48	67	67	78	78	83	89	99	107	113	122	127	132	136	---	---	---
18	0	24	47	67	78	87	89	94	101	107	119	124	134	142	146	146	---	---	---
19	0	29	50	70	82	89	89	94	99	107	111	116	124	127	132	138	---	---	---
20	0	23	41	58	64	71	73	75	79	87	96	99	105	109	114	114	---	---	---
21	0	22	43	60	72	78	78	82	89	95	97	104	105	109	113	116	---	---	---
22	0	28	57	73	89	98	99	103	110	116	120	125	130	135	142	145	---	---	---
23	0	30	57	76	91	90	91	95	107	119	126	134	136	141	150	153	---	---	---
24	0	26	54	76	91	100	99	104	105	103	105	112	116	124	133	133	---	---	---
25	0	27	52	74	80	88	87	91	96	99	102	111	116	122	128	131	---	---	---
GROUP 3 (300 MG/KG)																			
26	0	20	45	67	75	84	85	86	91	94	99	98	102	110	113	111	---	---	---
27	0	22	45	60	71	79	80	81	87	92	95	96	102	106	112	112	---	---	---
28	0	21	44	63	74	81	83	87	94	101	101	106	110	118	125	123	---	---	---
29	0	16	28	51	61	71	71	66	80	68	88	95	98	101	104	101	---	---	---
30	0	23	40	56	63	65	66	65	70	76	78	82	82	87	93	98	---	---	---
31	0	28	56	75	90	99	99	102	108	110	116	120	127	136	144	145	---	---	---
32	0	24	44	55	65	68	71	67	79	83	83	84	86	92	96	101	---	---	---
33	0	23	41	51	56	66	68	69	77	83	87	91	94	98	105	105	---	---	---
34	0	26	44	57	63	70	72	57	73	77	81	88	94	96	94	97	---	---	---
35	0	19	49	67	75	83	82	84	92	96	101	103	107	107	109	114	---	---	---
GROUP 4 (600 MG/KG)																			
36	0	20	40	52	48	57	59	66	70	71	76	72	---	---	---	---	---	---	---
37	0	22	38	51	56	60	58	63	71	76	78	83	83	86	85	91	---	---	---
38	0	20	35	35	53	56	57	62	67	71	66	66	73	77	48	61	---	---	---
39	0	23	43	59	71	75	74	80	90	90	93	94	98	101	90	103	---	---	---
40	0	5	24	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
41	0	14	40	56	64	70	71	75	86	92	97	94	102	98	95	99	---	---	---
42	0	21	42	61	66	75	75	78	83	89	89	89	84	91	88	99	---	---	---
43	0	20	44	56	67	72	72	77	85	91	88	93	97	96	94	101	85	---	101
44	0	20	43	63	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
45	0	19	45	61	48	64	67	74	91	99	103	106	112	111	113	110	97	---	112
46	0	19	41	60	63	67	67	66	81	92	97	99	103	107	110	114	96	---	112
47	0	19	41	58	24	---	---	---	---	---	---	---	---	---	---	---	---	---	---
48	0	10	33	44	39	49	52	60	60	51	35	---	---	---	---	---	---	---	---
49	0	13	27	44	48	54	54	61	76	87	88	91	97	95	94	94	72	---	85
50	0	16	34	49	39	43	26	28	37	30	44	39	29	23	17	---	---	---	---

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.7 BODY WEIGHT GAIN (%) MALES

	RECOVERY		
DAYS	15	22	28
WEEKS	3	4	4
ANIMAL			

GROUP 1 (CONTROL)

1	---	---	---
2	---	---	---
3	---	---	---
4	---	---	---
5	---	---	---
6	---	---	---
7	---	---	---
8	---	---	---
9	---	---	---
10	---	---	---
11	123	129	132
12	135	137	142
13	166	169	173
14	131	136	140
15	156	159	162

GROUP 2 (100 MG/KG)

16
17
18
19
20
21
22
23
24
25

GROUP 3 (300 MG/KG)

26
27
28
29
30
31
32
33
34
35

GROUP 4 (600 MG/KG)

36	---	---	---
37	---	---	---
38	---	---	---
39	---	---	---
40	---	---	---
41	---	---	---
42	---	---	---
43	115	121	121
44	---	---	---
45	126	132	140
46	128	136	141
47	---	---	---
48	---	---	---
49	101	104	107
50	---	---	---

**2.7 BODY WEIGHT GAIN (%)
FEMALES**

DAYS WEEKS ANIMAL	TREATMENT															
	1	8	15	22	29	33	34	36	43	50	57	64	71	78	85	91
	1	2	3	4	5	5	5	6	7	8	9	10	11	12	13	13
GROUP 1 (CONTROL)																
51	0	20	37	52	54	59	67	72	74	74	86	91	87	87	96	99
52	0	18	31	47	59	61	63	64	68	76	79	82	82	86	88	86
53	0	12	26	37	44	45	46	46	47	54	58	60	59	61	63	67
54	0	17	30	47	57	61	61	64	63	76	81	79	79	84	86	85
55	0	12	27	41	47	52	55	53	64	69	70	73	72	79	80	83
56	0	12	35	46	55	63	64	60	68	85	76	76	85	86	83	90
57	0	18	35	43	49	54	54	54	61	64	63	75	77	71	78	80
58	0	10	33	38	51	56	59	55	62	69	74	80	80	80	78	85
59	0	11	26	35	40	44	45	44	50	54	52	57	64	64	66	69
60	0	19	36	40	55	61	55	67	69	69	82	84	84	80	89	89
61	0	18	34	43	50	55	59	63	66	69	72	75	75	76	75	80
62	0	16	27	43	55	58	59	64	64	78	84	81	80	91	90	85
63	0	15	35	47	52	58	60	57	67	76	81	76	81	85	88	89
64	0	18	37	50	63	66	69	64	70	82	82	87	81	89	89	85
65	0	21	37	48	53	58	63	69	71	75	76	83	85	88	86	91
GROUP 2 (100 MG/KG)																
66	0	19	34	46	51	56	57	64	71	76	78	85	85	89	92	96
67	0	18	32	35	48	50	57	57	62	65	66	71	75	77	77	77
68	0	15	32	40	47	55	54	42	59	64	66	67	69	70	72	73
69	0	22	36	46	50	51	59	60	65	70	70	74	76	77	75	83
70	0	18	28	45	55	60	61	63	64	65	73	79	80	77	85	81
71	0	13	35	49	49	57	59	53	65	70	68	78	76	78	83	81
72	0	15	32	40	52	58	54	63	68	70	77	82	84	86	90	95
73	0	13	31	44	50	56	60	65	69	70	73	84	86	88	86	90
74	0	17	25	33	47	49	48	52	58	57	69	65	70	78	78	67
75	0	17	29	36	44	47	50	52	54	65	68	68	69	75	77	74
GROUP 3 (300 MG/KG)																
76	0	12	27	36	43	46	50	52	53	62	64	64	65	64	71	71
77	0	12	29	33	46	50	46	54	59	61	69	74	71	---	---	---
78	0	16	34	43	48	51	55	58	67	70	76	79	80	84	82	84
79	0	16	31	39	44	45	47	51	57	60	61	66	67	69	69	71
80	0	14	24	34	46	50	54	55	54	71	74	74	69	81	85	78
81	0	17	35	49	53	59	60	56	68	76	76	76	84	82	87	84
82	0	14	25	37	41	41	45	47	44	51	58	54	61	57	64	66
83	0	22	40	53	57	60	66	71	76	83	77	89	94	93	95	101
84	0	16	31	43	49	51	57	57	66	72	69	76	78	74	71	78
85	0	19	30	40	45	45	50	51	49	53	59	60	60	58	52	57
GROUP 4 (600 MG/KG)																
86	0	15	30	39	49	45	50	57	59	60	63	65	65	68	70	68
87	0	20	29	38	43	46	48	59	64	67	57	69	76	73	76	76
88	0	11	26	10	---	---	---	---	---	---	---	---	---	---	---	---
89	0	12	30	37	52	54	52	57	70	72	72	81	84	85	87	90
90	0	13	29	42	56	55	57	63	72	78	76	80	87	85	81	88
91	0	20	39	47	61	56	57	59	66	70	70	74	77	77	76	83
92	0	15	33	47	54	58	60	68	72	77	83	87	88	87	85	91
93	0	13	23	---	---	---	---	---	---	---	---	---	---	---	---	---
94	0	17	32	38	46	48	45	43	57	62	66	68	76	74	70	86
95	0	15	34	50	58	58	57	59	67	75	76	84	81	82	84	89
96	0	22	41	58	68	---	---	---	---	---	---	---	---	---	---	---
97	0	16	32	42	42	42	44	49	52	59	57	62	61	61	65	65
98	0	13	24	37	45	45	46	43	51	63	60	66	63	69	69	73
99	0	17	34	43	57	55	48	60	63	68	76	79	76	77	82	82
100	0	16	36	45	56	53	53	65	72	78	85	---	---	---	---	---

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.8 FOOD CONSUMPTION (G/ANIMAL/DAY) MALES

DAYS WEEKS CAGE	TREATMENT												
	1-8	8-15	15-22	22-29	29-36	36-43	43-50	50-57	57-64	64-71	71-78	78-85	85-91
	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	11-12	12-13	13
GROUP 1 (CONTROL)													
1	18	22	21	21	19	20	20	20	20	18	18	19	17
2	19	22	22	22	21	21	21	21	21	20	20	20	19
3	18	21	21	22	20	20	20	20	21	20	20	19	19
GROUP 2 (100 MG/KG)													
4	18	22	22	20	20	20	20	20	20	20	20	20	19
5	18	23	23	23	20	21	20	20	20	19	20	20	19
GROUP 3 (300 MG/KG)													
6	17	21	22	21	19	20	18	21	20	19	21	21	19
7	18	22	22	21	18	19	18	19	20	19	20	19	19
GROUP 4 (600 MG/KG)													
8	16	20	17	21	21	20	19	20	21	18	22	16	21
9	16	22	22	19	24	23	22	22	22	21	22	20	22
10	15	20	20	16	18	19	20	18	17	20	20	19	20

MALES

DAYS WEEKS CAGE	RECOVERY			
	2-8	8-15	15-22	22-28
	1-2	2-3	3-4	4
GROUP 1 (CONTROL)				
1	---	---	---	---
2	---	---	---	---
3	20	21	6 (B)	20
GROUP 2 (100 MG/KG)				
4				
5				
GROUP 3 (300 MG/KG)				
6				
7				
GROUP 4 (600 MG/KG)				
8	---	---	---	---
9	24	25	27	22
10	22	23	26	20

(B) Diet supplemented, value excluded

**2.8 FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES**

DAYS WEEKS CAGE	TREATMENT												
	1-8 1-2	8-15 2-3	15-22 3-4	22-29 4-5	29-36 5-6	36-43 6-7	43-50 7-8	50-57 8-9	57-64 9-10	64-71 10-11	71-78 11-12	78-85 12-13	85-91 13
GROUP 1 (CONTROL)													
11	13	16	15	16	15	15	16	15	15	15	14	15	14
12	13	16	15	16	14	15	15	15	15	15	14	15	14
13	13	16	15	16	15	15	15	16	15	15	14	14	14
GROUP 2 (100 MG/KG)													
14	13	15	14	15	14	14	14	14	14	13	14	14	12
15	14	16	15	15	15	15	15	15	16	15	15	15	13
GROUP 3 (300 MG/KG)													
16	13	16	16	17	15	17	17	17	17	15	15	16	15
17	13	15	15	16	15	15	16	16	17	15	16	16	15
GROUP 4 (600 MG/KG)													
18	11	16	14	17	17	17	18	17	18	17	18	17	17
19	12	17	14	18	17	17	18	18	18	17	17	16	18
20	12	16	17	19	15	15	17	17	13	15	15	16	15

**2.8 FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES**

	RECOVERY			
DAYS	1-8	8-15	15-22	22-28
WEEKS	1-2	2-3	3-4	4
CAGE				
GROUP 1 (CONTROL)				
11	---	---	---	---
12	---	---	---	---
13	17	---	12	16
GROUP 4 (1000 MG/KG)				
18	---	---	---	---
19	18	---	---	18
20	17	---	11	14

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

		TREATMENT											
DAYS	1-8	8-15	15-22	22-29	29-36	36-43	43-50	50-57	57-64	64-71	71-78	78-85	85-91
WEEKS	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	11-12	12-13	13
CAGE													
GROUP 1 (CONTROL)													
1	87	87	74	70	62	59	57	55	54	50	48	49	43
2	89	86	76	70	65	61	58	57	56	52	52	50	47
3	87	85	77	73	65	60	58	57	57	53	52	49	47
GROUP 2 (100 MG/KG)													
4	86	87	78	69	64	60	59	58	57	55	53	51	49
5	81	86	77	73	62	60	56	54	53	50	50	49	47
GROUP 3 (300 MG/KG)													
6	83	85	79	72	63	63	57	62	60	56	60	59	53
7	85	87	82	74	61	61	57	57	58	56	56	54	51
GROUP 4 (600 MG/KG)													
8	81	88	65	79	75	67	64	65	68	56	67	53	64
9	79	90	81	67	81	72	67	65	66	63	63	58	64
10	77	90	81	68	69	67	73	65	57	68	68	66	61

MALES

		RECOVERY			
DAYS	2-8	8-15	15-22	22-28	
WEEKS	1-2	2-3	3-4	4	
CAGE					
GROUP 1 (CONTROL)					
1	---	---	---	---	
2	---	---	---	---	
3	52	52	15 (B)	49	
GROUP 2 (100 MG/KG)					
4					
5					
GROUP 3 (300 MG/KG)					
6					
7					
GROUP 4 (600 MG/KG)					
8	---	---	---	---	
9	66	66	67	55	
10	69	65	70	54	

(B) Diet supplemented, value excluded

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

DAYS WEEKS CAGE	TREATMENT												
	1-8 1-2	8-15 2-3	15-22 3-4	22-29 4-5	29-36 5-6	36-43 6-7	43-50 7-8	50-57 8-9	57-64 9-10	64-71 10-11	71-78 11-12	78-85 12-13	85-91 13
GROUP 1 (CONTROL)													
11	80	88	76	76	67	68	66	64	63	59	58	59	56
12	86	86	77	79	67	69	67	64	64	60	59	60	56
13	85	87	77	78	70	68	65	65	62	61	57	58	56
GROUP 2 (100 MG/KG)													
14	83	83	74	76	70	66	63	64	60	57	58	59	51
15	87	88	75	75	70	68	65	65	65	59	60	59	53
GROUP 3 (300 MG/KG)													
16	83	89	80	82	73	75	73	72	72	64	60	63	59
17	85	87	78	81	73	71	73	74	73	64	70	68	64
GROUP 4 (600 MG/KG)													
18	72	92	77	86	84	74	79	78	78	73	74	72	69
19	73	93	69	87	82	77	76	74	75	69	70	66	70
20	78	91	87	93	79	73	79	76	58	69	70	72	65

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

	RECOVERY			
DAYS	1-8	8-15	15-22	22-28
WEEKS	1-2	2-3	3-4	4
CAGE				
GROUP 1 (CONTROL)				
11	---	---	---	---
12	---	---	---	---
13	68	---	46	63
GROUP 4 (1000 MG/KG)				
18	---	---	---	---
19	70	---	---	66
20	77	---	47	63

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.10 HAEMATOLOGY MALES END OF TREATMENT

ANIMAL	WBC 10E9/L	Neutrophils %WBC	Lymphocytes %WBC	Monocytes %WBC	Eosinophils %WBC
GROUP 1 (CONTROL)					
1	11.3	23.4	73.7	1.5	1.3
2	---	---	---	---	---
3	7.6	17.2	79.1	1.8	1.8
4	---	---	---	---	---
5	9.3	16.4	81.0	1.6	0.7
6	9.9	15.4	80.6	2.4	1.4
7	7.1	18.9	75.6	2.2	3.2
8	7.3	14.8	82.1	1.7	1.2
9	7.7	13.7	83.8	1.1	1.3
10	5.4	13.1	83.8	1.3	1.7
11	---	---	---	---	---
12	11.1	19.3	76.4	1.4	2.8
13	6.2	19.1	77.4	2.0	1.5
14	5.3	11.0	84.0	2.0	3.0
15	8.5	13.2	84.6	1.1	1.0
GROUP 2 (100 MG/KG)					
16	5.0	16.8	81.4	1.0	0.8
17	7.9	20.2	75.8	1.5	2.3
18	8.0	11.3	86.6	1.0	1.1
19	6.6	15.7	81.4	1.4	1.5
20	7.1	17.3	79.6	1.6	1.2
21	9.3	14.1	82.8	1.6	1.4
22	11.4	13.6	83.6	1.3	1.2
23	8.2	8.8	89.0	1.2	1.0
24	6.1	20.4	76.4	1.8	1.3
25	8.1	15.9	81.2	1.7	1.0
GROUP 3 (300 MG/KG)					
26	7.1	16.6	79.3	1.7	2.3
27	7.3	8.3	88.2	1.2	2.0
28	11.4	21.0	74.0	3.0	2.0
29	5.9	16.2	78.3	4.3	1.1
30	6.6	20.3	76.8	1.2	1.6
31	7.5	14.3	81.7	2.5	1.3
32	5.3	14.2	83.1	1.3	1.3
33	9.1	18.0	78.8	1.7	1.5
34	---	---	---	---	---
35	8.0	9.0	84.0	4.0	3.0
GROUP 4 (600 MG/KG)					
37	2.9	27.6	68.6	1.7	1.9
38	10.6	25.7	70.8	2.3	0.9
39	7.4	19.2	77.1	1.9	1.7
41	8.9	15.2	81.0	2.1	1.6
42	8.6	19.9	78.0	1.1	0.9
43	7.1	14.6	83.2	0.9	1.1
45	---	---	---	---	---
46	9.8	12.4	85.1	1.1	1.2
49	8.7	31.8	64.9	2.4	0.8

MALES END OF TREATMENT

ANIMAL	Basophils %WBC	Red blood cells 10E12/L	Reticulocytes %RBC	RDW %	Haemoglobin mmol/L
GROUP 1 (CONTROL)					
1	0.1	9.70	2.9	12.9	10.4

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.10 HAEMATOLOGY MALES END OF TREATMENT

ANIMAL	Basophils %WBC	Red blood cells 10E12/L	Reticulocytes %RBC	RDW %	Haemoglobin mmol/L
GROUP 1 (CONTROL)					
2	---	---	---	---	---
3	0.1	9.92	2.1	12.3	10.0
4	---	---	---	---	---
5	0.3	9.63	3.3	13.2	10.1
6	0.1	9.31	2.0	12.9	10.2
7	0.1	10.21	1.7	12.5	9.9
8	0.2	10.02	2.0	12.2	10.1
9	0.1	9.26	2.2	12.8	9.7
10	0.1	10.51	2.0	12.6	10.5
11	---	---	---	---	---
12	0.2	9.35	2.4	12.5	9.7
13	0.1	9.21	2.4	11.9	9.9
14	0.0	9.34	2.4	12.0	10.0
15	0.1	9.58	2.5	12.9	9.9
GROUP 2 (100 MG/KG)					
16	0.1	8.94	2.3	13.0	9.6
17	0.1	9.68	2.2	11.6	10.6
18	0.1	9.35	2.1	12.9	9.9
19	0.0	8.60	2.0	12.4	9.3
20	0.2	9.69	1.8	12.0	10.2
21	0.1	9.52	2.0	11.9	10.2
22	0.2	9.32	2.1	12.6	9.3
23	0.0	9.69	1.6	12.2	10.1
24	0.0	9.30	2.9	13.4	9.7
25	0.2	9.53	2.3	12.3	9.8
GROUP 3 (300 MG/KG)					
26	0.1	9.25	1.7	12.9	9.7
27	0.1	8.88	1.5	12.7	9.2
28	0.0	9.05	2.0	13.0	9.5
29	0.1	8.49	1.7	12.4	9.2
30	0.1	9.06	3.3	13.9	9.4
31	0.2	8.88	2.3	13.7	9.5
32	0.0	8.24	1.8	11.7	8.7
33	0.1	8.79	2.0	12.5	9.2
34	---	---	---	---	---
35	0.0	8.34	2.3	21.9	9.3
GROUP 4 (600 MG/KG)					
37	0.1	8.07	2.5	13.0	8.7
38	0.2	9.48	2.5	14.1	9.5
39	0.1	9.85	1.9	13.2	9.7
41	0.1	8.97	2.2	12.6	9.3
42	0.1	9.09	4.1	14.3	9.7
43	0.2	8.69	2.5	13.4	9.5
45	---	---	---	---	---
46	0.1	9.12	2.2	13.0	9.6
49	0.1	10.00	2.5	13.0	10.4

MALES END OF TREATMENT

ANIMAL	Haematocrit L/L	MCV fL	MCH fmol	MCHC mmol/L	Platelets 10E9/L
GROUP 1 (CONTROL)					
1	0.499	51.4	1.07	20.85	912
2	---	---	---	---	---

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.10 HAEMATOLOGY MALES END OF TREATMENT

ANIMAL	Haematocrit L/L	MCV fL	MCH fmol	MCHC mmol/L	Platelets 10E9/L
GROUP 1 (CONTROL)					
3	0.498	50.2	1.01	20.15	681
4	---	---	---	---	---
5	0.484	50.3	1.05	20.96	796
6	0.481	51.7	1.09	21.12	745
7	0.495	48.5	0.97	20.09	854
8	0.508	50.6	1.01	19.93	776
9	0.473	51.1	1.05	20.59	730
10	0.517	49.2	1.00	20.27	825
11	---	---	---	---	---
12	0.476	50.9	1.04	20.42	650
13	0.486	52.7	1.07	20.29	716
14	0.492	52.6	1.07	20.25	613
15	0.495	51.7	1.03	19.94	888
GROUP 2 (100 MG/KG)					
16	0.467	52.3	1.08	20.57	876
17	0.501	51.8	1.09	21.11	694
18	0.489	52.4	1.06	20.18	703
19	0.451	52.5	1.08	20.66	776
20	0.515	53.2	1.06	19.88	685
21	0.509	53.5	1.07	19.97	820
22	0.462	49.6	1.00	20.08	727
23	0.502	51.8	1.04	20.13	766
24	0.485	52.1	1.04	19.98	867
25	0.483	50.7	1.03	20.31	763
GROUP 3 (300 MG/KG)					
26	0.461	49.9	1.05	20.95	678
27	0.462	52.1	1.03	19.81	779
28	0.472	52.2	1.06	20.23	761
29	0.446	52.5	1.08	20.57	976
30	0.460	50.8	1.04	20.38	834
31	0.474	53.4	1.06	19.92	940
32	0.420	51.0	1.05	20.66	720
33	0.460	52.3	1.05	20.10	770
34	---	---	---	---	---
35	0.426	51.0	1.11	21.76	760
GROUP 4 (600 MG/KG)					
37	0.416	51.5	1.08	20.87	769
38	0.464	48.9	1.00	20.52	778
39	0.485	49.3	0.98	19.92	871
41	0.470	52.5	1.03	19.70	667
42	0.479	52.7	1.06	20.17	750
43	0.465	53.5	1.10	20.52	680
45	---	---	---	---	---
46	0.466	51.1	1.05	20.50	844
49	0.507	50.7	1.04	20.60	522

MALES END OF TREATMENT

ANIMAL	PT s	APTT s
GROUP 1 (CONTROL)		
1	---	---
2	---	---
3	17.6	18.6

**2.10 HAEMATOLOGY
MALES
END OF TREATMENT**

ANIMAL	PT s	APTT s
--------	---------	-----------

GROUP 1 (CONTROL)

4	15.8	16.3
5	16.6	21.8
6	16.4	18.6
7	16.9	21.8
8	18.1	19.9
9	16.9	17.7
10	17.9	20.8
11	---	---
12	16.4	17.2
13	16.2	21.4
14	15.5	15.8
15	15.6	17.6

GROUP 2 (100 MG/KG)

16	16.3	19.9
17	16.2	18.6
18	16.0	19.9
19	16.4	16.8
20	16.4	20.3
21	15.6	18.0
22	15.9	21.8
23	17.3	21.7
24	15.7	20.0
25	17.3	21.9

GROUP 3 (300 MG/KG)

26	17.8	22.4
27	16.6	21.0
28	16.7	20.7
29	15.7	18.7
30	17.8	21.0
31	15.7	16.5
32	15.6	17.9
33	15.2	16.7
34	---	---
35	14.9	18.8

GROUP 4 (600 MG/KG)

37	15.6	18.4
38	20.0	21.2
39	15.7	16.2
41	17.2	17.8
42	16.3	20.1
43	16.5	16.8
45	---	---
46	15.7	17.1
49	16.1	19.0

**MALES
END OF RECOVERY**

ANIMAL	WBC 10E9/L	Neutrophils %WBC	Lymphocytes %WBC	Monocytes %WBC	Eosinophils %WBC
--------	---------------	---------------------	---------------------	-------------------	---------------------

GROUP 1 (CONTROL)

11	8.0	18.2	78.3	1.6	1.6
12	7.7	15.9	81.5	0.9	1.6
13	6.9	19.6	77.3	1.5	1.4
14	4.7	15.9	80.8	1.9	1.4

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.10 HAEMATOLOGY MALES END OF RECOVERY

ANIMAL	WBC 10E9/L	Neutrophils %WBC	Lymphocytes %WBC	Monocytes %WBC	Eosinophils %WBC
GROUP 1 (CONTROL)					
15	7.8	18.5	77.9	1.4	2.1
GROUP 4 (600 MG/KG)					
43	6.4	10.9	86.0	1.3	1.7
45	7.2	13.3	84.9	1.0	0.8
46	8.5	15.1	82.5	1.3	1.0
49	7.5	21.9	75.5	1.5	0.9

MALES END OF RECOVERY

ANIMAL	Basophils %WBC	Red blood cells 10E12/L	Reticulocytes %RBC	RDW %	Haemoglobin mmol/L
GROUP 1 (CONTROL)					
11	0.3	9.60	1.7	12.5	10.7
12	0.1	9.36	1.7	12.8	9.9
13	0.2	8.79	2.1	12.4	9.6
14	0.1	9.56	2.2	12.4	10.3
15	0.1	9.28	2.2	13.0	9.8
GROUP 4 (600 MG/KG)					
43	0.2	8.55	1.8	12.4	9.5
45	0.1	8.99	2.2	13.1	9.6
46	0.1	9.07	2.0	12.9	9.6
49	0.2	9.38	1.7	12.5	9.9

MALES END OF RECOVERY

ANIMAL	Haematocrit L/L	MCV fL	MCH fmol	MCHC mmol/L	Platelets 10E9/L
GROUP 1 (CONTROL)					
11	0.501	52.2	1.11	21.33	685
12	0.485	51.8	1.05	20.36	828
13	0.468	53.2	1.09	20.54	675
14	0.510	53.4	1.08	20.25	688
15	0.485	52.3	1.06	20.28	838
GROUP 4 (600 MG/KG)					
43	0.466	54.4	1.11	20.32	818
45	0.461	51.2	1.07	20.81	893
46	0.469	51.7	1.06	20.56	776
49	0.482	51.4	1.05	20.48	648

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.10 HAEMATOLOGY MALES END OF RECOVERY

ANIMAL	PT s	APTT s
GROUP 1 (CONTROL)		
11	16.0	16.9
12	15.7	16.0
13	16.6	20.5
14	20.3	16.4
15	17.9	18.7
GROUP 4 (600 MG/KG)		
43	17.9	19.7
45	19.7	19.8
46	19.3	18.5
49	18.0	16.8

FEMALES END OF TREATMENT

ANIMAL	WBC 10E9/L	Neutrophils %WBC	Lymphocytes %WBC	Monocytes %WBC	Eosinophils %WBC
GROUP 1 (CONTROL)					
51	---	---	---	---	---
52	5.1	7.9	89.5	1.4	1.0
53	3.8	21.6	75.9	1.8	0.7
54	4.5	8.0	88.0	3.0	1.0
55	4.6	18.0	77.6	2.0	2.2
56	4.1	13.0	86.0	1.0	0.0
57	3.7	15.2	81.1	2.1	1.5
58	5.4	13.7	84.1	1.2	0.9
59	---	---	---	---	---
60	2.4	16.0	82.0	1.0	1.0
61	5.2	19.7	77.0	2.0	1.1
62	6.3	8.0	88.9	1.9	1.1
63	7.6	14.0	84.0	2.0	0.0
64	8.3	13.5	83.6	1.7	1.0
65	5.6	18.0	78.0	2.7	1.3
GROUP 2 (100 MG/KG)					
66	6.1	16.2	79.1	2.9	1.7
67	5.4	17.0	78.2	2.8	1.9
68	8.8	10.5	85.2	2.7	1.4
69	5.4	16.5	79.3	2.1	2.1
70	5.8	14.1	82.4	1.7	1.5
71	5.0	18.0	78.0	2.0	2.0
72	5.8	25.0	71.0	3.0	1.0
73	5.7	19.3	77.0	1.9	1.7
74	---	---	---	---	---
75	5.6	8.5	89.3	1.5	0.7
GROUP 3 (300 MG/KG)					
76	5.3	21.9	73.4	2.0	2.6
78	7.0	26.8	69.2	1.7	2.1
79	6.3	24.1	71.5	2.7	1.7
80	4.7	14.0	82.1	2.1	1.7
81	7.3	15.8	80.8	1.6	1.7
82	6.7	24.0	70.0	6.0	0.0
83	6.0	12.0	85.0	3.0	0.0
84	7.6	14.4	82.2	2.1	1.2
85	3.8	17.9	78.1	1.4	2.7

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.10 HAEMATOLOGY FEMALES END OF TREATMENT

ANIMAL	WBC 10E9/L	Neutrophils %WBC	Lymphocytes %WBC	Monocytes %WBC	Eosinophils %WBC
GROUP 4 (600 MG/KG)					
86	6.3	28.7	67.1	2.2	1.9
87	9.9	15.7	80.2	1.6	2.4
89	6.5	19.7	75.9	2.6	1.6
90	7.1	22.5	73.2	1.9	2.2
91	8.0	13.8	82.5	2.3	1.3
92	12.5	14.0	81.0	3.0	2.0
94	6.8	24.0	70.0	6.0	0.0
95	10.1	15.2	82.3	1.6	0.8
97	6.5	13.2	84.3	1.3	1.1
98	9.0	24.0	71.4	2.2	2.3
99	8.0	20.3	76.2	1.8	1.6

FEMALES END OF TREATMENT

ANIMAL	Basophils %WBC	Red blood cells 10E12/L	Reticulocytes %RBC	RDW %	Haemoglobin mmol/L
GROUP 1 (CONTROL)					
51	---	---	---	---	---
52	0.1	7.40	6.4	14.0	8.5
53	0.1	6.50	9.9	15.3	7.5
54	0.0	7.66	8.1	14.7	8.7
55	0.1	6.68	9.8	16.1	8.0
56	0.0	7.81	5.9	13.1	8.7
57	0.1	7.15	9.6	15.6	8.4
58	0.2	7.81	7.6	14.2	9.1
59	---	---	---	---	---
60	0.0	7.04	11.9	20.7	8.0
61	0.1	9.25	2.4	10.7	10.1
62	0.1	8.11	3.3	12.6	9.8
63	0.0	8.98	1.8	12.2	9.3
64	0.2	9.22	2.0	11.2	9.8
65	0.1	8.64	2.5	11.4	9.3
GROUP 2 (100 MG/KG)					
66	0.2	8.68	2.4	11.3	9.5
67	0.1	7.56	3.0	10.7	8.9
68	0.1	8.13	2.7	11.4	8.9
69	0.0	8.15	2.6	11.1	9.0
70	0.2	8.03	2.6	11.3	9.0
71	0.0	8.69	2.4	11.2	9.6
72	0.0	8.67	2.9	11.9	9.3
73	0.1	9.02	3.1	11.4	10.0
74	---	---	---	---	---
75	0.0	8.08	2.9	11.5	9.1
GROUP 3 (300 MG/KG)					
76	0.1	8.24	2.7	12.0	9.4
78	0.1	9.23	1.8	11.9	9.8
79	0.1	8.72	3.4	12.8	9.2
80	0.1	7.92	2.7	12.2	9.0
81	0.1	8.11	1.9	11.2	9.2
82	0.0	8.54	2.4	11.1	9.6
83	0.0	8.27	2.7	13.0	9.0
84	0.1	7.87	1.9	11.1	8.8
85	0.0	7.93	3.4	12.0	9.1

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.10 HAEMATOLOGY FEMALES END OF TREATMENT

ANIMAL	Basophils %WBC	Red blood cells 10E12/L	Reticulocytes %RBC	RDW %	Haemoglobin mmol/L
GROUP 4 (600 MG/KG)					
86	0.1	8.81	2.8	12.7	9.4
87	0.1	8.30	2.0	11.6	9.1
89	0.1	8.52	4.0	13.5	8.9
90	0.2	9.04	2.5	12.2	9.8
91	0.1	8.15	3.1	12.6	8.8
92	0.0	9.57	1.9	12.9	10.1
94	0.0	8.37	2.8	13.1	9.3
95	0.2	9.62	0.7	12.3	9.9
97	0.1	7.83	3.0	12.4	8.5
98	0.1	8.59	3.1	12.4	9.7
99	0.1	9.16	1.9	11.7	9.7

FEMALES END OF TREATMENT

ANIMAL	Haematocrit L/L	MCV fL	MCH fmol	MCHC mmol/L	Platelets 10E9/L
GROUP 1 (CONTROL)					
51	---	---	---	---	---
52	0.408	55.0	1.15	20.85	1065
53	0.371	57.0	1.16	20.32	813
54	0.410	53.6	1.13	21.19	651
55	0.376	56.3	1.20	21.25	765
56	0.422	54.0	1.11	20.51	758
57	0.414	57.9	1.18	20.31	1041
58	0.436	55.9	1.16	20.80	886
59	---	---	---	---	---
60	0.392	55.6	1.13	20.40	786
61	0.486	52.5	1.09	20.75	815
62	0.451	55.6	1.21	21.71	605
63	0.455	50.7	1.04	20.49	507
64	0.477	51.7	1.06	20.48	696
65	0.453	52.5	1.07	20.41	772
GROUP 2 (100 MG/KG)					
66	0.462	53.2	1.10	20.57	822
67	0.416	55.1	1.17	21.34	715
68	0.433	53.3	1.10	20.55	657
69	0.439	53.9	1.11	20.53	578
70	0.440	54.9	1.13	20.53	733
71	0.471	54.2	1.10	20.33	753
72	0.464	53.5	1.07	19.98	635
73	0.485	53.8	1.11	20.61	842
74	---	---	---	---	---
75	0.440	54.5	1.13	20.75	742
GROUP 3 (300 MG/KG)					
76	0.455	55.2	1.14	20.73	721
78	0.471	51.1	1.06	20.84	587
79	0.449	51.4	1.05	20.46	704
80	0.422	53.3	1.14	21.44	659
81	0.435	53.6	1.13	21.11	756
82	0.464	54.3	1.12	20.68	609
83	0.425	51.4	1.09	21.15	522
84	0.423	53.7	1.12	20.88	728
85	0.444	55.9	1.15	20.48	744

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.10 HAEMATOLOGY FEMALES END OF TREATMENT

ANIMAL	Haematocrit L/L	MCV fL	MCH fmol	MCHC mmol/L	Platelets 10E9/L
GROUP 4 (600 MG/KG)					
86	0.460	52.2	1.06	20.38	826
87	0.436	52.5	1.09	20.78	761
89	0.439	51.6	1.04	20.17	636
90	0.470	52.0	1.08	20.78	564
91	0.432	53.0	1.08	20.28	677
92	0.475	49.6	1.05	21.20	488
94	0.447	53.4	1.11	20.86	609
95	0.471	49.0	1.03	21.08	748
97	0.408	52.2	1.08	20.75	611
98	0.464	54.1	1.13	20.89	1017
99	0.470	51.3	1.06	20.64	714

FEMALES END OF TREATMENT

ANIMAL	PT s	APTT s
GROUP 1 (CONTROL)		
51	---	---
52	16.1	17.5
53	15.5	17.3
54	16.0	22.2
55	16.5	17.0
56	15.6	14.4
57	15.6	15.8
58	16.3	21.2
59	---	---
60	15.9	16.7
61	15.6	19.3
62	15.8	19.1
63	16.5	19.9
64	15.7	18.4
65	15.7	19.1
GROUP 2 (100 MG/KG)		
66	16.4	20.7
67	16.2	21.7
68	15.9	22.3
69	16.5	20.3
70	15.7	22.4
71	15.0	19.4
72	15.9	20.8
73	16.3	20.4
74	---	---
75	15.7	21.3
GROUP 3 (300 MG/KG)		
76	16.1	19.3
78	15.5	19.8
79	15.3	19.2
80	16.8	19.8
81	15.7	19.0
82	15.8	20.6
83	16.1	19.4
84	15.6	18.5
85	16.1	20.5

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.10 HAEMATOLOGY FEMALES END OF TREATMENT

ANIMAL	PT s	APTT s
GROUP 4 (600 MG/KG)		
86	15.6	20.3
87	16.5	19.1
89	16.5	15.8
90	15.8	19.5
91	16.0	15.1
92	15.6	16.5
94	16.2	18.8
95	16.4	17.8
97	16.3	14.8
98	15.5	15.9
99	16.5	18.6

FEMALES END OF RECOVERY

ANIMAL	WBC 10E9/L	Neutrophils %WBC	Lymphocytes %WBC	Monocytes %WBC	Eosinophils %WBC
GROUP 1 (CONTROL)					
61	3.8	19.7	75.8	2.5	2.0
62	5.4	10.1	85.9	2.8	1.0
63	5.3	14.0	82.2	2.0	1.6
64	3.8	13.8	83.6	1.1	1.4
65	1.8	12.7	84.0	1.5	1.8
GROUP 4 (600 MG/KG)					
94	3.6	20.0	74.0	3.3	2.5
95	5.0	9.3	87.1	2.2	1.3
97	6.6	10.2	86.9	1.4	1.4
98	5.9	18.9	76.8	1.9	2.3
99	4.4	9.2	87.7	1.5	1.5

FEMALES END OF RECOVERY

ANIMAL	Basophils %WBC	Red blood cells 10E12/L	Reticulocytes %RBC	RDW %	Haemoglobin mmol/L
GROUP 1 (CONTROL)					
61	0.1	9.35	2.1	11.0	10.5
62	0.2	8.15	2.3	13.8	10.1
63	0.1	9.51	1.7	12.2	10.2
64	0.1	8.99	1.8	11.7	9.7
65	0.1	7.71	2.1	11.8	8.7
GROUP 4 (600 MG/KG)					
94	0.2	8.89	2.2	11.9	10.0
95	0.1	9.25	1.2	13.0	9.9
97	0.1	8.41	1.4	11.9	9.6
98	0.1	8.87	2.1	11.2	10.2
99	0.1	8.92	1.9	11.7	9.7

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.10 HAEMATOLOGY FEMALES END OF RECOVERY

ANIMAL	Haematocrit L/L	MCV fL	MCH fmol	MCHC mmol/L	Platelets 10E9/L
GROUP 1 (CONTROL)					
61	0.500	53.5	1.12	20.94	789
62	0.456	56.0	1.23	22.03	708
63	0.495	52.0	1.07	20.63	393
64	0.482	53.6	1.08	20.22	800
65	0.412	53.4	1.12	21.03	660
GROUP 4 (600 MG/KG)					
94	0.484	54.5	1.13	20.68	582
95	0.485	52.5	1.07	20.32	904
97	0.462	55.0	1.14	20.77	843
98	0.493	55.5	1.15	20.61	1003
99	0.470	52.7	1.09	20.69	808

FEMALES END OF RECOVERY

ANIMAL	PT s	APTT s
GROUP 1 (CONTROL)		
61	---	---
62	16.9	16.1
63	18.4	15.7
64	19.0	16.1
65	17.4	15.0
GROUP 4 (600 MG/KG)		
94	16.4	18.9
95	17.5	16.8
97	18.1	17.0
98	15.5	17.3
99	16.7	17.9

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.11 CLINICAL BIOCHEMISTRY MALES END OF TREATMENT

ANIMAL	ALAT U/L	ASAT U/L	ALP U/L	Total protein g/L	Albumin g/L
GROUP 1 (CONTROL)					
1	52.0	82.2	123	63.6	32.2
2	47.1	84.1	158	65.1	32.0
3	48.9	90.6	205	62.2	33.2
4	27.6	62.4	165	64.4	32.8
5	43.4	74.1	134	57.5	30.4
6	40.8	92.0	137	66.8	33.0
7	50.5	83.2	165	64.1	32.4
8	50.1	161.9	274	64.5	32.5
9	60.6	77.0	211	62.2	31.4
10	39.0	98.3	233	64.1	33.1
11	43.6	80.2	164	59.3	31.2
12	45.5	112.0	176	57.4	30.6
13	43.9	138.1	192	62.4	32.5
14	35.9	66.3	125	63.5	32.7
15	59.7	86.5	205	65.0	34.9
GROUP 2 (100 MG/KG)					
16	45.1	72.5	110	62.5	33.5
17	54.5	75.5	166	64.2	33.5
18	49.5	72.4	155	64.8	33.2
19	46.7	73.2	208	59.1	31.1
20	38.9	68.1	168	62.6	33.1
21	44.8	83.8	170	67.0	33.2
22	42.6	63.5	134	65.4	33.5
23	57.2	72.1	216	65.0	32.6
24	61.1	83.0	171	63.8	33.5
25	64.3	77.9	147	65.4	33.1
GROUP 3 (300 MG/KG)					
26	67.2	86.9	222	61.4	33.8
27	47.7	68.4	318	60.3	32.4
28	64.7	78.0	355	58.4	31.4
29	205.9	147.5	176	56.4	32.2
30	79.0	101.8	172	63.1	33.8
31	51.6	79.1	266	64.1	35.0
32	75.4	81.1	333	57.2	31.8
33	59.9	102.2	303	59.2	32.3
34	94.6	92.2	307	59.6	31.2
35	49.1	77.5	189	61.6	33.4
GROUP 4 (600 MG/KG)					
37	85.1	98.2	303	62.5	34.4
38	117.3	97.5	474	57.0	32.0
39	85.0	85.2	221	60.4	33.8
41	86.0	84.9	290	55.8	32.6
42	121.2	88.3	313	61.3	35.3
43	397.0	203.1	359	55.1	31.7
45	132.4	109.2	213	58.9	33.2
46	97.4	107.5	283	55.4	32.0
49	53.2	70.7	237	62.9	34.5

MALES END OF TREATMENT

ANIMAL	Total bilirubin umol/L	Urea mmol/L	Creatinine umol/L	Glucose mmol/L	Cholesterol mmol/L
GROUP 1 (CONTROL)					
1	1.7	6.6	38.9	9.28	1.44

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.11 CLINICAL BIOCHEMISTRY MALES END OF TREATMENT

ANIMAL	Total bilirubin umol/L	Urea mmol/L	Creatinine umol/L	Glucose mmol/L	Cholesterol mmol/L
GROUP 1 (CONTROL)					
2	1.9	7.4	42.6	7.73	1.93
3	1.7	8.4	41.4	8.61	1.32
4	1.6	7.8	44.5	10.16	1.99
5	1.7	6.0	37.1	12.17	1.13
6	2.1	6.8	49.4	8.08	2.74
7	1.8	10.4	47.5	8.29	1.04
8	1.7	7.7	43.9	8.09	1.47
9	1.9	7.5	44.5	9.62	1.63
10	1.8	6.9	42.0	9.26	1.19
11	1.9	6.4	41.4	6.91	1.75
12	1.3	8.4	38.9	7.81	1.20
13	2.0	6.9	42.0	10.03	1.45
14	2.3	5.6	37.7	10.06	2.07
15	2.1	8.2	35.3	8.42	1.68
GROUP 2 (100 MG/KG)					
16	1.6	7.1	43.2	6.78	1.31
17	1.9	7.2	41.4	9.38	1.44
18	2.2	9.2	50.0	8.81	1.98
19	1.4	9.3	42.0	8.12	1.14
20	1.7	6.8	46.9	8.82	1.16
21	1.9	5.6	52.4	8.63	1.46
22	1.7	7.0	46.9	8.95	1.96
23	2.1	7.3	48.1	8.34	1.55
24	1.3	7.4	43.2	10.60	1.02
25	1.5	6.8	43.9	8.31	1.05
GROUP 3 (300 MG/KG)					
26	2.3	6.5	43.9	5.88	0.80
27	2.3	7.1	50.6	8.21	0.72
28	2.2	8.1	56.1	8.10	0.95
29	3.1	7.9	45.1	9.50	1.35
30	2.1	8.1	45.7	6.76	0.86
31	2.1	6.1	56.1	9.10	1.01
32	2.4	9.4	48.2	6.82	0.69
33	2.3	8.3	50.6	7.15	1.30
34	2.9	9.9	54.9	7.27	1.21
35	1.9	6.7	43.2	7.94	0.94
GROUP 4 (600 MG/KG)					
37	2.6	8.7	44.5	5.92	1.06
38	4.1	12.2	51.8	5.36	0.75
39	2.5	9.8	46.9	7.23	0.77
41	4.2	6.9	46.9	6.20	0.84
42	3.3	12.4	47.5	7.21	0.84
43	2.9	9.1	50.0	5.57	0.72
45	3.1	11.5	47.5	5.84	0.68
46	3.6	9.0	44.5	6.16	0.86
49	2.2	6.2	43.2	6.21	0.76

MALES END OF TREATMENT

ANIMAL	Bile Acids umol/L	Sodium mmol/L	Potassium mmol/L	Chloride mmol/L	Calcium mmol/L
GROUP 1 (CONTROL)					
1	38.5	140.2	3.86	103	2.52
2	33.5	141.7	5.37	99	2.65

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.11 CLINICAL BIOCHEMISTRY MALES END OF TREATMENT

ANIMAL	Bile Acids umol/L	Sodium mmol/L	Potassium mmol/L	Chloride mmol/L	Calcium mmol/L
GROUP 1 (CONTROL)					
3	18.0	141.4	3.61	101	2.51
4	16.9	141.6	3.79	102	2.57
5	28.0	139.0	4.03	99	2.51
6	25.5	140.6	3.85	101	2.60
7	26.3	141.7	3.99	101	2.51
8	39.4	140.4	4.05	102	2.57
9	21.1	140.2	4.13	101	2.48
10	12.6	139.8	4.05	101	2.55
11	14.5	140.6	3.87	103	2.43
12	39.5	141.9	4.31	103	2.50
13	14.1	140.5	3.99	102	2.51
14	30.4	141.9	3.88	102	2.67
15	36.5	140.0	4.11	102	2.60
GROUP 2 (100 MG/KG)					
16	21.0	142.1	3.76	103	2.50
17	26.7	141.6	4.19	102	2.60
18	25.3	143.0	3.86	100	2.59
19	14.6	143.5	4.01	103	2.51
20	24.7	143.7	3.90	105	2.51
21	13.7	143.2	3.87	103	2.52
22	23.9	143.9	4.06	102	2.54
23	45.2	144.6	3.97	102	2.54
24	28.1	141.6	3.80	101	2.53
25	15.7	143.9	3.67	104	2.58
GROUP 3 (300 MG/KG)					
26	35.8	144.7	3.71	103	2.47
27	20.2	144.7	3.85	105	2.50
28	31.7	143.4	3.75	104	2.42
29	81.8	143.3	3.66	103	2.57
30	21.8	144.5	3.68	102	2.49
31	32.3	143.3	3.99	102	2.64
32	53.4	142.8	4.05	102	2.42
33	20.9	143.6	4.13	103	2.52
34	29.1	142.1	4.45	101	2.55
35	24.4	141.8	4.21	103	2.49
GROUP 4 (600 MG/KG)					
37	38.7	142.7	3.97	101	2.59
38	59.5	142.4	3.88	99	2.45
39	34.8	143.2	3.80	102	2.57
41	50.9	142.1	3.71	103	2.49
42	82.5	140.3	4.21	99	2.53
43	60.9	141.4	3.99	102	2.40
45	55.5	138.9	4.37	99	2.48
46	35.9	139.1	4.33	97	2.46
49	48.0	142.8	3.66	101	2.60

MALES END OF TREATMENT

ANIMAL	Inorg.Phos mmol/L
GROUP 1 (CONTROL)	
1	1.67
2	2.09
3	1.63

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.11 CLINICAL BIOCHEMISTRY MALES END OF TREATMENT

ANIMAL	Inorg.Phos mmol/L
--------	----------------------

GROUP 1 (CONTROL)

4	1.68
5	1.54
6	2.11
7	1.85
8	2.00
9	1.91
10	1.63
11	1.55
12	2.43
13	1.72
14	1.51
15	2.07

GROUP 2 (100 MG/KG)

16	1.68
17	1.46
18	1.62
19	2.14
20	1.67
21	1.59
22	1.85
23	1.83
24	1.58
25	1.74

GROUP 3 (300 MG/KG)

26	1.85
27	1.90
28	2.01
29	1.36
30	1.99
31	1.78
32	1.85
33	2.16
34	2.06
35	1.82

GROUP 4 (600 MG/KG)

37	1.99
38	2.71
39	2.17
41	2.13
42	2.49
43	2.18
45	2.34
46	2.46
49	2.55

MALES END OF RECOVERY

ANIMAL	ALAT U/L	ASAT U/L	ALP U/L	Total protein g/L	Albumin g/L
GROUP 1 (CONTROL)					
11	43.9	84.3	195	67.2	33.6
12	37.6	81.4	163	61.5	30.9
13	25.5	72.0	126	67.6	33.8
14	88.6	157.0	128	69.5	33.4

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.11 CLINICAL BIOCHEMISTRY MALES END OF RECOVERY

ANIMAL	ALAT U/L	ASAT U/L	ALP U/L	Total protein g/L	Albumin g/L
GROUP 1 (CONTROL)					
15	40.4	71.8	189	71.2	35.9
GROUP 4 (600 MG/KG)					
43	46.5	67.7	136	67.3	32.4
45	43.8	72.1	111	66.5	31.4
46	42.4	60.4	137	74.3	35.5
49	37.3	76.9	135	69.3	34.1

MALES END OF RECOVERY

ANIMAL	Total bilirubin umol/L	Urea mmol/L	Creatinine umol/L	Glucose mmol/L	Cholesterol mmol/L
GROUP 1 (CONTROL)					
11	2.2	7.3	36.5	8.84	2.51
12	1.5	6.2	34.5	8.79	1.85
13	2.2	7.4	42.4	10.24	1.88
14	2.6	9.8	41.7	13.21	2.51
15	1.5	8.2	33.2	8.98	2.38
GROUP 4 (600 MG/KG)					
43	1.2	5.9	32.6	7.99	2.59
45	1.6	6.7	32.6	8.92	1.86
46	2.1	7.9	35.2	8.66	2.21
49	2.4	9.0	37.1	9.12	1.98

MALES END OF RECOVERY

ANIMAL	Bile Acids umol/L	Sodium mmol/L	Potassium mmol/L	Chloride mmol/L	Calcium mmol/L
GROUP 1 (CONTROL)					
11	37.0	141.2	4.12	104	2.69
12	17.8	141.2	4.29	104	2.59
13	25.4	142.4	4.11	106	2.65
14	27.6	141.0	4.23	101	2.68
15	20.0	142.4	4.31	104	2.70
GROUP 4 (600 MG/KG)					
43	20.7	142.1	4.25	104	2.71
45	49.9	142.6	4.24	104	2.67
46	63.1	142.6	4.02	102	2.71
49	64.2	141.5	4.34	104	2.61

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.11 CLINICAL BIOCHEMISTRY MALES END OF RECOVERY

ANIMAL	Inorg.Phos mmol/L
--------	----------------------

GROUP 1 (CONTROL)

11	1.72
12	2.12
13	1.74
14	1.50
15	1.90

GROUP 4 (600 MG/KG)

43	2.02
45	1.88
46	1.88
49	1.98

FEMALES END OF TREATMENT

ANIMAL	ALAT U/L	ASAT U/L	ALP U/L	Total protein g/L	Albumin g/L
--------	-------------	-------------	------------	----------------------	----------------

GROUP 1 (CONTROL)

51	---	---	---	---	---
52	61.6	78.8	36	65.5	33.3
53	37.1	60.2	59	64.5	32.1
54	58.1	90.8	39	67.1	34.6
55	59.8	100.9	139	62.5	32.7
56	49.7	92.8	123	64.9	32.9
57	42.9	69.2	78	69.2	35.9
58	55.2	69.1	85	70.2	35.7
59	49.2	84.4	39	65.2	33.7
60	35.7	70.1	49	64.9	33.5
61	37.3	71.4	45	68.6	35.3
62	66.6	79.9	108	67.4	33.6
63	52.7	78.8	121	65.5	33.2
64	56.3	85.1	77	69.8	35.6
65	38.6	73.1	162	68.2	35.8

GROUP 2 (100 MG/KG)

66	67.1	83.2	64	67.0	35.3
67	38.3	66.2	97	68.2	36.5
68	61.8	66.9	44	74.5	39.5
69	61.3	103.6	84	61.9	32.7
70	40.4	59.1	102	70.3	37.4
71	80.6	85.9	164	67.2	37.1
72	45.8	72.8	86	73.7	37.7
73	39.1	79.7	55	64.9	32.4
74	---	---	---	---	---
75	64.7	85.6	58	66.0	34.4

GROUP 3 (300 MG/KG)

76	85.5	97.3	59	75.1	38.4
78	30.1	69.9	42	74.9	39.0
79	65.3	72.4	129	68.7	37.2
80	112.4	104.1	134	60.6	32.3
81	88.8	95.9	83	67.9	35.0
82	88.2	84.2	190	66.6	35.4
83	59.1	90.2	124	68.1	36.6
84	61.9	79.4	60	67.0	36.1
85	69.6	84.1	53	65.9	35.6

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.11 CLINICAL BIOCHEMISTRY FEMALES END OF TREATMENT

ANIMAL	ALAT U/L	ASAT U/L	ALP U/L	Total protein g/L	Albumin g/L
GROUP 4 (600 MG/KG)					
86	65.7	68.3	118	65.4	36.3
87	87.9	109.1	144	63.1	35.2
89	78.1	75.2	178	66.3	37.4
90	76.1	82.4	80	66.0	35.0
91	74.8	99.0	227	65.8	36.0
92	140.5	215.3	367	60.7	34.7
94	75.7	98.6	206	61.0	33.8
95	143.7	219.3	161	47.8	26.4
97	59.7	102.9	219	59.9	34.3
98	73.0	81.8	206	70.9	37.0
99	66.3	85.7	176	62.0	32.6

FEMALES END OF TREATMENT

ANIMAL	Total bilirubin umol/L	Urea mmol/L	Creatinine umol/L	Glucose mmol/L	Cholesterol mmol/L
GROUP 1 (CONTROL)					
51	---	---	---	---	---
52	1.8	8.7	47.9	6.85	1.41
53	1.7	7.1	46.6	8.54	1.45
54	1.8	8.3	47.2	7.77	1.66
55	2.0	10.7	44.6	7.37	2.07
56	2.1	7.6	45.3	8.70	1.75
57	1.7	8.1	43.3	8.08	1.71
58	1.9	7.5	45.9	10.03	1.83
59	2.1	8.3	43.3	7.56	2.11
60	2.9	7.9	43.9	8.24	1.07
61	2.5	6.4	45.9	6.93	1.41
62	2.5	8.6	43.9	7.21	2.60
63	2.0	9.5	43.9	6.07	0.94
64	2.5	7.7	44.6	7.21	1.96
65	2.7	8.5	45.3	9.57	1.80
GROUP 2 (100 MG/KG)					
66	2.4	7.9	45.3	5.74	1.97
67	2.2	5.4	42.6	7.74	1.73
68	3.2	7.7	43.3	8.20	2.12
69	2.2	9.4	42.6	8.91	1.68
70	3.1	10.0	49.2	7.15	2.26
71	2.8	8.4	46.6	5.87	1.80
72	3.2	6.0	42.6	7.96	1.34
73	1.8	8.6	52.5	8.36	1.56
74	---	---	---	---	---
75	2.5	9.6	45.3	8.17	2.09
GROUP 3 (300 MG/KG)					
76	2.9	8.6	46.6	5.42	2.01
78	1.9	8.5	50.6	7.81	1.59
79	2.9	8.6	46.6	8.90	1.60
80	2.5	8.9	47.9	6.34	1.69
81	2.6	9.7	46.6	5.75	1.94
82	2.7	11.9	51.9	5.51	1.30
83	2.5	8.0	48.6	7.30	1.28
84	2.6	8.1	53.2	6.92	1.38
85	2.3	6.7	43.9	9.04	1.98

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.11 CLINICAL BIOCHEMISTRY FEMALES END OF TREATMENT

ANIMAL	Total bilirubin umol/L	Urea mmol/L	Creatinine umol/L	Glucose mmol/L	Cholesterol mmol/L
GROUP 4 (600 MG/KG)					
86	2.7	8.3	43.9	5.93	1.36
87	2.5	8.5	51.2	6.13	0.86
89	2.4	10.0	47.9	5.62	1.42
90	2.6	5.7	42.6	8.52	1.69
91	3.0	7.9	43.9	4.96	1.91
92	5.4	9.4	53.9	4.40	1.15
94	3.3	7.1	47.2	5.40	1.17
95	3.5	6.8	43.9	4.45	1.16
97	4.2	6.6	44.6	5.45	1.41
98	3.0	11.5	47.2	5.23	2.17
99	2.0	7.3	42.0	6.61	1.45

FEMALES END OF TREATMENT

ANIMAL	Bile Acids umol/L	Sodium mmol/L	Potassium mmol/L	Chloride mmol/L	Calcium mmol/L
GROUP 1 (CONTROL)					
51	---	---	---	---	---
52	29.1	138.9	3.35	101	2.61
53	47.6	141.2	3.42	104	2.59
54	49.1	137.3	3.87	100	2.59
55	68.6	137.5	3.66	99	2.47
56	49.7	138.9	3.73	103	2.64
57	19.2	138.2	3.27	101	2.71
58	36.9	136.7	3.27	99	2.63
59	16.3	138.1	4.12	100	2.63
60	5.1	141.7	3.60	101	2.64
61	26.6	139.4	3.83	103	2.55
62	90.6	139.4	3.71	102	2.56
63	37.2	140.2	3.57	104	2.48
64	39.3	139.6	3.70	102	2.55
65	61.0	140.1	3.68	103	2.60
GROUP 2 (100 MG/KG)					
66	46.4	143.1	4.08	103	2.60
67	11.4	141.2	3.26	105	2.53
68	154.0	140.0	3.79	103	2.74
69	46.2	139.4	3.95	103	2.45
70	33.1	139.1	3.44	102	2.66
71	58.3	138.8	3.56	102	2.63
72	19.5	141.1	3.32	102	2.68
73	32.8	138.2	3.90	103	2.51
74	---	---	---	---	---
75	62.4	139.4	3.64	103	2.58
GROUP 3 (300 MG/KG)					
76	46.0	139.1	3.47	99	2.65
78	39.6	138.6	3.27	99	2.65
79	87.0	138.9	3.72	98	2.65
80	49.3	139.0	3.42	102	2.42
81	61.8	139.0	3.53	102	2.57
82	71.2	138.9	3.40	101	2.57
83	26.8	140.8	3.47	104	2.61
84	36.5	140.8	3.88	103	2.59
85	51.6	139.9	3.51	101	2.56

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.11 CLINICAL BIOCHEMISTRY FEMALES END OF TREATMENT

ANIMAL	Bile Acids umol/L	Sodium mmol/L	Potassium mmol/L	Chloride mmol/L	Calcium mmol/L
GROUP 4 (600 MG/KG)					
86	58.4	140.3	3.66	99	2.66
87	27.9	138.4	3.37	100	2.55
89	51.5	138.6	3.76	103	2.61
90	51.8	140.4	3.41	101	2.54
91	70.0	140.5	3.35	102	2.61
92	56.2	138.0	3.46	94	2.56
94	46.1	138.2	3.58	100	2.60
95	54.2	134.0	3.05	95	2.24
97	67.2	140.9	3.20	102	2.48
98	89.5	137.6	3.38	96	2.63
99	62.0	139.5	3.52	102	2.51

FEMALES END OF TREATMENT

ANIMAL	Inorg.Phos mmol/L
GROUP 1 (CONTROL)	
51	---
52	1.37
53	1.41
54	1.69
55	1.74
56	1.84
57	1.70
58	2.16
59	2.57
60	1.79
61	1.59
62	1.42
63	1.59
64	1.37
65	1.22
GROUP 2 (100 MG/KG)	
66	1.52
67	1.37
68	1.50
69	1.89
70	1.69
71	1.38
72	1.40
73	1.43
74	---
75	1.35
GROUP 3 (300 MG/KG)	
76	1.89
78	1.76
79	1.61
80	1.48
81	1.61
82	1.82
83	1.79
84	1.53
85	1.22

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.11 CLINICAL BIOCHEMISTRY FEMALES END OF TREATMENT

ANIMAL	Inorg.Phos mmol/L
--------	----------------------

GROUP 4 (600 MG/KG)

86	2.23
87	2.07
89	2.16
90	1.63
91	1.92
92	2.24
94	1.77
95	1.83
97	1.55
98	1.85
99	1.56

FEMALES END OF RECOVERY

ANIMAL	ALAT U/L	ASAT U/L	ALP U/L	Total protein g/L	Albumin g/L
--------	-------------	-------------	------------	----------------------	----------------

GROUP 1 (CONTROL)

61	26.1	66.4	30	68.1	35.3
62	31.1	81.0	51	65.2	33.5
63	19.3	69.2	53	69.3	34.9
64	34.7	76.2	58	68.4	34.9
65	26.4	77.7	70	66.2	35.4

GROUP 4 (600 MG/KG)

94	22.8	65.9	43	64.8	33.5
95	28.5	68.5	69	66.6	33.6
97	22.8	69.2	68	66.3	34.2
98	27.8	73.1	45	66.5	33.4
99	26.0	84.5	122	63.8	32.8

FEMALES END OF RECOVERY

ANIMAL	Total bilirubin umol/L	Urea mmol/L	Creatinine umol/L	Glucose mmol/L	Cholesterol mmol/L
--------	---------------------------	----------------	----------------------	-------------------	-----------------------

GROUP 1 (CONTROL)

61	1.9	6.7	44.6	7.69	1.49
62	2.1	6.9	41.3	6.86	2.37
63	1.7	6.3	41.3	7.30	1.02
64	1.9	8.2	46.7	7.93	2.05
65	1.8	7.5	40.6	7.84	1.86

GROUP 4 (600 MG/KG)

94	2.2	6.5	40.6	8.04	1.44
95	1.9	6.8	38.5	7.12	2.75
97	1.5	9.6	44.6	6.48	1.53
98	1.6	7.4	38.5	6.31	1.56
99	1.6	6.6	39.2	7.29	1.80

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.11 CLINICAL BIOCHEMISTRY FEMALES END OF RECOVERY

ANIMAL	Bile Acids umol/L	Sodium mmol/L	Potassium mmol/L	Chloride mmol/L	Calcium mmol/L
GROUP 1 (CONTROL)					
61	8.5	139.1	3.49	102	2.57
62	55.2	141.0	3.46	105	2.62
63	23.4	141.8	3.70	105	2.64
64	53.7	140.3	3.43	104	2.57
65	23.8	141.1	4.12	106	2.68
GROUP 4 (600 MG/KG)					
94	9.8	139.7	3.90	105	2.64
95	41.6	140.6	3.76	106	2.57
97	10.7	142.4	3.88	105	2.59
98	14.3	142.2	3.70	104	2.60
99	41.8	140.8	3.58	105	2.57

FEMALES END OF RECOVERY

ANIMAL	Inorg.Phos mmol/L
GROUP 1 (CONTROL)	
61	1.47
62	1.48
63	1.42
64	1.46
65	2.02
GROUP 4 (600 MG/KG)	
94	1.29
95	1.44
97	1.76
98	1.44
99	1.44

**2.12 MACROSCOPIC FINDINGS
MALES****ALL NECROPSIES**

ANIMAL	ORGAN	FINDING	DAY OF DEATH
GROUP 1 (CONTROL)			
1		No findings noted	Scheduled sacrifice, 26May2016
2		No findings noted	Scheduled sacrifice, 26May2016
3	Stomach	Glandular mucosa: focus/foci, isolated, reddish.	Scheduled sacrifice, 26May2016
	Liver	Left lateral lobe: accessory lobe.	
	Preputial glands	Both sides: reduced in size.	
4	Seminal vesicles	Left side: reduced in size.	Scheduled sacrifice, 26May2016
5		No findings noted	Scheduled sacrifice, 26May2016
6		No findings noted	Scheduled sacrifice, 26May2016
7	Liver	Right medial lobe: accessory lobe.	Scheduled sacrifice, 26May2016
8		No findings noted	Scheduled sacrifice, 26May2016
9		No findings noted	Scheduled sacrifice, 26May2016
10		No findings noted	Scheduled sacrifice, 26May2016
11		No findings noted	Scheduled sacrifice, 23Jun2016
12		No findings noted	Scheduled sacrifice, 23Jun2016
13		No findings noted	Scheduled sacrifice, 23Jun2016
14	Stomach	Glandular mucosa: focus/foci, isolated, dark red.	Scheduled sacrifice, 23Jun2016
15	Thyroid gland	Both sides: enlarged.	Scheduled sacrifice, 23Jun2016
GROUP 2 (100 MG/KG)			
16	Mandibular lymph n	Right side: discolouration, reddish.	Scheduled sacrifice, 26May2016
17	Stomach	Forestomach: irregular surface.	Scheduled sacrifice, 26May2016
18	Kidneys	Both sides: discolouration, greenish.	Scheduled sacrifice, 26May2016
	Preputial glands	Both sides: reduced in size.	
19		No findings noted	Scheduled sacrifice, 26May2016
20		No findings noted	Scheduled sacrifice, 26May2016
21	Lacrimal glands	Right side: reduced in size.	Scheduled sacrifice, 26May2016
22	Liver	Enlarged.	Scheduled sacrifice, 26May2016
	Preputial glands	Both sides: reduced in size.	
23	Kidneys	Both sides: enlarged.	Scheduled sacrifice, 26May2016
24	Liver	Enlarged.	Scheduled sacrifice, 26May2016
	Preputial glands	Both sides: reduced in size.	
25	Stomach	Glandular mucosa: focus/foci, isolated, reddish.	Scheduled sacrifice, 26May2016
GROUP 3 (300 MG/KG)			
26	Liver	Enlarged.	Scheduled sacrifice, 26May2016
	Thyroid gland	Discolouration, red-brown.	
	Thymus	Both sides: enlarged.	
		Reduced in size.	
27	Liver	Enlarged.	Scheduled sacrifice, 26May2016
	Kidneys	Both sides: discolouration, greenish.	
28	Liver	Right medial lobe: accessory lobe.	Scheduled sacrifice, 26May2016
		Accentuated lobular pattern.	
		Enlarged.	
		Discolouration, red-brown.	
	Thymus	Enlarged.	
29	Liver	Enlarged.	Scheduled sacrifice, 26May2016
30	Liver	Enlarged.	Scheduled sacrifice, 26May2016
		Discolouration, red-brown.	
	Prostate	Reduced in size.	
31	Liver	Enlarged.	Scheduled sacrifice, 26May2016
	Kidneys	Both sides: discolouration, greenish.	
32	Liver	Enlarged.	Scheduled sacrifice, 26May2016
		Discolouration, red-brown.	
	Thymus	Focus/foci, isolated, reddish.	
33	Liver	Enlarged.	Scheduled sacrifice, 26May2016
	Kidneys	Both sides: discolouration, greenish.	
34	Liver	Enlarged.	Scheduled sacrifice, 26May2016
	Preputial glands	Reduced in size.	
	Thyroid gland	Both sides: enlarged.	
	Thymus	Right side: discolouration, reddish.	

**2.12 MACROSCOPIC FINDINGS
MALES****ALL NECROPSIES**

ANIMAL	ORGAN	FINDING	DAY OF DEATH
GROUP 3 (300 MG/KG)			
35	Liver	Enlarged.	Scheduled sacrifice, 26May2016
GROUP 4 (1000/600 MG/KG)			
36	Stomach	Glandular mucosa: focus/foci, many, dark red. Forestomach: focus/foci, isolated, black-brown.	Killed in extremis, 04May2016
	Liver	Glandular mucosa: irregular surface. Left lateral lobe: focus/foci, isolated, gray-white. Right medial lobe: focus/foci, isolated, gray-white.	
	Kidneys	Both sides: discolouration, greenish.	
	Prostate	Reduced in size.	
	Seminal vesicles	Both sides: reduced in size.	
	Thymus	Reduced in size.	
37	Stomach	Glandular mucosa: focus/foci, isolated, reddish.	Scheduled sacrifice, 26May2016
	Liver	Enlarged. Discolouration, red-brown.	
38	Kidneys	Both sides: discolouration, red-brown.	
	Stomach	Forestomach: irregular surface.	Scheduled sacrifice, 26May2016
	Liver	Enlarged. Discolouration, red-brown.	
	Kidneys	Both sides: discolouration, red-brown.	
	Prostate	Reduced in size.	
	Seminal vesicles	Both sides: reduced in size.	
	Preputial glands	Both sides: reduced in size.	
	Spleen	Reduced in size.	
	Thymus	Reduced in size.	
	Mesenteric lymph n	Reduced in size.	
39	Liver	Enlarged. Discolouration, red-brown.	Scheduled sacrifice, 26May2016
	Kidneys	Both sides: discolouration, greenish.	
	Urinary bladder	Contains gravel. Wall: thickened.	
40	General observations	Gi-tractus: distended with gas. Emaciated.	Killed in extremis, 15Mar2016
	Heart	Reduced in size.	
	Liver	Focus/foci, many, gray-white.	
	Prostate	Reduced in size.	
	Seminal vesicles	Both sides: reduced in size.	
	Preputial glands	Reduced in size.	
	Spleen	Reduced in size.	
	Thymus	Reduced in size.	
41	Stomach	Forestomach: irregular surface.	Scheduled sacrifice, 26May2016
	Liver	Enlarged. Discolouration, red-brown.	
42	Kidneys	Both sides: discolouration, greenish.	
	Liver	Enlarged. Discolouration, red-brown.	Scheduled sacrifice, 26May2016
	Kidneys	Both sides: discolouration, greenish.	
	Thymus	Reduced in size.	
43		No findings noted	Scheduled sacrifice, 23Jun2016
44	Trachea	Perforation(s), at height of lungs.	Spontaneous death, 21Mar2016
	Esophagus	Discolouration, dark red, at height of lungs.	
	Stomach	Glandular mucosa: focus/foci, isolated, reddish.	
	Liver	Enlarged.	
	Kidneys	Both sides: enlarged.	
	Body cavities	Thoracic cavity: contains red fluid/clots.	

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.12 MACROSCOPIC FINDINGS MALES

ALL NECROPSIES

ANIMAL	ORGAN	FINDING	DAY OF DEATH
GROUP 4 (1000/600 MG/KG)			
45	Liver	Discolouration, red-brown.	Scheduled sacrifice, 23Jun2016
	Thyroid gland	Both sides: enlarged.	
46		No findings noted	Scheduled sacrifice, 23Jun2016
47	General observations	Emaciated.	Killed in extremis, 25Mar2016
	Stomach	Irregular surface.	
	Liver	Focus/foci, several, gray-white.	
		Enlarged.	
	Kidneys	Discolouration, dark red.	
		Right side: focus/foci, many, black-brown.	
		Right side: discolouration, dark red.	
	Preputial glands	Both sides: reduced in size.	
	Thymus	Reduced in size.	
48	General observations	Gi-tractus: distended with gas.	Killed in extremis, 26Apr2016
		Emaciated.	
	Stomach	Glandular mucosa: focus/foci, many, reddish.	
	Liver	Focus/foci, several, gray-white.	
	Kidneys	Both sides: focus/foci, several, yellowish.	
	Prostate	Reduced in size.	
	Seminal vesicles	Both sides: reduced in size.	
	Thymus	Reduced in size.	
49	Liver	Discolouration, red-brown.	Scheduled sacrifice, 23Jun2016
50	General observations	Gi-tractus: distended with gas.	Killed in extremis, 19May2016
		Emaciated.	
	Trachea	Contains fluid, watery-clear.	
	Lungs	Focus/foci, several, tan.	
		Enlarged.	
	Stomach	Glandular mucosa: focus/foci, isolated, reddish.	
		Glandular mucosa: irregular surface.	
	Liver	Enlarged.	
		Discolouration, black-brown.	
	Prostate	Reduced in size.	
	Seminal vesicles	Both sides: reduced in size.	
	Spleen	Reduced in size.	
	Thymus	Reduced in size.	
	Harderian glands	Both sides: discolouration, pale.	

FEMALES

ALL NECROPSIES

ANIMAL	ORGAN	FINDING	DAY OF DEATH
GROUP 1 (CONTROL)			
51	Body cavities	Abdominal cavity, uterine adipose tissue, right side: nodule(s), d=8x5 mm, reddish, soft.	Scheduled sacrifice, 27May2016
52		No findings noted	Scheduled sacrifice, 31May2016
53	Uterus	Contains fluid.	Scheduled sacrifice, 31May2016
	Mandibular lymph n	Right side: discolouration, dark red.	
54		No findings noted	Scheduled sacrifice, 31May2016
55	Uterus	Contains fluid.	Scheduled sacrifice, 31May2016
56	Uterus	Contains fluid.	Scheduled sacrifice, 31May2016
57	Uterus	Contains fluid.	Scheduled sacrifice, 31May2016
58	Uterus	Contains fluid.	Scheduled sacrifice, 31May2016
59		No findings noted	Scheduled sacrifice, 31May2016
60	Liver	Papillary process: focus/foci, many, gray-white.	Scheduled sacrifice, 31May2016

**2.12 MACROSCOPIC FINDINGS
FEMALES****ALL NECROPSIES**

ANIMAL	ORGAN	FINDING	DAY OF DEATH
GROUP 1 (CONTROL)			
		Papillary process, left side: enlarged.	
		Papillary process: discolouration, black-brown.	
	Uterus	Contains fluid.	
61	Uterus	Contains fluid.	Scheduled sacrifice, 28Jun2016
62	Uterus	Contains fluid.	Scheduled sacrifice, 28Jun2016
63	Uterus	Contains fluid.	Scheduled sacrifice, 28Jun2016
64	Uterus	Contains fluid.	Scheduled sacrifice, 28Jun2016
65	Uterus	Contains fluid.	Scheduled sacrifice, 28Jun2016
GROUP 2 (100 MG/KG)			
66	Stomach	Glandular mucosa: focus/foci, isolated, black-brown.	Scheduled sacrifice, 31May2016
	Liver	Left median lobe: diaphragmatic hernia.	
67		No findings noted	Scheduled sacrifice, 31May2016
68	Uterus	Contains fluid.	Scheduled sacrifice, 31May2016
69	Uterus	Contains fluid.	Scheduled sacrifice, 31May2016
	Parathyroid lymph n.	Enlarged.	
70	Stomach	Glandular mucosa: focus/foci, isolated, reddish.	Scheduled sacrifice, 31May2016
71		No findings noted	Scheduled sacrifice, 31May2016
72	Uterus	Contains fluid.	Scheduled sacrifice, 31May2016
73	Lungs	Left lobe: discolouration, pale.	Scheduled sacrifice, 31May2016
	Stomach	Forestomach: focus/foci, isolated, reddish.	
74	General observations	Emaciated.	Spontaneous death, 26May2016
		Beginning autolysis.	
	Spleen	Reduced in size.	
	Thymus	Discolouration, reddish.	
	Mesenteric lymph n	Discolouration, black-brown.	
	Mandibular lymph n	Discolouration, black-brown.	
75	Uterus	Contains fluid.	Scheduled sacrifice, 31May2016
GROUP 3 (300 MG/KG)			
76		No findings noted	Scheduled sacrifice, 31May2016
77	General observations	Partial cannibalism	Spontaneous death, 12May2016
		Advanced autolysis.	
	Stomach	Glandular mucosa: focus/foci, many, black-brown.	
		Glandular mucosa: irregular surface.	
	Liver	Enlarged.	
	Adrenal glands	Both sides: enlarged.	
	Thymus	Focus/foci, several, reddish.	
	Renal lymph node	Both sides: enlarged.	
	Body cavities	Thoracic cavity: contains fluid, reddish, watery-cloudy.	
78	Stomach	Forestomach: focus/foci, isolated, black.	Scheduled sacrifice, 31May2016
	Liver	Accentuated lobular pattern.	
		Enlarged.	
		Discolouration, red-brown.	
79	Uterus	Contains fluid.	Scheduled sacrifice, 31May2016
80	Liver	Accentuated lobular pattern.	Scheduled sacrifice, 31May2016
		Enlarged.	
		Discolouration, red-brown.	
	Kidneys	Both sides: discolouration, greenish.	
	Thyroid gland	Both sides: enlarged.	
81	Liver	Accentuated lobular pattern.	Scheduled sacrifice, 31May2016
		Enlarged.	
		Discolouration, red-brown.	
	Kidneys	Both sides: pelvic dilation.	
		Both sides: enlarged.	
	Ovaries	Both sides: enlarged.	

**2.12 MACROSCOPIC FINDINGS
FEMALES****ALL NECROPSIES**

ANIMAL	ORGAN	FINDING	DAY OF DEATH
GROUP 3 (300 MG/KG)			
	Uterus	Contains fluid.	
82		No findings noted	Scheduled sacrifice, 31May2016
83	Uterus	Contains fluid.	Scheduled sacrifice, 31May2016
	Thyroid gland	Both sides: enlarged.	
	Mandibular lymph n	Right side: discolouration, reddish.	
84		No findings noted	Scheduled sacrifice, 31May2016
85	Uterus	Contains fluid.	Scheduled sacrifice, 31May2016
GROUP 4 (1000/600 MG/KG)			
86	Stomach	Forestomach: focus/foci, isolated, reddish.	Scheduled sacrifice, 31May2016
	Liver	Enlarged.	
	Kidneys	Discolouration, red-brown.	
	Uterus	Both sides: discolouration, greenish.	
87	Liver	Contains fluid.	Scheduled sacrifice, 31May2016
		Enlarged.	
	Kidneys	Discolouration, black-brown.	
88	General observations	Both sides: discolouration, greenish.	Killed in extremis, 18Mar2016
	Stomach	Emaciated.	
		Focus/foci, isolated, gray-white.	
	Spleen	Glandular mucosa: irregular surface.	
	Thymus	Reduced in size.	
89	Liver	Reduced in size.	Scheduled sacrifice, 31May2016
		Enlarged.	
	Uterus	Discolouration, red-brown.	
	Thyroid gland	Contains fluid.	
90	Stomach	Both sides: enlarged.	Scheduled sacrifice, 31May2016
		Forestomach: focus/foci, isolated, reddish.	
	Liver	Enlarged.	
		Discolouration, red-brown.	
	Kidneys	Both sides: discolouration, greenish.	
91	Uterus	Contains fluid.	Scheduled sacrifice, 31May2016
	Liver	Enlarged.	
		Discolouration, red-brown.	
	Kidneys	Both sides: discolouration, greenish.	
92	Uterus	Contains fluid.	Scheduled sacrifice, 31May2016
	Stomach	Forestomach: focus/foci, isolated, reddish.	
	Liver	Enlarged.	
		Discolouration, red-brown.	
93	Kidneys	Both sides: discolouration, greenish.	Spontaneous death, 15Mar2016
	General observations	Partial cannibalism	
		Advanced autolysis.	
94	Thymus	Discolouration, dark red.	Scheduled sacrifice, 28Jun2016
	Liver	Discolouration, red-brown.	
	Kidneys	Both sides: discolouration, greenish.	
	Uterus	Contains fluid.	
	Clitoral glands	Left side: focus/foci, isolated, tan.	
	Adrenal glands	Both sides: enlarged.	
95	Thymus	Right side: focus/foci, many, reddish.	Scheduled sacrifice, 28Jun2016
	Kidneys	Both sides: discolouration, greenish.	
	Uterus	Contains fluid.	
96	Lungs	Right medial lobe: focus/foci, d=9x8 mm, black-brown.	Spontaneous death, 25Mar2016
	Liver	Enlarged.	
	Kidneys	Both sides: discolouration, dark red.	
	Thymus	Discolouration, dark red.	
	Renal lymph node	Both sides: enlarged.	
		Both sides: discolouration, dark red.	
	Body cavities	Thoracic cavity: contents: dark red, watery-clear.	
97		No findings noted	Scheduled sacrifice, 28Jun2016

**2.12 MACROSCOPIC FINDINGS
FEMALES**

ALL NECROPSIES

ANIMAL	ORGAN	FINDING	DAY OF DEATH
GROUP 4 (1000/600 MG/KG)			
98	Liver	Discolouration, black-brown.	Scheduled sacrifice, 28Jun2016
99		No findings noted	Scheduled sacrifice, 28Jun2016
100	General observations	Emaciated.	Killed in extremis, 27Apr2016
	Liver	Enlarged.	
	Thymus	Reduced in size.	

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.13 ORGAN WEIGHTS (GRAM) MALES END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (GRAM)	HEART (GRAM)	LIVER (GRAM)
GROUP 1 (CONTROL)				
1	344	2.01	0.870	10.66
2	413	1.97	1.112	11.75
3	343	1.94	0.916	10.13
4	381	2.05	0.942	11.96
5	342	2.02	0.859	10.23
6	453	2.17	1.108	13.05
7	346	2.05	0.917	10.11
8	390	1.92	1.113	11.96
9	369	2.02	0.917	10.61
10	338	2.04	0.924	9.57
GROUP 2 (100 MG/KG)				
16	401	2.06	0.941	13.23
17	359	1.98	0.963	11.01
18	365	1.91	0.870	12.46
19	354	2.05	0.968	12.20
20	367	1.95	0.890	11.37
21	346	2.11	0.813	10.70
22	420	2.08	1.038	14.46
23	399	2.17	1.076	12.92
24	356	2.15	0.864	12.31
25	381	2.07	1.055	12.47
GROUP 3 (300 MG/KG)				
26	328	1.95	0.858	13.10
27	341	1.99	0.883	13.74
28	367	1.86	0.826	14.55
29	328	1.98	0.885	15.39
30	323	1.98	0.849	13.42
31	389	2.21	0.886	17.30
32	323	2.05	0.813	14.17
33	319	2.03	0.789	14.30
34	324	2.01	0.889	13.12
35	326	1.99	0.912	13.40
GROUP 4 (1000/600 MG/KG)				
36	---	---	---	---
37	300	1.90	0.798	16.95
38	266	2.00	0.734	15.04
39	325	2.05	0.842	17.63
40	---	---	---	---
41	306	1.98	0.772	19.60
42	292	1.86	0.733	19.06
44	---	---	---	---

MALES END OF TREATMENT

ANIMAL	THYROIDES (GRAM)	THYMUS (GRAM)	KIDNEYS (GRAM)	ADRENALS (GRAM)
GROUP 1 (CONTROL)				
1	0.015	0.250	2.45	0.048
2	0.018	0.375	2.45	0.060
3	0.015	0.284	2.27	0.058
4	0.012	0.370	2.53	0.061
5	0.016	0.242	2.46	0.052
6	0.018	0.346	2.64	0.046
7	0.014	0.249	2.30	0.055

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.13 ORGAN WEIGHTS (GRAM) MALES END OF TREATMENT

ANIMAL	THYROIDS (GRAM)	THYMUS (GRAM)	KIDNEYS (GRAM)	ADRENALS (GRAM)
GROUP 1 (CONTROL)				
8	0.014	0.329	2.67	0.057
9	0.015	0.265	2.31	0.055
10	0.012	0.286	2.32	0.050
GROUP 2 (100 MG/KG)				
16	0.020	0.318	2.81	0.050
17	0.016	0.310	2.72	0.053
18	0.012	0.238	2.72	0.051
19	0.016	0.303	2.94	0.048
20	0.021	0.354	2.35	0.057
21	0.018	0.299	2.39	0.042
22	0.021	0.489	2.74	0.061
23	0.017	0.425	3.09	0.056
24	0.013	0.295	3.00	0.046
25	0.016	0.284	2.91	0.050
GROUP 3 (300 MG/KG)				
26	0.018	0.238	2.81	0.063
27	0.019	0.369	2.53	0.047
28	0.020	0.432	2.78	0.054
29	0.016	0.227	2.80	0.046
30	0.018	0.320	2.63	0.046
31	0.016	0.300	3.23	0.055
32	0.015	0.395	2.90	0.046
33	0.018	0.265	2.51	0.042
34	0.026	0.234	2.65	0.064
35	0.018	0.367	2.89	0.049
GROUP 4 (1000/600 MG/KG)				
36	---	---	---	---
37	0.016	0.222	2.45	0.062
38	0.017	0.145	2.78	0.069
39	0.017	0.222	2.90	0.058
40	---	---	---	---
41	0.014	0.212	2.78	0.056
42	0.016	0.235	2.65	0.069
44	---	---	---	---

MALES END OF TREATMENT

ANIMAL	SPLEEN (GRAM)	TESTES (GRAM)	PROSTATE GLAND (GRAM)	EPIDIDYMIDES (GRAM)
GROUP 1 (CONTROL)				
1	0.552	3.29	0.742	1.217
2	0.637	3.59	0.718	1.204
3	0.549	3.28	0.736	1.070
4	0.690	4.04	1.005	1.278
5	0.564	3.56	0.693	1.184
6	0.647	3.91	0.582	1.241
7	0.423	3.56	0.643	1.111
8	0.588	3.23	0.861	1.174
9	0.444	3.87	0.937	1.251
10	0.387	3.47	0.777	1.264
GROUP 2 (100 MG/KG)				
16	0.550	3.64	0.837	1.152
17	0.542	3.64	0.556	1.211

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.13 ORGAN WEIGHTS (GRAM) MALES END OF TREATMENT

ANIMAL	SPLEEN (GRAM)	TESTES (GRAM)	PROSTATE GLAND (GRAM)	EPIDIDYMIDES (GRAM)
GROUP 2 (100 MG/KG)				
18	0.527	2.92	0.462	0.982
19	0.577	3.59	0.705	1.209
20	0.522	3.21	0.803	0.955
21	0.527	3.39	0.831	1.105
22	0.734	4.25	---	1.339
23	0.621	3.93	0.645	1.340
24	0.456	3.43	0.759	1.132
25	0.494	3.53	0.566	1.095
GROUP 3 (300 MG/KG)				
26	0.469	4.07	0.590	1.296
27	0.495	3.54	0.816	1.074
28	0.527	3.23	0.809	1.085
29	0.535	3.18	0.713	1.182
30	0.528	3.55	0.405	1.184
31	0.484	3.79	0.711	1.196
32	0.475	3.20	0.515	1.071
33	0.489	3.36	0.730	0.997
34	0.561	3.73	0.792	1.298
35	0.462	3.59	0.478	1.224
GROUP 4 (1000/600 MG/KG)				
36	---	---	---	---
37	0.533	3.63	0.777	1.143
38	0.305	3.24	0.406	1.078
39	0.412	3.45	0.709	1.145
40	---	---	---	---
41	0.461	3.92	0.739	1.101
42	0.469	3.59	0.577	1.214
44	---	---	---	---

MALES END OF TREATMENT

ANIMAL	SEMINAL VESICLES (GRAM)
GROUP 1 (CONTROL)	
1	1.373
2	1.287
3	1.157
4	1.225
5	1.225
6	0.932
7	1.031
8	1.075
9	1.528
10	1.064
GROUP 2 (100 MG/KG)	
16	1.457
17	1.257
18	1.295
19	1.434
20	1.040
21	0.927
22	1.366
23	1.322
24	1.479

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.13 ORGAN WEIGHTS (GRAM) MALES END OF TREATMENT

ANIMAL	SEMINAL VESICLES (GRAM)
--------	----------------------------

GROUP 2 (100 MG/KG)

25	1.392
----	-------

GROUP 3 (300 MG/KG)

26	1.382
27	1.169
28	1.129
29	1.278
30	1.744
31	1.413
32	0.980
33	0.891
34	1.206
35	1.517

GROUP 4 (1000/600 MG/KG)

36	---
37	1.072
38	0.551
39	0.995
40	---
41	0.882
42	1.185
44	---

MALES END OF RECOVERY

ANIMAL	BODY W. (GRAM)	BRAIN (GRAM)	HEART (GRAM)	LIVER (GRAM)
--------	-------------------	-----------------	-----------------	-----------------

GROUP 1 (CONTROL)

11	355	2.03	0.925	8.26
12	383	2.01	0.965	8.25
13	425	2.07	1.395	9.12
14	390	1.91	0.955	9.19
15	400	2.00	0.995	10.02

GROUP 4 (1000/600 MG/KG)

43	376	2.08	1.030	9.17
45	389	2.00	1.015	9.41
46	389	2.06	1.070	10.13
47	---	---	---	---
48	---	---	---	---
49	300	2.07	0.815	7.21
50	---	---	---	---

MALES END OF RECOVERY

ANIMAL	THYROIDS (GRAM)	THYMUS (GRAM)	KIDNEYS (GRAM)	ADRENALS (GRAM)
--------	--------------------	------------------	-------------------	--------------------

GROUP 1 (CONTROL)

11	0.016	0.220	1.99	0.045
12	0.014	0.405	2.26	0.050
13	0.014	0.330	2.36	0.060

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.13 ORGAN WEIGHTS (GRAM) MALES END OF RECOVERY

ANIMAL	THYROIDS (GRAM)	THYMUS (GRAM)	KIDNEYS (GRAM)	ADRENALS (GRAM)
GROUP 1 (CONTROL)				
14	0.011	0.175	2.08	0.050
15	0.023	0.315	2.30	0.045
GROUP 4 (1000/600 MG/KG)				
43	0.020	0.440	2.61	0.050
45	0.021	0.340	2.68	0.050
46	0.018	0.410	2.73	0.045
47	---	---	---	---
48	---	---	---	---
49	0.016	0.235	2.11	0.045
50	---	---	---	---

MALES END OF RECOVERY

ANIMAL	SPLEEN (GRAM)	TESTES (GRAM)	PROSTATE GLAND (GRAM)	EPIDIDYMIDES (GRAM)
GROUP 1 (CONTROL)				
11	0.450	3.47	0.460	1.285
12	0.480	3.36	0.795	1.190
13	0.740	4.00	0.790	1.370
14	0.515	3.47	0.745	1.360
15	0.480	3.66	0.775	1.290
GROUP 4 (1000/600 MG/KG)				
43	0.535	3.84	0.690	1.290
45	0.570	3.83	0.665	1.185
46	0.570	4.09	0.685	1.485
47	---	---	---	---
48	---	---	---	---
49	0.600	3.27	0.590	1.115
50	---	---	---	---

MALES END OF RECOVERY

ANIMAL	SEMINAL VESICLES (GRAM)
GROUP 1 (CONTROL)	
11	1.525
12	1.315
13	1.615
14	0.940
15	1.650
GROUP 4 (1000/600 MG/KG)	
43	1.320
45	1.335
46	1.265
47	---
48	---
49	1.520
50	---

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.13 ORGAN/BODY WEIGHT RATIOS (%)

MALES

END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (%)	HEART (%)	LIVER (%)
GROUP 1 (CONTROL)				
1	344	0.58	0.253	3.10
2	413	0.48	0.270	2.85
3	343	0.56	0.267	2.95
4	381	0.54	0.247	3.14
5	342	0.59	0.251	2.99
6	453	0.48	0.245	2.88
7	346	0.59	0.265	2.93
8	390	0.49	0.285	3.06
9	369	0.55	0.248	2.87
10	338	0.60	0.273	2.83
GROUP 2 (100 MG/KG)				
16	401	0.51	0.235	3.30
17	359	0.55	0.269	3.07
18	365	0.52	0.239	3.42
19	354	0.58	0.274	3.45
20	367	0.53	0.243	3.10
21	346	0.61	0.235	3.10
22	420	0.50	0.247	3.44
23	399	0.54	0.270	3.24
24	356	0.60	0.243	3.46
25	381	0.54	0.277	3.28
GROUP 3 (300 MG/KG)				
26	328	0.59	0.262	4.00
27	341	0.58	0.259	4.03
28	367	0.51	0.225	3.96
29	328	0.60	0.270	4.70
30	323	0.61	0.263	4.16
31	389	0.57	0.228	4.44
32	323	0.63	0.252	4.39
33	319	0.64	0.248	4.49
34	324	0.62	0.274	4.05
35	326	0.61	0.280	4.11
GROUP 4 (1000/600 MG/KG)				
36	---	---	---	---
37	300	0.63	0.266	5.65
38	266	0.75	0.276	5.66
39	325	0.63	0.259	5.42
40	---	---	---	---
41	306	0.65	0.253	6.42
42	292	0.64	0.251	6.54
44	---	---	---	---

MALES

END OF TREATMENT

ANIMAL	THYROIDS (%)	THYMUS (%)	KIDNEYS (%)	ADRENALS (%)
GROUP 1 (CONTROL)				
1	0.004	0.073	0.71	0.014
2	0.004	0.091	0.59	0.015
3	0.004	0.083	0.66	0.017
4	0.003	0.097	0.66	0.016
5	0.005	0.071	0.72	0.015
6	0.004	0.076	0.58	0.010
7	0.004	0.072	0.66	0.016

2.13 ORGAN/BODY WEIGHT RATIOS (%)

MALES

END OF TREATMENT

ANIMAL	THYROIDS (%)	THYMUS (%)	KIDNEYS (%)	ADRENALS (%)
GROUP 1 (CONTROL)				
8	0.004	0.084	0.68	0.015
9	0.004	0.072	0.63	0.015
10	0.004	0.085	0.69	0.015
GROUP 2 (100 MG/KG)				
16	0.005	0.079	0.70	0.012
17	0.004	0.086	0.76	0.015
18	0.003	0.065	0.74	0.014
19	0.004	0.086	0.83	0.014
20	0.006	0.096	0.64	0.016
21	0.005	0.086	0.69	0.012
22	0.005	0.116	0.65	0.015
23	0.004	0.107	0.77	0.014
24	0.004	0.083	0.84	0.013
25	0.004	0.075	0.76	0.013
GROUP 3 (300 MG/KG)				
26	0.006	0.073	0.86	0.019
27	0.006	0.108	0.74	0.014
28	0.005	0.118	0.76	0.015
29	0.005	0.069	0.85	0.014
30	0.006	0.099	0.81	0.014
31	0.004	0.077	0.83	0.014
32	0.004	0.122	0.90	0.014
33	0.006	0.083	0.79	0.013
34	0.008	0.072	0.82	0.020
35	0.006	0.113	0.89	0.015
GROUP 4 (1000/600 MG/KG)				
36	---	---	---	---
37	0.005	0.074	0.82	0.021
38	0.006	0.055	1.05	0.026
39	0.005	0.068	0.89	0.018
40	---	---	---	---
41	0.005	0.069	0.91	0.018
42	0.006	0.081	0.91	0.024
44	---	---	---	---

MALES

END OF TREATMENT

ANIMAL	SPLEEN (%)	TESTES (%)	PROSTATE GLAND (%)	EPIDIDYMIDES (%)
GROUP 1 (CONTROL)				
1	0.160	0.95	0.216	0.354
2	0.154	0.87	0.174	0.292
3	0.160	0.96	0.215	0.312
4	0.181	1.06	0.264	0.335
5	0.165	1.04	0.202	0.346
6	0.143	0.86	0.129	0.274
7	0.122	1.03	0.186	0.322
8	0.151	0.83	0.221	0.301
9	0.120	1.05	0.254	0.339
10	0.114	1.03	0.230	0.374
GROUP 2 (100 MG/KG)				
16	0.137	0.91	0.209	0.287
17	0.151	1.01	0.155	0.338

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.13 ORGAN/BODY WEIGHT RATIOS (%)

MALES

END OF TREATMENT

ANIMAL	SPLEEN (%)	TESTES (%)	PROSTATE GLAND (%)	EPIDIDYMIDES (%)
GROUP 2 (100 MG/KG)				
18	0.145	0.80	0.127	0.269
19	0.163	1.01	0.199	0.342
20	0.142	0.87	0.219	0.260
21	0.152	0.98	0.240	0.320
22	0.175	1.01	---	0.319
23	0.156	0.98	0.162	0.336
24	0.128	0.96	0.213	0.318
25	0.130	0.93	0.149	0.288
GROUP 3 (300 MG/KG)				
26	0.143	1.24	0.180	0.396
27	0.145	1.04	0.240	0.315
28	0.144	0.88	0.220	0.296
29	0.163	0.97	0.218	0.361
30	0.164	1.10	0.126	0.367
31	0.124	0.97	0.183	0.307
32	0.147	0.99	0.159	0.332
33	0.154	1.06	0.229	0.313
34	0.173	1.15	0.244	0.401
35	0.142	1.10	0.147	0.376
GROUP 4 (1000/600 MG/KG)				
36	---	---	---	---
37	0.178	1.21	0.259	0.381
38	0.115	1.22	0.153	0.406
39	0.127	1.06	0.218	0.352
40	---	---	---	---
41	0.151	1.28	0.242	0.360
42	0.161	1.23	0.198	0.416
44	---	---	---	---

MALES

END OF TREATMENT

ANIMAL	SEMINAL VESICLES (%)
GROUP 1 (CONTROL)	
1	0.399
2	0.312
3	0.337
4	0.321
5	0.358
6	0.206
7	0.298
8	0.275
9	0.414
10	0.315
GROUP 2 (100 MG/KG)	
16	0.363
17	0.351
18	0.355
19	0.405
20	0.283
21	0.268
22	0.325
23	0.331
24	0.415

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.13 ORGAN/BODY WEIGHT RATIOS (%)

MALES

END OF TREATMENT

ANIMAL	SEMINAL VESICLES (%)
--------	----------------------

GROUP 2 (100 MG/KG)

25	0.366
----	-------

GROUP 3 (300 MG/KG)

26	0.422
27	0.343
28	0.308
29	0.390
30	0.541
31	0.363
32	0.303
33	0.280
34	0.372
35	0.466

GROUP 4 (1000/600 MG/KG)

36	---
37	0.358
38	0.207
39	0.306
40	---
41	0.289
42	0.407
44	---

MALES

END OF RECOVERY

ANIMAL	BODY W. (GRAM)	BRAIN (%)	HEART (%)	LIVER (%)
--------	----------------	-----------	-----------	-----------

GROUP 1 (CONTROL)

11	355	0.57	0.260	2.32
12	383	0.52	0.252	2.15
13	425	0.49	0.329	2.15
14	390	0.49	0.245	2.36
15	400	0.50	0.249	2.51

GROUP 4 (1000/600 MG/KG)

43	376	0.55	0.274	2.44
45	389	0.51	0.261	2.42
46	389	0.53	0.275	2.60
47	---	---	---	---
48	---	---	---	---
49	300	0.69	0.272	2.40
50	---	---	---	---

MALES

END OF RECOVERY

ANIMAL	THYROIDS (%)	THYMUS (%)	KIDNEYS (%)	ADRENALS (%)
--------	--------------	------------	-------------	--------------

GROUP 1 (CONTROL)

11	0.004	0.062	0.56	0.013
12	0.004	0.106	0.59	0.013
13	0.003	0.078	0.56	0.014

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.13 ORGAN/BODY WEIGHT RATIOS (%)

MALES

END OF RECOVERY

ANIMAL	THYROIDS (%)	THYMUS (%)	KIDNEYS (%)	ADRENALS (%)
GROUP 1 (CONTROL)				
14	0.003	0.045	0.53	0.013
15	0.006	0.079	0.57	0.011
GROUP 4 (1000/600 MG/KG)				
43	0.005	0.117	0.69	0.013
45	0.005	0.087	0.69	0.013
46	0.005	0.105	0.70	0.012
47	---	---	---	---
48	---	---	---	---
49	0.005	0.078	0.70	0.015
50	---	---	---	---

MALES

END OF RECOVERY

ANIMAL	SPLEEN (%)	TESTES (%)	PROSTATE GLAND (%)	EPIDIDYMIDES (%)
GROUP 1 (CONTROL)				
11	0.127	0.98	0.130	0.362
12	0.125	0.88	0.208	0.311
13	0.174	0.94	0.186	0.323
14	0.132	0.89	0.191	0.349
15	0.120	0.92	0.194	0.323
GROUP 4 (1000/600 MG/KG)				
43	0.142	1.02	0.184	0.344
45	0.147	0.98	0.171	0.305
46	0.146	1.05	0.176	0.382
47	---	---	---	---
48	---	---	---	---
49	0.200	1.09	0.197	0.372
50	---	---	---	---

MALES

END OF RECOVERY

ANIMAL	SEMINAL VESICLES (%)
GROUP 1 (CONTROL)	
11	0.429
12	0.343
13	0.380
14	0.241
15	0.413
GROUP 4 (1000/600 MG/KG)	
43	0.352
45	0.343
46	0.325
47	---
48	---
49	0.507
50	---

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.13 ORGAN WEIGHTS (GRAM) FEMALES END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (GRAM)	HEART (GRAM)	LIVER (GRAM)
GROUP 1 (CONTROL)				
51	269	1.99	0.792	10.04
52	253	1.94	0.760	9.88
53	223	1.91	0.720	7.96
54	255	1.96	0.745	8.98
55	238	1.97	0.750	8.72
56	241	1.98	0.685	8.19
57	215	1.80	0.700	7.56
58	253	1.99	0.740	10.24
59	240	1.87	0.815	8.95
60	236	1.89	0.730	9.01
GROUP 2 (100 MG/KG)				
66	238	1.83	0.760	8.07
67	204	1.87	0.655	7.15
68	220	1.79	0.750	9.20
69	231	1.80	0.715	8.27
70	233	1.91	0.790	8.99
71	252	1.87	0.765	9.69
72	263	1.87	0.820	8.84
73	251	1.85	0.735	9.12
74	---	---	---	---
75	219	1.96	0.660	8.65
GROUP 3 (300 MG/KG)				
76	245	1.95	0.800	9.64
77	---	---	---	---
78	212	1.91	0.650	10.56
79	228	1.94	0.660	10.12
80	244	1.96	0.755	10.22
81	220	1.99	0.710	11.65
82	204	1.85	0.690	9.34
83	228	1.84	0.655	10.32
84	217	1.95	0.675	10.25
85	203	1.91	0.680	10.33
GROUP 4 (1000/600 MG/KG)				
86	221	1.87	0.680	13.95
87	224	1.97	0.715	12.10
88	---	---	---	---
89	222	1.83	0.625	13.09
90	237	1.94	0.720	12.64
91	207	1.79	0.635	11.06
92	232	1.90	0.680	12.75
93	---	---	---	---

FEMALES END OF TREATMENT

ANIMAL	THYROID (GRAM)	THYMUS (GRAM)	KIDNEYS (GRAM)	ADRENALS (GRAM)
GROUP 1 (CONTROL)				
51	0.016	0.352	1.90	0.083
52	0.016	0.395	1.47	0.090
53	0.017	0.320	1.66	0.065
54	0.017	0.335	1.85	0.095
55	0.017	0.245	1.56	0.055
56	0.012	0.220	1.70	0.090
57	0.011	0.440	1.44	0.050

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.13 ORGAN WEIGHTS (GRAM) FEMALES END OF TREATMENT

ANIMAL	THYROIDS (GRAM)	THYMUS (GRAM)	KIDNEYS (GRAM)	ADRENALS (GRAM)
GROUP 1 (CONTROL)				
58	0.022	0.310	1.80	0.075
59	0.015	0.220	1.72	0.070
60	0.020	0.220	1.70	0.090
GROUP 2 (100 MG/KG)				
66	0.016	0.275	1.67	0.075
67	0.012	0.220	1.65	0.055
68	0.016	0.360	1.82	0.065
69	0.016	0.250	1.66	0.055
70	0.016	0.365	1.76	0.070
71	0.013	0.345	1.91	0.075
72	0.018	0.300	2.09	0.090
73	0.015	0.295	1.78	0.085
74	---	---	---	---
75	0.016	0.295	1.67	0.060
GROUP 3 (300 MG/KG)				
76	0.020	0.235	2.15	0.075
77	---	---	---	---
78	0.013	0.250	1.72	0.085
79	0.017	0.265	1.82	0.070
80	0.024	0.235	1.95	0.080
81	0.019	0.180	2.22	0.075
82	0.015	0.240	1.73	0.070
83	0.024	0.260	1.82	0.090
84	0.017	0.250	1.77	0.060
85	0.016	0.210	1.81	0.075
GROUP 4 (1000/600 MG/KG)				
86	0.017	0.215	2.20	0.070
87	0.019	0.240	2.00	0.070
88	---	---	---	---
89	0.023	0.225	2.05	0.080
90	0.014	0.340	2.08	0.080
91	0.020	0.260	1.90	0.065
92	0.011	0.190	2.27	0.085
93	---	---	---	---

FEMALES END OF TREATMENT

ANIMAL	SPLEEN (GRAM)	OVARIES (GRAM)	UTERUS (GRAM)
GROUP 1 (CONTROL)			
51	0.470	0.160	0.856
52	0.595	0.170	0.495
53	0.545	0.180	1.495
54	0.570	0.125	0.800
55	0.470	0.150	1.060
56	0.495	0.185	1.785
57	0.605	0.175	1.115
58	0.545	0.190	2.115
59	0.650	0.160	0.565
60	0.645	0.160	1.090
GROUP 2 (100 MG/KG)			
66	0.430	0.130	0.790
67	0.440	0.135	0.585

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.13 ORGAN WEIGHTS (GRAM) FEMALES END OF TREATMENT

ANIMAL	SPLEEN (GRAM)	OVARIES (GRAM)	UTERUS (GRAM)
GROUP 2 (100 MG/KG)			
68	0.505	0.145	1.295
69	0.505	0.165	2.085
70	0.445	0.155	0.545
71	0.485	0.145	0.535
72	0.475	0.205	0.910
73	0.430	0.165	0.725
74	---	---	---
75	0.480	0.165	1.035
GROUP 3 (300 MG/KG)			
76	0.435	0.120	0.450
77	---	---	---
78	0.385	0.140	0.480
79	0.455	0.120	1.585
80	0.530	0.145	0.615
81	0.400	0.175	1.245
82	0.355	0.150	0.465
83	0.480	0.170	1.705
84	0.400	0.135	0.415
85	0.365	0.130	1.930
GROUP 4 (1000/600 MG/KG)			
86	0.365	0.135	0.880
87	0.460	0.185	0.485
88	---	---	---
89	0.505	0.155	3.980
90	0.490	0.155	1.140
91	0.455	0.145	1.270
92	0.325	0.145	0.395
93	---	---	---

FEMALES END OF RECOVERY

ANIMAL	BODY W. (GRAM)	BRAIN (GRAM)	HEART (GRAM)	LIVER (GRAM)
GROUP 1 (CONTROL)				
61	233	1.92	0.705	6.02
62	237	1.92	0.745	6.03
63	258	1.97	0.880	6.45
64	236	1.92	0.670	5.37
65	239	1.92	0.755	6.05
GROUP 4 (1000/600 MG/KG)				
94	253	1.99	0.795	6.90
95	240	1.84	0.685	5.69
96	---	---	---	---
97	199	1.88	0.610	5.11
98	201	1.84	0.690	5.74
99	235	1.86	0.680	5.66
100	---	---	---	---

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.13 ORGAN WEIGHTS (GRAM) FEMALES END OF RECOVERY

ANIMAL	THYROIDS (GRAM)	THYMUS (GRAM)	KIDNEYS (GRAM)	ADRENALS (GRAM)
GROUP 1 (CONTROL)				
61	0.014	0.305	1.62	0.065
62	0.015	0.195	1.68	0.065
63	0.015	0.365	1.87	0.085
64	0.017	0.335	1.55	0.050
65	0.017	0.255	1.56	0.065
GROUP 4 (1000/600 MG/KG)				
94	0.016	0.315	2.05	0.100
95	0.015	0.435	1.59	0.050
96	---	---	---	---
97	0.019	0.395	1.68	0.055
98	0.014	0.390	1.57	0.075
99	0.016	0.350	1.59	0.060
100	---	---	---	---

FEMALES END OF RECOVERY

ANIMAL	SPLEEN (GRAM)	OVARIES (GRAM)	UTERUS (GRAM)
GROUP 1 (CONTROL)			
61	0.435	0.140	3.490
62	0.490	0.140	1.075
63	0.560	0.240	3.040
64	0.350	0.130	2.125
65	0.470	0.140	1.160
GROUP 4 (1000/600 MG/KG)			
94	0.465	0.205	2.305
95	0.390	0.140	1.215
96	---	---	---
97	0.420	0.135	0.425
98	0.400	0.115	0.580
99	0.430	0.145	0.705
100	---	---	---

Final Report

MTDID 7831
APPENDIX 2

Project 511505

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

ANIMAL	BODY W. (GRAM)	BRAIN (%)	HEART (%)	LIVER (%)
GROUP 1 (CONTROL)				
51	269	0.74	0.294	3.73
52	253	0.77	0.301	3.91
53	223	0.86	0.323	3.57
54	255	0.77	0.293	3.53
55	238	0.83	0.315	3.66
56	241	0.82	0.285	3.40
57	215	0.84	0.326	3.52
58	253	0.79	0.293	4.06
59	240	0.78	0.340	3.73
60	236	0.80	0.310	3.82
GROUP 2 (100 MG/KG)				
66	238	0.77	0.320	3.40
67	204	0.92	0.322	3.51
68	220	0.81	0.340	4.17
69	231	0.78	0.309	3.57
70	233	0.82	0.339	3.85
71	252	0.74	0.303	3.84
72	263	0.71	0.312	3.37
73	251	0.74	0.293	3.63
74	---	---	---	---
75	219	0.89	0.302	3.95
GROUP 3 (300 MG/KG)				
76	245	0.80	0.327	3.93
77	---	---	---	---
78	212	0.90	0.307	4.98
79	228	0.85	0.289	4.43
80	244	0.80	0.310	4.19
81	220	0.90	0.322	5.29
82	204	0.91	0.339	4.58
83	228	0.80	0.287	4.52
84	217	0.90	0.311	4.72
85	203	0.94	0.335	5.09
GROUP 4 (1000/600 MG/KG)				
86	221	0.84	0.307	6.30
87	224	0.88	0.319	5.40
88	---	---	---	---
89	222	0.82	0.282	5.90
90	237	0.82	0.304	5.34
91	207	0.87	0.307	5.34
92	232	0.82	0.293	5.50
93	---	---	---	---

FEMALES END OF TREATMENT

ANIMAL	THYROIDS (%)	THYMUS (%)	KIDNEYS (%)	ADRENALS (%)
GROUP 1 (CONTROL)				
51	0.006	0.131	0.71	0.031
52	0.006	0.156	0.58	0.036
53	0.008	0.144	0.74	0.029
54	0.007	0.132	0.72	0.037
55	0.007	0.103	0.65	0.023
56	0.005	0.091	0.71	0.037
57	0.005	0.205	0.67	0.023

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

ANIMAL	THYROIDS (%)	THYMUS (%)	KIDNEYS (%)	ADRENALS (%)
GROUP 1 (CONTROL)				
58	0.009	0.123	0.71	0.030
59	0.006	0.092	0.72	0.029
60	0.008	0.093	0.72	0.038
GROUP 2 (100 MG/KG)				
66	0.007	0.116	0.70	0.032
67	0.006	0.108	0.81	0.027
68	0.007	0.163	0.83	0.029
69	0.007	0.108	0.72	0.024
70	0.007	0.157	0.75	0.030
71	0.005	0.137	0.76	0.030
72	0.007	0.114	0.79	0.034
73	0.006	0.118	0.71	0.034
74	---	---	---	---
75	0.007	0.135	0.76	0.027
GROUP 3 (300 MG/KG)				
76	0.008	0.096	0.88	0.031
77	---	---	---	---
78	0.006	0.118	0.81	0.040
79	0.007	0.116	0.80	0.031
80	0.010	0.096	0.80	0.033
81	0.008	0.082	1.01	0.034
82	0.007	0.118	0.85	0.034
83	0.010	0.114	0.80	0.039
84	0.008	0.115	0.82	0.028
85	0.008	0.103	0.89	0.037
GROUP 4 (1000/600 MG/KG)				
86	0.008	0.097	0.99	0.032
87	0.008	0.107	0.89	0.031
88	---	---	---	---
89	0.010	0.101	0.92	0.036
90	0.006	0.144	0.88	0.034
91	0.010	0.126	0.92	0.031
92	0.005	0.082	0.98	0.037
93	---	---	---	---

FEMALES**END OF TREATMENT**

ANIMAL	SPLEEN (%)	OVARIES (%)	UTERUS (%)
GROUP 1 (CONTROL)			
51	0.175	0.059	0.318
52	0.236	0.067	0.196
53	0.245	0.081	0.671
54	0.224	0.049	0.314
55	0.197	0.063	0.445
56	0.206	0.077	0.742
57	0.281	0.081	0.519
58	0.216	0.075	0.838
59	0.271	0.067	0.236
60	0.274	0.068	0.462
GROUP 2 (100 MG/KG)			
66	0.181	0.055	0.332
67	0.216	0.066	0.287

Final Report

MTDID 7831
APPENDIX 2

Project 511505

2.13 ORGAN/BODY WEIGHT RATIOS (%)

FEMALES

END OF TREATMENT

ANIMAL	SPLEEN (%)	OVARIES (%)	UTERUS (%)
GROUP 2 (100 MG/KG)			
68	0.229	0.066	0.588
69	0.218	0.071	0.901
70	0.191	0.066	0.234
71	0.192	0.057	0.212
72	0.181	0.078	0.347
73	0.171	0.066	0.289
74	---	---	---
75	0.219	0.075	0.473
GROUP 3 (300 MG/KG)			
76	0.178	0.049	0.184
77	---	---	---
78	0.182	0.066	0.227
79	0.199	0.053	0.694
80	0.217	0.059	0.252
81	0.182	0.079	0.565
82	0.174	0.074	0.228
83	0.211	0.075	0.748
84	0.184	0.062	0.191
85	0.180	0.064	0.951
GROUP 4 (1000/600 MG/KG)			
86	0.165	0.061	0.398
87	0.205	0.083	0.217
88	---	---	---
89	0.228	0.070	1.795
90	0.207	0.066	0.482
91	0.220	0.070	0.614
92	0.140	0.063	0.170
93	---	---	---

FEMALES

END OF RECOVERY

ANIMAL	BODY W. (GRAM)	BRAIN (%)	HEART (%)	LIVER (%)
GROUP 1 (CONTROL)				
61	233	0.82	0.302	2.58
62	237	0.81	0.314	2.54
63	258	0.76	0.341	2.50
64	236	0.81	0.284	2.27
65	239	0.80	0.316	2.53
GROUP 4 (1000/600 MG/KG)				
94	253	0.78	0.314	2.73
95	240	0.77	0.285	2.37
96	---	---	---	---
97	199	0.94	0.306	2.57
98	201	0.91	0.343	2.85
99	235	0.79	0.290	2.41
100	---	---	---	---

2.13 ORGAN/BODY WEIGHT RATIOS (%)
FEMALES
END OF RECOVERY

ANIMAL	THYROIDS (%)	THYMUS (%)	KIDNEYS (%)	ADRENALS (%)
GROUP 1 (CONTROL)				
61	0.006	0.131	0.69	0.028
62	0.006	0.082	0.71	0.027
63	0.006	0.141	0.72	0.033
64	0.007	0.142	0.65	0.021
65	0.007	0.107	0.65	0.027
GROUP 4 (1000/600 MG/KG)				
94	0.006	0.125	0.81	0.040
95	0.006	0.181	0.66	0.021
96	---	---	---	---
97	0.010	0.198	0.84	0.028
98	0.007	0.194	0.78	0.037
99	0.007	0.149	0.68	0.026
100	---	---	---	---

FEMALES
END OF RECOVERY

ANIMAL	SPLEEN (%)	OVARIES (%)	UTERUS (%)
GROUP 1 (CONTROL)			
61	0.187	0.060	1.497
62	0.206	0.059	0.453
63	0.217	0.093	1.177
64	0.148	0.055	0.900
65	0.197	0.059	0.486
GROUP 4 (1000/600 MG/KG)			
94	0.184	0.081	0.911
95	0.162	0.058	0.506
96	---	---	---
97	0.211	0.068	0.213
98	0.199	0.057	0.289
99	0.183	0.062	0.301
100	---	---	---

2.14 KEY TO MISSING VALUES/REMARKS**BODY WEIGHTS**

Recovery period				
Day 3		Day 18		
Animal(s):	Body Weight	Animal(s):	Body Weight (g)	
61	249	11	361	
62	245	12	390	
63	278	13	450	
64	249	14	400	
65	249	15	417	
94	277	43	393	
95	223	45	396	
		46	400	
		49	317	
All Recovery females	Body weight gain compared to Day 1 in females is not calculated from Day 93 onwards since a separate project number is used from Day 93 onwards. Absolute body weight are recorded and evaluated.			

CLINICAL LABORATORY INVESTIGATIONS

All animals	Samples were stored at $\leq -75^{\circ}\text{C}$ prior to analysis on the STA Compact and AU400
-------------	--

End of Treatment		
Haematology:		
Animal(s):		
2,4,11,34,45,59	---	= EDTA sample clotted
1,2,11,34,45,59	---	= Citrate sample clotted
14,28,35,54,56,60,63,71,72,82,83,92,94		Differential leucocyte count was also performed manually because of a technical error / an abnormal plot in the automated count and these manual results are reported
Clinical Biochemistry:		
Animal(s)	BACID	
11	14.5	Serum sample was haemolytic, therefore BACID was not included in the tables.

End of Recovery		
Haematology:		
Animal(s):		
61	---	= Citrate sample clotted
46 and 49		Due to identification error, the samples were identified as 48 and 50. These samples are representing two individual values in the high dose group. However correlations with haematology in individual animals have to be interpreted with caution.
Clinical Biochemistry: No remarks		
BACID		The QC1 was slightly lower compared to the supplier range (7.0 instead of 7.5-10.9, which is 6.7% lower). All values were between QC1 and QC2, which means that the values are possibly 6.7% too low and therefore have to be interpreted with caution.

MACROSCOPIC EXAMINATION

Animal(s):	
77	Organs missing due to partial cannibalism: tail, both hindlimbs, rectum, uterus, cervix, vagina
93	Organs missing due to partial cannibalism: all abdominal organs except right kidney and right adrenal gland and stomach

APPENDIX 3
PHASE REPORT FORMULATION ANALYSIS

TABLE OF CONTENTS

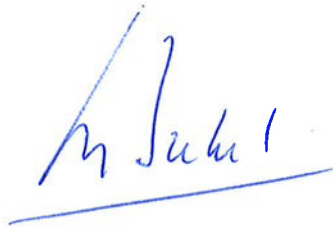
1.	REPORT APPROVAL.....	3
2.	SUMMARY	4
3.	INTRODUCTION	5
3.1.	Study schedule analytical phase.....	5
3.2.	Purpose of the study.....	5
4.	MATERIALS AND METHODS	5
4.1.	Reagents.....	5
4.2.	Study samples	5
4.3.	Analytical method.....	6
4.3.1.	Analytical conditions	6
4.3.2.	Preparation of solutions	6
4.3.3.	Sample injections.....	6
4.4.	Electronic systems for data acquisition.....	6
4.5.	Formulas	7
4.6.	Specifications.....	7
5.	RESULTS.....	8
5.1.	Calibration curves	8
5.2.	Samples.....	8
5.2.1.	QC samples	8
5.2.2.	Study samples	8

TABLES

Table 1	QC samples	9
Table 2	Accuracy and homogeneity test - Week 1	10
Table 3	Stability test – storage at room temperature for 6 hours.....	11
Table 4	Stability test – storage in the refrigerator for 8 days.....	11
Table 5	Accuracy and homogeneity test - Week 6	12
Table 6	Accuracy and homogeneity test - Week 13	13

1. REPORT APPROVAL

Charles River Laboratories Den Bosch B.V.



Signature:

Name: M.J.C. Brekelmans, MSc.

Title: Principal Scientist
Analytical Chemistry

Date: *February 01, 2017*

2. SUMMARY

The purpose of this part of the study was to determine the accuracy of preparation, homogeneity and stability of the test item in formulations.

Accuracy of preparation

The concentrations analysed in the formulations of Group 2, Group 3 and Group 4 were in agreement with target concentrations (i.e. mean accuracies between 85% and 115%).

No test item was detected in the Group 1 formulations.

Homogeneity

The formulations of Group 2 and Group 4 were homogeneous (i.e. coefficient of variation $\leq 10\%$).

Stability

Group 2 and Group 4 formulations were stable when stored at room temperature under normal laboratory light conditions for at least 6 hours and in a refrigerator protected from light for at least 8 days.

3. INTRODUCTION

3.1. Study schedule analytical phase

Experimental starting date : 03 March 2016
Experimental completion date : 20 May 2016

3.2. Purpose of the study

The purpose of the analytical phase was to determine the accuracy of preparation, homogeneity and stability of the test item in formulations.

4. MATERIALS AND METHODS

4.1. Reagents

Water	Tap water purified by a Milli-Q water purification system (Millipore, Bedford, MA, USA)
Acetonitrile	Biosolve, Valkenswaard, The Netherlands
Tetrahydrofuran (THF)	VWR International, Leuven, Belgium
Arachis Oil	See main report

All reagents were of analytical grade, unless specified otherwise.

4.2. Study samples

Accuracy, homogeneity and stability were determined for formulations prepared for use in Week 1, Week 6 and Week 13.

Duplicate samples (approximately 500 mg), which were taken from the formulations using a pipette, were accurately weighed into volumetric flasks of 25 mL. For determination of accuracy, samples were taken at middle position (50% height) or at top, middle and bottom position (90%, 50% and 10% height). The samples taken at 90%, 50% and 10% height were also used for the determination of the homogeneity of the formulations. For determination of stability, additional samples were taken at 50% height and stored at room temperature under normal laboratory light conditions for at least 6 hours and in a refrigerator protected from light for at least 8 days.

The volumetric flasks were filled up to the mark with THF. The solutions were further diluted with THF to obtain concentrations within the calibration range.

4.3. Analytical method

4.3.1. Analytical conditions

Analysis was based on the analytical method validated for the test item in project 511509.

Analytical conditions:

Instrument	Acquity UPLC system (Waters, Milford, MA, USA)
Detector	Acquity UPLC TUV and PDA detector (Waters)
Column	Acquity UPLC BEH C18, 50 mm × 2.1 mm i.d., dp = 1.7 µm (Waters)
Column temperature	40°C ± 1°C
Injection volume	1 µL
Mobile phase	65/35 (v/v) acetonitrile/water
Flow	0.6 mL/min
UV detection	210 nm

4.3.2. Preparation of solutions

Stock and spiking solutions

Stock and spiking solutions of the test item were prepared in THF at concentrations of 2000 mg/L.

Calibration solutions

Solutions with the test item in the concentration range of 0.8 - 120 mg/L were prepared in THF from two stock solutions.

Quality control (QC) samples

Approximately 500 mg blank vehicle was spiked with the test item at a target concentration of 1 mg/g and approximately 400 mg blank vehicle was spiked with the test item at a target concentration of 200 mg/g. The QC samples were treated similarly as the study samples (see paragraph 4.2 'Study samples').

4.3.3. Sample injections

Calibration solutions were injected in duplicate. Study samples and QC samples were analysed by single injection.

4.4. Electronic systems for data acquisition

System control, data acquisition and data processing were performed using the following program:

- Empower 3 database version 7.21 (Waters, Milford, MA, USA).

Temperature, relative humidity and/or atmospheric pressure during sample storage and/or performance of the studies was monitored continuously using the following program:

- REES Centron Environmental Monitoring system version SQL 2.0 (REES Scientific, Trenton, NJ, USA).

4.5. Formulas

Response (R) Peak area test item [units]

Calibration curve $R = a C_N + b$

where:

 C_N = nominal concentration [mg/L]

a = slope [units × L/mg]

b = intercept [units]

Analysed concentration (C_A) $C_A = \frac{(R - b)}{a} \times \frac{V \times d}{w}$ [mg/g]

where:

w = weight sample [mg]

V = volume volumetric flask [mL]

d = dilution factor

Accuracy $\frac{C_A}{C_N} \times 100$ [%]*QC samples*

where:

 C_N = nominal concentration [mg/g]Accuracy $\frac{C_A}{C_T} \times 100$ [%]*Study samples*

where:

 C_T = target concentration [mg/g]Relative difference $\frac{C_t - C_0}{C_0} \times 100$ [%]

where:

 C_t = mean concentration of stored samples [mg/g] C_0 = mean concentration of non-stored samples [mg/g]**4.6. Specifications**

Preparation of formulations was considered acceptable if the mean accuracy was in the range 85-115% of the target concentration and was considered homogeneous if the coefficient of variation was $\leq 10\%$. Formulations were considered stable if the relative difference between the stored and freshly taken samples was $\leq 10\%$.

5. RESULTS

5.1. Calibration curves

Calibration curves were constructed using five concentrations. For each concentration, two responses were used. Linear regression analysis was performed using the least squares method with a $1/\text{concentration}^2$ weighting factor. The coefficient of correlation (r) was > 0.99 for each curve.

5.2. Samples

5.2.1. QC samples

The results of the QC samples are given in [Table 1](#).

The mean accuracies of the QC samples were within the criterion range of 85-115%. It demonstrated that the analytical method was adequate for the determination of the test item in the study samples.

5.2.2. Study samples

The results of the study samples are given in [Table 2](#), [Table 3](#), [Table 4](#), [Table 5](#) and [Table 6](#).

Accuracy of preparation

In the Group 1 formulations, no test item was detected.

The concentrations analysed in the formulations of Group 2, Group 3 and Group 4 were in agreement with target concentrations (i.e. mean accuracies between 85% and 115%).

Homogeneity

The formulations of Group 2 and Group 4 were homogeneous (i.e. coefficient of variation $\leq 10\%$).

Stability

Analysis of Group 2 and Group 4 formulations after storage yielded a relative difference of $\leq 10\%$. Based on this, the formulations were found to be stable during storage at room temperature under normal laboratory light conditions for at least 6 hours and in a refrigerator protected from light for at least 8 days.

TABLES**Table 1 QC samples**

Date of analysis	Concentration [mg/g]			Accuracy [%]	
	Target	Nominal	Analysed	Individual	Mean
04-Mar-2016	1	1.02 0.937	0.917 0.893	90 95	93
04-Mar-2016	200	185 187	177 181	96 97	96
04-Mar-2016 ¹	1	0.988 0.934	0.959 0.844	97 90	94
04-Mar-2016 ¹	200	198 204	192 195	97 96	96
12-Mar-2016	1	0.917 0.947	0.871 0.915	95 97	96
12-Mar-2016	200	196 213	184 197	94 92	93
04-Apr-2016	1	0.978 0.944	0.960 0.916	98 97	98
04-Apr-2016	200	200 202	185 204	92 101	97
20-May-2016	1	0.964 1.01	0.852 0.872	88 87	87
20-May-2016	200	195 207	195 200	100 97	98

¹ Samples were prepared on 03-Mar-2016, stored in the freezer and analysed on 04-Mar-2016 to check freeze-thaw stability.

Table 2 Accuracy and homogeneity test - Week 1

Date of analysis	04-Mar-2016
------------------	-------------

Group	Sample position	Concentration		Accuracy		Homogeneity (coefficient of variation) [%]
		[mg/g]		[%]		
		Target	Analysed	Individual	Mean	
1	50% height	0.00	n.d.	n.a.	n.a.	n.a.
		0.00	n.d.	n.a.		
2	90% height	22.5	21.6	96	94	3.7
		22.5	21.5	96		
	50% height	22.5	19.7	87		
		22.5	21.7	96		
	10% height	22.5	20.7	92		
		22.5	21.5	95		
3	50% height	67.3	65.9	98	98	n.a.
		67.3	65.7	98		
4	90% height	220	217	99	99	1.1
		220	220	100		
	50% height	220	220 ¹	100		
		220	220	100		
	10% height	220	215	98		
		220	215	98		

¹ Value calculated by extrapolation of the calibration curve.

n.d. Not detected.

n.a. Not applicable.

Table 3 Stability test – storage at room temperature for 6 hours

Date of analysis	04-Mar-2016
------------------	-------------

Group	Sample position	Concentration [mg/g]		Accuracy [%]		Relative difference ¹ [%]
		Target	Analysed	Individual	Mean	
2	50% height	22.5	21.4	95	95	1.1
		22.5	21.3	95		
4	50% height	220	216	98	98	-0.93
		220	216	98		

¹ Relative difference between the mean accuracy of the stability samples and six samples taken at t=0 at 10%, 50% and 90% height (see [Table 2](#)).

Table 4 Stability test – storage in the refrigerator for 8 days

Date of analysis	12-Mar-2016
------------------	-------------

Group	Sample position	Concentration [mg/g]		Accuracy [%]		Relative difference ¹ [%]
		Target	Analysed	Individual	Mean	
2	50% height	22.5	20.2	90	90	-3.6
		22.5	20.5	91		
4	50% height	220	201	91	92	-6.8
		220	205	93		

¹ Relative difference between the mean accuracy of the stability samples and six samples taken at t=0 at 10%, 50% and 90% height (see [Table 2](#)).

Table 5 Accuracy and homogeneity test - Week 6

Date of analysis		04-Apr-2016				
Group	Sample position	Concentration		Accuracy		Homogeneity (coefficient of variation) [%]
		[mg/g]		[%]		
		Target	Analysed	Individual	Mean	
1	50% height	0.00	n.d.	n.a.	n.a.	n.a.
		0.00	n.d.	n.a.		
2	90% height	22.5	21.4	95	97	4.3
		22.5	21.4	95		
	50% height	22.5	21.3	95		
		22.5	21.3	95		
	10% height	22.5	21.4	95		
		22.5	23.7	105		
3	50% height	67.3	64.1	95	94	n.a.
		67.3	62.6	93		
4	90% height	134	131	98	97	1.3
		134	128	96		
	50% height	134	131	98		
		134	130	97		
	10% height	134	251	188 ¹		
		134	127	95		
4	90% height	134	134 ²	101	100	0.44
		134	133 ²	100		
	50% height	134	134 ²	101		
		134	135 ²	101		
	10% height	134	133 ²	100		
		134	134 ²	101		

¹ Outlier according to the Dixon's Q-test at 90% confidence level.

² On 05-Apr-2016, these samples were ultrasonicated for 10 minutes and diluted again. The results were in agreement with the results obtained on 04-Apr-2016.

n.d. Not detected.

n.a. Not applicable.

Table 6 Accuracy and homogeneity test - Week 13

Date of analysis	20-May-2016
------------------	-------------

Group	Sample position	Concentration		Accuracy		Homogeneity (coefficient of variation) [%]
		[mg/g]		[%]		
		Target	Analysed	Individual	Mean	
1	50% height	0.00	n.d.	n.a.	n.a.	n.a.
		0.00	n.d.	n.a.		
2	90% height	22.5	21.3	95	95	0.65
		22.5	21.4	95		
	50% height	22.5	21.2	94		
		22.5	21.5	95		
	10% height	22.5	21.3	95		
		22.5	21.6	96		
3	50% height	67.3	65.2	97	96	n.a.
		67.3	63.9	95		
4	90% height	134	130	97	96	3.9
		134	119	89		
	50% height	134	131	98		
		134	132	99		
	10% height	134	127	95		
		134	132	99		

n.d. Not detected.

n.a. Not applicable

APPENDIX 4
PHASE REPORT HISTOPATHOLOGY

TABLE OF CONTENTS

1. SUMMARY3
2. INTRODUCTION6
3. STUDY DESIGN6
4. METHODS6
4.1. Macroscopic Examination6
4.2. Organ Weights7
4.3. Microscopic Examination7
4.4. Internal Peer Review8
5. RESULTS9
5.1. Mortality9
5.2. Clinical Pathology11
5.3. Macroscopic Findings11
5.4. Organ Weights12
5.5. Microscopic Findings14
6. DISCUSSION21
7. CONCLUSIONS23
8. REFERENCES23
9. REPORT AUTHENTICATION25

LIST OF APPENDICES

APPENDIX 1 HISTOPATHOLOGY TABLES

1. SUMMARY

Pathomorphologic examination was performed on 100 Wistar (Han) rats (50 males, 50 females) which had been subjected to a 90-day oral (gavage) toxicity study with the test item **MTDID 7831**, followed by a 28-day recovery period.

The rats were assigned to 4 dose groups, Groups 1 and 4 containing 15 males and 15 females, and Groups 2 and 3 containing 10 males and 10 females. The test item was administered once daily by gavage at doses of 100, 300 and 600 mg/kg/day (Day 1-Day 30: 1000 mg/kg/day) (dose Groups 2, 3 and 4 respectively). The rats of the control Group 1 received the vehicle, Arachis Oil, alone.

At the end of the 90-day treatment period all surviving rats from the main groups were euthanized and subjected to complete necropsies. The animals of the recovery groups were euthanized following a 28-day treatment-free recovery period. Histopathologic examination was performed on an extensive list of organs and tissues from all main Group 1 and 4 animals, all animals that were found dead or were euthanized for ethical reasons, as well as macroscopic findings from all rats. In addition, sections of thyroid gland, stomach, liver, kidney, urinary bladder, bone marrow (sternum) of both sexes and thymus, spleen, and adrenal gland of all females of Groups 2 and 3 and the recovery animals of Groups 1 and 4 were prepared and examined.

There were twelve premature decedents in the study:

Animals 36, 40, 47, 48, 50 (males, 1000/600 mg/kg/day) and animals 88 and 100 (females, 1000/600 mg/kg/day) were euthanized for ethical reasons after respectively 70, 19, 30, 62, 84, 22 and 63 days of treatment. Main cause of morbidity was hepatocellular necrosis of the centrilobular area of the liver and/or degenerative findings in the kidney.

Animal 74 (female, 100 mg/kg/day), animal 77 (female 300 mg/kg/day) and animal 93 (female, 1000 mg/kg/day) were found dead after respectively 91, 77 and 19 days of treatment. No cause of death could be determined from the sections examined.

Animal 44 (male, 1000 mg/kg/day) and animal 96 (female, 1000 mg/kg/day) were found dead after respectively 26 and 30 days of treatment. Cause of death for these animals was a gavage accident.

Test item-related macroscopic findings were present in the following organs:

Liver: An *enlarged* liver was recorded in Main Group males starting at 100 mg/kg/day and females starting at 300 mg/kg/day (microscopic correlate: *centrilobular/diffuse hepatocellular hypertrophy*). *Discoloration (red-brown or black-brown)* at the end of the treatment period was recorded in both sexes starting at 300 mg/kg/day (microscopic correlate: *centrilobular/diffuse hepatocellular hypertrophy with eosinophilic cytoplasm*). This was also recorded in some recovery rats (microscopic correlate in recovery animals: *brown pigment deposition*). An *accentuated lobular pattern* was recorded in a few Main Group animals of both sexes at 300 mg/kg/day (microscopic correlate: *centrilobular/diffuse hepatocellular hypertrophy*).

Kidney: *Discolouration (red-brown or greenish)* was recorded in Main Group males starting at 100 mg/kg/day and females starting at 300 mg/kg/day (no microscopic correlate).

Thyroid gland: An *enlarged* thyroid gland was recorded in some Main and Recovery Group animals, including controls (microscopic correlate *hypertrophy of follicular cells* in a single male and female at 1000/600 mg/kg/day).

Stomach: Macroscopic findings were recorded in several Main Group animals including controls consisting of *dark red/reddish/ black-brown foci in the glandular mucosa* of the stomach in some males and females including controls (microscopic correlate: *congestion*), *reddish/black foci in the forestomach* in females starting at 100 mg/kg/day (microscopic correlate: *erosion/ulceration, hemorrhage*) and an *irregular surface of the forestomach* in males at 100 mg/kg/day and 1000/600 mg/kg/day (microscopic correlate: *hyperplasia squamous epithelium or cyst*).

Statistically significant organ weight changes were noted in the following organs:

Liver: Higher absolute liver weights in the Main Groups of both sexes starting at 300 mg/kg/day and relative to body weight in Main Group males starting at 100 mg/kg/day and in Main Group females starting at 300 mg/kg/day (microscopic correlate: *centrilobular/diffuse hepatocellular hypertrophy*), with complete recovery.

Kidney: Higher kidney weights (absolute and relative to body weights) in Main Group males starting at 100 mg/kg/day. In Main Group females the relative to body weight was increased starting at 100 mg/kg/day and in the absolute kidney weight was increased starting at 300 mg/kg/day (no microscopic correlate), with partial recovery in males and complete recovery in females

Thyroid gland (males): An apparent increase in Main and Recovery Group males (only statistically significant increase of absolute thyroid gland weight in males at 300 mg/kg/day). The microscopic correlate was *hypertrophy of follicular cells*.

Adrenal gland (males): Higher adrenal gland weights (absolute and relative to body weights) in Main Group males at 1000/600 mg/kg/day, with complete recovery (no microscopic correlate).

Thymus (females): An apparent decrease in thymus weight in Main Group females starting at 300 mg/kg/day, only statistically significant absolute weight decrease at 300 mg/kg/day (microscopic correlate: *increased lymphocytolysis*), with complete recovery

Spleen (females): Lower spleen weights (absolute and relative to body weights) in Main Group females starting at 100 mg/kg/day (microscopic correlate: *decreased extramedullary hematopoiesis*), with complete recovery.

The remaining organ weight changes were in line with the decrease in terminal body weight.

Adverse test item-related microscopic findings were present in the following organs:

Liver: A combination of *centrilobular/diffuse hepatocellular hypertrophy with eosinophilic cytoplasm* starting at 100 mg/kg/day; *hepatocellular necrosis of the centrilobular area* (in some instances with additional brown pigmentation) in females starting at 300 mg/kg/day and in males at 1000/600 mg/kg/day; *focal/multifocal coagulative necrosis* at an increased incidence and severity in males at 1000/600 mg/kg/day.

There was partial recovery for *hepatocellular necrosis of the centrilobular area* in females and complete recovery for the remaining findings in females and all three liver findings in males. *Yellow-brown pigment deposition* was recorded after the 28-day recovery period in a single male and a few females at 1000/600 mg/kg/day.

Kidney: A combination of *tubular basophilia* at an increased incidence and/or severity at 1000/600 mg/kg/day; *vacuolar degeneration/necrosis* in one male surviving the 90 day

treatment period; *eosinophilic content of the tubuli* at an increased incidence and/or severity at 1000/600 mg/kg/day; *eosinophilic content of the papil* in a few females starting at 300 mg/kg/day; *hyperplasia of the epithelium of the papil with cellular debris/casts* in a few males and females at 1000/600 mg/kg/day; a *calculus in the papil or pelvis* in a few females at 1000/600 mg/kg/day. There was complete recovery for these findings.

After a 28-day treatment-free recovery period *yellow-brown tubular pigment* was recorded in a few males at 1000/600 mg/kg/day.

Urinary bladder: Hypertrophy/hyperplasia of the urothelium of the urinary in both sexes starting at 300 mg/kg/day. There was no recovery for this finding.

Non-adverse test item-related microscopic findings were present in the following organs:

Thyroid gland: An increased incidence and severity of *hypertrophy of the follicular cells* of the thyroid gland in males starting at 100 mg/kg/day and females at 1000/600 mg/kg/day, with complete recovery.

Bone marrow (sternum): A slightly increased number of adipocytes (incidence and/or severity) in a few males and females starting at 100 mg/kg/day, with partial recovery.

Thymus (females): A minor increase in incidence and severity of lymphocytolysis in the thymus in females starting at 100 mg/kg/day, with complete recovery.

Adrenal gland (females): A minor increase in incidence and severity of vacuolation of the zona glomerulosa in females at 1000/600 mg/kg/day, with complete recovery.

Treatment-related microscopic findings considered unrelated to the test item:

Stomach: Microscopic findings consisted of *lymphogranulocytic inflammation, hyperplasia of squamous cells, erosions/ulcerations* and *edema* in all dose groups including controls, with complete recovery in males, partial recovery in females, which was probably related to the treatment procedure (gavage) with Arachis Oil.

Spleen (females): A high incidence and severity of extramedullary hematopoiesis was recorded in the spleen of females of the main control group after the 90-day treatment period. This was related to the blood sampling five days prior to the necropsy and subsequent reactive increase in hematopoiesis and not related to the treatment with MTDID 7831.

CONCLUSION

Adverse test item-related morphologic alterations in Wistar (Han) rats subjected to 90-Day oral gavage toxicity study, followed by a 4-week recovery period with MTDID 7831 up to a dose of 1000/600 mg/kg/day were present in liver (*hepatocellular necrosis of the centrilobular area, coagulative necrosis*), kidney (*vacuolar degeneration/necrosis, granular casts, increased severity of tubular basophilia*) and urinary bladder (*hypertrophy/hyperplasia of the urothelium*) of both sexes starting at 300 mg/kg/day. In addition there were MTDID 7831-related unscheduled deaths in the 1000/600 mg/kg/day treated dose group.

There were no adverse test item-related morphologic alterations at 100 mg/kg/day.

2. INTRODUCTION

The nature and purpose of this toxicity study was to assess the toxic potential of the test item when administered to rats by daily oral gavage for a period of 13 weeks, followed by a 28-day recovery period. This study should provide part of a rational basis for toxicological risk assessment in man. The oral route was selected as it is a possible route of human exposure during manufacture, handling or use of the test item.

This pathology report addresses the anatomical pathology endpoints of the study. It is based on the study plan and any study plan amendment.

3. STUDY DESIGN

Male and female Wistar (Han) rats, approximately 6 weeks of age on study Day 1, were administered MTDID 7831 via oral gavage daily for at least 90 consecutive days (Groups 1, 2 and 3) as indicated in the following table. The animals of Group 4 were treated at 1000 mg/kg/day from Day 1- Day 30 (inclusive), discontinued on Day 31- Day 34 based on the health status of the animals and recommenced on Day 35 (and onwards) at a dose level of 600 mg/kg/day.

Group	Dose level mg/kg	Number of animals		Animal numbers	
		Males	Females	Males	Females
1 Main	0 ^a	10	10	1-10	51-60
1 Recovery	0 ^a	5	5	11-15	61-65
2 Main	100	10	10	16-25	66-75
3 Main	300	10	10	26-35	76-85
4 Main	1000/600	7	8	36-42	86-93
4 Recovery	1000/600	8	7	43-50	94-100

^a The vehicle was Arachis Oil, specific gravity 0.885.

4. METHODS

4.1. Macroscopic Examination

Complete postmortem examinations were performed on all animals. Animals (excluding the spontaneous deaths) were anesthetized using isoflurane and subsequently exsanguinated. At the time of necropsy, the following tissues and organs were collected and placed in 10% neutral-buffered formalin fixative unless otherwise noted:

Identification marks: not processed	Ovaries
Adrenal glands	Pancreas
Aorta	Peyer's patches [jejunum, ileum] if detectable
Brain -cerebellum, midbrain, cortex (7 levels)	Pituitary gland
Caecum	(Preputial gland)
Cervix	Prostate gland
(Clitoral gland)	Rectum
Colon	Salivary glands - mandibular, sublingual
Duodenum	Sciatic nerve
Epididymides *	Seminal vesicles including coagulating gland
Eyes with optic nerve [if detectable] and	(Skeletal muscle)
Harderian gland *	Skin

Female mammary gland area (Femur including joint)	Spinal cord -cervical, midthoracic, lumbar
Heart	Spleen
Ileum	Sternum with bone marrow
Jejunum	Stomach
Kidneys	Testes *
Larynx	Thymus
(Lacrimal gland, exorbital)	Thyroid including parathyroid [if detectable]
Liver	(Tongue)
Lung, infused with formalin	Trachea
Lymph nodes - mandibular, mesenteric	Urinary bladder
(Nasopharynx)	Uterus
Oesophagus	Vagina
	All gross lesions

Tissues/organs mentioned in parentheses were not examined by the pathologist.

* Initially fixed in modified Davidson's solution.

4.2. Organ Weights

The following organ weights (and terminal body weight) were recorded from all animals at the scheduled necropsy:

Adrenal glands	Spleen
Brain	Testes
Epididymides	Thymus
Heart	Uterus (including cervix)
Kidneys	Prostate
Liver	Seminal vesicles including coagulating glands
Ovaries	Thyroid including parathyroid

Paired organs were weighed together. Absolute organ weights were reported and organ to terminal body weights were calculated and presented in the main study report.

In the discussion of organ weights, statistical significance refers to the $p < 0.05$ level. The discussion of organ weights refers to group mean values unless stated otherwise.

4.3. Microscopic Examination

Microscopic examination of routinely prepared hematoxylin-eosin stained paraffin sections was performed on all tissues collected at necropsy (with exceptions as indicated on the tissue list above) from all animals of the control group and 1000/600 mg/kg/day treated main animals, as well as all unscheduled deaths. Slides of the thyroid gland, stomach, liver, kidney, urinary bladder, bone marrow (sternum) of both sexes and thymus, spleen, and adrenal gland of all females of the main animals treated at 100 and 300 mg/kg/day and all recovery animals (control and 1000/600 mg/kg/day treated animals) were prepared and examined after microscopic examination of the initially prepared sections. Gross lesions were examined from all animals and correlated to microscopic findings if possible.

The animal data and macroscopic findings were electronically transferred from the necropsy raw data files of ToxData system® into the computer system PathData®. Stained histologic sections were examined by light microscopy in the period 9 June – 19 July 2016 and the microscopic findings were recorded by the undersigned pathologist using on-line input under pathology number 21614 BRH.

Severity grades were assigned to non-neoplastic histopathologic diagnoses, as presented in the following table. Severity grades were assigned based on the severity of alterations in the examined histologic sections and may not reflect the overall severity of the pathologic

process in the entire tissue, organ, or animal. The PathData® histopathology tables contain all of the recorded data and serve as the basis for this narrative report.

In the separate pathology tables file, all macroscopic and microscopic findings are given for each animal in text form under "Text of Gross and Microscopic Findings". The incidence of microscopic findings is also presented in tabular form: "Incidence table – Selected findings with grades", "Incidence table - all microscopic findings" and "Incidence table – Unscheduled deaths". Incidence tables were created by computer.

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

Severity scores were assigned as follows:

Present	Finding present, grading not scored.
Grade 1	Minimal/very few/very small.
Grade 2	Slight/few/small.
Grade 3	Moderate/moderate number/moderate size.
Grade 4	Marked/many/large.
Grade 5	Massive/extensive number/extensive size.
N.A.D.	No Abnormality Detected

4.4. Internal Peer Review

Pathology findings were subjected to an internal review conducted by Joost Lensen, PhD (Dutch CRP/TP Certified Toxicologic Pathologist). Following the peer review, a consensus was reached between the study pathologist and the peer review pathologist with regard to diagnoses and interpretation. Histopathology data entries in PathData® and pathology data presented in the pathology report reflect this consensus.

5. RESULTS

5.1. Mortality

There were twelve premature decedents in the study, one female at 100 mg/kg/day, one female at 300 mg/kg/day and six males and four females at 1000/600 mg/kg/day:

Animals 36, 40, 47, 48, 50 (males, 1000/600 mg/kg/day) and animals 88 and 100 (females, 1000/600 mg/kg/day) were euthanized for ethical reasons:

Male 36 (1000/600 mg/kg/day) was euthanized for ethical reasons after 70 days of treatment. Main findings consisted of marked centrilobular hepatocellular necrosis with brown pigment, moderate hepatocellular hypertrophy and slight coagulative necrosis of the liver (correlating to gray-white foci recorded at necropsy). In the kidney slight tubular vacuolar degeneration/necrosis was recorded. The stomach of this animal showed moderate hyperplasia of the squamous epithelium and slight erosion/ulceration of the forestomach (correlating to black brown foci in the forestomach recorded at necropsy). The findings recorded for the thymus (moderate lymphoid depletion) and bone marrow (moderate diffuse atrophy) and the reduced size/degenerative findings recorded for the prostate gland and seminal vesicles were considered to be secondary to the poor condition of this animal. Main cause of moribundity was considered the marked centrilobular hepatocellular necrosis of the liver.

Male 40 (1000 mg/kg/day) was euthanized for ethical reasons after 19 days of treatment. Main findings consisted of slight centrilobular hepatocellular necrosis, slight hepatocellular hypertrophy and moderate coagulative necrosis of the liver (correlating to gray-white foci recorded at necropsy). In the kidney moderate tubular vacuolar degeneration/necrosis was recorded. The stomach of this animal showed moderate hyperplasia of the squamous epithelium and minimal erosion/ulceration in the forestomach. The findings recorded for the thymus (marked lymphoid depletion), spleen (marked diffuse lymphoid depletion) and bone marrow (moderate diffuse atrophy) and the reduced size/degenerative findings recorded for the prostate gland, seminal vesicles and preputial glands were considered to be secondary to the poor condition of this animal. Main cause of moribundity were considered the moderate coagulative necrosis of the liver and the moderate vacuolar degeneration/necrosis of the kidney.

Male 47 (1000 mg/kg/day) was euthanized for ethical reasons after 30 days of treatment. Main findings consisted of moderate centrilobular hepatocellular necrosis with brown pigment, slight hepatocellular hypertrophy (correlating to an enlarged liver recorded at necropsy) and moderate coagulative necrosis of the liver (correlating to gray-white foci recorded at necropsy). In the kidney slight tubular vacuolar degeneration/necrosis was recorded. The stomach of this animal showed moderate hyperplasia of the squamous epithelium (correlating to an irregular surface recorded at necropsy), slight inflammatory infiltrate and minimal erosion/ulceration in the forestomach. The findings recorded for the thymus (moderate lymphoid depletion), mesenteric lymph node (slight lymphoid depletion), bone marrow (moderate diffuse atrophy), the degranulation recorded for the pancreas and the reduced size/degenerative findings recorded for the prostate gland and seminal vesicles were considered to be secondary to the poor condition of this animal. Main cause of moribundity was considered the moderate centrilobular hepatocellular necrosis of the liver.

Male 48 (1000/600 mg/kg/day) was euthanized for ethical reasons after 62 days of treatment. Main findings consisted of marked centrilobular hepatocellular necrosis with brown pigment, slight hepatocellular hypertrophy and slight coagulative necrosis of the liver (correlating to gray-white foci recorded at necropsy). In the kidney slight tubular vacuolar degeneration/necrosis was recorded (correlating to yellowish foci recorded at necropsy) and moderate tubular basophilia. The findings recorded for the thymus (marked lymphoid depletion) and the reduced size/degenerative findings recorded for the prostate gland and seminal vesicles were considered to be secondary to the poor condition of this animal. Main cause of moribundity was considered the marked centrilobular hepatocellular necrosis of the liver.

Male 50 (1000/600 mg/kg/day) was euthanized for ethical reasons after 84 days of treatment. Main findings consisted of moderate centrilobular hepatocellular necrosis with brown pigment and moderate hepatocellular hypertrophy of the liver (correlating to black-brown discoloration and an enlarged liver recorded at necropsy). The findings recorded for the thymus (moderate lymphoid depletion) and bone marrow (minimal diffuse atrophy) and the reduced size/degenerative findings recorded for the prostate gland and seminal vesicles were considered to be secondary to the poor condition of this animal. Main cause of moribundity was considered the moderate centrilobular hepatocellular necrosis of the liver.

Female 88 (1000 mg/kg/day) was euthanized for ethical reasons after 22 days of treatment. Main findings consisted of moderate coagulative necrosis of the liver, minimal centrilobular hepatocellular necrosis and slight hepatocellular hypertrophy. In the kidney marked tubular basophilia, slight granular casts and moderate mineralization was recorded. The findings recorded for the thymus (marked lymphoid depletion), bone marrow (moderate diffuse atrophy), the degranulation recorded for the pancreas and the degenerative findings recorded for the uterus and vagina were considered to be secondary to the poor condition of this animal. Main cause of moribundity was considered the moderate coagulative necrosis of the liver and the marked tubular basophilia in the kidney.

Female 100 (1000/600 mg/kg/day) was euthanized for ethical reasons after 63 days of treatment. Main findings consisted of marked centrilobular hepatocellular necrosis with brown pigment and moderate hepatocellular hypertrophy (correlating to an enlarged liver recorded at necropsy). The stomach of this animal showed slight hyperplasia of the squamous epithelium and minimal erosion/ulceration in the forestomach. The findings recorded for the thymus (moderate lymphoid depletion), bone marrow (slight diffuse atrophy), the degranulation recorded for the pancreas and the degenerative findings recorded for the uterus were considered to be secondary to the poor condition of this animal. Main cause of moribundity was considered the marked centrilobular hepatocellular necrosis of the liver.

Animals 44, 74, 77, 93 and 96 were found dead:

Animal 44 (male, 1000 mg/kg/day) was found dead after 26 days of treatment. Main cause of death was considered a gavage accident, based on the necropsy finding of perforation of the trachea and the presence of blood clots and hemorrhagic fluid in the thoracic cavity. Other findings of note were present in the liver and consisted of slight centrilobular hepatocellular necrosis and slight hepatocellular hypertrophy (correlating to an enlarged liver recorded at necropsy).

Animal 74 (female, 100 mg/kg/day) was found dead after 91 days of treatment. No cause of death could be determined from the sections examined.

Animal 77 (female 300 mg/kg/day) was found dead after 77 days of treatment. This animal was partly cannibalized and autolytic. No cause of death could be determined from the organs examined.

Animal 93 (female, 1000 mg/kg/day) was found dead after 19 days of treatment. This animal was partly cannibalized and autolytic. No cause of death could be determined from the organs examined.

Animal 96 (female, 1000 mg/kg/day) was found dead after 30 days of treatment. Main cause of death for this animal was considered a gavage accident, based on the necropsy finding of dark red, watery-clear contents of the thoracic cavity and black-brown foci of the right medial lobe of the lung, which correlated to focal hemorrhage in the lung, probably due to trauma caused by the gavage needle. Other findings of note were present in the liver and consisted of minimal centrilobular hepatocellular necrosis and slight hepatocellular hypertrophy (correlating to an enlarged liver recorded at necropsy).

5.2. Clinical Pathology

Clinical pathology data were evaluated and discussed by the study pathologist and the study director. Clinical pathology results are presented in the main toxicology report.

5.3. Macroscopic Findings

Test item-related macroscopic findings in the surviving rats were present in the following organs:

Liver: An *enlarged* liver at the end of the treatment period was recorded in 2/10 males at 100 mg/kg/day, in 10/10 males and 3/9 females at 300 mg/kg/day and in 5/5 males and 6/6 females at 1000/600 mg/kg/day. The microscopic correlate for this finding was *centrilobular/diffuse hepatocellular hypertrophy*. After a 28-day treatment-free recovery period enlargement of the liver was not recorded. *Discoloration (red-brown or black-brown)* at the end of the treatment period was recorded 4/10 males and 3/9 females at 300 mg/kg/day and in 5/5 males and 6/6 females at 1000/600 mg/kg/day. The microscopic correlate for this finding was *eosinophilic cytoplasmic change in some cases with yellow brown pigment deposition*. After a 28 day treatment-free recovery period red-brown discoloration for the liver was recorded in 2/4 males and 2/5 females at 1000/600 mg/kg/day (microscopic correlate: *brown pigment deposition*). An *accentuated lobular pattern* in the liver was recorded in 1/10 males and 3/9 females at 300 mg/kg/day, correlating to *centrilobular/diffuse hepatocellular hypertrophy*. This finding was not recorded after a 28-day treatment-free recovery period.

Kidney: *Discolouration (red-brown or greenish)* was recorded 1/10 males at 100 mg/kg/day, 3/10 males and 1/9 females at 300 mg/kg/day and 5/5 males and 5/6 females at 1000/600 mg/kg/day, with no microscopic correlate. After a 28 day treatment-free recovery period discoloration of the kidneys was recorded in 2/5 females at 1000/600 mg/kg/day.

Thyroid gland: An *enlarged* thyroid gland, was recorded in 2/10 males and 2/9 females at 300 mg/kg/day, in 1/6 main females at 1000/600 mg/kg/day and in the recovery group in 1/5 males of the control and 1/4 males of the 1000/600 mg/kg/day treated group. The microscopic correlate for this finding was in some cases *hypertrophy of follicular cells*. After

a 28-day treatment-free recovery period enlarged thyroid glands were recorded at comparable incidences in control and treated rats.

Stomach: Macroscopic findings were recorded in all dose groups including controls. These findings consisted of *dark red/reddish/black-brown foci in the glandular mucosa* of the stomach in 1/10 males of Main Group 1, 1/5 males of the Recovery Group 1, 1/10 males and 2/9 females at 100 mg/kg/day, 1/5 males at 1000/600 mg/kg/day (microscopic correlate: *congestion* or no microscopic correlate), *reddish/black foci in the forestomach* in 1/9 females at 100 mg/kg/day, 1/9 females at 300 mg/kg/day and 3/6 females at 1000/600 mg/kg/day (microscopic correlate: *erosion/ulceration, hemorrhage* or no microscopic correlate) and an *irregular surface of the forestomach* in 1/10 males at 100 mg/kg/day and 2/5 males at 1000/600 mg/kg/day (microscopic correlate: *hyperplasia squamous epithelium* or *cyst*). There was complete recovery for the stomach findings after a 28 day treatment-free recovery period. The macroscopic findings recorded at the end of the treatment period were considered to be related to the gavage treatment procedure with Arachis Oil with or without test item.

The remainder of the recorded macroscopic findings were within the range of background gross observations encountered in rats of this age and strain.

5.4. Organ Weights

Statistically significant organ weight changes were noted in liver and kidney of both sexes, thyroid gland and adrenal gland of males and thymus and spleen of females as shown in text table 1 (males) and text table 2 (females).

Text Table 1
Mean Percent Organ Weight Differences from Control Groups - Males

Dose level (mg/kg/day):	100	Main 300	1000/600	Recovery 1000/600
LIVER				
Absolute	+12	+30**	+61**	0
Relative to body weight	+11*	+43**	+101**	+7
KIDNEY				
Absolute	+14**	+14**	+11*	+15
Relative to body weight	+12*	24**	+38**	+25**
THYROID GLAND				
Absolute	+13	+20*	+7	+19
Relative to body weight	0	+25**	+25**	+25
ADRENAL GLAND				
Absolute	-6	-6	+17*	-4
Relative to body weight	-7	0	+40**	0

*: P<0.05, **: P<0.01

Text Table 2
Mean Percent Organ Weight Differences from Control Groups - Females

Dose level (mg/kg/day):	100	Main 300	1000/600	Recovery 1000/600
LIVER				
Absolute	-3	+15**	+41**	-3
Relative to body weight	0	+26**	+53**	+4
KIDNEYS				
Absolute	+6	+13*	+24**	+3
Relative to body weight	+10*	+23**	+35**	+9
THYMUS				
Absolute	-2	-23*	-20	+30*
Relative to body weight	+1	-16	-13	+40*
SPLEEN				
Absolute	-17**	-24**	-23**	-9
Relative to body weight	-14*	-18**	-16*	-2

*: P<0.05, **: P<0.01

Liver: At the end of the 90-day treatment period statistically significant higher absolute liver weights were noted in both sexes starting at 300 mg/kg/day and relative to body weight was noted in males starting at 100 mg/kg/day and in females starting at 300 mg/kg/day. The microscopic correlate for this finding was *centrilobular/diffuse hepatocellular hypertrophy*.

There was complete recovery in males and females after the 28-day recovery period.

Kidney: At the end of the 90-day treatment period statistically significant higher kidney weights (absolute and relative to body weights) were noted in males starting at 100 mg/kg/day. In females the relative to body weight was increased starting at 100 mg/kg/day and in the absolute kidney weight was increased starting at 300 mg/kg/day. There was partial recovery for this increase in males (significant relative to body weight) and complete recovery in females at 1000/600 mg/kg/day after the 28-day recovery period. There was no microscopic correlate for this weight increase.

Thyroid gland (males): At the end of the 90-day treatment period an apparent increase in thyroid gland weight (relative to body weights) was noted starting at 300 mg/kg/day (only statistically significant increase of absolute thyroid gland weight at 300 mg/kg/day). There was partial recovery for this increase (apparent increase, not statistically significant) at 1000/600 mg/kg/day after the 28-day recovery period. The microscopic correlate was *hypertrophy of follicular cells*.

Adrenal gland (males): At the end of the 90-day treatment period statistically significant higher adrenal gland weights (absolute and relative to body weights) were noted at 1000/600 mg/kg/day. There was no microscopic correlate for this weight increase. There was complete recovery after the 28-day recovery period.

Thymus (females): At the end of the 90-day treatment period an apparent decrease in thymus weight was noted starting at 300 mg/kg/day (only statistically significant decrease of absolute thymus weight at 300 mg/kg/day). There was complete recovery for this decrease at 1000/600 mg/kg/day after the 28-day recovery period, the thymus weight of the recovery females at 1000/600 mg/kg/day was statistically higher compared to the control recovery females. The microscopic correlate for the lower thymus weights was a slightly *increased lymphocytolysis*.

Spleen (females): At the end of the 90-day treatment period a statistically significant decrease in spleen weight (absolute and relative to body weights) was noted starting at 100 mg/kg/day. There was complete recovery for this decrease at 1000/600 mg/kg/day after the 28-day recovery period. The microscopic correlate was *decreased extramedullary hematopoiesis* in test item-treated females compared to the control females.

The remaining (statistically significant) organ weight differences compared to the control group were considered to be the result of a test item-related decrease in final body weight.

5.5. Microscopic Findings

Treatment-related microscopic findings after treatment with MTDID 7831 were noted in the thyroid gland, stomach, liver, kidney, urinary bladder and bone marrow (sternum) of both sexes and thymus, adrenal gland and spleen of females and are summarized in text tables 3 – 11.

THYROID GLAND:

Text Table 3.
Summary Test Item-Related Microscopic Thyroid Gland Findings – Scheduled Euthanasia Animals

Dose level (mg/kg/day):	MAIN				RECOVERY	
	0	100	300	600	0	600
THYROID GLAND MALES ^a	10	10	10	5	5	4
<i>Hypertrophy follicular cell</i>						
Minimal	3	3	4	-	2	1
Slight	2	3	4	4	-	1
Moderate	-	2	-	1	-	-
THYROID GLAND FEMALES ^a	10	9	9	6	5	5
<i>Hypertrophy follicular cell</i>						
Minimal	1	2	3	3	1	1
Slight	-	-	-	3	-	-

^a = Number of tissues examined from each group.

An increased incidence and severity of *hypertrophy of the follicular cells* of the thyroid gland was recorded in males starting at 100 mg/kg/day and females at 1000/600 mg/kg/day. There was complete recovery for this finding after a 28 day treatment-free recovery period. The incidences and severities recorded for females at 100 and 300 mg/kg/day and the males and females of the recovery groups were within background pathology for rats of this age and strain.

STOMACH:

Text Table 4.
Summary Test Item-Related Microscopic Stomach Findings – Scheduled Euthanasia Animals

Dose level (mg/kg/day):	MAIN				RECOVERY	
	0	100	300	600	0	600
STOMACH MALES ^a	10	10	10	5	5	4
<i>Inflammation forestomach</i>						
Minimal	6	2	3	1	-	-
Slight	2	-	2	-	-	-
<i>Hyperplasia squamous cell</i>						
Minimal	3	2	3	2	-	-
Slight	5	2	4	1	-	-
Moderate	-	-	-	1	-	-
<i>Erosion/ulceration</i>						
Minimal	-	-	1	1	-	-
Slight	1	-	-	-	-	-
<i>Edema</i>						
Minimal	1	4	-	-	-	-
Slight	2	1	2	-	-	-
Moderate	1	-	-	-	-	-
STOMACH FEMALES ^a	10	9	9	6	5	5
<i>Inflammation forestomach</i>						
Minimal	1	1	1	1	-	1
Slight	2	2	1	2	-	-
Moderate	-	1	-	-	-	-
<i>Hyperplasia squamous cell</i>						
Minimal	1	2	2	3	-	1
Slight	3	2	-	-	-	-
Moderate	-	1	2	2	-	-
<i>Erosion/ulceration</i>						
Minimal	-	1	-	1	-	-
Slight	1	1	1	1	-	-
<i>Edema</i>						
Minimal	1	3	-	-	-	-
Slight	2	1	1	1	-	-

^a = Number of tissues examined from each group.

Microscopic findings above background incidences and severities were recorded for the stomach (forestomach) of all dose groups including controls. These microscopic findings consisted of *lymphogranulocytic inflammation*, *hyperplasia of squamous cells*, *erosions/ulcerations* and *edema*. There was complete recovery for these findings in males and almost complete recovery in females after the 28-day treatment-free recovery period.

LIVER:

Text Table 5.
Summary Test Item-Related Microscopic Liver Findings – Scheduled Euthanasia Animals

Dose level (mg/kg/day):	MAIN				RECOVERY	
	0	100	300	600	0	600
LIVER MALES ^a	10	10	10	5	5	4
<i>Hypertrophy, centrilobular/diffuse</i>						
Minimal	-	10	2	-	-	-
Slight	-	-	7	1	-	-
Moderate	-	-	1	4	-	-
<i>Necrosis hepatocellular, centrilobular</i>						
Minimal	-	-	-	1	-	-
Slight	-	-	-	4	-	-
<i>Necrosis coagulative</i>						
Minimal	-	-	1	1	-	-
Slight	-	-	-	1	-	-
<i>Pigment deposition yellow-brown</i>						
Slight	-	-	-	-	-	1
LIVER FEMALES ^a	10	9	9	6	5	5
<i>Hypertrophy, centrilobular/diffuse</i>						
Minimal	-	2	6	-	-	-
Slight	-	-	3	-	-	-
Moderate	-	-	-	6	-	-
<i>Necrosis hepatocellular, centrilobular</i>						
Minimal	-	-	1	2	-	1
Slight	-	-	-	3	-	-
Moderate	-	-	-	1	-	-
<i>Necrosis coagulative</i>						
Minimal	-	-	-	1	1	-
Slight	-	-	-	-	-	-
<i>Pigment deposition yellow-brown</i>						
Minimal	-	-	-	-	-	1
Slight	-	-	-	-	1	1

^a = Number of tissues examined from each group.

A combination of findings was recorded for the liver of males and females:

Centrilobular/diffuse hepatocellular hypertrophy with eosinophilic cytoplasm was recorded starting at 100 mg/kg/day. There was complete recovery for this finding after a 28-day treatment-free recovery period.

Hepatocellular necrosis of the centrilobular area (in some instances with additional brown pigmentation) was recorded in females starting at 300 mg/kg/day and in males at 1000/600 mg/kg/day. There was complete recovery this finding in males and partial recovery in females.

Focal/multifocal coagulative necrosis was recorded at an increased incidence and severity in males at 1000/600 mg/kg/day. There was complete recovery for this finding after a 28 day

treatment-free recovery period. The single incidences of minimal coagulative necrosis recorded in the remaining dose groups including the control recovery females is considered to be within background pathology of rats of this age and strain.

Yellow-brown pigment deposition was recorded in a single male and a few females at 1000/600 mg/kg/day of the recovery group.

KIDNEY:

Text Table 6.
Summary Test Item-Related Microscopic Kidney Findings – Scheduled Euthanasia Animals

Dose level (mg/kg/day):	MAIN				RECOVERY	
	0	100	300	600	0	600
KIDNEY MALES ^a	10	10	10	5	5	4
<i>Basophilia tubule</i>						
Minimal	3	-	1	1	1	-
Slight	-	-	-	1	-	-
<i>Vacuolar degeneration/necrosis</i>						
Minimal	-	-	-	1	-	-
<i>Granular cast</i>						
Slight	-	-	-	1	-	-
<i>Eosinophilic content tubular</i>						
Minimal	1	1	-	3	-	-
Slight	-	-	-	2	-	-
<i>Papil hyperplasia epithelium</i>						
Minimal	-	-	-	2	-	-
<i>Pigment yellow-brown</i>						
Minimal	-	-	-	-	-	3
KIDNEY FEMALES ^a	10	9	9	6	5	5
<i>Basophilia tubule</i>						
Minimal	2	-	1	-	-	1
Slight	-	-	-	-	-	-
Moderate	-	-	-	1	-	-
<i>Eosinophilic content tubular</i>						
Minimal	-	-	-	2	-	-
<i>Papil hyperplasia epithelium</i>						
Slight	-	-	-	2	-	-
<i>Papil eosinophilic content</i>						
Minimal	-	-	3	-	-	-
Slight	-	-	-	1	-	-
<i>Calculus</i>						
Slight	-	-	-	1	-	-
Moderate	-	-	-	1	-	-

^a = Number of tissues examined from each group.

A combination of findings was recorded for the kidney of males and females:

Tubular basophilia was recorded at an increased severity in both sexes at 1000/600 mg/kg/day. There was complete recovery for this finding after a 28-day treatment-free recovery period. The incidences and severities recorded for the males and females of the remaining dose groups including controls were considered to be within background pathology for rats of this age and strain.

Vacuolar degeneration/necrosis was recorded in one male surviving the 90-day treatment period. There was complete recovery for this finding after a 28-day treatment-free recovery period.

Granular casts were recorded in one male at 1000/600 mg/kg/day. There was complete recovery for this finding after a 28-day treatment-free recovery period.

Eosinophilic content of the tubuli was recorded at an increased incidence and severity in males and females at 1000/600 mg/kg/day. There was complete recovery for this finding after a 28-day treatment-free recovery period.

Eosinophilic content of the papil was recorded in a few females starting at 300 mg/kg/day. There was complete recovery for this finding after a 28-day treatment-free recovery period.

Hyperplasia of the epithelium of the papil with cellular debris/casts was recorded in a few males and females at 1000/600 mg/kg/day. There was complete recovery for this finding after a 28 day treatment-free recovery period.

A calculus in the papil or pelvis was recorded in a few females at 1000/600 mg/kg/day. There was complete recovery for this finding after a 28 day treatment-free recovery period.

After a 28 day treatment-free recovery period *yellow-brown tubular pigment* was recorded in a few males at 1000/600 mg/kg/day.

URINARY BLADDER:

Text Table 7.
Summary Test Item-Related Microscopic Urinary Bladder Findings – Scheduled Euthanasia Animals

Dose level (mg/kg/day):	MAIN				RECOVERY	
	0	100	300	600	0	600
URINARY BLADDER MALES ^a <i>Hyperplasia/hypertrophy urothelium</i>	10	10	10	5	5	4
Minimal	-	-	2	2	-	1
Slight	-	-	2	1	-	2
Moderate	-	-	-	1	-	-
URINARY BLADDER FEMALES ^a <i>Hyperplasia/hypertrophy urothelium</i>	10	9	9	6	5	5
Minimal	-	-	2	3	-	3
Slight	-	-	-	-	-	1

^a = Number of tissues examined from each group.

Hypertrophy/hyperplasia of the urothelium of the urinary bladder was recorded in both sexes starting at 300 mg/kg/day. There was no recovery for this finding after a 28 day treatment-free recovery period.

BONE MARROW (STERNUM):

Text Table 8.

Summary Test Item-Related Microscopic Bone Marrow (sternum) findings – Scheduled Euthanasia Animals

Dose level (mg/kg/day):	MAIN				RECOVERY	
	0	100	300	600	0	600
BONE MARROW MALES ^a	10	10	10	5	5	4
<i>Increased adipocytes</i>						
Minimal	-	2	3	-	-	1
Slight	-	-	1	-	-	1
Moderate	-	-	-	1	-	-
BONE MARROW FEMALES ^a	10	9	9	6	5	5
<i>Increased adipocytes</i>						
Minimal	-	1	2	2	-	1

^a = Number of tissues examined from each group.

An increased number of adipocytes (incidence and/or severity) in the bone marrow (sternum) was recorded in a few males and females starting at 100 mg/kg/day. There was partial recovery for this finding after a 28-day treatment-free recovery period.

THYMUS (FEMALES):

Text Table 9.

Summary Test Item-Related Microscopic Thymus Findings – Scheduled Euthanasia Animals

Dose level (mg/kg/day):	MAIN				RECOVERY	
	0	100	300	600	0	600
THYMUS ^a	10	9	9	6	5	5
<i>Lymphocytolysis increased</i>						
Minimal	-	1	1	2	-	-

^a = Number of tissues examined from each group.

A minor increase in incidence and severity of lymphocytolysis in the thymus was recorded in females starting at 100 mg/kg/day. There was complete recovery for this finding after a 28-day treatment-free recovery period.

ADRENAL GLAND (FEMALES):

Text Table 10.

Summary Test Item-Related Microscopic Adrenal Gland Findings – Scheduled Euthanasia Animals

Dose level (mg/kg/day):	MAIN				RECOVERY	
	0	100	300	600	0	600
ADRENAL GLAND FEMALES ^a	10	9	9	6	5	5
<i>Vacuolation zona glomerulosa</i>						
Minimal	1	2	4	2	2	1
Slight	-	-	-	2	-	-

^a = Number of tissues examined from each group.

A minor increase in incidence and severity of vacuolation of the zona glomerulosa of the adrenal gland was recorded in females at 1000/600 mg/kg/day. There was complete recovery for this finding after a 28-day treatment-free recovery period. The incidences and severities recorded for females at 100 and 300 mg/kg/day and the recovery groups were within background pathology for female rats of this age and strain.

SPLEEN (FEMALES):

Text Table 11.
 Summary Treatment-Related Microscopic Spleen Findings – Scheduled Euthanasia Animals

Dose level (mg/kg/day):	MAIN				RECOVERY	
	0	100	300	600	0	600
SPLEEN FEMALES ^a	10	9	9	6	5	5
<i>Hematopoiesis extramedullary</i>						
Minimal	2	5	3	4	-	-
Slight	5	-	-	-	-	-
Moderate	3	-	-	-	-	-

^a = Number of tissues examined from each group.

A high incidence and severity of extramedullary hematopoiesis was recorded for the spleen of females of the Control group after the 90-day treatment period, compared to the test item-treated dose groups. There was no extramedullary hematopoiesis in the spleen after the 28 day treatment-free recovery period in females of the control and 1000/600 mg/kg/day treated females, suggesting complete recovery.

Remaining histologic changes were considered to be incidental. There was no test item-related alteration in the prevalence, severity, or histologic character of those incidental tissue alterations.

6. DISCUSSION

Relationships were suspected between gross necropsy, organ weight, clinical pathology, and histopathology observations, as presented in Text Table 12. These proposed relationships were based on subjective interpretation rather than a statistical analysis of correlation.

Text Table 12.
Correlations of Treatment Related Observations

Necropsy	Organ Weight	Clinical Pathology	Histopathology
Liver: <i>Discoloration</i>		ALAT, ASAT, ALP, total bilirubine, bile acids↑	<i>Hepatocellular hypertrophy with eosinophilic cytoplasm and/or brown pigment</i>
Liver: <i>Enlarged</i>	↑	ALAT, ASAT, ALP, total bilirubine, bile acids↑	<i>Hepatocellular hypertrophy</i>
Liver: <i>Accentuated lobular pattern</i>			
Kidneys: No correlating necropsy finding	↑	Urea, creatinine↑	<i>Degenerative kidney findings</i>
Thyroid gland: <i>Enlarged</i>	↑	-	<i>Hypertrophy follicular cells</i>
Forestomach: <i>Focus/foci</i>	n.a.	-	<i>Erosion/ulceration, Hemorrhage</i>
Forestomach: <i>Irregular surface</i>	n.a.	-	<i>Hyperplasia squamous epithelium</i>
Thymus: No findings	↓	-	<i>Increased lymphocytolysis</i>

- = no findings / no correlate, n.a.= not applicable

For the **liver** the *hepatocellular necrosis of the centrilobular area* and *focal/multifocal coagulative necrosis* are degenerative findings and therefore considered adverse in nature. The brown pigmentation of the liver in some recovery animals at 1000/600 mg/kg/day are probably digested remnants of necrotic cellular material, resulting from the hepatocellular necrosis recorded at the end of the treatment period. The minimal *hepatocellular hypertrophy* of the liver recorded for the males and females at 100 mg/kg/day, in the absence of any degenerative findings is considered to be a non-adverse finding (Kerlin et. al., 2016).

For the **kidney** the *vacuolar degeneration/necrosis* and the *granular casts* recorded in males and the high severity of *tubular basophilia* recorded in females are degenerative in nature and therefore considered to be adverse microscopic findings.

The *hypertrophy/hyperplasia of the urothelium* of the **urinary bladder**, with no recovery is considered to be an adverse microscopic finding (Sahota et. al., 2013).

Thyroid gland hypertrophy in rats is usually an adaptive response to induction of hepatic enzymes. This results in increase in the hepatic/biliary clearance of T3/T4 leading to increase in TSH and compensatory follicular cell hypertrophy and/or hyperplasia (Wu and Farrelly, 2006).

The findings recorded in **bone marrow (sternum)**, **female thymus** and **female adrenal gland** in a few animals of the test item-treated dose groups can be seen as spontaneous background findings, were not accompanied by any degenerative findings and showed complete or partial recovery. Therefore these findings are considered to be non-adverse (Kerlin et. al., 2016).

Macroscopic and microscopic findings were recorded for the **stomach** of all dose groups including controls. There was no dose relationship and therefore these findings were considered to be due to the gavage treatment procedure with Arachis Oil as vehicle and not related to the treatment with MTDID 7831.

The differences in severity of extramedullary hematopoiesis and the difference in organ weight noticed in the **spleen** of females of all test item-treated dose groups compared to the control females at the end of the treatment period were considered to be related to the blood sampling procedure: Blood samples were collected from the females of the Main Control group after 92 days of treatment and these animals (except animal 51) were subsequently necropsied after 96 days of treatment on Day 97. No blood samples were collected of the remaining females on Day 92. The differences in the red blood cell parameters (decreased red blood cell counts and increased reticulocytes), increased organ weight of the spleen and microscopic finding (increased extramedullary hematopoiesis) in the spleen of the Main Control females after the treatment period, represent a physiological response after the blood sampling procedure and these differences between the control and test item treated groups are therefore regarded to be unrelated to the test item.

7. CONCLUSIONS

Adverse test item-related morphologic alterations in Wistar (Han) rats subjected to 90-Day oral gavage toxicity study, followed by a 4-week recovery period with MTDID 7831 up to a dose of 1000/600 mg/kg/day were present in liver (*hepatocellular necrosis of the centrilobular area, coagulative necrosis*), kidney (*vacuolar degeneration/necrosis, granular casts, increased severity of tubular basophilia*) and urinary bladder (*hypertrophy/hyperplasia of the urothelium*) of both sexes starting at 300 mg/kg/day. In addition there were MTDID 7831-related unscheduled deaths in the 1000/600 mg/kg/day treated dose group.

There were no adverse test item-related morphologic alterations at 100 mg/kg/day.

8. REFERENCES

Kerlin, R., Bolon, B., Burkhardt, J., Francke, S., Greaves, P., Meador, V., Popp, P. (2016). Scientific and Regulatory Policy Committee: Recommended (“Best”) Practice for Determining, Communicating, and Using Adverse Effect Data from Nonclinical Studies. *Toxicol. Pathol.* 44(2), 147-162.

Sahota P.S., Popp J.A., Hardisty J.F., Gopinath, C. (2013). *Toxicologic Pathology - Nonclinical Safety Assessment*. CRC Press, Taylor& Francis Group, Boca Raton, 450-451, 472.

Wu K.M., Farrelly, J.G. (2006) Preclinical development of new drugs that enhance thyroid hormone metabolism and clearance: inadequacy of using rats as an animal model for predicting human risks in an IND and NDA. *Am J Ther* 13; 141-144.

9. REPORT AUTHENTICATION

I, the undersigned, was responsible for the histopathology evaluation and reporting of the pathology data. The histopathology data in this report were compiled by me, and they reflect accurately the primary data records. Histopathology tables were created in PathData® under number 21614 BRH.

FINAL histopathology tables generated 01-February-2017
Project 511505 Pathology Report

Report and Histopathology Tables Submitted By:



Hetty van den Brink-Knol, DVM
Dutch CRP/TP Certified Toxicologic Pathologist
Study Pathologist



Date

APPENDIX 1
HISTOPATHOLOGY TABLES

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF CONTENTS

PAGE :

EXPLANATION OF CODES AND SYMBOLS	1
SUMMARY TABLES	
SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX NECROPSY STATUS: TERMINAL SACRIFICE GROUP (K0), EXCEPT DEATHS Incidence table - Selected findings with grades	2 - 4
SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX NECROPSY STATUS: RECOVERY / POST-TREATMENT GROUP (R1), EXCEPT DEATHS Incidence table - Selected findings with grades	5 - 6
NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX STATUS AT NECROPSY: K0, EXCEPT DEATHS Incidence table - All microscopic findings	7 - 28
NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX STATUS AT NECROPSY: R1, EXCEPT DEATHS Incidence table - All microscopic findings	29 - 34
NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX STATUS AT NECROPSY: K0, DEATHS ONLY Incidence table - Unscheduled deaths	35 - 42
NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX STATUS AT NECROPSY: R1, DEATHS ONLY Incidence table - Unscheduled deaths	43 - 50
INDIVIDUAL ANIMAL DATA	
TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)	51 - 84
ANIMAL HEADING DATA DOSE GROUP 01	85

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF CONTENTS

	PAGE :
TEXT OF GROSS AND MICROSCOPIC FINDINGS DOSE GROUP 01	86 - 123
ANIMAL HEADING DATA DOSE GROUP 02	124
TEXT OF GROSS AND MICROSCOPIC FINDINGS DOSE GROUP 02	125 - 146
ANIMAL HEADING DATA DOSE GROUP 03	147
TEXT OF GROSS AND MICROSCOPIC FINDINGS DOSE GROUP 03	148 - 172
ANIMAL HEADING DATA DOSE GROUP 04	173
TEXT OF GROSS AND MICROSCOPIC FINDINGS DOSE GROUP 04	174 - 231

TEST ITEM	: MTDID 7831	PATHOL. NO.:	21614 BRH
TEST SYSTEM	: RAT, 90 Days + Rec., Gavage	FINALIZED	: 01-FEB-17
SPONSOR	: 3M Belgium BVBA	PathData@System	V6.2e2

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
+2 = Sacrificed moribund

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
* = Comment in text of individual animal data
0 = Tissue not present for histologic examination
' = Histologic examination not required
+ = Organ examined, findings present
- = Organ examined, no pathologic findings noted (AOFT only)
(= Only one of paired organs examined/present

CODES AND SYMBOLS USED AT FINDING LEVEL:

GRADE 1 = Minimal / very few / very small
GRADE 2 = Slight / few / small
GRADE 3 = Moderate / moderate number / moderate size
GRADE 4 = Marked / many / large
P = Finding present, severity not scored
(= Finding unilateral in paired organs
* = Comment in text of individual animal data

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX									
Necropsy Status: TERMINAL SACRIFICE GROUP (K0), Except Deaths									
Incidence table - Selected findings with grades									
Sex	Males				Females				
Dose Group	01	02	03	04	01	02	03	04	
No. Animals per Dose Group	10	10	10	5	10	9	9	6	
THYMUS	No.Examined	10	-	4	5	10	9	9	6
- Lymphocytolysis increased	GRADE 1	-	-	-	-	-	1	1	2
	GRADE 2	1	-	-	-	-	-	-	-
	TOTAL AFFECTED	1	-	-	-	-	1	1	2
	MEAN GRADE/TOISS.AFFECTED	2.0	-	-	-	-	1.0	1.0	1.0
THYROID GLAND	No.Examined	10	10	10	5	10	9	9	6
- Hypertrophy follicular cell	GRADE 1	3	3	4	-	1	2	3	3
	GRADE 2	2	3	4	4	-	-	-	3
	GRADE 3	-	2	-	1	-	-	-	-
	TOTAL AFFECTED	5	8	8	5	1	2	3	6
	MEAN GRADE/TOISS.AFFECTED	1.4	1.9	1.5	2.2	1.0	1.0	1.0	1.5
STOMACH	No.Examined	10	10	10	5	10	9	9	6
- Inflammation forestomach	GRADE 1	6	2	3	1	1	1	1	1
	GRADE 2	2	-	2	-	2	2	1	2
	GRADE 3	-	-	-	-	-	1	-	-
	TOTAL AFFECTED	8	2	5	1	3	4	2	3
	MEAN GRADE/TOISS.AFFECTED	1.3	1.0	1.4	1.0	1.7	2.0	1.5	1.7
- Hyperplasia squamous cell	GRADE 1	3	2	3	2	1	2	2	3
	GRADE 2	5	2	4	1	3	2	-	-
	GRADE 3	-	-	-	1	-	1	2	2
	TOTAL AFFECTED	8	4	7	4	4	5	4	5
	MEAN GRADE/TOISS.AFFECTED	1.6	1.5	1.6	1.8	1.8	1.8	2.0	1.8
- Erosion/ulceration	GRADE 1	-	-	1	1	-	1	-	1
	GRADE 2	1	-	-	-	1	1	1	1
	TOTAL AFFECTED	1	-	1	1	1	2	1	2
	MEAN GRADE/TOISS.AFFECTED	2.0	-	1.0	1.0	2.0	1.5	2.0	1.5
- Edema	GRADE 1	1	4	-	-	1	3	-	-
	GRADE 2	2	1	2	-	2	1	1	1
	GRADE 3	1	-	-	-	-	-	-	-
	TOTAL AFFECTED	4	5	2	-	3	4	1	1
	MEAN GRADE/TOISS.AFFECTED	2.0	1.2	2.0	-	1.7	1.3	2.0	2.0
LIVER	No.Examined	10	10	10	5	10	9	9	6
- Hypertrophy centrilobular/diffuse+eosinophilic cytopl	GRADE 1	-	10	2	-	-	2	6	-
	GRADE 2	-	-	7	1	-	-	3	-
	GRADE 3	-	-	1	4	-	-	-	6
	TOTAL AFFECTED	-	10	10	5	-	2	9	6
	MEAN GRADE/TOISS.AFFECTED	-	1.0	1.9	2.8	-	1.0	1.3	3.0
- Necrosis hepatocellular centrilobular	GRADE 1	-	-	-	1	-	-	1	2
	GRADE 2	-	-	-	4	-	-	-	3
	GRADE 3	-	-	-	-	-	-	-	1
	TOTAL AFFECTED	-	-	-	5	-	-	1	6
	MEAN GRADE/TOISS.AFFECTED	-	-	-	1.8	-	-	1.0	1.8

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG); females: MTDID 7831 (0 MG/KG)
 Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
 Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
 Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX								
Necropsy Status: TERMINAL SACRIFICE GROUP (K0), Except Deaths								
Incidence table - Selected findings with grades								
Sex	Males				Females			
Dose Group	01	02	03	04	01	02	03	04
No. Animals per Dose Group	10	10	10	5	10	9	9	6
LIVER								
cont.d	10	10	10	5	10	9	9	6
- Necrosis coagulative								
GRADE 1	-	-	1	1	-	-	-	1
GRADE 2	-	-	-	1	-	-	-	-
TOTAL AFFECTED	-	-	1	2	-	-	-	1
MEAN GRADE/TISS.AFFECTED	-	-	1.0	1.5	-	-	-	1.0
SPLEEN								
No.Examined	10	-	-	5	10	9	9	6
- Hematopoiesis								
extramedullary								
GRADE 1	-	-	-	-	2	5	3	4
GRADE 2	-	-	-	1	5	-	-	-
GRADE 3	-	-	-	-	3	-	-	-
TOTAL AFFECTED	-	-	-	1	10	5	3	4
MEAN GRADE/TISS.AFFECTED	-	-	-	2.0	2.1	1.0	1.0	1.0
KIDNEYS								
No.Examined	10	10	10	5	10	9	9	6
- Basophilia tubule								
GRADE 1	3	-	1	1	2	-	1	-
GRADE 2	-	-	-	1	-	-	-	-
GRADE 3	-	-	-	-	-	-	-	1
TOTAL AFFECTED	3	-	1	2	2	-	1	1
MEAN GRADE/TISS.AFFECTED	1.0	-	1.0	1.5	1.0	-	1.0	3.0
- Vacuolar degeneration/								
necrosis tubular								
GRADE 1	-	-	-	1	-	-	-	-
TOTAL AFFECTED	-	-	-	1	-	-	-	-
MEAN GRADE/TISS.AFFECTED	-	-	-	1.0	-	-	-	-
- Eosinophilic content								
tubular								
GRADE 1	1	1	-	3	-	-	-	2
GRADE 2	-	-	-	2	-	-	-	-
TOTAL AFFECTED	1	1	-	5	-	-	-	2
MEAN GRADE/TISS.AFFECTED	1.0	1.0	-	1.4	-	-	-	1.0
- Casts granular								
GRADE 2	-	-	-	1	-	-	-	-
TOTAL AFFECTED	-	-	-	1	-	-	-	-
MEAN GRADE/TISS.AFFECTED	-	-	-	2.0	-	-	-	-
- Papil hyperplasia epit								
helium with cellular debris/cas								
GRADE 1	-	-	-	2	-	-	-	-
GRADE 2	-	-	-	-	-	-	-	2
TOTAL AFFECTED	-	-	-	2	-	-	-	2
MEAN GRADE/TISS.AFFECTED	-	-	-	1.0	-	-	-	2.0
- Papil eosinophilic								
content								
GRADE 1	-	-	-	-	-	-	3	-
GRADE 2	-	-	-	-	-	-	-	1
TOTAL AFFECTED	-	-	-	-	-	-	3	1
MEAN GRADE/TISS.AFFECTED	-	-	-	-	-	-	1.0	2.0
- Calculus								
GRADE 2	-	-	-	-	-	-	-	1
GRADE 3	-	-	-	-	-	-	-	1
TOTAL AFFECTED	-	-	-	-	-	-	-	2
MEAN GRADE/TISS.AFFECTED	-	-	-	-	-	-	-	2.5

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG); females: MTDID 7831 (0 MG/KG)
 Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
 Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
 Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX								
Necropsy Status: TERMINAL SACRIFICE GROUP (K0), Except Deaths								
Incidence table - Selected findings with grades								
Sex	Males				Females			
Dose Group	01	02	03	04	01	02	03	04
No. Animals per Dose Group	10	10	10	5	10	9	9	6
URINARY BLADDER No.Examined	10	10	9	5	10	9	8	6
- Hyperplasia/hypertrophyGRADE 1 urothelium	-	-	2	2	-	-	2	3
GRADE 2	-	-	2	1	-	-	-	-
GRADE 3	-	-	-	1	-	-	-	-
TOTAL AFFECTED	-	-	4	4	-	-	2	3
MEAN GRADE/TISS.AFFECTED	-	-	1.5	1.8	-	-	1.0	1.0
ADRENAL GLANDS No.Examined	10	-	-	5	10	9	9	6
- Vacuolation zona glomerulosa GRADE 1	-	-	-	1	1	2	4	2
GRADE 2	-	-	-	-	-	-	-	2
TOTAL AFFECTED	-	-	-	1	1	2	4	4
MEAN GRADE/TISS.AFFECTED	-	-	-	1.0	1.0	1.0	1.0	1.5
BONE MARROW, STERNUM No.Examined	10	10	10	5	10	9	9	6
- Increased adipocytes GRADE 1	-	2	3	-	-	1	2	2
GRADE 2	-	-	1	-	-	-	-	-
GRADE 3	-	-	-	1	-	-	-	-
TOTAL AFFECTED	-	2	4	1	-	1	2	2
MEAN GRADE/TISS.AFFECTED	-	1.0	1.3	3.0	-	1.0	1.0	1.0

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG); females: MTDID 7831 (0 MG/KG)
 Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
 Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
 Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX Necropsy Status: RECOVERY / POST-TREATMENT GROUP (R1), Except Deaths Incidence table - Selected findings with grades								
Sex	Males				Females			
Dose Group	01	02	03	04	01	02	03	04
No. Animals per Dose Group	5	-	-	4	5	-	-	5
THYROID GLAND No.Examined	5	-	-	4	5	-	-	5
- Hypertrophy follicular GRADE 1	2	-	-	1	1	-	-	1
cell								
GRADE 2	-	-	-	1	-	-	-	-
TOTAL AFFECTED	2	-	-	2	1	-	-	1
MEAN GRADE/TISS.AFFECTED	1.0	-	-	1.5	1.0	-	-	1.0
STOMACH No.Examined	5	-	-	4	5	-	-	5
- Inflammation GRADE 1	-	-	-	-	-	-	-	1
forestomach								
TOTAL AFFECTED	-	-	-	-	-	-	-	1
MEAN GRADE/TISS.AFFECTED	-	-	-	-	-	-	-	1.0
- Hyperplasia squamous GRADE 1	-	-	-	-	-	-	-	1
cell								
TOTAL AFFECTED	-	-	-	-	-	-	-	1
MEAN GRADE/TISS.AFFECTED	-	-	-	-	-	-	-	1.0
LIVER No.Examined	5	-	-	4	5	-	-	5
- Pigment deposition yel GRADE 1	-	-	-	-	-	-	-	1
low-brown centrilobular								
GRADE 2	-	-	-	1	-	-	-	1
TOTAL AFFECTED	-	-	-	1	-	-	-	2
MEAN GRADE/TISS.AFFECTED	-	-	-	2.0	-	-	-	1.5
- Necrosis GRADE 1	-	-	-	-	-	-	-	1
hepatocellular centrilobular								
TOTAL AFFECTED	-	-	-	-	-	-	-	1
MEAN GRADE/TISS.AFFECTED	-	-	-	-	-	-	-	1.0
- Necrosis coagulative GRADE 1	-	-	-	-	1	-	-	-
TOTAL AFFECTED	-	-	-	-	1	-	-	-
MEAN GRADE/TISS.AFFECTED	-	-	-	-	1.0	-	-	-
KIDNEYS No.Examined	5	-	-	4	5	-	-	5
- Basophilia tubule GRADE 1	1	-	-	-	-	-	-	1
TOTAL AFFECTED	1	-	-	-	-	-	-	1
MEAN GRADE/TISS.AFFECTED	1.0	-	-	-	-	-	-	1.0
- Pigment yellow-brown GRADE 1	-	-	-	3	-	-	-	-
TOTAL AFFECTED	-	-	-	3	-	-	-	-
MEAN GRADE/TISS.AFFECTED	-	-	-	1.0	-	-	-	-
URINARY BLADDER No.Examined	5	-	-	4	5	-	-	5
- Hyperplasia/hypertrophy GRADE 1	-	-	-	1	-	-	-	3
urothelium								
GRADE 2	-	-	-	2	-	-	-	1
TOTAL AFFECTED	-	-	-	3	-	-	-	4
MEAN GRADE/TISS.AFFECTED	-	-	-	1.7	-	-	-	1.3

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG); females: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX Necropsy Status: RECOVERY / POST-TREATMENT GROUP (R1), Except Deaths Incidence table - Selected findings with grades								
Sex	Males				Females			
Dose Group	01	02	03	04	01	02	03	04
No. Animals per Dose Group	5	-	-	4	5	-	-	5
ADRENAL GLANDS No.Examined	-	-	-	-	5	-	-	5
- Vacuolation zona glomerulosa GRADE 1	-	-	-	-	2	-	-	1
TOTAL AFFECTED	-	-	-	-	2	-	-	1
MEAN GRADE/TISS.AFFECTED	-	-	-	-	1.0	-	-	1.0
BONE MARROW, STERNUM No.Examined	5	-	-	4	5	-	-	5
- Increased adipocytes GRADE 1	-	-	-	1	-	-	-	1
GRADE 2	-	-	-	1	-	-	-	-
TOTAL AFFECTED	-	-	-	2	-	-	-	1
MEAN GRADE/TISS.AFFECTED	-	-	-	1.5	-	-	-	1.0

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG); females: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

SEX :	MALE			
DOSE GROUP:	01	02	03	04
NO. ANIMALS:	10	10	10	5
HEART	10	-	-	5
N.A.D.	6	-	-	5
.....				
- Infiltrate inflamm. :	1	-	-	-
Grade 1:	1	-	-	-
- Necrosis, myofibers :	2	-	-	-
Grade 1:	1	-	-	-
Grade 2:	1	-	-	-
- Cardiopathy, progr. :	1	-	-	-
Grade 2:	1	-	-	-
AORTA	10	-	-	5
N.A.D.	10	-	-	5
LUNG	10	-	-	5
N.A.D.	6	-	-	1
.....				
- Inflamm. alv. acute :	1	-	-	-
Grade 1:	1	-	-	-
- Alveolar macrophages:	2	-	-	3
Grade 1:	1	-	-	-
Grade 2:	1	-	-	3
- Inflamm. peribronch.:	2	-	-	3
Grade 1:	2	-	-	3
Grade 2:	-	-	-	-
- Edema alveolar/bron.:	1	-	-	-
Grade 2:	1	-	-	-
- Mineralization vasc.:	1	-	-	1
Grade 1:	1	-	-	1

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA
PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

SEX :	MALE			
DOSE GROUP:	01	02	03	04
NO. ANIMALS:	10	10	10	5
THYMUS :	10	-	4	5
N.A.D. :	7	-	2	3
.....				
- Congestion/hemorrh. :	-	-	2	-
Grade 1:	-	-	2	-
- Depletion, lymphoid :	1	-	-	2
Grade 1:	1	-	-	2
- Lymphocytolysis inc.:	1	-	-	-
Grade 1:	-	-	-	-
Grade 2:	1	-	-	-
- Hyperplasia, epith. :	1	-	-	-
Grade 1:	1	-	-	-
.....				
TRACHEA :	10	-	-	5
N.A.D. :	8	-	-	4
.....				
- Infiltrate inflamm. :	1	-	-	-
Grade 1:	1	-	-	-
- Ectasia subm. glands:	1	-	-	1
Grade 1:	1	-	-	1
.....				
ESOPHAGUS :	10	-	-	5
N.A.D. :	7	-	-	5
.....				
- Degen./necr. muscle :	3	-	-	-
Grade 1:	3	-	-	-

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

SEX :	MALE			
DOSE GROUP:	01	02	03	04
NO. ANIMALS:	10	10	10	5
THYROID GLAND :	10	10	10	5
N.A.D. :	5	2	1	-
.....				
- Hypertrophy foll. c.:	5	8	8	5
Grade 1:	3	3	4	-
Grade 2:	2	3	4	4
Grade 3:	-	2	-	1
- Cyst, ultimobranch. :	-	-	1	-
Grade 1:	-	-	1	-
Grade 2:	-	-	-	-
.....				
PARATHYROID GLANDS :	10	-	-	5
N.A.D. :	10	-	-	5

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

	SEX :	MALE			
	DOSE GROUP:	01	02	03	04
	NO. ANIMALS:	10	10	10	5
STOMACH	:	10	10	10	5
	N.A.D. :	1	5	2	1
.....					
- Inflammation forest.:		8	2	5	1
Grade 1:		6	2	3	1
Grade 2:		2	-	2	-
Grade 3:		-	-	-	-
- Inflammation, gland.:		-	-	-	1
Grade 2:		-	-	-	1
- Hyperplasia squamous:		8	4	7	4
Grade 1:		3	2	3	2
Grade 2:		5	2	4	1
Grade 3:		-	-	-	1
- Erosion/ulceration :		1	-	1	1
Grade 1:		-	-	1	1
Grade 2:		1	-	-	-
- Hemorrhage :		1	-	-	-
Grade 1:		1	-	-	-
Grade 2:		-	-	-	-
- Cyst(s) :		-	-	-	1
Grade 2:		-	-	-	1
- Edema :		4	5	2	-
Grade 1:		1	4	-	-
Grade 2:		2	1	2	-
Grade 3:		1	-	-	-
.....					
DUODENUM	:	10	-	-	5
	N.A.D. :	10	-	-	5
.....					
JEJUNUM	:	10	-	-	5
	N.A.D. :	10	-	-	5
.....					
ILEUM	:	10	-	-	5
	N.A.D. :	10	-	-	5

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

SEX :	MALE			
DOSE GROUP:	01	02	03	04
NO. ANIMALS:	10	10	10	5
PEYER'S PATCHES :	10	-	-	5
N.A.D. :	6	-	-	5
.....				
- Vacuolation, incr. :	4	-	-	-
Grade 1:	4	-	-	-
Grade 2:	-	-	-	-
Grade 3:	-	-	-	-
CECUM :	10	-	-	5
N.A.D. :	10	-	-	5
COLON :	10	-	-	5
N.A.D. :	10	-	-	5
RECTUM :	10	-	-	5
N.A.D. :	10	-	-	5

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

	SEX :	MALE			
	DOSE GROUP:	01	02	03	04
	NO.ANIMALS:	10	10	10	5
LIVER	:	10	10	10	5
N.A.D.	:	-	-	-	-
.....					
- Infiltrate inflamm.	:	9	5	7	4
Grade 1:		9	5	7	4
- Hematopoiesis extram.:		-	1	-	-
Grade 1:		-	1	-	-
Grade 2:		-	-	-	-
- Infiltrat. peribil. :		1	-	-	-
Grade 1:		1	-	-	-
- Hypertrophy hepatoc.:		-	10	10	5
Grade 1:		-	10	2	-
Grade 2:		-	-	7	1
Grade 3:		-	-	1	4
- Accessory lobe :		2	-	1	-
- Necrosis hepatocell.:		-	-	-	5
Grade 1:		-	-	-	1
Grade 2:		-	-	-	4
Grade 3:		-	-	-	-
- Necrosis coagulat. :		-	-	1	2
Grade 1:		-	-	1	1
Grade 2:		-	-	-	1
.....					
SPLEEN	:	10	-	-	5
- Hematopoiesis extra.:		-	-	-	1
Grade 1:		-	-	-	-
Grade 2:		-	-	-	1
Grade 3:		-	-	-	-
- Pigmentation, hemos.:		10	-	-	5
Grade 1:		6	-	-	1
Grade 2:		4	-	-	4
Grade 3:		-	-	-	-

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

SEX :	MALE			
DOSE GROUP:	01	02	03	04
NO. ANIMALS:	10	10	10	5
MESENT. LYMPH NODE :	10	-	-	5
N.A.D. :	7	-	-	1
.....				
- Erythrocytes, sinus :	-	-	-	2
Grade 1:	-	-	-	2
- Incr. macrophages :	3	-	-	2
Grade 1:	3	-	-	2
Grade 2:	-	-	-	-
- Sinus histiocytosis :	-	-	-	1
Grade 2:	-	-	-	1
.....				
PANCREAS :	10	-	-	5
N.A.D. :	10	-	-	5
.....				
MANDIB. LYMPH NODES :	10	1	-	5
N.A.D. :	9	-	-	4
.....				
- Erythrocytes, sinus :	1	1	-	1
Grade 1:	-	-	-	-
Grade 2:	1	1	-	1
Grade 3:	-	-	-	-
.....				
SUBLINGUAL GLANDS :	10	-	-	5
N.A.D. :	10	-	-	5
.....				
MANDIBULAR GLANDS :	10	-	-	5
N.A.D. :	10	-	-	5

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

	SEX :	MALE			
	DOSE GROUP:	01	02	03	04
	NO. ANIMALS:	10	10	10	5
KIDNEYS		10	9	10	5
	N.A.D. :	1	5	7	-
.....					
- Infiltrate inflamm. :		-	-	-	1
Grade 1:		-	-	-	1
Grade 2:		-	-	-	-
- Hyaline droplet acc.:		8	4	2	2
Grade 1:		4	4	2	2
Grade 2:		4	-	-	-
- Basophilia tubule :		3	-	1	2
Grade 1:		3	-	1	1
Grade 2:		-	-	-	1
Grade 3:		-	-	-	-
- Vacuolar deg./necr. :		-	-	-	1
Grade 1:		-	-	-	1
- Eosinophilic content:		1	1	-	5
Grade 1:		1	1	-	3
Grade 2:		-	-	-	2
- Casts hyaline :		1	-	-	-
Grade 1:		1	-	-	-
- Casts granular :		-	-	-	1
Grade 2:		-	-	-	1
- Dilation, tubule :		3	-	-	-
Grade 1:		1	-	-	-
Grade 2:		2	-	-	-
- Papil hyperplasia :		-	-	-	2
Grade 1:		-	-	-	2
Grade 2:		-	-	-	-

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

SEX :	MALE			
DOSE GROUP:	01	02	03	04
NO. ANIMALS:	10	10	10	5
URINARY BLADDER :	10	10	9	5
N.A.D. :	10	10	5	1
.....				
- Infiltrate inflamm. :	-	-	2	2
Grade 1:	-	-	1	1
Grade 2:	-	-	1	1
- Hyperpl/hypert urot.:	-	-	4	4
Grade 1:	-	-	2	2
Grade 2:	-	-	2	1
Grade 3:	-	-	-	1
- Uroliths :	-	-	-	1
- Edema :	-	-	1	-
Grade 1:	-	-	1	-
.....				
ADRENAL GLANDS :	10	-	-	5
N.A.D. :	7	-	-	4
.....				
- Cortical tissue, ac.:	3	-	-	-
- Vacuol. glomerulosa :	-	-	-	1
Grade 1:	-	-	-	1
Grade 2:	-	-	-	-
- Vacuol. fasciculata :	-	-	-	1
Grade 1:	-	-	-	1
.....				
BRAIN :	10	-	-	5
N.A.D. :	10	-	-	5
.....				
PITUITARY GLAND :	10	-	-	5
N.A.D. :	10	-	-	5
.....				
SCIATIC NERVE, LEFT :	10	-	-	5
N.A.D. :	10	-	-	5

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

SEX	MALE			
DOSE GROUP:	01	02	03	04
NO.ANIMALS:	10	10	10	5
TESTES	: 10	-	-	5
N.A.D.	: 9	-	-	5
.....				
- Atrophy, tubular	: 1	-	-	-
Grade 1:	1	-	-	-
EPIDIDYMIDES	: 10	-	-	5
N.A.D.	: 10	-	-	5
PROSTATE GLAND	: 10	-	1	5
N.A.D.	: 9	-	1	5
.....				
- Infiltrate inflamm.	: 1	-	-	-
Grade 1:	1	-	-	-
SEMINAL VESICLES	: 10	-	-	5
N.A.D.	: 10	-	-	5
COAGULATING GLANDS	: 10	-	-	5
N.A.D.	: 10	-	-	5
SKIN/SUBCUTIS	: 10	-	-	5
N.A.D.	: 9	-	-	5
.....				
- Inflamm. exudative	: 1	-	-	-
Grade 1:	1	-	-	-
LARYNX	: 10	-	-	5
N.A.D.	: 10	-	-	5
EYES	: 10	-	-	5
N.A.D.	: 10	-	-	5

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

SEX :	MALE			
DOSE GROUP:	01	02	03	04
NO. ANIMALS:	10	10	10	5
<hr/>				
OPTIC NERVES :	10	-	-	5
N.A.D. :	10	-	-	5
<hr/>				
HARDERIAN GLANDS :	10	-	-	5
N.A.D. :	8	-	-	4
<hr/>				
- Infiltrate inflamm. :	1	-	-	-
Grade 1:	1	-	-	-
Grade 2:	-	-	-	-
- Hemorrhage :	2	-	-	1
Grade 1:	1	-	-	1
Grade 2:	1	-	-	-
<hr/>				
SPINAL CORD, CERVIC. :	10	-	-	5
N.A.D. :	10	-	-	5
<hr/>				
SPINAL CORD, THORAC. :	10	-	-	5
N.A.D. :	10	-	-	5
<hr/>				
SPINAL CORD, LUMBAR :	10	-	-	5
N.A.D. :	10	-	-	5
<hr/>				
BONE, STERNUM :	10	10	10	5
N.A.D. :	10	10	10	5
<hr/>				
BONE MARROW, STERNUM :	10	10	10	5
N.A.D. :	10	8	6	4
<hr/>				
- Increased adipocytes:	-	2	4	1
Grade 1:	-	2	3	-
Grade 2:	-	-	1	-
Grade 3:	-	-	-	1

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
 STATUS AT NECROPSY: K0, EXCEPT DEATHS
 Incidence table - All microscopic findings

SEX :	MALE			
DOSE GROUP:	01	02	03	04
NO.ANIMALS:	10	10	10	5
PREPUTIAL GLANDS :	1	3	1	1
N.A.D. :	1	3	1	-
.....				
- Infiltrate inflamm. :	-	-	-	1
Grade 1:	-	-	-	1
.....				
LACRIMAL GLANDS :	-	1	-	-
- Atrophy, glandular :	-	1	-	-
Grade 3:	-	1	-	-

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG)
 Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG)
 Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG)
 Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

	SEX :	FEMALE			
	DOSE GROUP:	01	02	03	04
	NO. ANIMALS:	10	9	9	6
HEART	:	10	-	-	6
	N.A.D. :	10	-	-	6
AORTA	:	10	-	-	6
	N.A.D. :	10	-	-	6
LUNG	:	10	1	-	6
	N.A.D. :	6	-	-	4
.....					
- Alveolar macrophages:		-	1	-	1
Grade 1:		-	1	-	1
Grade 2:		-	-	-	-
- Inflamm. peribronch.:		3	-	-	-
Grade 1:		2	-	-	-
Grade 2:		1	-	-	-
- Inflamm. granulomat.:		-	-	-	1
Grade 1:		-	-	-	1
- Mineralization vasc.:		1	1	-	-
Grade 1:		1	1	-	-
THYMUS	:	10	9	9	6
	N.A.D. :	10	8	4	3
.....					
- Congestion/hemorrh. :		-	-	1	1
Grade 1:		-	-	1	1
- Lymphocytolysis inc.:		-	1	1	2
Grade 1:		-	1	1	2
Grade 2:		-	-	-	-
- Hyperplasia, epith. :		-	-	2	1
Grade 1:		-	-	2	1
- Cystic ducts :		-	-	1	-
Grade 1:		-	-	1	-

Group 01, CONTROL, females: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

SEX :	FEMALE			
DOSE GROUP:	01	02	03	04
NO. ANIMALS:	10	9	9	6
TRACHEA :	10	-	-	6
N.A.D. :	10	-	-	5
.....				
- Infiltrate inflamm. :	-	-	-	1
Grade 1:	-	-	-	1
.....				
ESOPHAGUS :	10	-	-	6
N.A.D. :	10	-	-	6
.....				
THYROID GLAND :	10	9	9	6
N.A.D. :	8	6	6	-
.....				
- Thymus, ectopic :	-	1	-	1
- Hypertrophy foll. c.:	1	2	3	6
Grade 1:	1	2	3	3
Grade 2:	-	-	-	3
Grade 3:	-	-	-	-
- Cyst, ultimobranch. :	1	-	-	1
Grade 1:	-	-	-	1
Grade 2:	1	-	-	-
.....				
PARATHYROID GLANDS :	10	-	-	6
N.A.D. :	10	-	-	6

Group 01, CONTROL, females: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

	SEX :	FEMALE			
	DOSE GROUP:	01	02	03	04
	NO. ANIMALS:	10	9	9	6
STOMACH	:	10	9	9	6
N.A.D.	:	6	3	5	1
.....					
- Inflammation forest.	:	3	4	2	3
Grade 1:		1	1	1	1
Grade 2:		2	2	1	2
Grade 3:		-	1	-	-
- Hyperplasia squamous:		4	5	4	5
Grade 1:		1	2	2	3
Grade 2:		3	2	-	-
Grade 3:		-	1	2	2
- Erosion/ulceration :		1	2	1	2
Grade 1:		-	1	-	1
Grade 2:		1	1	1	1
- Hemorrhage :		-	-	-	1
Grade 1:		-	-	-	-
Grade 2:		-	-	-	1
- Edema :		3	4	1	1
Grade 1:		1	3	-	-
Grade 2:		2	1	1	1
Grade 3:		-	-	-	-
.....					
DUODENUM	:	10	-	-	6
N.A.D.	:	10	-	-	6
.....					
JEJUNUM	:	10	-	-	6
N.A.D.	:	10	-	-	6
.....					
ILEUM	:	10	-	-	6
N.A.D.	:	10	-	-	6

Group 01, CONTROL, females: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

SEX :					FEMALE
DOSE GROUP:	01	02	03	04	
NO. ANIMALS:	10	9	9	6	
PEYER'S PATCHES :	10	-	-	6	
N.A.D. :	7	-	-	6	
.....					
- Vacuolation, incr. :	3	-	-	-	
Grade 1:	-	-	-	-	
Grade 2:	2	-	-	-	
Grade 3:	1	-	-	-	
CECUM :	10	-	-	6	
N.A.D. :	10	-	-	6	
COLON :	10	-	-	6	
N.A.D. :	10	-	-	6	
RECTUM :	10	-	-	6	
N.A.D. :	10	-	-	6	

Group 01, CONTROL, females: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

		SEX : FEMALE				
		DOSE GROUP:	01	02	03	04
		NO. ANIMALS:	10	9	9	6
LIVER	:	10	9	9	6	
	N.A.D. :	1	-	-	-	
.....						
- Infiltrate inflamm.	:	8	9	9	4	
	Grade 1:	8	9	9	4	
- Hematopoiesis extram.	:	8	1	-	-	
	Grade 1:	7	1	-	-	
	Grade 2:	1	-	-	-	
- Hypertrophy hepatoc.	:	-	2	9	6	
	Grade 1:	-	2	6	-	
	Grade 2:	-	-	3	-	
	Grade 3:	-	-	-	6	
- Hepatodiaphr. nodule:	:	-	1	-	-	
- Necrosis hepatocell.	:	-	-	1	6	
	Grade 1:	-	-	1	2	
	Grade 2:	-	-	-	3	
	Grade 3:	-	-	-	1	
- Necrosis coagulat.	:	-	-	-	1	
	Grade 1:	-	-	-	1	
	Grade 2:	-	-	-	-	
- Infarction/torsion	:	1	-	-	-	
.....						
SPLEEN	:	10	9	9	6	
- Hematopoiesis extra.	:	10	5	3	4	
	Grade 1:	2	5	3	4	
	Grade 2:	5	-	-	-	
	Grade 3:	3	-	-	-	
- Pigmentation, hemos.	:	10	9	9	6	
	Grade 1:	3	2	2	-	
	Grade 2:	6	7	5	4	
	Grade 3:	1	-	2	2	

Group 01, CONTROL, females: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

SEX :	FEMALE			
DOSE GROUP:	01	02	03	04
NO.ANIMALS:	10	9	9	6
MESENT. LYMPH NODE :	10	-	-	6
N.A.D. :	3	-	-	1
.....				
- Incr. macrophages :	7	-	-	5
Grade 1:	3	-	-	5
Grade 2:	4	-	-	-
.....				
PANCREAS :	10	-	-	6
N.A.D. :	10	-	-	6
.....				
MANDIB.LYMPH NODES :	10	-	1	6
N.A.D. :	7	-	-	4
.....				
- Congestion :	2	-	-	-
Grade 1:	2	-	-	-
- Erythrocytes, sinus :	1	-	1	1
Grade 1:	-	-	-	1
Grade 2:	1	-	-	-
Grade 3:	-	-	1	-
- Pigmentation :	-	-	-	1
Grade 1:	-	-	-	1
.....				
SUBLINGUAL GLANDS :	10	-	-	6
N.A.D. :	10	-	-	6
.....				
MANDIBULAR GLANDS :	10	-	-	6
N.A.D. :	10	-	-	6

Group 01, CONTROL, females: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

	SEX :					FEMALE
	DOSE GROUP:	01	02	03	04	
	NO.ANIMALS:	10	9	9	6	
KIDNEYS	:	10	9	9	6	
	N.A.D. :	6	8	4	2	
.....						
- Infiltrate inflamm.	:	1	-	-	1	
	Grade 1:	1	-	-	-	
	Grade 2:	-	-	-	1	
- Basophilia tubule	:	2	-	1	1	
	Grade 1:	2	-	1	-	
	Grade 2:	-	-	-	-	
	Grade 3:	-	-	-	1	
- Eosinophilic content:	:	-	-	-	2	
	Grade 1:	-	-	-	2	
	Grade 2:	-	-	-	-	
- Casts hyaline	:	1	-	-	-	
	Grade 1:	1	-	-	-	
- Cyst	:	-	1	-	-	
	Grade 2:	-	1	-	-	
- Dilation, tubule	:	-	-	-	1	
	Grade 1:	-	-	-	1	
	Grade 2:	-	-	-	-	
- Papil hyperplasia	:	-	-	-	2	
	Grade 1:	-	-	-	-	
	Grade 2:	-	-	-	2	
- Papil eosin. content:	:	-	-	3	1	
	Grade 1:	-	-	3	-	
	Grade 2:	-	-	-	1	
- Calculus,	:	-	-	-	2	
	Grade 2:	-	-	-	1	
	Grade 3:	-	-	-	1	
- Mineralization	:	-	-	2	1	
	Grade 1:	-	-	2	1	
- Dilation, pelvis	:	-	-	1	-	
	Grade 3:	-	-	1	-	

Group 01, CONTROL, females: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

SEX :	FEMALE			
DOSE GROUP:	01	02	03	04
NO. ANIMALS:	10	9	9	6
URINARY BLADDER :	10	9	8	6
N.A.D. :	10	9	6	3
.....				
- Hyperpl/hypert urot.:	-	-	2	3
Grade 1:	-	-	2	3
Grade 2:	-	-	-	-
Grade 3:	-	-	-	-
.....				
ADRENAL GLANDS :	10	9	9	6
N.A.D. :	9	7	4	2
.....				
- Cortical tissue, ac.:	-	-	2	-
- Vacuol. glomerulosa :	1	2	4	4
Grade 1:	1	2	4	2
Grade 2:	-	-	-	2
- Hematopoiese extram.:	1	-	-	-
Grade 1:	1	-	-	-
.....				
BRAIN :	10	-	-	6
N.A.D. :	10	-	-	6
.....				
PITUITARY GLAND :	10	-	-	6
N.A.D. :	10	-	-	6
.....				
SCIATIC NERVE, LEFT :	10	-	-	6
N.A.D. :	10	-	-	6
.....				
OVARIES :	10	-	1	6
N.A.D. :	8	-	1	5
.....				
- Hypertr. interst. c.:	2	-	-	1
Grade 1:	2	-	-	1

Group 01, CONTROL, females: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

	SEX :					FEMALE
	DOSE GROUP:	01	02	03	04	
	NO.ANIMALS:	10	9	9	6	
UTERUS	:	10	4	4	6	
	N.A.D. :	4	-	-	2	
.....						
- Cyclic dilation	:	6	4	4	4	
CERVIX	:	10	-	-	6	
	N.A.D. :	10	-	-	6	
VAGINA	:	10	-	-	6	
- Cycle: Proestrus	:	4	-	-	-	
- Cycle: Estrus	:	3	-	-	4	
- Cycle: Metestrus	:	2	-	-	1	
- Cycle: Diestrus	:	1	-	-	1	
SKIN/SUBCUTIS	:	10	-	-	6	
	N.A.D. :	10	-	-	6	
MAMMARY GLAND	:	10	-	-	6	
	N.A.D. :	10	-	-	6	
LARYNX	:	10	-	-	6	
	N.A.D. :	10	-	-	6	
EYES	:	10	-	-	6	
	N.A.D. :	10	-	-	6	
OPTIC NERVES	:	10	-	-	6	
	N.A.D. :	10	-	-	6	

Group 01, CONTROL, females: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, EXCEPT DEATHS
Incidence table - All microscopic findings

SEX :	FEMALE			
DOSE GROUP:	01	02	03	04
NO.ANIMALS:	10	9	9	6
HARDERIAN GLANDS :	10	-	-	6
N.A.D. :	9	-	-	6
.....				
- Infiltrate inflamm. :	1	-	-	-
Grade 1:	-	-	-	-
Grade 2:	1	-	-	-
.....				
SPINAL CORD, CERVIC. :	10	-	-	6
N.A.D. :	10	-	-	6
.....				
SPINAL CORD, THORAC. :	10	-	-	6
N.A.D. :	10	-	-	6
.....				
SPINAL CORD, LUMBAR :	10	-	-	6
N.A.D. :	10	-	-	6
.....				
BONE, STERNUM :	10	9	9	6
N.A.D. :	10	9	9	6
.....				
BONE MARROW, STERNUM :	10	9	9	6
N.A.D. :	10	8	7	4
.....				
- Increased adipocytes:	-	1	2	2
Grade 1:	-	1	2	2
Grade 2:	-	-	-	-
Grade 3:	-	-	-	-
.....				
PARATHYMIC LN. :	-	1	-	-
- Lymphoid hyperplasia:	-	1	-	-
Grade 1:	-	1	-	-
.....				
BODY CAVITIES :	1	-	-	-
- Fat necrosis :	1	-	-	-
Grade 2:	1	-	-	-

Group 01, CONTROL, females: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1, EXCEPT DEATHS
Incidence table - All microscopic findings

SEX :	MALE			
DOSE GROUP:	01	02	03	04
NO. ANIMALS:	5	-	-	4
THYROID GLAND :	5	-	-	4
N.A.D. :	2	-	-	2
.....				
- Thymus, ectopic :	1	-	-	-
- Hypertrophy foll. c.:	2	-	-	2
Grade 1:	2	-	-	1
Grade 2:	-	-	-	1
.....				
STOMACH :	5	-	-	4
N.A.D. :	2	-	-	1
.....				
- Inflammation, gland.:	-	-	-	3
Grade 1:	-	-	-	2
Grade 2:	-	-	-	1
- Congestion :	1	-	-	-
Grade 2:	1	-	-	-
- Cyst(s) :	2	-	-	-
Grade 1:	1	-	-	-
Grade 3:	1	-	-	-
- Vacuolation, lim. r.:	-	-	-	3
Grade 1:	-	-	-	1
Grade 2:	-	-	-	2

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1, EXCEPT DEATHS
Incidence table - All microscopic findings

	SEX :					MALE
	DOSE GROUP:	01	02	03	04	
	NO. ANIMALS:	5	-	-	4	
LIVER		5	-	-	4	
	N.A.D. :	3	-	-	3	
.....						
- Infiltrate inflamm. :		1	-	-	1	
	Grade 1:	1	-	-	1	
	Grade 2:	-	-	-	-	
	Grade 3:	-	-	-	-	
- Infiltrat. peribil. :		1	-	-	-	
	Grade 1:	1	-	-	-	
- Pigment deposition :		-	-	-	1	
	Grade 1:	-	-	-	-	
	Grade 2:	-	-	-	1	
.....						
KIDNEYS		5	-	-	4	
	N.A.D. :	3	-	-	1	
.....						
- Hyaline droplet acc.:		2	-	-	-	
	Grade 1:	2	-	-	-	
- Basophilia tubule :		1	-	-	-	
	Grade 1:	1	-	-	-	
- Pigment yellow-brown:		-	-	-	3	
	Grade 1:	-	-	-	3	
.....						
URINARY BLADDER		5	-	-	4	
	N.A.D. :	4	-	-	1	
.....						
- Infiltrate inflamm. :		1	-	-	1	
	Grade 1:	1	-	-	1	
- Hyperpl/hypert urot.:		-	-	-	3	
	Grade 1:	-	-	-	1	
	Grade 2:	-	-	-	2	
.....						
BONE, STERNUM		5	-	-	4	
	N.A.D. :	5	-	-	4	

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1, EXCEPT DEATHS
Incidence table - All microscopic findings

SEX :	MALE			
DOSE GROUP:	01	02	03	04
NO.ANIMALS:	5	-	-	4
BONE MARROW, STERNUM :	5	-	-	4
N.A.D. :	5	-	-	2
.....				
- Increased adipocytes:	-	-	-	2
Grade 1:	-	-	-	1
Grade 2:	-	-	-	1

Group 01, CONTROL, males: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1, EXCEPT DEATHS
Incidence table - All microscopic findings

SEX :	FEMALE			
DOSE GROUP:	01	02	03	04
NO. ANIMALS:	5	-	-	5
THYMUS	5	-	-	5
N.A.D. :	5	-	-	4
- Congestion/hemorrh. :	-	-	-	1
Grade 1:	-	-	-	1
THYROID GLAND	5	-	-	5
N.A.D. :	4	-	-	4
- Hypertrophy foll. c.:	1	-	-	1
Grade 1:	1	-	-	1
Grade 2:	-	-	-	-
STOMACH	5	-	-	5
N.A.D. :	4	-	-	4
- Inflammation forest.:	-	-	-	1
Grade 1:	-	-	-	1
- Hyperplasia squamous:	-	-	-	1
Grade 1:	-	-	-	1
- Vacuolation, lim. r.:	1	-	-	1
Grade 1:	1	-	-	1
Grade 2:	-	-	-	-
- Dilated gastric pits:	-	-	-	1
Grade 1:	-	-	-	1

Group 01, CONTROL, females: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1, EXCEPT DEATHS
Incidence table - All microscopic findings

	SEX :					FEMALE
	DOSE GROUP:	01	02	03	04	
	NO. ANIMALS:	5	-	-	5	
LIVER	:	5	-	-	5	
N.A.D.	:	-	-	-	-	
.....						
- Infiltrate inflamm.	:	5	-	-	5	
Grade 1:		3	-	-	5	
Grade 2:		1	-	-	-	
Grade 3:		1	-	-	-	
- Vacuolation hepatoc.:		-	-	-	4	
Grade 1:		-	-	-	3	
Grade 2:		-	-	-	1	
- Pigment deposition :		-	-	-	2	
Grade 1:		-	-	-	1	
Grade 2:		-	-	-	1	
- Necrosis hepatocell.:		-	-	-	1	
Grade 1:		-	-	-	1	
- Necrosis coagulat. :		1	-	-	-	
Grade 1:		1	-	-	-	
.....						
SPLEEN	:	5	-	-	5	
- Pigmentation, hemos.:		5	-	-	5	
Grade 1:		1	-	-	-	
Grade 2:		4	-	-	5	
.....						
KIDNEYS	:	5	-	-	5	
N.A.D.	:	5	-	-	4	
.....						
- Basophilia tubule :		-	-	-	1	
Grade 1:		-	-	-	1	

Group 01, CONTROL, females: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1, EXCEPT DEATHS
Incidence table - All microscopic findings

SEX :	FEMALE			
DOSE GROUP:	01	02	03	04
NO. ANIMALS:	5	-	-	5
URINARY BLADDER :	5	-	-	5
N.A.D. :	5	-	-	1
.....				
- Hyperpl/hypert urot.:	-	-	-	4
Grade 1:	-	-	-	3
Grade 2:	-	-	-	1
.....				
ADRENAL GLANDS :	5	-	-	5
N.A.D. :	3	-	-	3
.....				
- Cortical tissue, ac.:	-	-	-	1
- Vacuol. glomerulosa :	2	-	-	1
Grade 1:	2	-	-	1
- Vacuol. fasciculata :	1	-	-	-
Grade 2:	1	-	-	-
.....				
UTERUS :	5	-	-	2
- Cyclic dilation :	5	-	-	2
.....				
BONE, STERNUM :	5	-	-	5
N.A.D. :	5	-	-	5
.....				
BONE MARROW, STERNUM :	5	-	-	5
N.A.D. :	5	-	-	4
.....				
- Increased adipocytes:	-	-	-	1
Grade 1:	-	-	-	1
Grade 2:	-	-	-	-
.....				
CLITORAL GLANDS :	-	-	-	1
- Dilated duct :	-	-	-	1
Grade 2:	-	-	-	1

Group 01, CONTROL, females: MTDID 7831 (0 MG/KG)
Group 02, 100 MG/KG, females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, DEATHS ONLY
Incidence table - Unscheduled deaths

DOSE GROUP:		02		03		04	
SEX :		M	F	M	F	M	F
NO.ANIMALS:		-	1	-	1	3	2
GENERAL OBSERVATIONS :		-	-	-	-	1	-
- Gavage accident :		-	-	-	-	1	-
LUNG :		-	-	-	1	3	2
N.A.D. :		-	-	-	-	3	1
- Inflamm. alv. acute :		-	-	-	-	-	1
Grade 1:		-	-	-	-	-	1
- Mineralization vasc.:		-	-	-	1	-	-
Grade 1:		-	-	-	1	-	-
THYMUS :		-	1	-	1	3	2
N.A.D. :		-	-	-	-	1	-
- Congestion/hemorrh. :		-	1	-	1	-	1
Grade 2:		-	1	-	1	-	-
Grade 4:		-	-	-	-	-	1
- Depletion, lymphoid :		-	-	-	-	2	2
Grade 3:		-	-	-	-	1	-
Grade 4:		-	-	-	-	1	2
TRACHEA :		-	-	-	1	3	2
N.A.D. :		-	-	-	1	2	2
- Inflammation granul.:		-	-	-	-	1	-
Grade 1:		-	-	-	-	1	-
ESOPHAGUS :		-	1	-	1	3	2
N.A.D. :		-	1	-	1	2	2
- Hemorrhage :		-	-	-	-	1	-
Grade 3:		-	-	-	-	1	-

Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, DEATHS ONLY
Incidence table - Unscheduled deaths

	DOSE GROUP: 02		03		04	
SEX :	M	F	M	F	M	F
NO. ANIMALS:	-	1	-	1	3	2
THYROID GLAND :	-	1	-	-	3	1
N.A.D. :	-	1	-	-	2	1
.....						
- Hypertrophy foll. c.:	-	-	-	-	1	-
Grade 1:	-	-	-	-	1	-
.....						
STOMACH :	-	1	-	-	3	2
N.A.D. :	-	1	-	-	-	1
.....						
- Inflammation forest.:	-	-	-	-	1	1
Grade 1:	-	-	-	-	-	1
Grade 2:	-	-	-	-	1	-
- Inflammation, gland.:	-	-	-	-	1	-
Grade 1:	-	-	-	-	1	-
- Hyperplasia squamous:	-	-	-	-	2	1
Grade 1:	-	-	-	-	-	1
Grade 3:	-	-	-	-	2	-
- Erosion/ulceration :	-	-	-	-	2	1
Grade 1:	-	-	-	-	1	1
Grade 2:	-	-	-	-	1	-
- Hemorrhage :	-	-	-	-	1	-
Grade 1:	-	-	-	-	1	-
- Congestion :	-	-	-	-	3	-
Grade 1:	-	-	-	-	3	-

Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, DEATHS ONLY
Incidence table - Unscheduled deaths

	DOSE GROUP: 02		03		04	
SEX :	M	F	M	F	M	F
NO.ANIMALS:	-	1	-	1	3	2
LIVER :	-	1	-	1	3	1
- Infiltrate inflamm. :	-	-	-	1	-	1
Grade 1:	-	-	-	-	-	1
Grade 2:	-	-	-	1	-	-
- Hypertrophy hepatoc.:	-	1	-	1	3	1
Grade 2:	-	1	-	1	2	1
Grade 3:	-	-	-	-	1	-
- Necrosis hepatocell.:	-	-	-	-	3	1
Grade 1:	-	-	-	-	-	1
Grade 2:	-	-	-	-	2	-
Grade 4:	-	-	-	-	1	-
- Necrosis coagulat. :	-	1	-	-	2	1
Grade 2:	-	1	-	-	1	-
Grade 3:	-	-	-	-	1	1
SPLEEN :	-	-	-	-	3	1
- Hematopoiesis extra.:	-	-	-	-	1	-
Grade 1:	-	-	-	-	1	-
- Pigmentation, hemos.:	-	-	-	-	1	-
Grade 1:	-	-	-	-	1	-
- Atrophy red pulp :	-	-	-	-	-	1
Grade 2:	-	-	-	-	-	1
- Depletion, lymphoid :	-	-	-	-	1	-
Grade 4:	-	-	-	-	1	-
MESENT. LYMPH NODE :	-	1	-	-	3	1
N.A.D. :	-	1	-	-	2	1
.....						
- Depletion, lymphoid :	-	-	-	-	1	-
Grade 2:	-	-	-	-	1	-

Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, DEATHS ONLY
Incidence table - Unscheduled deaths

	DOSE GROUP: 02		03		04	
SEX :	M	F	M	F	M	F
NO. ANIMALS:	-	1	-	1	3	2
PANCREAS :	-	1	-	-	3	1
N.A.D. :	-	1	-	-	2	-
.....						
- Vacuolation, acinar :	-	-	-	-	1	-
Grade 1:	-	-	-	-	1	-
- Degranulation acinar:	-	-	-	-	-	1
Grade 2:	-	-	-	-	-	1
.....						
MANDIB. LYMPH NODES :	-	1	-	1	3	2
N.A.D. :	-	-	-	1	3	2
.....						
- Congestion :	-	1	-	-	-	-
Grade 2:	-	1	-	-	-	-
.....						
MANDIBULAR GLANDS :	-	1	-	-	3	1
N.A.D. :	-	1	-	-	2	1
.....						
- Reduced cont/atrophy:	-	-	-	-	1	-
Grade 3:	-	-	-	-	1	-

Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, DEATHS ONLY
Incidence table - Unscheduled deaths

	DOSE GROUP:		02		03		04	
	SEX :		M	F	M	F	M	F
NO.ANIMALS:			-	1	-	1	3	2
KIDNEYS	:		-	-	-	-	3	1
N.A.D.	:		-	-	-	-	1	-
.....								
- Infiltrate inflamm.	:		-	-	-	-	1	-
Grade 1:			-	-	-	-	1	-
- Basophilia tubule	:		-	-	-	-	1	1
Grade 2:			-	-	-	-	1	-
Grade 4:			-	-	-	-	-	1
- Vacuolar deg./necr.	:		-	-	-	-	2	-
Grade 2:			-	-	-	-	1	-
Grade 3:			-	-	-	-	1	-
- Eosinophilic content:			-	-	-	-	1	1
Grade 1:			-	-	-	-	1	1
- Casts granular	:		-	-	-	-	-	1
Grade 2:			-	-	-	-	-	1
- Dilation, tubule	:		-	-	-	-	2	-
Grade 1:			-	-	-	-	1	-
Grade 2:			-	-	-	-	1	-
- Papil hyperplasia	:		-	-	-	-	2	1
Grade 1:			-	-	-	-	1	1
Grade 3:			-	-	-	-	1	-
- Papil inflamm. inf.	:		-	-	-	-	1	-
Grade 1:			-	-	-	-	1	-
- Mineralization	:		-	-	-	-	-	1
Grade 3:			-	-	-	-	-	1
.....								
URINARY BLADDER	:		-	1	-	-	3	1
N.A.D.	:		-	1	-	-	2	1
.....								
- Infiltrate inflamm.	:		-	-	-	-	1	-
Grade 1:			-	-	-	-	1	-
- Hyperpl/hypert urot.:			-	-	-	-	1	-
Grade 2:			-	-	-	-	1	-

Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, DEATHS ONLY
Incidence table - Unscheduled deaths

	DOSE GROUP: 02		03		04	
SEX :	M	F	M	F	M	F
NO. ANIMALS:	-	1	-	1	3	2
ADRENAL GLANDS :	-	1	-	-	3	2
N.A.D. :	-	1	-	-	-	2
.....						
- Vacuol. glomerulosa :	-	-	-	-	1	-
Grade 3:	-	-	-	-	1	-
- Vacuol. fasciculata :	-	-	-	-	2	-
Grade 1:	-	-	-	-	1	-
Grade 2:	-	-	-	-	1	-
.....						
SCIATIC NERVE, LEFT :	-	1	-	-	3	1
N.A.D. :	-	1	-	-	2	1
.....						
- Infiltrate inflamm. :	-	-	-	-	1	-
Grade 2:	-	-	-	-	1	-
.....						
EPIDIDYMIDES :	-	-	-	-	3	-
N.A.D. :	-	-	-	-	2	-
.....						
- Cell debris, luminal:	-	-	-	-	1	-
Grade 2:	-	-	-	-	1	-
.....						
PROSTATE GLAND :	-	-	-	-	3	-
N.A.D. :	-	-	-	-	1	-
.....						
- Reduced ac. content :	-	-	-	-	2	-
Grade 2:	-	-	-	-	2	-
.....						
SEMINAL VESICLES :	-	-	-	-	3	-
N.A.D. :	-	-	-	-	1	-
.....						
- Reduced ac. content :	-	-	-	-	2	-
Grade 2:	-	-	-	-	2	-

Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0, DEATHS ONLY
Incidence table - Unscheduled deaths

	DOSE GROUP:	02		03		04	
SEX :		M	F	M	F	M	F
NO. ANIMALS:		-	1	-	1	3	2
UTERUS	:	-	1	-	-	-	1
N.A.D.	:	-	1	-	-	-	-
.....							
- Atrophy	:	-	-	-	-	-	1
Grade 3:		-	-	-	-	-	1
VAGINA	:	-	1	-	-	-	1
- Cycle: Estrus	:	-	1	-	-	-	-
- Atrophy, epithelial	:	-	-	-	-	-	1
Grade 2:		-	-	-	-	-	1
LARYNX	:	-	-	-	1	3	2
N.A.D.	:	-	-	-	1	2	2
.....							
- Inflammation, acute	:	-	-	-	-	1	-
Grade 1:		-	-	-	-	1	-
- Erosion/ulceration	:	-	-	-	-	1	-
Grade 2:		-	-	-	-	1	-
HARDERIAN GLANDS	:	-	1	-	1	3	2
N.A.D.	:	-	1	-	1	2	2
.....							
- Dilation glandular	:	-	-	-	-	1	-
Grade 1:		-	-	-	-	1	-
BONE MARROW, STERNUM	:	-	1	-	1	3	2
N.A.D.	:	-	1	-	1	1	-
.....							
- Increased adipocytes:		-	-	-	-	1	-
Grade 3:		-	-	-	-	1	-
- Atrophy	:	-	-	-	-	2	2
Grade 2:		-	-	-	-	-	1
Grade 3:		-	-	-	-	2	1

Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
 STATUS AT NECROPSY: K0, DEATHS ONLY
 Incidence table - Unscheduled deaths

	DOSE GROUP: 02		03		04	
SEX :	M	F	M	F	M	F
NO.ANIMALS:	-	1	-	1	3	2
PREPUTIAL GLANDS :	-	-	-	-	1	-
- Atrophy :	-	-	-	-	1	-
Grade 2:	-	-	-	-	1	-

Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
 Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
 Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1, DEATHS ONLY
Incidence table - Unscheduled deaths

	DOSE GROUP: 02		03		04	
SEX :	M	F	M	F	M	F
NO. ANIMALS:	-	-	-	-	3	2
GENERAL OBSERVATIONS :	-	-	-	-	-	1
- Gavage accident :	-	-	-	-	-	1
LUNG :	-	-	-	-	3	2
N.A.D. :	-	-	-	-	2	1
- Hemorrhage, pulmon. :	-	-	-	-	-	1
Grade 3:	-	-	-	-	-	1
- Inflamm. alv. acute :	-	-	-	-	1	-
Grade 1:	-	-	-	-	1	-
- Alveolar macrophages:	-	-	-	-	1	-
Grade 2:	-	-	-	-	1	-
- Inflamm. peribronch.:	-	-	-	-	-	1
Grade 1:	-	-	-	-	-	1
- Mineralization vasc.:	-	-	-	-	1	-
Grade 1:	-	-	-	-	1	-
THYMUS :	-	-	-	-	3	2
- Congestion/hemorrh. :	-	-	-	-	-	1
Grade 1:	-	-	-	-	-	1
- Depletion, lymphoid :	-	-	-	-	3	1
Grade 3:	-	-	-	-	2	1
Grade 4:	-	-	-	-	1	-
TRACHEA :	-	-	-	-	3	2
N.A.D. :	-	-	-	-	2	1
- Infiltrate inflamm. :	-	-	-	-	1	1
Grade 1:	-	-	-	-	1	1
ESOPHAGUS :	-	-	-	-	3	2
N.A.D. :	-	-	-	-	2	2
- Degen./necr. muscle :	-	-	-	-	1	-
Grade 1:	-	-	-	-	1	-

Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1, DEATHS ONLY
Incidence table - Unscheduled deaths

	DOSE GROUP: 02		03		04	
	SEX : M	F	M	F	M	F
NO. ANIMALS:	-	-	-	-	3	2
THYROID GLAND :	-	-	-	-	3	2
- Hypertrophy foll. c.:	-	-	-	-	3	2
Grade 1:	-	-	-	-	3	1
Grade 2:	-	-	-	-	-	1
- Cyst, ultimobranch. :	-	-	-	-	1	-
Grade 1:	-	-	-	-	1	-
STOMACH :	-	-	-	-	3	2
N.A.D. :	-	-	-	-	-	1
.....						
- Inflammation forest.:	-	-	-	-	1	1
Grade 1:	-	-	-	-	-	1
Grade 2:	-	-	-	-	1	-
- Hyperplasia squamous:	-	-	-	-	3	1
Grade 2:	-	-	-	-	2	1
Grade 3:	-	-	-	-	1	-
- Erosion/ulceration :	-	-	-	-	1	1
Grade 1:	-	-	-	-	1	1
- Hemorrhage :	-	-	-	-	1	-
Grade 2:	-	-	-	-	1	-
- Congestion :	-	-	-	-	2	-
Grade 1:	-	-	-	-	2	-

Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1, DEATHS ONLY
Incidence table - Unscheduled deaths

	DOSE GROUP: 02		03		04	
	SEX : M	F	M	F	M	F
NO. ANIMALS:	-	-	-	-	3	2
<hr/>						
LIVER :	-	-	-	-	3	2
- Infiltrate inflamm. :	-	-	-	-	3	1
Grade 1:	-	-	-	-	2	1
Grade 2:	-	-	-	-	1	-
- Hematopoiesis extram.:	-	-	-	-	-	1
Grade 1:	-	-	-	-	-	1
- Hypertrophy hepatoc.:	-	-	-	-	3	2
Grade 2:	-	-	-	-	2	1
Grade 3:	-	-	-	-	1	1
- Necrosis hepatocell.:	-	-	-	-	3	2
Grade 1:	-	-	-	-	-	1
Grade 3:	-	-	-	-	2	-
Grade 4:	-	-	-	-	1	1
- Necrosis coagulat. :	-	-	-	-	2	-
Grade 2:	-	-	-	-	1	-
Grade 3:	-	-	-	-	1	-
<hr/>						
SPLEEN :	-	-	-	-	3	2
N.A.D. :	-	-	-	-	1	-
<hr/>						
- Hematopoiesis extra.:	-	-	-	-	-	1
Grade 1:	-	-	-	-	-	1
- Pigmentation, hemos.:	-	-	-	-	2	2
Grade 1:	-	-	-	-	1	1
Grade 2:	-	-	-	-	1	1
<hr/>						
MESENT. LYMPH NODE :	-	-	-	-	3	2
N.A.D. :	-	-	-	-	-	2
<hr/>						
- Depletion, lymphoid :	-	-	-	-	2	-
Grade 2:	-	-	-	-	2	-
- Erythrocytes, sinus :	-	-	-	-	1	-
Grade 1:	-	-	-	-	1	-
- Sinus histiocytosis :	-	-	-	-	1	-
Grade 2:	-	-	-	-	1	-

Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1, DEATHS ONLY
Incidence table - Unscheduled deaths

	DOSE GROUP: 02		03		04	
SEX :	M	F	M	F	M	F
NO. ANIMALS:	-	-	-	-	3	2
PANCREAS :	-	-	-	-	3	2
N.A.D. :	-	-	-	-	2	1
.....						
- Degranulation acinar:	-	-	-	-	1	1
Grade 3:	-	-	-	-	1	1
.....						
MANDIB. LYMPH NODES :	-	-	-	-	2	2
N.A.D. :	-	-	-	-	1	2
.....						
- Erythrocytes, sinus :	-	-	-	-	1	-
Grade 1:	-	-	-	-	1	-
.....						
MANDIBULAR GLANDS :	-	-	-	-	3	2
N.A.D. :	-	-	-	-	2	2
.....						
- Reduced cont/atrophy:	-	-	-	-	1	-
Grade 2:	-	-	-	-	1	-

Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1, DEATHS ONLY
Incidence table - Unscheduled deaths

	DOSE GROUP: 02		03		04	
SEX :	M	F	M	F	M	F
NO. ANIMALS:	-	-	-	-	3	2
KIDNEYS :	-	-	-	-	3	2
- Infiltrate inflamm. :	-	-	-	-	2	-
Grade 1:	-	-	-	-	2	-
- Basophilia tubule :	-	-	-	-	3	-
Grade 2:	-	-	-	-	1	-
Grade 3:	-	-	-	-	2	-
- Congestion :	-	-	-	-	1	1
Grade 2:	-	-	-	-	1	1
- Vacuolar deg./necr. :	-	-	-	-	2	-
Grade 2:	-	-	-	-	2	-
- Eosinophilic content:	-	-	-	-	2	-
Grade 1:	-	-	-	-	2	-
- Casts hyaline :	-	-	-	-	-	1
Grade 2:	-	-	-	-	-	1
- Dilation, tubule :	-	-	-	-	3	1
Grade 2:	-	-	-	-	3	1
- Papil hyperplasia :	-	-	-	-	2	-
Grade 2:	-	-	-	-	2	-
- Papil inflamm. inf. :	-	-	-	-	1	-
Grade 1:	-	-	-	-	1	-
- Vacuolation tubular :	-	-	-	-	-	1
Grade 2:	-	-	-	-	-	1
URINARY BLADDER :	-	-	-	-	3	2
N.A.D. :	-	-	-	-	2	2
.....						
- Hyperpl/hypert urot.:	-	-	-	-	1	-
Grade 1:	-	-	-	-	1	-

Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1, DEATHS ONLY
Incidence table - Unscheduled deaths

	DOSE GROUP: 02		03		04	
SEX :	M	F	M	F	M	F
NO. ANIMALS:	-	-	-	-	3	2
ADRENAL GLANDS :	-	-	-	-	3	2
N.A.D. :	-	-	-	-	1	1
.....						
- Cortical tissue, ac.:	-	-	-	-	1	-
- Vacuol. glomerulosa :	-	-	-	-	1	-
Grade 1:	-	-	-	-	1	-
- Vacuol. fasciculata :	-	-	-	-	1	1
Grade 1:	-	-	-	-	1	-
Grade 2:	-	-	-	-	-	1
.....						
SCIATIC NERVE, LEFT :	-	-	-	-	3	2
N.A.D. :	-	-	-	-	2	2
.....						
- Demyelination :	-	-	-	-	1	-
Grade 2:	-	-	-	-	1	-
.....						
TESTES :	-	-	-	-	3	-
N.A.D. :	-	-	-	-	2	-
.....						
- Degenerat. germ cell:	-	-	-	-	1	-
Grade 2:	-	-	-	-	1	-
.....						
EPIDIDYMIDES :	-	-	-	-	3	-
N.A.D. :	-	-	-	-	2	-
.....						
- Cell debris, luminal:	-	-	-	-	1	-
Grade 1:	-	-	-	-	1	-
.....						
PROSTATE GLAND :	-	-	-	-	3	-
- Reduced ac. content :	-	-	-	-	3	-
Grade 1:	-	-	-	-	1	-
Grade 2:	-	-	-	-	2	-

Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: R1, DEATHS ONLY
Incidence table - Unscheduled deaths

	DOSE GROUP: 02		03		04	
SEX :	M	F	M	F	M	F
NO. ANIMALS:	-	-	-	-	3	2
SEMINAL VESICLES :	-	-	-	-	3	-
- Reduced ac. content :	-	-	-	-	3	-
Grade 1:	-	-	-	-	1	-
Grade 3:	-	-	-	-	2	-
UTERUS :	-	-	-	-	-	2
N.A.D. :	-	-	-	-	-	1
.....						
- Atrophy :	-	-	-	-	-	1
Grade 1:	-	-	-	-	-	1
VAGINA :	-	-	-	-	-	2
- Cycle: Metestrus :	-	-	-	-	-	2
- Infiltrate inflamm. :	-	-	-	-	-	2
Grade 1:	-	-	-	-	-	1
Grade 2:	-	-	-	-	-	1
LARYNX :	-	-	-	-	3	2
N.A.D. :	-	-	-	-	2	2
.....						
- Squamous metaplasia :	-	-	-	-	1	-
Grade 2:	-	-	-	-	1	-
BONE MARROW, STERNUM :	-	-	-	-	3	2
N.A.D. :	-	-	-	-	-	1
.....						
- Increased adipocytes:	-	-	-	-	3	1
Grade 1:	-	-	-	-	-	1
Grade 2:	-	-	-	-	2	-
Grade 3:	-	-	-	-	1	-
- Atrophy :	-	-	-	-	2	1
Grade 1:	-	-	-	-	1	-
Grade 2:	-	-	-	-	-	1
Grade 3:	-	-	-	-	1	-

Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
 STATUS AT NECROPSY: R1, DEATHS ONLY
 Incidence table - Unscheduled deaths

	DOSE GROUP: 02		03		04	
SEX :	M	F	M	F	M	F
NO.ANIMALS:	-	-	-	-	3	2
PREPUTIAL GLANDS :	-	-	-	-	1	-
- Atrophy :	-	-	-	-	1	-
Grade 2:	-	-	-	-	1	-

Group 02, 100 MG/KG, males: MTDID 7831 (100 MG/KG); females: MTDID 7831 (100 MG/KG)
 Group 03, 300 MG/KG, males: MTDID 7831 (300 MG/KG); females: MTDID 7831 (300 MG/KG)
 Group 04, 600 MG/KG, males: MTDID 7831 (600 MG/KG); females: MTDID 7831 (600 MG/KG)

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 01, CONTROL

ANIMAL NUMBER :

	1	2	3	4	5	6	7	8	9	10
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
HEART	-	+	-	-	-	-	-	+	+	+
- Infiltrate inflamm.	1.	.
- Necrosis, myofibers	2.	.	1.
- Cardiopathy, progr.	.	2.
.....										
AORTA	-	-	-	-	-	-	-	-	-	-
.....										
LUNG	-	-	-	+	-	+	-	-	+	+
- Inflamm. alv. acute	1.
- Alveolar macrophages	2.	.	.	.	1.
- Inflamm. peribronch.	.	.	.	1.	.	1.
- Edema alveolar/bron.	2.
- Mineralization vasc.	1.	.
.....										
THYMUS	-	-	+	+	+	-	-	-	-	-
- Depletion, lymphoid	1.
- Lymphocytolysis inc.	.	.	.	2.
- Hyperplasia, epith.	.	.	1.
.....										
TRACHEA	+	-	-	-	-	-	+	-	-	-
- Infiltrate inflamm.	1.	.	.	.
- Ectasia subm. glands	1.
.....										
ESOPHAGUS	+	+	-	+	-	-	-	-	-	-
- Degen./necr. muscle	1.	1.	.	1.
.....										
THYROID GLAND	+	+	-	+	-	+	-	-	+	-
- Hypertrophy foll. c.	2.	1.	.	1.	.	2.	.	.	1.	.
.....										
PARATHYROID GLANDS	-	(-	-	-	-	-	-	-	-
.....										
STOMACH	+	+	-G	+	+	+	+	+	+	+
- Inflammation forest.	2.	1.	.	1.	1.	1.	1.	2.	.	1.
- Hyperplasia squamous	2.	1.	.	.	2.	1.	2.	2.	1.	2.
- Erosion/ulceration	2.	.	.
- Hemorrhage	1.
- Edema	.	1.	.	.	.	2.	.	3.	.	2.
.....										
DUODENUM	-	-	-	-	-	-	-	-	-	-
.....										

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 01, CONTROL

ANIMAL NUMBER :

	1	2	3	4	5	6	7	8	9	10
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
JEJUNUM	-	-	-	-	-	-	-	-	-	-
.....										
ILEUM	-	-	-	-	-	-	-	-	-	-
.....										
PEYER'S PATCHES	-	+	+	-	-	-	-	+	+	-
- Vacuolation, incr.	.	1.	1.	1.	1.	.
.....										
CECUM	-	-	-	-	-	-	-	-	-	-
.....										
COLON	-	-	-	-	-	-	-	-	-	-
.....										
RECTUM	-	-	-	-	-	-	-	-	-	-
.....										
LIVER	+	+	+G	+	+	+	+G	+	+	+
- Infiltrate inflamm.	1.	.	1.	1.	1.	1.	1.	1.	1.	1.
- Infiltrat. peribil.	.	1.
- Accessory lobe	.	.	P.	.	.	.	P.	.	.	.
.....										
SPLEEN	+	+	+	+	+	+	+	+	+	+
- Pigmentation, hemos.	1.	1.	1.	1.	1.	1.	2.	2.	2.	2.
.....										
MESENT. LYMPH NODE	-	-	+	-	+	+	-	-	-	-
- Incr. macrophages	.	.	1.	.	1.	1.
.....										
PANCREAS	-	-	-	-	-	-	-	-	-	-
.....										
MANDIB. LYMPH NODES	-	-	-	-	-	-	-	-	+	-
- Erythrocytes, sinus	(2.	.
.....										
SUBLINGUAL GLANDS	-	-	-	-	-	-	-	-	-	-
.....										
MANDIBULAR GLANDS	-	-	-	-	-	-	-	-	-	-
.....										
KIDNEYS	+	+	-	+	+	+	+	+	+	+
- Hyaline droplet acc.	.	1.	.	1.	1.	1.	2.	2.	2.	2.
- Basophilia tubule	.	(1.	.	.	.	(1.	.	.	1.	.
- Eosinophilic content	(1.
- Casts hyaline	(1.
- Dilation, tubule	1.	.	.	2.	2.
.....										

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 01, CONTROL

ANIMAL NUMBER :

	1	2	3	4	5	6	7	8	9	10
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
URINARY BLADDER	-	-	-	-	-	-	-	-	-	-
ADRENAL GLANDS	-	-	+	-	-	-	-	-	+	+
- Cortical tissue, ac.	.	.	(P.	(P.	(P.
BRAIN	-	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	-	-	-	-	-	-	-	-	-	-
SCIATIC NERVE, LEFT	-	-	-	-	-	-	-	-	-	-
TESTES	-	-	-	+	-	-	-	-	-	-
- Atrophy, tubular	.	.	.	(1.
EPIDIDYMIDES	-	-	-	-	-	-	-	-	-	-
PROSTATE GLAND	+	-	-	-	-	-	-	-	-	-
- Infiltrate inflamm.	1.
SEMINAL VESICLES	-	-	-	-G	-	-	-	-	-	-
COAGULATING GLANDS	-	-	-	-	-	-	-	-	-	-
SKIN/SUBCUTIS	-	-	+	-	-	-	-	-	-	-
- Inflamm. exudative	.	.	1.
LARYNX	-	-	-	-	-	-	-	-	-	-
EYES	-	-	-	-	-	-	-	-	-	-
OPTIC NERVES	-	-	-	-	-	-	-	-	-	-
HARDERIAN GLANDS	+	-	+	-	-	-	-	-	-	-
- Infiltrate inflamm.	.	.	(1.
- Hemorrhage	(1.	.	(2.
SPINAL CORD, CERVIC.	-	-	-	-	-	-	-	-	-	-
SPINAL CORD, THORAC.	-	-	-	-	-	-	-	-	-	-

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 54/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, CONTROL

ANIMAL NUMBER :

	1	2	3	4	5	6	7	8	9	10
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
SPINAL CORD, LUMBAR	-	-	-	-	-	-	-	-	-	-
.....										
BONE, STERNUM	-	-	-	-	-	-	-	-	-	-
.....										
BONE MARROW, STERNUM	-	-	-	-	-	-	-	-	-	-
.....										
PREPUTIAL GLANDS	'	'	-G	'	'	'	'	'	'	'
.....										

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 01, CONTROL

ANIMAL NUMBER :

	11	12	13	14	15
	MR1	MR1	MR1	MR1	MR1
THYROID GLAND	-	+	+	-	+G
- Thymus, ectopic	(P.
- Hypertrophy foll. c.	.	1.	1.	.	.
.....					
STOMACH	+	-	-	+G	+
- Congestion	.	.	.	2.	.
- Cyst(s)	3.	.	.	.	1.
.....					
LIVER	+	-	+	-	-
- Infiltrate inflamm.	.	.	1.	.	.
- Infiltrat. peribil.	1.
.....					
KIDNEYS	-	+	-	-	+
- Hyaline droplet acc.	.	1.	.	.	1.
- Basophilia tubule	.	(1.	.	.	.
.....					
URINARY BLADDER	-	-	-	+	-
- Infiltrate inflamm.	.	.	.	1.	.
.....					
BONE, STERNUM	-	-	-	-	-
.....					
BONE MARROW, STERNUM	-	-	-	-	-
.....					

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 01, CONTROL

ANIMAL NUMBER :

	51	52	53	54	55	56	57	58	59	60
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
HEART	-	-	-	-	-	-	-	-	-	-
AORTA	-	-	-	-	-	-	-	-	-	-
LUNG	-	-	+	+	+	-	-	-	+	-
- Inflamm. peribronch.	.	.	.	1.	2.	.	.	.	1.	.
- Mineralization vasc.	.	.	1.
THYMUS	-	-	-	-	-	-	-	-	-	-
TRACHEA	-	-	-	-	-	-	-	-	-	-
ESOPHAGUS	-	-	-	-	-	-	-	-	-	-
THYROID GLAND	+	-	-	-	-	-	-	+	-	-
- Hypertrophy foll. c.	1.	.	.
- Cyst, ultimobranch. (2.
PARATHYROID GLANDS	-	-	-	-	(-	-	(-	-	-	-
STOMACH	-	-	-	+	-	+	+	-	-	+
- Inflammation forest.	.	.	.	2.	.	2.	.	.	.	1.
- Hyperplasia squamous	.	.	.	2.	.	2.	2.	.	.	1.
- Erosion/ulceration	2.
- Edema	.	.	.	2.	.	2.	.	.	.	1.
DUODENUM	-	-	-	-	-	-	-	-	-	-
JEJUNUM	-	-	-	-	-	-	-	-	-	-
ILEUM	-	-	-	-	-	-	-	-	-	-
PEYER'S PATCHES	-	-	-	-	+	+	-	+	-	-
- Vacuolation, incr.	2.	2.	.	3.	.	.
CECUM	-	-	-	-	-	-	-	-	-	-
COLON	-	-	-	-	-	-	-	-	-	-

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 01, CONTROL

ANIMAL NUMBER :

	51 FK0	52 FK0	53 FK0	54 FK0	55 FK0	56 FK0	57 FK0	58 FK0	59 FK0	60 FK0
RECTUM	-	-	-	-	-	-	-	-	-	-
LIVER	-	+	+	+	+	+	+	+	+	+G
- Infiltrate inflamm.	.	1.	1.	1.	1.	1.	1.	1.	.	1.
- Hematopoiesis extram.	.	.	1.	1.	1.	1.	1.	1.	1.	2.
- Infarction/torsion	P.
SPLEEN	+	+	+	+	+	+	+	+	+	+
- Hematopoiesis extra.	1.	2.	3.	1.	2.	2.	3.	2.	2.	3.
- Pigmentation, hemos.	2.	3.	1.	2.	2.	2.	2.	2.	1.	1.
MESENT. LYMPH NODE	+	+	+	-	+	-	+	-	+	+
- Incr. macrophages	1.	2.	2.	.	1.	.	2.	.	2.	1.
PANCREAS	-	-	-	-	-	-	-	-	-	-
MANDIB. LYMPH NODES	-	-	+G	-	-	-	-	+	+	-
- Congestion	(1.	(1.	.
- Erythrocytes, sinus	.	.	(2.
SUBLINGUAL GLANDS	-	-	-	-	-	-	-	-	-	-
MANDIBULAR GLANDS	-	-	-	-	-	-	-	-	-	-
KIDNEYS	-	+	-	+	-	-	+	+	-	-
- Infiltrate inflamm.	.	(1.
- Basophilia tubule	.	.	.	(1.	.	.	1.	.	.	.
- Casts hyaline	(1.	.	.
URINARY BLADDER	-	-	-	-	-	-	-	-	-	-
ADRENAL GLANDS	-	-	-	-	-	-	-	-	-	+
- Vacuol. glomerulosa	1.
- Hematopoiesis extram.	(1.
BRAIN	-	-	-	-	-	-	-	-	-	-
PITUITARY GLAND	-	-	-	-	-	-	-	-	-	-

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 01, CONTROL

ANIMAL NUMBER :

	51	52	53	54	55	56	57	58	59	60
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
SCIATIC NERVE, LEFT	-	-	-	-	-	-	-	-	-	-
.....										
OVARIES	-	-	-	-	+	+	-	-	-	-
- Hypertr. interst. c.	1.	1.
.....										
UTERUS	-	-	+G	-	+G	+G	+G	+G	-	+G
- Cyclic dilation	.	.	P.	.	P.	P.	P.	P.	.	P.
.....										
CERVIX	-	-	-	-	-	-	-	-	-	-
.....										
VAGINA	+	+	+	+	+	+	+	+	+	+
- Cycle: Proestrus	P.	.	P.	.	.	.	P.	.	.	P.
- Cycle: Estrus	P.	P.	.	P.	.	.
- Cycle: Metestrus	.	.	.	P.	P.	.
- Cycle: Diestrus	.	P.
.....										
SKIN/SUBCUTIS	-	-	-	-	-	-	-	-	-	-
.....										
MAMMARY GLAND	-	-	-	-	-	-	-	-	-	-
.....										
LARYNX	-	-	-	-	-	-	-	-	-	-
.....										
EYES	-	-	-	-	-	-	-	-	-	-
.....										
OPTIC NERVES	-	-	-	-	-	-	-	-	-	-
.....										
HARDERIAN GLANDS	-	-	-	+	-	-	-	-	-	-
- Infiltrate inflamm.	.	.	.	(2.
.....										
SPINAL CORD, CERVIC.	-	-	-	-	-	-	-	-	-	-
.....										
SPINAL CORD, THORAC.	-	-	-	-	-	-	-	-	-	-
.....										
SPINAL CORD, LUMBAR	-	-	-	-	-	-	-	-	-	-
.....										
BONE, STERNUM	-	-	-	-	-	-	-	-	-	-
.....										
BONE MARROW, STERNUM	-	-	-	-	-	-	-	-	-	-
.....										

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 59/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, CONTROL

ANIMAL NUMBER :

51 52 53 54 55 56 57 58 59 60
FK0 FK0 FK0 FK0 FK0 FK0 FK0 FK0 FK0 FK0

BODY CAVITIES +G ' ' ' ' ' ' ' ' ' '
- Fat necrosis 2.
.....

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 01, CONTROL

ANIMAL NUMBER :

	61	62	63	64	65
	FR1	FR1	FR1	FR1	FR1
THYMUS	-	-	-	-	-
.....					
THYROID GLAND	-	-	+	-	-
- Hypertrophy foll. c.	.	.	1.	.	.
.....					
STOMACH	-	-	+	-	-
- Vacuolation, lim. r.	.	.	1.	.	.
.....					
LIVER	+	+	+	+	+
- Infiltrate inflamm.	2.	1.	3.	1.	1.
- Necrosis coagulat.	.	.	1.	.	.
.....					
SPLEEN	+	+	+	+	+
- Pigmentation, hemos.	2.	2.	1.	2.	2.
.....					
KIDNEYS	-	-	-	-	-
.....					
URINARY BLADDER	-	-	-	-	-
.....					
ADRENAL GLANDS	-	+	-	+	-
- Vacuol. glomerulosa	.	(1.	.	1.	.
- Vacuol. fasciculata	.	2.	.	.	.
.....					
UTERUS	+G	+G	+G	+G	+G
- Cyclic dilation	P.	P.	P.	P.	P.
.....					
BONE, STERNUM	-	-	-	-	-
.....					
BONE MARROW, STERNUM	-	-	-	-	-
.....					

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 02, 100 MG/KG

ANIMAL NUMBER :

	16	17	18	19	20	21	22	23	24	25
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
THYROID GLAND	+	+	+	+	+	+	+	-	-	+
- Hypertrophy foll. c.	1.	2.	3.	1.	2.	3.	2.	.	.	1.
STOMACH	-	+G	+	-	+	+	-	-	-	+G
- Inflammation forest.	1.	1.
- Hyperplasia squamous	.	1.	1.	.	2.	2.
- Edema	.	1.	1.	.	2.	1.	.	.	.	1.
LIVER	+	+	+	+	+	+	+G	+	+G	+
- Infiltrate inflamm.	1.	.	.	.	1.	.	.	1.	1.	1.
- Hematopoiesis extram.	.	1.
- Hypertrophy hepatoc.	1.	1.	1.	1.	1.	1.	1.	1.	1.	1.
MANDIB.LYMPH NODES	+G	'	'	'	'	'	'	'	'	'
- Erythrocytes, sinus (2.										
KIDNEYS	+	-	-G	+	-	-	+	G	-	+
- Hyaline droplet acc.	1.	.	.	1.	.	.	1.	.	.	1.
- Eosinophilic content	1.
URINARY BLADDER	-	-	-	-	-	-	-	-	-	-
BONE, STERNUM	-	-	-	-	-	-	-	-	-	-
BONE MARROW, STERNUM	+	-	-	-	-	-	-	+	-	-
- Increased adipocytes	1.	1.	.	.
PREPUTIAL GLANDS	'	'	-G	'	'	'	-G	'	-G	'
LACRIMAL GLANDS	'	'	'	'	'	+G	'	'	'	'
- Atrophy, glandular						(3.				

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 02, 100 MG/KG

ANIMAL NUMBER :

	66	67	68	69	70	71	72	73	74	75
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0+	FK0
GENERAL OBSERVATIONS	'	'	'	'	'	'	'	'	'!	'
HEART	'	'	'	'	'	'	'	'	-	'
AORTA	'	'	'	'	'	'	'	'	-	'
LUNG	'	'	'	'	'	'	'	+G	A	'
- Alveolar macrophages								1.	.	
- Mineralization vasc.								1.	.	
THYMUS	-	-	-	+	-	-	-	-	+G	-
- Congestion/hemorrh.	2.	.
- Lymphocytolysis inc.	.	.	.	1.
TRACHEA	'	'	'	'	'	'	'	'	A	'
ESOPHAGUS	'	'	'	'	'	'	'	'	-	'
THYROID GLAND	-	+	-	-	+	-	+	-	-	-
- Thymus, ectopic	(P.
- Hypertrophy foll. c.	.	1.	1.	.	.	.
PARATHYROID GLANDS	'	'	'	'	'	'	'	'	-	'
STOMACH	+G	-	+	-	+G	+	+	+G	-	-
- Inflammation forest.	2.	.	.	.	1.	.	2.	3.	.	.
- Hyperplasia squamous	2.	.	1.	.	.	1.	2.	3.	.	.
- Erosion/ulceration	1.	2.	.	.
- Edema	2.	.	.	.	1.	.	1.	1.	.	.
DUODENUM	'	'	'	'	'	'	'	'	A	'
JEJUNUM	'	'	'	'	'	'	'	'	A	'
ILEUM	'	'	'	'	'	'	'	'	A	'
PEYER'S PATCHES	'	'	'	'	'	'	'	'	-	'
CECUM	'	'	'	'	'	'	'	'	A	'

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 02, 100 MG/KG

ANIMAL NUMBER :

	66	67	68	69	70	71	72	73	74	75
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0+	FK0
COLON	†	†	†	†	†	†	†	†	A	†
RECTUM	†	†	†	†	†	†	†	†	A	†
LIVER	+G	+	+	+	+	+	+	+	+*	+
- Infiltrate inflamm.	1.	1.	1.	1.	1.	1.	1.	1.	.	1.
- Hematopoiesis extram.	1.
- Hypertrophy hepatoc.	1.	1.	.	.	2.	.
- Hepatodiaphr. nodule	P.
- Necrosis coagulat.	2.	.
SPLEEN	+	+	+	+	+	+	+	+	AG	+
- Hematopoiesis extra.	.	1.	.	.	1.	1.	1.	1.	.	.
- Pigmentation, hemos.	2.	2.	1.	2.	2.	2.	1.	2.	.	2.
MESENT. LYMPH NODE	†	†	†	†	†	†	†	†	-G	†
PANCREAS	†	†	†	†	†	†	†	†	-	†
MANDIB. LYMPH NODES	†	†	†	†	†	†	†	†	+G	†
- Congestion									2.	
SUBLINGUAL GLANDS	†	†	†	†	†	†	†	†	-	†
MANDIBULAR GLANDS	†	†	†	†	†	†	†	†	-	†
KIDNEYS	-	-	-	-	-	-	-	-	A	+
- Cyst	(2.
URINARY BLADDER	-	-	-	-	-	-	-	-	-	-
ADRENAL GLANDS	-	-	-	-	+	-	-	-	-	+
- Vacuol. glomerulosa	1.	1.
BRAIN	†	†	†	†	†	†	†	†	-	†
PITUITARY GLAND	†	†	†	†	†	†	†	†	-	†
SCIATIC NERVE, LEFT	†	†	†	†	†	†	†	†	-	†

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 02, 100 MG/KG

ANIMAL NUMBER :

	66	67	68	69	70	71	72	73	74	75
	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0+	FK0
OVARIES	'	'	'	'	'	'	'	'	-	'
UTERUS	'	'	+G	+G	'	'	+G	'	-	+G
- Cyclic dilation			P.	P.			P.		.	P.
CERVIX	'	'	'	'	'	'	'	'	-	'
VAGINA	'	'	'	'	'	'	'	'	+	'
- Cycle: Estrus									P.	
SKIN/SUBCUTIS	'	'	'	'	'	'	'	'	-	'
MAMMARY GLAND	'	'	'	'	'	'	'	'	-	'
LARYNX	'	'	'	'	'	'	'	'	A	'
EYES	'	'	'	'	'	'	'	'	A	'
OPTIC NERVES	'	'	'	'	'	'	'	'	-	'
HARDERIAN GLANDS	'	'	'	'	'	'	'	'	-	'
SPINAL CORD, CERVIC.	'	'	'	'	'	'	'	'	-	'
SPINAL CORD, THORAC.	'	'	'	'	'	'	'	'	-	'
SPINAL CORD, LUMBAR	'	'	'	'	'	'	'	'	-	'
BONE, STERNUM	-	-	-	-	-	-	-	-	-	-
BONE MARROW, STERNUM	-	-	-	-	-	-	+	-	-	-
- Increased adipocytes	1.	.	.	.
PARATHYMIC LN.	'	'	'	+G	'	'	'	'	'	'
- Lymphoid hyperplasia				1.						

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 03, 300 MG/KG

ANIMAL NUMBER :

	26	27	28	29	30	31	32	33	34	35
	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0	MK0
THYMUS	-G	'	-G	'	'	'	+G	'	+G	'
- Congestion/hemorrh.	1.	.	1.	.
THYROID GLAND	+G	+	+	+	+	+	+	+	-G	+
- Hypertrophy foll. c.	2.	1.	.	2.	2.	1.	1.	1.	.	2.
- Cyst, ultimobranch.	.	.	1.
STOMACH	+	+	+	+	+	-	+	-	+	+
- Inflammation forest.	1.	1.	2.	2.	1.
- Hyperplasia squamous	2.	1.	2.	1.	1.	.	2.	.	2.	.
- Erosion/ulceration	1.	.
- Edema	2.	.	2.
LIVER	+G	+G	+G	+G	+G	+G	+G	+G	+G	+G
- Infiltrate inflamm.	1.	1.	.	.	1.	1.	1.	.	1.	1.
- Hypertrophy hepatoc.	2.	1.	3.	2.	2.	2.	1.	2.	2.	2.
- Accessory lobe	.	.	P.
- Necrosis coagulat.	.	1.
KIDNEYS	-	-G	-	-	+	-G	+	-G	-	+
- Hyaline droplet acc.	1.	1.
- Basophilia tubule	(1.	.	.	.
URINARY BLADDER	0	+	-	-	-	-	-	+	+	+
- Infiltrate inflamm.	2.	.	1.
- Hyperpl/hypert urot.	.	1.	2.	1.	2.
- Edema	1.	.	.
PROSTATE GLAND	'	'	'	'	-G	'	'	'	'	'
BONE, STERNUM	-	-	-	-	-	-	-	-	-	-
BONE MARROW, STERNUM	-	-	-	+	+	+	-	-	+	-
- Increased adipocytes	.	.	.	2.	1.	1.	.	.	1.	.
PREPUTIAL GLANDS	'	'	'	'	'	'	'	'	-G	'

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 03, 300 MG/KG

ANIMAL NUMBER :

	76	77	78	79	80	81	82	83	84	85
	FK0	FK0+	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
GENERAL OBSERVATIONS	†	†	†	†	†	†	†	†	†	†
HEART	†	-	†	†	†	†	†	†	†	†
AORTA	†	-	†	†	†	†	†	†	†	†
LUNG	†	+	†	†	†	†	†	†	†	†
- Mineralization vasc.		1.								
THYMUS	+	+G	+	+	-	-	-	-	+	+
- Congestion/hemorrh.	.	2.	1.
- Lymphocytolysis inc.	.	.	1.
- Hyperplasia, epith.	.	.	.	1.	1.	.
- Cystic ducts	1.
TRACHEA	†	-	†	†	†	†	†	†	†	†
ESOPHAGUS	†	-	†	†	†	†	†	†	†	†
THYROID GLAND	-	A	+	-	-G	-	+	-G	-	+
- Hypertrophy foll. c.	.	.	1.	.	.	.	1.	.	.	1.
PARATHYROID GLANDS	†	A	†	†	†	†	†	†	†	†
STOMACH	-	AG	+G	-	-	+	+	+	-	-
- Inflammation forest.	.	.	2.	1.	.	.
- Hyperplasia squamous	.	.	3.	.	.	1.	1.	3.	.	.
- Erosion/ulceration	.	.	2.
- Edema	2.	.	.
DUODENUM	†	A	†	†	†	†	†	†	†	†
JEJUNUM	†	A	†	†	†	†	†	†	†	†
ILEUM	†	0	†	†	†	†	†	†	†	†
PEYER'S PATCHES	†	0	†	†	†	†	†	†	†	†
CECUM	†	0	†	†	†	†	†	†	†	†

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 03, 300 MG/KG

ANIMAL NUMBER :

	76	77	78	79	80	81	82	83	84	85
	FK0	FK0+	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
COLON	'	0	'	'	'	'	'	'	'	'
RECTUM	'	0	'	'	'	'	'	'	'	'
LIVER	+	+G	+G	+	+G	+G	+	+	+	+
- Infiltrate inflamm.	1.	2.	1.	1.	1.	1.	1.	1.	1.	1.
- Hypertrophy hepatoc.	1.	2.	1.	2.	1.	2.	1.	1.	1.	2.
- Necrosis hepatocell.	1.	.
SPLEEN	+	A	+	+	+	+	+	+	+	+
- Hematopoiesis extra.	.	.	.	1.	1.	.	.	1.	.	3.
- Pigmentation, hemos.	2.	.	1.	2.	2.	2.	3.	2.	1.	3.
MESENT. LYMPH NODE	'	0	'	'	'	'	'	'	'	'
PANCREAS	'	A	'	'	'	'	'	'	'	'
MANDIB. LYMPH NODES	'	-	'	'	'	'	'	+G	'	'
- Erythrocytes, sinus		.						(3.		
SUBLINGUAL GLANDS	'	A	'	'	'	'	'	'	'	'
MANDIBULAR GLANDS	'	A	'	'	'	'	'	'	'	'
KIDNEYS	+	A	-	+	+G	+G	-	-	-	+
- Basophilia tubule	(1.
- Papil eosin. content	.	.	.	1.	(1.	(1.
- Mineralization	(1.	.	.	(1.
- Dilation, pelvis	3.
URINARY BLADDER	0	0	+	+	-	-	-	-	-	-
- Hyperpl/hypert urot.	.	.	1.	1.
ADRENAL GLANDS	-	AG	-	+	-	+	+	+	-	+
- Cortical tissue, ac.	(P.	.	(P.	.	.
- Vacuol. glomerulosa	.	.	.	1.	.	1.	1.	.	.	1.
BRAIN	'	-	'	'	'	'	'	'	'	'

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 03, 300 MG/KG

ANIMAL NUMBER :

	76	77	78	79	80	81	82	83	84	85
	FK0	FK0+	FK0	FK0	FK0	FK0	FK0	FK0	FK0	FK0
PITUITARY GLAND	†	-	†	†	†	†	†	†	†	†
SCIATIC NERVE, LEFT	†	0	†	†	†	†	†	†	†	†
OVARIES	†	0	†	†	†	-G	†	†	†	†
UTERUS	†	0	†	+G	†	+G	†	+G	†	+G
- Cyclic dilation		.		P.		P.		P.		P.
CERVIX	†	0	†	†	†	†	†	†	†	†
VAGINA	†	0	†	†	†	†	†	†	†	†
SKIN/SUBCUTIS	†	-	†	†	†	†	†	†	†	†
MAMMARY GLAND	†	0	†	†	†	†	†	†	†	†
LARYNX	†	-	†	†	†	†	†	†	†	†
EYES	†	A	†	†	†	†	†	†	†	†
OPTIC NERVES	†	-	†	†	†	†	†	†	†	†
HARDERIAN GLANDS	†	-	†	†	†	†	†	†	†	†
SPINAL CORD, CERVIC.	†	-	†	†	†	†	†	†	†	†
SPINAL CORD, THORAC.	†	-	†	†	†	†	†	†	†	†
SPINAL CORD, LUMBAR	†	-	†	†	†	†	†	†	†	†
BONE, STERNUM	-	-	-	-	-	-	-	-	-	-
BONE MARROW, STERNUM	-	-	+	-	-	+	-	-	-	-
- Increased adipocytes	.	.	1.	.	.	1.
RENAL LYMPH NODE	†	0G	†	†	†	†	†	†	†	†
BODY CAVITIES	†	†	†	†	†	†	†	†	†	†

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 04, 600 MG/KG

ANIMAL NUMBER :

	36	37	38	39	40	41	42	43	44	45
	MK0+	MK0	MK0	MK0	MK0+	MK0	MK0	MR1	MK0+	MR1
GENERAL OBSERVATIONS	'	'	'	'	'!	'	'	'	+	'
- Gavage accident									P.	
HEART	-	-	-	-	-G	-	-	'	-	'
AORTA	-	-	-	-	-	-	-	'	-	'
LUNG	-	-	+	+	-	+	+	'	-	'
- Alveolar macrophages	.	.	2.	.	.	2.	2.		.	
- Inflamm. peribronch.	.	.	1.	1.	.	1.	.		.	
- Mineralization vasc.	1.	.		.	
THYMUS	+G	-	+G	-	+G	-	+G	'	-	'
- Depletion, lymphoid	3.	.	1.	.	4.	.	1.		.	
TRACHEA	-	-	-	-	+	+	-	'	-G	'
- Inflammation granul.	1*	.	.		.	
- Ectasia subm. glands	1.	.		.	
ESOPHAGUS	-	-	-	-	-	-	-	'	+G	'
- Hemorrhage		3.	
THYROID GLAND	-	+	+	+	-	+	+	-	+	+G
- Hypertrophy foll. c.	.	2.	2.	2.	.	3.	2.	.	1.	2.
PARATHYROID GLANDS	0	-	-	-	-	-	-	'	-	'
STOMACH	+G	-G	+G	+	+	+G	+	+	+G	-
- Inflammation forest.	2.	.	.	1.
- Inflammation, gland.	1.	2.	.	2.	.	.
- Hyperplasia squamous	3.	.	1.	2.	3.	3.	1.	.	.	.
- Erosion/ulceration	2.	.	.	.	1.	1.
- Hemorrhage	1.
- Congestion	1.	.	.	.	1.	.	.	.	1.	.
- Cyst(s)	.	.	2.
- Vacuolation, lim. r.	2.	.	.
DUODENUM	-	-	-	-	-	-	-	'	-	'

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 04, 600 MG/KG

ANIMAL NUMBER :

	36	37	38	39	40	41	42	43	44	45
	MK0+	MK0	MK0	MK0	MK0+	MK0	MK0	MR1	MK0+	MR1
JEJUNUM	-	-	-	-	-	-	-	!	-	!
.....										
ILEUM	-	-	-	-	-	-	-	!	-	!
.....										
PEYER'S PATCHES	-	-	-	-	-	-	-	!	-	!
.....										
CECUM	-	-	-	-	-	-	-	!	-	!
.....										
COLON	-	-	-	-	-	-	-	!	-	!
.....										
RECTUM	-	-	-	-	-	-	-	!	-	!
.....										
LIVER	+G	+G	+G	+G	+G	+G	+G	-	+G	-G
- Infiltrate inflamm.	.	1.	.	1.	.	1.	1.	.	.	.
- Hypertrophy hepatoc.	3.	2.	3.	3.	2.	3.	3.	.	2.	.
- Necrosis hepatocell.	4.	1.	2.	2.	2.	2.	2.	.	2.	.
- Necrosis coagulat.	2.	.	1.	.	3.	.	2.	.	.	.
.....										
SPLEEN	+	+	+G	+	+G	+	+	!	+	!
- Hematopoiesis extra.	2.	.	1.	.
- Pigmentation, hemos.	1.	2.	2.	2.	.	2.	1.	.	.	.
- Depletion, lymphoid	4.
.....										
MESENT. LYMPH NODE	-	-	+G	+	+	+	+	!	-	!
- Depletion, lymphoid	2.
- Erythrocytes, sinus	1.	1.	.	.	.
- Incr. macrophages	.	.	1.	1.
- Sinus histiocytosis	2.
.....										
PANCREAS	-	-	-	-	-	-	-	!	+	!
- Vacuolation, acinar	1.	.
.....										
MANDIB. LYMPH NODES	-	-	(-	+	-	-	-	!	-	!
- Erythrocytes, sinus	.	.	.	(2.
.....										
SUBLINGUAL GLANDS	-	-	-	-	-	-	-	!	-	!
.....										
MANDIBULAR GLANDS	-	-	-	-	+	-	-	!	-	!
- Reduced cont/atrophy	3.
.....										

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 04, 600 MG/KG

ANIMAL NUMBER :

	36	37	38	39	40	41	42	43	44	45
	MK0+	MK0	MK0	MK0	MK0+	MK0	MK0	MR1	MK0+	MR1
KIDNEYS	+G	+G	+G	+G	+	+G	+G	+	-G	+
- Infiltrate inflamm.	(1.	.	1.
- Hyaline droplet acc.	.	1.	.	1.
- Basophilia tubule	(2.	.	2.	.	.	(1.
- Vacuolar deg./necr.	(2.	.	.	.	3.	.	(1.	.	.	.
- Eosinophilic content	.	(2.	2.	1.	1.	1.	(1.	.	.	.
- Casts granular	.	.	2.
- Pigment yellow-brown	1.	.	1.
- Dilation, tubule	1.	.	.	.	2.
- Papil hyperplasia	1.	.	1.	.	3.	.	(1.	.	.	.
- Papil inflamm. inf.	(1.
.....										
URINARY BLADDER	+	+	+	+G	-	+	-	+	-	+
- Infiltrate inflamm.	1.	.	.	1.	.	2.
- Hyperpl/hypert urot.	2.	1.	1.	3.	.	2.	.	2.	.	1.
- Uroliths	.	.	.	P*
.....										
ADRENAL GLANDS	+	+	-	-	+	-	-	!	+	!
- Vacuol. glomerulosa	3.	1.
- Vacuol. fasciculata	.	1.	.	.	2.	.	.	.	1.	.
.....										
BRAIN	-	-	-	-	-*	-	-	!	-	!
.....										
PITUITARY GLAND	-	-	-	-	-	-	-	!	-	!
.....										
SCIATIC NERVE, LEFT	-	-	-	-	+	-	-	!	-	!
- Infiltrate inflamm.	2.
.....										
TESTES	-	-	-	-	-	-	-	!	-	!
.....										
EPIDIDYMIDES	-	-	-	-	+	-	-	!	-	!
- Cell debris, luminal	2.
.....										
PROSTATE GLAND	+G	-	-G	-	+G	-	-	!	-	!
- Reduced ac. content	2.	.	.	.	2.
.....										
SEMINAL VESICLES	+G	-	-G	-	+G	-	-	!	-	!
- Reduced ac. content	2.	.	.	.	2.
.....										

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 04, 600 MG/KG

ANIMAL NUMBER :

	36	37	38	39	40	41	42	43	44	45
	MK0+	MK0	MK0	MK0	MK0+	MK0	MK0	MR1	MK0+	MR1
COAGULATING GLANDS	-	-	-	-	-	-	-	'	-	'
SKIN/SUBCUTIS	-	-	-	-	-	-	-	'	-	'
LARYNX	-	-	-	-	+	-	-	'	-	'
- Inflammation, acute	1.
- Erosion/ulceration	2.
EYES	-	-	-	-	-	-	-	'	-	'
OPTIC NERVES	-	-	-	-	-	-	(-	' (-	-	'
HARDERIAN GLANDS	+	-	-	+	-	-	-	'	-	'
- Dilation glandular	1.
- Hemorrhage	.	.	.	(1.
SPINAL CORD, CERVIC.	-	-	-	-	-	-	-	'	-	'
SPINAL CORD, THORAC.	-	-	-	-	-	-	-	'	-	'
SPINAL CORD, LUMBAR	-	-	-	-	-	-	-	'	-	'
BONE, STERNUM	-	-	-	-	-	-	-	-	-	-
BONE MARROW, STERNUM	+	-	+	-	+	-	-	+	-	+
- Increased adipocytes	3.	.	3.	1.	.	2.
- Atrophy	3.	.	.	.	3.
PREPUTIAL GLANDS	'	'	+G	'	+G	'	'	'	'	'
- Infiltrate inflamm.	.	.	(1.
- Atrophy	2.
BODY CAVITIES	'	'	'	'	'	'	'	'	'	'

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 04, 600 MG/KG

ANIMAL NUMBER :

46 47 48 49 50
 MR1 MR1+ MR1+ MR1 MR1+

GENERAL OBSERVATIONS	46 MR1	47 MR1+	48 MR1+	49 MR1	50 MR1+
HEART	'	'!	'!	'	'!
AORTA	'	-	-	'	-
LUNG	'	-	-	'	+G
- Inflamm. alv. acute		.	.		1.
- Alveolar macrophages		.	.		2.
- Mineralization vasc.		.	.		1.
THYMUS	'	+G	+G	'	+G
- Depletion, lymphoid		3.	4.		3.
TRACHEA	'	-	-	'	+G
- Infiltrate inflamm.		.	.		1.
ESOPHAGUS	'	+	-	'	-
- Degen./necr. muscle		1.	.		.
THYROID GLAND	-	+	+	+	+
- Hypertrophy foll. c.	.	1.	1.	1.	1.
- Cyst, ultimobranch.	.	.	(1.	.	.
PARATHYROID GLANDS	'	-	-	'	-
STOMACH	+	+G	+G	+	+G
- Inflammation forest.	.	2.	.	.	.
- Inflammation, gland.	1.	.	.	1.	.
- Hyperplasia squamous	.	3.	2.	.	2.
- Erosion/ulceration	.	1.	.	.	.
- Hemorrhage	.	.	2.	.	.
- Congestion	.	1.	.	.	1.
- Vacuolation, lim. r.	2.	.	.	1.	.
DUODENUM	'	-	-	'	-
JEJUNUM	'	-	-	'	-

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 04, 600 MG/KG

ANIMAL NUMBER :

	46	47	48	49	50
	MR1	MR1+	MR1+	MR1	MR1+
ILEUM	'	-	-	'	-
.....					
PEYER'S PATCHES	'	-	-	'	-
.....					
CECUM	'	-	-	'	-
.....					
COLON	'	-	-	'	-
.....					
RECTUM	'	-	-	'	-
.....					
LIVER	-	+G	+G	+G	+G
- Infiltrate inflamm.	.	1.	2.	1.	1.
- Hypertrophy hepatoc.	.	2.	2.	.	3.
- Pigment deposition	.	.	.	2.	.
- Necrosis hepatocell.	.	3.	4.	.	3.
- Necrosis coagulat.	.	3.	2.	.	.
.....					
SPLEEN	'	-	+	'	+G
- Pigmentation, hemos.	.	.	2.	.	1.
.....					
MESENT. LYMPH NODE	'	+	+	'	+
- Depletion, lymphoid	.	2.	2.	.	.
- Erythrocytes, sinus	.	1.	.	.	.
- Sinus histiocytosis	2.
.....					
PANCREAS	'	+	-	'	-
- Degranulation acinar	.	3.	.	.	.
.....					
MANDIB. LYMPH NODES	'	0	+	'	-
- Erythrocytes, sinus	.	(1.	.	.	.
.....					
SUBLINGUAL GLANDS	'	-	-	'	-
.....					
MANDIBULAR GLANDS	'	+	-	'	-
- Reduced cont/atrophy	.	2.	.	.	.
.....					

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 04, 600 MG/KG

ANIMAL NUMBER :

	46	47	48	49	50
	MR1	MR1+	MR1+	MR1	MR1+
KIDNEYS	+	+G	+G	-	+
- Infiltrate inflamm.	. (1.	.	.	. (1.	.
- Basophilia tubule	. (2.	(3.	.	.	3.
- Congestion	.	2.	.	.	.
- Vacuolar deg./necr.	.	2.	2*	.	.
- Eosinophilic content	.	1.	1.	.	.
- Pigment yellow-brown	1.
- Dilatation, tubule	.	2.	(2.	.	2.
- Papil hyperplasia	.	.	2*	.	2.
- Papil inflamm. inf.	(1.
.....					
URINARY BLADDER	-	-	-	+	+
- Infiltrate inflamm.	.	.	.	1.	.
- Hyperpl/hypert urot.	.	.	.	2.	1.
.....					
ADRENAL GLANDS	'	-	+	'	+
- Cortical tissue, ac.	.	.	.	(P.	.
- Vacuol. glomerulosa	1.
- Vacuol. fasciculata	.	(1.	.	.	.
.....					
BRAIN	'	-	-	'	-
.....					
PITUITARY GLAND	'	-	-	'	-
.....					
SCIATIC NERVE, LEFT	'	-	+	'	-
- Demyelination	.	.	2.	.	.
.....					
TESTES	'	-	-	'	+
- Degenerat. germ cell	.	.	.	(2.	.
.....					
EPIDIDYMIDES	'	-	-	'	+
- Cell debris, luminal	.	.	.	(1.	.
.....					
PROSTATE GLAND	'	+	+G	'	+G
- Reduced ac. content	.	1.	2.	.	2.
.....					
SEMINAL VESICLES	'	+	+G	'	+G
- Reduced ac. content	.	1.	3.	.	3.
.....					

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 04, 600 MG/KG

ANIMAL NUMBER :

	46	47	48	49	50
	MR1	MR1+	MR1+	MR1	MR1+
COAGULATING GLANDS	†	-	-	†	-
SKIN/SUBCUTIS	†	-	-	†	-
LARYNX	†	-	-	†	+
- Squamous metaplasia		.	.		2.
EYES	†	-	-	†	-
OPTIC NERVES	†	-	-	†	-
HARDERIAN GLANDS	†	-	-	†	-G
SPINAL CORD, CERVIC.	†	-	-	†	-
SPINAL CORD, THORAC.	†	-	-	†	-
SPINAL CORD, LUMBAR	†	-	-	†	-
BONE, STERNUM	-	-	-	-	-
BONE MARROW, STERNUM	-	+	+	-	+
- Increased adipocytes	.	2.	3.	.	2.
- Atrophy	.	3.	.	.	1.
PREPUTIAL GLANDS	†	+G	†	†	†
- Atrophy		2.			

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 04, 600 MG/KG

ANIMAL NUMBER :

	86	87	88	89	90	91	92	93	94	95
	FK0	FK0	FK0+	FK0	FK0	FK0	FK0	FK0+	FR1	FR1
GENERAL OBSERVATIONS	'	'	'!	'	'	'	'	'!	'	'
HEART	-	-	-	-	-	-	-	-	'	'
AORTA	-	-	-	-	-	-	-	-	'	'
LUNG	-	+	-	-	-	-	+	+	'	'
- Inflamm. alv. acute	1.	.	.
- Alveolar macrophages	1.	.	.	.
- Inflamm. granulomat.	.	1.
THYMUS	+	-	+G	-	-	+	+	+G	+G	-
- Congestion/hemorrh.	1.	4.	1.	.
- Depletion, lymphoid	.	.	4.	4.	.	.
- Lymphocytolysis inc.	1.	1.	.	.	.
- Hyperplasia, epith.	1.
TRACHEA	-	-	-	-	-	+	-	-	'	'
- Infiltrate inflamm.	1.
ESOPHAGUS	-	-	-	-	-	-	-	-	'	'
THYROID GLAND	+	+	-	+G	+	+	+	A	+	-
- Thymus, ectopic	.	.	.	P.
- Hypertrophy foll. c.	2.	1.	.	1.	2.	2.	1.	.	1.	.
- Cyst, ultimobranch.	(1.
PARATHYROID GLANDS	-	-	(-	-	(-	-	(-	-	'	'
STOMACH	-G	+	+G	+	+G	+	+G	-	+	-
- Inflammation forest.	.	1.	1.	.	2.	.	2.	.	1.	.
- Hyperplasia squamous	.	1.	1.	1.	3.	1.	3.	.	1.	.
- Erosion/ulceration	.	.	1.	.	2.	.	1.	.	.	.
- Hemorrhage	2.
- Vacuolation, lim. r.	1.	.
- Dilated gastric pits	1.	.
- Edema	2.
DUODENUM	-	-	-	-	-	-	-	0	'	'

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 04, 600 MG/KG

ANIMAL NUMBER :

	86	87	88	89	90	91	92	93	94	95
	FK0	FK0	FK0+	FK0	FK0	FK0	FK0	FK0+	FR1	FR1
JEJUNUM	-	-	-	-	-	-	-	0	'	'
.....										
ILEUM	-	-	-	-	-	-	-	0	'	'
.....										
PEYER'S PATCHES	-	-	-	-	-	-	-	0	'	'
.....										
CECUM	-	-	-	-	-	-	-	0	'	'
.....										
COLON	-	-	-	-	-	-	-	0	'	'
.....										
RECTUM	-	-	-	-	-	-	-	0	'	'
.....										
LIVER	+G	+G	+	+G	+G	+G	+G	0	+G	+
- Infiltrate inflamm.	1.	.	1.	1.	1.	1.	.	.	1.	1.
- Hypertrophy hepatoc.	3.	3.	2.	3.	3.	3.	3.	.	.	.
- Vacuolation hepatoc.	1.	2.
- Pigment deposition	2.
- Necrosis hepatocell.	1.	2.	1.	2.	2.	1.	3.	.	1.	.
- Necrosis coagulat.	.	.	3.	.	.	.	1.	.	.	.
.....										
SPLEEN	+	+	+G	+	+	+	+	0	+	+
- Hematopoiesis extra.	1.	.	.	1.	1.	1.
- Pigmentation, hemos.	2.	3.	.	2.	2.	2.	3.	.	2.	2.
- Atrophy red pulp	.	.	2.
.....										
MESENT. LYMPH NODE	+	+	-	+	-	+	+	0	'	'
- Incr. macrophages	1.	1.	.	1.	.	1.	1.	.		
.....										
PANCREAS	-	-	+	-	-	-	-	0	'	'
- Degranulation acinar	.	.	2.		
.....										
MANDIB. LYMPH NODES	-	-	-	+	-	+	(-	(-	'	'
- Erythrocytes, sinus	.	.	.	(1.		
- Pigmentation	(1.	.	.		
.....										
SUBLINGUAL GLANDS	-	-	-	-	-	-	-	-	'	'
.....										
MANDIBULAR GLANDS	-	-	-	-	-	-	-	A	'	'
.....										

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 04, 600 MG/KG

ANIMAL NUMBER :

	86	87	88	89	90	91	92	93	94	95
	FK0	FK0	FK0+	FK0	FK0	FK0	FK0	FK0+	FR1	FR1
KIDNEYS	+G	+G	+	-	-G	+G	+G (A		+G	-G
- Infiltrate inflamm.	(2.	.	.	.
- Basophilia tubule	.	.	4.	.	.	.	3*	.	1.	.
- Eosinophilic content	(1.	(1.	(1.
- Casts granular	.	.	2.
- Dilation, tubule	(1.
- Papil hyperplasia	2.	.	(1.	.	.	.	2.	.	.	.
- Papil eosin. content	2*	.	.	.
- Calculus,	(3*	(2.	.	.	.
- Mineralization	.	.	3.	.	.	.	(1.	.	.	.
.....										
URINARY BLADDER	+	+	-	+	-	-	-	0	+	+
- Hyperpl/hypert urot.	1.	1.	.	1.	2.	1.
.....										
ADRENAL GLANDS	-	-	-	+	+	+	+	(-	+G	-
- Cortical tissue, ac.	(P.	.
- Vacuol. glomerulosa	.	.	.	1.	2.	1.	2.	.	.	.
.....										
BRAIN	-	-	-*	-	-	-	-	-	'	'
.....										
PITUITARY GLAND	-	-	-	-	-	-	-	-	'	'
.....										
SCIATIC NERVE, LEFT	-	-	-	-	-	-	-	0	'	'
.....										
OVARIES	-	-	-	-	+	-	-	0	'	'
- Hypertr. interst. c.	1.
.....										
UTERUS	+G	-	+	+G	+G	+G	-	0	+G	+G
- Cyclic dilation	P.	.	.	P.	P.	P.	.	.	P.	P.
- Atrophy	.	.	3.
.....										
CERVIX	-	-	-	-	-	-	-	0	'	'
.....										
VAGINA	+	+	+	+	+	+	+	0	'	'
- Cycle: Estrus	P.	.	.	P.	P.	P.
- Cycle: Metestrus	P.	.	.	.
- Cycle: Diestrus	.	P.
- Atrophy, epithelial	.	.	2.
.....										

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 04, 600 MG/KG

ANIMAL NUMBER :

	86	87	88	89	90	91	92	93	94	95
	FK0	FK0	FK0+	FK0	FK0	FK0	FK0	FK0+	FR1	FR1
SKIN/SUBCUTIS	-	-	-	-	-	-	-	-	'	'
MAMMARY GLAND	-	-	-	-	-	-	-	0	'	'
LARYNX	-	-	-	-	-	-	-	-	'	'
EYES	-	-	-	-	-	-	-	A	'	'
OPTIC NERVES	-	-	-	-	-	-	-	(-	'	'
HARDERIAN GLANDS	-	-	-	-	-	-	-	-	'	'
SPINAL CORD, CERVIC.	-	-	-*	-	-	-	-	A	'	'
SPINAL CORD, THORAC.	-	-	-*	-	-	-	-	A	'	'
SPINAL CORD, LUMBAR	-	-	-	-	-	-	-	A	'	'
BONE, STERNUM	-	-	-	-	-	-	-	-	-	-
BONE MARROW, STERNUM	+	-	+	-	-	-	+	+	-	+
- Increased adipocytes	1.	1.	.	.	1.
- Atrophy	.	.	3.	2.	.	.
CLITORAL GLANDS	'	'	'	'	'	'	'	'	+G	'
- Dilated duct									(2.	

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 04, 600 MG/KG

ANIMAL NUMBER :

	96	97	98	99	100
	FR1+	FR1	FR1	FR1	FR1+
GENERAL OBSERVATIONS	+	'	'	'	'!
- Gavage accident	P.				
HEART	-	'	'	'	-
AORTA	-	'	'	'	-
LUNG	+G	'	'	'	-
- Hemorrhage, pulmon.	3*				.
- Inflamm. peribronch.	1.				.
THYMUS	+G	-	-	-	+G
- Congestion/hemorrh.	1.
- Depletion, lymphoid	3.
TRACHEA	+	'	'	'	-
- Infiltrate inflamm.	1.				.
ESOPHAGUS	-	'	'	'	-*
THYROID GLAND	+	-	-	-	+
- Hypertrophy foll. c.	2.	.	.	.	1.
PARATHYROID GLANDS	-	'	'	'	-
STOMACH	-	-	-	-	+
- Inflammation forest.	1.
- Hyperplasia squamous	2.
- Erosion/ulceration	1.
DUODENUM	-	'	'	'	-
JEJUNUM	-	'	'	'	-
ILEUM	-	'	'	'	-
PEYER'S PATCHES	-	'	'	'	-
CECUM	-	'	'	'	-

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 04, 600 MG/KG

ANIMAL NUMBER :

	96	97	98	99	100
	FR1+	FR1	FR1	FR1	FR1+
COLON	-	'	'	'	-
RECTUM	-	'	'	'	-
LIVER	+G	+	+G	+	+G
- Infiltrate inflamm.	1.	1.	1.	1.	.
- Hematopoiesis extram.	1.
- Hypertrophy hepatoc.	2.	.	.	.	3.
- Vacuolation hepatoc.	.	1.	1.	.	.
- Pigment deposition	.	1.	.	.	.
- Necrosis hepatocell.	1.	.	.	.	4.
SPLEEN	+	+	+	+	+
- Hematopoiesis extra.	1.
- Pigmentation, hemos.	1.	2.	2.	2.	2.
MESENT. LYMPH NODE	-	'	'	'	-
PANCREAS	-	'	'	'	+
- Degranulation acinar	3.
MANDIB. LYMPH NODES	-	'	'	'	-
SUBLINGUAL GLANDS	-	'	'	'	-
MANDIBULAR GLANDS	-	'	'	'	-
KIDNEYS	+G	-	-	-	+
- Congestion	2.
- Casts hyaline	(2.
- Dilatation, tubule	2.
- Vacuolation tubular	2.
URINARY BLADDER	-	+	+	-	-
- Hyperpl/hypert urot.	.	1.	1.	.	.
ADRENAL GLANDS	-	-	-	+	+
- Vacuol. glomerulosa	.	.	.	1.	.
- Vacuol. fasciculata	2.

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 04, 600 MG/KG

ANIMAL NUMBER :

	96	97	98	99	100
	FR1+	FR1	FR1	FR1	FR1+
BRAIN	-*	'	'	'	-
PITUITARY GLAND	-	'	'	'	-
SCIATIC NERVE, LEFT	-	'	'	'	-
OVARIES	-	'	'	'	-
UTERUS	-	'	'	'	+
- Atrophy	.				1.
CERVIX	-	'	'	'	-
VAGINA	+	'	'	'	+
- Cycle: Metestrus	P.				P.
- Infiltrate inflamm.	2.				1.
SKIN/SUBCUTIS	-	'	'	'	-
MAMMARY GLAND	-	'	'	'	-
LARYNX	-	'	'	'	-
EYES	-	'	'	'	-
OPTIC NERVES	-	'	'	'	-
HARDERIAN GLANDS	-	'	'	'	-
SPINAL CORD, CERVIC.	-*	'	'	'	-
SPINAL CORD, THORAC.	-*	'	'	'	-
SPINAL CORD, LUMBAR	-*	'	'	'	-
BONE, STERNUM	-	-	-	-	-

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
 DOSE GROUP : 04, 600 MG/KG

ANIMAL NUMBER :

	96	97	98	99	100
	FR1+	FR1	FR1	FR1	FR1+
BONE MARROW, STERNUM	-	-	-	-	+
- Increased adipocytes	1.
- Atrophy	2.
.....					
RENAL LYMPH NODE	0G	'	'	'	'
.....					
BODY CAVITIES	'!	'	'	'	'
.....					

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

ANIMAL HEADING DATA
 DOSE GROUP : 01, CONTROL

ANIMAL NUMBER	SEX M/F	DEFINED STATE	AND FINAL NECROPSY	TEST DAYS	FIRST DAY	AND LAST DAY UNDER TEST	DATE OF NECROPSY
1	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
2	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
3	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
4	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
5	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
6	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
7	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
8	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
9	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
10	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
11	M	R1	R1	92	25-FEB-16	26-MAY-16	23-JUN-16
12	M	R1	R1	92	25-FEB-16	26-MAY-16	23-JUN-16
13	M	R1	R1	92	25-FEB-16	26-MAY-16	23-JUN-16
14	M	R1	R1	92	25-FEB-16	26-MAY-16	23-JUN-16
15	M	R1	R1	92	25-FEB-16	26-MAY-16	23-JUN-16
51	F	K0	K0	92	25-FEB-16	26-MAY-16	27-MAY-16
52	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
53	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
54	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
55	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
56	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
57	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
58	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
59	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
60	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
61	F	R1	R1	124	25-FEB-16	27-JUN-16	28-JUN-16
62	F	R1	R1	124	25-FEB-16	27-JUN-16	28-JUN-16
63	F	R1	R1	124	25-FEB-16	27-JUN-16	28-JUN-16
64	F	R1	R1	124	25-FEB-16	27-JUN-16	28-JUN-16
65	F	R1	R1	124	25-FEB-16	27-JUN-16	28-JUN-16

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 1

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TRACHEA:

-Ectasia submucosal glands, grade 1

ESOPHAGUS:

-Degeneration/necrosis muscle, grade 1

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 2

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 2

-Hyperplasia squamous cell, forestomach, grade 2

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 1

KIDNEYS:

-Dilation, tubule, bilateral, grade 1

PROSTATE GLAND:

-Infiltrate inflammatory cell, mononuclear, grade 1

HARDERIAN GLANDS:

-Hemorrhage post-traumatic, unilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 87/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

CONT./FF. ANIMAL NO. : 1

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, THYMUS, PARATHYROID GLANDS, DUODENUM,
JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, MESENTERIC
LYMPH NODE, PANCREAS, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS,
MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER,
ADRENAL GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) ,
TESTES, EPIDIDYMIDES, SEMINAL VESICLES, COAGULATING GLANDS
(ANTERIOR PROSTATE), SKIN/SUBCUTIS, LARYNX, EYES, OPTIC NERVES,
SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT),
SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM), BONE MARROW
(STERNUM) .

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 2

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

HEART:

-Cardiopathy, progressive, papillary muscle, grade 2

ESOPHAGUS:

-Degeneration/necrosis muscle, grade 1

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

PARATHYROID GLANDS:

Only one of paired organs examined/present

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 1

-Hyperplasia squamous cell, forestomach, grade 1

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

CONT./FF. ANIMAL NO. : 2

.....
-Edema, forestomach, grade 1
PEYER'S PATCHES:
-Vacuolation, increased, grade 1
LIVER:
-Infiltration, peribiliary (intrahepatic), grade 1
SPLEEN:
-Pigmentation, hemosiderin, grade 1
KIDNEYS:
-Hyaline droplet accumulation, bilateral, grade 1
-Basophilia tubule, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- AORTA, LUNG, THYMUS, TRACHEA, PARATHYROID GLANDS, DUODENUM,
JEJUNUM, ILEUM, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE,
PANCREAS, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR
(SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER, ADRENAL
GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , TESTES,
EPIDIDYIMIDES, PROSTATE GLAND, SEMINAL VESICLES, COAGULATING
GLANDS (ANTERIOR PROSTATE), SKIN/SUBCUTIS, LARYNX, EYES, OPTIC
NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL
CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE
(STERNUM), BONE MARROW (STERNUM).

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

* STATE AT NECROPSY: K0
DAYS ON TEST : 91 * ANIMAL NO. : 3

* NECROPSY FINDINGS

STOMACH:
01: GLANDULAR MUCOSA: FOCUS/FOCI, ISOLATED, REDDISH.
LIVER:
01: LEFT LATERAL LOBE: ACCESSORY LOBE.
PREPUTIAL GLANDS (INGUINAL GLANDS):
01: BOTH SIDES: REDUCED IN SIZE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:
-Hyperplasia, epithelial tubules and cords, grade 1
STOMACH:
No microscopic finding corresponding to necropsy observation no. 01.
PEYER'S PATCHES:
-Vacuolation, increased, grade 1
LIVER:
-Infiltrate inflammatory cell, mononuclear, grade 1
-Accessory lobe
This finding corresponds to necropsy observation no: 01.
SPLEEN:
-Pigmentation, hemosiderin, grade 1
MESENTERIC LYMPH NODE:
-Increased macrophage foci, grade 1
ADRENAL GLANDS:
-Cortical tissue, accessory, unilateral
SKIN/SUBCUTIS:
-Inflammation exudative, with crust formation, grade 1
HARDERIAN GLANDS:
-Infiltrate inflammatory cell, lymphocytic, unilateral, grade 1
-Hemorrhage post-traumatic, unilateral, grade 2

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

CONT./FF. ANIMAL NO. : 3

PREPUTIAL GLANDS (INGUINAL GLANDS):

No microscopic finding corresponding to necropsy observation no. 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, TRACHEA, ESOPHAGUS , THYROID GLAND (BOTH LOBES), PARATHYROID GLANDS, STOMACH, DUODENUM, JEJUNUM, ILEUM, CECUM, COLON, RECTUM, PANCREAS, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, KIDNEYS, URINARY BLADDER, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , TESTES, EPIDIDYMIDES, PROSTATE GLAND, SEMINAL VESICLES, COAGULATING GLANDS (ANTERIOR PROSTATE), LARYNX, EYES, OPTIC NERVES, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM), BONE MARROW (STERNUM), PREPUTIAL GLANDS (INGUINAL GLANDS).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 4

* NECROPSY FINDINGS

SEMINAL VESICLES:

01: LEFT SIDE: REDUCED IN SIZE.
NO OTHER NECROPSY OBSERVATIONS NOTED

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 91/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

CONT./FF. ANIMAL NO. : 4

* MICROSCOPIC FINDINGS

LUNG:

-Inflammation peribronchial/perivascular, grade 1

THYMUS:

-Lymphocytolysis increased, grade 2

ESOPHAGUS:

-Degeneration/necrosis muscle, grade 1

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 1

KIDNEYS:

-Hyaline droplet accumulation, bilateral, grade 1

-Dilation, tubule, bilateral, grade 2

TESTES:

-Atrophy, tubular, unilateral, grade 1

SEMINAL VESICLES:

No microscopic finding corresponding to necropsy observation no. 01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 92/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

CONT./FF. ANIMAL NO. : 4

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, TRACHEA, PARATHYROID GLANDS, DUODENUM, JEJUNUM,
ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, MESENTERIC LYMPH
NODE, PANCREAS, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS,
MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER,
ADRENAL GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) ,
EPIDIDYMIDES, PROSTATE GLAND, SEMINAL VESICLES, COAGULATING
GLANDS (ANTERIOR PROSTATE), SKIN/SUBCUTIS, LARYNX, EYES, OPTIC
NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL
CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE
(STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 5

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

THYMUS:

-Depletion, lymphoid, grade 1

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 1

-Hyperplasia squamous cell, forestomach, grade 2

-Hemorrhage, forestomach, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 1

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 93/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

CONT./FF. ANIMAL NO. : 5

MESENTERIC LYMPH NODE:

-Increased macrophage foci, grade 1

KIDNEYS:

-Hyaline droplet accumulation, bilateral, grade 1

-Casts hyaline, unilateral, grade 1

-Dilation, tubule, bilateral, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, TRACHEA, ESOPHAGUS , THYROID GLAND (BOTH LOBES), PARATHYROID GLANDS, DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, PANCREAS, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER, ADRENAL GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , TESTES, EPIDIDYMIDES, PROSTATE GLAND, SEMINAL VESICLES, COAGULATING GLANDS (ANTERIOR PROSTATE), SKIN/SUBCUTIS, LARYNX, EYES, OPTIC NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM), BONE MARROW (STERNUM) .

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 6

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 94/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

CONT./FF. ANIMAL NO. : 6

* MICROSCOPIC FINDINGS

LUNG:

- Inflammation bronchioalveolar, acute, grade 1
- Alveolar macrophage aggregation, grade 2
- Inflammation peribronchial/perivascular, grade 1
- Edema alveolar/bronchiolar, focal, grade 2

THYROID GLAND (BOTH LOBES):

- Hypertrophy follicular cell, bilateral, grade 2

STOMACH:

- Inflammation forestomach, lymphogranulocytic, grade 1
- Hyperplasia squamous cell, forestomach, grade 1
- Edema, forestomach, grade 2

LIVER:

- Infiltrate inflammatory cell, mononuclear, grade 1

SPLEEN:

- Pigmentation, hemosiderin, grade 1

MESENTERIC LYMPH NODE:

- Increased macrophage foci, grade 1

KIDNEYS:

- Hyaline droplet accumulation, bilateral, grade 1
- Basophilia tubule, unilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 95/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

CONT./FF. ANIMAL NO. : 6

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, THYMUS, TRACHEA, ESOPHAGUS , PARATHYROID GLANDS,
DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM,
PANCREAS, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR
(SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER, ADRENAL
GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , TESTES,
EPIDIDYMIDES, PROSTATE GLAND, SEMINAL VESICLES, COAGULATING
GLANDS (ANTERIOR PROSTATE), SKIN/SUBCUTIS, LARYNX, EYES, OPTIC
NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL
CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE
(STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 7

* NECROPSY FINDINGS

LIVER:

01: RIGHT MEDIAL LOBE: ACCESSORY LOBE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

TRACHEA:

-Infiltrate inflammatory cell, lymphogranulocytic, grade 1

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 1

-Hyperplasia squamous cell, forestomach, grade 2

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Accessory lobe

This finding corresponds to necropsy observation no: 01.

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

CONT./FF. ANIMAL NO. : 7

SPLEEN:

-Pigmentation, hemosiderin, grade 2

KIDNEYS:

-Hyaline droplet accumulation, bilateral, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, THYMUS, ESOPHAGUS , THYROID GLAND (BOTH LOBES), PARATHYROID GLANDS, DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, PANCREAS, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER, ADRENAL GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , TESTES, EPIDIDYMITES, PROSTATE GLAND, SEMINAL VESICLES, COAGULATING GLANDS (ANTERIOR PROSTATE), SKIN/SUBCUTIS, LARYNX, EYES, OPTIC NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM) , BONE MARROW (STERNUM) .

* STATE AT NECROPSY: K0
DAYS ON TEST : 91

* ANIMAL NO. : 8

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

CONT./FF. ANIMAL NO. : 8

* MICROSCOPIC FINDINGS

HEART:

-Necrosis, myofibers, ventricular wall, grade 2

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 2

-Hyperplasia squamous cell, forestomach, grade 2

-Erosion/ulceration, forestomach, grade 2

-Edema, forestomach, grade 3

PEYER'S PATCHES:

-Vacuolation, increased, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 2

KIDNEYS:

-Hyaline droplet accumulation, bilateral, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- AORTA, LUNG, THYMUS, TRACHEA, ESOPHAGUS , THYROID GLAND (BOTH LOBES), PARATHYROID GLANDS, DUODENUM, JEJUNUM, ILEUM, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, PANCREAS, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER, ADRENAL GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , TESTES, EPIDIDYMIDES, PROSTATE GLAND, SEMINAL VESICLES, COAGULATING GLANDS (ANTERIOR PROSTATE), SKIN/SUBCUTIS, LARYNX, EYES, OPTIC NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM), BONE MARROW (STERNUM) .

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 98/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 9

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

HEART:

-Infiltrate inflammatory cell, mononuclear, left ventricle,
grade 1

LUNG:

-Mineralization vascular, grade 1

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

STOMACH:

-Hyperplasia squamous cell, forestomach, grade 1

PEYER'S PATCHES:

-Vacuolation, increased, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 2

MANDIBULAR LYMPH NODES:

-Erythrocytes, intrasinusoidal, unilateral, grade 2

KIDNEYS:

-Hyaline droplet accumulation, bilateral, grade 2

-Basophilia tubule, bilateral, grade 1

ADRENAL GLANDS:

-Cortical tissue, accessory, unilateral

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

CONT./FF. ANIMAL NO. : 9

* ORGANS WITHOUT ABNORMALITIES

- AORTA, THYMUS, TRACHEA, ESOPHAGUS , PARATHYROID GLANDS, DUODENUM,
JEJUNUM, ILEUM, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE,
PANCREAS, SUBLINGUAL GLANDS, MANDIBULAR
(SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER, BRAIN,
PITUITARY GLAND, SCIATIC NERVE (LEFT) , TESTES, EPIDIDYMIDES,
PROSTATE GLAND, SEMINAL VESICLES, COAGULATING GLANDS (ANTERIOR
PROSTATE), SKIN/SUBCUTIS, LARYNX, EYES, OPTIC NERVES, HARDERIAN
GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC
SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM), BONE
MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 10

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

HEART:

-Necrosis, myofibers, right ventricle, grade 1

LUNG:

-Alveolar macrophage aggregation, grade 1

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 1

-Hyperplasia squamous cell, forestomach, grade 2

-Edema, forestomach, grade 2

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

CONT./FF. ANIMAL NO. : 10

SPLEEN:

-Pigmentation, hemosiderin, grade 2

KIDNEYS:

-Hyaline droplet accumulation, bilateral, grade 2
-Eosinophilic content tubular, unilateral, grade 1

ADRENAL GLANDS:

-Cortical tissue, accessory, unilateral

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- AORTA, THYMUS, TRACHEA, ESOPHAGUS , THYROID GLAND (BOTH LOBES),
PARATHYROID GLANDS, DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES,
CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, PANCREAS, MANDIBULAR
LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR
(SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER, BRAIN,
PITUITARY GLAND, SCIATIC NERVE (LEFT) , TESTES, EPIDIDYMIDES,
PROSTATE GLAND, SEMINAL VESICLES, COAGULATING GLANDS (ANTERIOR
PROSTATE), SKIN/SUBCUTIS, LARYNX, EYES, OPTIC NERVES, HARDERIAN
GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC
SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM), BONE
MARROW (STERNUM).

* STATE AT NECROPSY: R1

DAYS ON TEST : 92

* ANIMAL NO. : 11

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 101/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

CONT./FF. ANIMAL NO. : 11

* MICROSCOPIC FINDINGS

STOMACH:

-Cyst(s), squamous, with chronic mononuclear infiltrate,
grade 3

LIVER:

-Infiltration, peribiliary (intrahepatic), grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYROID GLAND (BOTH LOBES), KIDNEYS, URINARY BLADDER, BONE
(STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: R1

DAYS ON TEST : 92

* ANIMAL NO. : 12

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

KIDNEYS:

-Hyaline droplet accumulation, bilateral, grade 1

-Basophilia tubule, unilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 102/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

CONT./FF. ANIMAL NO. : 12

* ORGANS WITHOUT ABNORMALITIES

- STOMACH, LIVER, URINARY BLADDER, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: R1

DAYS ON TEST : 92

* ANIMAL NO. : 13

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- STOMACH, KIDNEYS, URINARY BLADDER, BONE (STERNUM), BONE MARROW (STERNUM).

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

* STATE AT NECROPSY: R1

DAYS ON TEST : 92

* ANIMAL NO. : 14

* NECROPSY FINDINGS

STOMACH:

01: GLANDULAR MUCOSA: FOCUS/FOCI, ISOLATED, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

STOMACH:

-Congestion, glandular mucosa, grade 2

This finding corresponds to necropsy observation no: 01.

URINARY BLADDER:

-Infiltrate inflammatory cell, lymphocytic, focal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYROID GLAND (BOTH LOBES), LIVER, KIDNEYS, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: R1

DAYS ON TEST : 92

* ANIMAL NO. : 15

* NECROPSY FINDINGS

THYROID GLAND (BOTH LOBES):

01: BOTH SIDES: ENLARGED.

NO OTHER NECROPSY OBSERVATIONS NOTED

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 104/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

MALE

CONT./FF. ANIMAL NO. : 15

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Thymus, ectopic, unilateral

This finding corresponds to necropsy observation no: 01.

STOMACH:

-Cyst(s), glandular mucosa, grade 1

KIDNEYS:

-Hyaline droplet accumulation, bilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- LIVER, URINARY BLADDER, BONE (STERNUM), BONE MARROW (STERNUM).

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 105/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 92

* ANIMAL NO. : 51

* NECROPSY FINDINGS

BODY CAVITIES:

01: ABDOMINAL CAVITY, UTERINE ADIPOSE TISSUE, RIGHT SIDE:
NODULE(S), D=8X5 MM, REDDISH, SOFT.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Cyst, ultimobranchial, unilateral, grade 2

SPLEEN:

-Hematopoiesis extramedullary, grade 1

-Pigmentation, hemosiderin, grade 2

MESENTERIC LYMPH NODE:

-Increased macrophage foci, grade 1

VAGINA:

-Cycle: proestrus

BODY CAVITIES:

-Fat necrosis, with hemorrhage, grade 2

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 106/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

CONT./FF. ANIMAL NO. : 51

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, THYMUS, TRACHEA, ESOPHAGUS , PARATHYROID
GLANDS, STOMACH, DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES,
CECUM, COLON, RECTUM, LIVER, PANCREAS, MANDIBULAR LYMPH NODES,
SUBLINGUAL GLANDS, MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY)
GLANDS, KIDNEYS, URINARY BLADDER, ADRENAL GLANDS, BRAIN,
PITUITARY GLAND, SCIATIC NERVE (LEFT) , OVARIES, UTERUS, CERVIX,
SKIN/SUBCUTIS, MAMMARY GLAND, LARYNX, EYES, OPTIC NERVES,
HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD
(THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM),
BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 52

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

SPLEEN:

-Hematopoiesis extramedullary, grade 2

-Pigmentation, hemosiderin, grade 3

MESENTERIC LYMPH NODE:

-Increased macrophage foci, grade 2

KIDNEYS:

-Infiltrate inflammatory cell, lymphocytic, unilateral, grade 1

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 107/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

CONT./FF. ANIMAL NO. : 52

VAGINA:

-Cycle: diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, THYMUS, TRACHEA, ESOPHAGUS , THYROID GLAND
(BOTH LOBES), PARATHYROID GLANDS, STOMACH, DUODENUM, JEJUNUM,
ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, PANCREAS,
MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR
(SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER, ADRENAL
GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , OVARIES,
UTERUS, CERVIX, SKIN/SUBCUTIS, MAMMARY GLAND, LARYNX, EYES, OPTIC
NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL
CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE
(STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 53

* NECROPSY FINDINGS

MANDIBULAR LYMPH NODES:

01: RIGHT SIDE: DISCOLOURATION, DARK RED.

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

CONT./FF. ANIMAL NO. : 53

* MICROSCOPIC FINDINGS

LUNG:

-Mineralization vascular, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Extramedullary hematopoiesis, grade 1

SPLEEN:

-Hematopoiesis extramedullary, grade 3

-Pigmentation, hemosiderin, grade 1

MESENTERIC LYMPH NODE:

-Increased macrophage foci, grade 2

MANDIBULAR LYMPH NODES:

-Erythrocytes, intrasinusoidal, unilateral, grade 2

This finding corresponds to necropsy observation no: 01.

UTERUS:

-Cyclic dilation, proestrus stage

This finding corresponds to necropsy observation no: 01.

VAGINA:

-Cycle: proestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, THYMUS, TRACHEA, ESOPHAGUS , THYROID GLAND (BOTH LOBES), PARATHYROID GLANDS, STOMACH, DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, PANCREAS, SUBLINGUAL GLANDS, MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, KIDNEYS, URINARY BLADDER, ADRENAL GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , OVARIES, CERVIX, SKIN/SUBCUTIS, MAMMARY GLAND, LARYNX, EYES, OPTIC NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM), BONE MARROW (STERNUM).

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 109/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 54

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LUNG:

-Inflammation peribronchial/perivascular, grade 1

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 2

-Hyperplasia squamous cell, forestomach, grade 2

-Edema, forestomach, grade 2

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Extramedullary hematopoiesis, grade 1

SPLEEN:

-Hematopoiesis extramedullary, grade 1

-Pigmentation, hemosiderin, grade 2

KIDNEYS:

-Basophilia tubule, unilateral, grade 1

VAGINA:

-Cycle: metestrus

HARDERIAN GLANDS:

-Infiltrate inflammatory cell, lymphocytic, unilateral, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 110/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

CONT./FF. ANIMAL NO. : 54

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, THYMUS, TRACHEA, ESOPHAGUS , THYROID GLAND (BOTH LOBES), PARATHYROID GLANDS, DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, PANCREAS, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER, ADRENAL GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , OVARIES, UTERUS, CERVIX, SKIN/SUBCUTIS, MAMMARY GLAND, LARYNX, EYES, OPTIC NERVES, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 55

* NECROPSY FINDINGS

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LUNG:

-Inflammation peribronchial/perivascular, grade 2

PARATHYROID GLANDS:

Only one of paired organs examined/present

PEYER'S PATCHES:

-Vacuolation, increased, grade 2

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Extramedullary hematopoiesis, grade 1

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

CONT./FF. ANIMAL NO. : 55

SPLEEN:

- Hematopoiesis extramedullary, grade 2
- Pigmentation, hemosiderin, grade 2

MESENTERIC LYMPH NODE:

- Increased macrophage foci, grade 1

OVARIES:

- Hypertrophy interstitial cell, bilateral, grade 1

UTERUS:

- Cyclic dilation, estrus stage

This finding corresponds to necropsy observation no: 01.

VAGINA:

- Cycle: estrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, THYMUS, TRACHEA, ESOPHAGUS , THYROID GLAND (BOTH LOBES), PARATHYROID GLANDS, STOMACH, DUODENUM, JEJUNUM, ILEUM, CECUM, COLON, RECTUM, PANCREAS, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, KIDNEYS, URINARY BLADDER, ADRENAL GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , CERVIX, SKIN/SUBCUTIS, MAMMARY GLAND, LARYNX, EYES, OPTIC NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM), BONE MARROW (STERNUM) .

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 112/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 56

* NECROPSY FINDINGS

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 2

-Hyperplasia squamous cell, forestomach, grade 2

-Erosion/ulceration, forestomach, grade 2

-Edema, forestomach, grade 2

PEYER'S PATCHES:

-Vacuolation, increased, grade 2

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Extramedullary hematopoiesis, grade 1

SPLEEN:

-Hematopoiesis extramedullary, grade 2

-Pigmentation, hemosiderin, grade 2

OVARIES:

-Hypertrophy interstitial cell, bilateral, grade 1

UTERUS:

-Cyclic dilation, estrus stage

This finding corresponds to necropsy observation no: 01.

VAGINA:

-Cycle: estrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

CONT./FF. ANIMAL NO. : 56

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, THYMUS, TRACHEA, ESOPHAGUS , THYROID GLAND
(BOTH LOBES), PARATHYROID GLANDS, DUODENUM, JEJUNUM, ILEUM,
CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, PANCREAS, MANDIBULAR
LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR
(SUBMANDIBULAR/SUBMAXILLARY) GLANDS, KIDNEYS, URINARY BLADDER,
ADRENAL GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) ,
CERVIX, SKIN/SUBCUTIS, MAMMARY GLAND, LARYNX, EYES, OPTIC NERVES,
HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD
(THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM),
BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 57

* NECROPSY FINDINGS

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

PARATHYROID GLANDS:

Only one of paired organs examined/present

STOMACH:

-Hyperplasia squamous cell, forestomach, grade 2

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Extramedullary hematopoiesis, grade 1

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 114/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

CONT./FF. ANIMAL NO. : 57

.....
SPLEEN:

- Hematopoiesis extramedullary, grade 3
- Pigmentation, hemosiderin, grade 2

MESENTERIC LYMPH NODE:

- Increased macrophage foci, grade 2

KIDNEYS:

- Basophilia tubule, bilateral, grade 1

UTERUS:

- Cyclic dilation, proestrus stage

This finding corresponds to necropsy observation no: 01.

VAGINA:

- Cycle: proestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, THYMUS, TRACHEA, ESOPHAGUS , THYROID GLAND (BOTH LOBES), PARATHYROID GLANDS, DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, PANCREAS, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER, ADRENAL GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , OVARIES, CERVIX, SKIN/SUBCUTIS, MAMMARY GLAND, LARYNX, EYES, OPTIC NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM), BONE MARROW (STERNUM) .

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 115/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 58

* NECROPSY FINDINGS

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

PEYER'S PATCHES:

-Vacuolation, increased, grade 3

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Extramedullary hematopoiesis, grade 1

SPLEEN:

-Hematopoiesis extramedullary, grade 2

-Pigmentation, hemosiderin, grade 2

MANDIBULAR LYMPH NODES:

-Congestion, unilateral, grade 1

KIDNEYS:

-Casts hyaline, unilateral, grade 1

UTERUS:

-Cyclic dilation, estrus stage

This finding corresponds to necropsy observation no: 01.

VAGINA:

-Cycle: estrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 116/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

CONT./FF. ANIMAL NO. : 58

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, THYMUS, TRACHEA, ESOPHAGUS , PARATHYROID
GLANDS, STOMACH, DUODENUM, JEJUNUM, ILEUM, CECUM, COLON, RECTUM,
MESENTERIC LYMPH NODE, PANCREAS, SUBLINGUAL GLANDS, MANDIBULAR
(SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER, ADRENAL
GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , OVARIES,
CERVIX, SKIN/SUBCUTIS, MAMMARY GLAND, LARYNX, EYES, OPTIC NERVES,
HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD
(THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM),
BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 59

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LUNG:

-Inflammation peribronchial/perivascular, grade 1

LIVER:

-Extramedullary hematopoiesis, grade 1

SPLEEN:

-Hematopoiesis extramedullary, grade 2

-Pigmentation, hemosiderin, grade 1

MESENTERIC LYMPH NODE:

-Increased macrophage foci, grade 2

MANDIBULAR LYMPH NODES:

-Congestion, unilateral, grade 1

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 117/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

CONT./FF. ANIMAL NO. : 59

VAGINA:

-Cycle: metestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, THYMUS, TRACHEA, ESOPHAGUS , THYROID GLAND (BOTH LOBES), PARATHYROID GLANDS, STOMACH, DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, PANCREAS, SUBLINGUAL GLANDS, MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, KIDNEYS, URINARY BLADDER, ADRENAL GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , OVARIES, UTERUS, CERVIX, SKIN/SUBCUTIS, MAMMARY GLAND, LARYNX, EYES, OPTIC NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 60

* NECROPSY FINDINGS

LIVER:

01: PAPILLARY PROCESS, LEFT SIDE: ENLARGED.

02: PAPILLARY PROCESS: DISCOLOURATION, BLACK-BROWN.

03: PAPILLARY PROCESS: FOCUS/FOCI, MANY, GRAY-WHITE.

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 118/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

CONT./FF. ANIMAL NO. : 60

* MICROSCOPIC FINDINGS

STOMACH:

- Inflammation forestomach, lymphogranulocytic, grade 1
- Hyperplasia squamous cell, forestomach, grade 1
- Edema, forestomach, grade 1

LIVER:

- Infiltrate inflammatory cell, mononuclear, grade 1
 - Extramedullary hematopoiesis, grade 2
 - Infarction/torsion lobar, chronic
- This finding corresponds to necropsy observations nos: 01,02,03.

SPLEEN:

- Hematopoiesis extramedullary, grade 3
- Pigmentation, hemosiderin, grade 1

MESENTERIC LYMPH NODE:

- Increased macrophage foci, grade 1

ADRENAL GLANDS:

- Vacuolation zona glomerulosa, bilateral, grade 1
- Extramedullary hematopoiesis, unilateral, grade 1

UTERUS:

- Cyclic dilation, proestrus stage
- This finding corresponds to necropsy observation no: 01.

VAGINA:

- Cycle: proestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 119/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

CONT./FF. ANIMAL NO. : 60

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, THYMUS, TRACHEA, ESOPHAGUS , THYROID GLAND
(BOTH LOBES), PARATHYROID GLANDS, DUODENUM, JEJUNUM, ILEUM,
PEYER'S PATCHES, CECUM, COLON, RECTUM, PANCREAS, MANDIBULAR LYMPH
NODES, SUBLINGUAL GLANDS, MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY)
GLANDS, KIDNEYS, URINARY BLADDER, BRAIN, PITUITARY GLAND, SCIATIC
NERVE (LEFT) , OVARIES, CERVIX, SKIN/SUBCUTIS, MAMMARY GLAND,
LARYNX, EYES, OPTIC NERVES, HARDERIAN GLANDS, SPINAL CORD
(CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD
(LUMBAR SEGMENT), BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: R1

DAYS ON TEST : 124

* ANIMAL NO. : 61

* NECROPSY FINDINGS

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:

-Infiltrate inflammatory cell, granulomatous, grade 2

SPLEEN:

-Pigmentation, hemosiderin, grade 2

UTERUS:

-Cyclic dilation, estrus stage

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 120/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

CONT./FF. ANIMAL NO. : 61

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, THYROID GLAND (BOTH LOBES), STOMACH, KIDNEYS, URINARY
BLADDER, ADRENAL GLANDS, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: R1

DAYS ON TEST : 124

* ANIMAL NO. : 62

* NECROPSY FINDINGS

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 2

ADRENAL GLANDS:

-Vacuolation zona glomerulosa, unilateral, grade 1

-Vacuolation zona fasciculata, bilateral, grade 2

UTERUS:

-Cyclic dilation, proestrus stage

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 121/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

CONT./FF. ANIMAL NO. : 62

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, THYROID GLAND (BOTH LOBES), STOMACH, KIDNEYS, URINARY
BLADDER, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: R1

DAYS ON TEST : 124

* ANIMAL NO. : 63

* NECROPSY FINDINGS

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

STOMACH:

-Vacuolation, limiting ridge, grade 1

LIVER:

-Infiltrate inflammatory cell, granulomatous, grade 3

-Necrosis coagulative, focal/multifocal, grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 1

UTERUS:

-Cyclic dilation, estrus stage

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 122/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

CONT./FF. ANIMAL NO. : 63

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, KIDNEYS, URINARY BLADDER, ADRENAL GLANDS, BONE (STERNUM),
BONE MARROW (STERNUM).

* STATE AT NECROPSY: R1

DAYS ON TEST : 124

* ANIMAL NO. : 64

* NECROPSY FINDINGS

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 2

ADRENAL GLANDS:

-Vacuolation zona glomerulosa, bilateral, grade 1

UTERUS:

-Cyclic dilation, estrus stage

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 123/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

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

FEMALE

CONT./FF. ANIMAL NO. : 64

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, THYROID GLAND (BOTH LOBES), STOMACH, KIDNEYS, URINARY
BLADDER, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: R1

DAYS ON TEST : 124

* ANIMAL NO. : 65

* NECROPSY FINDINGS

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 2

UTERUS:

-Cyclic dilation, proestrus stage

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, THYROID GLAND (BOTH LOBES), STOMACH, KIDNEYS, URINARY
BLADDER, ADRENAL GLANDS, BONE (STERNUM), BONE MARROW (STERNUM).

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

ANIMAL HEADING DATA
DOSE GROUP : 02, 100 MG/KG

ANIMAL NUMBER	SEX M/F	DEFINED STATE	AND FINAL NECROPSY	TEST DAYS	FIRST DAY	AND LAST DAY UNDER TEST	DATE OF NECROPSY
16	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
17	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
18	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
19	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
20	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
21	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
22	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
23	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
24	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
25	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
66	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
67	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
68	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
69	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
70	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
71	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
72	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
73	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
74	F	K0	+1	91	25-FEB-16	25-MAY-16	26-MAY-16
75	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 125/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

MALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 16

* NECROPSY FINDINGS

MANDIBULAR LYMPH NODES:

01: RIGHT SIDE: DISCOLOURATION, REDDISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 1

MANDIBULAR LYMPH NODES:

-Erythrocytes, intrasinusoidal, unilateral, grade 2

This finding corresponds to necropsy observation no: 01.

KIDNEYS:

-Hyaline droplet accumulation, bilateral, grade 1

-Eosinophilic content tubular, bilateral, grade 1

BONE MARROW (STERNUM):

-Increased adipocytes, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- STOMACH, URINARY BLADDER, BONE (STERNUM).

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 126/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

MALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 17

* NECROPSY FINDINGS

STOMACH:

01: FORESTOMACH: IRREGULAR SURFACE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 2

STOMACH:

-Hyperplasia squamous cell, forestomach, grade 1

This finding corresponds to necropsy observation no: 01.

-Edema, forestomach, grade 1

LIVER:

-Extramedullary hematopoiesis, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- KIDNEYS, URINARY BLADDER, BONE (STERNUM), BONE MARROW (STERNUM).

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

MALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 18

* NECROPSY FINDINGS

KIDNEYS:

01: BOTH SIDES: DISCOLOURATION, GREENISH.

PREPUTIAL GLANDS (INGUINAL GLANDS):

01: BOTH SIDES: REDUCED IN SIZE.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 3

STOMACH:

-Hyperplasia squamous cell, forestomach, grade 1

-Edema, forestomach, grade 1

LIVER:

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 1

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

PREPUTIAL GLANDS (INGUINAL GLANDS):

No microscopic finding corresponding to necropsy observation no. 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- KIDNEYS, URINARY BLADDER, BONE (STERNUM), BONE MARROW (STERNUM),
PREPUTIAL GLANDS (INGUINAL GLANDS).

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 128/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

MALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 19

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

LIVER:

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 1

KIDNEYS:

-Hyaline droplet accumulation, bilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- STOMACH, URINARY BLADDER, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 20

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 129/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

MALE

CONT./FF. ANIMAL NO. : 20

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 2

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 1

-Hyperplasia squamous cell, forestomach, grade 2

-Edema, forestomach, grade 2

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- KIDNEYS, URINARY BLADDER, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 21

* NECROPSY FINDINGS

LACRIMAL GLANDS:

01: RIGHT SIDE: REDUCED IN SIZE.

NO OTHER NECROPSY OBSERVATIONS NOTED

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 130/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

MALE

CONT./FF. ANIMAL NO. : 21

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 3

STOMACH:

-Edema, forestomach, grade 1

LIVER:

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 1

LACRIMAL GLANDS:

-Atrophy, glandular, unilateral, grade 3

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- KIDNEYS, URINARY BLADDER, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 22

* NECROPSY FINDINGS

LIVER:

01: ENLARGED.

PREPUTIAL GLANDS (INGUINAL GLANDS):

01: BOTH SIDES: REDUCED IN SIZE.

NO OTHER NECROPSY OBSERVATIONS NOTED

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 131/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

MALE

CONT./FF. ANIMAL NO. : 22

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 2

LIVER:

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 1

This finding corresponds to necropsy observation no: 01.

KIDNEYS:

-Hyaline droplet accumulation, bilateral, grade 1

PREPUTIAL GLANDS (INGUINAL GLANDS):

No microscopic finding corresponding to necropsy observation no. 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- STOMACH, URINARY BLADDER, BONE (STERNUM), BONE MARROW (STERNUM),
PREPUTIAL GLANDS (INGUINAL GLANDS).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 23

* NECROPSY FINDINGS

KIDNEYS:

01: BOTH SIDES: ENLARGED.

NO OTHER NECROPSY OBSERVATIONS NOTED

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 132/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

MALE

CONT./FF. ANIMAL NO. : 23

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

Organ examined, no pathologic findings noted

STOMACH:

Organ examined, no pathologic findings noted

LIVER:

- Infiltrate inflammatory cell, mononuclear, grade 1
- Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm, grade 1

KIDNEYS:

Organ not examined

No microscopic finding corresponding to necropsy observation no. 01.

URINARY BLADDER:

Organ examined, no pathologic findings noted

BONE (STERNUM):

Organ examined, no pathologic findings noted

BONE MARROW (STERNUM):

- Increased adipocytes, grade 1

* ORGANS WITHOUT ABNORMALITIES

- THYROID GLAND (BOTH LOBES), STOMACH, URINARY BLADDER, BONE (STERNUM) .

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

MALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 24

* NECROPSY FINDINGS

LIVER:

01: ENLARGED.

PREPUTIAL GLANDS (INGUINAL GLANDS):

01: BOTH SIDES: REDUCED IN SIZE.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 1

This finding corresponds to necropsy observation no: 01.

PREPUTIAL GLANDS (INGUINAL GLANDS):

No microscopic finding corresponding to necropsy observation no. 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYROID GLAND (BOTH LOBES), STOMACH, KIDNEYS, URINARY BLADDER,
BONE (STERNUM), BONE MARROW (STERNUM), PREPUTIAL GLANDS (INGUINAL
GLANDS).

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 134/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

MALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 25

* NECROPSY FINDINGS

STOMACH:

01: GLANDULAR MUCOSA: FOCUS/FOCI, ISOLATED, REDDISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

STOMACH:

No microscopic finding corresponding to necropsy observation no. 01.

-Inflammation forestomach, lymphogranulocytic, grade 1

-Hyperplasia squamous cell, forestomach, grade 2

-Edema, forestomach, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 1

KIDNEYS:

-Hyaline droplet accumulation, bilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- URINARY BLADDER, BONE (STERNUM), BONE MARROW (STERNUM).

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 66

* NECROPSY FINDINGS

STOMACH:

01: GLANDULAR MUCOSA: FOCUS/FOCI, ISOLATED, BLACK-BROWN.

LIVER:

01: LEFT MEDIAN LOBE: DIAPHRAGMATIC HERNIA.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

STOMACH:

No microscopic finding corresponding to necropsy observation no. 01.

- Inflammation forestomach, lymphogranulocytic, grade 2
- Hyperplasia squamous cell, forestomach, grade 2
- Erosion/ulceration, forestomach, grade 1
- Edema, forestomach, grade 2

LIVER:

- Infiltrate inflammatory cell, mononuclear, grade 1
- Hepatodiaphragmatic nodule

This finding corresponds to necropsy observation no: 01.

SPLEEN:

- Pigmentation, hemosiderin, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, THYROID GLAND (BOTH LOBES), KIDNEYS, URINARY BLADDER, ADRENAL GLANDS, BONE (STERNUM), BONE MARROW (STERNUM).

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 136/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 02, 100 MG/KG FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 96 * ANIMAL NO. : 67
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

SPLEEN:

-Hematopoiesis extramedullary, grade 1

-Pigmentation, hemosiderin, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, STOMACH, KIDNEYS, URINARY BLADDER, ADRENAL GLANDS, BONE
(STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0
DAYS ON TEST : 96 * ANIMAL NO. : 68
.....

* NECROPSY FINDINGS

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 137/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 68

* MICROSCOPIC FINDINGS

STOMACH:

-Hyperplasia squamous cell, forestomach, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 1

UTERUS:

-Cyclic dilation, proestrus stage

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, THYROID GLAND (BOTH LOBES), KIDNEYS, URINARY BLADDER,
ADRENAL GLANDS, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 69

* NECROPSY FINDINGS

UTERUS:

01: CONTAINS FLUID.

PARATHYMIC LYMPH NODE:

01: ENLARGED.

NO OTHER NECROPSY OBSERVATIONS NOTED

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 138/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 69

* MICROSCOPIC FINDINGS

THYMUS:

-Lymphocytolysis increased, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 2

UTERUS:

-Cyclic dilation, estrus stage

This finding corresponds to necropsy observation no: 01.

PARATHYMIC LYMPH NODE:

-Lymphoid hyperplasia, bilateral, grade 1

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYROID GLAND (BOTH LOBES), STOMACH, KIDNEYS, URINARY BLADDER,
ADRENAL GLANDS, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 70

* NECROPSY FINDINGS

STOMACH:

01: GLANDULAR MUCOSA: FOCUS/FOCI, ISOLATED, REDDISH.

NO OTHER NECROPSY OBSERVATIONS NOTED

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 70

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Thymus, ectopic, unilateral

STOMACH:

No microscopic finding corresponding to necropsy observation no. 01.

-Inflammation forestomach, lymphogranulocytic, grade 1

-Edema, forestomach, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Extramedullary hematopoiesis, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 1

SPLEEN:

-Hematopoiesis extramedullary, grade 1

-Pigmentation, hemosiderin, grade 2

ADRENAL GLANDS:

-Vacuolation zona glomerulosa, bilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, KIDNEYS, URINARY BLADDER, BONE (STERNUM), BONE MARROW
(STERNUM).

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 140/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 02, 100 MG/KG

FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 71

.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

STOMACH:

-Hyperplasia squamous cell, forestomach, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 1

SPLEEN:

-Hematopoiesis extramedullary, grade 1

-Pigmentation, hemosiderin, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, THYROID GLAND (BOTH LOBES), KIDNEYS, URINARY BLADDER,
ADRENAL GLANDS, BONE (STERNUM), BONE MARROW (STERNUM).

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 72

* NECROPSY FINDINGS

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 2

-Hyperplasia squamous cell, forestomach, grade 2

-Edema, forestomach, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

SPLEEN:

-Hematopoiesis extramedullary, grade 1

-Pigmentation, hemosiderin, grade 1

UTERUS:

-Cyclic dilation, proestrus stage

This finding corresponds to necropsy observation no: 01.

BONE MARROW (STERNUM):

-Increased adipocytes, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, KIDNEYS, URINARY BLADDER, ADRENAL GLANDS, BONE (STERNUM).

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 142/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 73

* NECROPSY FINDINGS

LUNG:

01: LEFT LOBE: DISCOLOURATION, PALE.

STOMACH:

01: FORESTOMACH: FOCUS/FOCI, ISOLATED, REDDISH.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LUNG:

No microscopic finding corresponding to necropsy observation no. 01.

-Alveolar macrophage aggregation, grade 1

-Mineralization vascular, grade 1

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 3

-Hyperplasia squamous cell, forestomach, grade 3

-Erosion/ulceration, forestomach, grade 2

This finding corresponds to necropsy observation no: 01.

-Edema, forestomach, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

SPLEEN:

-Hematopoiesis extramedullary, grade 1

-Pigmentation, hemosiderin, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, THYROID GLAND (BOTH LOBES), KIDNEYS, URINARY BLADDER,
ADRENAL GLANDS, BONE (STERNUM), BONE MARROW (STERNUM).

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

FEMALE

* STATE AT NECROPSY: K0/+1
DAYS ON TEST : 91

* ANIMAL NO. : 74

* NECROPSY FINDINGS

GENERAL OBSERVATIONS:

- 01: EMACIATED.
- 02: BEGINNING AUTOLYSIS.

THYMUS:

- 01: DISCOLOURATION, REDDISH.

SPLEEN:

- 01: REDUCED IN SIZE.

MESENTERIC LYMPH NODE:

- 01: DISCOLOURATION, BLACK-BROWN.

MANDIBULAR LYMPH NODES:

- 01: DISCOLOURATION, BLACK-BROWN.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LUNG:

Severe autolysis, evaluation not possible

THYMUS:

-Congestion/hemorrhage, grade 2

This finding corresponds to necropsy observation no: 01.

TRACHEA:

Severe autolysis, evaluation not possible

DUODENUM:

Severe autolysis, evaluation not possible

JEJUNUM:

Severe autolysis, evaluation not possible

ILEUM:

Severe autolysis, evaluation not possible

CECUM:

Severe autolysis, evaluation not possible

COLON:

Severe autolysis, evaluation not possible

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 144/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 74

RECTUM:

Severe autolysis, evaluation not possible

LIVER:

Advanced autolysis.

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 2

-Necrosis coagulative, focal/multifocal, grade 2

SPLEEN:

Severe autolysis, evaluation not possible

Organ autolytic, evaluation not possible

MESENTERIC LYMPH NODE:

No microscopic finding corresponding to necropsy observation no. 01.

MANDIBULAR LYMPH NODES:

-Congestion, bilateral, grade 2

This finding corresponds to necropsy observation no: 01.

KIDNEYS:

Severe autolysis, evaluation not possible

VAGINA:

-Cycle: estrus

LARYNX:

Severe autolysis, evaluation not possible

EYES:

Severe autolysis, evaluation not possible

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 145/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 74

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, ESOPHAGUS , THYROID GLAND (BOTH LOBES), PARATHYROID GLANDS, STOMACH, PEYER'S PATCHES, MESENTERIC LYMPH NODE, PANCREAS, SUBLINGUAL GLANDS, MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER, ADRENAL GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , OVARIES, UTERUS, CERVIX, SKIN/SUBCUTIS, MAMMARY GLAND, OPTIC NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 75

* NECROPSY FINDINGS

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 2

KIDNEYS:

-Cyst, medulla, single, unilateral, grade 2

ADRENAL GLANDS:

-Vacuolation zona glomerulosa, bilateral, grade 1

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 146/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, 100 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 75

UTERUS:

-Cyclic dilation, proestrus stage

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, THYROID GLAND (BOTH LOBES), STOMACH, URINARY BLADDER,
BONE (STERNUM), BONE MARROW (STERNUM).

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

ANIMAL HEADING DATA
DOSE GROUP : 03, 300 MG/KG

ANIMAL NUMBER	SEX M/F	DEFINED STATE	AND FINAL NECROPSY	TEST DAYS	FIRST DAY	AND LAST DAY UNDER TEST	DATE OF NECROPSY
26	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
27	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
28	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
29	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
30	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
31	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
32	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
33	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
34	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
35	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
76	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
77	F	K0	+1	77	25-FEB-16	11-MAY-16	12-MAY-16
78	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
79	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
80	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
81	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
82	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
83	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
84	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
85	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 148/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

MALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 26

* NECROPSY FINDINGS

THYMUS:

01: REDUCED IN SIZE.

THYROID GLAND (BOTH LOBES):

01: BOTH SIDES: ENLARGED.

LIVER:

01: ENLARGED.

02: DISCOLOURATION, RED-BROWN.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:

No microscopic finding corresponding to necropsy observation no. 01.

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 2

This finding corresponds to necropsy observation no: 01.

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 1

-Hyperplasia squamous cell, forestomach, grade 2

-Edema, forestomach, grade 2

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 2

This finding corresponds to necropsy observations nos: 01,02.

URINARY BLADDER:

Tissue not present for histologic examination

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 149/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

MALE

CONT./FF. ANIMAL NO. : 26

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, KIDNEYS, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 27

* NECROPSY FINDINGS

LIVER:

01: ENLARGED.

KIDNEYS:

01: BOTH SIDES: DISCOLOURATION, GREENISH.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 1

-Hyperplasia squamous cell, forestomach, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 1

This finding corresponds to necropsy observation no: 01.

-Necrosis coagulative, focal/multifocal, grade 1

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

URINARY BLADDER:

-Hyperplasia/hypertrophy urothelium, grade 1

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 150/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

MALE

CONT./FF. ANIMAL NO. : 27

.....
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- KIDNEYS, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 28

* NECROPSY FINDINGS

THYMUS:

01: ENLARGED.

LIVER:

01: RIGHT MEDIAL LOBE: ACCESSORY LOBE.

02: ACCENTUATED LOBULAR PATTERN.

03: DISCOLOURATION, RED-BROWN.

04: ENLARGED.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:

No microscopic finding corresponding to necropsy observation no. 01.

THYROID GLAND (BOTH LOBES):

-Cyst, ultimobranchial, bilateral, grade 1

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 2

-Hyperplasia squamous cell, forestomach, grade 2

-Edema, forestomach, grade 2

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 151/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

MALE

CONT./FF. ANIMAL NO. : 28

LIVER:

- Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 3
This finding corresponds to necropsy observations nos: 02,03,04.
 - Accessory lobe
This finding corresponds to necropsy observation no: 01.
- ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, KIDNEYS, URINARY BLADDER, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 29

* NECROPSY FINDINGS

LIVER:

- 01: ENLARGED.
- NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

- Hypertrophy follicular cell, bilateral, grade 2

STOMACH:

- Hyperplasia squamous cell, forestomach, grade 1

LIVER:

- Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 2
This finding corresponds to necropsy observation no: 01.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 152/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

MALE

CONT./FF. ANIMAL NO. : 29

BONE MARROW (STERNUM):

-Increased adipocytes, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- KIDNEYS, URINARY BLADDER, BONE (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 30

* NECROPSY FINDINGS

LIVER:

01: ENLARGED.

02: DISCOLOURATION, RED-BROWN.

PROSTATE GLAND:

01: REDUCED IN SIZE.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 2

STOMACH:

-Hyperplasia squamous cell, forestomach, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 2

This finding corresponds to necropsy observations nos: 01,02.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 153/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

MALE

CONT./FF. ANIMAL NO. : 30

KIDNEYS:

-Hyaline droplet accumulation, bilateral, grade 1

PROSTATE GLAND:

No microscopic finding corresponding to necropsy observation no. 01.

BONE MARROW (STERNUM):

-Increased adipocytes, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- URINARY BLADDER, PROSTATE GLAND, BONE (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 31

* NECROPSY FINDINGS

LIVER:

01: ENLARGED.

KIDNEYS:

01: BOTH SIDES: DISCOLOURATION, GREENISH.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 2

This finding corresponds to necropsy observation no: 01.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 154/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

MALE

CONT./FF. ANIMAL NO. : 31

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.
BONE MARROW (STERNUM):
-Increased adipocytes, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- STOMACH, KIDNEYS, URINARY BLADDER, BONE (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 32

* NECROPSY FINDINGS

THYMUS:

01: FOCUS/FOCI, ISOLATED, REDDISH.

LIVER:

01: ENLARGED.

02: DISCOLOURATION, RED-BROWN.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:

-Congestion/hemorrhage, grade 1

This finding corresponds to necropsy observation no: 01.

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

STOMACH:

-Hyperplasia squamous cell, forestomach, grade 2

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 155/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

MALE

CONT./FF. ANIMAL NO. : 32

LIVER:

- Infiltrate inflammatory cell, mononuclear, grade 1
 - Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm, grade 1
- This finding corresponds to necropsy observations nos: 01,02.

KIDNEYS:

- Basophilia tubule, unilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- URINARY BLADDER, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 33

* NECROPSY FINDINGS

LIVER:

01: ENLARGED.

KIDNEYS:

01: BOTH SIDES: DISCOLOURATION, GREENISH.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

- Hypertrophy follicular cell, bilateral, grade 1

LIVER:

- Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm, grade 2

This finding corresponds to necropsy observation no: 01.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 156/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

MALE

CONT./FF. ANIMAL NO. : 33

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

URINARY BLADDER:

- Infiltrate inflammatory cell, lymphogranulocytic, grade 2
- Hyperplasia/hypertrophy urothelium, grade 2
- Edema, submucosa, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- STOMACH, KIDNEYS, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 34

* NECROPSY FINDINGS

THYMUS:

01: RIGHT SIDE: DISCOLOURATION, REDDISH.

THYROID GLAND (BOTH LOBES):

01: BOTH SIDES: ENLARGED.

LIVER:

01: ENLARGED.

PREPUTIAL GLANDS (INGUINAL GLANDS):

01: REDUCED IN SIZE.

NO OTHER NECROPSY OBSERVATIONS NOTED

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

MALE

CONT./FF. ANIMAL NO. : 34

* MICROSCOPIC FINDINGS

THYMUS:

-Congestion/hemorrhage, grade 1

This finding corresponds to necropsy observation no: 01.

THYROID GLAND (BOTH LOBES):

No microscopic finding corresponding to necropsy observation no. 01.

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 2

-Hyperplasia squamous cell, forestomach, grade 2

-Erosion/ulceration, focal, forestomach, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 2

This finding corresponds to necropsy observation no: 01.

URINARY BLADDER:

-Hyperplasia/hypertrophy urothelium, grade 1

BONE MARROW (STERNUM):

-Increased adipocytes, grade 1

PREPUTIAL GLANDS (INGUINAL GLANDS):

No microscopic finding corresponding to necropsy observation no. 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYROID GLAND (BOTH LOBES), KIDNEYS, BONE (STERNUM), PREPUTIAL
GLANDS (INGUINAL GLANDS).

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 158/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

MALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 35

* NECROPSY FINDINGS

LIVER:

01: ENLARGED.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 2

STOMACH:

-Inflammation forestomach, lymphocytic, focal, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 2

This finding corresponds to necropsy observation no: 01.

KIDNEYS:

-Hyaline droplet accumulation, bilateral, grade 1

URINARY BLADDER:

-Infiltrate inflammatory cell, lymphocytic, grade 1

-Hyperplasia/hypertrophy urothelium, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- BONE (STERNUM), BONE MARROW (STERNUM).

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 159/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 76

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

THYMUS:

-Cystic ducts, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 2

KIDNEYS:

-Mineralization, papillary, focal, unilateral, grade 1

URINARY BLADDER:

Tissue not present for histologic examination

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYROID GLAND (BOTH LOBES), STOMACH, ADRENAL GLANDS, BONE
(STERNUM), BONE MARROW (STERNUM).

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 160/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

FEMALE

* STATE AT NECROPSY: K0/+1
DAYS ON TEST : 77

* ANIMAL NO. : 77

* NECROPSY FINDINGS

GENERAL OBSERVATIONS:

01: CANNIBALISM:ORGAN MISSING, UTERUS, CERVIX, VAGINA, ILEUM,
CAECUM, COLON, MESENTERIC LYMPH N, URINARY BLADDER,
SKELETAL MUSCLE, OVARIES.

02: ADVANCED AUTOLYSIS.

03: CANNIBALISM:ORGAN MISSING: TAILBASE, BOTH HINDLEGS, RECTUM.

THYMUS:

01: FOCUS/FOCI, SEVERAL, REDDISH.

STOMACH:

01: GLANDULAR MUCOSA: FOCUS/FOCI, MANY, BLACK-BROWN.

02: GLANDULAR MUCOSA: IRREGULAR SURFACE.

LIVER:

01: ENLARGED.

ADRENAL GLANDS:

01: BOTH SIDES: ENLARGED.

RENAL LYMPH NODE:

01: BOTH SIDES: ENLARGED.

BODY CAVITIES:

01: THORACIC CAVITY: CONTAINS FLUID, REDDISH, WATERY-CLOUDY.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LUNG:

-Mineralization vascular, grade 1

THYMUS:

-Congestion/hemorrhage, grade 2

This finding corresponds to necropsy observation no: 01.

THYROID GLAND (BOTH LOBES):

Severe autolysis, evaluation not possible

PARATHYROID GLANDS:

Severe autolysis, evaluation not possible

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 77

STOMACH:

Severe autolysis, evaluation not possible
No microscopic finding corresponding to necropsy observation
no. 01,02.

DUODENUM:

Severe autolysis, evaluation not possible

JEJUNUM:

Severe autolysis, evaluation not possible

ILEUM:

Tissue not present for histologic examination

PEYER'S PATCHES:

Tissue not present for histologic examination

CECUM:

Tissue not present for histologic examination

COLON:

Tissue not present for histologic examination

RECTUM:

Tissue not present for histologic examination

LIVER:

- Infiltrate inflammatory cell, mononuclear, grade 2
 - Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 2
- This finding corresponds to necropsy observation no: 01.

SPLEEN:

Severe autolysis, evaluation not possible

MESENTERIC LYMPH NODE:

Tissue not present for histologic examination

PANCREAS:

Severe autolysis, evaluation not possible

SUBLINGUAL GLANDS:

Severe autolysis, evaluation not possible

MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS:

Severe autolysis, evaluation not possible

KIDNEYS:

Severe autolysis, evaluation not possible

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 77

URINARY BLADDER:

Tissue not present for histologic examination

ADRENAL GLANDS:

Severe autolysis, evaluation not possible

No microscopic finding corresponding to necropsy observation no. 01.

SCIATIC NERVE (LEFT):

Tissue not present for histologic examination

OVARIES:

Tissue not present for histologic examination

UTERUS:

Tissue not present for histologic examination

CERVIX:

Tissue not present for histologic examination

VAGINA:

Tissue not present for histologic examination

MAMMARY GLAND:

Tissue not present for histologic examination

EYES:

Severe autolysis, evaluation not possible

RENAL LYMPH NODE:

Tissue not present for histologic examination

No microscopic finding corresponding to necropsy observation no. 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, TRACHEA, ESOPHAGUS , MANDIBULAR LYMPH NODES, BRAIN, PITUITARY GLAND, SKIN/SUBCUTIS, LARYNX, OPTIC NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM), BONE MARROW (STERNUM).

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 163/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 78

* NECROPSY FINDINGS

STOMACH:

01: FORESTOMACH: FOCUS/FOCI, ISOLATED, BLACK.

LIVER:

01: ENLARGED.

02: ACCENTUATED LOBULAR PATTERN.

03: DISCOLOURATION, RED-BROWN.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:

-Lymphocytolysis increased, grade 1

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 2

-Hyperplasia squamous cell, forestomach, grade 3

-Erosion/ulceration, forestomach, grade 2

This finding corresponds to necropsy observation no: 01.

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 1

This finding corresponds to necropsy observations nos: 01,02,03.

SPLEEN:

-Pigmentation, hemosiderin, grade 1

URINARY BLADDER:

-Hyperplasia/hypertrophy urothelium, grade 1

BONE MARROW (STERNUM):

-Increased adipocytes, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 164/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 78

* ORGANS WITHOUT ABNORMALITIES

- KIDNEYS, ADRENAL GLANDS, BONE (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 79

* NECROPSY FINDINGS

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:

-Hyperplasia, epithelial tubules and cords, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 2

SPLEEN:

-Hematopoiesis extramedullary, grade 1

-Pigmentation, hemosiderin, grade 2

KIDNEYS:

-Papil eosinophilic content, bilateral, grade 1

-Mineralization, pelvic, focal, unilateral, grade 1

URINARY BLADDER:

-Hyperplasia/hypertrophy urothelium, grade 1

ADRENAL GLANDS:

-Vacuolation zona glomerulosa, bilateral, grade 1

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 165/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 79

UTERUS:

-Cyclic dilation, proestrus stage

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYROID GLAND (BOTH LOBES), STOMACH, BONE (STERNUM), BONE MARROW (STERNUM) .

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 80

* NECROPSY FINDINGS

THYROID GLAND (BOTH LOBES):

01: BOTH SIDES: ENLARGED.

LIVER:

01: DISCOLOURATION, RED-BROWN.

02: ACCENTUATED LOBULAR PATTERN.

03: ENLARGED.

KIDNEYS:

01: BOTH SIDES: DISCOLOURATION, GREENISH.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

No microscopic finding corresponding to necropsy observation no. 01.

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 166/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 80

grade 1

This finding corresponds to necropsy observations nos: 01,02,03.

SPLEEN:

-Hematopoiesis extramedullary, grade 1

-Pigmentation, hemosiderin, grade 2

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

-Papil eosinophilic content, unilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, THYROID GLAND (BOTH LOBES), STOMACH, URINARY BLADDER,
ADRENAL GLANDS, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 81

* NECROPSY FINDINGS

LIVER:

01: ENLARGED.

02: DISCOLOURATION, RED-BROWN.

03: ACCENTUATED LOBULAR PATTERN.

KIDNEYS:

01: BOTH SIDES: ENLARGED.

02: BOTH SIDES: PELVIC DILATION.

OVARIES:

01: BOTH SIDES: ENLARGED.

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 81

* MICROSCOPIC FINDINGS

STOMACH:

-Hyperplasia squamous cell, forestomach, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 2

This finding corresponds to necropsy observations nos: 01,02,03.

SPLEEN:

-Pigmentation, hemosiderin, grade 2

KIDNEYS:

-Basophilia tubule, unilateral, grade 1

-Dilation, pelvis, bilateral, grade 3

This finding corresponds to necropsy observations nos: 01,02.

ADRENAL GLANDS:

-Cortical tissue, accessory, unilateral

-Vacuolation zona glomerulosa, bilateral, grade 1

OVARIES:

Large organ, normal histology

UTERUS:

-Cyclic dilation, estrus stage

This finding corresponds to necropsy observation no: 01.

BONE MARROW (STERNUM):

-Increased adipocytes, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, THYROID GLAND (BOTH LOBES), URINARY BLADDER, OVARIES,
BONE (STERNUM).

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 168/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 82

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

STOMACH:

-Hyperplasia squamous cell, forestomach, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 3

ADRENAL GLANDS:

-Vacuolation zona glomerulosa, bilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, KIDNEYS, URINARY BLADDER, BONE (STERNUM), BONE MARROW
(STERNUM) .

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 169/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 83

* NECROPSY FINDINGS

THYROID GLAND (BOTH LOBES):

01: BOTH SIDES: ENLARGED.

MANDIBULAR LYMPH NODES:

01: RIGHT SIDE: DISCOLOURATION, REDDISH.

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

No microscopic finding corresponding to necropsy observation no. 01.

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 1

-Hyperplasia squamous cell, forestomach, grade 3

-Edema, forestomach, grade 2

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 1

SPLEEN:

-Hematopoiesis extramedullary, grade 1

-Pigmentation, hemosiderin, grade 2

MANDIBULAR LYMPH NODES:

-Erythrocytes, intrasinusoidal, unilateral, grade 3

This finding corresponds to necropsy observation no: 01.

ADRENAL GLANDS:

-Cortical tissue, accessory, unilateral

UTERUS:

-Cyclic dilation, estrus stage

This finding corresponds to necropsy observation no: 01.

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 83

.....
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, THYROID GLAND (BOTH LOBES), KIDNEYS, URINARY BLADDER,
BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 84

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

THYMUS:

-Hyperplasia, epithelial tubules and cords, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 1

-Necrosis hepatocellular centrilobular, grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 171/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 84

* ORGANS WITHOUT ABNORMALITIES

- THYROID GLAND (BOTH LOBES), STOMACH, KIDNEYS, URINARY BLADDER,
ADRENAL GLANDS, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 85

* NECROPSY FINDINGS

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:

-Congestion/hemorrhage, grade 1

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 2

SPLEEN:

-Pigmentation, hemosiderin, grade 3

KIDNEYS:

-Papil eosinophilic content, unilateral, grade 1

ADRENAL GLANDS:

-Vacuolation zona glomerulosa, bilateral, grade 1

UTERUS:

-Cyclic dilation, estrus stage

This finding corresponds to necropsy observation no: 01.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 172/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 300 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 85

.....
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- STOMACH, URINARY BLADDER, BONE (STERNUM), BONE MARROW (STERNUM).

TEST ITEM : MTDID 7831
 TEST SYSTEM : RAT, 90 Days + Rec., Gavage
 SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
 FINALIZED : 01-FEB-17
 PathData@System V6.2e2

ANIMAL HEADING DATA
 DOSE GROUP : 04, 600 MG/KG

ANIMAL NUMBER	SEX M/F	DEFINED STATE	AND FINAL NECROPSY	TEST DAYS	FIRST DAY	AND LAST DAY UNDER TEST	DATE OF NECROPSY
36	M	K0	+2	70	25-FEB-16	04-MAY-16	04-MAY-16
37	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
38	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
39	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
40	M	K0	+2	19	25-FEB-16	14-MAR-16	15-MAR-16
41	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
42	M	K0	K0	91	25-FEB-16	25-MAY-16	26-MAY-16
43	M	R1	R1	92	25-FEB-16	26-MAY-16	23-JUN-16
44	M	K0	+1	26	25-FEB-16	21-MAR-16	21-MAR-16
45	M	R1	R1	92	25-FEB-16	26-MAY-16	23-JUN-16
46	M	R1	R1	92	25-FEB-16	26-MAY-16	23-JUN-16
47	M	R1	+2	30	25-FEB-16	25-MAR-16	25-MAR-16
48	M	R1	+2	62	25-FEB-16	26-APR-16	26-APR-16
49	M	R1	R1	92	25-FEB-16	26-MAY-16	23-JUN-16
50	M	R1	+2	84	25-FEB-16	18-MAY-16	19-MAY-16
86	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
87	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
88	F	K0	+2	22	25-FEB-16	17-MAR-16	18-MAR-16
89	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
90	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
91	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
92	F	K0	K0	96	25-FEB-16	30-MAY-16	31-MAY-16
93	F	K0	+1	19	25-FEB-16	14-MAR-16	15-MAR-16
94	F	R1	R1	124	25-FEB-16	27-JUN-16	28-JUN-16
95	F	R1	R1	124	25-FEB-16	27-JUN-16	28-JUN-16
96	F	R1	+1	30	25-FEB-16	25-MAR-16	25-MAR-16
97	F	R1	R1	124	25-FEB-16	27-JUN-16	28-JUN-16
98	F	R1	R1	124	25-FEB-16	27-JUN-16	28-JUN-16
99	F	R1	R1	124	25-FEB-16	27-JUN-16	28-JUN-16
100	F	R1	+2	63	25-FEB-16	27-APR-16	27-APR-16

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

* STATE AT NECROPSY: K0/+2
DAYS ON TEST : 70

* ANIMAL NO. : 36

* CAUSE OF DEATH / MORBIDITY

LIVER:

-Necrosis hepatocellular centrilobular, grade 4

* NECROPSY FINDINGS

THYMUS:

01: REDUCED IN SIZE.

STOMACH:

- 01: GLANDULAR MUCOSA: IRREGULAR SURFACE.
- 02: GLANDULAR MUCOSA: FOCUS/FOCI, MANY, DARK RED.
- 03: FORESTOMACH: FOCUS/FOCI, ISOLATED, BLACK-BROWN.

LIVER:

- 01: LEFT LATERAL LOBE: FOCUS/FOCI, ISOLATED, GRAY-WHITE.
- 02: RIGHT MEDIAL LOBE: FOCUS/FOCI, ISOLATED, GRAY-WHITE.

KIDNEYS:

01: BOTH SIDES: DISCOLOURATION, GREENISH.

PROSTATE GLAND:

01: REDUCED IN SIZE.

SEMINAL VESICLES:

01: BOTH SIDES: REDUCED IN SIZE.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:

-Depletion, lymphoid, grade 3

This finding corresponds to necropsy observation no: 01.

PARATHYROID GLANDS:

Tissue not present for histologic examination

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 36

STOMACH:

- No microscopic finding corresponding to necropsy observation no. 01.
- Inflammation forestomach, lymphogranulocytic, grade 2
- Hyperplasia squamous cell, forestomach, grade 3
- Erosion/ulceration, forestomach, focal, grade 2
- This finding corresponds to necropsy observation no: 03.
- Hemorrhage, nonglandular stomach, grade 1
- Congestion, glandular stomach, grade 1
- This finding corresponds to necropsy observation no: 02.

LIVER:

- Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm, grade 3
- Necrosis hepatocellular centrilobular, with brown pigment, grade 4
- Necrosis coagulative, focal/multifocal, grade 2
- This finding corresponds to necropsy observations nos: 01,02.

SPLEEN:

- Pigmentation, hemosiderin, grade 1

KIDNEYS:

- No microscopic finding corresponding to necropsy observation no. 01.
- Infiltrate inflammatory cell, lymphocytic, unilateral, grade 1
- Basophilia tubule, unilateral, grade 2
- Vacuolar degeneration/necrosis tubular, unilateral, grade 2
- Dilation, tubule, bilateral, grade 1
- Papil hyperplasia epithelium with cellular debris/casts, bilateral, grade 1
- Papil inflammatory infiltrate, unilateral, grade 1

URINARY BLADDER:

- Infiltrate inflammatory cell, lymphocytic, grade 1
- Hyperplasia/hypertrophy urothelium, grade 2

ADRENAL GLANDS:

- Vacuolation zona glomerulosa, bilateral, grade 3

PROSTATE GLAND:

- Reduced acinar content, grade 2
- This finding corresponds to necropsy observation no: 01.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 176/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 36

SEMINAL VESICLES:

-Reduced acinar content, bilateral, grade 2
This finding corresponds to necropsy observation no: 01.

HARDERIAN GLANDS:

-Dilation glandular, bilateral, grade 1

BONE MARROW (STERNUM):

-Increased adipocytes, grade 3
-Atrophy, diffuse, grade 3

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, TRACHEA, ESOPHAGUS , THYROID GLAND (BOTH LOBES), DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, PANCREAS, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , TESTES, EPIDIDYMIDES, COAGULATING GLANDS (ANTERIOR PROSTATE), SKIN/SUBCUTIS, LARYNX, EYES, OPTIC NERVES, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM) .

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 37

* NECROPSY FINDINGS

STOMACH:

01: GLANDULAR MUCOSA: FOCUS/FOCI, ISOLATED, REDDISH.

LIVER:

01: ENLARGED.

02: DISCOLOURATION, RED-BROWN.

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 37

KIDNEYS:

01: BOTH SIDES: DISCOLOURATION, RED-BROWN.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 2

STOMACH:

No microscopic finding corresponding to necropsy observation no. 01.

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 2

This finding corresponds to necropsy observations nos: 01,02.

-Necrosis hepatocellular centrilobular, grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 2

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

-Hyaline droplet accumulation, bilateral, grade 1

-Eosinophilic content tubular, unilateral, grade 2

URINARY BLADDER:

-Hyperplasia/hypertrophy urothelium, grade 1

ADRENAL GLANDS:

-Vacuolation zona glomerulosa, bilateral, grade 1

-Vacuolation zona fasciculata, bilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 178/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 37

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, THYMUS, TRACHEA, ESOPHAGUS , PARATHYROID
GLANDS, STOMACH, DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES,
CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, PANCREAS, MANDIBULAR
LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR
(SUBMANDIBULAR/SUBMAXILLARY) GLANDS, BRAIN, PITUITARY GLAND,
SCIATIC NERVE (LEFT) , TESTES, EPIDIDYMIDES, PROSTATE GLAND,
SEMINAL VESICLES, COAGULATING GLANDS (ANTERIOR PROSTATE) ,
SKIN/SUBCUTIS, LARYNX, EYES, OPTIC NERVES, HARDERIAN GLANDS,
SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT) ,
SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM), BONE MARROW
(STERNUM) .

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 38

* NECROPSY FINDINGS

THYMUS:

01: REDUCED IN SIZE.

STOMACH:

01: FORESTOMACH: IRREGULAR SURFACE.

LIVER:

01: ENLARGED.

02: DISCOLOURATION, RED-BROWN.

SPLEEN:

01: REDUCED IN SIZE.

MESENTERIC LYMPH NODE:

01: REDUCED IN SIZE.

KIDNEYS:

01: BOTH SIDES: DISCOLOURATION, RED-BROWN.

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 38

PROSTATE GLAND:

01: REDUCED IN SIZE.

SEMINAL VESICLES:

01: BOTH SIDES: REDUCED IN SIZE.

PREPUTIAL GLANDS (INGUINAL GLANDS):

01: BOTH SIDES: REDUCED IN SIZE.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LUNG:

- Alveolar macrophage aggregation, grade 2
- Inflammation peribronchial/perivascular, grade 1

THYMUS:

- Depletion, lymphoid, grade 1

This finding corresponds to necropsy observation no: 01.

THYROID GLAND (BOTH LOBES):

- Hypertrophy follicular cell, bilateral, grade 2

STOMACH:

- Hyperplasia squamous cell, forestomach, grade 1
- Cyst(s), forestomach, grade 2

This finding corresponds to necropsy observation no: 01.

LIVER:

- Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm, grade 3

This finding corresponds to necropsy observations nos: 01,02.

- Necrosis hepatocellular centrilobular, with brown pigment, grade 2

This finding corresponds to necropsy observation no: 02.

- Necrosis coagulative, focal/multifocal, grade 1

SPLEEN:

No microscopic finding corresponding to necropsy observation no. 01.

- Pigmentation, hemosiderin, grade 2

MESENTERIC LYMPH NODE:

No microscopic finding corresponding to necropsy observation no. 01.

- Increased macrophage foci, grade 1

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 180/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 38

MANDIBULAR LYMPH NODES:

Only one of paired organs examined/present

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

-Infiltrate inflammatory cell, lymphogranulocytic, bilateral,
grade 1

-Basophilia tubule, bilateral, grade 2

-Eosinophilic content tubular, bilateral, grade 2

-Casts granular, bilateral, grade 2

-Papil hyperplasia epithelium with cellular debris/casts,
bilateral, grade 1

URINARY BLADDER:

-Hyperplasia/hypertrophy urothelium, grade 1

PROSTATE GLAND:

No microscopic finding corresponding to necropsy observation no. 01.

SEMINAL VESICLES:

No microscopic finding corresponding to necropsy observation no. 01.

BONE MARROW (STERNUM):

-Increased adipocytes, grade 3

PREPUTIAL GLANDS (INGUINAL GLANDS):

No microscopic finding corresponding to necropsy observation no. 01.

-Infiltrate inflammatory cell, mononuclear, unilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 181/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 38

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, TRACHEA, ESOPHAGUS , PARATHYROID GLANDS, DUODENUM,
JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, PANCREAS,
MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR
(SUBMANDIBULAR/SUBMAXILLARY) GLANDS, ADRENAL GLANDS, BRAIN,
PITUITARY GLAND, SCIATIC NERVE (LEFT) , TESTES, EPIDIDYMIDES,
PROSTATE GLAND, SEMINAL VESICLES, COAGULATING GLANDS (ANTERIOR
PROSTATE), SKIN/SUBCUTIS, LARYNX, EYES, OPTIC NERVES, HARDERIAN
GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC
SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 39

* NECROPSY FINDINGS

LIVER:

- 01: ENLARGED.
- 02: DISCOLOURATION, RED-BROWN.

KIDNEYS:

- 01: BOTH SIDES: DISCOLOURATION, GREENISH.

URINARY BLADDER:

- 01: CONTAINS GRAVEL.
- 02: WALL: THICKENED.

NO OTHER NECROPSY OBSERVATIONS NOTED

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 39

* MICROSCOPIC FINDINGS

LUNG:

-Inflammation peribronchial/perivascular, grade 1

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 2

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 1

-Hyperplasia squamous cell, forestomach, grade 2

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 3

This finding corresponds to necropsy observations nos: 01,02.

-Necrosis hepatocellular centrilobular, with brown pigment,
grade 2

This finding corresponds to necropsy observation no: 02.

SPLEEN:

-Pigmentation, hemosiderin, grade 2

MESENTERIC LYMPH NODE:

-Increased macrophage foci, grade 1

MANDIBULAR LYMPH NODES:

-Erythrocytes, intrasinusoidal, unilateral, grade 2

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

-Hyaline droplet accumulation, bilateral, grade 1

-Eosinophilic content tubular, bilateral, grade 1

URINARY BLADDER:

-Infiltrate inflammatory cell, lymphocytic, grade 1

-Hyperplasia/hypertrophy urothelium, grade 3

This finding corresponds to necropsy observation no: 02.

-Uroliths

Present on slide 24.

This finding corresponds to necropsy observation no: 01.

HARDERIAN GLANDS:

-Hemorrhage post-traumatic, unilateral, grade 1

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 39

.....
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, THYMUS, TRACHEA, ESOPHAGUS , PARATHYROID GLANDS,
DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM,
PANCREAS, SUBLINGUAL GLANDS, MANDIBULAR
(SUBMANDIBULAR/SUBMAXILLARY) GLANDS, ADRENAL GLANDS, BRAIN,
PITUITARY GLAND, SCIATIC NERVE (LEFT) , TESTES, EPIDIDYMIDES,
PROSTATE GLAND, SEMINAL VESICLES, COAGULATING GLANDS (ANTERIOR
PROSTATE), SKIN/SUBCUTIS, LARYNX, EYES, OPTIC NERVES, SPINAL CORD
(CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD
(LUMBAR SEGMENT), BONE (STERNUM), BONE MARROW (STERNUM) .

* STATE AT NECROPSY: K0/+2
DAYS ON TEST : 19

* ANIMAL NO. : 40

* CAUSE OF DEATH / MORBIDITY

LIVER:

-Necrosis coagulative, grade 3

KIDNEYS:

-Vacuolar degeneration/necrosis tubular, grade 3

* NECROPSY FINDINGS

GENERAL OBSERVATIONS:

01: GI-TRACTUS: DISTENDED WITH GAS.

02: EMACIATED.

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 40

HEART:
01: REDUCED IN SIZE.
THYMUS:
01: REDUCED IN SIZE.
LIVER:
01: FOCUS/FOCI, MANY, GRAY-WHITE.
SPLEEN:
01: REDUCED IN SIZE.
PROSTATE GLAND:
01: REDUCED IN SIZE.
SEMINAL VESICLES:
01: BOTH SIDES: REDUCED IN SIZE.
PREPUTIAL GLANDS (INGUINAL GLANDS):
01: REDUCED IN SIZE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

HEART:
No microscopic finding corresponding to necropsy observation no. 01.
THYMUS:
-Depletion, lymphoid, grade 4
This finding corresponds to necropsy observation no: 01.
TRACHEA:
-Inflammation granulomatous, focal, grade 1
with multinucleated giant cells.
STOMACH:
-Inflammation, glandular stomach, lymphogranulocytic, grade 1
-Hyperplasia squamous cell, forestomach, grade 3
-Erosion/ulceration, forestomach, grade 1
-Congestion, glandular stomach, grade 1
LIVER:
-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 2
-Necrosis hepatocellular centrilobular, grade 2
-Necrosis coagulative, focal/multifocal, grade 3

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 40

.....
This finding corresponds to necropsy observation no: 01.

SPLEEN:

-Depletion, lymphoid, diffuse, grade 4

This finding corresponds to necropsy observation no: 01.

MESENTERIC LYMPH NODE:

-Depletion, lymphoid, grade 2

MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS:

-Reduced acinar contents/atrophy, bilateral, grade 3

KIDNEYS:

-Vacuolar degeneration/necrosis tubular, bilateral, grade 3

-Eosinophilic content tubular, bilateral, grade 1

-Dilation, tubule, bilateral, grade 2

-Papil hyperplasia epithelium with cellular debris/casts,
bilateral, grade 3

ADRENAL GLANDS:

-Vacuolation zona fasciculata, bilateral, grade 2

BRAIN:

Artefactual vacuolation cerebellum/pons.

SCIATIC NERVE (LEFT):

-Infiltrate inflammatory cell, surrounding tissue, grade 2

EPIDIDYMIDES:

-Cell debris, luminal, bilateral, grade 2

PROSTATE GLAND:

-Reduced acinar content, grade 2

This finding corresponds to necropsy observation no: 01.

SEMINAL VESICLES:

-Reduced acinar content, bilateral, grade 2

This finding corresponds to necropsy observation no: 01.

LARYNX:

-Inflammation, acute, grade 1

-Erosion/ulceration, grade 2

BONE MARROW (STERNUM):

-Atrophy, diffuse, grade 3

PREPUTIAL GLANDS (INGUINAL GLANDS):

-Atrophy, bilateral, grade 2

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 186/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 40

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, ESOPHAGUS , THYROID GLAND (BOTH LOBES),
PARATHYROID GLANDS, DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES,
CECUM, COLON, RECTUM, PANCREAS, MANDIBULAR LYMPH NODES,
SUBLINGUAL GLANDS, URINARY BLADDER, BRAIN, PITUITARY GLAND,
TESTES, COAGULATING GLANDS (ANTERIOR PROSTATE), SKIN/SUBCUTIS,
EYES, OPTIC NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL
SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR
SEGMENT), BONE (STERNUM) .

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 41

* NECROPSY FINDINGS

STOMACH:

01: FORESTOMACH: IRREGULAR SURFACE.

LIVER:

01: ENLARGED.

02: DISCOLOURATION, RED-BROWN.

KIDNEYS:

01: BOTH SIDES: DISCOLOURATION, GREENISH.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LUNG:

-Alveolar macrophage aggregation, grade 2

-Inflammation peribronchial/perivascular, grade 1

-Mineralization vascular, grade 1

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 187/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 41

TRACHEA:

-Ectasia submucosal glands, grade 1

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 3

STOMACH:

-Inflammation, glandular stomach, lymphogranulocytic, grade 2

-Hyperplasia squamous cell, forestomach, grade 3

This finding corresponds to necropsy observation no: 01.

-Erosion/ulceration, forestomach, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 3

This finding corresponds to necropsy observations nos: 01,02.

-Necrosis hepatocellular centrilobular, with brown pigment,
grade 2

This finding corresponds to necropsy observation no: 02.

SPLEEN:

-Pigmentation, hemosiderin, grade 2

MESENTERIC LYMPH NODE:

-Erythrocytes, intrasinusoidal, grade 1

-Sinus histiocytosis, grade 2

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

-Basophilia tubule, unilateral, grade 1

-Eosinophilic content tubular, bilateral, grade 1

URINARY BLADDER:

-Infiltrate inflammatory cell, lymphogranulocytic, grade 2

-Hyperplasia/hypertrophy urothelium, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 188/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 41

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, THYMUS, ESOPHAGUS , PARATHYROID GLANDS, DUODENUM,
JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, PANCREAS,
MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR
(SUBMANDIBULAR/SUBMAXILLARY) GLANDS, ADRENAL GLANDS, BRAIN,
PITUITARY GLAND, SCIATIC NERVE (LEFT) , TESTES, EPIDIDYMIDES,
PROSTATE GLAND, SEMINAL VESICLES, COAGULATING GLANDS (ANTERIOR
PROSTATE), SKIN/SUBCUTIS, LARYNX, EYES, OPTIC NERVES, HARDERIAN
GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC
SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM), BONE
MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 91

* ANIMAL NO. : 42

* NECROPSY FINDINGS

THYMUS:

01: REDUCED IN SIZE.

LIVER:

01: ENLARGED.

02: DISCOLOURATION, RED-BROWN.

KIDNEYS:

01: BOTH SIDES: DISCOLOURATION, GREENISH.

NO OTHER NECROPSY OBSERVATIONS NOTED

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 42

* MICROSCOPIC FINDINGS

LUNG:

-Alveolar macrophage aggregation, grade 2

THYMUS:

-Depletion, lymphoid, grade 1

This finding corresponds to necropsy observation no: 01.

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 2

STOMACH:

-Hyperplasia squamous cell, forestomach, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 3

This finding corresponds to necropsy observations nos: 01,02.

-Necrosis hepatocellular centrilobular, grade 2

-Necrosis coagulative, focal/multifocal, grade 2

SPLEEN:

-Hematopoiesis extramedullary, grade 2

-Pigmentation, hemosiderin, grade 1

MESENTERIC LYMPH NODE:

-Erythrocytes, intrasinusoidal, grade 1

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

-Vacuolar degeneration/necrosis tubular, unilateral, grade 1

-Eosinophilic content tubular, unilateral, grade 1

-Papil hyperplasia epithelium with cellular debris/casts,
unilateral, grade 1

OPTIC NERVES:

Only one of paired organs examined/present

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 42

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, TRACHEA, ESOPHAGUS , PARATHYROID GLANDS, DUODENUM,
JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, PANCREAS,
MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR
(SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER, ADRENAL
GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , TESTES,
EPIDIDYMIDES, PROSTATE GLAND, SEMINAL VESICLES, COAGULATING
GLANDS (ANTERIOR PROSTATE), SKIN/SUBCUTIS, LARYNX, EYES, OPTIC
NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL
CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE
(STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: R1

DAYS ON TEST : 92

* ANIMAL NO. : 43

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

STOMACH:

- Inflammation, glandular stomach, lymphogranulocytic, grade 2
- Vacuolation, limiting ridge, grade 2

KIDNEYS:

- Pigment yellow-brown, tubular, bilateral, grade 1

URINARY BLADDER:

- Hyperplasia/hypertrophy urothelium, grade 2

BONE MARROW (STERNUM):

- Increased adipocytes, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 191/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 43

* ORGANS WITHOUT ABNORMALITIES

- THYROID GLAND (BOTH LOBES), LIVER, BONE (STERNUM).

* STATE AT NECROPSY: K0/+1
DAYS ON TEST : 26

* ANIMAL NO. : 44

* CAUSE OF DEATH / MORBIDITY

GENERAL OBSERVATIONS:

-Gavage accident

* NECROPSY FINDINGS

TRACHEA:

01: PERFORATION(S), AT HEIGHT OF LUNGS.

ESOPHAGUS:

01: DISCOLOURATION, DARK RED, AT HEIGHT OF LUNGS.

STOMACH:

01: GLANDULAR MUCOSA: FOCUS/FOCI, ISOLATED, REDDISH.

LIVER:

01: ENLARGED.

KIDNEYS:

01: BOTH SIDES: ENLARGED.

BODY CAVITIES:

01: THORACIC CAVITY: CONTAINS BLOOD/BLOOD CLOTS.

02: THORACIC CAVITY: CONTAINS HEMORRHAGIC FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 192/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 44

* MICROSCOPIC FINDINGS

GENERAL OBSERVATIONS:

-Gavage accident, based on macroscopic findings

TRACHEA:

No microscopic finding corresponding to necropsy observation no. 01.

ESOPHAGUS:

-Hemorrhage, submucosa, muscle and surrounding tissue, grade 3

This finding corresponds to necropsy observation no: 01.

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

STOMACH:

-Congestion, glandular stomach, grade 1

This finding corresponds to necropsy observation no: 01.

LIVER:

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 2

This finding corresponds to necropsy observation no: 01.

-Necrosis hepatocellular centrilobular, grade 2

SPLEEN:

-Hematopoiesis extramedullary, grade 1

PANCREAS:

-Vacuolation, acinar cells, grade 1

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

ADRENAL GLANDS:

-Vacuolation zona fasciculata, bilateral, grade 1

OPTIC NERVES:

Only one of paired organs examined/present

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 193/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 44

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, THYMUS, TRACHEA, PARATHYROID GLANDS,
DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM,
MESENTERIC LYMPH NODE, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS,
MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, KIDNEYS, URINARY
BLADDER, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , TESTES,
EPIDIDYIMIDES, PROSTATE GLAND, SEMINAL VESICLES, COAGULATING
GLANDS (ANTERIOR PROSTATE), SKIN/SUBCUTIS, LARYNX, EYES, OPTIC
NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL
CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE
(STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: R1

DAYS ON TEST : 92

* ANIMAL NO. : 45

* NECROPSY FINDINGS

THYROID GLAND (BOTH LOBES):

01: BOTH SIDES: ENLARGED.

LIVER:

01: DISCOLOURATION, RED-BROWN.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 2

This finding corresponds to necropsy observation no: 01.

LIVER:

No microscopic finding corresponding to necropsy observation no. 01.

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 45

KIDNEYS:

-Pigment yellow-brown, tubular, bilateral, grade 1

URINARY BLADDER:

-Hyperplasia/hypertrophy urothelium, grade 1

BONE MARROW (STERNUM):

-Increased adipocytes, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- STOMACH, LIVER, BONE (STERNUM).

* STATE AT NECROPSY: R1

DAYS ON TEST : 92

* ANIMAL NO. : 46

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

STOMACH:

-Inflammation, glandular stomach, lymphogranulocytic, grade 1

-Vacuolation, limiting ridge, grade 2

KIDNEYS:

-Pigment yellow-brown, tubular, bilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 195/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 46

* ORGANS WITHOUT ABNORMALITIES

- THYROID GLAND (BOTH LOBES), LIVER, URINARY BLADDER, BONE
(STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: R1/+2
DAYS ON TEST : 30

* ANIMAL NO. : 47

* CAUSE OF DEATH / MORBIDITY

LIVER:

-Necrosis hepatocellular centrilobular, grade 3

* NECROPSY FINDINGS

GENERAL OBSERVATIONS:

01: EMACIATED.

THYMUS:

01: REDUCED IN SIZE.

STOMACH:

01: IRREGULAR SURFACE.

LIVER:

01: ENLARGED.

02: DISCOLOURATION, DARK RED.

03: FOCUS/FOCI, SEVERAL, GRAY-WHITE.

KIDNEYS:

01: RIGHT SIDE: DISCOLOURATION, DARK RED.

02: RIGHT SIDE: FOCUS/FOCI, MANY, BLACK-BROWN.

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 47

PREPUTIAL GLANDS (INGUINAL GLANDS):
01: BOTH SIDES: REDUCED IN SIZE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:

-Depletion, lymphoid, grade 3
This finding corresponds to necropsy observation no: 01.

ESOPHAGUS:

-Degeneration/necrosis muscle, grade 1

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 2
-Hyperplasia squamous cell, forestomach, grade 3
This finding corresponds to necropsy observation no: 01.
-Erosion/ulceration, forestomach, grade 1
-Congestion, glandular stomach, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1
-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 2
This finding corresponds to necropsy observations nos: 01,02.
-Necrosis hepatocellular centrilobular, with brown pigment,
grade 3
-Necrosis coagulative, focal/multifocal, grade 3
This finding corresponds to necropsy observation no: 03.

MESENTERIC LYMPH NODE:

-Depletion, lymphoid, grade 2
-Erythrocytes, intrasinusoidal, grade 1

PANCREAS:

-Degranulation acinar cells, grade 3

MANDIBULAR LYMPH NODES:

Tissue not present for histologic examination

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 47

MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS:

-Reduced acinar contents/atrophy, bilateral, grade 2

KIDNEYS:

-Infiltrate inflammatory cell, lymphocytic, unilateral, grade 1

-Basophilia tubule, unilateral, grade 2

-Congestion, bilateral, grade 2

This finding corresponds to necropsy observations nos: 01,02.

-Vacuolar degeneration/necrosis tubular, bilateral, grade 2

-Eosinophilic content tubular, bilateral, grade 1

-Dilation, tubule, bilateral, grade 2

PROSTATE GLAND:

-Reduced acinar content, grade 1

SEMINAL VESICLES:

-Reduced acinar content, bilateral, grade 1

BONE MARROW (STERNUM):

-Increased adipocytes, grade 2

-Atrophy, diffuse, grade 3

PREPUTIAL GLANDS (INGUINAL GLANDS):

-Atrophy, bilateral, grade 2

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, TRACHEA, PARATHYROID GLANDS, DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, SPLEEN, SUBLINGUAL GLANDS, URINARY BLADDER, ADRENAL GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , TESTES, EPIDIDYMIDES, COAGULATING GLANDS (ANTERIOR PROSTATE), SKIN/SUBCUTIS, LARYNX, EYES, OPTIC NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM) .

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

* STATE AT NECROPSY: R1/+2
DAYS ON TEST : 62

* ANIMAL NO. : 48

* CAUSE OF DEATH / MORBIDITY

LIVER:

-Necrosis hepatocellular centrilobular, grade 4

* NECROPSY FINDINGS

GENERAL OBSERVATIONS:

- 01: EMACIATED.
- 02: GI-TRACTUS: DISTENDED WITH GAS.

THYMUS:

- 01: REDUCED IN SIZE.

STOMACH:

- 01: GLANDULAR MUCOSA: FOCUS/FOCI, MANY, REDDISH.

LIVER:

- 01: FOCUS/FOCI, SEVERAL, GRAY-WHITE.

KIDNEYS:

- 01: BOTH SIDES: FOCUS/FOCI, SEVERAL, YELLOWISH.

PROSTATE GLAND:

- 01: REDUCED IN SIZE.

SEMINAL VESICLES:

- 01: BOTH SIDES: REDUCED IN SIZE.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:

-Depletion, lymphoid, grade 4

This finding corresponds to necropsy observation no: 01.

THYROID GLAND (BOTH LOBES):

- Hypertrophy follicular cell, bilateral, grade 1
- Cyst, ultimobranchial, unilateral, grade 1

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 48

STOMACH:

- Hyperplasia squamous cell, forestomach, grade 2
 - Hemorrhage, glandular stomach, multifocal, grade 2
- This finding corresponds to necropsy observation no: 01.

LIVER:

- Infiltrate inflammatory cell, mononuclear, grade 2
 - Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm, grade 2
 - Necrosis hepatocellular centrilobular, with brown pigment, grade 4
 - Necrosis coagulative, focal/multifocal, grade 2
- This finding corresponds to necropsy observation no: 01.

SPLEEN:

- Pigmentation, hemosiderin, grade 2

MESENTERIC LYMPH NODE:

- Depletion, lymphoid, grade 2

MANDIBULAR LYMPH NODES:

- Erythrocytes, intrasinusoidal, unilateral, grade 1

KIDNEYS:

- Basophilia tubule, unilateral, grade 3
 - Vacuolar degeneration/necrosis tubular, bilateral, grade 2
- Grade 1 in contralateral organ
- This finding corresponds to necropsy observation no: 01.
- Eosinophilic content tubular, bilateral, grade 1
 - Dilation, tubule, unilateral, grade 2
 - Papil hyperplasia epithelium with cellular debris/casts, bilateral, grade 2
- Grade 1 in contralateral organ

ADRENAL GLANDS:

- Vacuolation zona fasciculata, unilateral, grade 1

SCIATIC NERVE (LEFT):

- Demyelination, grade 2

PROSTATE GLAND:

- Reduced acinar content, grade 2
- This finding corresponds to necropsy observation no: 01.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 200/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 48

SEMINAL VESICLES:

-Reduced acinar content, bilateral, grade 3

This finding corresponds to necropsy observation no: 01.

BONE MARROW (STERNUM):

-Increased adipocytes, grade 3

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, TRACHEA, ESOPHAGUS , PARATHYROID GLANDS,
DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM,
PANCREAS, SUBLINGUAL GLANDS, MANDIBULAR
(SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER, BRAIN,
PITUITARY GLAND, TESTES, EPIDIDYMIDES, COAGULATING GLANDS
(ANTERIOR PROSTATE), SKIN/SUBCUTIS, LARYNX, EYES, OPTIC NERVES,
HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD
(THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM).

* STATE AT NECROPSY: R1

DAYS ON TEST : 92

* ANIMAL NO. : 49

* NECROPSY FINDINGS

LIVER:

01: DISCOLOURATION, RED-BROWN.

NO OTHER NECROPSY OBSERVATIONS NOTED

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 49

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

STOMACH:

-Inflammation, glandular stomach, lymphogranulocytic, grade 1

-Vacuolation, limiting ridge, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Pigment deposition yellow-brown centrilobular, grade 2

This finding corresponds to necropsy observation no: 01.

URINARY BLADDER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hyperplasia/hypertrophy urothelium, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- KIDNEYS, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: R1/+2
DAYS ON TEST : 84

* ANIMAL NO. : 50

* CAUSE OF DEATH / MORBIDITY

LIVER:

-Necrosis hepatocellular centrilobular, grade 3

* NECROPSY FINDINGS

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG MALE

CONT./FF. ANIMAL NO. : 50

GENERAL OBSERVATIONS:

- 01: EMACIATED.
 - 02: GI-TRACTUS: DISTENDED WITH GAS.
 - LUNG:
 - 01: ENLARGED.
 - 02: FOCUS/FOCI, SEVERAL, TAN.
 - THYMUS:
 - 01: REDUCED IN SIZE.
 - TRACHEA:
 - 01: CONTAINS FLUID, WATERY-CLEAR.
 - STOMACH:
 - 01: GLANDULAR MUCOSA: FOCUS/FOCI, ISOLATED, REDDISH.
 - 02: GLANDULAR MUCOSA: IRREGULAR SURFACE.
 - LIVER:
 - 01: ENLARGED.
 - 02: DISCOLOURATION, BLACK-BROWN.
 - SPLEEN:
 - 01: REDUCED IN SIZE.
 - PROSTATE GLAND:
 - 01: REDUCED IN SIZE.
 - SEMINAL VESICLES:
 - 01: BOTH SIDES: REDUCED IN SIZE.
 - HARDERIAN GLANDS:
 - 01: BOTH SIDES: DISCOLOURATION, PALE.
- NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

- LUNG:
- No microscopic finding corresponding to necropsy observation no. 01.
 - Inflammation bronchioalveolar, acute, grade 1
 - Alveolar macrophage aggregation, grade 2
 - This finding corresponds to necropsy observation no: 02.
 - Mineralization vascular, grade 1

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 50

THYMUS:

-Depletion, lymphoid, grade 3
This finding corresponds to necropsy observation no: 01.

TRACHEA:

No microscopic finding corresponding to necropsy observation no. 01.
-Infiltrate inflammatory cell, lymphogranulocytic, grade 1

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

STOMACH:

No microscopic finding corresponding to necropsy observation no. 02.
-Hyperplasia squamous cell, forestomach, grade 2
-Congestion, glandular stomach, grade 1
This finding corresponds to necropsy observation no: 01.

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1
-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm, grade 3
This finding corresponds to necropsy observations nos: 01,02.
-Necrosis hepatocellular centrilobular, with brown pigment, grade 3
This finding corresponds to necropsy observation no: 02.

SPLEEN:

Small organ, normal histology
-Pigmentation, hemosiderin, grade 1

MESENTERIC LYMPH NODE:

-Sinus histiocytosis, grade 2

KIDNEYS:

-Infiltrate inflammatory cell, lymphocytic, unilateral, grade 1
-Basophilia tubule, bilateral, grade 3
-Dilation, tubule, bilateral, grade 2
-Papil hyperplasia epithelium with cellular debris/casts, bilateral, grade 2
-Papil inflammatory infiltrate, unilateral, grade 1

URINARY BLADDER:

-Hyperplasia/hypertrophy urothelium, grade 1

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

MALE

CONT./FF. ANIMAL NO. : 50

ADRENAL GLANDS:

- Cortical tissue, accessory, unilateral
- Vacuolation zona glomerulosa, bilateral, grade 1

TESTES:

- Degeneration, germ cell, unilateral, grade 2

EPIDIDYMIDES:

- Cell debris, luminal, unilateral, grade 1

PROSTATE GLAND:

- Reduced acinar content, grade 2

This finding corresponds to necropsy observation no: 01.

SEMINAL VESICLES:

- Reduced acinar content, bilateral, grade 3

This finding corresponds to necropsy observation no: 01.

LARYNX:

- Squamous metaplasia, grade 2

HARDERIAN GLANDS:

No microscopic finding corresponding to necropsy observation no. 01.

BONE MARROW (STERNUM):

- Increased adipocytes, grade 2
- Atrophy, diffuse, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, ESOPHAGUS , PARATHYROID GLANDS, DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, PANCREAS, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , COAGULATING GLANDS (ANTERIOR PROSTATE), SKIN/SUBCUTIS, EYES, OPTIC NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM).

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 205/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 86

* NECROPSY FINDINGS

STOMACH:

01: FORESTOMACH: FOCUS/FOCI, ISOLATED, REDDISH.

LIVER:

01: ENLARGED.

02: DISCOLOURATION, RED-BROWN.

KIDNEYS:

01: BOTH SIDES: DISCOLOURATION, GREENISH.

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:

-Congestion/hemorrhage, focal, grade 1

-Lymphocytolysis increased, grade 1

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 2

-Cyst, ultimobranchial, unilateral, grade 1

STOMACH:

No microscopic finding corresponding to necropsy observation no. 01.

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 3

This finding corresponds to necropsy observations nos: 01,02.

-Necrosis hepatocellular centrilobular, with brown pigment,
grade 1

This finding corresponds to necropsy observation no: 02.

SPLEEN:

-Hematopoiesis extramedullary, grade 1

-Pigmentation, hemosiderin, grade 2

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 86

MESENTERIC LYMPH NODE:

-Increased macrophage foci, grade 1

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

-Eosinophilic content tubular, unilateral, grade 1

-Dilation, tubule, unilateral, grade 1

-Papil hyperplasia epithelium with cellular debris/casts,
bilateral, grade 2

URINARY BLADDER:

-Hyperplasia/hypertrophy urothelium, grade 1

UTERUS:

-Cyclic dilation, estrus stage

This finding corresponds to necropsy observation no: 01.

VAGINA:

-Cycle: estrus

BONE MARROW (STERNUM):

-Increased adipocytes, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, TRACHEA, ESOPHAGUS , PARATHYROID GLANDS,
STOMACH, DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON,
RECTUM, PANCREAS, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS,
MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, ADRENAL GLANDS,
BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , OVARIES, CERVIX,
SKIN/SUBCUTIS, MAMMARY GLAND, LARYNX, EYES, OPTIC NERVES,
HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD
(THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM).

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 207/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 87

* NECROPSY FINDINGS

LIVER:

01: ENLARGED.

02: DISCOLOURATION, BLACK-BROWN.

KIDNEYS:

01: BOTH SIDES: DISCOLOURATION, GREENISH.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LUNG:

-Inflammation granulomatous, grade 1

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 1

-Hyperplasia squamous cell, forestomach, grade 1

LIVER:

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 3

This finding corresponds to necropsy observations nos: 01,02.

-Necrosis hepatocellular centrilobular, grade 2

This finding corresponds to necropsy observation no: 02.

SPLEEN:

-Pigmentation, hemosiderin, grade 3

MESENTERIC LYMPH NODE:

-Increased macrophage foci, grade 1

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

-Eosinophilic content tubular, unilateral, grade 1

URINARY BLADDER:

-Hyperplasia/hypertrophy urothelium, grade 1

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 87

VAGINA:

-Cycle: diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, THYMUS, TRACHEA, ESOPHAGUS , PARATHYROID GLANDS,
DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM,
PANCREAS, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR
(SUBMANDIBULAR/SUBMAXILLARY) GLANDS, ADRENAL GLANDS, BRAIN,
PITUITARY GLAND, SCIATIC NERVE (LEFT) , OVARIES, UTERUS, CERVIX,
SKIN/SUBCUTIS, MAMMARY GLAND, LARYNX, EYES, OPTIC NERVES,
HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD
(THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM),
BONE MARROW (STERNUM) .

* STATE AT NECROPSY: K0/+2

DAYS ON TEST : 22

* ANIMAL NO. : 88

* CAUSE OF DEATH / MORBIDITY

LIVER:

-Necrosis coagulative, grade 3

KIDNEYS:

-Basophilia tubule, grade 4

* NECROPSY FINDINGS

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 88

GENERAL OBSERVATIONS:

01: EMACIATED.

THYMUS:

01: REDUCED IN SIZE.

STOMACH:

01: FOCUS/FOCI, ISOLATED, GRAY-WHITE.
02: GLANDULAR MUCOSA: IRREGULAR SURFACE.

SPLEEN:

01: REDUCED IN SIZE.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:

-Depletion, lymphoid, grade 4
This finding corresponds to necropsy observation no: 01.

PARATHYROID GLANDS:

Only one of paired organs examined/present

STOMACH:

No microscopic finding corresponding to necropsy observation no. 02.
-Inflammation forestomach, lymphogranulocytic, grade 1
-Hyperplasia squamous cell, forestomach, grade 1
-Erosion/ulceration, forestomach, grade 1
This finding corresponds to necropsy observation no: 01.

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1
-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm, grade 2
-Necrosis hepatocellular centrilobular, grade 1
-Necrosis coagulative, focal/multifocal, grade 3

SPLEEN:

-Atrophy red pulp, grade 2
This finding corresponds to necropsy observation no: 01.

PANCREAS:

-Degranulation acinar cells, grade 2

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 88

KIDNEYS:

- Basophilia tubule, bilateral, grade 4
- Eosinophilic content tubular, unilateral, grade 1
- Casts granular, bilateral, grade 2
- Papil hyperplasia epithelium with cellular debris/casts, unilateral, grade 1
- Mineralization, tubular, corticomedullary, multifocal, bilateral, grade 3

BRAIN:

Artefactual vacuolation cerebellum.

UTERUS:

- Atrophy, diffuse, grade 3

VAGINA:

- Atrophy, epithelial, with granulocytic infiltrate in lumen, grade 2

SPINAL CORD (CERVICAL SEGMENT):

Artefactual vacuolation.

SPINAL CORD (THORACIC SEGMENT):

Artefactual vacuolation.

BONE MARROW (STERNUM):

- Atrophy, diffuse, grade 3

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, TRACHEA, ESOPHAGUS , THYROID GLAND (BOTH LOBES), PARATHYROID GLANDS, DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER, ADRENAL GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , OVARIES, CERVIX, SKIN/SUBCUTIS, MAMMARY GLAND, LARYNX, EYES, OPTIC NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM).

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 211/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 89

* NECROPSY FINDINGS

THYROID GLAND (BOTH LOBES):

01: BOTH SIDES: ENLARGED.

LIVER:

01: ENLARGED.

02: DISCOLOURATION, RED-BROWN.

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

-Thymus, ectopic, bilateral

-Hypertrophy follicular cell, bilateral, grade 1

This finding corresponds to necropsy observation no: 01.

STOMACH:

-Hyperplasia squamous cell, forestomach, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 3

This finding corresponds to necropsy observations nos: 01,02.

-Necrosis hepatocellular centrilobular, with brown pigment,
grade 2

This finding corresponds to necropsy observation no: 02.

SPLEEN:

-Hematopoiesis extramedullary, grade 1

-Pigmentation, hemosiderin, grade 2

MESENTERIC LYMPH NODE:

-Increased macrophage foci, grade 1

MANDIBULAR LYMPH NODES:

-Erythrocytes, intrasinusoidal, unilateral, grade 1

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 212/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 89

URINARY BLADDER:

-Hyperplasia/hypertrophy urothelium, grade 1

ADRENAL GLANDS:

-Vacuolation zona glomerulosa, bilateral, grade 1

UTERUS:

-Cyclic dilation, estrus stage

This finding corresponds to necropsy observation no: 01.

VAGINA:

-Cycle: estrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, THYMUS, TRACHEA, ESOPHAGUS , PARATHYROID
GLANDS, DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON,
RECTUM, PANCREAS, SUBLINGUAL GLANDS, MANDIBULAR
(SUBMANDIBULAR/SUBMAXILLARY) GLANDS, KIDNEYS, BRAIN, PITUITARY
GLAND, SCIATIC NERVE (LEFT) , OVARIES, CERVIX, SKIN/SUBCUTIS,
MAMMARY GLAND, LARYNX, EYES, OPTIC NERVES, HARDERIAN GLANDS,
SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD (THORACIC SEGMENT),
SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM), BONE MARROW
(STERNUM) .

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 90

* NECROPSY FINDINGS

STOMACH:

01: FORESTOMACH: FOCUS/FOCI, ISOLATED, REDDISH.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 213/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 90

LIVER:

- 01: ENLARGED.
- 02: DISCOLOURATION, RED-BROWN.

KIDNEYS:

- 01: BOTH SIDES: DISCOLOURATION, GREENISH.

UTERUS:

- 01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYROID GLAND (BOTH LOBES):

- Hypertrophy follicular cell, bilateral, grade 2

PARATHYROID GLANDS:

Only one of paired organs examined/present

STOMACH:

- Inflammation forestomach, lymphogranulocytic, grade 2
- Hyperplasia squamous cell, forestomach, grade 3
- Erosion/ulceration, forestomach, grade 2
- Hemorrhage, focal, forestomach, grade 2
- This finding corresponds to necropsy observation no: 01.
- Edema, forestomach, grade 2

LIVER:

- Infiltrate inflammatory cell, mononuclear, grade 1
- Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm, grade 3
- This finding corresponds to necropsy observations nos: 01,02.
- Necrosis hepatocellular centrilobular, with brown pigment, grade 2
- This finding corresponds to necropsy observation no: 02.

SPLEEN:

- Hematopoiesis extramedullary, grade 1
- Pigmentation, hemosiderin, grade 2

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 214/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 90

ADRENAL GLANDS:

-Vacuolation zona glomerulosa, bilateral, grade 2

OVARIES:

-Hypertrophy interstitial cell, bilateral, grade 1

UTERUS:

-Cyclic dilation, estrus stage

This finding corresponds to necropsy observation no: 01.

VAGINA:

-Cycle: estrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, THYMUS, TRACHEA, ESOPHAGUS , PARATHYROID
GLANDS, DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON,
RECTUM, MESENTERIC LYMPH NODE, PANCREAS, MANDIBULAR LYMPH NODES,
SUBLINGUAL GLANDS, MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY)
GLANDS, KIDNEYS, URINARY BLADDER, BRAIN, PITUITARY GLAND, SCIATIC
NERVE (LEFT) , CERVIX, SKIN/SUBCUTIS, MAMMARY GLAND, LARYNX,
EYES, OPTIC NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL
SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR
SEGMENT), BONE (STERNUM), BONE MARROW (STERNUM) .

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 91

* NECROPSY FINDINGS

LIVER:

01: DISCOLOURATION, RED-BROWN.

02: ENLARGED.

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 91

KIDNEYS:

01: BOTH SIDES: DISCOLOURATION, GREENISH.

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:

-Hyperplasia, epithelial tubules and cords, grade 1

TRACHEA:

-Infiltrate inflammatory cell, lymphocytic, grade 1

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 2

STOMACH:

-Hyperplasia squamous cell, forestomach, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 3

This finding corresponds to necropsy observations nos: 01,02.

-Necrosis hepatocellular centrilobular, with brown pigment,
grade 1

This finding corresponds to necropsy observation no: 01.

SPLEEN:

-Hematopoiesis extramedullary, grade 1

-Pigmentation, hemosiderin, grade 2

MESENTERIC LYMPH NODE:

-Increased macrophage foci, grade 1

MANDIBULAR LYMPH NODES:

-Pigmentation, macrophages, yellow-brown, unilateral, grade 1

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

-Calculus, pelvis, unilateral, grade 3
with hyperplasia urothelium pelvis.

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 91

ADRENAL GLANDS:

-Vacuolation zona glomerulosa, bilateral, grade 1

UTERUS:

-Cyclic dilation

This finding corresponds to necropsy observation no: 01.

VAGINA:

-Cycle: estrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, ESOPHAGUS, PARATHYROID GLANDS, DUODENUM,
JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, PANCREAS,
SUBLINGUAL GLANDS, MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY)
GLANDS, URINARY BLADDER, BRAIN, PITUITARY GLAND, SCIATIC NERVE
(LEFT), OVARIES, CERVIX, SKIN/SUBCUTIS, MAMMARY GLAND, LARYNX,
EYES, OPTIC NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL
SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR
SEGMENT), BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: K0

DAYS ON TEST : 96

* ANIMAL NO. : 92

* NECROPSY FINDINGS

STOMACH:

01: FORESTOMACH: FOCUS/FOCI, ISOLATED, REDDISH.

LIVER:

01: ENLARGED.

02: DISCOLOURATION, RED-BROWN.

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG FEMALE

CONT./FF. ANIMAL NO. : 92

KIDNEYS:

01: BOTH SIDES: DISCOLOURATION, GREENISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LUNG:

-Alveolar macrophage aggregation, grade 1

THYMUS:

-Lymphocytolysis increased, grade 1

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

PARATHYROID GLANDS:

Only one of paired organs examined/present

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 2

-Hyperplasia squamous cell, forestomach, grade 3

-Erosion/ulceration, forestomach, grade 1

This finding corresponds to necropsy observation no: 01.

LIVER:

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 3

This finding corresponds to necropsy observations nos: 01,02.

-Necrosis hepatocellular centrilobular, with brown pigment,
grade 3

This finding corresponds to necropsy observation no: 02.

-Necrosis coagulative, focal/multifocal, grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 3

MESENTERIC LYMPH NODE:

-Increased macrophage foci, grade 1

MANDIBULAR LYMPH NODES:

Only one of paired organs examined/present

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

-Infiltrate inflammatory cell, lymphocytic, unilateral, grade 2

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 92

-
- Basophilia tubule, bilateral, grade 3
Grade 2 in contralateral organ
 - Papil hyperplasia epithelium with cellular debris/casts,
bilateral, grade 2
 - Papil eosinophilic content, bilateral, grade 2
Grade 1 in contralateral organ
 - Calculus, papil, unilateral, grade 2
 - Mineralization, papillary, focal, unilateral, grade 1
- ADRENAL GLANDS:
-Vacuolation zona glomerulosa, bilateral, grade 2
- VAGINA:
-Cycle: metestrus
- BONE MARROW (STERNUM):
-Increased adipocytes, grade 1
- ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, TRACHEA, ESOPHAGUS , PARATHYROID GLANDS, DUODENUM,
JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, PANCREAS,
MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, MANDIBULAR
(SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER, BRAIN,
PITUITARY GLAND, SCIATIC NERVE (LEFT) , OVARIES, UTERUS, CERVIX,
SKIN/SUBCUTIS, MAMMARY GLAND, LARYNX, EYES, OPTIC NERVES,
HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD
(THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM).

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 219/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

* STATE AT NECROPSY: K0/+1
DAYS ON TEST : 19

* ANIMAL NO. : 93

* NECROPSY FINDINGS

GENERAL OBSERVATIONS:

- 01: ADVANCED AUTOLYSIS.
- 02: CANNIBALISM:ORGAN MISSING PARTIAL

THYMUS:

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

* MICROSCOPIC FINDINGS

LUNG:

- Inflammation bronchioalveolar, acute, grade 1

THYMUS:

- Congestion/hemorrhage, grade 4
This finding corresponds to necropsy observation no: 01.
- Depletion, lymphoid, grade 4

THYROID GLAND (BOTH LOBES):

- Severe autolysis, evaluation not possible

DUODENUM:

- Tissue not present for histologic examination

JEJUNUM:

- Tissue not present for histologic examination

ILEUM:

- Tissue not present for histologic examination

PEYER'S PATCHES:

- Tissue not present for histologic examination

CECUM:

- Tissue not present for histologic examination

COLON:

- Tissue not present for histologic examination

RECTUM:

- Tissue not present for histologic examination

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 93

LIVER:

Tissue not present for histologic examination

SPLEEN:

Tissue not present for histologic examination

MESENTERIC LYMPH NODE:

Tissue not present for histologic examination

PANCREAS:

Tissue not present for histologic examination

MANDIBULAR LYMPH NODES:

Only one of paired organs examined/present

MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS:

Severe autolysis, evaluation not possible

KIDNEYS:

Only one of paired organs examined/present

Severe autolysis, evaluation not possible

URINARY BLADDER:

Tissue not present for histologic examination

ADRENAL GLANDS:

Only one of paired organs examined/present

SCIATIC NERVE (LEFT):

Tissue not present for histologic examination

OVARIES:

Tissue not present for histologic examination

UTERUS:

Tissue not present for histologic examination

CERVIX:

Tissue not present for histologic examination

VAGINA:

Tissue not present for histologic examination

MAMMARY GLAND:

Tissue not present for histologic examination

EYES:

Severe autolysis, evaluation not possible

OPTIC NERVES:

Only one of paired organs examined/present

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 221/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 93

SPINAL CORD (CERVICAL SEGMENT):

Severe autolysis, evaluation not possible

SPINAL CORD (THORACIC SEGMENT):

Severe autolysis, evaluation not possible

SPINAL CORD (LUMBAR SEGMENT):

Severe autolysis, evaluation not possible

BONE MARROW (STERNUM):

-Atrophy, diffuse, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, TRACHEA, ESOPHAGUS , PARATHYROID GLANDS, STOMACH,
MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS, ADRENAL GLANDS, BRAIN,
PITUITARY GLAND, SKIN/SUBCUTIS, LARYNX, OPTIC NERVES, HARDERIAN
GLANDS, BONE (STERNUM).

* STATE AT NECROPSY: R1

DAYS ON TEST : 124

* ANIMAL NO. : 94

* NECROPSY FINDINGS

THYMUS:

01: RIGHT SIDE: FOCUS/FOCI, MANY, REDDISH.

LIVER:

01: DISCOLOURATION, RED-BROWN.

KIDNEYS:

01: BOTH SIDES: DISCOLOURATION, GREENISH.

ADRENAL GLANDS:

01: BOTH SIDES: ENLARGED.

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 94

UTERUS:

01: CONTAINS FLUID.

CLITORAL GLANDS:

01: LEFT SIDE: FOCUS/FOCI, ISOLATED, TAN.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:

-Congestion/hemorrhage, grade 1

This finding corresponds to necropsy observation no: 01.

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 1

-Hyperplasia squamous cell, forestomach, grade 1

-Vacuolation, limiting ridge, grade 1

-Dilated gastric pits, grade 1

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Vacuolation hepatocellular, scattered, grade 1

-Necrosis hepatocellular centrilobular, with brown pigment,
grade 1

This finding corresponds to necropsy observation no: 01.

SPLEEN:

-Pigmentation, hemosiderin, grade 2

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

-Basophilia tubule, bilateral, grade 1

URINARY BLADDER:

-Hyperplasia/hypertrophy urothelium, grade 2

ADRENAL GLANDS:

Large organ, normal histology

-Cortical tissue, accessory, unilateral

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 223/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 94

UTERUS:

-Cyclic dilation, estrus stage

This finding corresponds to necropsy observation no: 01.

CLITORAL GLANDS:

-Dilated duct with contents, unilateral, grade 2

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: R1

DAYS ON TEST : 124

* ANIMAL NO. : 95

* NECROPSY FINDINGS

KIDNEYS:

01: BOTH SIDES: DISCOLOURATION, GREENISH.

UTERUS:

01: CONTAINS FLUID.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Vacuolation hepatocellular, periportal, focal, grade 2

-Pigment deposition yellow-brown centrilobular, grade 2

SPLEEN:

-Pigmentation, hemosiderin, grade 2

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 224/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 95

KIDNEYS:

No microscopic finding corresponding to necropsy observation no. 01.

URINARY BLADDER:

-Hyperplasia/hypertrophy urothelium, grade 1

UTERUS:

-Cyclic dilation, proestrus stage

This finding corresponds to necropsy observation no: 01.

BONE MARROW (STERNUM):

-Increased adipocytes, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, THYROID GLAND (BOTH LOBES), STOMACH, KIDNEYS, ADRENAL GLANDS, BONE (STERNUM).

* STATE AT NECROPSY: R1/+1

DAYS ON TEST : 30

* ANIMAL NO. : 96

* CAUSE OF DEATH / MORBIDITY

GENERAL OBSERVATIONS:

-Gavage accident

LUNG:

-Hemorrhage, grade 3

* NECROPSY FINDINGS

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 96

LUNG:

01: RIGHT MEDIAL LOBE: FOCUS/FOCI, D=9X8 MM, BLACK-BROWN.

THYMUS:

01: DISCOLOURATION, DARK RED.

LIVER:

01: ENLARGED.

KIDNEYS:

01: BOTH SIDES: DISCOLOURATION, DARK RED.

RENAL LYMPH NODE:

01: BOTH SIDES: DISCOLOURATION, DARK RED.

02: BOTH SIDES: ENLARGED.

BODY CAVITIES:

01: THORACIC CAVITY: CONTENTS: DARK RED, WATERY-CLEAR.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

GENERAL OBSERVATIONS:

-Gavage accident

LUNG:

-Hemorrhage, pulmonary, focal, traumatic, grade 3 probably gavage accident.

This finding corresponds to necropsy observation no: 01.

-Inflammation peribronchial/perivascular, grade 1

THYMUS:

-Congestion/hemorrhage, grade 1

This finding corresponds to necropsy observation no: 01.

TRACHEA:

-Infiltrate inflammatory cell, lymphogranulocytic, grade 1

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 2

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

-Extramedullary hematopoiesis, grade 1

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm, grade 2

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 226/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 96

.....

This finding corresponds to necropsy observation no: 01.
-Necrosis hepatocellular centrilobular, grade 1
SPLEEN:
-Hematopoiesis extramedullary, grade 1
-Pigmentation, hemosiderin, grade 1
KIDNEYS:
-Congestion, bilateral, grade 2
This finding corresponds to necropsy observation no: 01.
BRAIN:
Artefactual vacuolation cerebellum.
VAGINA:
-Cycle: metestrus
-Infiltrate inflammatory cell, lymphogranulocytic, lumen,
grade 2
SPINAL CORD (CERVICAL SEGMENT):
Artefactual vacuolation.
SPINAL CORD (THORACIC SEGMENT):
Artefactual vacuolation.
SPINAL CORD (LUMBAR SEGMENT):
Artefactual vacuolation.
RENAL LYMPH NODE:
Tissue not present for histologic examination
No lymph node on slide 24.
No microscopic finding corresponding to necropsy observation no. 02.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 227/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 96

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, ESOPHAGUS , PARATHYROID GLANDS, STOMACH, DUODENUM,
JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM, MESENTERIC
LYMPH NODE, PANCREAS, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS,
MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER,
ADRENAL GLANDS, BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) ,
OVARIES, UTERUS, CERVIX, SKIN/SUBCUTIS, MAMMARY GLAND, LARYNX,
EYES, OPTIC NERVES, HARDERIAN GLANDS, SPINAL CORD (CERVICAL
SEGMENT), SPINAL CORD (THORACIC SEGMENT), SPINAL CORD (LUMBAR
SEGMENT), BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: R1

DAYS ON TEST : 124

* ANIMAL NO. : 97

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:

- Infiltrate inflammatory cell, mononuclear, grade 1
- Vacuolation hepatocellular, scattered, grade 1
- Pigment deposition yellow-brown centrilobular, grade 1

SPLEEN:

- Pigmentation, hemosiderin, grade 2

URINARY BLADDER:

- Hyperplasia/hypertrophy urothelium, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 228/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 97

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, THYROID GLAND (BOTH LOBES), STOMACH, KIDNEYS, ADRENAL
GLANDS, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: R1

DAYS ON TEST : 124

* ANIMAL NO. : 98

* NECROPSY FINDINGS

LIVER:

01: DISCOLOURATION, BLACK-BROWN.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:

No microscopic finding corresponding to necropsy observation no. 01.
-Infiltrate inflammatory cell, mononuclear, grade 1
-Vacuolation hepatocellular, scattered, grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 2

URINARY BLADDER:

-Hyperplasia/hypertrophy urothelium, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, THYROID GLAND (BOTH LOBES), STOMACH, KIDNEYS, ADRENAL
GLANDS, BONE (STERNUM), BONE MARROW (STERNUM).

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 04, 600 MG/KG FEMALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 124 * ANIMAL NO. : 99
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:

-Infiltrate inflammatory cell, mononuclear, grade 1

SPLEEN:

-Pigmentation, hemosiderin, grade 2

ADRENAL GLANDS:

-Vacuolation zona glomerulosa, bilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- THYMUS, THYROID GLAND (BOTH LOBES), STOMACH, KIDNEYS, URINARY
BLADDER, BONE (STERNUM), BONE MARROW (STERNUM).

* STATE AT NECROPSY: R1/+2
DAYS ON TEST : 63 * ANIMAL NO. : 100
.....

* CAUSE OF DEATH / MORBIDITY

LIVER:

-Necrosis hepatocellular centrilobular, grade 4

* NECROPSY FINDINGS

PATHOLOGY REPORT (FINAL)
INDIVIDUAL ANIMAL DATA

PAGE : 230/ 231
TOX : 511505

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 100

GENERAL OBSERVATIONS:

01: EMACIATED.

THYMUS:

01: REDUCED IN SIZE.

LIVER:

01: ENLARGED.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:

-Depletion, lymphoid, grade 3

This finding corresponds to necropsy observation no: 01.

ESOPHAGUS:

Food remnants in lumen esophagus.

THYROID GLAND (BOTH LOBES):

-Hypertrophy follicular cell, bilateral, grade 1

STOMACH:

-Inflammation forestomach, lymphogranulocytic, grade 1

-Hyperplasia squamous cell, forestomach, grade 2

-Erosion/ulceration, forestomach, grade 1

LIVER:

-Hypertrophy centrilobular/diffuse+eosinophilic cytoplasm,
grade 3

This finding corresponds to necropsy observation no: 01.

-Necrosis hepatocellular centrilobular, with brown pigment,
grade 4

SPLEEN:

-Pigmentation, hemosiderin, grade 2

PANCREAS:

-Degranulation acinar cells, grade 3

KIDNEYS:

-Casts hyaline, unilateral, grade 2

-Dilation, tubule, bilateral, grade 2

-Vacuolation tubular, tubular, medulla, bilateral, grade 2

TEST ITEM : MTDID 7831
TEST SYSTEM : RAT, 90 Days + Rec., Gavage
SPONSOR : 3M Belgium BVBA

PATHOL. NO.: 21614 BRH
FINALIZED : 01-FEB-17
PathData@System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, 600 MG/KG

FEMALE

CONT./FF. ANIMAL NO. : 100

ADRENAL GLANDS:

-Vacuolation zona fasciculata, bilateral, grade 2

UTERUS:

-Atrophy, diffuse, grade 1

VAGINA:

-Cycle: metestrus

-Infiltrate inflammatory cell, lymphogranulocytic, lumen,
grade 1

BONE MARROW (STERNUM):

-Increased adipocytes, grade 1

-Atrophy, diffuse, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* ORGANS WITHOUT ABNORMALITIES

- HEART, AORTA, LUNG, TRACHEA, ESOPHAGUS , PARATHYROID GLANDS,
DUODENUM, JEJUNUM, ILEUM, PEYER'S PATCHES, CECUM, COLON, RECTUM,
MESENTERIC LYMPH NODE, MANDIBULAR LYMPH NODES, SUBLINGUAL GLANDS,
MANDIBULAR (SUBMANDIBULAR/SUBMAXILLARY) GLANDS, URINARY BLADDER,
BRAIN, PITUITARY GLAND, SCIATIC NERVE (LEFT) , OVARIES, CERVIX,
SKIN/SUBCUTIS, MAMMARY GLAND, LARYNX, EYES, OPTIC NERVES,
HARDERIAN GLANDS, SPINAL CORD (CERVICAL SEGMENT), SPINAL CORD
(THORACIC SEGMENT), SPINAL CORD (LUMBAR SEGMENT), BONE (STERNUM) .



United States Environmental Protection Agency
Washington, DC 20460

Section 8(e) Notice

This is an original submission:



This is an amendment:



CERTIFICATION

I hereby certify to the best of my knowledge and belief that all information entered on this form is complete and accurate. I further certify that, pursuant to 15 U.S.C. § 2613(c), for all claims for protection for any confidential information made with this submission, all information submitted to substantiate such claims is true and correct, and that it is true and correct that the person submitting the claim has:

- (i) taken reasonable measures to protect the confidentiality of the information;
- (ii) determined that the information is not required to be disclosed or otherwise made available to the public under any other Federal law;
- (iii) a reasonable basis to conclude that disclosure of the information is likely to cause substantial harm to the competitive position of the person; and
- (iv) a reasonable basis to believe that the information is not readily discoverable through reverse engineering.

Any knowing and willful misrepresentation is subject to criminal penalty pursuant to 18 U.S.C. § 1001.

Signature:

ES/Jonathan M. Gerber

Official Title:

Advanced Regulatory Specialist

Contact Person:

Jonathan M. Gerber

Email Address:

jmgrber1@mmm.com

Date Signed:

03/06/2017

PART 1

Contact Information

Submission Information

Case Number:

Submission Alias:

File 252

Date Submitted:

03/06/2017

Submitter Information

CBI:

Yes: No:

Company Name:

3M

Address:

3M CENTER

	Contact Person: Jonathan M. Gerber	ST. PAUL, MN, 55144	
	Phone Number: 6517330226	Email Address: jmgerber1@mmm.com	
Technical Contact	CBI: Yes: <input type="checkbox"/> No: <input checked="" type="checkbox"/>		
	Company Name: 3M	Address: 3M CENTER ST. PAUL, MN, 55144 United States	
	Contact Person: Mr Jonathan M. Gerber		
	Phone Number: 6517330226	Email Address: jmgerber1@mmm.com	
PART 2	Chemical Reports		
Chemical Identification	Chemical Report Folder Alias: 67584-55-8		
	Chemical Identifying #: CASRN: 67584-55-8	CBI: Yes: <input type="checkbox"/> No: <input checked="" type="checkbox"/>	
	Chemical Name: 2-Propenoic acid, 2-[methyl[(1,1,2,2,3,3,4,4,4-n onafluorobutyl)sulfonyl]amino]ethyl ester		
Attached Document(s)	Report Study Title: Repeated Dose 90-Day Oral Toxicity Study with MTDID 7831 by Daily Gavage in the Rat followed by a 28-Day Recovery Period		
	Original Document: FINAL REPORT File 252_no CBI.pdf	Submission Type: Final Report Submission	
	Summary Original Document: FINAL CL File 252_no CBI.pdf		
	Effects: Health Effects	Endpoints: Repeated Dose toxicity: oral	

Paperwork Reduction Act

The information collection requirements contained in the information collection request (ICR) have been submitted for OMB approval under 15 U.S.C. 2607(e). The ICR prepared by EPA, identified under EPA ICR No. 0794.13 and OMB control number 2070-0046, is available in the docket for the ICR. ICR No. 0794.13 addresses the incremental changes to the currently approved ICR documents that cover the existing reporting and record keeping programs that are approved under OMB control number 2070-0046. An agency may not conduct or sponsor, and a person is not required to, respond to a collection of information unless it displays a currently valid OMB control number.

Authority

The Government Paperwork Elimination Act (GPEA) (44 U.S.C. 3504) provides that, when practicable, Federal organizations use electronic forms, electronic filings, and electronic signatures to conduct official business with the public. EPA's Cross-Media Electronic Reporting Regulation (CROMERR) (40 CFR part 3) (Ref. 2), provides that any requirement in title 40 of the CFR to submit a report directly to EPA can be satisfied with an electronic submission that meets certain conditions once the Agency published a document in the **Federal Register** announcing that EPA is prepared to receive certain documents in electronic form. For more information about CROMERR, go to <http://www.epa.gov/cromerr/>.