FINAL REPORT

PROTOCOL 418-028

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST

SPONSOR'S STUDY NUMBER: T-7706.1

FINAL REPORT DATE: 31 JULY 2003

PROTOCOL 418-028 - ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST

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TABLE OF CONTENTS

SUBJECT		PAGE
1.	SUMMARY AND CONCLUSION	1-1
1.1.	Methods	1-1
1.2.	Results	1-3
1.3.	Conclusion	1-6
2.	DESCRIPTION OF TEST PROCEDURES	2-1
2.1.	Conduct of Study	2-1
2.2.	Test Substance Information	2-4
2.3.	Vehicle Information	2-4
2.4.	Test Substance Preparation and Storage Conditions	2-5
2.5.	Test System	2-6
2.6.	Husbandry	2-7
2.7.	Methods	2-10
3.	RESULTS - Male Rats	3-1
3.1.	Mortality, Clinical and Necropsy Observations	3-1
3.2.	Terminal Body Weights and Organ Weights and Ratios (%) of Organ Weight to Terminal Body Weight and Brain Weight	3-2

SUBJECT		PAGE
3.3.	Hematology and Clinical Chemistry	3-2
3.4.	Body Weights and Body Weight Changes	3-3
3.5.	Absolute (g/day) and Relative (g/kg/day) Feed Consumption Values	3-3
3.6.	Mating and Fertility	3-3
3.7.	Functional Observational Battery	3-3
3.8.	Motor Activity	3-4
3.9.	Sperm	3-4
4.	RESULTS - Female Rats	4-1
4.1.	Mortality, Clinical and Necropsy Observations	4-1
4.2.	Terminal Body Weights, Organ Weights and Ratios (%) of Organ Weight to Terminal Body Weight and Brain Weight and Primordial Follicle Counts	4-2
4.3.	Hematology and Clinical Chemistry	4-2
4.4.	Body Weights and Body Weight Changes	4-3
4.5	Absolute (g/day) and Relative (g/kg/day) Feed Consumption Values	4-3
4.6.	Estrous Cycling, Mating and Fertility	4-4
4.7.	Functional Observational Battery	4-4
4.8.	Motor Activity	4-4
4.9.	Natural Delivery and Litter Observations	4-5
4.10.	Pup Clinical and Necropsy Observations	4-5
4.11.	Pup Liver Weight and Ratio of Liver Weight to Terminal Body Weight	4-5
REFERENCES		4-6
APPENDIX A - REPORT FIGURES		
Figure 1.	Fo Generation Male Rats	A-1

SUBJECT		PAGE
Figure 2.	Fo Generation Female Rats	A-2
Figure 3.	Motor Activity - Number of Movements - Fo Generation Male Rats	A-3
Figure 4.	Motor Activity - Time Spent in Movement - Fo Generation Male Rats	A-4
Figure 5.	Motor Activity - Number of Movements - Fo Generation Female Rats	A-5
Figure 6.	Motor Activity - Time Spent in Movement - Fo Generation Female Rats	A-6
APPENDIX B - REPORT TABLES - Fo GENERATION MALE RATS		
Table B1.	Clinical Observations - Summary - Fo Generation Male Rats	B-1
Table B2.	Necropsy Observations - Summary - Fo Generation Male Rats	B-2
Table B3.	Terminal Body Weights and Organ Weights - Summary - Fo Generation Male Rats	B-3
Table B4.	Ratios (%) of Organ Weight to Terminal Body Weight - Summary - Fo Generation Male Rats	B-5
Table B5.	Ratios (%) of Organ Weight to Brain Weight - Summary - Fo Generation Male Rats	B-7
Table B6.	Hematology - Summary - Fo Generation Male Rats	B-9
Table B7.	Clinical Chemistry - Summary - Fo Generation Male Rats	B-12
Table B8.	Body Weights - Summary - Fo Generation Male Rats	B-15
Table B9.	Body Weight Changes - Summary - Fo Generation Male Rats	B-16
Table B10.	Absolute Feed Consumption Values (g/day) - Summary - Fo Generation Male Rats	B-17
Table B11.	Relative Feed Consumption Values (g/kg/day) - Summary - Fo Generation Male Rats	B-18
Table B12.	Mating and Fertility - Summary - Fo Generation Male Rats	B-19
Table B13.	Functional Observational Battery Observations - Summary - Fo Generation Male Rats	B-20

SUBJECT		PAGE
Table B14.	Motor Activity - Summary - Fo Generation Male Rats	B-26
Table B15.	Sperm Motility, Count and Density - Summary - Fo Generation Male Rats	B-28
Table B16.	Sperm Morphology - Summary - Fo Generation Male Rats	B-29
Table B17.	Clinical Observations - Individual Data - Fo Generation Male Rats	B-30
Table B18.	Necropsy Observations - Individual Data - Fo Generation Male Rats	B-33
Table B19.	Terminal Body Weights and Organ Weights and Ratios (%) of Organ Weight to Terminal Body Weight - Individual Data - Fo Generation Male Rats	B-38
Table B20.	Organ Weights and Ratios (%) Of Organ Weight to Brain Weight - Individual Data - Fo Generation Male Rats	B-48
Table B21.	Body Weights - Individual Data - Fo Generation Male Rats	B-58
Table B22.	Feed Consumption Values - Individual Data - Fo Generation Male Rats	B-68
Table B23.	Mating and Fertility - Individual Data - Fo Generation Male Rats	B-71
Table B24.	Functional Observational Battery Observations - Individual Data - Fo Generation Male Rats	B-74
Table B25.	Motor Activity - Individual Data - Fo Generation Male Rats	B-79
Table B26.	Sperm Motility, Count and Density - Individual Data - Fo Generation Male Rats	B-89
Table B27.	Sperm Morphology - Individual Data - Fo Generation Male Rats	B-92
APPENDIX C - REPORT TABLES - Fo GENERATION FEMALE RATS		
Table C1.	Clinical Observations - Summary - Fo Generation Female Rats	C-1
Table C2.	Necropsy Observations - Summary - Fo Generation Female Rats	C-4
Table C3.	Terminal Body Weights and Organ Weights and Primordial Follicle Count - Summary - Fo Generation Female Rats	C-5

SUBJECT		PAGE
Table C4.	Ratios (%) of Organ Weight to Terminal Body Weight - Summary - Fo Generation Female Rats	C-7
Table C5.	Ratios (%) of Organ Weight to Brain Weight - Summary - Fo Generation Female Rats	C-8
Table C6.	Hematology - Summary - Fo Generation Female Rats	C-9
Table C7.	Clinical Chemistry - Summary - Fo Generation Female Rats	C-12
Table C8.	Body Weights - Precohabitation - Summary - Fo Generation Female Rats	C-15
Table C9.	Body Weight Changes - Precohabitation - Summary - Fo Generation Female Rats	C-16
Table C10.	Maternal Body Weights - Gestation - Summary - Fo Generation Female Rats	C-17
Table C11.	Maternal Body Weight Changes - Gestation - Summary - Fo Generation Female Rats	C-19
Table C12.	Maternal Body Weights - Lactation - Summary - Fo Generation Female Rats	C-20
Table C13.	Maternal Body Weight Changes - Lactation - Summary - Fo Generation Female Rats	C-22
Table C14.	Absolute Feed Consumption Values (g/day) - Precohabitation - Summary - Fo Generation Female Rats	C-23
Table C15.	Relative Feed Consumption Values (g/kg/day) - Precohabitation - Summary - Fo Generation Female Rats	C-24
Table C16.	Maternal Absolute Feed Consumption Values (g/day) - Gestation - Summary - Fo Generation Female Rats	C-25
Table C17.	Maternal Relative Feed Consumption Values (g/kg/day) - Gestation - Summary - Fo Generation Female Rats	C-26
Table C18.	Maternal Absolute Feed Consumption Values (g/day) - Lactation - Summary - Fo Generation Female Rats	C-27

SUBJECT		PAGE
Table C19.	Maternal Relative Feed Consumption Values (g/kg/day) - Lactation - Summary - Fo Generation Female Rats	C-28
Table C20.	Mating and Fertility, Estrous Cycling and Days in Cohabitation - Summary - Fo Generation Female Rats	C-29
Table C21.	Functional Observational Battery - Summary - Fo Generation Female Rats	C-31
Table C22.	Motor Activity - Summary - Fo Generation Female Rats	C-37
Table C23.	Natural Delivery Observations - Summary - Fo Generation Female Rats	C-39
Table C24.	Litter Observations (Naturally Delivered Pups) - Summary - F1 Generation Litters	C-40
Table C25.	Clinical Observations from Birth to Day 22 Postpartum - Summary - F1 Generation Pups	C-43
Table C26.	Necropsy Observations - Summary - F1 Generation Pups	C-44
Table C27.	Pup Liver Weights - Summary - F1 Generation Pups	C-45
Table C28.	Clinical Observations - Individual Data - Fo Generation Female Rats	C-46
Table C29.	Necropsy Observations - Individual Data - Fo Generation Female Rats	C-51
Table C30.	Terminal Body Weights and Organ Weights and Ratios (%) of Organ Weight to Terminal Body Weight - Individual Data - Fo Generation Female Rats	C-55
Table C31.	Organ Weights and Ratios (%) Of Organ Weight to Brain Weight - Individual Data - Fo Generation Female Rats	C-60
Table C32.	Primordial Follicle Count - Individual Data - Fo Generation Female Rats	C-65
Table C33.	Body Weights - Precohabitation - Individual Data - Fo Generation Female Rats	C-67

SUBJECT		PAGE
Table C34.	Maternal Body Weights - Presumed Gestation - Individual Data - Fo Generation Female Rats	C-70
Table C35.	Maternal Body Weights - Lactation - Individual Data - Fo Generation Female Rats	C-75
Table C36.	Feed Consumption Values - Precohabitation - Individual Data - Fo Generation Female Rats	C-80
Table C37.	Maternal Feed Consumption Values - Presumed Gestation - Individual Data - Fo Generation Female Rats	C-83
Table C38.	Maternal Feed Consumption Values - Lactation - Individual Data - Fo Generation Female Rats	C-86
Table C39.	Mating and Fertility, Estrous Cycling and Days in Cohabitation - Individual Data - Fo Generations Female Rats	C-89
Table C40.	Functional Observational Battery - Individual Data - Fo Generation Female Rats	C-92
Table C41.	Motor Activity - Individual Data - Fo Generation Female Rats	C-97
Table C42.	Natural Delivery, Implantation Sites, and Pup Viability and Sex - Individual Data - Fo Generation Female Rats/F1 Generation Litters	C-107
Table C43.	Pup Body Weight Litter Averages from Birth to Day 22 Postpartum - Individual Data - F1 Generation Litters	C-110
Table C44.	Pup Body Weights from Birth to Day 22 Postpartum - Individual Data - F1 Generation Pups	C-113
Table C45.	Pup Vital Status and Sex from Birth to Day 22 Postpartum - Individual Data - F1 Generation Pups	C-125
Table C46.	Clinical Observations from Birth to Day 22 Postpartum - Individual Data - F1 Generation Pups	C-128
Table C47.	Necropsy Observations - Individual Data - F1 Generation Pups	C-130
Table C48.	Pup Liver Weights - Individual Date - F1 Generation Pups	C-136
APPENDIX D -	PROTOCOL AND AMENDMENTS	D-1 to D-52

SUBJECT		PAGE
APPENDIX E -	DEVIATIONS FROM THE PROTOCOL AND THE STANDARD OPERATING PROCEDURES OF THE TESTING FACILITY	E-1 to E-3
APPENDIX F -	CERTIFICATE OF ANALYSIS	F-1 to F-3
APPENDIX G -	ANALYTICAL AND BIOANALYTICAL REPORT	G-1 to G-153
APPENDIX H -	TEMPERATURE AND RELATIVE HUMIDITY REPORT	H-1
APPENDIX I -	POSITIVE CONTROL DATA	I-1 to I-4
APPENDIX J -	HISTOPATHOLOGY REPORT	J-1 to J-105
APPENIDX K -	HEMATOLOGY AND CLINICAL CHEMISTRY REPORTS	K-1 to K-150
APPENDIX L -	STATEMENT OF THE STUDY DIRECTOR	L-1
APPENIDIX M -	QUALITY ASSURANCE STATEMENT	M-1 to M-2

TITLE: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST

ARGUS RESEARCH PROTOCOL NUMBER: 418-028
SPONSOR'S STUDY NUMBER: T-7706.1

1. SUMMARY AND CONCLUSION

1.1. Methods[a]

Seventy-five Crl:CD®(SD)IGS VAF/Plus® rats per sex were assigned to five dosage groups (Groups I through V), 15 rats per sex per group. An additional three rats per sex per group were assigned to Groups I through V for toxicokinetic sample collection. The test substance, T-7706 [Perfluorohexane Sulfonate Potassium Salt (PFHS)], or vehicle, aqueous 0.5% carboxymethylcellulose (CMC), was administered via gavage to male rats once daily beginning 14 days before cohabitation and continuing through the day before sacrifice, after completion of the cohabitation period, after a minimum of 42 days of administration, and to female rats once daily beginning 14 days before cohabitation and continuing through the day before sacrifice, day 21 of lactation (DL 21) or day 25 of presumed gestation (DG 25, rats that did not deliver a litter). Dosages were 0, 0.3, 1, 3 and 10 mg/kg/day. The dosage volume, 10 mL/kg, was adjusted daily on the basis of the individual body weights recorded before intubation. F1 generation pups were not directly administered the test substance or vehicle.

Within each dosage group, rats were assigned to cohabitation, one male rat per female rat.

Rats were observed for viability at least twice each day of the study. Observations for clinical signs of effects of the test substance and deaths were made on the first day of dosage at approximately hourly intervals for the first four hours and at the end of the normal working day. Observations for clinical signs of effects of the test substance and deaths were made on subsequent days daily before dosage and approximately 60 ± 10 minutes after dosage administration and on the day of sacrifice. Once before the first dosage and at least once weekly thereafter, detailed clinical observations were conducted for all male and female rats assigned to the main study.

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a. Detailed descriptions of all procedures used in the conduct of this study are provided in the appropriate sections of this report and in APPENDIX D (PROTOCOL AND AMENDMENTS).

Body weights were recorded daily during the dosage period and at sacrifice. Feed consumption values for male rats assigned to the main study were recorded weekly during the dosage period. Feed consumption values for female rats assigned to the main study were recorded weekly to cohabitation, on DGs 0, 7, 10, 12, 15, 18, 20 and 25 (if necessary) and on DLs 1, 5, 8 and 15. During cohabitation, individual values were not recorded or tabulated.

Estrous cycling was evaluated in rats assigned to the main study by examination of vaginal cytology beginning with the day after the first administration and then until spermatozoa were observed in a smear of the vaginal contents and/or a copulatory plug was observed *in situ* during the cohabitation period. Estrous cycling was evaluated in rats assigned to the toxicokinetic study during the cohabitation period until spermatozoa were observed in a smear of the vaginal contents and/or a copulatory plug was observed *in situ.*

Female rats were evaluated for adverse clinical signs observed during parturition, duration of gestation, litter sizes and pup viability at birth. Maternal behavior was evaluated on DLs 1, 5, 8, 15 and 22.

Shortly before scheduled sacrifice, a functional observational battery (FOB) was conducted and motor activity was evaluated on 10 male and 10 female rats per group.

On days 14 and 42 of study, blood samples were collected from each male rat assigned to the toxicokinetic sample collection portion of the study and on day 14 of study and DG 21, blood samples were collected from each female rat assigned to the toxicokinetic sample collection portion of the study.

Each litter was evaluated for viability at least twice daily. The pups in each litter were counted once daily. Clinical observations were recorded once daily. Pup body weights were recorded on DLs 1, 8, 15 and 22.

Male and female rats assigned to the toxicokinetic study were sacrificed on day 42 of study and DG 21, respectively. Liver weights were recorded. The median liver lobe was shipped for analysis. Blood samples were collected from each fetus and pooled by litter and serum was shipped for analysis. The liver from each fetus was collected, pooled per litter and shipped for analysis. The number of implantation sites was recorded.

Male and female rats assigned to the main study were sacrificed after a minimum of 42 days of dosage and on DL 22, respectively. A gross necropsy of the thoracic, abdominal and pelvic viscera was performed. The number of implantation sites were recorded. Gross lesions were examined histologically.

Ten rats per sex per group assigned to functional observational battery and motor activity tests were assigned to histological evaluations. The following organs were individually weighed: liver, kidneys, adrenals, thymus, testes, right epididymis, left epididymis (corpus and caput), seminal vesicles (with and without fluid), prostate, spleen, brain, heart, ovaries and uterus (with cervix). The following tissues or representative samples

were retained: brain, small and large intestines, lungs, lymph nodes, peripheral nerve, stomach, kidneys, spleen, thymus, trachea, urinary bladder, spinal cord, liver, adrenals, heart, thyroid/parathyroid, bone marrow, testes, prostate, seminal vesicles, ovaries, uterus, vagina, mammary gland (female rats only) and gross lesions. Histological examination of retained tissues, including reproductive organs, was conducted for the assigned ten rats per sex from the control and high dosage groups. A quantitative evaluation of primordial follicles was conducted for Fo generation female rats.

Sperm evaluations (concentration, motility and morphology) were performed for 10 male rats in each dosage group.

At scheduled sacrifice, blood samples were collected from the 10 male and 10 female rats per group assigned to hematology and clinical chemistry sample collection. The following hematologic parameters were evaluated: erythrocyte count, hematocrit, hemoglobin, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, mean corpuscular volume, total leukocyte count, differential leukocyte count, platelet count, mean platelet volume and cell morphology. Two blood smear slides were prepared for measurements of differential leukocyte count. Plasma samples evaluated for prothrombin time and activated partial thromboplastin time. Sera samples were evaluated for total protein, triglycerides, albumin, globulin, albumin/globulin ratio, glucose, cholesterol, total bilirubin, urea nitrogen, creatinine, creatinine kinase, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, calcium, phosphorus, sodium, potassium and chloride.

On DL 22, pups were sacrificed and examined for gross lesions. Necropsy included a single cross-section of the head at the level of the frontal-parietal suture and examination of the cross-sectioned brain for apparent hydrocephaly.

Blood samples were collected from five pups per sex per litter from the 10 female rats per group selected for FOB and motor activity assessment, blood sample collection for hematology and clinical chemistry and histological evaluations. Sera was shipped for analysis. The liver from each selected pup was weighed.

1.2. Results

1.2.1. Male Rats

All male rats survived to scheduled sacrifice and all clinical and necropsy observations were considered unrelated to the test substance.

Body weight gains were significantly reduced in the 0.3, 3 and 10 mg/kg/day dosage groups on study days (DSs) 29 to 36. Significantly reduced body weight gain occurred in the 0.3, 1, 3 and 10 mg/kg/day dosage groups on study days DS 29 to termination. Body weight gain was also significantly reduced for the 10 mg/kg/day dosage group for the entire dosage period. Absolute and relative feed consumption values for the male rats were unaffected by dosages of the test substance as high as 10 mg/kg/day.

Terminal body weights of the male rats were slightly reduced in the 10 mg/kg/day dosage group. The absolute weights of the liver, the ratios of the liver weights to terminal body weights and ratios of the liver weights to brain weight were significantly increased in the 3 and 10 mg/kg/day dosage groups. The ratio of the heart weights to brain weight was significantly decreased in the 10 mg/kg/day dosage group.

Hemoglobin concentrations were significantly decreased in the 1, 3 and 10 mg/kg/day dosage groups and average values for red blood cells and hematocrit were significantly decreased in the 3 and 10 mg/kg/day dosage groups. Prothrombin time was significantly increased in the 0.3, 3 and 10 mg/kg/day dosage groups. Average values for cholesterol were significantly decreased in the 0.3, 1, 3 and 10 mg/kg/day dosage groups and the average values for triglycerides was significantly decreased in the 10 mg/kg/day dosage group. Albumin, blood urea nitrogen, alkaline phosphatase, calcium and albumin/globulin ratio levels were significantly increased in the 10 mg/kg/day dosage group.

Treatment-related microscopic changes were observed in the liver and thyroid gland of male rats in the 3 and 10 mg/kg/day dosage groups. The treatment-related microscopic changes in the liver consisted of minimal to moderate enlargement of centrilobular hepatocytes and in the thyroid gland as an increased incidence of hypertrophy of follicular cells and hyperplasia. These microscopic changes are consistent with the known effects of compounds that cause microsomal enzyme induction where the hepatocellular hypertrophy results in a compensatory hypertrophy and hyperplasia of the thyroid due to increased plasma turnover of thyroxine and associated stimulation of thyroid-stimulating hormone in rats[1]. There were no treatment-related microscopic changes observed in the liver of the F1 generation pups from the dams given up to 10 mg/kg/day of the test substance.

All mating and fertility parameters were unaffected by dosages of the test substance as high as 10 mg/kg/day. There were no other statistically significant or biologically important differences among the four dosage groups in the measures of the functional observational battery (FOB) or motor activity on DSs 36 through 39.

Sperm motility was unaffected by dosages of the test substance as high as 10 mg/kg/day. The sperm count and sperm density were comparable among the five dosage groups.

1.2.2. Female Rats

All female rats survived to scheduled sacrifice and all clinical and necropsy observations were considered unrelated to the test substance.

Body weights, body weight gains, and absolute and relative feed consumption values were comparable and did not differ significantly during the precohabitation, gestation or lactation periods at dosages of the test substance up to 10 mg/kg/day.

Terminal body weights, absolute and relative weights of the reproductive organs, brain, liver, left and right kidneys and adrenals, spleen, thymus and heart of the female rats were

comparable among dosage groups. Average primordial follicle counts for the 10 mg/kg/day dosage group were comparable to the control group.

No treatment-related microscopic changes were observed in any of the female rats administered up to 10 mg/kg/day of the test substance. There were no treatment-related microscopic changes observed in the liver of the F1 generation pups from the dams given up to 10 mg/kg/day of the test substance.

Dosages as high as 10 mg/kg/day did not affect any hematology or clinical chemistry values evaluated.

The average numbers of estrous stages per 13 days were comparable among the five dosage groups. All mating and fertility parameters, including the gestation index, viability index and lactation indices were unaffected by dosages of the test substance as high as 10 mg/kg/day.

There were no statistically significant or biologically important differences among the five dosage groups in the measures of the functional observational battery (FOB) or motor activity on DL 17.

All pregnant dams delivered a litter of one or more live pups. Values for the numbers of dams delivering litters, the duration of gestation, averages for implantation sites per delivered litter, the numbers of dams with stillborn pups, the numbers of dams with no liveborn pups, dams with all pups dying, were comparable among the five dosage groups. The number of pups surviving per litter, pup sex ratios, litter size and pup body weights per litter were comparable among the five dosage groups.

No clinical or necropsy observations in the F1 generation pups were attributable to dosages of the test substance as high as 10 mg/kg/day. F1 generation male and female pup terminal body weights, absolute liver weight and ratio of liver weight to terminal body weight were comparable across all five dosage groups.

1.3. Conclusion

On the basis of these data, the maternal no-observable-adverse-effect-level (NOAEL) for T-7706 [Perfluorohexane Sulfonate Potassium Salt] is greater than 10 mg/kg/day (the 10 mg/kg/day dosage caused no deaths, adverse clinical or necropsy/pathology observations, changes in body weight, feed consumption, or hematology or clinical chemistry values throughout precohabitation, gestation or lactation. The paternal NOAEL is less than 0.3 mg/kg/day (the 0.3 and 1 mg/kg/day dosages caused significant differences in body weight gain, hematology and clinical chemistry values and the 3 and 10 mg/kg/day dosages caused significant changes in absolute and relative organ weights and microscopic changes in the liver and thyroid gland).

The reproductive NOAEL is greater than 10 mg/kg/day (the 10 mg/kg/day dosage had no effect on the durations of gestation and parturition or any mating and fertility parameters. There was no effect on the sperm parameters in the male rats).

The NOAEL for viability and growth in the offspring is also greater than 10 mg/kg/day (dosages of 10 mg/kg/day had no effect on perinatal mortality, clinical or necropsy observations or body or liver weights in the F1 generation offspring).

A. Hoberman 31-JUL-03

Alan M. Hoberman, Ph.D., DABT Date
Director of Research
Study Director

Raymond G. York 31 JUL 2003

Raymond G. York, Ph.D., DABT Date
Associate Director of Research
Study Director

2. DESCRIPTION OF TEST PROCEDURES

2.1. Conduct of Study

2.1.1. Sponsor

3M Corporate Toxicology, 3M Center, Building 220-2E-02, St. Paul, Minnesota 55144-1000

2.1.2. Testing Facility

Argus Research, 905 Sheehy Drive, Building A, Horsham, Pennsylvania 19044-1297

2.1.3. Study Number

418-028

2.1.4. Sponsor's Study Number

T-7706.1

2.1.5. Purpose of the Study

The purpose of this study was to provide information on the possible health hazards that may result from repeated exposure of Crl:CD®(SD)IGS BR VAF/Plus® male and female rats to a test substance beginning before cohabitation, through mating and continuing for at least 42 days (male rats) or through parturition until day 21 of lactation (female rats). This repeated dose study incorporated a reproduction/developmental toxicity screening test that can be used to provide initial information on possible effects on male and female reproductive performance (e.g., gonadal function, mating behavior, conception, development of the conceptus and parturition). The study also placed emphasis on neurological effects as a specific endpoint and should identify the neurotoxic potential of a test substance, which may warrant further in-depth investigation.

Because of the selectivity of the endpoints and the short duration of the study, the screening test did not provide evidence for definitive claims of no reproductive/ developmental effects. In particular, it offered only limited means of detecting postnatal manifestations of prenatal exposure or effects that may be induced during postnatal exposure.

2.1.6. Study Design

The requirements of the Organisation for Economic Co-operation and Development (OECD)[2] were used as the basis for study design.

2.1.7. Regulatory Compliance

This study was conducted in compliance with Good Laboratory Practice (GLP) regulations of the OECD[3],U.S. Food and Drug Administration (FDA)[4], the Japanese

Ministry of Health and Welfare (MHW)[5]. There were no deviations from the GLP regulations that affected the quality or integrity of the study. Quality Assurance Unit findings derived from the inspections during the conduct of this study are documented and have been provided to the Study Director and the Testing Facility Management.

2.1.8. Ownership of the Study

The Sponsor owns the study. All raw data, analyses, reports and preserved tissues are the property of the Sponsor.

2.1.9. Study Monitor

John Butenhoff, Ph.D., CIH, DABT

2.1.10. Study Director

Raymond G. York, Ph.D., DABT (Associate Director of Research)
Address as cited previously for Testing Facility.

2.1.11. Technical Performance

John F. Barnett, B.S. (Director of Laboratory Operations)
Joseph W. Lech, B.S. (Senior Research Associate)
Mary P. Howard, B.S. (Team Leader - General Laboratory)
Jaclyn S. Fox, B.S. (Laboratory Technician)
Josette M. Provost, B.S. (Necropsy Laboratory Technician/Fixed Tissue Coordinator)
Christopher K. Ruppert, B.S. (Formulation Laboratory Technician)

2.1.12. Report Preparation

Raymond G. York, Ph.D., DABT
Jo Ann Frazee, M.S. (Study Coordinator)
JoAnne M. Conklin, B.S. (Data Management Specialist)
Cristina Petrescu (Report Administrator)

2.1.13. Report Review

Valerie A. Sharper, M.S. (Director of Study Management)

2.1.14. Date Protocol Signed

26 March 2002

2.1.15. Dates of Technical Performance

2.1.15.1. Male Rats

Rat Arrival	26 MAR 02
Dosage Period (14 days before cohabitation and through a 14-day cohabitation period until sacrifice after at least 42 days of dosage)	01 APR 02 - 16 MAY 02
FOB and Motor Activity Evaluation	06 MAY 02 - 09 MAY 02
Toxicokinetic Sample Collections	
DS[a] 14	14 APR 02
DS 42	12 MAY 02
Scheduled Sacrifice - Toxicokinetic Study	12 MAY 02
Scheduled Sacrifice - Main Study	13 MAY 02 - 17 MAY 02

2.1.15.2. Female Rats

Rat Arrival	26 MAR 02
Dosage Period (14 days before cohabitation through DL[b] 21)	01 APR 02 - 09 JUN 02
Cohabitation Period	
Male 1	14 APR 02 PM - 21 APR 02 AM
Male 2	21 APR 02 PM - 28 APR 02 AM
Toxicokinetic Sample Collections	
DS 14	14 APR 02
DG[c] 21	06 MAY 02 - 19 MAY 02
DG 0	15 APR 02 - 28 APR 02
DG 25 Sacrifice (Rats that did not deliver a litter)	10 MAY 02 - 23 MAY 02
Delivery Period[d] (DL 1)	07 MAY 02 - 20 MAY 02
FOB and Motor Activity Evaluation	23 MAY 02 - 26 MAY 02
DL 22 Sacrifice Female Rats and Pups	28 MAY 02 - 10 JUN 02

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a. DS is an abbreviation used for day of study.
b. DL is an abbreviation used for day of lactation/postpartum.
c. DG is an abbreviation used for day of (presumed) gestation.
d. The day of birth is designated lactation day 0 (postpartum day 0) in the Health Effects Test Guidelines - Reproduction and Fertility Effects (Office of Prevention, Pesticides and Toxic Substances 870.3800, August, 1998) and in the OECD Guideline for the Testing of Chemicals - Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (Section 4, No. 422, 22 March 1966). This same day is designated day 1 postpartum (day 1 of lactation) in the Standard Operating Procedures of the Testing Facility. Throughout this study, the day of birth was designated as day 1 postpartum (day 1 of lactation) and all subsequent ages of the F1 generation rats and days of the lactation period were determined and cited accordingly.

2.1.16. Records Maintained

The original report, raw data and reserve samples of each lot of bulk test substance and bulk vehicle components are retained in the archives of Argus Research. Any preserved tissues are retained in the archives of the Testing Facility for one year after the mailing of the draft final report, after which time the Sponsor will decide their final disposition. All unused prepared formulations were discarded at the Testing Facility. All remaining bulk test substance was returned to the Sponsor.

2.2. Test Substance Information

2.2.1. Description

T-7706 [Perfluorohexane Sulfonate Potassium Salt (PFHS)] - a white powder

2.2.2. Date Received and Storage Conditions

The test substance was received on 11 March 2002 and stored at room temperature.

2.2.3. Special Handling Instructions

Standard safety precautions (use of protective clothing, gloves, dust-mist/HEPA-filtered mask, safety goggles or safety glasses and a face-shield) were taken during formulation preparation and dosage. A half-face respirator was worn during formulation preparation.

2.2.4. Analysis of Purity

Information to document or certify the identity, composition, method of synthesis, strength and purity of the test substance was provided by the Sponsor to the Testing Facility. A Certificate of Analysis is available in APPENDIX F.

2.3. Vehicle Information

2.3.1. Description

Aqueous 0.5% carboxymethylcellulose (CMC) (sodium salt; medium viscosity) prepared using carboxymethylcellulose (sodium salt; medium viscosity), an off-white powder, and reverse osmosis membrane processed deionized water (R.O. deionized water).

2.3.2. Lot Number

120K0252

2.3.3. Date Received and Storage Conditions

The carboxymethylcellulose was received from Sigma Chemical Co., St. Louis, Missouri, on 11 September 2001 and stored at room temperature. R.O. deionized water is available from a continuous source at the Testing Facility and is maintained at room temperature.

2.3.4. Special Handling Instructions

Standard safety precautions (use of protective clothing, gloves, dust-mist/HEPA-filtered mask, safety goggles or safety glasses and a face-shield) were taken when handling the vehicle components and prepared vehicle.

2.3.5. Analysis of Purity

Neither the Sponsor nor the Study Director was aware of any potential contaminants likely to have been present in the vehicle that would have interfered with the results of this study. The expiration date for the carboxymethylcellulose is September 2005.

2.4. Test Substance Preparation and Storage Conditions

Formulations were prepared weekly at the Testing Facility. Prepared test substance and vehicle formulations were stored refrigerated (2°C to 8°C).

2.4.1. Sample Information

Sample Type	Size	Date Retained	Storage Conditions	Shipped To/ Shipping Conditions	Date Shipped
Bulk Test Substance[a]	1 g	09 JUN 02	Room temperature	Exygen[b]/ Ambient conditions	10 JUN 02
Homogeneity[c] (all levels)	2 mL	29 MAR 02	Refrigerated	Sponsor/ Refrigerated	01 APR 02
Concentration[d] (all levels)	2 mL	24 MAY 02[e] 07 JUN 02[f]	Refrigerated	Exygen[b] / Refrigerated	28 MAY 02 10 JUN 02
Stability[g]	2 mL	29 MAR 02	Refrigerated	Sponsor/ Refrigerated	01 APR 02
Bulk Test Substance Reserve	1 g	10 JUN 02	Room temperature	Testing Facility Archives	10 JUN 02
Vehicle Components Reserve			Room temperature	Testing Facility Archives	
Carboxymethylcellulose	1 g	10 JUN 02			10 JUN 02
R.O. deionized water	5 mL	10 JUN 02			10 JUN 02

a. A sample of the test article was retained on the last day of treatment and shipped for analysis.
b. Exygen Research, State College, Pennsylvania.
c. Quadruplicate samples were taken from the top, middle and bottom of each concentration on the first day of preparation. Two samples from each quadruplicate set were shipped for analysis. The remaining samples were retained at the Testing Facility as backup samples.
d. Quadruplicate samples were taken from each concentration on the last day of preparation. Two samples from each quadruplicate set were shipped for analysis. The remaining samples were retained at the Testing Facility as backup samples.
e. Samples for 0.03, 0.1 and 1 mg/mL concentrations only.
f. Samples for 0 and 0.3 mg/mL concentrations only.
g. Two sets of duplicate samples from each concentration were taken on the first day of preparation. One sample of each duplicate set was shipped on the day of preparation. These samples were analyzed as soon as possible after preparation and ten days after the first analysis. The remaining samples were retained at the Testing Facility as backup samples.

2.4.2. Analytical Results

Results of the analytical analyses are available in APPENDIX G.

2.5. Test System

2.5.1. Species

Rat

2.5.2. Strain

Crl:CD®(SD)IGS VAF/Plus®

2.5.3. Supplier (Source)

Charles River Laboratories, Inc.
Male Rats - St. Constant, Quebec, CANADA
Female Rats - Raleigh, North Carolina

2.5.4. Sex

Male and Female

2.5.5. Rationale for Test System

The Crl:CD®(SD)IGS BR VAF/Plus® rat was selected as the Test System because: 1) it is one mammalian species accepted for use in toxicity studies and it has been widely used throughout industry; 2) this strain of rat has been demonstrated to be sensitive to reproductive and developmental toxins; and 3) historical data and experience exist at the Testing Facility[6-8].

2.5.6. Test System Data

2.5.6.1. Male Rats

Number of Rats	100
Approximate Date of Birth	20 JAN 02
Approximate Age at Arrival	66 days
Weight (g) the Day after Arrival	277 - 318
Weight (g) at Study Assignment	305 - 348

2.5.6.2. Female Rats

Number of Rats	100
Approximate Date of Birth	21 JAN 02
Approximate Age at Arrival	65 days
Weight (g) the Day after Arrival	195 - 227
Weight (g) at Study Assignment	207 - 230

2.5.7. Method of Randomization

Upon arrival, the male and female rats were assigned to individual housing on the basis of computer-generated random units. During an acclimation period of at least five days, male and female rats were selected for study on the basis of physical appearance and body weights recorded during acclimation. The rats were assigned to five dosage groups (Groups I through V), 15 rats per sex per group, using a computer-generated (weight-ordered) randomization procedure. An additional three rats per sex per group were assigned to Groups I through V for toxicokinetic sample collection. At study initiation, the weight variation of the rats did not exceed ± 20% of the mean weight of each sex.

Litters were not culled during the lactation period because random selection of pups for culling could have resulted in potential biases in pup viabilities and body weight gains over this period.

Within each dosage group, consecutive order was used to assign the first 10 male and the first 10 female Fo generation rats to a functional observational battery (FOB) and motor activity assessment, blood sample collection for clinical chemistry and hematology and histological evaluations.

On DL 22, a table of random units was used to select five male and five female pups per litter for blood sample and liver collection. These pups were only selected from the 10 dams selected for FOB, motor activity, clinical chemistry and hematology and histological evaluation.

2.5.8. System of Identification

Male and female rats were assigned temporary numbers at receipt and given unique permanent identification numbers when assigned to the study before administration of the first dosage. Rats were permanently identified using a Monel® self-piercing ear tag (Gey Band and Tag Co., Inc., No. MSPT 20101). Cage tags were marked with the study number, permanent rat number, sex, test substance identification, generation, dosage group and dosage level.

Pups were not individually identified during lactation; all parameters were evaluated in terms of the litter.

2.6. Husbandry

2.6.1. Research Facility Registration

USDA Registration No. 14-R-0144 under the Animal Welfare Act, 7 U.S.C. 2131 *et seq.*

2.6.2. Study Room

The study room was maintained under conditions of positive airflow relative to a hallway and independently supplied with a minimum of ten changes per hour of 100% fresh air that had been passed through 99.97% HEPA filters. Room temperature and humidity

were monitored constantly throughout the study. Room temperature was targeted at 64°F to 79°F (18°C to 26°C); relative humidity was targeted at 30% to 70%[a].

2.6.3. Housing

Rats were individually housed in stainless steel, wire-bottomed cages except during cohabitation and postpartum periods. During cohabitation, each pair of male and female rats was housed in the male rat's cage. Beginning no later than DG 20, Fo generation female rats were individually housed in nesting boxes until they either naturally delivered litters or were sacrificed (DG 25). Each dam and delivered litter was housed in a common nesting box during the postpartum period. All cage sizes and housing conditions were in compliance with the *Guide for the Care and Use of Laboratory Animals*[9]. Argus Research is an AAALAC-accredited facility.

2.6.4. Lighting

An automatically-controlled fluorescent light cycle was maintained at 12-hours light: 12-hours dark, with each dark period beginning at 1900 hours EST.

2.6.5. Sanitization

Cage pan liners were changed at least three times weekly. Cages were changed approximately every other week. Bedding was changed as often as necessary to keep the rats dry and clean.

2.6.6. Feed

Rats were given *ad libitum* access to Certified Rodent Diet®#5002 (PMI Nutrition International, Inc., St. Louis, Missouri) in individual feeders. Feed was removed the evening prior to the scheduled sacrifice[b].

2.6.7. Feed Analysis

Analyses were routinely performed by the feed supplier. No contaminants at levels exceeding the maximum concentration for certified feed or deviations from expected nutritional requirements were detected by these analyses. Copies of the results of the feed analyses are available in the raw data.

Neither the Sponsor nor the Study Director was aware of any potential contaminants likely to have been present in the feed at concentrations that would have interfered with the results of this study.

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a. See APPENDIX H (TEMPERATURE AND RELATIVE HUMIDITY REPORT).

b. See APPENDIX E (DEVIATIONS FROM THE PROTOCOL AND THE STANDARD OPERATING PROCEDURES OF THE TESTING FACILITY), item 1.

2.6.8. Water

Local water that had been processed by passage through a reverse osmosis membrane (R.O. water) was available to the rats *ad libitum* from individual water bottles attached to the cages and/or from an automatic watering access system. Chlorine was added to the processed water as a bacteriostat.

2.6.9. Water Analysis

The processed water is analyzed twice annually for possible chemical contamination (Lancaster Laboratories, Lancaster, Pennsylvania) and monthly for possible bacterial contamination (Analytical Laboratories, Inc., Chalfont, Pennsylvania). Copies of the results of the water analyses are available in the raw data.

Neither the Sponsor nor the Study Director was aware of any potential contaminants likely to have been present in the water that would have interfered with the results of this study.

2.6.10. Bedding Material

Bed-o'cobs® bedding (The Andersons Industrial Products Group, Maumee, Ohio) was used as the nesting material.

2.6.11. Bedding Analysis

Analyses for possible contamination are conducted semi-annually. Copies of the restults of the bedding analyses are available in the raw data.

Neither the Sponsor nor the Study Director was aware of any potential contaminants likely to have been present in the bedding that would have interfered with the results of this study.

2.7. Methods

2.7.1. Dosage Administration

Dosage Group	Dosage[a] (mg/kg/day)	Concentration (mg/mL)	Dosage Volume (mL/kg)	Number of Rats per Sex	Assigned Numbers	
					Male Rats	Female Rats
I	0	0	10	15 + 3[b]	Main Study: 19109, 19115, 19116, 19119, 19122, 19125, 19131, 19132, 19134, 19135, 19143, 19151, 19157, 19161, 19167 Toxicokinetic Study: 19176 - 19178	Main Study: 19010, 19012, 19019, 19021, 19023, 19041, 19042, 19044, 19050, 19053, 19065, 19068, 19072, 19074, 19075 Toxicokinetic Study: 19076 - 19078
II	0.3	0.03	10	15 + 3[b]	Main Study: 19102, 19106, 19108, 19110, 19113, 19120, 19129, 19136, 19138, 19139, 19147, 19153, 19164, 19165, 19171 Toxicokinetic Study: 19179 - 19181	Main Study: 19004, 19009, 19016, 19018, 19026, 19036, 19037, 19043, 19047, 19048, 19052, 19055, 19061, 19067, 19071 Toxicokinetic Study: 19079 - 19081
III	1	0.1	10	15 + 3[b]	Main Study: 19101, 19105, 19107, 19112, 19114, 19121, 19123, 19130, 19137, 19146, 19155, 19159, 19172, 19173, 19174 Toxicokinetic Study: 19182 - 19184	Main Study: 19003, 19007, 19008, 19013, 19014, 19015, 19017, 19024, 19029, 19034, 19038, 19056, 19057, 19060, 19064 Toxicokinetic Study: 19082 - 19084
IV	3	0.3	10	15 + 3[b]	Main Study: 19100, 19103, 19104, 19118, 19133, 19141, 19142, 19144, 19148, 19150, 19156, 19160, 19162, 19163, 19166 Toxicokinetic Study: 19185 - 19187	Main Study: 19002, 19005, 19035, 19039, 19040, 19045, 19046, 19051, 19054, 19058, 19062, 19063, 19066, 19069, 19073 Toxicokinetic Study: 19085 - 19087
V	10	1	10	15 + 3[b]	Main Study: 19111, 19117, 19124, 19126, 19127, 19128, 19140, 19145, 19149, 19152, 19154, 19158, 19168, 19169, 19170 Toxicokinetic Study: 19188 - 19190	Main Study: 19001, 19006, 19011, 19020, 19022, 19025, 19027, 19028, 19030, 19031, 19032, 19033, 19049, 19059, 19070 Toxicokinetic Study: 19088 - 19090

a. The test substance was considered 100% pure for the purpose of dosage calculations.
b. Three additional rats per sex were assigned to toxicokinetic sample collection.

2.7.2. Rationale for Dosage Selection

Dosages were selected by the Sponsor based on previous studies conducted with the test substance, taking into account possible differences in sensitivity between pregnant and nonpregnant rats. The highest dosage was expected to cause toxic effects but not mortality or obvious suffering. The descending sequence of the lower dosage levels was selected for the purpose of demonstrating any dosage-related response, with no adverse effects expected at the lowest level.

2.7.3. Route and Rationale for Route of Administration

The oral (gavage) route was selected for use because: 1) in comparison with the dietary route, the exact dosage can be accurately administered; and 2) it is one of the possible routes for environmental exposure.

2.7.4. Frequency of Administration

2.7.4.1. Fo Generation Rats

Male rats were administered the test substance or the vehicle once daily beginning 14 days before cohabitation (maximum 14 days) and continuing through the day before sacrifice, after completion of the cohabitation period, after a minimum of 42 days of administration. Female rats were administered the test substance or the vehicle once daily beginning 14 days before cohabitation (maximum 14 days) and continuing through the day before sacrifice, DL 21 or DG 24 (rats that did not deliver a litter). The dosage volume was adjusted daily on the basis of the individual body weights recorded before intubation. The rats were intubated once daily at approximately the same time each day. The first day of dosage was designated as DS 1. Dams in the process of delivering pups were not intubated until completion of parturition, in order to preclude possible disruption of maternal behavior and/or cannibalization of pups. Consequently, some dams were not administered one daily dosage during the delivery period. No dam missed more than one daily dosage.

2.7.4.2. F1 Generation Pups

F1 generation pups were not directly administered the test substance or vehicle, but may have been possibly exposed to the test substance or vehicle during maternal gestation (*in utero* exposure) or via maternal milk during the lactation period.

2.7.5. Method of Study Performance

2.7.5.1. Fo Generation Rats

Within each dosage group, consecutive order was used to assign rats to cohabitation, one male rat per female rat. The cohabitation period consisted of a maximum of 14 days. Female rats with spermatozoa observed in a smear of the vaginal contents and/or a copulatory plug *in situ* were considered to be DG 0 and assigned to individual housing. Female rats not mated with a male rat within the first seven days of cohabitation were assigned an alternate male rat that had mated (same dosage group) and remained in cohabitation for a maximum of seven additional days.

Rats were observed for viability at least twice each day of the study. Rats were examined for clinical observations and general appearance weekly during the acclimation period. Observations for clinical signs of effects of the test substance and deaths were made on the first day of dosage at approximately hourly intervals for the first four hours and at the end of the normal working day. Observations for clinical signs of effects of the test

substance and deaths were made on subsequent days daily before dosage and approximately 60 ± 10 minutes after dosage administration and on the day of sacrifice[a].

Once before the first dosage and at least once weekly thereafter, detailed clinical observations were conducted for all male and female rats assigned to the main study[b]. These observations were made outside the cage in a standard arena at the same time each day of conduct. Effort was made to ensure that variations in the test conditions were minimal and that observations were conducted by observers unaware of treatment groups. The rats were observed for (but observations were not limited to) the following signs: changes in skin, fur, eyes, mucous membranes, occurrence of secretions and excretions and autonomic activity (e.g., lacrimation, piloerection, pupil size, unusual respiratory pattern). Changes in gait, posture and response to handling as well as the presence of clonic or tonic movements, stereotypic behavior (e.g., excessive grooming, repetitive circling), difficult or prolonged parturition or bizarre behavior (e.g., self-mutilation, walking backwards) were also recorded.

Body weights were recorded weekly during the acclimation period, daily during the dosage period and at sacrifice. Feed consumption values for male rats assigned to the main study were recorded weekly during the dosage period. Feed consumption values for female rats assigned to the main study were recorded weekly to cohabitation, on DGs 0, 7, 10, 12, 15, 18, 20 and 25 (if necessary) and on DLs 1, 5, 8 and 15[c]. Because pups begin to consume maternal feed on or about DL 15, feed consumption values were not tabulated after DL 15. During cohabitation, when two rats occupied the same cage with one feed jar, replenishment of the feed jars was documented but individual values were not recorded or tabulated.

Estrous cycling was evaluated in rats assigned to the main study by examination of vaginal cytology beginning with the day after the first administration and then until spermatozoa were observed in a smear of the vaginal contents and/or a copulatory plug was observed *in situ* during the cohabitation period. Estrous cycling was evaluated in rats assigned to the toxicokinetic study during the cohabitation period until spermatozoa were observed in a smear of the vaginal contents and/or a copulatory plug was observed *in situ*.

Female rats were evaluated for adverse clinical signs observed during parturition, duration of gestation (DG 0 to the day the first pup was observed), litter sizes (all pups delivered) and pup viability at birth. Maternal behavior was evaluated on DLs 1, 5, 8, 15 and 22. Variations from expected maternal behavior were recorded, if and when present, on all other days of the postpartum period.

On one occasion during the course of the study, a functional observational battery (FOB)[10-13] was conducted on 10 male and 10 female rats per group. For male rats, this assessment was conducted shortly before scheduled sacrifice, but prior to blood sample

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a. See APPENDIX E, items 2 and 3.
b. See APPENDIX E, item 4.
c. See APPENDIX E, item 5.

collection for hematology and clinical chemistry evaluations. Female rats were tested during the lactation period, shortly before scheduled sacrifice.

The FOB evaluation was conducted by an observer unaware of the group assignment of the rat. The following parameters were assessed:

1. Lacrimation, salivation, palpebral closure, prominence of the eye, pupillary reaction to light, piloerection, respiration, and urination and defecation (autonomic functions).

2. Sensorimotor responses to visual, auditory, tactile and painful stimuli (reactivity and sensitivity).

3. Reactions to handling and behavior in the open field (excitability).

4. Gait pattern in the open field, severity of gait abnormalities, air righting reaction and landing foot splay (gait and sensorimotor coordination).

5. Forelimb and hindlimb grip strength.

6. Abnormal clinical signs including but not limited to convulsions, tremors and other unusual behavior, hypotonia or hypertonia, emaciation, dehydration, unkempt appearance and deposits around the eyes, nose or mouth.

The ability of this battery to detect the effects of positive control substances has been established (Testing Facility Positive Control Data) and is available in APPENDIX I.

Motor activity was evaluated on 10 male and 10 female rats per group once, shortly before scheduled sacrifice, prior to blood sample collection. The movements of each rat were monitored by a passive infrared sensor mounted outside a stainless steel, wire-bottomed cage (40.6 x 25.4 x 17.8 cm). Each test session was 1.5 hours in duration with the number of movements and time spent in movement tabulated at each five-minute interval. The apparatus monitored a rack of up to 32 cages and sensors during each session, with each rat tested in the same location on the rack across test sessions. Groups were counterbalanced across testing sessions and cages. Data demonstrating that the test system is capable of detecting increases in activity produced by positive control substances (Testing Facility Positive Control Data) is available in APPENDIX I.

On DSs 14 and 42, blood samples (approximately 1 mL each) were collected from each male rat assigned to the toxicokinetic sample collection portion of the study (three rats per group) and on DS 14 and DG 21, blood samples (approximately 1 mL each) were collected from each female rat assigned to the toxicokinetic sample collection portion of the study (three rats per group). Samples were collected prior to dosage on DS 14. The time of each blood collection was recorded in the raw data. Blood was collected from the orbital sinus on DS 14 of the study and from the vena cava on DS 42 of study (male rats) and DG 21 (female rats). The samples were transferred into EDTA-coated (purple top) tubes and spun in a centrifuge. The resulting serum was transferred into polypropylene

tubes labeled with the protocol number, Sponsor study number, rat number, sex, group number, dosage level, day of study, collection interval, date of collection, species, generation and storage conditions. All samples were immediately frozen on dry ice and maintained frozen (≤-70°C) until shipment to Exygen Research, State College, Pennsylvania, for analysis. Results of these analyses are available in APPENDIX G.

2.7.5.2. F1 Generation Pups

Day 1 of lactation (postpartum) was defined as the day of birth and was also the first day on which all pups in a litter were individually weighed (pup body weights were recorded after all pups in a litter were delivered and groomed by the dam).

Each litter was evaluated for viability at least twice daily. The pups in each litter were counted once daily. Clinical observations were recorded once daily[a]. Pups were observed if they were warm and clean, for evidence of a nest and if pups were grouped together and nursing or had milk in stomach. Each pup was examined for general shape of the head, trunk, limbs, tail and presence of anus. Pup body weights were recorded on DLs 1, 8, 15 and 22 (terminal weight).

2.7.6. Gross Necropsy

2.7.6.1. Fo Generation Rats

Male and female rats assigned to the toxicokinetic study were sacrificed by carbon dioxide asphyxiation on DS 42 and DG 21, respectively. Blood samples were collected from the rats as previously described. After sacrifice, the liver of each rat was excised and the liver weight was recorded. The median liver lobe was frozen and stored (≤-20°C) until shipment for analysis[b]. The fetuses were removed from the uterus and blood samples were collected from each fetus via decapitation. Blood was placed into tubes, pooled per litter, allowed to clot and spun in a centrifuge. The resulting serum was transferred into labeled polypropylene tubes. All samples were immediately frozen on dry ice and maintained frozen (≤-70°C) until shipment for analysis. The liver from each fetus was collected, pooled per litter and placed into labeled tubes. The samples were frozen and stored (≤-20°C) until shipment for analysis. The number of implantation sites was recorded. Carcasses were discarded without further evaluation. The livers were shipped to Exygen Research, State College, Pennsylvania, for analysis. Results of the analyses are available in APPENDIX G.

Male and female rats assigned to the main study were sacrificed by carbon dioxide asphyxiation following the last dosage administration, after a minimum of 42 days of dosage and on DL 22, respectively. A gross necropsy of the thoracic, abdominal and pelvic viscera was performed. Gross necropsy included an initial physical examination of external surfaces and all orifices, as well as the cranial, thoracic and abdominal cavities and their contents. Special attention was paid to the organs of the reproductive system. The ovaries and the uterus with cervix of each female rat were weighed, and the

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a. See APPENDIX E, items 6 and 7.
b. See APPENDIX E, item 8.

ovaries, uterus, vagina and a mammary gland were retained in neutral buffered 10% formalin. The number of implantation sites were recorded. Uteri of apparently nonpregnant rats were examined after being pressed between glass plates to confirm the absence of implantation sites and were retained in neutral buffered 10% formalin. Gross lesions were retained in neutral buffered 10% formalin and examined histologically. Representative photographs of gross lesions are available in the raw data. Tissue trimming and histopathology were performed under the supervision of or by a Board Certified Veterinary Pathologist.

Ten rats per sex per group assigned to functional observational battery and motor activity tests were assigned to histological evaluations. The following organs were excised, trimmed and individually weighed as soon as possible after excision to avoid drying: liver, kidneys, adrenals, thymus, testes, right epididymis, left epididymis (corpus and caput), seminal vesicles (with and without fluid), prostate, spleen, brain, heart, ovaries and uterus (with cervix). The following tissues or representative samples were retained in neutral buffered 10% formalin: brain (representative regions including cerebrum, cerebellum, pons), small and large intestines (including Peyer's patches), lungs (perfused with neutral buffered 10% formalin), lymph nodes (submandibular and mediastinal), peripheral nerve (sciatic or tibial), stomach, kidneys, spleen, thymus, trachea, urinary bladder, spinal cord (cervical, thoracic and lumbar), liver, adrenals, heart, thyroid/parathyroid, bone marrow (sternum), testes (fixed in Bouin's solution for 48 to 96 hours before being retained in neutral buffered 10% formalin), prostate, seminal vesicles (with coagulating gland), the remaining portion of the left epididymis (corpus and caput), the right epididymis, ovaries, uterus, vagina, mammary gland (female rats only) and gross lesions. Histological examination of retained tissues, including reproductive organs, was conducted for the assigned ten rats per sex from the control and high dosage groups. A quantitative evaluation of primordial follicles was conducted for Fo generation female rats. Examination included enumeration of number of primordial follicles, which were combined with small growing follicles, for comparison of ovaries of rats assigned to treated and control groups. Tissues that were examined histologically were shipped to Research Pathology Services, Inc., New Britain, Pennsylvania, for evaluation. Results of the histological evaluation are available in APPENDIX J.

To assess the potential toxicity of the test substance on the male reproductive system, sperm evaluations were performed for 10 male rats in each dosage group. Sperm concentration and motility were evaluated using computer-assisted sperm analysis (CASA). Motility was evaluated by the Hamilton Thorne IVOS by collection of a sample from the left vas deferens. A homogenate was prepared from the left cauda epididymis for evaluation by the Hamilton Thorne IVOS to determine sperm concentration (sperm per gram of tissue weight). The remaining portion of the left cauda epididymis was used to manually evaluate sperm morphology. Sperm morphology evaluations included the following: 1) determination of the percentage of normal sperm in a sample of at least 200; and 2) qualitative evaluation of abnormal sperm, including such categories as abnormal head, abnormal tail, and abnormal head and tail.

At scheduled sacrifice, the 10 male and 10 female rats per group assigned to hematology and clinical chemistry sample collection were exsanguinated from the inferior vena cava following sacrifice. Rats were fasted overnight before sacrifice[a]. Approximately 5 mL of blood was collected. The tubes containing the samples were labeled with the protocol number, Sponsor study number, rat number, sex, group number, dosage level, day of study, collection interval, date of collection, species, generation and storage conditions.

Approximately 1 mL of blood was collected into EDTA-coated tubes and maintained on wet ice or refrigerated until shipment for analysis of the following hematologic parameters: erythrocyte count (RBC), hematocrit (HCT), hemoglobin (HGB), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular volume (MCV), total leukocyte count (WBC), differential leukocyte count, platelet count (PLAT), mean platelet volume (MPV) and cell morphology. Two blood smear slides were prepared at the Testing Facility for each sample for measurements of differential leukocyte count.

Approximately 1.8 mL of blood was added to a tube containing 0.2 mL of sodium citrate (0.129 M). The contents were mixed and maintained on wet ice until the tubes were centrifuged (within 30 minutes of the collection time). The resulting plasma was transferred to 2.0 mL polypropylene tubes and immediately frozen. Plasma samples were maintained on dry ice or in a freezer (≤-70°C) until shipment for measurement of prothrombin time (PT) and activated partial thromboplastin time (APTT).

Approximately 2 mL of blood was collected into serum separator tubes and centrifuged. The resulting sera samples were immediately frozen on dry ice and maintained frozen (≤-70°C) until shipment for analysis of the following parameters: total protein (TP), triglycerides (TRI), albumin (A), globulin (G), albumin/globulin Ratio (A/G), glucose (GLU), cholesterol (CHOL), total bilirubin (TBILI), urea nitrogen (BUN), creatinine (CREAT), creatinine kinase (CK), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALK), calcium (CA), phosphorus (PHOS), sodium (NA), potassium (K) and chloride (CL).

Samples for hematology and clinical chemistry analyses were shipped to Redfield Laboratories, A Division of CRL-DDS, Redfield, Arkansas. Samples were shipped on dry ice and slides were shipped at ambient conditions. Results of these analyses are available in APPENDIX K.

Female rats that did not deliver a litter were sacrificed on DG 25. Gross necropsy, examination and tissue retention were conducted as described above for rats at scheduled sacrifice. Gross lesions were preserved in neutral buffered 10% formalin for possible future evaluation. Representative photographs of gross lesions are available in the raw data.

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a. See APPENDIX E, item 1.

2.7.6.2. F1 Generation Pups

On DL 22, pups were sacrificed by carbon dioxide asphyxiation and examined for gross lesions. Necropsy included a single cross-section of the head at the level of the frontal-parietal suture and examination of the cross-sectioned brain for apparent hydrocephaly. Gross lesions were preserved in neutral buffered 10% formalin for possible future evaluation. Representative photographs of gross lesions are available in the raw data.

Blood samples were collected from each selected pup (five per sex per litter from the 10 female rats per group selected for FOB and motor activity assessment, blood sample collection for hematology and clinical chemistry and histological evaluations) from the vena cava. The blood was placed into tubes, pooled per litter, allowed to clot and spun in a centrifuge; the resulting serum was transferred into labeled polypropylene tubes. All samples were immediately frozen on dry ice and maintained frozen (≤-70°C) until shipment for analysis. The liver from each selected pup was excised and the organ weight recorded[a]. The median lobe was frozen and stored (≤-20°C) until shipment for possible analysis. The remaining portion of each liver was retained in neutral buffered 10% formalin for possible histological evaluation. The livers were processed and evaluated histologically as described for the Fo generation rats.

Pups that died before initial examination of the litter for pup viability were evaluated for vital status at birth. The lungs were removed and immersed in water. Pups with lungs that sink were identified as stillborn; pups with lungs that float were identified as liveborn, and to have died shortly after birth. Pups found dead were examined for gross lesions and for the cause of death.

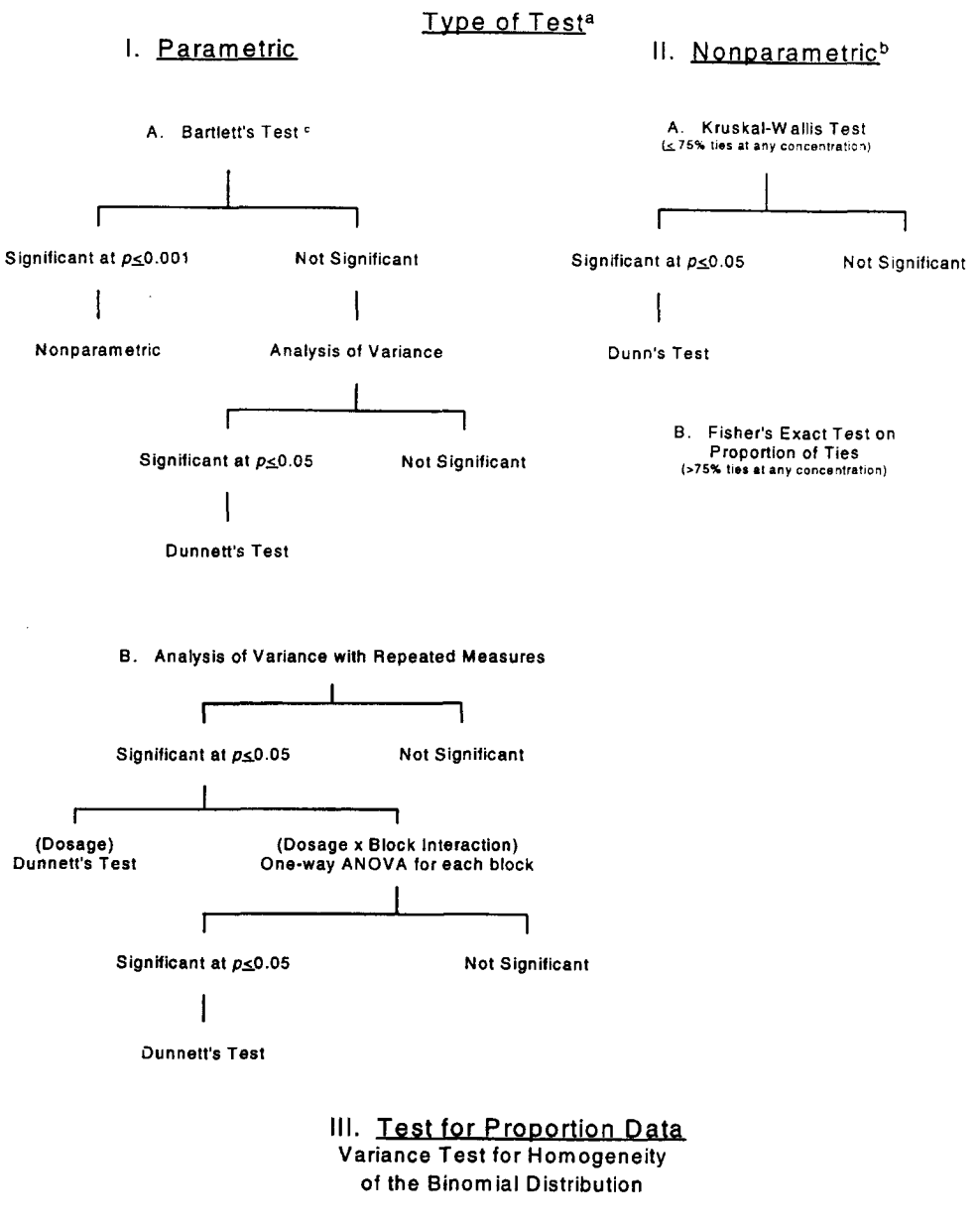
2.7.7. Data Collection and Statistical Analyses

Data generated during the course of this study were recorded either by hand or using the *Argus Automated Data Collection and Management System*, the *Vivarium Temperature and Relative Humidity Monitoring System*, the *Coulbourn Instruments Passive Infrared Motor Activity System*, the *Coulbourn Instruments Auditory Startle System*, the *Coulbourn Instruments Spatial Delayed Alternation System*, and/or the passive avoidance software. All data were tabulated, summarized and/or statistically analyzed using the *Argus Automated Data Collection and Management System*, the *Vivarium Temperature and Relative Humidity Monitoring System*, *Microsoft Excel* [part of Microsoft Office 97 (version SR-2)] and/or *The SAS System* (version 6.12).

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a. See APPENDIX E, item 9.

Averages and percentages were calculated. Litter values were used where appropriate. The following schematic represents the statistical analyses of the data:



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a. Statistically significant probabilities are reported as either $p \leq 0.05$ or $p \leq 0.01$.
b. Proportion data are not included in this category.
c. Test for homogeneity of variance.

Adult data was evaluated with the individual rat as the unit measured. Litter values were used in evaluation of pup data, as appropriate.

Variables with interval or ratio scales of measurement, such as body weights, feed consumption values, latency and errors per trial scores in behavioral tests and percent mortality per litter were analyzed as described under the Parametric heading of the schematic. Bartlett's Test of Homogeneity of Variances[14] was used to estimate the probability that the dosage groups have different variances. A non-significant result ($p>0.001$) indicated that an assumption of homogeneity of variance was not inappropriate, and the data was compared using the Analysis of Variance[15]. If that test was significant ($p\leq0.05$), the groups given the test substance were compared with the control group using Dunnett's Test[16]. If Bartlett's Test was significant ($p\leq0.001$), the Analysis of Variance Test was not appropriate, and the data was analyzed as described under the Nonparametric heading of the schematic. When 75% or fewer of the scores in all the groups were tied, the Kruskal-Wallis Test[17] was used to analyze the data, and in the event of a significant result ($p\leq0.05$), Dunn's Test[18] was used to compare the groups given the test substance with the control group. When more than 75% of the scores in any dosage group were tied, Fisher's Exact Test[19] was used to compare the proportion of ties in the groups.

Data from the motor activity test, with measurements recorded at intervals (Blocks) throughout each test session, were analyzed using an Analysis of Variance with Repeated Measures[20], as described under that heading in the schematic. A significant result ($p\leq0.05$) in that test could have appeared as effect of Concentration (differences among dosage groups in the totals of all measurements in a session) or as an interaction between Concentration and Block (differences in the patterns of dosage group values across the measurement periods). If the Concentration effect was significant, the totals for the control group and the groups given the test substance were compared using Dunnett's Test[16]. If the Concentration x Block interaction was significant, an Analysis of Variance[15] was used to evaluate the data at each measurement period, and a significant result ($p\leq0.05$) was followed by a comparison of the dosage groups using Dunnett's Test[16].

Variables that had graded or count scores, such as litter size, the number of trials to a criterion in a behavioral test or the day a developmental landmark appeared, were analyzed using the procedures described under the Nonparametric heading of the schematic.

Clinical observation incidence data, as well as the descriptive and quantal data from the FOB, were analyzed as contingency tables using the Variance Test for Homogeneity of the Binomial Distribution[21].

Sperm motility data were expressed as percentages and analyzed, as indicated above, by parametric methods.

3. RESULTS - Male Rats

3.1. Mortality, Clinical and Necropsy Observations (Summaries - Tables B1 and B2; Individual Data - Tables B17 and B18)

3.1.1. Mortality

All male rats survived to scheduled sacrifice.

3.1.2. Clinical Observations

All clinical observations were considered unrelated to the test substance because: 1) the incidences were not dosage-dependent; and/or 2) the observation occurred in only one or two male rats in any dosage group. These observations included chromorhinorrea, missing/broken or misaligned incisors, chromodacryorrhea, lacrimation, localized alopecia on the head, underside or limbs, dry, brown perioral substance, soft or liquid feces, scab on head and dehydration.

3.1.3. Necropsy Observations

All necropsy observations were considered unrelated to the test substance because the incidences were not dosage-dependent; and/or 2) the observation occurred in only one or two male rats in any dosage group. These observations included discolored/mottled kidneys, slight pelvic dilation of the left kidney, small epididymides, small testes and diverticulum jejunum.

3.1.4. Histopathology (APPENDIX J)

No treatment-related microscopic changes were observed in any of the male rats administered 0.3 or 1 mg/kg/day of the test substance. Treatment-related microscopic changes were observed in the liver and thyroid gland of male rats in the 3 and 10 mg/kg/day dosage groups. The treatment-related microscopic changes in the liver consisted of minimal to moderate enlargement (hypertrophy) of centrilobular hepatocytes. The affected hepatocytes were enlarged with an increased amount of dense eosinophilic granular cytoplasm.

The treatment-related microscopic changes in the thyroid gland consisted of an increased incidence of the male rats in the 3 and 10 mg/kg/day dosage groups with hypertrophy (enlargement) of follicular cells and hyperplasia (increased follicular cells and small follicles). Although the incidence in the 10 mg/kg/day dosage group was minimally increased over the control group values, the hypertrophy and hyperplasia could have been associated with the liver-cell changes.

3.2. Terminal Body Weights and Organ Weights and Ratios (%) of Organ Weight to Terminal Body Weight and Brain Weight (Summaries - Tables B3 through B5; Individual Data - Tables B19 and B20)

Terminal body weights of the male rats were slightly reduced (approximately 6%), albeit not significantly, in the 10 mg/kg/day dosage group, as compared with control group values.

The absolute weights of the liver, the ratios of the liver weights to terminal body weights and ratios of the liver weights to brain weight were significantly increased ($p \leq 0.05$ and/or $p \leq 0.01$) in the 3 and 10 mg/kg/day dosage groups, as compared with the control group value. The ratio of the heart weights to brain weight was significantly decreased ($p \leq 0.05$) in the 10 mg/kg/day dosage group, as compared with the control group value.

The absolute and relative (terminal body and brain) weights of the male reproductive organs (left and right epididymes, left cauda epididymes, left and right testes, seminal vesicles with and without fluid and prostate), brain, left and right kidneys and adrenals, spleen, thymus and heart (except relative heart weight as described above) were comparable across dosage groups and did not differ significantly.

3.3. Hematology and Clinical Chemistry (Summaries - Tables B6 and B7; Individual Data - APPENDIX K)

Hemoglobin concentrations (HGB) were significantly decreased ($p \leq 0.05$ or $p \leq 0.01$) in the 1, 3 and 10 mg/kg/day dosage groups and average values for red blood cells (RBC) and hematocrit (HCT) were significantly decreased ($p \leq 0.05$ or $p \leq 0.01$) in the 3 and 10 mg/kg/day dosage groups, as compared with the control group values. Prothrombin time (PT) was significantly increased ($p \leq 0.05$ or $p \leq 0.01$) in the 0.3, 3 and 10 mg/kg/day dosage groups.

Dosages of the test substance as high as 10 mg/kg/day did not affect mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelets (PLAT), mean platelet volume (MPV), volume, white blood counts (WBC), activated partial thromboplastin time (APTT), nucleated red blood cell count (NRBC), lymphocytes, segmented neutrophils, bands, monocytes, eosinophils, basophils and abnormal lymphocytes in male rats. These values were comparable among the four dosage groups and did not differ significantly.

Average values for cholesterol (CHOL) were significantly decreased ($p \leq 0.05$ or $p \leq 0.01$) in the 0.3, 1, 3 and 10 mg/kg/day dosage groups and the average values for triglycerides (TRIG) was significantly decreased ($p \leq 0.01$) in the 10 mg/kg/day dosage group. Albumin (A), blood urea nitrogen (BUN), alkaline phosphatase (ALK), calcium (CA) and albumin/globulin ratio (A/G) levels were significantly increased ($p \leq 0.01$) in the 10 mg/kg/day dosage group.

Clinical chemistry values for total protein (TP), glucose (GLU), total bilirubin (TBILI), creatinine (CREAT), creatinine kinase (CK), alanine aminotransferase (ALT), aspartate

aminotransferase (AST), phosphorus (PHOS), sodium (NA), potassium (K), chloride (CL) and globulin (G) in male rats were comparable among the four dosage groups and did not differ significantly.

3.4. Body Weights and Body Weight Changes (Figure 1; Summaries - Tables B8 and B9; Individual Data - Table B21)

Body weight gains were significantly reduced ($p \leq 0.05$ or $p \leq 0.01$) in the 0.3, 3 and 10 mg/kg/day dosage groups on study days (DSs) 29 to 36. As a result of these reductions, significantly reduced ($p \leq 0.05$ or $p \leq 0.01$) body weight gain occurred in the 0.3, 1, 3 and 10 mg/kg/day dosage groups on study days DS 29 to termination. Body weight gain was also significantly reduced ($p \leq 0.01$) for the 10 mg/kg/day dosage group for the entire dosage period (calculated as DS 1 to termination).

3.5. Absolute (g/day) and Relative (g/kg/day) Feed Consumption Values (Summaries - Tables B10 and B11; Individual Data - Table B22)

Absolute (g/day) and relative (g/kg/day) feed consumption values for the male rats were unaffected by dosages of the test substance as high as 10 mg/kg/day.

3.6. Mating and Fertility (Summary - Table B12; Individual Data - Table B23)

All mating and fertility parameters (numbers of days in cohabitation, rats that mated, fertility index, rats with confirmed mating dates during the first and second week of cohabitation and the number of pregnant rats per number of rats in cohabitation) were unaffected by dosages of the test substance as high as 10 mg/kg/day.

3.7. Functional Observational Battery (Summary - Table B13; Individual Data - Table B24)

Home cage behavior of sleeping and immobile/awake were significantly different ($p \leq 0.01$) in the 3 mg/kg/day dosage group, compared to the control group. These increases were not considered treatment-related because they were not dosage-dependent.

There were no other statistically significant or biologically important differences among the four dosage groups in the measures of the functional observational battery (FOB). There were no alterations in autonomic functions (lacrimation, salivation, palpebral closure, prominence of the eye, pupillary reaction to light, piloerection, respiration, defecation and urination), sensorimotor functions [responses to visual, auditory, tactile and painful stimuli (reactivity and sensitivity)], excitability (reactions to handling and behavior in the open field), gait and sensorimotor coordination (gait pattern in the open field, severity of gait abnormalities, air righting reaction and landing foot splay) and forelimb and hindlimb grip strength and abnormal clinical observations including but not limited to: convulsions, tremors, unusual behavior, hypotonia or hypertonia, emaciation, dehydration, unkempt appearance and deposits around the eyes, nose or mouth.

Body weights recorded during the functional operational battery for the treated groups were not significantly different than the control group for the male rats.

3.8. Motor Activity (Figures 3 and 4; Summary - Table B14; Individual Data - Table B25)

There were no statistically significant or biologically important differences among the five dosage groups in the number of movements or time (in seconds) spent in movement measures of motor activity on DSs 36 through 39.

3.9. Sperm (Summary - Tables B15 and B16; Individual Data - Tables B26 and B27)

3.9.1. Sperm Motility

Sperm motility was unaffected by dosages of the test substance as high as 10 mg/kg/day. Group mean values were comparable among the five dosage groups and ranged from 85.5% to 93.2% motile sperm.

3.9.2. Sperm Count and Sperm Density

The sperm count and sperm density were comparable among the five dosage groups. No treatment-related differences were observed.

3.9.3. Sperm Morphology

A low incidence of head and/or tail abnormalities was observed for the male rats in all dosage groups. No treatment-related differences were observed.

4. RESULTS - Female Rats

4.1. Mortality, Clinical and Necropsy Observations (Summaries - Tables C1 and C2; Individual Data - Tables C28 and C29)

4.1.1. Mortality

All female rats survived to scheduled sacrifice.

4.1.2. Clinical Observations

All clinical observations were considered unrelated to the test substance because: 1) the incidences were not dosage-dependent; and/or 2) the observation occurred in only one female rat in any dosage group except for localized alopecia which is a common finding in rats that are allowed to deliver. These observations included brown perioral substance, rales, localized alopecia on the limbs, back or head, urine-stained abdominal fur, miosis, abdominal distention, emaciation, cold to touch, swollen nose, scab or ulceration on back or head, dehydration and tip of tail missing.

4.1.3. Necropsy Observations

All necropsy observations were considered unrelated to the test substance because: 1) the incidences were not dosage-dependent; and/or 2) the observation occurred in only one female rat in each of the 1, 3 and 10 mg/kg/day dosage groups. These observations included the cortex of the right kidney adhered to the right lateral liver lobe in a 1 mg/kg/day dosage group female rat (19907), small left ovaries (0.003g) in one 3 mg/kg/day dosage group female rat (19051) that was not pregnant, outer capsule of spleen adhered to the omentum in another 3 mg/kg/day dosage group female rat (19063) and the large and small intestines distented with gas, small spleen and thymus, large adrenals, and approximately 12 black areas (pinpoint to 0.3 cm) on the fundic mucosal surface of the stomach in a 10 mg/kg/day dosage group female rat (19020).

4.1.4. Histopathology (APPENDIX J)

No treatment-related microscopic changes were observed in any of the female rats administered up to 10 mg/kg/day of the test substance.

There were no treatment-related microscopic changes observed in the liver of the F1 generation pups from the dams given up to 10 mg/kg/day of the test article. There were a few microscopic changes observed in the various organs and tissues which were considered to have occurred spontaneously and not to be treatment-related.

4.2. Terminal Body Weights, Organ Weights and Ratios (%) of Organ Weight to Terminal Body Weight and Brain Weight and Primordial Follicle Counts (Summaries - Tables C3 through C5; Individual Data - Tables C30 through C32)

Terminal body weights of the female rats were comparable among dosage groups and did not differ significantly.

The absolute and relative weights (to terminal body and to brain weight) of the female reproductive organs (left and right ovaries and uterus with cervix), brain, liver, left and right kidneys and adrenals, spleen, thymus and heart were comparable across dosage groups and did not differ significantly (except on one occasion). The ratio of the left kidney to the brain weight of the female rats in the 3 mg/kg/day dosage group was significantly increased ($p \leq 0.05$) over the corresponding control group value. This significant finding was not considered treatment-related because: 1) the incidence was not dosage-dependent; and/or 2) the observation was a single occurrence.

Average primordial follicle counts for the 10 mg/kg/day dosage group were comparable to the control group and did not differ significantly.

4.3. Hematology and Clinical Chemistry (Summaries - Tables C6 and C7; Individual Data - APPENDIX K)

Dosages as high as 10 mg/kg/day did not affect any hematology or clinical chemistry values evaluated. Average values for red blood cells (RBC), white blood cells (WBC), hemoglobin concentration (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelets (PLAT), mean platelet volume (MPV), prothrombin time (PT), activated partial thromboplastin time (APTT), nucleated red blood cell count (NRBC), lymphocytes, segmented neutrophils, bands, monocytes, eosinophils, basophils, abnormal lymphocytes in female rats were comparable among the five dosage groups and did not differ significantly (except on one occasion). The concentration of WBCs (lymphocytes) for of the female rats in the 0.3 mg/kg/day dosage group was significantly increased ($p \leq 0.05$) over the corresponding control group value. This significant finding was not considered treatment-related because: 1) the incidence was not dosage-dependent; and/or 2) the observation was a single occurrence.

Average values for total protein (TP), albumin (A), glucose (GLU), cholesterol (CHOL), total bilirubin (TBILI), blood urea nitrogen (BUN), creatinine (CREAT), creatinine kinase (CK), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALK), calcium (CA), phosphorus (PHOS), triglycerides (TRIG), sodium (NA), potassium (K), chloride (CL), globulin (G) and albumin/globulin ratio (A/G) in female rats were comparable among the five dosage groups and did not differ significantly (except on two occasions). The concentration of G was significantly decreased ($p \leq 0.01$) and the concentration of A/G was significantly increased ($p \leq 0.01$) for of the female rats in the 0.3 mg/kg/day dosage group over the corresponding control group values. These significant findings were not considered treatment-related because:

1) the incidences were not dosage-dependent; and/or 2) the observations were a single occurrence for both parameters.

4.4. Body Weights and Body Weight Changes (Figure 2; Summaries - Tables C8 through C13; Individual Data - Tables C33 through C35)

4.4.1. Precohabitation

Body weights and body weight gains were comparable and did not differ significantly during the precohabitation period at dosages of the test substance up to 10 mg/kg/day.

4.4.2. Gestation

Body weights and body weight gains were comparable and did not differ significantly during the gestation period at dosages of the test substance up to 10 mg/kg/day.

4.4.3. Lactation

Body weight gains were not significantly affected by dosages of the test substance up to 10 mg/kg/day during lactation.

Body weights were significantly reduced ($p \leq 0.05$ or $p \leq 0.01$) on days of lactation (DLs) 4, 6 through 8, 11 and 13 in the 0.3 mg/kg/day dosage group, DLs 7 and 8 in the 3 mg/kg/day dosage group, DLs 4, 6 through 9, 11, 13 and 14 in the 10 mg/kg/day dosage group. These significant findings were not considered treatment-related because they were not dosage-dependent or they did not persist.

4.5. Absolute (g/day) and Relative (g/kg/day) Feed Consumption Values (Summaries - Tables C14 through C19; Individual Data - Tables C36 through C38)

4.5.1. Precohabitation

Absolute (g/day) and relative (g/kg/day) feed consumption values were not significantly affected by dosages of the test substance up to 10 mg/kg/day during the precohabitation period.

4.5.2. Gestation

Absolute (g/day) and relative (g/kg/day) feed consumption values were not significantly affected by dosages of the test substance up to 10 mg/kg/day during the gestation period.

4.5.3. Lactation

Absolute and relative feed consumption values were not affected by dosages of the test substance up to 10 mg/kg/day during lactation.

Absolute feed consumption values were significantly reduced ($p \leq 0.05$ or $p \leq 0.01$) on DLs 1 to 5 and 8 to 15 in the 0.3 mg/kg/day dosage group, DLs 1 to 5 and 8 to 15 in the 3 mg/kg/day dosage group and DLs 8 to 15 in the 10 mg/kg/day dosage group. Relative feed consumption values were significantly reduced ($p \leq 0.01$) on DLs 1 to 5 in the 0.3 mg/kg/day and DLs 5 to 8 in the 3 mg/kg/day dosage group. These significant findings were not considered treatment-related because they were not dosage-dependent and they did not persist.

4.6. Estrous Cycling, Mating and Fertility (Summary - Table C20; Individual Data - Table C39)

The average numbers of estrous stages per 13 days were comparable among the five dosage groups and did not significantly differ. The number of rats with six or more consecutive days of diestrus or estrus did not differ significantly.

All mating and fertility parameters (numbers of days in cohabitation, rats that mated, fertility index, rats with confirmed mating dates during the first and second week of cohabitation and the number of pregnant rats per number of rats in cohabitation) were unaffected by dosages of the test substance as high as 10 mg/kg/day.

4.7. Functional Observational Battery (Summary - Table C21; Individual Data - Table C40)

There were no statistically significant or biologically important differences among the five dosage groups in the measures of the functional observational battery (FOB). There were no alterations in home cage behavior, autonomic functions (lacrimation, salivation, palpebral closure, prominence of the eye, pupillary reaction to light, piloerection, respiration, defecation and urination), sensorimotor functions [responses to visual, auditory, tactile and painful stimuli (reactivity and sensitivity)], excitability (reactions to handling and behavior in the open field), gait and sensorimotor coordination (gait pattern in the open field, severity of gait abnormalities, air righting reaction and landing foot splay) and forelimb and hindlimb grip strength and abnormal clinical observations including but not limited to: convulsions, tremors, unusual behavior, hypotonia or hypertonia, emaciation, dehydration, unkempt appearance and deposits around the eyes, nose or mouth.

Body weights recorded during the functional operational battery for the treated groups were not significantly different than the control group for the female rats.

4.8. Motor Activity (Figures 5 and 6; Summary - Table C22; Individual Data - Table C41)

There were no statistically significant or biologically important differences among the five dosage groups in the measures of number of movements or time (in seconds) spent in movement motor activity on DL 17.

4.9. Natural Delivery and Litter Observations (Summary - Tables C23 and C24; Individual Data - Tables C42 through C45)

Pregnancy occurred in all 15 (100%) rats assigned to the 0 (Vehicle), 0.3 and 10 mg/kg/day dosage groups and 13 (88.7%) of the rats assigned to the 1 and 3 mg/kg/day dosage groups. All pregnant dams delivered a litter of one or more liveborn pups. Values for the numbers of dams that delivered litters, the duration of gestation (calculated in days), averages for implantation sites per delivered litter, the numbers of dams with stillborn pups, the numbers of dams with no liveborn pups, dams with all pups dying days 1 to 4 and 5 to 22, were comparable among the five dosage groups and did not significantly differ. The number of liveborn pups, the number of pups found dead or presumed cannibalized on day 1, and days 2 to 8, 9 to 15 and 16 to 22 postpartum were comparable among the five dosage groups and did not significantly differ.

The gestation index (number of dams with one or more liveborn pups per number of pregnant rats), viability index (number of live pups on DL 8 per number of liveborn pups on DL 1) and lactation index (number of live pups on DL 22 per number of liveborn pups on DL 8) were compared to the control group value and did not differ significantly.

The number of pups surviving per litter, pup sex ratios, litter size and pup body weights per litter on DLs 1, 8, 15 and 22 were comparable among the five dosage groups and did not significantly differ.

4.10. Pup Clinical and Necropsy Observations (Summary - Tables C25 and C26; Individual Data - Tables C46 and C47)

No clinical or necropsy observations in the F1 generation pups were attributable to dosages of the test substance as high as 10 mg/kg/day because: 1) the incidences were not dosage-dependent; and 2) the observation occurred in only one to two litters. These clinical observations included: not nursing, emaciation, dehydration, whole body discolored purple, scab, cold to touch, left eye discolored purple, right eye enlarged, laceration on right hindlimb, bruise on back, not nesting, pale in appearance and corneal opacity of right eye. Necropsy observations of 228, 203, 196, 172 and 211 pups in the five respective dosage groups on postpartum days 5 and 22 were limited to moderate dilation of the renal pelvis of one pup from a 0.3 mg/kg/day dosage group litter.

4.11. Pup Liver Weight and Ratio of Liver Weight to Terminal Body Weight (Summary - Table C27; Individual Data - Table C48)

F1 generation male and female pup terminal body weights, absolute liver weight (by sex) and ratio of liver weight to terminal body weight (by sex) were comparable across all five dosage groups and did not differ significantly.

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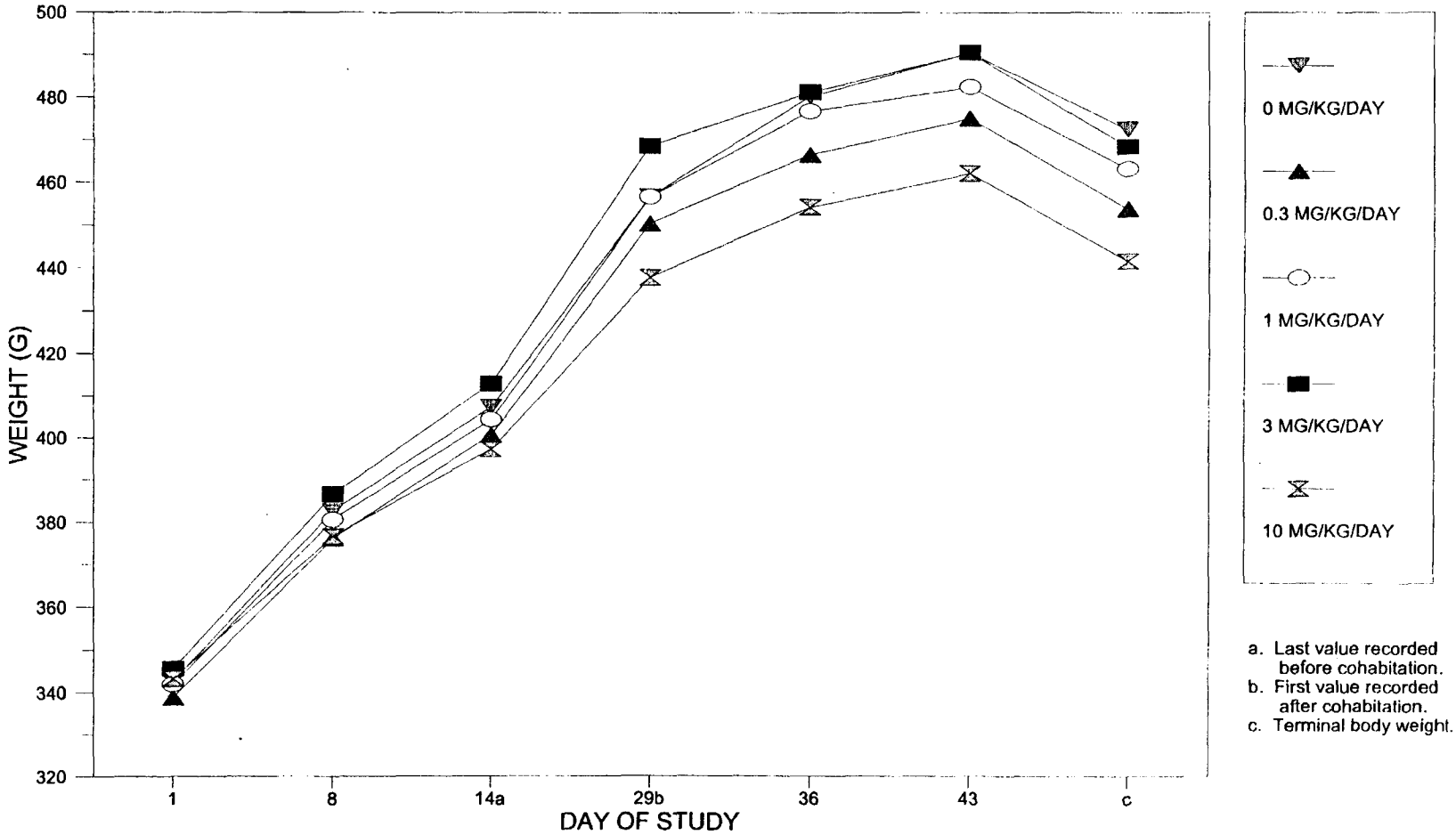
APPENDIX A

REPORT FIGURES

BODY WEIGHTS

Fo GENERATION MALE RATS

Figure 1



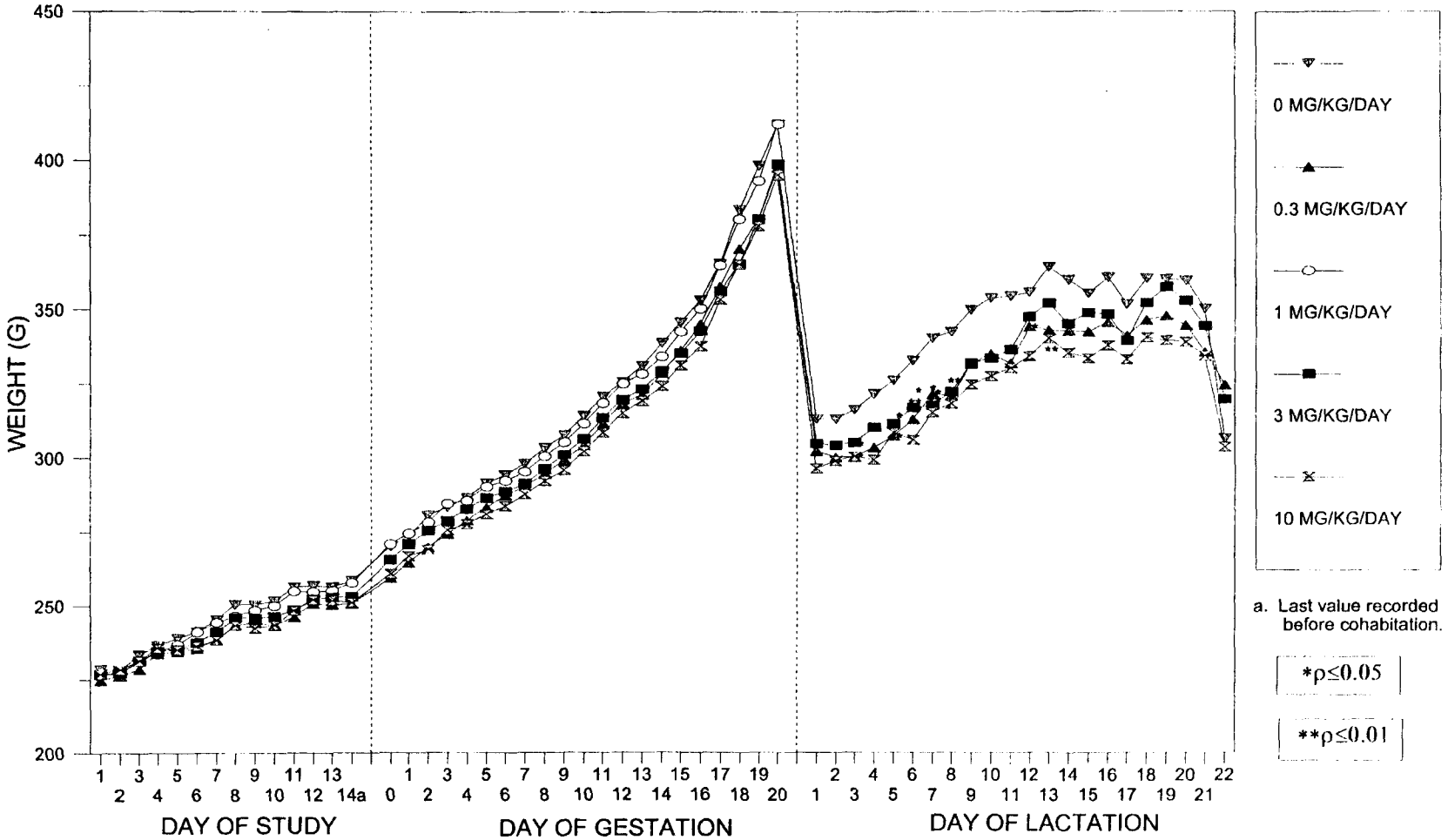
a. Last value recorded before cohabitation.
b. First value recorded after cohabitation.
c. Terminal body weight.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

BODY WEIGHTS

Fo GENERATION FEMALE RATS

Figure 2



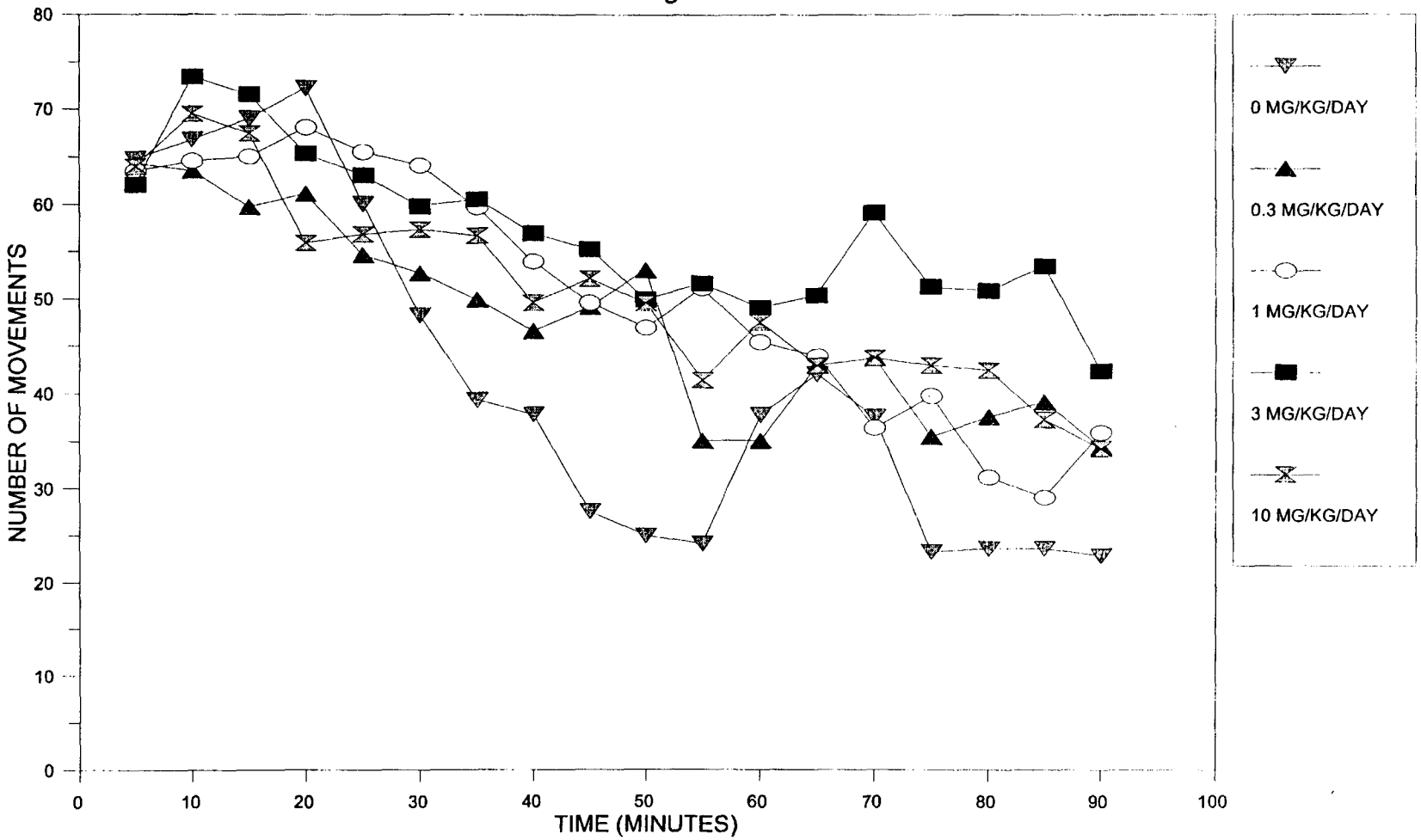
a. Last value recorded before cohabitation.

*ρ≤0.05

**ρ≤0.01

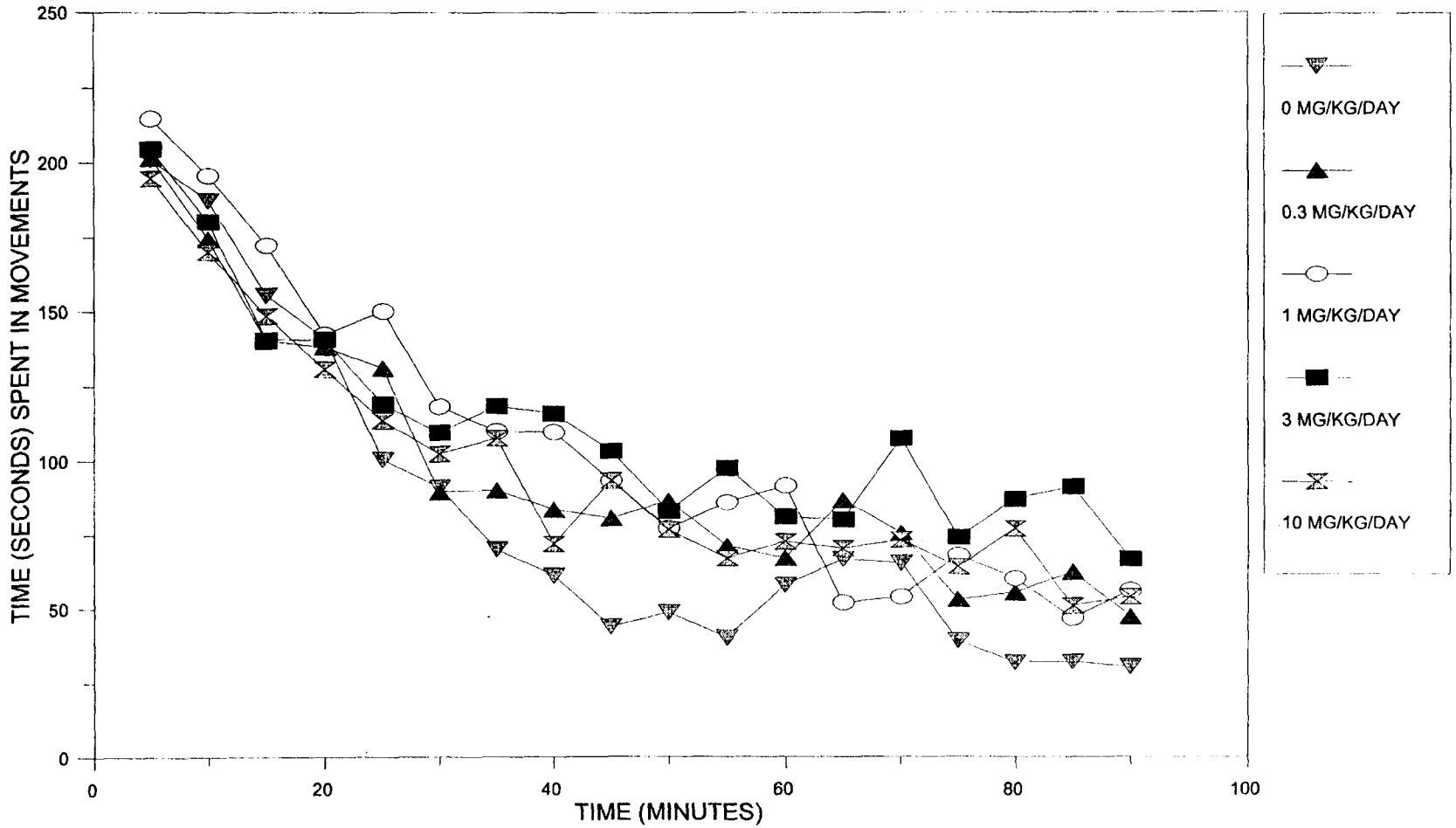
MOTOR ACTIVITY - NUMBER OF MOVEMENTS - Fo GENERATION MALE RATS

Figure 3



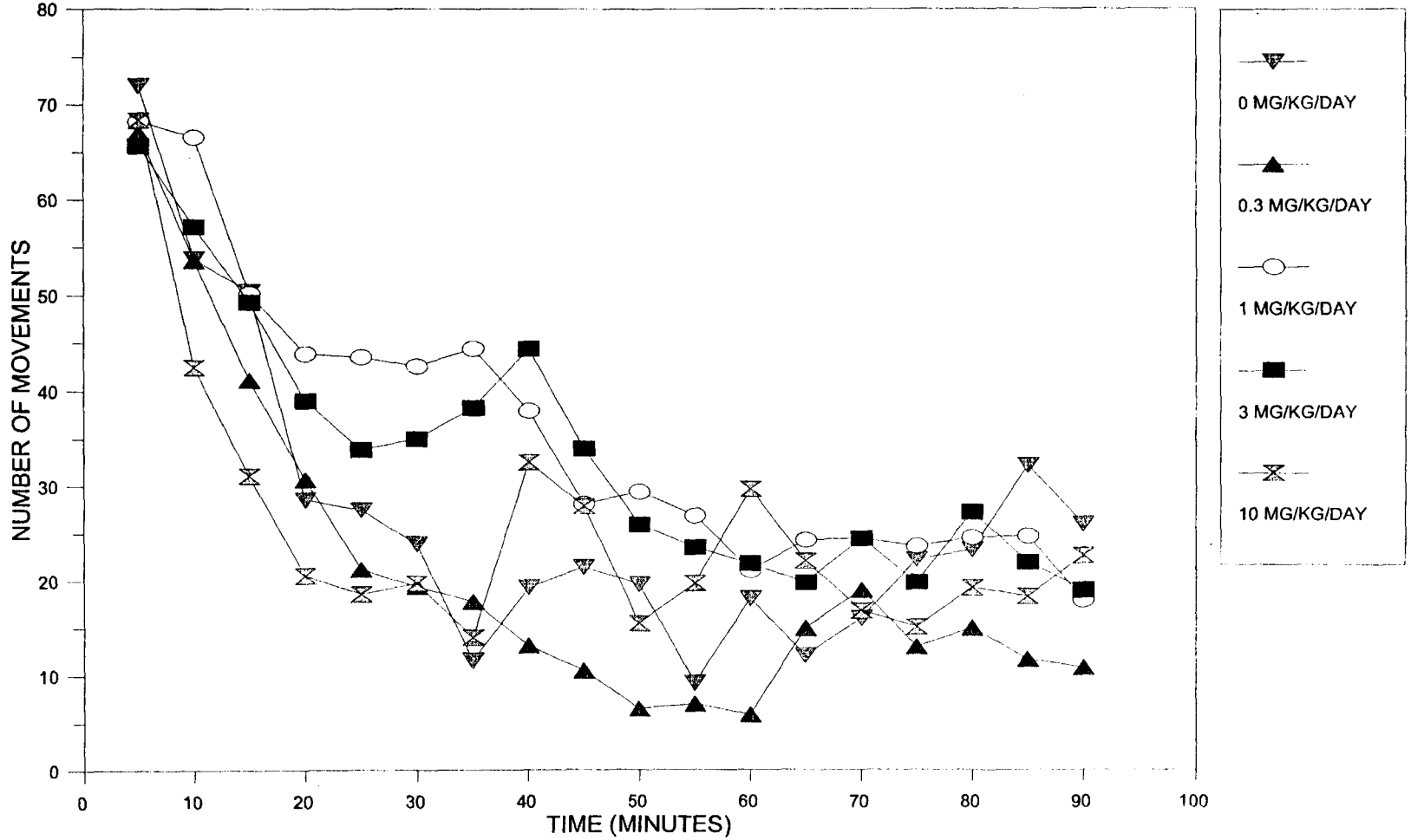
MOTOR ACTIVITY - TIME SPENT IN MOVEMENT - Fo GENERATION MALE RATS

Figure 4



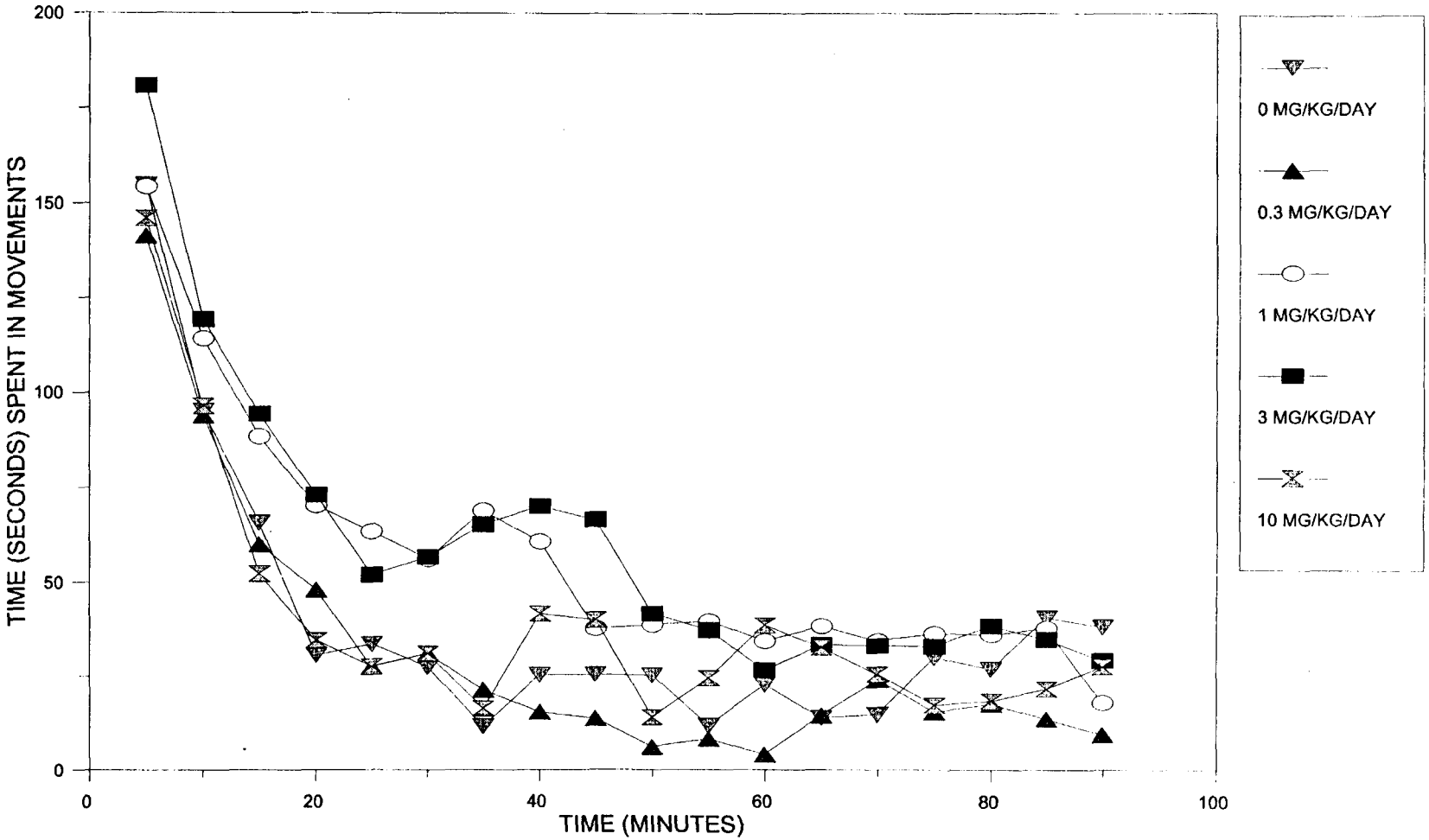
MOTOR ACTIVITY - NUMBER OF MOVEMENTS - Fo GENERATION FEMALE RATS

Figure 5



MOTOR ACTIVITY - TIME SPENT IN MOVEMENT - Fo GENERATION FEMALE RATS

Figure 6



APPENDIX B

REPORT TABLES - Fo GENERATION MALE RATS

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B1 (PAGE 1): CLINICAL OBSERVATIONS - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP	I	II	III	IV	V
DOSAGE (MG/KG/DAY)	0	0.3	1	3	10
MAXIMUM POSSIBLE INCIDENCE	680/ 15	680/ 15	680/ 15	680/ 15	680/ 15
MORTALITY	0	0	0	0	0
CHROMORHINORRHEA	0/ 0	1/ 1	1/ 1	1/ 1	2/ 2
INCISORS: TOTAL	2/ 1	0/ 0	0/ 0	13/ 1	13/ 1
MISSING/BROKEN	2/ 1	0/ 0	0/ 0	6/ 1	13/ 1
MISALIGNED	0/ 0	0/ 0	0/ 0	13/ 1	0/ 0
CHROMODACRYORRHEA	0/ 0	0/ 0	3/ 1	9/ 1	2/ 1
LACRIMATION	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
LOCALIZED ALOPECIA: TOTAL	0/ 0	27/ 2	3/ 2	14/ 1	0/ 0
HEAD	0/ 0	16/ 1	0/ 0	14/ 1	0/ 0
UNDERSIDE	0/ 0	0/ 0	2/ 1	0/ 0	0/ 0
LIMBS	0/ 0	11/ 1	1/ 1	0/ 0	0/ 0
DRY, BROWN PERIORAL SUBSTANCE	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0
SOFT OR LIQUID FECES	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0
HEAD: SCAB	8/ 1	0/ 0	0/ 0	0/ 0	0/ 0
DEHYDRATION	7/ 1	0/ 0	0/ 0	0/ 0	0/ 0

STATISTICAL ANALYSES OF CLINICAL OBSERVATION DATA WERE RESTRICTED TO THE NUMBER OF RATS WITH OBSERVATIONS.
MAXIMUM POSSIBLE INCIDENCE = (DAYS x RATS)/NUMBER OF RATS EXAMINED PER GROUP.
N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF RATS WITH OBSERVATION.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B2 (PAGE 1): NECROPSY OBSERVATIONS - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS EXAMINED a	N	15	15	15	15	15
MORTALITY	N	0	0	0	0	0
APPEARED NORMAL	N	14	12	15	14	14
KIDNEYS:						
BILATERAL, MOTTLED, MOTTLED TAN AND RED OR MOTTLED DARK RED	N	1	2	0	0	0
LEFT, PELVIS, SLIGHT DILATION	N	0	1	0	0	0
EPIDIDYMIDES:						
BILATERAL, SMALL	N	0	0	0	1	0
LEFT CAUDA, SMALL	N	0	0	0	1	0
TESTES:						
BILATERAL, SMALL	N	0	0	0	1	0
JEJUNUM:						
DIVERTICULUM	N	0	0	0	0	1

a. Refer to the individual clinical observations table (Table B17) for external observations confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B3 (PAGE 1): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0	II 0.3	III 1	IV 3	V 10
RATS TESTED	N	10	10	10	10	10
TERMINAL BODY WEIGHT	MEAN±S.D.	469.7 ± 31.6	448.8 ± 37.8	455.8 ± 55.2	472.3 ± 38.3	440.8 ± 12.6
EPIDIDYMIS LEFT	MEAN±S.D.	0.6476 ±0.0367	0.6358 ±0.0397	0.6277 ±0.0505	0.5916 ±0.1092	0.6134 ±0.0472
CAUDA EPIDIDYMIS LEFT	MEAN±S.D.	0.3308 ±0.0294	0.3182 ±0.0266	0.3232 ±0.0285	0.2913 ±0.0650	0.3041 ±0.0309
TESTIS LEFT	MEAN±S.D.	1.6591 ±0.0879	1.7154 ±0.1239	1.6717 ±0.1646	1.6116 ±0.3330	1.7483 ±0.1549
SEMINAL VESICLES WITH FLUID	MEAN±S.D.	1.7055 ±0.2370	1.5439 ±0.2672	1.6385 ±0.2912	1.5473 ±0.3182	1.4424 ±0.2669
SEMINAL VESICLES WITHOUT FLUID	MEAN±S.D.	0.8440 ±0.1038	0.8118 ±0.1117	0.7965 ±0.1068	0.7670 ±0.1477	0.7772 ±0.1163
EPIDIDYMIS RIGHT	MEAN±S.D.	0.6745 ±0.0424	0.6546 ±0.0409	0.6534 ±0.0555	0.6106 ±0.1218	0.6261 ±0.0409
TESTIS RIGHT	MEAN±S.D.	1.6777 ±0.0936	1.7281 ±0.1287	1.6922 ±0.1642	1.6175 ±0.3393	1.7604 ±0.1447
PROSTATE	MEAN±S.D.	1.2902 ±0.2968	1.2000 ±0.1297	1.2267 ±0.2694	1.2734 ±0.1659	1.1918 ±0.2344
BRAIN	MEAN±S.D.	2.40 ± 0.11	2.44 ± 0.11	2.38 ± 0.09	2.38 ± 0.09	2.40 ± 0.10

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B3 (PAGE 2): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0	II 0.3	III 1	IV 3	V 10
RATS TESTED	N	10	10	10	10	10
TERMINAL BODY WEIGHT	MEAN±S.D.	469.7 ± 31.6	448.8 ± 37.8	455.8 ± 55.2	472.3 ± 38.3	440.8 ± 12.6
LIVER	MEAN±S.D.	14.63 ± 1.81	14.22 ± 1.58	15.94 ± 3.56	17.60 ± 1.64*	22.83 ± 2.73**
KIDNEY LEFT	MEAN±S.D.	1.98 ± 0.25	1.86 ± 0.12	1.96 ± 0.26	2.04 ± 0.17	2.01 ± 0.18
KIDNEY RIGHT	MEAN±S.D.	2.02 ± 0.26	1.90 ± 0.15	2.00 ± 0.24	2.13 ± 0.18	2.04 ± 0.14
ADRENAL LEFT	MEAN±S.D.	0.035 ± 0.007	0.035 ± 0.007	0.034 ± 0.005	0.032 ± 0.006	0.032 ± 0.004
ADRENAL RIGHT	MEAN±S.D.	0.034 ± 0.006	0.034 ± 0.006	0.030 ± 0.007	0.032 ± 0.007	0.029 ± 0.007
SPLEEN	MEAN±S.D.	0.79 ± 0.14	0.81 ± 0.07	0.76 ± 0.12	0.88 ± 0.19	0.78 ± 0.10
THYMUS	MEAN±S.D.	0.41 ± 0.12	0.45 ± 0.09	0.36 ± 0.10	0.42 ± 0.09	0.42 ± 0.05
HEART	MEAN±S.D.	1.55 ± 0.10	1.52 ± 0.12	1.54 ± 0.13	1.60 ± 0.13	1.44 ± 0.07

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
* Significantly different from the Group I value ($p \leq 0.05$).
** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B4 (PAGE 1): RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	10	10	10	10	10
TERMINAL BODY WEIGHT	MEAN±S.D.	469.7 ± 31.6	448.8 ± 37.8	455.8 ± 55.2	472.3 ± 38.3	440.8 ± 12.6
EPIDIDYMIS LEFT	MEAN±S.D.	0.138 ± 0.014	0.142 ± 0.015	0.138 ± 0.018	0.126 ± 0.027	0.138 ± 0.011
CAUDA EPIDIDYMIS LEFT	MEAN±S.D.	0.068 ± 0.009	0.071 ± 0.012	0.071 ± 0.007	0.063 ± 0.015	0.068 ± 0.008
TESTIS LEFT	MEAN±S.D.	0.354 ± 0.024	0.385 ± 0.047	0.370 ± 0.041	0.342 ± 0.078	0.397 ± 0.041
SEMINAL VESICLES WITH FLUID	MEAN±S.D.	0.366 ± 0.064	0.348 ± 0.073	0.359 ± 0.063	0.329 ± 0.081	0.326 ± 0.062
SEMINAL VESICLES WITHOUT FLUID	MEAN±S.D.	0.181 ± 0.031	0.183 ± 0.038	0.176 ± 0.022	0.163 ± 0.038	0.176 ± 0.026
EPIDIDYMIS RIGHT	MEAN±S.D.	0.143 ± 0.016	0.147 ± 0.018	0.145 ± 0.016	0.127 ± 0.028	0.141 ± 0.012
TESTIS RIGHT	MEAN±S.D.	0.357 ± 0.030	0.386 ± 0.049	0.374 ± 0.042	0.344 ± 0.078	0.400 ± 0.035
PROSTATE	MEAN±S.D.	0.276 ± 0.073	0.267 ± 0.022	0.271 ± 0.061	0.274 ± 0.052	0.270 ± 0.054
BRAIN	MEAN±S.D.	0.510 ± 0.030	0.546 ± 0.053	0.528 ± 0.050	0.506 ± 0.041	0.545 ± 0.027

ALL WEIGHTS WERE RECORDED IN GRAMS (G). RATIOS (%) = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B4 (PAGE 2): RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	10	10	10	10	10
TERMINAL BODY WEIGHT	MEAN±S.D.	469.7 ± 31.6	448.8 ± 37.8	455.8 ± 55.2	472.3 ± 38.3	440.8 ± 12.6
LIVER	MEAN±S.D.	3.109 ± 0.264	3.165 ± 0.208	3.466 ± 0.396	3.728 ± 0.212**	5.190 ± 0.702**
KIDNEY LEFT	MEAN±S.D.	0.419 ± 0.032	0.415 ± 0.033	0.429 ± 0.030	0.433 ± 0.025	0.456 ± 0.042
KIDNEY RIGHT	MEAN±S.D.	0.428 ± 0.036	0.426 ± 0.044	0.441 ± 0.030	0.450 ± 0.032	0.463 ± 0.034
ADRENAL LEFT a	MEAN±S.D.	7.419 ± 1.226	7.837 ± 1.573	7.427 ± 1.196	6.929 ± 1.461	7.280 ± 0.836
ADRENAL RIGHT a	MEAN±S.D.	7.202 ± 1.181	7.587 ± 1.353	6.603 ± 1.636	6.788 ± 1.503	6.680 ± 1.514
SPLEEN	MEAN±S.D.	0.168 ± 0.025	0.180 ± 0.024	0.167 ± 0.019	0.183 ± 0.030	0.177 ± 0.023
THYMUS	MEAN±S.D.	0.086 ± 0.024	0.099 ± 0.017	0.077 ± 0.019	0.089 ± 0.019	0.095 ± 0.013
HEART	MEAN±S.D.	0.331 ± 0.021	0.339 ± 0.014	0.340 ± 0.024	0.337 ± 0.015	0.327 ± 0.012

ALL WEIGHTS WERE RECORDED IN GRAMS (G). RATIOS (%) = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.

a. Value was multiplied by 1000.

** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B5 (PAGE 1): RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0	II 0.3	III 1	IV 3	V 10
RATS TESTED	N	10	10	10	10	10
BRAIN WEIGHT	MEAN±S.D.	2.40 ± 0.11	2.44 ± 0.11	2.38 ± 0.09	2.38 ± 0.09	2.40 ± 0.10
EPIDIDYMIS LEFT	MEAN±S.D.	27.10 ± 2.14	26.11 ± 1.77	26.39 ± 1.99	24.77 ± 4.51	25.55 ± 2.21
CAUDA EPIDIDYMIS LEFT	MEAN±S.D.	13.83 ± 1.28	13.05 ± 0.96	13.59 ± 1.18	12.20 ± 2.80	12.66 ± 1.32
TESTIS LEFT	MEAN±S.D.	69.36 ± 4.17	70.39 ± 4.40	70.28 ± 6.50	67.41 ± 13.64	72.79 ± 6.71
SEMINAL VESICLES WITH FLUID	MEAN±S.D.	71.40 ± 11.06	63.64 ± 12.45	68.84 ± 12.04	64.77 ± 12.58	59.83 ± 10.03
SEMINAL VESICLES WITHOUT FLUID	MEAN±S.D.	35.34 ± 4.98	33.48 ± 5.71	33.44 ± 4.03	32.14 ± 5.94	32.30 ± 4.57
EPIDIDYMIS RIGHT	MEAN±S.D.	28.22 ± 2.23	26.90 ± 2.06	27.47 ± 2.16	25.57 ± 5.13	26.08 ± 2.00
TESTIS RIGHT	MEAN±S.D.	70.19 ± 5.17	70.94 ± 5.02	71.14 ± 6.42	67.66 ± 13.99	73.30 ± 6.34
PROSTATE	MEAN±S.D.	54.35 ± 14.08	49.41 ± 6.63	51.57 ± 11.28	53.52 ± 7.70	49.48 ± 9.23

ALL WEIGHTS WERE RECORDED IN GRAMS (G). RATIOS (%) = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B5 (PAGE 2): RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	10	10	10	10	10
BRAIN WEIGHT	MEAN±S.D.	2.40 ± 0.11	2.44 ± 0.11	2.38 ± 0.09	2.38 ± 0.09	2.40 ± 0.10
LIVER	MEAN±S.D.	611.89 ± 79.55	584.43 ± 68.39	667.08 ±129.02	739.11 ± 73.28**	948.61 ± 95.12**
KIDNEY LEFT	MEAN±S.D.	82.68 ± 9.11	76.46 ± 5.95	82.16 ± 9.05	85.78 ± 7.04	83.64 ± 8.05
KIDNEY RIGHT	MEAN±S.D.	84.22 ± 9.20	77.94 ± 6.26	84.13 ± 7.94	89.26 ± 6.52	85.00 ± 6.56
ADRENAL LEFT	MEAN±S.D.	1.46 ± 0.27	1.44 ± 0.31	1.42 ± 0.24	1.36 ± 0.25	1.34 ± 0.18
ADRENAL RIGHT	MEAN±S.D.	1.41 ± 0.25	1.40 ± 0.26	1.26 ± 0.33	1.34 ± 0.26	1.23 ± 0.29
SPLEEN	MEAN±S.D.	32.90 ± 5.93	33.34 ± 3.91	31.83 ± 4.39	36.64 ± 7.27	32.44 ± 3.96
THYMUS	MEAN±S.D.	17.22 ± 5.29	18.37 ± 4.02	14.93 ± 4.04	17.75 ± 3.63	17.46 ± 2.39
HEART	MEAN±S.D.	64.91 ± 3.78	62.49 ± 5.04	64.67 ± 4.56	66.89 ± 4.77	59.97 ± 3.51*

ALL WEIGHTS WERE RECORDED IN GRAMS (G). RATIOS (%) = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.

* Significantly different from the Group I value ($p \leq 0.05$).

** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B6 (PAGE 1): HEMATOLOGY - SUMMARY - Fo GENERATION MALE RATS
(See abbreviations on the last page of this table.)

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	10	10	10	10	10
WBC (THSN/CU MM)	MEAN ± S.D.	15.3 ± 1.63	14.9 ± 3.03	13.8 ± 2.84	16.2 ± 3.97	14.7 ± 3.07
RBC (MILL/CU MM)	MEAN ± S.D.	7.51 ± 0.648	7.33 ± 0.396	7.32 ± 0.441	6.93 ± 0.305*	6.99 ± 0.442*
HGB (GRAMS/DL)	MEAN ± S.D.	16.5 ± 1.16	15.9 ± 0.42	15.7 ± 0.59*	15.4 ± 0.67**	15.6 ± 0.81*
HCT (%)	MEAN ± S.D.	43.5 ± 3.48	42.2 ± 1.57	42.0 ± 2.22	40.2 ± 2.29**	40.7 ± 1.81*
MCV (CU MICRONS)	MEAN ± S.D.	57.9 ± 1.89	57.7 ± 2.27	57.4 ± 1.78	57.9 ± 1.15	58.3 ± 1.37
MCH (PICO GRAMS)	MEAN ± S.D.	22.0 ± 0.87	21.8 ± 1.13	21.5 ± 0.75	22.2 ± 0.45	22.3 ± 0.56
MCHC (%)	MEAN ± S.D.	38.0 ± 0.93	37.7 ± 1.15	37.5 ± 0.79	38.4 ± 0.80	38.3 ± 0.70
PLAT (THSN/CU MM)	MEAN ± S.D.	1179 ± 130.9	1131 ± 183.7	1115 ± 149.2	1104 ± 91.4	1148 ± 159.9
MPV (CU MICRONS)	MEAN ± S.D.	8.1 ± 0.52	7.9 ± 0.54	8.2 ± 0.72	8.2 ± 0.76	8.0 ± 0.59

* Significantly different from the Group I value ($p \leq 0.05$).
** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B6 (PAGE 2): HEMATOLOGY - SUMMARY - Fo GENERATION MALE RATS
(See abbreviations on the last page of this table.)

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	10	10	10	10	10
PT (SECONDS)	MEAN ± S.D.	13.4 ± 0.24	14.2 ± 0.27**	13.6 ± 0.23	13.8 ± 0.40*	14.0 ± 0.47**
APTT (SECONDS)	MEAN ± S.D.	21.0 ± 3.09	22.1 ± 4.41	20.6 ± 2.38	21.2 ± 2.24	21.3 ± 1.43
NRBC COUNT	MEAN ± S.D.	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0
Lymphocytes (THSN/CU MM)	MEAN ± S.D.	11.9 ± 1.72	11.0 ± 2.68	10.8 ± 2.02	12.1 ± 3.57	12.4 ± 2.75
Segmented (THSN/CU MM)	MEAN ± S.D.	2.2 ± 0.73	2.9 ± 1.18	2.0 ± 1.06	2.8 ± 0.73	1.6 ± 0.78
Bands (THSN/CU MM)	MEAN ± S.D.	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.03	0.0 ± 0.03	0.0 ± 0.00
Monocytes (THSN/CU MM)	MEAN ± S.D.	0.8 ± 0.56	0.7 ± 0.50	0.6 ± 0.51	0.8 ± 0.67	0.5 ± 0.33
Eosinophils (THSN/CU MM)	MEAN ± S.D.	0.3 ± 0.20	0.3 ± 0.21	0.3 ± 0.21	0.3 ± 0.26	0.2 ± 0.15
Basophils (THSN/CU MM)	MEAN ± S.D.	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00
Abnormal L (THSN/CU MM)	MEAN ± S.D.	0.1 ± 0.20	0.1 ± 0.14	0.1 ± 0.07	0.2 ± 0.22	0.1 ± 0.21
Other (THSN/CU MM)	MEAN ± S.D.	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00

* Significantly different from the Group I value ($p \leq 0.05$).
** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B6 (PAGE 3): HEMATOLOGY - SUMMARY - Fo GENERATION MALE RATS

KEY TO HEMATOLOGY TABLE

ABBREVIATION	TERMINOLOGY
WBC	White Blood Cells (Leukocytes)
RBC	Red Blood Cells (Erythrocytes)
HGB	Hemoglobin
HCT	Hematocrit (Packed Cell Volume)
MCV	Mean Corpuscular Volume
MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hemoglobin Concentration
PLAT	Platelet Count
MPV	Mean Platelet Volume
PT	Prothrombin Time
APTT	Activated Partial Thromboplastin
NRBC	Nucleated Red Blood Cell Count
Segmented	Segmented Neutrophils
Abnormal L	Abnormal Lymphocytes
Other	Other Cells

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B7 (PAGE 1): CLINICAL CHEMISTRY - SUMMARY - Fo GENERATION MALE RATS
(See abbreviations on the last page of this table.)

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	10	10	10	10	10
TP (G/DL)	MEAN ± S.D.	6.3 ± 0.36	6.1 ± 0.28	6.3 ± 0.33	6.2 ± 0.28	6.3 ± 0.28
A (G/DL)	MEAN ± S.D.	4.3 ± 0.22	4.1 ± 0.19	4.3 ± 0.15	4.2 ± 0.17	4.5 ± 0.20**
GLU (MG/DL)	MEAN ± S.D.	145 ± 16.8	141 ± 26.0	182 ± 58.2	162 ± 25.2	165 ± 33.7
CHOL (MG/DL)	MEAN ± S.D.	57 ± 8.3	41 ± 11.1**	46 ± 11.6*	43 ± 13.1**	33 ± 7.2**
TBILI (MG/DL)	MEAN ± S.D.	0.2 ± 0.07	0.1 ± 0.05	0.1 ± 0.06	0.1 ± 0.05	0.2 ± 0.06
BUN (MG/DL)	MEAN ± S.D.	16 ± 1.5	16 ± 0.8	16 ± 1.8	17 ± 1.6	21 ± 2.4**
CREAT (MG/DL)	MEAN ± S.D.	0.3 ± 0.04	0.3 ± 0.05	0.3 ± 0.06	0.3 ± 0.03	0.3 ± 0.05
CK (U/L)	MEAN ± S.D.	288 ± 172.6	246 ± 111.5	239 ± 112.9	196 ± 53.5	243 ± 117.4
ALT (U/L)	MEAN ± S.D.	42 ± 6.0	63 ± 69.9	60 ± 34.4	95 ± 124.1	45 ± 7.0

* Significantly different from the Group I value ($p \leq 0.05$).
** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B7 (PAGE 2): CLINICAL CHEMISTRY - SUMMARY - Fo GENERATION MALE RATS
(See abbreviations on the last page of this table.)

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	10	10	10	10	10
AST (U/L)	MEAN ± S.D.	96 ± 22.4	121 ± 92.6	117 ± 40.9	198 ± 248.7	97 ± 15.6
ALK (U/L)	MEAN ± S.D.	105 ± 14.3	111 ± 36.9	100 ± 12.4	115 ± 25.1	144 ± 37.5**
CA (MG/DL)	MEAN ± S.D.	10.9 ± 0.48	10.7 ± 0.44	11.1 ± 0.44	11.1 ± 0.34	11.5 ± 0.38**
PHOS (MG/DL)	MEAN ± S.D.	9.5 ± 1.40	9.4 ± 1.11	9.9 ± 2.09	9.7 ± 1.43	10.2 ± 1.33
TRI (MG/DL)	MEAN ± S.D.	52 ± 21.8	47 ± 17.2	36 ± 13.8	36 ± 27.9	17 ± 8.0**
NA (MMOL/L)	MEAN ± S.D.	146 ± 1.4	146 ± 1.3	147 ± 1.6	147 ± 1.0	146 ± 2.2
K (MMOL/L)	MEAN ± S.D.	6.6 ± 2.10	6.1 ± 0.89	6.5 ± 1.27	6.0 ± 0.60	6.9 ± 1.55
CL (MMOL/L)	MEAN ± S.D.	98 ± 2.7	99 ± 1.5	100 ± 2.3	100 ± 2.7	100 ± 1.2
G (G/DL)	MEAN ± S.D.	2.0 ± 0.19	2.0 ± 0.16	2.0 ± 0.24	2.0 ± 0.16	1.8 ± 0.13
A/G (NONE)	MEAN ± S.D.	2.1 ± 0.18	2.1 ± 0.16	2.2 ± 0.26	2.2 ± 0.15	2.5 ± 0.17**

** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B7 (PAGE 3): CLINICAL CHEMISTRY - SUMMARY - Fo GENERATION MALE RATS

KEY TO CLINICAL CHEMISTRY TABLE

ABBREVIATION	TERMINOLOGY
TP	Total Protein
A	Albumin
GLU	Glucose
CHOL	Cholesterol
TBILI	Total Bilirubin
BUN	Blood Urea Nitrogen
CREAT	Creatinine
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
ALK	Alkaline Phosphatase
CA	Calcium
PHOS	Phosphorus
TRI	Triglycerides
NA	Sodium
K	Potassium
CL	Chloride
G	Globulin
A/G	Albumin/Globulin Ratio

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B8 (PAGE 1): BODY WEIGHTS - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0	II 0.3	III 1	IV 3	V 10
RATS TESTED	N	15	15	15	15	15
BODY WEIGHT (G)						
DAY 1	MEAN±S.D.	342.7 ± 12.6	338.9 ± 13.1	341.9 ± 14.7	345.6 ± 11.2	343.3 ± 12.4
DAY 8	MEAN±S.D.	382.7 ± 22.2	376.1 ± 19.5	380.5 ± 21.6	386.6 ± 21.5	376.7 ± 11.7
DAY 14a	MEAN±S.D.	407.3 ± 25.4	400.7 ± 23.7	404.3 ± 29.8	412.9 ± 25.4	397.3 ± 12.3
DAY 29b	MEAN±S.D.	456.6 ± 38.9	450.3 ± 30.9	456.6 ± 44.6	468.5 ± 32.0	437.7 ± 15.4
DAY 36	MEAN±S.D.	480.2 ± 38.2	466.5 ± 32.6	476.8 ± 47.7	481.1 ± 33.1	454.1 ± 16.6
DAY 43	MEAN±S.D.	490.5 ± 37.2	475.1 ± 38.3	482.5 ± 53.1	490.5 ± 40.2	462.1 ± 22.0
TERMINAL BODY WEIGHT	MEAN±S.D.	472.5 ± 33.9	453.7 ± 34.3	463.1 ± 48.2	468.3 ± 37.1	441.5 ± 16.5

DAY = DAY OF STUDY
a. Last value recorded before cohabitation.
b. First value recorded after cohabitation.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B9 (PAGE 1): BODY WEIGHT CHANGES - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	15	15	15	15	15
BODY WEIGHT CHANGE (G)						
DAYS 1 - 8	MEAN±S.D.	+39.9 ± 12.3	+37.2 ± 11.0	+38.5 ± 10.0	+41.0 ± 12.1	+33.4 ± 5.6
DAYS 8 - 14a	MEAN±S.D.	+24.7 ± 6.8	+24.6 ± 5.0	+23.8 ± 11.1	+26.3 ± 8.2	+20.6 ± 4.8
DAYS 1 - 14a	MEAN±S.D.	+64.6 ± 16.5	+61.8 ± 14.6	+62.3 ± 18.3	+67.3 ± 16.3	+54.0 ± 7.0
DAYS 29b- 36	MEAN±S.D.	+23.6 ± 8.6	+16.2 ± 7.8*	+20.2 ± 5.6	+12.6 ± 5.4**	+16.5 ± 8.4*
DAYS 36 - 43	MEAN±S.D.	+10.3 ± 10.8	+8.7 ± 11.2	+5.7 ± 14.4	+9.4 ± 12.9	+7.9 ± 13.7
DAYS 29b-TERMINATION	MEAN±S.D.	+15.9 ± 11.7	+3.4 ± 7.9**	+6.5 ± 10.1*	-0.2 ± 7.7**	+3.8 ± 11.8**
DAYS 1 - TERMINATION	MEAN±S.D.	+129.8 ± 25.5	+114.8 ± 27.5	+121.2 ± 37.7	+122.7 ± 30.0	+98.2 ± 13.9**

DAY(S) = DAY(S) OF STUDY
a. Last value recorded before cohabitation.
b. First value recorded after cohabitation.
* Significantly different from the Group I value ($p \leq 0.05$).
** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B10 (PAGE 1): ABSOLUTE FEED CONSUMPTION VALUES (G/DAY) - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	15	15	15	15	15
FEED CONSUMPTION (G/DAY)						
DAYS 1 - 8a	MEAN±S.D.	28.4 ± 3.1	27.8 ± 2.0	29.1 ± 3.3	28.8 ± 2.6	26.9 ± 1.4
DAYS 29b- 36	MEAN±S.D.	30.2 ± 2.6 [14]c	28.8 ± 2.5	29.8 ± 2.5	29.3 ± 2.8	28.2 ± 2.2

DAYS = DAYS OF STUDY
[ ] = NUMBER OF VALUES AVERAGED
a. Last value recorded before cohabitation.
b. First value recorded after cohabitation.
c. Excludes values that were associated with spillage.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B11 (PAGE 1): RELATIVE FEED CONSUMPTION VALUES (G/KG/DAY) - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	15	15	15	15	15
FEED CONSUMPTION (G/KG/DAY)						
DAYS 1 - 8a	MEAN±S.D.	78.3 ± 7.2	77.7 ± 3.9	80.1 ± 6.9	78.2 ± 4.3	74.7 ± 3.3
DAYS 29b- 36	MEAN±S.D.	64.2 ± 3.2 [14]c	62.8 ± 4.5	64.1 ± 4.2	61.7 ± 3.7	63.2 ± 3.6

DAYS = DAYS OF STUDY
[ ] = NUMBER OF VALUES AVERAGED
a. Last value recorded before cohabitation.
b. First value recorded after cohabitation.
c. Excludes values that were associated with spillage.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B12 (PAGE 1): MATING AND FERTILITY - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0	II 0.3	III 1	IV 3	V 10
RATS IN COHABITATION	N	15	15	15	15	15
DAYS IN COHABITATION a	MEAN±S.D.	3.2 ± 1.4	1.9 ± 1.2	2.8 ± 1.2	3.1 ± 2.0	2.5 ± 1.4
RATS THAT MATED	N(%)	14(93.3)	15(100.0)	15(100.0)	13(86.7)	15(100.0)
FERTILITY INDEX b	N/N (%)	14/ 14 (100.0)	15/ 15 (100.0)	13/ 15 (86.7)	12/ 13 (92.3)	15/ 15 (100.0)
RATS WITH CONFIRMED MATING DATES f	N	14	15	15	13	15
MATED WITH FIRST FEMALE c DAYS 1-7	N(%)	14(100.0)	15(100.0)	15(100.0)	13(100.0)	15(100.0)
RATS PREGNANT/RATS IN COHABITATION	N/N (%)	14/ 15 (93.3)	15/ 15 (100.0)	13/ 15 (86.7)	12/ 15 (80.0)	15/ 15 (100.0)

a. Restricted to rats with a confirmed mating date and rats that did not mate.
b. Number of pregnancies/number of rats that mated.
c. Includes only one mating for each male rat.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B13 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
MALE RATS	N	10	10	10	10	10
HOME CAGE BEHAVIOR						
1: Sleeping	N	2	3	3	8**	2
2: Awake, Immobile	N	8	7	7	2**	8
3: Normal movement	N	0	0	0	0	0
4: Unusual posture	N	0	0	0	0	0
5: Unusual behavior	N	0	0	0	0	0
ALTERATIONS (HOME CAGE)						
1: None	N	9	10	10	10	10
2: Stereotyped behavior	N	1a	0	0	0	0
3: Bizarre behavior	N	0	0	0	0	0
4: Limb twitches/tremor	N	0	0	0	0	0
5: Whole body tremor/spasm	N	0	0	0	0	0
6: Unusual posture	N	0	0	0	0	0
7: Tonic-clonic seizure	N	0	0	0	0	0
REACTION TO REMOVAL						
(1) Sits quietly	N	10	10	10	10	10
(2) Vocalization	N	0	0	0	0	0
(3) Runs or freezes	N	0	0	0	0	0
(4) Tail or throat rattles	N	0	0	0	0	0
	MEAN SCORE	1.0	1.0	1.0	1.0	1.0
REACTION TO HANDLING						
(1) No resistance	N	10	10	10	10	10
(2) Vocalization	N	0	0	0	0	0
(3) Tense	N	0	0	0	0	0
(4) Squirming	N	0	0	0	0	0
	MEAN SCORE	1.0	1.0	1.0	1.0	1.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Excludes a value for rat 19131, which appeared incorrectly recorded.

** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B13 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
MALE RATS	N	10	10	10	10	10
REARS IN OPEN FIELD	MEAN±S.D.	3.3 ± 2.5	6.2 ± 3.2	3.9 ± 1.9	4.5 ± 2.1	4.5 ± 3.1
DEFECATION IN OPEN FIELD						
1: None	N	10	8	7	9	9
2: Feces normal	N	0	2	3	1	1
3: Soft or liquid feces	N	0	0	0	0	0
URINATION IN OPEN FIELD						
(1) None	N	6	1	6	2	3
(2) Normal urination	N	4	9	4	8	7
(3) Excess urination	N	0	0	0	0	0
	MEAN SCORE	1.4	1.9	1.4	1.8	1.7
LEVEL OF AROUSAL						
(1) Stuporous	N	0	0	0	0	0
(2) Sluggish	N	0	0	0	0	0
(3) Apparently normal	N	10	10	10	10	10
(4) Sudden darting	N	0	0	0	0	0
(5) Freezing, vocalization	N	0	0	0	0	0
	MEAN SCORE	3.0	3.0	3.0	3.0	3.0
ALTERATIONS (OPEN FIELD)						
1: None	N	10	10	10	10	10
2: Stereotyped behavior	N	0	0	0	0	0
3: Bizarre behavior	N	0	0	0	0	0
4: Limb twitches/tremor	N	0	0	0	0	0
5: Whole body tremor/spasm	N	0	0	0	0	0
6: Unusual posture	N	0	0	0	0	0
7: Tonic-clonic seizure	N	0	0	0	0	0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B13 (PAGE 3): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
MALE RATS	N	10	10	10	10	10
GAIT PATTERN						
1: Apparently normal	N	10	10	10	10	10
2: Ataxic	N	0	0	0	0	0
3: Limbs splay or drag	N	0	0	0	0	0
4: Spastic, tip-toe	N	0	0	0	0	0
5: Duck-walk	N	0	0	0	0	0
6: Scissors gait	N	0	0	0	0	0
GAIT ABNORMALITY, SEVERITY						
(1) Normal gait	N	10	10	10	10	10
(2) Slight	N	0	0	0	0	0
(3) Moderate	N	0	0	0	0	0
(4) Extreme	N	0	0	0	0	0
	MEAN SCORE	1.0	1.0	1.0	1.0	1.0
PALPEBRAL CLOSURE						
(1) Wide open	N	10	10	10	10	10
(2) Slightly drooping	N	0	0	0	0	0
(3) Half-closed	N	0	0	0	0	0
(4) Completely shut	N	0	0	0	0	0
	MEAN SCORE	1.0	1.0	1.0	1.0	1.0
PROMINENCE OF THE EYE						
1: Normal	N	10	10	10	10	10
2: Exophthalmos	N	0	0	0	0	0
3: Enophthalmos	N	0	0	0	0	0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B13 (PAGE 4): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
MALE RATS	N	10	10	10	10	10
LACRIMATION						
(1) No excess	N	10	10	10	10	10
(2) Excess at eyelid margin	N	0	0	0	0	0
(3) Margin persistently damp	N	0	0	0	0	0
(4) Extends beyond margin	N	0	0	0	0	0
	MEAN SCORE	1.0	1.0	1.0	1.0	1.0
SALIVATION						
(1) No excess	N	10	10	10	10	10
(2) Margin of mouth wet	N	0	0	0	0	0
(3) 1/4 to 1/2 submandibular	N	0	0	0	0	0
(4) Entire submandibular	N	0	0	0	0	0
	MEAN SCORE	1.0	1.0	1.0	1.0	1.0
PILOERECTION	N	0	0	0	0	0
ABNORMAL RESPIRATION	N	0	0	0	0	0
APPEARANCE						
(1) Clean and groomed	N	10	10	10	10	10
(2) Unkempt	N	0	0	0	0	0
(3) Urine and/or fecal stain	N	0	0	0	0	0
	MEAN SCORE	1.0	1.0	1.0	1.0	1.0
VISUAL REACTION						
(1) None	N	0	0	0	0	0
(2) Orienting	N	10	10	10	10	10
(3) Startle	N	0	0	0	0	0
(4) More energetic reaction	N	0	0	0	0	0
(5) Attacks	N	0	0	0	0	0
	MEAN SCORE	2.0	2.0	2.0	2.0	2.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B13 (PAGE 5): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
MALE RATS	N	10	10	10	10	10
TACTILE REACTION						
(1) None	N	0	0	0	0	0
(2) Orienting	N	10	10	10	10	10
(3) Startle	N	0	0	0	0	0
(4) More energetic reaction	N	0	0	0	0	0
(5) Attacks	N	0	0	0	0	0
	MEAN SCORE	2.0	2.0	2.0	2.0	2.0
AUDITORY REACTION						
(1) None	N	0	0	0	0	0
(2) Orienting	N	0	0	0	0	0
(3) Startle	N	10	10	10	10	10
(4) More energetic reaction	N	0	0	0	0	0
(5) Intense vocalization	N	0	0	0	0	0
	MEAN SCORE	3.0	3.0	3.0	3.0	3.0
TAIL-PINCH REACTION						
(1) None	N	0	0	0	0	0
(2) Orienting	N	10	10	10	10	10
(3) Startle	N	0	0	0	0	0
(4) More energetic reaction	N	0	0	0	0	0
(5) Attacks	N	0	0	0	0	0
	MEAN SCORE	2.0	2.0	2.0	2.0	2.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B13 (PAGE 6): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
MALE RATS	N	10	10	10	10	10
AIR RIGHTING RESPONSE						
(1) All feet land on ground	N	10	10	10	10	10
(2) Lands on side	N	0	0	0	0	0
(3) Lands on back	N	0	0	0	0	0
	MEAN SCORE	1.0	1.0	1.0	1.0	1.0
PUPIL RESPONSE TO LIGHT	N	10	10	10	10	10
FORELIMB GRIP TEST						
Maximum (G)	MEAN±S.D.	444.0 ± 49.6	451.5 ± 57.5	456.0 ± 111.1	418.5 ± 125.8	406.5 ± 120.7
Average (G)	MEAN±S.D.	410.5 ± 52.7	400.6 ± 62.7	409.4 ± 93.7	367.5 ± 109.0	359.2 ± 104.6
HINDLIMB GRIP TEST						
Maximum (G)	MEAN±S.D.	386.0 ± 128.8	456.0 ± 109.4	457.0 ± 102.5	414.5 ± 58.9	467.5 ± 113.4
Average (G)	MEAN±S.D.	360.9 ± 121.8	400.8 ± 101.1	419.5 ± 97.8	364.5 ± 67.5	439.4 ± 95.8
LANDING FOOT SPLAY						
Average (CM)	MEAN±S.D.	7.5 ± 1.0	8.6 ± 2.2	9.0 ± 1.3	8.6 ± 1.9	8.0 ± 2.1
BODY WEIGHT (G)	N	484.2 ± 34.1	465.5 ± 36.8	477.1 ± 58.8	493.2 ± 36.6	461.9 ± 13.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B14 (PAGE 1): MOTOR ACTIVITY - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
NUMBER OF MALE RATS	N	10	10	10	10	10
NUMBER OF MOVEMENTS						
BLOCK 1	MEAN ± S.D	64.8 ± 6.6	64.3 ± 6.7	63.5 ± 8.6	62.1 ± 10.0	64.0 ± 8.0
BLOCK 2	MEAN ± S.D	66.9 ± 9.4	63.6 ± 11.5	64.6 ± 9.0	73.5 ± 4.4	69.6 ± 7.2
BLOCK 3	MEAN ± S.D	69.1 ± 6.8	59.8 ± 16.2	65.1 ± 8.3	71.6 ± 11.7	67.5 ± 7.8
BLOCK 4	MEAN ± S.D	72.3 ± 10.5	61.2 ± 20.0	68.2 ± 12.1	65.4 ± 11.9	56.0 ± 11.7
BLOCK 5	MEAN ± S.D	60.1 ± 12.0	54.7 ± 23.1	65.6 ± 5.4	63.1 ± 16.5	56.9 ± 15.6
BLOCK 6	MEAN ± S.D	48.3 ± 25.4	52.8 ± 26.8	64.2 ± 12.8	59.9 ± 14.9	57.4 ± 9.9
BLOCK 7	MEAN ± S.D	39.4 ± 21.0	50.0 ± 25.8	59.8 ± 14.7	60.6 ± 8.2	56.8 ± 11.5
BLOCK 8	MEAN ± S.D	37.9 ± 34.6	46.7 ± 24.8	54.0 ± 19.9	57.0 ± 19.4	49.7 ± 22.2
BLOCK 9	MEAN ± S.D	27.6 ± 25.2	49.2 ± 22.8	49.7 ± 23.4	55.3 ± 20.4	52.2 ± 16.9
BLOCK 10	MEAN ± S.D	25.0 ± 30.2	53.1 ± 20.5	47.0 ± 28.9	50.0 ± 23.1	49.6 ± 15.6
BLOCK 11	MEAN ± S.D	24.2 ± 27.1	35.1 ± 28.3	51.2 ± 25.5	51.7 ± 26.7	41.5 ± 21.2
BLOCK 12	MEAN ± S.D	37.8 ± 28.0	35.1 ± 25.7	45.5 ± 25.9	49.1 ± 26.0	47.6 ± 13.0
BLOCK 13	MEAN ± S.D	42.1 ± 31.9	43.0 ± 34.6	44.0 ± 35.4	50.4 ± 25.6	43.0 ± 22.3
BLOCK 14	MEAN ± S.D	37.6 ± 30.7	43.8 ± 29.4	36.5 ± 26.3	59.2 ± 19.0	43.8 ± 29.6
BLOCK 15	MEAN ± S.D	23.3 ± 26.0	35.5 ± 22.3	39.8 ± 36.2	51.3 ± 21.1	43.0 ± 25.4
BLOCK 16	MEAN ± S.D	23.6 ± 31.2	37.6 ± 28.5	31.2 ± 31.0	50.9 ± 22.7	42.5 ± 29.4
BLOCK 17	MEAN ± S.D	23.6 ± 26.8	39.2 ± 30.2	29.1 ± 25.9	53.5 ± 24.3	37.3 ± 29.6
BLOCK 18	MEAN ± S.D	22.8 ± 24.7	34.4 ± 23.6	35.9 ± 30.2	42.4 ± 27.0	34.2 ± 23.1
TOTAL	MEAN ± S.D	746.4 ± 217.7	859.1 ± 251.7	914.9 ± 212.7	1027.0 ± 176.0	912.6 ± 139.0

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B14 (PAGE 2): MOTOR ACTIVITY - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
NUMBER OF MALE RATS	N	10	10	10	10	10
TIME (SECONDS) SPENT IN MOVEMENT						
BLOCK 1	MEAN ± S.D	201.1 ± 24.1	201.8 ± 17.8	214.8 ± 13.0	204.6 ± 23.7	194.8 ± 27.2
BLOCK 2	MEAN ± S.D	187.4 ± 22.6	174.4 ± 32.9	195.8 ± 33.8	180.2 ± 20.9	170.1 ± 32.5
BLOCK 3	MEAN ± S.D	155.5 ± 26.2	140.3 ± 63.3	172.5 ± 35.6	140.6 ± 27.5	148.7 ± 39.4
BLOCK 4	MEAN ± S.D	141.4 ± 33.3	138.3 ± 53.0	142.4 ± 24.7	140.9 ± 34.1	130.9 ± 50.6
BLOCK 5	MEAN ± S.D	100.7 ± 28.5	131.1 ± 71.4	150.3 ± 20.6	119.2 ± 29.0	113.8 ± 45.7
BLOCK 6	MEAN ± S.D	91.2 ± 54.3	89.7 ± 52.6	118.4 ± 41.2	109.7 ± 48.8	102.7 ± 40.8
BLOCK 7	MEAN ± S.D	70.2 ± 44.2	90.2 ± 55.5	110.2 ± 46.9	118.6 ± 45.9	107.9 ± 38.8
BLOCK 8	MEAN ± S.D	61.3 ± 60.8	83.7 ± 55.9	109.9 ± 52.7	116.1 ± 50.9	72.0 ± 35.9
BLOCK 9	MEAN ± S.D	44.0 ± 46.2	80.9 ± 40.5	93.6 ± 59.3	103.6 ± 56.4	93.6 ± 47.3
BLOCK 10	MEAN ± S.D	48.9 ± 68.7	86.6 ± 40.3	77.4 ± 55.3	83.1 ± 47.0	76.8 ± 44.1
BLOCK 11	MEAN ± S.D	40.2 ± 59.5	71.4 ± 63.0	86.0 ± 49.1	97.7 ± 61.8	67.2 ± 40.0
BLOCK 12	MEAN ± S.D	58.1 ± 46.2	67.1 ± 60.9	91.7 ± 62.1	81.1 ± 49.1	72.9 ± 33.7
BLOCK 13	MEAN ± S.D	66.9 ± 56.7	86.9 ± 82.2	52.1 ± 44.8	80.2 ± 41.2	70.5 ± 48.9
BLOCK 14	MEAN ± S.D	65.6 ± 58.7	75.7 ± 55.9	54.1 ± 47.4	107.8 ± 40.9	73.3 ± 59.7
BLOCK 15	MEAN ± S.D	39.1 ± 49.7	53.1 ± 46.5	68.0 ± 65.3	74.2 ± 35.4	64.2 ± 36.9
BLOCK 16	MEAN ± S.D	31.9 ± 45.1	55.5 ± 47.5	60.3 ± 73.9	87.2 ± 43.5	77.1 ± 68.2
BLOCK 17	MEAN ± S.D	32.0 ± 38.5	62.5 ± 56.4	46.9 ± 53.5	91.4 ± 49.7	51.0 ± 44.8
BLOCK 18	MEAN ± S.D	30.5 ± 39.6	47.4 ± 46.1	56.3 ± 54.7	66.9 ± 43.5	54.1 ± 41.8
TOTAL	MEAN ± S.D	1466.0 ± 453.9	1736.6 ± 607.9	1900.7 ± 469.7	2003.1 ± 453.4	1741.6 ± 463.4

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B15 (PAGE 1): SPERM MOTILITY, COUNT AND DENSITY - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	10	10	10	10	10
NUMBER MOTILE	MEAN±S.D.	289.1 ± 51.3	307.4 ± 77.3	312.0 ± 80.2	307.3 ± 149.6	325.4 ± 81.5
MOTILE PERCENT	MEAN±S.D.	92.1 ± 3.1	93.3 ± 2.8	92.5 ± 3.4	85.5 ± 22.3	91.1 ± 7.4
STATIC COUNT (NONMOTILE)	MEAN±S.D.	25.2 ± 11.3	23.5 ± 14.4	23.1 ± 7.8	32.7 ± 15.3	32.4 ± 23.4
TOTAL COUNT a	MEAN±S.D.	314.3 ± 57.7	330.9 ± 89.7	335.1 ± 75.6	340.0 ± 152.4	357.8 ± 81.2
SPERM COUNT b	MEAN±S.D.	170.1 ± 48.8	158.2 ± 55.2	161.0 ± 41.6	124.6 ± 50.2	174.5 ± 37.9
SPERM DENSITY c	MEAN±S.D.	1494.26 ± 440.40	1430.20 ± 458.01	1441.89 ± 344.28	1214.68 ± 407.71	1664.03 ± 370.30

a. Sum of number motile and static count. Groups of five fields were evaluated until a sperm count of at least 200 was achieved or 20 fields were evaluated.

b. Sperm count used in the calculation of sperm density. Ten fields were evaluated.

c. The sperm density was calculated by dividing the sperm count by the volume in the image area (34.3×10^{-6} mL), multiplying by 2 (dilution factor) and multiplying by 10^{-6} to obtain the sperm concentration. The calculated sperm concentration value (rounded to 1 decimal place) was multiplied by 50 (volume) and divided by the weight of the left cauda epididymis (see Table B19 for the weight of the left cauda epididymis) to obtain the sperm density. The calculated value will vary by approximately 0.8% from the Computer Automated Sperm Analysis because the digital image evaluated is slightly smaller (4 pixels) than the actual field causing a slight underestimate of the actual volume and an overestimate of the concentration.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B16 (PAGE 1): SPERM MORPHOLOGY - SUMMARY - Fo GENERATION MALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	10	10	10	10	10
NORMAL	MEAN±S.D.	192.3 ± 3.1	193.3 ± 3.0	193.3 ± 3.5	173.8 ± 59.8	193.3 ± 3.1
DETACHED HEAD	MEAN±S.D.	3.7 ± 2.4	3.6 ± 2.2	3.1 ± 2.0	6.8 ± 11.0	3.8 ± 2.6
NO HEAD	MEAN±S.D.	3.4 ± 1.7	2.1 ± 1.2	2.6 ± 1.4	10.5 ± 23.1	1.8 ± 1.3
BROKEN FLAGELLUM	MEAN±S.D.	0.4 ± 0.5	0.8 ± 0.8	0.7 ± 0.7	8.5 ± 24.8	1.0 ± 0.9
BENT FLAGELLUM	MEAN±S.D.	0.2 ± 0.4	0.2 ± 0.4	0.3 ± 0.7	0.4 ± 1.3	0.1 ± 0.3
PERCENT ABNORMAL	MEAN±S.D.	3.8 ± 1.5	3.4 ± 1.5	3.4 ± 1.8	13.1 ± 29.9	3.4 ± 1.6

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B17 (PAGE 1): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT #		DESCRIPTION
DOSAGE GROUP I		0 MG/KG/DAY
19109		NO ADVERSE FINDINGS
19115		NO ADVERSE FINDINGS
19116		NO ADVERSE FINDINGS
19119		NO ADVERSE FINDINGS
19122		NO ADVERSE FINDINGS
19125		NO ADVERSE FINDINGS
19131		NO ADVERSE FINDINGS
19132		NO ADVERSE FINDINGS
19134		NO ADVERSE FINDINGS
19135		NO ADVERSE FINDINGS
19143		NO ADVERSE FINDINGS
19151		NO ADVERSE FINDINGS
19157	DS(25- 32)	HEAD: SCAB (0.5 CM IN DIAMETER)
19161	DS(43- 44)	INCISORS: MISSING/BROKEN
19167	DS(23- 29)	DEHYDRATION
DOSAGE GROUP II		0.3 MG/KG/DAY
19102		NO ADVERSE FINDINGS
19106	DS(23)	CHROMORHINORRHEA
19108		NO ADVERSE FINDINGS
19110		NO ADVERSE FINDINGS
19113		NO ADVERSE FINDINGS
19120		NO ADVERSE FINDINGS
19129		NO ADVERSE FINDINGS
19136		NO ADVERSE FINDINGS
19138		NO ADVERSE FINDINGS
19139		NO ADVERSE FINDINGS
19147		NO ADVERSE FINDINGS
19153	DS(36- 46)	LOCALIZED ALOPECIA: LIMBS a
19164		NO ADVERSE FINDINGS
19165	DS(6)	SOFT OR LIQUID FECES
	DS(11)	DRY, BROWN PERIORAL SUBSTANCE
19171	DS(17- 32)	LOCALIZED ALOPECIA: HEAD

DS = DAY OF STUDY
a. Observation confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B17 (PAGE 2): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT #		DESCRIPTION
DOSAGE GROUP III		1 MG/KG/DAY
19101		NO ADVERSE FINDINGS
19105		NO ADVERSE FINDINGS
19107	DS(43)	LOCALIZED ALOPECIA: LIMBS a
19112		NO ADVERSE FINDINGS
19114	DS(11- 13)	CHROMODACRYORRHEA
19121		NO ADVERSE FINDINGS
19123	DS(41)	CHROMORHINORRHEA
19130		NO ADVERSE FINDINGS
19137		NO ADVERSE FINDINGS
19146		NO ADVERSE FINDINGS
19155		NO ADVERSE FINDINGS
19159		NO ADVERSE FINDINGS
19172		NO ADVERSE FINDINGS
19173	DS(46- 47)	LOCALIZED ALOPECIA: UNDERSIDE a
19174		NO ADVERSE FINDINGS
DOSAGE GROUP IV		3 MG/KG/DAY
19100		NO ADVERSE FINDINGS
19103		NO ADVERSE FINDINGS
19104		NO ADVERSE FINDINGS
19118		NO ADVERSE FINDINGS
19133		NO ADVERSE FINDINGS
19141		NO ADVERSE FINDINGS
19142	DS(41)	CHROMORHINORRHEA
19144		NO ADVERSE FINDINGS
19148		NO ADVERSE FINDINGS
19150	DS(34- 39)	INCISORS: MISSING/BROKEN
	DS(34- 42)	CHROMODACRYORRHEA
	DS(34- 46)	INCISORS: MISALIGNED a
19156		NO ADVERSE FINDINGS
19160		NO ADVERSE FINDINGS
19162	DS(19- 32)	LOCALIZED ALOPECIA: HEAD
19163		NO ADVERSE FINDINGS
19166		NO ADVERSE FINDINGS

DS = DAY OF STUDY
a. Observation confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B17 (PAGE 3): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP V		10 MG/KG/DAY
RAT #		DESCRIPTION
19111		NO ADVERSE FINDINGS
19117		NO ADVERSE FINDINGS
19124		NO ADVERSE FINDINGS
19126		NO ADVERSE FINDINGS
19127		NO ADVERSE FINDINGS
19128	DS(7- 8)	CHROMODACRYORRHEA
19140		NO ADVERSE FINDINGS
19145	DS(34)	LACRIMATION
19149		NO ADVERSE FINDINGS
19152		NO ADVERSE FINDINGS
19154	DS(25)	CHROMORHINORRHEA
19158	DS(25- 37)	INCISORS: MISSING/BROKEN
	DS(34)	CHROMORHINORRHEA
19168		NO ADVERSE FINDINGS
19169		NO ADVERSE FINDINGS
19170		NO ADVERSE FINDINGS

DS = DAY OF STUDY

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B18 (PAGE 1): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	DOSES ADMINISTERED	OBSERVATIONS a
I				
0	19109	DS 43	42	ALL TISSUES APPEARED NORMAL.
	19115	DS 43	42	ALL TISSUES APPEARED NORMAL.
	19116	DS 44	43	KIDNEYS: BILATERAL, MOTTLED TAN AND RED. ALL OTHER TISSUES APPEARED NORMAL.
	19119	DS 44	43	ALL TISSUES APPEARED NORMAL.
	19122	DS 44	43	ALL TISSUES APPEARED NORMAL.
	19125	DS 45	44	ALL TISSUES APPEARED NORMAL.
	19131	DS 45	44	ALL TISSUES APPEARED NORMAL.
	19132	DS 45	44	ALL TISSUES APPEARED NORMAL.
	19134	DS 46	45	ALL TISSUES APPEARED NORMAL.
	19135	DS 46	45	ALL TISSUES APPEARED NORMAL.
	19143	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19151	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19157	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19161	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19167	DS 47	46	ALL TISSUES APPEARED NORMAL.

DS = DAY OF STUDY
a. Refer to the individual clinical observations table (Table B17) for external observations confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B18 (PAGE 2): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	DOSES ADMINISTERED	OBSERVATIONS a
II 0.3	19102	DS 43	42	KIDNEYS: BILATERAL, MOTTLED TAN AND DARK RED. ALL OTHER TISSUES APPEARED NORMAL.
	19106	DS 43	42	ALL TISSUES APPEARED NORMAL.
	19108	DS 44	43	ALL TISSUES APPEARED NORMAL.
	19110	DS 44	43	ALL TISSUES APPEARED NORMAL.
	19113	DS 44	43	KIDNEYS: LEFT, PELVIS, SLIGHT DILATION. ALL OTHER TISSUES APPEARED NORMAL.
	19120	DS 45	44	ALL TISSUES APPEARED NORMAL.
	19129	DS 45	44	ALL TISSUES APPEARED NORMAL.
	19136	DS 45	44	KIDNEYS: BILATERAL, MOTTLED. ALL OTHER TISSUES APPEARED NORMAL.
	19138	DS 46	45	ALL TISSUES APPEARED NORMAL.
	19139	DS 46	45	ALL TISSUES APPEARED NORMAL.
	19147	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19153	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19164	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19165	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19171	DS 47	46	ALL TISSUES APPEARED NORMAL.

DS = DAY OF STUDY

a. Refer to the individual clinical observations table (Table B17) for external observations confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B18 (PAGE 3): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	DOSES ADMINISTERED	OBSERVATIONS a
III				
1	19101	DS 43	42	ALL TISSUES APPEARED NORMAL.
	19105	DS 43	42	ALL TISSUES APPEARED NORMAL.
	19107	DS 43	42	ALL TISSUES APPEARED NORMAL.
	19112	DS 44	43	ALL TISSUES APPEARED NORMAL.
	19114	DS 44	43	ALL TISSUES APPEARED NORMAL.
	19121	DS 45	44	ALL TISSUES APPEARED NORMAL.
	19123	DS 45	44	ALL TISSUES APPEARED NORMAL.
	19130	DS 46	45	ALL TISSUES APPEARED NORMAL.
	19137	DS 46	45	ALL TISSUES APPEARED NORMAL.
	19146	DS 46	45	ALL TISSUES APPEARED NORMAL.
	19155	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19159	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19172	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19173	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19174	DS 47	46	ALL TISSUES APPEARED NORMAL.

DS = DAY OF STUDY

a. Refer to the individual clinical observations table (Table B17) for external observations confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B18 (PAGE 4): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	DOSES ADMINISTERED	OBSERVATIONS a
IV				
3	19100	DS 43	42	ALL TISSUES APPEARED NORMAL.
	19103	DS 43	42	ALL TISSUES APPEARED NORMAL.
	19104	DS 44	43	ALL TISSUES APPEARED NORMAL.
	19118	DS 44	43	ALL TISSUES APPEARED NORMAL.
	19133	DS 44	43	ALL TISSUES APPEARED NORMAL.
	19141	DS 45	44	ALL TISSUES APPEARED NORMAL.
	19142	DS 45	44	EPIDIDYMIDES: BILATERAL, SMALL; LEFT CAUDA, SMALL. TESTES: BILATERAL, SMALL. ALL OTHER TISSUES APPEARED NORMAL.
	19144	DS 45	44	ALL TISSUES APPEARED NORMAL.
	19148	DS 46	45	ALL TISSUES APPEARED NORMAL.
	19150	DS 46	45	ALL TISSUES APPEARED NORMAL.
	19156	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19160	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19162	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19163	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19166	DS 47	46	ALL TISSUES APPEARED NORMAL.

DS = DAY OF STUDY

a. Refer to the individual clinical observations table (Table B17) for external observations confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B18 (PAGE 5): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	DOSES ADMINISTERED	OBSERVATIONS a
V				
10	19111	DS 43	42	JEJUNUM: DIVERTICULUM (1.5 CM X 0.6 CM X 0.4 CM). ALL OTHER TISSUES APPEARED NORMAL.
	19117	DS 43	42	ALL TISSUES APPEARED NORMAL.
	19124	DS 43	42	ALL TISSUES APPEARED NORMAL.
	19126	DS 44	43	ALL TISSUES APPEARED NORMAL.
	19127	DS 44	43	ALL TISSUES APPEARED NORMAL.
	19128	DS 45	44	ALL TISSUES APPEARED NORMAL.
	19140	DS 45	44	ALL TISSUES APPEARED NORMAL.
	19145	DS 46	45	ALL TISSUES APPEARED NORMAL.
	19149	DS 46	45	ALL TISSUES APPEARED NORMAL.
	19152	DS 46	45	ALL TISSUES APPEARED NORMAL.
	19154	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19158	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19168	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19169	DS 47	46	ALL TISSUES APPEARED NORMAL.
	19170	DS 47	46	ALL TISSUES APPEARED NORMAL.

DS = DAY OF STUDY

a. Refer to the individual clinical observations table (Table B17) for external observations confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B19 (PAGE 1): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP I — 0 MG/KG/DAY

RAT NUMBER	TERMINAL BODY WEIGHT	EPIDIDYMIS LEFT ABS. WT.	EPIDIDYMIS LEFT REL. % TBW	CAUDA EPIDIDYMIS LEFT ABS. WT.	CAUDA EPIDIDYMIS LEFT REL. % TBW	TESTIS LEFT ABS. WT.	TESTIS LEFT REL. % TBW	SEMINAL VESICLES WITH FLUID ABS. WT.	SEMINAL VESICLES WITH FLUID REL. % TBW	SEMINAL VESICLES WITHOUT FLUID ABS. WT.	SEMINAL VESICLES WITHOUT FLUID REL. % TBW	EPIDIDYMIS RIGHT ABS. WT.	EPIDIDYMIS RIGHT REL. % TBW
19109	438.	0.6013	0.14	0.2822	0.06	1.5706	0.36	1.3331	0.30	0.7867	0.18	0.6317a	0.14
19115	466.	0.6976a	0.15	0.3438	0.07	1.6971	0.36	2.1021	0.45	1.0227	0.22	0.7252	0.16
19116	490.	0.6499	0.13	0.3209	0.06	1.6213	0.33	1.5369	0.31	0.6846	0.14	0.6497	0.13
19119	505.	0.6541	0.13	0.3489	0.07	1.7174	0.34	1.6464	0.33	0.8014	0.16	0.6728	0.13
19122	451.	0.6661	0.15	0.3724	0.08	1.6754	0.37	1.9375	0.43	0.9217	0.20	0.7436	0.16
19125	508.	0.6160	0.12	0.3260	0.06	1.6621	0.33	1.6300	0.32	0.7377	0.14	0.6362	0.12
19131	499.	0.6482	0.13	0.3140	0.06	1.6865	0.34	1.5772	0.32	0.7764	0.16	0.6767	0.14
19132	439.	0.7103	0.16	0.3684	0.08	1.8079	0.41	1.9409	0.44	0.9312	0.21	0.7249	0.16
19134	419.	0.6278	0.15	0.3368	0.08	1.4801	0.35	1.8240	0.44	0.9106	0.22	0.6540	0.16
19135	482.	0.6052	0.12	0.2942	0.06	1.6728	0.35	1.5266	0.32	0.8672	0.18	0.6302	0.13

RAT NUMBER	TERMINAL BODY WEIGHT	TESTIS RIGHT ABS. WT.	TESTIS RIGHT REL. % TBW	PROSTATE ABS. WT.	PROSTATE REL. % TBW	BRAIN ABS. WT.	BRAIN REL. % TBW	LIVER ABS. WT.	LIVER REL. % TBW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % TBW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % TBW
19109	438.	1.6529	0.38	1.1854	0.27	2.29	0.52	14.18	3.24	1.51	0.34	1.51	0.34
19115	466.	1.6847	0.36	1.4274	0.31	2.27	0.49	16.71	3.58	1.99	0.43	1.99	0.43
19116	490.	1.6820	0.34	1.5838	0.32	2.28	0.46	15.18	3.10	2.16	0.44	2.12	0.43
19119	505.	1.6364	0.32	0.7632	0.15	2.63	0.52	14.66	2.90	2.26	0.45	2.38	0.47
19122	451.	1.6956	0.38	1.0942	0.24	2.45	0.54	13.10	2.90	1.92	0.42	1.81	0.40
19125	508.	1.6796	0.33	1.1823	0.23	2.44	0.48	16.13	3.18	2.31	0.45	2.29	0.45
19131	499.	1.6534	0.33	1.2496	0.25	2.45	0.49	16.94	3.39	2.13	0.43	2.22	0.44
19132	439.	1.8532	0.42	1.8597	0.42	2.34	0.53	11.94	2.72	1.78	0.40	1.89	0.43
19134	419.	1.4818	0.35	1.3858	0.33	2.35	0.56	12.01	2.87	1.76	0.42	1.84	0.44
19135	482.	1.7570	0.36	1.1710	0.24	2.45	0.51	15.48	3.21	2.00	0.41	2.15	0.45

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.
a. Damaged during processing (weight not affected).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B19 (PAGE 2): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP I 0 MG/KG/DAY

RAT NUMBER	TERMINAL BODY WEIGHT	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % TBW a	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % TBW a	SPLEEN ABS. WT.	SPLEEN REL. % TBW	THYMUS ABS. WT.	THYMUS REL. % TBW	HEART ABS. WT.	HEART REL. % TBW
19109	438.	0.027	6.16	0.027	6.16	0.56	0.13	0.37	0.08	1.41	0.32
19115	466.	0.041	8.80	0.040	8.58	0.77	0.16	0.41	0.09	1.62	0.35
19116	490.	0.035	7.14	0.035	7.14	0.95	0.19	0.49	0.10	1.51	0.31
19119	505.	0.048	9.50	0.046	9.11	0.79	0.16	0.30	0.06	1.62	0.32
19122	451.	0.033	7.32	0.031	6.87	0.79	0.18	0.33	0.07	1.68	0.37
19125	508.	0.034	6.69	0.031	6.10	0.76	0.15	0.70	0.14	1.54	0.30
19131	499.	0.041	8.22	0.036	7.21	1.03	0.21	0.47	0.09	1.67	0.33
19132	439.	0.036	8.20	0.038	8.66	0.73	0.17	0.27	0.06	1.40	0.32
19134	419.	0.024	5.73	0.025	5.97	0.60	0.14	0.44	0.10	1.46	0.35
19135	482.	0.031	6.43	0.030	6.22	0.90	0.19	0.33	0.07	1.63	0.34

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.
a. Value was multiplied by 1000.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B19 (PAGE 3): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP II — 0.3 MG/KG/DAY

RAT NUMBER	TERMINAL BODY WEIGHT	EPIDIDYMIS LEFT ABS. WT.	EPIDIDYMIS LEFT REL. % TBW	CAUDA EPIDIDYMIS LEFT ABS. WT.	CAUDA EPIDIDYMIS LEFT REL. % TBW	TESTIS LEFT ABS. WT.	TESTIS LEFT REL. % TBW	SEMINAL VESICLES WITH FLUID ABS. WT.	SEMINAL VESICLES WITH FLUID REL. % TBW	SEMINAL VESICLES WITHOUT FLUID ABS. WT.	SEMINAL VESICLES WITHOUT FLUID REL. % TBW	EPIDIDYMIS RIGHT ABS. WT.	EPIDIDYMIS RIGHT REL. % TBW
19102	428.	0.6197	0.14	0.2867	0.07	1.5498	0.36	1.7556	0.41	0.9426	0.22	0.6523	0.15
19106	476.	0.6623	0.14	0.2962	0.06	1.6495	0.35	1.0913	0.23	0.5991	0.12	0.6675	0.14
19108	474.	0.6465	0.14	0.3502	0.07	1.8847	0.40	1.2460	0.26	0.7062	0.15	0.6572	0.14
19110	453.	0.5411	0.12	0.2779	0.06	1.4915	0.33	1.8646	0.41	0.8697	0.19	0.5439	0.12
19113	444.	0.6310	0.14	0.3379	0.08	1.7844	0.40	1.7236	0.39	0.8319	0.19	0.6568	0.15
19120	486.	0.6180	0.13	0.3209	0.07	1.6588	0.34	1.6952	0.35	0.8335	0.17	0.6724	0.14
19129	435.	0.6644	0.15	0.3181	0.07	1.8000	0.41	1.7928	0.41	0.8254	0.19	0.6538	0.15
19136	495.	0.6785	0.14	0.3219	0.06	1.7629	0.36	1.2650	0.26	0.6950	0.14	0.6914	0.14
19138	365.	0.6686	0.18	0.3604	0.10	1.7956	0.49	1.5421	0.42	0.8728	0.24	0.6831	0.19
19139	432.	0.6280	0.14	0.3114	0.07	1.7773	0.41	1.4625	0.34	0.9423	0.22	0.6675	0.15

RAT NUMBER	TERMINAL BODY WEIGHT	TESTIS RIGHT ABS. WT.	TESTIS RIGHT REL. % TBW	PROSTATE ABS. WT.	PROSTATE REL. % TBW	BRAIN ABS. WT.	BRAIN REL. % TBW	LIVER ABS. WT.	LIVER REL. % TBW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % TBW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % TBW
19102	428.	1.5930	0.37	1.2374	0.29	2.19	0.51	14.53	3.39	1.92	0.45	1.95	0.46
19106	476.	1.6779	0.35	1.0360	0.22	2.57	0.54	17.19	3.61	1.97	0.41	2.00	0.42
19108	474.	1.9171	0.40	1.1892	0.25	2.52	0.53	14.75	3.11	1.90	0.40	1.98	0.42
19110	453.	1.4694	0.32	1.1812	0.26	2.42	0.53	13.95	3.08	1.96	0.43	2.00	0.44
19113	444.	1.7350	0.39	1.2130	0.27	2.58	0.58	13.08	2.94	1.96a	0.44	2.11	0.48
19120	486.	1.6765	0.34	1.4290	0.29	2.38	0.49	14.26	2.93	1.72	0.35	1.76	0.36
19129	435.	1.8164	0.42	1.1232	0.26	2.45	0.56	13.37	3.07	1.89	0.43	1.90	0.44
19136	495.	1.8039	0.36	1.3313	0.27	2.41	0.49	15.75	3.18	1.83	0.37	1.69	0.34
19138	365.	1.7840	0.49	0.9939	0.27	2.46	0.67	11.25	3.08	1.58	0.43	1.66	0.45
19139	432.	1.8078	0.42	1.2660	0.29	2.40	0.56	14.10	3.26	1.88	0.44	1.93	0.45

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.
a. Rat 19113 had slight dilation of the pelvis of the left kidney. See the individual necropsy observations table (Table B18).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B19 (PAGE 4): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP II 0.3 MG/KG/DAY

RAT NUMBER	TERMINAL BODY WEIGHT	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % TBW a	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % TBW a	SPLEEN ABS. WT.	SPLEEN REL. % TBW	THYMUS ABS. WT.	THYMUS REL. % TBW	HEART ABS. WT.	HEART REL. % TBW
19102	428.	0.041	9.58	0.038	8.88	0.89	0.21	0.52	0.12	1.38	0.32
19106	476.	0.024	5.04	0.024	5.04	0.86	0.18	0.42	0.09	1.56	0.33
19108	474.	0.030	6.33	0.030	6.33	0.73	0.15	0.47	0.10	1.64	0.34
19110	453.	0.037	8.17	0.038	8.39	0.85	0.19	0.41	0.09	1.59	0.35
19113	444.	0.046	10.36	0.044	9.91	0.81	0.18	0.48	0.11	1.47	0.33
19120	486.	0.042	8.64	0.038	7.82	0.83	0.17	0.40	0.08	1.56	0.32
19129	435.	0.037	8.50	0.034	7.82	0.76	0.17	0.34	0.08	1.55	0.36
19136	495.	0.033	6.67	0.034	6.87	0.72	0.14	0.58	0.12	1.71	0.34
19138	365.	0.028	7.67	0.027	7.40	0.73	0.20	0.30	0.08	1.30	0.36
19139	432.	0.032	7.41	0.032	7.41	0.92	0.21	0.54	0.12	1.46	0.34

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.
a. Value was multiplied by 1000.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B19 (PAGE 5): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP III — 1 MG/KG/DAY

RAT NUMBER	TERMINAL BODY WEIGHT	EPIDIDYMIS LEFT ABS. WT.	EPIDIDYMIS LEFT REL. % TBW	CAUDA EPIDIDYMIS LEFT ABS. WT.	CAUDA EPIDIDYMIS LEFT REL. % TBW	TESTIS LEFT ABS. WT.	TESTIS LEFT REL. % TBW	SEMINAL VESICLES WITH FLUID ABS. WT.	SEMINAL VESICLES WITH FLUID REL. % TBW	SEMINAL VESICLES WITHOUT FLUID ABS. WT.	SEMINAL VESICLES WITHOUT FLUID REL. % TBW	EPIDIDYMIS RIGHT ABS. WT.	EPIDIDYMIS RIGHT REL. % TBW
19101	353.	0.6021	0.17	0.2993	0.08	1.6371	0.46	1.1004	0.31	0.5923	0.17	0.6071	0.17
19105	505.	0.7012	0.14	0.3377	0.07	2.0077	0.40	1.7433	0.34	0.7941	0.16	0.7481	0.15
19107	437.	0.5355a	0.12	0.2667	0.06	1.4816	0.34	2.2034	0.50	0.9613	0.22	0.5625	0.13
19112	452.	0.6158	0.14	0.3199	0.07	1.6088	0.36	1.6734	0.37	0.8909	0.20	0.6460	0.14
19114	430.	0.5678	0.13	0.2915	0.07	1.4232	0.33	1.6586	0.38	0.7345	0.17	0.6091	0.14
19121	567.	0.6466	0.11	0.3316	0.06	1.8123	0.32	1.6481	0.29	0.8330	0.15	0.6559	0.12
19123	464.	0.6675	0.14	0.3384	0.07	1.7221	0.37	1.7452	0.38	0.9021	0.19	0.6825	0.15
19130	434.	0.6775	0.16	0.3513	0.08	1.7366	0.40	1.7430	0.40	0.7931	0.18	0.7227	0.17
19137	443.	0.6420	0.14	0.3467	0.08	1.6457	0.37	1.3000	0.29	0.7387	0.17	0.6680	0.15
19146	473.	0.6207	0.13	0.3492	0.07	1.6423	0.35	1.5693	0.33	0.7248	0.15	0.6320	0.13

RAT NUMBER	TERMINAL BODY WEIGHT	TESTIS RIGHT ABS. WT.	TESTIS RIGHT REL. % TBW	PROSTATE ABS. WT.	PROSTATE REL. % TBW	BRAIN ABS. WT.	BRAIN REL. % TBW	LIVER ABS. WT.	LIVER REL. % TBW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % TBW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % TBW
19101	353.	1.5806	0.45	0.8460	0.24	2.22	0.63	11.34	3.21	1.50	0.42	1.56	0.44
19105	505.	2.0016	0.40	1.5220	0.30	2.40	0.48	17.13	3.39	2.37	0.47	2.29	0.45
19107	437.	1.5096	0.34	1.5754	0.36	2.35	0.54	13.84	3.17	1.71	0.39	1.71	0.39
19112	452.	1.6041	0.35	1.3786	0.30	2.41	0.53	14.51	3.21	2.09	0.46	1.97	0.44
19114	430.	1.4506	0.34	1.1497	0.27	2.36	0.55	14.34	3.33	1.84	0.43	1.92	0.45
19121	567.	1.7745	0.31	1.0712	0.19	2.54	0.45	23.98	4.23	2.20	0.39	2.25	0.40
19123	464.	1.8031	0.39	0.9914	0.21	2.43	0.52	19.27	4.15	2.17	0.47	2.22	0.48
19130	434.	1.8184	0.42	1.6000	0.37	2.37	0.55	13.79	3.18	1.88	0.43	1.98	0.46
19137	443.	1.6928	0.38	1.0622	0.24	2.45	0.55	14.59	3.29	1.88	0.42	2.14	0.48
19146	473.	1.6866	0.36	1.0704	0.23	2.26	0.48	16.57	3.50	1.94	0.41	2.01	0.42

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.
a. Damaged during processing (weight not affected).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B19 (PAGE 6): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP III 1 MG/KG/DAY

RAT NUMBER	TERMINAL BODY WEIGHT	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % TBW a	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % TBW a	SPLEEN ABS. WT.	SPLEEN REL. % TBW	THYMUS ABS. WT.	THYMUS REL. % TBW	HEART ABS. WT.	HEART REL. % TBW
19101	353.	0.028	7.93	0.026	7.36	0.55	0.16	0.23	0.06	1.33	0.38
19105	505.	0.034	6.73	0.027	5.35	0.74	0.15	0.47	0.09	1.66	0.33
19107	437.	0.039	8.92	0.038	8.70	0.69	0.16	0.26	0.06	1.36	0.31
19112	452.	0.026	5.75	0.022	4.87	0.65	0.14	0.55	0.12	1.48	0.33
19114	430.	0.033	7.67	0.031	7.21	0.68	0.16	0.32	0.07	1.52	0.35
19121	567.	0.032	5.64	0.035	6.17	0.92	0.16	0.44	0.08	1.70	0.30
19123	464.	0.040	8.62	0.025	5.39	0.78	0.17	0.40	0.09	1.56	0.34
19130	434.	0.030	6.91	0.033	7.60	0.87	0.20	0.33	0.08	1.48	0.34
19137	443.	0.032	7.22	0.019	4.29	0.91	0.20	0.29	0.06	1.65	0.37
19146	473.	0.042	8.88	0.043	9.09	0.80	0.17	0.28	0.06	1.65	0.35

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.
a. Value was multiplied by 1000.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B19 (PAGE 7): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP IV 3 MG/KG/DAY

RAT NUMBER	TERMINAL BODY WEIGHT	EPIDIDYMIS LEFT ABS. WT.	EPIDIDYMIS LEFT REL. % TBW	CAUDA EPIDIDYMIS LEFT ABS. WT.	CAUDA EPIDIDYMIS LEFT REL. % TBW	TESTIS LEFT ABS. WT.	TESTIS LEFT REL. % TBW	SEMINAL VESICLES WITH FLUID ABS. WT.	SEMINAL VESICLES WITH FLUID REL. % TBW	SEMINAL VESICLES WITHOUT FLUID ABS. WT.	SEMINAL VESICLES WITHOUT FLUID REL. % TBW	EPIDIDYMIS RIGHT ABS. WT.	EPIDIDYMIS RIGHT REL. % TBW
19100	421.	0.6712	0.16	0.3355	0.08	1.7129	0.41	2.0456	0.48	1.0125	0.24	0.6970	0.16
19103	487.	0.6486	0.13	0.2909	0.06	1.6530	0.34	2.0607	0.42	1.0014	0.20	0.6457	0.13
19104	476.	0.6201	0.13	0.2961	0.06	1.7770	0.37	1.4443	0.30	0.7874	0.16	0.5846	0.12
19118	442.	0.5834	0.13	0.3022	0.07	1.5495	0.35	1.6316	0.37	0.7381	0.17	0.6169	0.14
19133	448.	0.5667	0.13	0.2961	0.07	1.7262	0.38	1.7327	0.39	0.8511	0.19	0.5492	0.12
19141	545.	0.6531	0.12	0.3098	0.06	1.7814	0.33	1.4610	0.27	0.7077	0.13	0.6801	0.12
19142	479.	0.3058a	0.06	0.1333a	0.03	0.6988a	0.14	1.1736	0.24	0.6729	0.14	0.3002a	0.06
19144	523.	0.5626	0.11	0.2529	0.05	1.6357	0.31	1.3813	0.26	0.6369	0.12	0.6547	0.12
19148	454.	0.6884	0.15	0.3851	0.08	1.8767	0.41	1.3721	0.30	0.6888	0.15	0.7389	0.16
19150	448.	0.6161	0.14	0.3111	0.07	1.7049	0.38	1.1701	0.26	0.5734	0.13	0.6388	0.14

RAT NUMBER	TERMINAL BODY WEIGHT	TESTIS RIGHT ABS. WT.	TESTIS RIGHT REL. % TBW	PROSTATE ABS. WT.	PROSTATE REL. % TBW	BRAIN ABS. WT.	BRAIN REL. % TBW	LIVER ABS. WT.	LIVER REL. % TBW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % TBW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % TBW
19100	421.	1.7274	0.41	1.5079	0.36	2.40	0.57	15.67	3.72	1.82	0.43	1.91	0.45
19103	487.	1.7657	0.36	1.4347	0.29	2.39	0.49	19.28	3.96	2.40	0.49	2.39	0.49
19104	476.	1.7025	0.36	1.2209	0.26	2.43	0.51	17.78	3.74	1.98	0.42	2.16	0.45
19118	442.	1.6129	0.36	1.3183	0.30	2.42	0.55	15.97	3.61	1.90	0.43	2.12	0.48
19133	448.	1.7045	0.38	1.2429	0.28	2.47	0.55	15.06	3.36	2.08	0.46	2.24	0.50
19141	545.	1.7406	0.32	1.0238	0.19	2.52	0.46	20.42	3.75	2.18	0.40	2.20	0.40
19142	479.	0.6700a	0.14	1.0863	0.23	2.23	0.46	17.61	3.68	2.00	0.42	2.07	0.43
19144	523.	1.6766	0.32	1.1080	0.21	2.40	0.46	18.23	3.48	2.21	0.42	2.36	0.45
19148	454.	1.8681	0.41	1.4524	0.32	2.24	0.49	18.08	3.98	1.91	0.42	1.92	0.42
19150	448.	1.7068	0.38	1.3391	0.30	2.35	0.52	17.94	4.00	1.97	0.44	1.92	0.43

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.

a. Rat 19142 had small testes, epididymides and left cauda epididymis. See the individual necropsy observations table (Table B18).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B19 (PAGE 8): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP IV 3 MG/KG/DAY

RAT NUMBER	TERMINAL BODY WEIGHT	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % TBW a	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % TBW a	SPLEEN ABS. WT.	SPLEEN REL. % TBW	THYMUS ABS. WT.	THYMUS REL. % TBW	HEART ABS. WT.	HEART REL. % TBW
19100	421.	0.028	6.65	0.032	7.60	0.86	0.20	0.40	0.10	1.42	0.34
19103	487.	0.040	8.21	0.046	9.44	0.88	0.18	0.39	0.08	1.56	0.32
19104	476.	0.030	6.30	0.026	5.46	1.10	0.23	0.40	0.08	1.64	0.34
19118	442.	0.030	6.79	0.032	7.24	0.69	0.16	0.37	0.08	1.44	0.32
19133	448.	0.043	9.60	0.041	9.15	0.74	0.16	0.36	0.08	1.60	0.36
19141	545.	0.024	4.40	0.030	5.50	1.15	0.21	0.57	0.10	1.84	0.34
19142	479.	0.028	5.84	0.028	5.84	0.74	0.15	0.48	0.10	1.54	0.32
19144	523.	0.037	7.07	0.032	6.12	1.15	0.22	0.34	0.06	1.74	0.33
19148	454.	0.028	6.17	0.026	5.73	0.78	0.17	0.35	0.08	1.55	0.34
19150	448.	0.037	8.26	0.026	5.80	0.67	0.15	0.57	0.13	1.62	0.36

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.
a. Value was multiplied by 1000.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B19 (PAGE 9): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP V — 10 MG/KG/DAY

RAT NUMBER	TERMINAL BODY WEIGHT	EPIDIDYMIS LEFT ABS. WT.	EPIDIDYMIS LEFT REL. % TBW	CAUDA EPIDIDYMIS LEFT ABS. WT.	CAUDA EPIDIDYMIS LEFT REL. % TBW	TESTIS LEFT ABS. WT.	TESTIS LEFT REL. % TBW	SEMINAL VESICLES WITH FLUID ABS. WT.	SEMINAL VESICLES WITH FLUID REL. % TBW	SEMINAL VESICLES WITHOUT FLUID ABS. WT.	SEMINAL VESICLES WITHOUT FLUID REL. % TBW	EPIDIDYMIS RIGHT ABS. WT.	EPIDIDYMIS RIGHT REL. % TBW
19111	432.	0.5886	0.14	0.2814	0.06	1.7973	0.42	1.4923	0.34	0.7724	0.18	0.6626	0.15
19117	462.	0.5554a	0.12	0.2921	0.06	1.5902	0.34	1.4692	0.32	0.8619	0.19	0.5723	0.12
19124	426.	0.7041	0.16	0.3378	0.08	1.9441	0.46	1.6428	0.38	0.8490	0.20	0.6631	0.16
19126	426.	0.5648	0.13	0.2550	0.06	1.5950	0.37	0.9950	0.23	0.5749	0.13	0.5576	0.13
19127	434.	0.5950	0.14	0.3045	0.07	1.7552	0.40	1.6404	0.38	0.7509	0.17	0.5793	0.13
19128	445.	0.5787	0.13	0.2725	0.06	1.5509	0.35	1.1019	0.25	0.6009	0.14	0.6242	0.14
19140	442.	0.6181	0.14	0.2951	0.07	1.6009	0.36	1.5387	0.35	0.8782	0.20	0.6487	0.15
19145	441.	0.6705	0.15	0.3537	0.08	1.8102	0.41	1.8705	0.42	0.9316	0.21	0.6428	0.14
19149	439.	0.6384	0.14	0.3200	0.07	1.9607	0.45	1.4543	0.33	0.8120	0.18	0.6610	0.15
19152	461.	0.6200	0.13	0.3288	0.07	1.8784	0.41	1.2190	0.26	0.7403	0.16	0.6498	0.14

RAT NUMBER	TERMINAL BODY WEIGHT	TESTIS RIGHT ABS. WT.	TESTIS RIGHT REL. % TBW	PROSTATE ABS. WT.	PROSTATE REL. % TBW	BRAIN ABS. WT.	BRAIN REL. % TBW	LIVER ABS. WT.	LIVER REL. % TBW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % TBW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % TBW
19111	432.	1.7246	0.40	1.0515	0.24	2.48	0.57	24.36	5.64	2.00	0.46	2.13	0.49
19117	462.	1.6160	0.35	1.0954	0.24	2.43	0.52	24.11	5.22	2.22	0.48	2.26	0.49
19124	426.	1.8910	0.44	1.5146	0.36	2.38	0.56	25.72	6.04	2.21	0.52	2.18	0.51
19126	426.	1.6044	0.38	0.7260	0.17	2.28	0.54	22.94	5.38	2.04	0.48	2.04	0.48
19127	434.	1.7997	0.41	1.4010	0.32	2.62	0.60	27.38	6.31	1.90	0.44	1.95	0.45
19128	445.	1.5952	0.36	0.9706	0.22	2.31	0.52	21.74	4.88	1.78	0.40	1.82	0.41
19140	442.	1.6407	0.37	1.2239	0.28	2.42	0.55	20.21	4.57	1.93	0.44	1.88	0.42
19145	441.	1.8340	0.42	1.3756	0.31	2.40	0.54	23.20	5.26	2.27	0.51	2.16	0.49
19149	439.	1.9989	0.46	1.2522	0.28	2.38	0.54	20.06	4.57	1.76	0.40	1.92	0.44
19152	461.	1.8997	0.41	1.3077	0.28	2.34	0.51	18.58	4.03	1.97	0.43	2.07	0.45

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.
a. Damaged during processing (weight not affected).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B19 (PAGE 10): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP V 10 MG/KG/DAY

RAT NUMBER	TERMINAL BODY WEIGHT	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % TBW a	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % TBW a	SPLEEN ABS. WT.	SPLEEN REL. % TBW	THYMUS ABS. WT.	THYMUS REL. % TBW	HEART ABS. WT.	HEART REL. % TBW
19111	432.	0.025	5.79	0.024	5.56	0.73	0.17	0.37	0.08	1.38	0.32
19117	462.	0.030	6.49	0.014	3.03	0.75	0.16	0.36	0.08	1.60	0.35
19124	426.	0.035	8.22	0.034	7.98	0.72	0.17	0.36	0.08	1.40	0.33
19126	426.	0.029	6.81	0.028	6.57	0.64	0.15	0.47	0.11	1.38	0.32
19127	434.	0.031	7.14	0.031	7.14	0.81	0.19	0.47	0.11	1.43	0.33
19128	445.	0.036	8.09	0.034	7.64	0.74	0.17	0.40	0.09	1.42	0.32
19140	442.	0.036	8.14	0.028	6.33	0.86	0.19	0.44	0.10	1.50	0.34
19145	441.	0.034	7.71	0.033	7.48	0.88	0.20	0.38	0.09	1.36	0.31
19149	439.	0.029	6.60	0.030	6.83	0.97	0.22	0.43	0.10	1.46	0.33
19152	461.	0.036	7.81	0.038	8.24	0.70	0.15	0.51	0.11	1.47	0.32

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.
a. Value was multiplied by 1000.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B20 (PAGE 1): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP I — 0 MG/KG/DAY

RAT NUMBER	BRAIN WEIGHT	EPIDIDYMIS LEFT ABS. WT.	EPIDIDYMIS LEFT REL. % BRW	CAUDA EPIDIDYMIS LEFT ABS. WT.	CAUDA EPIDIDYMIS LEFT REL. % BRW	TESTIS LEFT ABS. WT.	TESTIS LEFT REL. % BRW	SEMINAL VESICLES WITH FLUID ABS. WT.	SEMINAL VESICLES WITH FLUID REL. % BRW	SEMINAL VESICLES WITHOUT FLUID ABS. WT.	SEMINAL VESICLES WITHOUT FLUID REL. % BRW	EPIDIDYMIS RIGHT ABS. WT.	EPIDIDYMIS RIGHT REL. % BRW
19109	2.29	0.6013	26.26	0.2822	12.32	1.5706	68.58	1.3331	58.21	0.7867	34.35	0.6317a	27.58
19115	2.27	0.6976a	30.73	0.3438	15.14	1.6971	74.76	2.1021	92.60	1.0227	45.05	0.7252	31.95
19116	2.28	0.6499	28.50	0.3209	14.07	1.6213	71.11	1.5369	67.41	0.6846	30.03	0.6497	28.50
19119	2.63	0.6541	24.87	0.3489	13.27	1.7174	65.30	1.6464	62.60	0.8014	30.47	0.6728	25.58
19122	2.45	0.6661	27.19	0.3724	15.20	1.6754	68.38	1.9375	79.08	0.9217	37.62	0.7436	30.35
19125	2.44	0.6160	25.24	0.3260	13.36	1.6621	68.12	1.6300	66.80	0.7377	30.23	0.6362	26.07
19131	2.45	0.6482	26.46	0.3140	12.82	1.6865	68.84	1.5772	64.38	0.7764	31.69	0.6767	27.62
19132	2.34	0.7103	30.35	0.3684	15.74	1.8079	77.26	1.9409	82.94	0.9312	39.79	0.7249	30.98
19134	2.35	0.6278	26.71	0.3368	14.33	1.4801	62.98	1.8240	77.62	0.9106	38.75	0.6540	27.83
19135	2.45	0.6052	24.70	0.2942	12.01	1.6728	68.28	1.5266	62.31	0.8672	35.40	0.6302	25.72

RAT NUMBER	BRAIN WEIGHT	TESTIS RIGHT ABS. WT.	TESTIS RIGHT REL. % BRW	PROSTATE ABS. WT.	PROSTATE REL. % BRW	LIVER ABS. WT.	LIVER REL. % BRW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % BRW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % BRW	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % BRW
19109	2.29	1.6529	72.18	1.1854	51.76	14.18	619.21	1.51	65.94	1.51	65.94	0.027	1.18
19115	2.27	1.6847	74.22	1.4274	62.88	16.71	736.12	1.99	87.66	1.99	87.66	0.041	1.81
19116	2.28	1.6820	73.77	1.5838	69.46	15.18	665.79	2.16	94.74	2.12	92.98	0.035	1.54
19119	2.63	1.6364	62.22	0.7632	29.02	14.66	557.41	2.26	85.93	2.38	90.49	0.048	1.82
19122	2.45	1.6956	69.21	1.0942	44.66	13.10	534.69	1.92	78.37	1.81	73.88	0.033	1.35
19125	2.44	1.6796	68.84	1.1823	48.45	16.13	661.06	2.31	94.67	2.29	93.85	0.034	1.39
19131	2.45	1.6534	67.48	1.2496	51.00	16.94	691.43	2.13	86.94	2.22	90.61	0.041	1.67
19132	2.34	1.8532	79.20	1.8597	79.47	11.94	510.26	1.78	76.07	1.89	80.77	0.036	1.54
19134	2.35	1.4818	63.06	1.3858	58.97	12.01	511.06	1.76	74.89	1.84	78.30	0.024	1.02
19135	2.45	1.7570	71.71	1.1710	47.80	15.48	631.84	2.00	81.63	2.15	87.76	0.031	1.26

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.
a. Damaged during processing (weight not affected).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B20 (PAGE 2): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP I — 0 MG/KG/DAY

RAT NUMBER	BRAIN WEIGHT	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % BRW	SPLEEN ABS. WT.	SPLEEN REL. % BRW	THYMUS ABS. WT.	THYMUS REL. % BRW	HEART ABS. WT.	HEART REL. % BRW
19109	2.29	0.027	1.18	0.56	24.45	0.37	16.16	1.41	61.57
19115	2.27	0.040	1.76	0.77	33.92	0.41	18.06	1.62	71.36
19116	2.28	0.035	1.54	0.95	41.67	0.49	21.49	1.51	66.23
19119	2.63	0.046	1.75	0.79	30.04	0.30	11.41	1.62	61.60
19122	2.45	0.031	1.26	0.79	32.24	0.33	13.47	1.68	68.57
19125	2.44	0.031	1.27	0.76	31.15	0.70	28.69	1.54	63.11
19131	2.45	0.036	1.47	1.03	42.04	0.47	19.18	1.67	68.16
19132	2.34	0.038	1.62	0.73	31.20	0.27	11.54	1.40	59.83
19134	2.35	0.025	1.06	0.60	25.53	0.44	18.72	1.46	62.13
19135	2.45	0.030	1.22	0.90	36.73	0.33	13.47	1.63	66.53

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B20 (PAGE 3): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP II — 0.3 MG/KG/DAY

RAT NUMBER	BRAIN WEIGHT	EPIDIDYMIS LEFT ABS. WT.	EPIDIDYMIS LEFT REL. % BRW	CAUDA EPIDIDYMIS LEFT ABS. WT.	CAUDA EPIDIDYMIS LEFT REL. % BRW	TESTIS LEFT ABS. WT.	TESTIS LEFT REL. % BRW	SEMINAL VESICLES WITH FLUID ABS. WT.	SEMINAL VESICLES WITH FLUID REL. % BRW	SEMINAL VESICLES WITHOUT FLUID ABS. WT.	SEMINAL VESICLES WITHOUT FLUID REL. % BRW	EPIDIDYMIS RIGHT ABS. WT.	EPIDIDYMIS RIGHT REL. % BRW
19102	2.19	0.6197	28.30	0.2867	13.09	1.5498	70.77	1.7556	80.16	0.9426	43.04	0.6523	29.78
19106	2.57	0.6623	25.77	0.2962	11.52	1.6495	64.18	1.0913	42.46	0.5991	23.31	0.6675	25.97
19108	2.52	0.6465	25.65	0.3502	13.90	1.8847	74.79	1.2460	49.44	0.7062	28.02	0.6572	26.08
19110	2.42	0.5411	22.36	0.2779	11.48	1.4915	61.63	1.8646	77.05	0.8697	35.94	0.5439	22.48
19113	2.58	0.6310	24.46	0.3379	13.10	1.7844	69.16	1.7236	66.81	0.8319	32.24	0.6568	25.46
19120	2.38	0.6180	25.97	0.3209	13.48	1.6588	69.70	1.6952	71.23	0.8335	35.02	0.6724	28.25
19129	2.45	0.6644	27.12	0.3181	12.98	1.8000	73.47	1.7928	73.18	0.8254	33.69	0.6538	26.68
19136	2.41	0.6785	28.15	0.3219	13.36	1.7629	73.15	1.2650	52.49	0.6950	28.84	0.6914	28.69
19138	2.46	0.6686	27.18	0.3604	14.65	1.7956	72.99	1.5421	62.69	0.8728	35.48	0.6831	27.77
19139	2.40	0.6280	26.17	0.3114	12.98	1.7773	74.05	1.4625	60.94	0.9423	39.26	0.6675	27.81

RAT NUMBER	BRAIN WEIGHT	TESTIS RIGHT ABS. WT.	TESTIS RIGHT REL. % BRW	PROSTATE ABS. WT.	PROSTATE REL. % BRW	LIVER ABS. WT.	LIVER REL. % BRW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % BRW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % BRW	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % BRW
19102	2.19	1.5930	72.74	1.2374	56.50	14.53	663.47	1.92	87.67	1.95	89.04	0.041	1.87
19106	2.57	1.6779	65.29	1.0360	40.31	17.19	668.87	1.97	76.65	2.00	77.82	0.024	0.93
19108	2.52	1.9171	76.08	1.1892	47.19	14.75	585.32	1.90	75.40	1.98	78.57	0.030	1.19
19110	2.42	1.4694	60.72	1.1812	48.81	13.95	576.45	1.96	80.99	2.00	82.64	0.037	1.53
19113	2.58	1.7350	67.25	1.2130	47.02	13.08	506.98	1.96a	75.97	2.11	81.78	0.046	1.78
19120	2.38	1.6765	70.44	1.4290	60.04	14.26	599.16	1.72	72.27	1.76	73.95	0.042	1.76
19129	2.45	1.8164	74.14	1.1232	45.84	13.37	545.71	1.89	77.14	1.90	77.55	0.037	1.51
19136	2.41	1.8039	74.85	1.3313	55.24	15.75	653.53	1.83	75.93	1.69	70.12	0.033	1.37
19138	2.46	1.7840	72.52	0.9939	40.40	11.25	457.32	1.58	64.23	1.66	67.48	0.028	1.14
19139	2.40	1.8078	75.32	1.2660	52.75	14.10	587.50	1.88	78.33	1.93	80.42	0.032	1.33

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.

a. Rat 19113 had slight dilation of the pelvis of the left kidney. See the individual necropsy observations table (Table B18).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B20 (PAGE 4): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP II 0.3 MG/KG/DAY

RAT NUMBER	BRAIN WEIGHT	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % BRW	SPLEEN ABS. WT.	SPLEEN REL. % BRW	THYMUS ABS. WT.	THYMUS REL. % BRW	HEART ABS. WT.	HEART REL. % BRW
19102	2.19	0.038	1.74	0.89	40.64	0.52	23.74	1.38	63.01
19106	2.57	0.024	0.93	0.86	33.46	0.42	16.34	1.56	60.70
19108	2.52	0.030	1.19	0.73	28.97	0.47	18.65	1.64	65.08
19110	2.42	0.038	1.57	0.85	35.12	0.41	16.94	1.59	65.70
19113	2.58	0.044	1.70	0.81	31.40	0.48	18.60	1.47	56.98
19120	2.38	0.038	1.60	0.83	34.87	0.40	16.81	1.56	65.55
19129	2.45	0.034	1.39	0.76	31.02	0.34	13.88	1.55	63.26
19136	2.41	0.034	1.41	0.72	29.88	0.58	24.07	1.71	70.95
19138	2.46	0.027	1.10	0.73	29.67	0.30	12.20	1.30	52.84
19139	2.40	0.032	1.33	0.92	38.33	0.54	22.50	1.46	60.83

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B20 (PAGE 5): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP III — 1 MG/KG/DAY

RAT NUMBER	BRAIN WEIGHT	EPIDIDYMIS LEFT ABS. WT.	EPIDIDYMIS LEFT REL. % BRW	CAUDA EPIDIDYMIS LEFT ABS. WT.	CAUDA EPIDIDYMIS LEFT REL. % BRW	TESTIS LEFT ABS. WT.	TESTIS LEFT REL. % BRW	SEMINAL VESICLES WITH FLUID ABS. WT.	SEMINAL VESICLES WITH FLUID REL. % BRW	SEMINAL VESICLES WITHOUT FLUID ABS. WT.	SEMINAL VESICLES WITHOUT FLUID REL. % BRW	EPIDIDYMIS RIGHT ABS. WT.	EPIDIDYMIS RIGHT REL. % BRW
19101	2.22	0.6021	27.12	0.2993	13.48	1.6371	73.74	1.1004	49.57	0.5923	26.68	0.6071	27.35
19105	2.40	0.7012	29.22	0.3377	14.07	2.0077	83.65	1.7433	72.64	0.7941	33.09	0.7481	31.17
19107	2.35	0.5355a	22.79	0.2667	11.35	1.4816	63.05	2.2034	93.76	0.9613	40.91	0.5625	23.94
19112	2.41	0.6158	25.55	0.3199	13.27	1.6088	66.76	1.6734	69.44	0.8909	36.97	0.6460	26.80
19114	2.36	0.5678	24.06	0.2915	12.35	1.4232	60.30	1.6586	70.28	0.7345	31.12	0.6091	25.81
19121	2.54	0.6466	25.46	0.3316	13.06	1.8123	71.35	1.6481	64.88	0.8330	32.80	0.6559	25.82
19123	2.43	0.6675	27.47	0.3384	13.92	1.7221	70.87	1.7452	71.82	0.9021	37.12	0.6825	28.09
19130	2.37	0.6775	28.59	0.3513	14.82	1.7366	73.27	1.7430	73.54	0.7931	33.46	0.7227	30.49
19137	2.45	0.6420	26.20	0.3467	14.15	1.6457	67.17	1.3000	53.06	0.7387	30.15	0.6680	27.26
19146	2.26	0.6207	27.46	0.3492	15.45	1.6423	72.67	1.5693	69.44	0.7248	32.07	0.6320	27.96

RAT NUMBER	BRAIN WEIGHT	TESTIS RIGHT ABS. WT.	TESTIS RIGHT REL. % BRW	PROSTATE ABS. WT.	PROSTATE REL. % BRW	LIVER ABS. WT.	LIVER REL. % BRW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % BRW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % BRW	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % BRW
19101	2.22	1.5806	71.20	0.8460	38.11	11.34	510.81	1.50	67.57	1.56	70.27	0.028	1.26
19105	2.40	2.0016	83.40	1.5220	63.42	17.13	713.75	2.37	98.75	2.29	95.42	0.034	1.42
19107	2.35	1.5096	64.24	1.5754	67.04	13.84	588.94	1.71	72.76	1.71	72.76	0.039	1.66
19112	2.41	1.6041	66.56	1.3786	57.20	14.51	602.07	2.09	86.72	1.97	81.74	0.026	1.08
19114	2.36	1.4506	61.47	1.1497	48.72	14.34	607.63	1.84	77.97	1.92	81.36	0.033	1.40
19121	2.54	1.7745	69.86	1.0712	42.17	23.98	944.09	2.20	86.61	2.25	88.58	0.032	1.26
19123	2.43	1.8031	74.20	0.9914	40.80	19.27	793.00	2.17	89.30	2.22	91.36	0.040	1.65
19130	2.37	1.8184	76.72	1.6000	67.51	13.79	581.86	1.88	79.32	1.98	83.54	0.030	1.26
19137	2.45	1.6928	69.09	1.0622	43.36	14.59	595.51	1.88	76.73	2.14	87.35	0.032	1.31
19146	2.26	1.6866	74.63	1.0704	47.36	16.57	733.18	1.94	85.84	2.01	88.94	0.042	1.86

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.
a. Damaged during processing (weight not affected).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B20 (PAGE 6): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP III 1 MG/KG/DAY

RAT NUMBER	BRAIN WEIGHT	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % BRW	SPLEEN ABS. WT.	SPLEEN REL. % BRW	THYMUS ABS. WT.	THYMUS REL. % BRW	HEART ABS. WT.	HEART REL. % BRW
19101	2.22	0.026	1.17	0.55	24.77	0.23	10.36	1.33	59.91
19105	2.40	0.027	1.12	0.74	30.83	0.47	19.58	1.66	69.17
19107	2.35	0.038	1.62	0.69	29.36	0.26	11.06	1.36	57.87
19112	2.41	0.022	0.91	0.65	26.97	0.55	22.82	1.48	61.41
19114	2.36	0.031	1.31	0.68	28.81	0.32	13.56	1.52	64.41
19121	2.54	0.035	1.38	0.92	36.22	0.44	17.32	1.70	66.93
19123	2.43	0.025	1.03	0.78	32.10	0.40	16.46	1.56	64.20
19130	2.37	0.033	1.39	0.87	36.71	0.33	13.92	1.48	62.45
19137	2.45	0.019	0.78	0.91	37.14	0.29	11.84	1.65	67.35
19146	2.26	0.043	1.90	0.80	35.40	0.28	12.39	1.65	73.01

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B20 (PAGE 7): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP IV — 3 MG/KG/DAY

RAT NUMBER	BRAIN WEIGHT	EPIDIDYMIS LEFT ABS. WT.	EPIDIDYMIS LEFT REL. % BRW	CAUDA EPIDIDYMIS LEFT ABS. WT.	CAUDA EPIDIDYMIS LEFT REL. % BRW	TESTIS LEFT ABS. WT.	TESTIS LEFT REL. % BRW	SEMINAL VESICLES WITH FLUID ABS. WT.	SEMINAL VESICLES WITH FLUID REL. % BRW	SEMINAL VESICLES WITHOUT FLUID ABS. WT.	SEMINAL VESICLES WITHOUT FLUID REL. % BRW	EPIDIDYMIS RIGHT ABS. WT.	EPIDIDYMIS RIGHT REL. % BRW
19100	2.40	0.6712	27.97	0.3355	13.98	1.7129	71.37	2.0456	85.23	1.0125	42.19	0.6970	29.04
19103	2.39	0.6486	27.14	0.2909	12.17	1.6530	69.16	2.0607	86.22	1.0014	41.90	0.6457	27.02
19104	2.43	0.6201	25.52	0.2961	12.18	1.7770	73.13	1.4443	59.44	0.7874	32.40	0.5846	24.06
19118	2.42	0.5834	24.11	0.3022	12.49	1.5495	64.03	1.6316	67.42	0.7381	30.50	0.6169	25.49
19133	2.47	0.5667	22.94	0.2961	11.99	1.7262	69.89	1.7327	70.15	0.8511	34.46	0.5492	22.23
19141	2.52	0.6531	25.92	0.3098	12.29	1.7814	70.69	1.4610	57.98	0.7077	28.08	0.6801	26.99
19142	2.23	0.3058a	13.71	0.1333a	5.98	0.6988a	31.34	1.1736	52.63	0.6729	30.17	0.3002a	13.46
19144	2.40	0.5626	23.44	0.2529	10.54	1.6357	68.15	1.3813	57.55	0.6369	26.54	0.6547	27.28
19148	2.24	0.6884	30.73	0.3851	17.19	1.8767	83.78	1.3721	61.25	0.6888	30.75	0.7389	32.99
19150	2.35	0.6161	26.22	0.3111	13.24	1.7049	72.55	1.1701	49.79	0.5734	24.40	0.6388	27.18

RAT NUMBER	BRAIN WEIGHT	TESTIS RIGHT ABS. WT.	TESTIS RIGHT REL. % BRW	PROSTATE ABS. WT.	PROSTATE REL. % BRW	LIVER ABS. WT.	LIVER REL. % BRW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % BRW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % BRW	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % BRW
19100	2.40	1.7274	71.98	1.5079	62.83	15.67	652.92	1.82	75.83	1.91	79.58	0.028	1.17
19103	2.39	1.7657	73.88	1.4347	60.03	19.28	806.69	2.40	100.42	2.39	100.00	0.040	1.67
19104	2.43	1.7025	70.06	1.2209	50.24	17.78	731.69	1.98	81.48	2.16	88.89	0.030	1.23
19118	2.42	1.6129	66.65	1.3183	54.48	15.97	659.92	1.90	78.51	2.12	87.60	0.030	1.24
19133	2.47	1.7045	69.01	1.2429	50.32	15.06	609.72	2.08	84.21	2.24	90.69	0.043	1.74
19141	2.52	1.7406	69.07	1.0238	40.63	20.42	810.32	2.18	86.51	2.20	87.30	0.024	0.95
19142	2.23	0.6700a	30.04	1.0863	48.71	17.61	789.69	2.00	89.69	2.07	92.82	0.028	1.26
19144	2.40	1.6766	69.86	1.1080	46.17	18.23	759.58	2.21	92.08	2.36	98.33	0.037	1.54
19148	2.24	1.8681	83.40	1.4524	64.84	18.08	807.14	1.91	85.27	1.92	85.71	0.028	1.25
19150	2.35	1.7068	72.63	1.3391	56.98	17.94	763.40	1.97	83.83	1.92	81.70	0.037	1.57

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.

a. Rat 19142 had small testes, epididymides and left cauda epididymis. See the individual necropsy observations table (Table B18).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B20 (PAGE 8): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP IV 3 MG/KG/DAY

RAT NUMBER	BRAIN WEIGHT	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % BRW	SPLEEN ABS. WT.	SPLEEN REL. % BRW	THYMUS ABS. WT.	THYMUS REL. % BRW	HEART ABS. WT.	HEART REL. % BRW
19100	2.40	0.032	1.33	0.86	35.83	0.40	16.67	1.42	59.17
19103	2.39	0.046	1.92	0.88	36.82	0.39	16.32	1.56	65.27
19104	2.43	0.026	1.07	1.10	45.27	0.40	16.46	1.64	67.49
19118	2.42	0.032	1.32	0.69	28.51	0.37	15.29	1.44	59.50
19133	2.47	0.041	1.66	0.74	29.96	0.36	14.57	1.60	64.78
19141	2.52	0.030	1.19	1.15	45.63	0.57	22.62	1.84	73.02
19142	2.23	0.028	1.26	0.74	33.18	0.48	21.52	1.54	69.06
19144	2.40	0.032	1.33	1.15	47.92	0.34	14.17	1.74	72.50
19148	2.24	0.026	1.16	0.78	34.82	0.35	15.62	1.55	69.20
19150	2.35	0.026	1.11	0.67	28.51	0.57	24.26	1.62	68.94

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B20 (PAGE 9): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP V — 10 MG/KG/DAY

RAT NUMBER	BRAIN WEIGHT	EPIDIDYMIS LEFT ABS. WT.	EPIDIDYMIS LEFT REL. % BRW	CAUDA EPIDIDYMIS LEFT ABS. WT.	CAUDA EPIDIDYMIS LEFT REL. % BRW	TESTIS LEFT ABS. WT.	TESTIS LEFT REL. % BRW	SEMINAL VESICLES WITH FLUID ABS. WT.	SEMINAL VESICLES WITH FLUID REL. % BRW	SEMINAL VESICLES WITHOUT FLUID ABS. WT.	SEMINAL VESICLES WITHOUT FLUID REL. % BRW	EPIDIDYMIS RIGHT ABS. WT.	EPIDIDYMIS RIGHT REL. % BRW
19111	2.48	0.5886	23.73	0.2814	11.35	1.7973	72.47	1.4923	60.17	0.7724	31.14	0.6626	26.72
19117	2.43	0.5554a	22.86	0.2921	12.02	1.5902	65.44	1.4692	60.46	0.8619	35.47	0.5723	23.55
19124	2.38	0.7041	29.58	0.3378	14.19	1.9441	81.68	1.6428	69.02	0.8490	35.67	0.6631	27.86
19126	2.28	0.5648	24.77	0.2550	11.18	1.5950	69.96	0.9950	43.64	0.5749	25.21	0.5576	24.46
19127	2.62	0.5950	22.71	0.3045	11.62	1.7552	66.99	1.6404	62.61	0.7509	28.66	0.5793	22.11
19128	2.31	0.5787	25.05	0.2725	11.80	1.5509	67.14	1.1019	47.70	0.6009	26.01	0.6242	27.02
19140	2.42	0.6181	25.54	0.2951	12.19	1.6009	66.15	1.5387	63.58	0.8782	36.29	0.6487	26.80
19145	2.40	0.6705	27.94	0.3537	14.74	1.8102	75.42	1.8705	77.94	0.9316	38.82	0.6428	26.78
19149	2.38	0.6384	26.82	0.3200	13.44	1.9607	82.38	1.4543	61.10	0.8120	34.12	0.6610	27.77
19152	2.34	0.6200	26.50	0.3288	14.05	1.8784	80.27	1.2190	52.09	0.7403	31.64	0.6498	27.77

RAT NUMBER	BRAIN WEIGHT	TESTIS RIGHT ABS. WT.	TESTIS RIGHT REL. % BRW	PROSTATE ABS. WT.	PROSTATE REL. % BRW	LIVER ABS. WT.	LIVER REL. % BRW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % BRW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % BRW	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % BRW
19111	2.48	1.7246	69.54	1.0515	42.40	24.36	982.26	2.00	80.64	2.13	85.89	0.025	1.01
19117	2.43	1.6160	66.50	1.0954	45.08	24.11	992.18	2.22	91.36	2.26	93.00	0.030	1.23
19124	2.38	1.8910	79.45	1.5146	63.64	25.72	1080.67	2.21	92.86	2.18	91.60	0.035	1.47
19126	2.28	1.6044	70.37	0.7260	31.84	22.94	1006.14	2.04	89.47	2.04	89.47	0.029	1.27
19127	2.62	1.7997	68.69	1.4010	53.47	27.38	1045.04	1.90	72.52	1.95	74.43	0.031	1.18
19128	2.31	1.5952	69.06	0.9706	42.02	21.74	941.12	1.78	77.06	1.82	78.79	0.036	1.56
19140	2.42	1.6407	67.80	1.2239	50.57	20.21	835.12	1.93	79.75	1.88	77.68	0.036	1.49
19145	2.40	1.8340	76.42	1.3756	57.32	23.20	966.67	2.27	94.58	2.16	90.00	0.034	1.42
19149	2.38	1.9989	83.99	1.2522	52.61	20.06	842.86	1.76	73.95	1.92	80.67	0.029	1.22
19152	2.34	1.8997	81.18	1.3077	55.88	18.58	794.02	1.97	84.19	2.07	88.46	0.036	1.54

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.
a. Damaged during processing (weight not affected).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B20 (PAGE 10): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP V — 10 MG/KG/DAY

RAT NUMBER	BRAIN WEIGHT	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % BRW	SPLEEN ABS. WT.	SPLEEN REL. % BRW	THYMUS ABS. WT.	THYMUS REL. % BRW	HEART ABS. WT.	HEART REL. % BRW
19111	2.48	0.024	0.97	0.73	29.44	0.37	14.92	1.38	55.64
19117	2.43	0.014	0.58	0.75	30.86	0.36	14.81	1.60	65.84
19124	2.38	0.034	1.43	0.72	30.25	0.36	15.13	1.40	58.82
19126	2.28	0.028	1.23	0.64	28.07	0.47	20.61	1.38	60.53
19127	2.62	0.031	1.18	0.81	30.92	0.47	17.94	1.43	54.58
19128	2.31	0.034	1.47	0.74	32.03	0.40	17.32	1.42	61.47
19140	2.42	0.028	1.16	0.86	35.54	0.44	18.18	1.50	61.98
19145	2.40	0.033	1.38	0.88	36.67	0.38	15.83	1.36	56.67
19149	2.38	0.030	1.26	0.97	40.76	0.43	18.07	1.46	61.34
19152	2.34	0.038	1.62	0.70	29.91	0.51	21.79	1.47	62.82

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B21 (PAGE 1): BODY WEIGHTS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT #	DOSAGE GROUP I															
	0 MG/KG/DAY															
DAY	1	2	3	4	5	6	7	8	9	10	11	12	13	14a	15	16
19109	322.	326.	334.	342.	344.	352.	357.	359.	355.	363.	370.	374.	380.	380.	376.	384.
19115	357.	361.	370.	374.	377.	388.	385.	393.	402.	408.	412.	417.	423.	427.	422.	430.
19116	347.	348.	360.	363.	372.	378.	385.	388.	389.	394.	402.	402.	408.	403.	410.	416.
19119	350.	356.	370.	378.	388.	394.	400.	414.	420.	424.	431.	446.	450.	454.	449.	452.
19122	328.	329.	320.	312.	336.	346.	350.	354.	358.	366.	372.	379.	380.	382.	389.	396.
19125	359.	364.	372.	382.	384.	392.	400.	409.	414.	420.	428.	431.	436.	440.	435.	435.
19131	341.	350.	357.	362.	375.	384.	388.	388.	403.	400.	407.	407.	419.	417.	418.	418.
19132	338.	339.	343.	347.	348.	356.	361.	359.	353.	363.	363.	369.	370.	376.	376.	376.
19134	332.	330.	342.	345.	350.	356.	358.	358.	366.	367.	370.	373.	373.	380.	357.	378.
19135	358.	359.	372.	380.	381.	391.	393.	398.	395.	398.	408.	403.	416.	417.	416.	424.
19143	338.	334.	344.	347.	357.	358.	363.	366.	365.	374.	381.	381.	387.	390.	387.	388.
19151	346.	350.	362.	366.	370.	378.	380.	387.	389.	392.	400.	404.	407.	406.	404.	408.
19157	331.	337.	344.	350.	355.	362.	363.	370.	369.	377.	378.	384.	394.	393.	384.	392.
19161	362.	373.	385.	392.	399.	411.	417.	424.	425.	416.	436.	433.	436.	446.	449.	457.
19167	332.	340.	347.	351.	359.	365.	372.	373.	382.	382.	388.	391.	391.	399.	396.	401.

DAY	17	18	19	20	21	22	23	24	25	26	27	28	29b	30	31	32
19109	390.	391.	392.	398.	400.	398.	396.	403.	406.	409.	420.	420.	421.	427.	430.	435.
19115	429.	442.	443.	451.	449.	455.	458.	460.	465.	463.	462.	453.	472.	469.	479.	472.
19116	413.	422.	420.	425.	431.	432.	442.	448.	448.	452.	461.	469.	462.	466.	476.	479.
19119	455.	463.	470.	476.	478.	485.	483.	492.	494.	504.	513.	511.	504.	510.	518.	516.
19122	396.	399.	399.	405.	406.	409.	413.	420.	419.	421.	426.	432.	432.	434.	440.	441.
19125	435.	434.	442.	448.	452.	452.	465.	471.	478.	482.	486.	489.	491.	493.	500.	498.
19131	417.	432.	425.	438.	435.	440.	447.	450.	456.	458.	470.	470.	479.	479.	484.	494.
19132	384.	392.	393.	410.	415.	406.	407.	406.	418.	420.	424.	426.	428.	428.	431.	438.
19134	371.	377.	377.	380.	385.	381.	381.	387.	388.	394.	396.	404.	404.	406.	415.	419.
19135	426.	432.	430.	440.	437.	440.	442.	446.	449.	453.	464.	465.	468.	469.	470.	477.
19143	392.	393.	400.	406.	408.	407.	413.	414.	417.	426.	432.	440.	435.	440.	444.	453.
19151	411.	413.	408.	423.	424.	428.	430.	434.	446.	445.	450.	452.	463.	461.	457.	464.
19157	394.	397.	396.	410.	405.	409.	411.	420.	424.	429.	432.	409.	438.	434.	439.	441.
19161	463.	468.	474.	483.	488.	499.	502.	508.	517.	518.	532.	539.	546.	544.	548.	555.
19167	410.	409.	419.	425.	422.	378.	368.	363.	373.	389.	396.	405.	406.	414.	398.	421.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.
b. First value recorded after cohabitation.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B21 (PAGE 2): BODY WEIGHTS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT #	DOSAGE GROUP I														0 MG/KG/DAY
DAY	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47
19109	442.	446.	452.	443.	451.	447.	450.	455.	463.	466.	438.				
19115	439.	482.	485.	476.	490.	487.	491.	490.	498.	499.	466.				
19116	477.	485.	490.	491.	490.	492.	494.	501.	501.	503.	509.	490.			
19119	521.	532.	538.	533.	523.	526.	527.	529.	526.	537.	538.	505.			
19122	437.	451.	449.	455.	458.	467.	467.	468.	468.	475.	474.	451.			
19125	503.	509.	517.	517.	527.	517.	528.	528.	528.	534.	534.	543.	508.		
19131	492.	497.	501.	513.	512.	506.	514.	516.	515.	520.	528.	530.	499.		
19132	444.	446.	446.	448.	450.	439.	454.	458.	465.	466.	463.	474.	439.		
19134	421.	424.	426.	433.	438.	431.	434.	436.	441.	444.	436.	446.	445.	419.	
19135	485.	486.	493.	490.	504.	494.	496.	502.	502.	504.	504.	511.	509.	482.	
19143	458.	456.	466.	468.	472.	470.	477.	478.	476.	486.	491.	493.	495.	499.	469.
19151	473.	466.	461.	474.	481.	474.	481.	482.	482.	484.	482.	490.	500.	503.	470.
19157	441.	443.	447.	455.	458.	459.	460.	463.	470.	473.	478.	483.	491.	486.	462.
19161	557.	561.	560.	566.	567.	571.	564.	571.	562.	556.	559.	569.	575.	583.	549.
19167	424.	426.	438.	441.	445.	446.	445.	451.	451.	456.	458.	458.	462.	472.	441.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B21 (PAGE 3): BODY WEIGHTS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT #	DOSAGE GROUP II															0.3 MG/KG/DAY
DAY	1	2	3	4	5	6	7	8	9	10	11	12	13	14a	15	16
19102	315.	321.	322.	328.	336.	339.	348.	349.	353.	362.	367.	370.	365.	366.	363.	376.
19106	360.	356.	369.	379.	383.	398.	400.	405.	408.	415.	424.	432.	433.	438.	437.	441.
19108	340.	351.	361.	371.	377.	386.	389.	396.	401.	405.	415.	417.	422.	427.	428.	426.
19110	348.	356.	358.	368.	372.	385.	385.	389.	391.	392.	400.	404.	410.	416.	387.	390.
19113	328.	340.	344.	352.	354.	362.	368.	369.	369.	375.	389.	388.	396.	390.	391.	396.
19120	355.	358.	368.	376.	381.	387.	389.	396.	402.	404.	412.	414.	421.	423.	421.	433.
19129	333.	340.	346.	354.	361.	368.	367.	373.	366.	377.	386.	387.	392.	398.	388.	391.
19136	346.	352.	367.	370.	378.	389.	392.	396.	402.	404.	414.	413.	426.	421.	414.	414.
19138	314.	323.	319.	326.	326.	328.	331.	330.	330.	333.	336.	338.	344.	348.	334.	336.
19139	339.	343.	348.	350.	356.	366.	362.	369.	374.	378.	381.	385.	388.	391.	385.	388.
19147	331.	335.	346.	348.	356.	362.	366.	375.	370.	379.	387.	389.	397.	399.	397.	397.
19153	346.	345.	337.	362.	365.	371.	375.	379.	381.	392.	392.	398.	405.	409.	404.	417.
19164	338.	338.	344.	352.	360.	362.	369.	379.	382.	386.	395.	399.	404.	402.	407.	414.
19165	342.	347.	355.	357.	362.	359.	367.	371.	382.	384.	388.	392.	400.	400.	401.	409.
19171	348.	353.	356.	355.	363.	367.	368.	365.	366.	366.	368.	372.	378.	382.	375.	385.

DAY	17	18	19	20	21	22	23	24	25	26	27	28	29b	30	31	32
19102	375.	382.	389.	396.	399.	396.	403.	407.	411.	415.	421.	413.	424.	426.	430.	431.
19106	438.	444.	443.	446.	452.	453.	457.	459.	467.	469.	470.	476.	484.	485.	489.	482.
19108	429.	435.	436.	446.	442.	439.	444.	447.	451.	456.	461.	464.	471.	466.	483.	478.
19110	404.	410.	418.	422.	420.	423.	437.	431.	439.	442.	444.	447.	450.	453.	454.	461.
19113	396.	396.	406.	408.	412.	410.	417.	423.	421.	429.	433.	434.	436.	442.	447.	449.
19120	433.	441.	438.	447.	451.	454.	458.	457.	459.	467.	477.	479.	483.	481.	486.	490.
19129	402.	408.	408.	411.	417.	417.	424.	425.	429.	430.	433.	436.	445.	440.	449.	448.
19136	420.	429.	435.	440.	446.	446.	454.	455.	458.	465.	472.	480.	480.	481.	487.	491.
19138	340.	343.	346.	353.	358.	352.	353.	360.	360.	364.	370.	368.	371.	372.	372.	380.
19139	385.	392.	395.	403.	407.	406.	410.	412.	416.	419.	424.	430.	427.	432.	433.	433.
19147	396.	403.	412.	419.	420.	428.	430.	432.	434.	445.	447.	452.	459.	452.	462.	466.
19153	418.	425.	423.	433.	439.	444.	444.	449.	450.	457.	463.	469.	473.	470.	480.	481.
19164	411.	423.	429.	433.	442.	439.	453.	454.	453.	451.	463.	470.	472.	465.	476.	480.
19165	406.	412.	411.	422.	429.	424.	434.	434.	442.	448.	454.	459.	460.	455.	462.	468.
19171	384.	393.	386.	399.	395.	396.	401.	406.	408.	411.	415.	412.	419.	423.	423.	423.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.
b. First value recorded after cohabitation.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B21 (PAGE 4): BODY WEIGHTS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT #	DOSAGE GROUP II						0.3 MG/KG/DAY								
DAY	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47
19102	431.	436.	440.	443.	455.	450.	455.	461.	453.	456.	428.				
19106	489.	488.	488.	486.	499.	501.	508.	502.	501.	506.	476.				
19108	483.	484.	490.	486.	489.	479.	485.	485.	488.	495.	498.	474.			
19110	465.	464.	464.	461.	462.	471.	473.	474.	474.	481.	480.	453.			
19113	451.	453.	453.	464.	458.	456.	460.	463.	466.	464.	468.	444.			
19120	491.	496.	497.	503.	509.	493.	506.	508.	509.	505.	517.	524.	486.		
19129	448.	451.	451.	456.	450.	440.	455.	460.	461.	463.	459.	466.	435.		
19136	503.	506.	508.	511.	513.	504.	524.	523.	522.	528.	534.	537.	495.		
19138	375.	380.	379.	383.	389.	382.	382.	387.	386.	390.	388.	389.	396.	365.	
19139	433.	442.	451.	450.	451.	451.	447.	461.	450.	462.	458.	462.	464.	432.	
19147	466.	474.	471.	475.	478.	469.	478.	480.	484.	497.	481.	496.	499.	498.	470.
19153	482.	486.	490.	494.	495.	498.	498.	500.	505.	502.	504.	511.	513.	506.	487.
19164	487.	490.	497.	489.	501.	504.	493.	495.	500.	509.	516.	512.	517.	521.	484.
19165	470.	466.	464.	468.	470.	473.	478.	467.	476.	480.	486.	490.	489.	492.	455.
19171	426.	420.	425.	428.	428.	431.	424.	424.	427.	435.	434.	443.	444.	453.	421.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B21 (PAGE 5): BODY WEIGHTS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT #	DOSAGE GROUP III												1 MG/KG/DAY			
DAY	1	2	3	4	5	6	7	8	9	10	11	12	13	14a	15	16
19101	309.	308.	312.	317.	317.	320.	322.	324.	323.	318.	325.	327.	333.	335.	319.	326.
19105	368.	372.	383.	388.	395.	404.	411.	399.	420.	422.	418.	428.	432.	432.	429.	439.
19107	344.	350.	356.	367.	368.	380.	382.	387.	393.	390.	395.	400.	394.	411.	403.	414.
19112	345.	353.	360.	363.	371.	374.	378.	381.	386.	388.	387.	393.	400.	405.	406.	398.
19114	325.	331.	334.	338.	343.	348.	352.	353.	356.	359.	365.	364.	369.	371.	363.	361.
19121	359.	368.	381.	389.	403.	409.	403.	408.	433.	428.	444.	452.	452.	465.	445.	477.
19123	337.	339.	350.	356.	365.	371.	375.	386.	384.	386.	397.	404.	411.	415.	407.	415.
19130	345.	346.	354.	356.	363.	369.	371.	374.	378.	383.	385.	387.	392.	389.	384.	386.
19137	329.	330.	342.	349.	353.	355.	364.	367.	372.	370.	371.	383.	381.	387.	386.	393.
19146	354.	357.	367.	374.	379.	384.	393.	394.	396.	400.	407.	408.	412.	413.	405.	412.
19155	337.	341.	347.	354.	356.	367.	371.	374.	381.	370.	376.	380.	388.	398.	383.	396.
19159	346.	351.	367.	368.	376.	385.	390.	396.	390.	389.	398.	408.	403.	413.	401.	409.
19172	350.	350.	362.	373.	378.	388.	398.	402.	411.	415.	428.	430.	420.	434.	414.	437.
19173	351.	355.	363.	373.	376.	383.	388.	393.	395.	391.	402.	405.	410.	408.	409.	413.
19174	330.	334.	343.	346.	353.	360.	362.	369.	374.	377.	376.	383.	389.	388.	373.	386.

DAY	17	18	19	20	21	22	23	24	25	26	27	28	29b	30	31	32
19101	326.	337.	333.	340.	343.	335.	345.	341.	343.	346.	350.	353.	355.	359.	363.	365.
19105	430.	443.	454.	453.	455.	462.	461.	469.	473.	478.	481.	491.	497.	500.	509.	509.
19107	415.	413.	415.	424.	432.	428.	436.	438.	434.	441.	439.	442.	447.	451.	450.	450.
19112	407.	415.	415.	423.	424.	433.	433.	435.	444.	445.	451.	452.	458.	456.	458.	461.
19114	366.	367.	374.	370.	381.	379.	389.	390.	397.	400.	407.	408.	411.	422.	422.	423.
19121	474.	480.	488.	499.	502.	511.	522.	528.	528.	533.	538.	547.	557.	558.	568.	571.
19123	414.	418.	426.	433.	439.	438.	439.	448.	446.	454.	455.	460.	461.	468.	466.	468.
19130	389.	393.	397.	405.	406.	411.	415.	418.	419.	421.	428.	434.	433.	425.	438.	438.
19137	401.	402.	404.	406.	410.	417.	421.	424.	428.	429.	440.	436.	443.	443.	452.	449.
19146	409.	419.	426.	428.	435.	430.	444.	444.	452.	449.	457.	460.	462.	470.	471.	473.
19155	401.	405.	409.	416.	418.	422.	429.	437.	442.	443.	454.	457.	458.	457.	467.	471.
19159	416.	409.	417.	417.	428.	428.	431.	435.	433.	448.	463.	458.	462.	454.	460.	463.
19172	435.	440.	447.	456.	461.	464.	470.	479.	484.	487.	493.	500.	505.	506.	506.	514.
19173	426.	430.	432.	436.	442.	441.	443.	442.	448.	456.	459.	459.	463.	456.	460.	466.
19174	388.	388.	396.	401.	406.	411.	414.	418.	420.	428.	431.	433.	437.	437.	444.	447.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.
b. First value recorded after cohabitation.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B21 (PAGE 6): BODY WEIGHTS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT #	DOSAGE GROUP III							1 MG/KG/DAY							
DAY	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47
19101	369.	370.	374.	369.	373.	373.	374.	379.	375.	379.	353.				
19105	515.	522.	519.	528.	538.	537.	536.	535.	533.	532.	505.				
19107	454.	455.	461.	457.	458.	449.	449.	453.	456.	460.	437.				
19112	468.	463.	471.	470.	474.	473.	480.	480.	480.	478.	482.	452.			
19114	428.	430.	435.	436.	442.	442.	446.	445.	450.	451.	454.	430.			
19121	573.	576.	579.	584.	598.	590.	602.	600.	606.	606.	603.	616.	567.		
19123	472.	474.	481.	483.	478.	469.	482.	483.	489.	491.	497.	494.	464.		
19130	449.	447.	450.	449.	452.	454.	448.	452.	464.	466.	466.	461.	470.	434.	
19137	453.	457.	456.	462.	469.	465.	461.	474.	474.	471.	473.	473.	468.	443.	
19146	478.	478.	479.	481.	481.	483.	475.	480.	493.	493.	495.	496.	499.	473.	
19155	467.	474.	475.	479.	477.	481.	481.	486.	492.	494.	493.	502.	500.	504.	481.
19159	470.	466.	476.	480.	480.	482.	485.	483.	484.	494.	494.	484.	498.	506.	475.
19172	514.	508.	520.	528.	534.	531.	534.	531.	532.	538.	541.	547.	549.	556.	526.
19173	467.	471.	476.	486.	485.	483.	482.	466.	477.	483.	483.	485.	483.	486.	459.
19174	449.	453.	457.	460.	457.	462.	461.	457.	461.	461.	461.	466.	471.	473.	448.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B21 (PAGE 7): BODY WEIGHTS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT #	DOSAGE GROUP IV								3 MG/KG/DAY							
DAY	1	2	3	4	5	6	7	8	9	10	11	12	13	14a	15	16
19100	332.	332.	341.	344.	348.	356.	363.	363.	366.	366.	378.	377.	376.	381.	375.	382.
19103	363.	363.	379.	386.	393.	403.	415.	417.	428.	425.	434.	436.	439.	446.	435.	441.
19104	351.	360.	366.	375.	383.	389.	398.	401.	405.	400.	408.	412.	412.	423.	426.	432.
19118	342.	352.	358.	362.	363.	370.	374.	376.	380.	383.	389.	394.	397.	399.	399.	394.
19133	338.	338.	339.	347.	354.	357.	362.	364.	368.	372.	384.	393.	393.	388.	386.	395.
19141	363.	374.	382.	391.	396.	406.	414.	422.	426.	431.	438.	451.	450.	457.	452.	466.
19142	334.	338.	345.	354.	363.	368.	374.	379.	389.	387.	391.	398.	400.	410.	407.	415.
19144	348.	357.	368.	378.	386.	393.	405.	410.	418.	422.	434.	436.	430.	436.	434.	437.
19148	336.	343.	342.	355.	360.	366.	376.	378.	388.	378.	388.	389.	393.	398.	395.	403.
19150	356.	360.	372.	377.	384.	390.	391.	396.	399.	395.	404.	407.	410.	411.	406.	419.
19156	333.	330.	333.	337.	346.	358.	361.	360.	368.	366.	384.	386.	382.	394.	385.	395.
19160	351.	351.	364.	375.	376.	388.	395.	392.	392.	396.	404.	401.	412.	417.	396.	417.
19162	331.	333.	334.	338.	341.	344.	347.	351.	352.	354.	358.	369.	366.	369.	365.	372.
19163	350.	356.	364.	368.	379.	387.	393.	394.	401.	405.	418.	412.	410.	422.	412.	419.
19166	356.	359.	373.	385.	388.	398.	404.	396.	415.	416.	430.	430.	439.	443.	437.	447.

DAY	17	18	19	20	21	22	23	24	25	26	27	28	29b	30	31	32
19100	390.	391.	396.	400.	403.	405.	404.	408.	411.	414.	418.	425.	428.	428.	431.	432.
19103	451.	458.	457.	470.	468.	470.	479.	489.	483.	486.	488.	490.	492.	498.	497.	499.
19104	438.	439.	436.	452.	454.	454.	458.	461.	467.	464.	471.	478.	479.	481.	481.	481.
19118	398.	406.	409.	419.	425.	426.	430.	429.	433.	434.	442.	444.	446.	449.	447.	451.
19133	395.	404.	410.	415.	421.	421.	432.	427.	439.	440.	441.	445.	449.	446.	443.	451.
19141	462.	473.	476.	476.	486.	490.	499.	502.	505.	512.	519.	518.	531.	526.	533.	539.
19142	420.	425.	431.	435.	441.	438.	448.	450.	455.	463.	469.	471.	472.	475.	485.	490.
19144	435.	451.	444.	456.	459.	462.	471.	474.	480.	494.	497.	497.	509.	518.	519.	517.
19148	405.	412.	417.	421.	421.	424.	431.	434.	437.	438.	450.	452.	455.	451.	457.	465.
19150	418.	427.	432.	441.	440.	436.	448.	442.	454.	450.	462.	462.	464.	458.	467.	474.
19156	396.	392.	402.	411.	411.	409.	416.	417.	419.	423.	422.	430.	436.	436.	435.	438.
19160	421.	424.	427.	434.	437.	431.	446.	442.	449.	450.	461.	470.	464.	468.	475.	473.
19162	377.	376.	381.	382.	390.	392.	397.	402.	400.	408.	409.	410.	415.	414.	415.	417.
19163	429.	434.	438.	453.	455.	448.	462.	463.	459.	463.	468.	478.	484.	476.	481.	479.
19166	456.	460.	465.	473.	480.	480.	480.	487.	488.	493.	500.	502.	503.	505.	505.	505.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.
b. First value recorded after cohabitation.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B21 (PAGE 8): BODY WEIGHTS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT #	DOSAGE GROUP IV						3 MG/KG/DAY								
DAY	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47
19100	435.	438.	440.	441.	445.	447.	448.	455.	449.	454.	421.				
19103	497.	502.	503.	499.	508.	513.	516.	509.	511.	516.	487.				
19104	484.	488.	484.	486.	497.	499.	506.	506.	502.	506.	509.	476.			
19118	448.	452.	459.	458.	457.	459.	464.	467.	464.	469.	470.	442.			
19133	452.	453.	454.	461.	457.	464.	470.	474.	470.	475.	484.	448.			
19141	537.	537.	543.	545.	556.	557.	566.	570.	567.	564.	574.	585.	545.		
19142	494.	489.	491.	496.	510.	497.	501.	504.	500.	504.	505.	515.	479.		
19144	524.	524.	528.	531.	539.	533.	546.	536.	547.	552.	547.	553.	523.		
19148	460.	461.	469.	473.	482.	482.	481.	489.	485.	486.	482.	495.	495.	454.	
19150	468.	463.	466.	470.	470.	472.	472.	463.	478.	481.	476.	472.	479.	448.	
19156	438.	442.	441.	448.	446.	450.	447.	452.	452.	457.	453.	447.	455.	460.	433.
19160	473.	475.	479.	479.	485.	488.	486.	480.	483.	481.	478.	496.	493.	491.	461.
19162	419.	418.	426.	424.	429.	427.	431.	433.	435.	434.	435.	441.	449.	445.	415.
19163	491.	483.	490.	492.	494.	492.	497.	492.	500.	503.	508.	516.	513.	512.	486.
19166	511.	511.	517.	513.	519.	525.	525.	520.	522.	523.	528.	535.	531.	537.	506.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B21 (PAGE 9): BODY WEIGHTS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT #	DOSAGE GROUP V															10 MG/KG/DAY
DAY	1	2	3	4	5	6	7	8	9	10	11	12	13	14a	15	16
19111	326.	334.	339.	346.	351.	360.	370.	370.	374.	382.	390.	389.	391.	393.	389.	396.
19117	363.	365.	375.	381.	382.	387.	393.	393.	390.	392.	404.	401.	408.	416.	405.	416.
19124	345.	346.	354.	360.	365.	372.	372.	379.	382.	389.	389.	379.	389.	393.	385.	397.
19126	344.	349.	356.	360.	365.	370.	371.	371.	377.	377.	384.	383.	391.	389.	386.	390.
19127	329.	335.	342.	351.	357.	366.	365.	370.	376.	378.	379.	383.	387.	395.	362.	394.
19128	358.	358.	367.	372.	376.	382.	382.	385.	389.	394.	390.	406.	409.	408.	411.	415.
19140	331.	328.	347.	346.	353.	359.	362.	366.	373.	379.	380.	387.	388.	393.	386.	396.
19145	348.	349.	358.	366.	375.	375.	382.	386.	388.	393.	395.	398.	406.	406.	387.	394.
19149	325.	324.	331.	339.	339.	346.	352.	354.	352.	359.	368.	367.	367.	369.	368.	375.
19152	347.	360.	358.	367.	371.	378.	384.	385.	382.	388.	394.	396.	401.	405.	399.	407.
19154	346.	346.	354.	355.	363.	369.	376.	371.	378.	381.	388.	385.	394.	401.	397.	409.
19158	350.	351.	362.	368.	373.	379.	384.	387.	389.	385.	398.	395.	394.	401.	398.	408.
19168	329.	329.	338.	341.	342.	352.	356.	359.	360.	369.	376.	378.	380.	378.	374.	385.
19169	358.	360.	365.	372.	375.	379.	381.	388.	390.	391.	403.	403.	409.	410.	411.	424.
19170	350.	353.	359.	365.	368.	382.	382.	386.	386.	390.	396.	395.	402.	402.	400.	396.

DAY	17	18	19	20	21	22	23	24	25	26	27	28	29b	30	31	32
19111	401.	403.	407.	410.	412.	414.	426.	424.	427.	429.	437.	436.	438.	440.	440.	442.
19117	410.	424.	423.	427.	428.	430.	438.	446.	444.	445.	456.	456.	463.	460.	464.	466.
19124	403.	397.	402.	409.	409.	410.	415.	410.	413.	416.	419.	425.	430.	429.	428.	433.
19126	394.	393.	394.	400.	402.	400.	400.	400.	406.	407.	415.	420.	418.	422.	420.	423.
19127	388.	382.	384.	398.	402.	405.	464.c	417.	416.	421.	432.	436.	436.	435.	440.	446.
19128	414.	425.	429.	429.	430.	434.	436.	433.	430.	440.	439.	443.	444.	444.	451.	449.
19140	401.	407.	415.	417.	424.	417.	420.	428.	430.	436.	434.	442.	440.	446.	450.	448.
19145	399.	401.	407.	414.	418.	414.	421.	424.	424.	430.	435.	437.	440.	440.	447.	453.
19149	383.	376.	383.	386.	396.	399.	402.	405.	406.	407.	417.	417.	422.	422.	433.	434.
19152	412.	415.	416.	418.	426.	399.	406.	410.	417.	424.	430.	432.	430.	440.	445.	449.
19154	408.	409.	411.	412.	417.	416.	414.	415.	419.	427.	437.	437.	443.	448.	452.	463.
19158	412.	412.	414.	422.	427.	428.	432.	431.	432.	439.	440.	447.	447.	443.	446.	450.
19168	390.	394.	388.	391.	394.	390.	387.	392.	390.	396.	403.	404.	405.	404.	409.	414.
19169	424.	429.	431.	438.	438.	436.	446.	447.	444.	447.	454.	456.	463.	466.	461.	468.
19170	407.	412.	410.	418.	421.	420.	424.	428.	428.	433.	443.	443.	446.	448.	452.	455.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.
b. First value recorded after cohabitation.
c. Value appeared incorrectly recorded and was excluded from group averages and statistical analyses.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B21 (PAGE 10): BODY WEIGHTS - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT #	DOSAGE GROUP V														10 MG/KG/DAY
DAY	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47
19111	446.	456.	449.	449.	457.	456.	455.	461.	468.	466.	432.				
19117	465.	467.	473.	467.	477.	481.	484.	480.	486.	483.	462.				
19124	434.	437.	443.	438.	448.	445.	449.	445.	448.	450.	426.				
19126	430.	436.	431.	435.	429.	438.	437.	445.	446.	452.	452.	426.			
19127	448.	456.	448.	454.	444.	454.	453.	458.	455.	470.	467.	434.			
19128	458.	457.	459.	461.	473.	463.	473.	469.	472.	470.	481.	486.	445.		
19140	452.	449.	456.	453.	464.	454.	466.	465.	466.	469.	473.	486.	442.		
19145	454.	451.	455.	455.	460.	463.	459.	465.	464.	471.	473.	477.	466.	441.	
19149	443.	442.	444.	451.	453.	460.	454.	463.	460.	459.	462.	466.	468.	439.	
19152	450.	455.	458.	461.	464.	463.	464.	476.	479.	483.	485.	498.	491.	461.	
19154	458.	466.	468.	472.	479.	477.	480.	491.	488.	496.	490.	496.	498.	498.	466.
19158	449.	448.	450.	453.	461.	458.	456.	460.	462.	469.	474.	461.	478.	471.	453.
19168	412.	414.	418.	414.	417.	423.	423.	420.	412.	416.	416.	421.	421.	425.	402.
19169	471.	469.	472.	484.	485.	485.	479.	471.	474.	486.	479.	477.	482.	480.	448.
19170	456.	460.	459.	465.	460.	462.	466.	457.	452.	457.	459.	463.	467.	471.	445.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B22 (PAGE 1): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DAYS	1- 8a	29b-36
RAT #	DOSAGE GROUP I	0 MG/KG/DAY
19109	229.	c
19115	187.	199.
19116	188.	209.
19119	236.	238.
19122	164.	204.
19125	212.	235.
19131	213.	222.
19132	169.	189.
19134	184.	198.
19135	199.	208.
19143	196.	220.
19151	195.	190.
19157	195.	212.
19161	235.	244.
19167	187.	191.
RAT #	DOSAGE GROUP II	0.3 MG/KG/DAY
19102	193.	200.
19106	212.	192.
19108	222.	216.
19110	199.	202.
19113	200.	203.
19120	200.	195.
19129	196.	190.
19136	212.	226.
19138	169.	179.
19139	184.	201.
19147	189.	203.
19153	188.	201.
19164	196.	246.
19165	178.	189.
19171	187.	178.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.
b. First value recorded after cohabitation.
c. Spilled feed precluded the calculation of this value.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B22 (PAGE 2): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DAYS	1- 8a	29b-36
RAT #	DOSAGE GROUP III	1 MG/KG/DAY
19101	153.	186.
19105	207.	219.
19107	211.	204.
19112	209.	209.
19114	188.	199.
19121	224.	253.
19123	192.	204.
19130	190.	192.
19137	207.	219.
19146	190.	194.
19155	194.	208.
19159	251.	231.
19172	240.	222.
19173	206.	192.
19174	195.	197.
RAT #	DOSAGE GROUP IV	3 MG/KG/DAY
19100	186.	191.
19103	222.	218.
19104	204.	209.
19118	181.	188.
19133	194.	208.
19141	233.	236.
19142	195.	232.
19144	227.	238.
19148	199.	212.
19150	214.	181.
19156	176.	177.
19160	214.	207.
19162	171.	181.
19163	206.	197.
19166	200.	201.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.
b. First value recorded after cohabitation.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B22 (PAGE 3): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DAYS	1- 8a	29b-36
RAT #	DOSAGE GROUP V	10 MG/KG/DAY
19111	193.	186.
19117	183.	206.
19124	191.	178.
19126	181.	188.
19127	198.	198.
19128	197.	218.
19140	177.	193.
19145	191.	194.
19149	170.	206.
19152	187.	200.
19154	198.	227.
19158	202.	191.
19168	175.	168.
19169	198.	216.
19170	189.	198.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.
b. First value recorded after cohabitation.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B23 (PAGE 1): MATING AND FERTILITY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT #	DAYS IN COHABITATION	MATING STATUS	MATING DATE	FEMALE PREGNANCY STATUS
DOSAGE GROUP I		0 MG/KG/DAY		
19109	7	DID NOT MATE	-	-(19010)
19115	2	M	C	P(19012)
19116	3	M	C	P(19019)
19119	2	M	C	P(19021)
19122	4	M	C	P(19023)
19125	4	M	C	P(19041)
19131	3	M	C	P(19042)
19132	1	M	C	P(19044)
19134	4	M	C	P(19050)
19135	3	M	C	P(19053)
19143	3	M	C	P(19065)
19151	2	M	C	P(19068)
19157a	4	M	C	P(19072)
19157b	7	M	C	P(19010)
19161	2	M	C	P(19074)
19167	4	M	C	P(19075)
DOSAGE GROUP II		0.3 MG/KG/DAY		
19102	4	M	C	P(19004)
19106	1	M	C	P(19009)
19108	1	M	C	P(19016)
19110	2	M	C	P(19018)
19113	4	M	C	P(19026)
19120	1	M	C	P(19036)
19129	2	M	C	P(19037)
19136	1	M	C	P(19043)
19138	1	M	C	P(19047)
19139	4	M	C	P(19048)
19147	1	M	C	P(19052)
19153	1	M	C	P(19055)
19164	2	M	C	P(19061)
19165	3	M	C	P(19067)
19171	1	M	C	P(19071)

M = MATED ( ) = FEMALE RAT NUMBER
C = CONFIRMED
P = PREGNANT NP = NOT PREGNANT
a. Result of first cohabitation period.
b. Result of second cohabitation period.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B23 (PAGE 2): MATING AND FERTILITY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT #	DAYS IN COHABITATION	MATING STATUS	MATING DATE	FEMALE PREGNANCY STATUS
DOSAGE GROUP III		1 MG/KG/DAY		
19101	3	M	C	P(19003)
19105	3	M	C	P(19007)
19107	4	M	C	P(19008)
19112	2	M	C	P(19013)
19114	1	M	C	NP(19014)
19121	4	M	C	P(19015)
19123	1	M	C	P(19017)
19130	4	M	C	P(19024)
19137	2	M	C	P(19029)
19146	3	M	C	P(19034)
19155	1	M	C	NP(19038)
19159	4	M	C	P(19056)
19172	4	M	C	P(19057)
19173	2	M	C	P(19060)
19174	4	M	C	P(19064)
DOSAGE GROUP IV		3 MG/KG/DAY		
19100	7	DID NOT MATE	-	-(19002)
19103	4	M	C	P(19005)
19104	4	M	C	P(19035)
19118	2	M	C	P(19039)
19133	4	M	C	P(19040)
19141	1	M	C	P(19045)
19142	1	M	C	NP(19046)
19144	7	DID NOT MATE	-	-(19051)
19148	3	M	C	P(19054)
19150	1	M	C	P(19058)
19156a	4	M	C	P(19062)
19156b	6	M	C	P(19002)
19160	2	M	C	P(19063)
19162	4	M	C	P(19066)
19163a	2	M	C	P(19069)
19163b	7	DID NOT MATE	-	-(19051)
19166	1	M	C	P(19073)

M = MATED ( ) = FEMALE RAT NUMBER
C = CONFIRMED
P = PREGNANT NP = NOT PREGNANT
a. Result of first cohabitation period.
b. Result of second cohabitation period.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B23 (PAGE 3): MATING AND FERTILITY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT #	DAYS IN COHABITATION	MATING STATUS	MATING DATE	FEMALE PREGNANCY STATUS
DOSAGE GROUP V		10 MG/KG/DAY		
19111	1	M	C	P(19001)
19117	3	M	C	P(19006)
19124	4	M	C	P(19011)
19126	4	M	C	P(19020)
19127	4	M	C	P(19022)
19128	3	M	C	P(19025)
19140	4	M	C	P(19027)
19145	1	M	C	P(19028)
19149	4	M	C	P(19030)
19152	1	M	C	P(19031)
19154	4	M	C	P(19032)
19158	1	M	C	P(19033)
19168	1	M	C	P(19049)
19169	1	M	C	P(19059)
19170	1	M	C	P(19070)

M = MATED ( ) = FEMALE RAT NUMBER
C = CONFIRMED
P = PREGNANT NP = NOT PREGNANT

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B24 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP I	0 MG/KG/DAY									
RAT #	19109	19115	19116	19119	19122	19125	19131	19132	19134	19135
HOME CAGE BEHAVIOR	2	2	2	2	2	2	1	2	2	1
ALTERATIONS (HOME CAGE)	1	1	1	1	1	1	2a	1	1	1
REACTION TO REMOVAL	1	1	1	1	1	1	1	1	1	1
REACTION TO HANDLING	1	1	1	1	1	1	1	1	1	1
REARS IN OPEN FIELD	2	5	3	4	3	6	1	1	8	0
DEFECATION IN OPEN FIELD	1	1	1	1	1	1	1	1	1	1
URINATION IN OPEN FIELD	2	1	1	2	1	2	1	2	1	1
LEVEL OF AROUSAL	3	3	3	3	3	3	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1	1	1	1	1	1	1
GAIT PATTERN	1	1	1	1	1	1	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1	1	1	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1	1	1	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1	1	1	1	1	1	1
LACRIMATION	1	1	1	1	1	1	1	1	1	1
SALIVATION	1	1	1	1	1	1	1	1	1	1
PILOERECTION	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0	0	0	0	0	0	0
APPEARANCE	1	1	1	1	1b	1	1	1	1	1
VISUAL REACTION	2	2	2	2	2	2	2	2	2	2
TACTILE REACTION	2	2	2	2	2	2	2	2	2	2
AUDITORY REACTION	3	3	3	3	3	3	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2	2	2	2	2	2	2
AIR RIGHTING RESPONSE	1	1	1	1	1	1	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1	1	1	1	1	1	1
FORELIMB GRIP TEST #1 (G)	355	460	500	360	340	470	315	415	295	315
FORELIMB GRIP TEST #2 (G)	460	510	420	395	375	350	465	465	430	370
HINDLIMB GRIP TEST #1 (G)	450	320	620	315	315	490	255	300	280	345
HINDLIMB GRIP TEST #2 (G)	415	380	690	220	330	390	255	325	250	275
LANDING FOOT SPLAY #1 (CM)	6.7	9.8	8.8	7.9	4.5	8.5	7.8	8.0	7.7	8.4
LANDING FOOT SPLAY #2 (CM)	6.8	7.6	7.7	7.6	5.7	7.1	7.2	6.8	7.5	8.4
BODY WEIGHT (G)	452	487	495	527	464	529	507	445	433	503

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

a. Value appeared incorrectly recorded; value excluded from group averages and statistical analyses.

b. Chromorhinorrhea.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B24 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP II	0.3 MG/KG/DAY									
RAT #	19102	19106	19108	19110	19113	19120	19129	19136	19138	19139
HOME CAGE BEHAVIOR	2	2	2	2	2	2	2	1	1	1
ALTERATIONS (HOME CAGE)	1	1	1	1	1	1	1	1	1	1
REACTION TO REMOVAL	1	1	1	1	1	1	1	1	1	1
REACTION TO HANDLING	1	1	1	1	1	1	1	1	1	1
REARS IN OPEN FIELD	11	8	3	11	9	4	4	3	4	5
DEFECATION IN OPEN FIELD	1	1	1	1	2	2	1	1	1	1
URINATION IN OPEN FIELD	2	1	2	2	2	2	2	2	2	2
LEVEL OF AROUSAL	3	3	3	3	3	3	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1	1	1	1	1	1	1
GAIT PATTERN	1	1	1	1	1	1	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1	1	1	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1	1	1	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1	1	1	1	1	1	1
LACRIMATION	1	1	1	1	1	1	1	1	1	1
SALIVATION	1	1	1	1	1	1	1	1	1	1
PILOERECTION	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0	0	0	0	0	0	0
APPEARANCE	1	1	1	1	1	1	1	1	1	1
VISUAL REACTION	2	2	2	2	2	2	2	2	2	2
TACTILE REACTION	2	2	2	2	2	2	2	2	2	2
AUDITORY REACTION	3	3	3	3	3	3	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2	2	2	2	2	2	2
AIR RIGHTING RESPONSE	1	1	1	1	1	1	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1	1	1	1	1	1	1
FORELIMB GRIP TEST #1 (G)	355	375	395	415	455	245	250a	505	215	435
FORELIMB GRIP TEST #2 (G)	400	490	360	470	465	410	365	390	465	550
HINDLIMB GRIP TEST #1 (G)	345	435	610	365	315	250	315	155	435	465
HINDLIMB GRIP TEST #2 (G)	460	505	575	450	520	550	345b	220	365	335
LANDING FOOT SPLAY #1 (CM)	11.6	9.5	7.6	8.0	6.8	6.2	12.5	7.6	8.0	9.9
LANDING FOOT SPLAY #2 (CM)	9.7	8.4	6.5	7.8	6.5	4.8	12.7	7.8	9.2	11.5
BODY WEIGHT (G)	444	489	490	467	464	496	443	517	385	460

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

a. Vocalization and aggression observed during forelimb grip test.

b. Soft or liquid feces observed during hindlimb grip test.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B24 (PAGE 3): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP III						1 MG/KG/DAY				
RAT #	19101	19105	19107	19112	19114	19121	19123	19130	19137	19146
HOME CAGE BEHAVIOR	2	2	2	2	2	2	2	1	1	1
ALTERATIONS (HOME CAGE)	1	1	1	1	1	1	1	1	1	1
REACTION TO REMOVAL	1	1	1	1	1	1	1	1	1	1
REACTION TO HANDLING	1	1	1	1	1	1	1	1	1	1
REARS IN OPEN FIELD	3	3	7	2	2	3	2	5	6	6
DEFECATION IN OPEN FIELD	2	1	2	1	1	1	2	1	1	1
URINATION IN OPEN FIELD	2	2	2	1	2	1	1	1	1	1
LEVEL OF AROUSAL	3	3	3	3	3	3	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1	1	1	1	1	1	1
GAIT PATTERN	1	1	1	1	1	1	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1	1	1	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1	1	1	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1	1	1	1	1	1	1
LACRIMATION	1	1	1	1	1	1	1	1	1	1
SALIVATION	1	1	1	1	1	1	1	1	1	1
PILOERECTION	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0	0	0	0	0	0	0
APPEARANCE	1	1	1a	1	1	1	1	1	1	1
VISUAL REACTION	2	2	2	2	2	2	2	2	2	2
TACTILE REACTION	2	2	2	2	2	2	2	2	2	2
AUDITORY REACTION	3	3	3	3	3	3	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2	2	2	2b	2	2	2
AIR RIGHTING RESPONSE	1	1	1	1	1	1	1	1	1	1c
PUPIL RESPONSE TO LIGHT	1	1	1	1	1	1	1	1	1	1
FORELIMB GRIP TEST #1 (G)	215	500	480	490	270	550	405	395	340	570
FORELIMB GRIP TEST #2 (G)	175	430	545	400	430	395	395	515	330	360
HINDLIMB GRIP TEST #1 (G)	520	480	540	415	395	465	375	280	305	220
HINDLIMB GRIP TEST #2 (G)	545	580	415	525	395	475	490	435	255	280
LANDING FOOT SPLAY #1 (CM)	8.2	8.7	9.7	6.8	9.0	11.8	8.5	9.7	11.1	8.7
LANDING FOOT SPLAY #2 (CM)	6.7	7.5	10.3	7.5	8.8	10.2	9.5	7.8	10.7	7.6
BODY WEIGHT (G)	375	532	459	482	439	601	476	457	467	483

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

a. Localized alopecia: lower midline - right side (4.0 cm x 1.5 cm).

b. Soft or liquid feces observed during tail-pinch reaction.

c. Vocalization to touch and aggressive behavior observed during air righting response.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B24 (PAGE 4): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP IV	3 MG/KG/DAY									
RAT #	19100	19103	19104	19118	19133	19141	19142	19144	19148	19150
HOME CAGE BEHAVIOR	2	2	2	2	2	2	1	2	2	1
ALTERATIONS (HOME CAGE)	1	1	1	1	1	1	1	1	1	1
REACTION TO REMOVAL	1	1	1	1	1	1	1	1	1	1
REACTION TO HANDLING	1	1	1	1	1	1	1	1	1	1
REARS IN OPEN FIELD	7	6	1	4	4	2	6	7	3	5
DEFECATION IN OPEN FIELD	1	2	1	1	1	1	1	1	1	1
URINATION IN OPEN FIELD	2	2	1	2	2	1	2	2	2	2
LEVEL OF AROUSAL	3	3	3	3	3	3	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1	1	1	1	1	1	1
GAIT PATTERN	1	1	1	1	1	1	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1	1	1	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1	1	1	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1	1	1	1	1	1	1
LACRIMATION	1	1	1	1	1	1	1	1	1	1
SALIVATION	1	1	1	1	1	1	1	1	1	1
PILOERECTION	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0	0	0	0	0	0	0
APPEARANCE	1	1	1	1	1	1	1	1	1	1a
VISUAL REACTION	2	2	2	2	2	2	2	2	2	2
TACTILE REACTION	2	2	2	2	2	2	2	2	2	2
AUDITORY REACTION	3	3	3	3	3	3	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2	2	2	2	2	2	2
AIR RIGHTING RESPONSE	1	1	1	1	1	1	1b	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1	1	1	1	1	1	1
FORELIMB GRIP TEST #1 (G)	450	355	330	270	335	120	390	355	465	260
FORELIMB GRIP TEST #2 (G)	540	315	465	475	365	220	365	255	675	345
HINDLIMB GRIP TEST #1 (G)	425	520	450	380	350	270	215	200	405	270
HINDLIMB GRIP TEST #2 (G)	385	420	335	415	265	420	365	340	485	375
LANDING FOOT SPLAY #1 (CM)	7.6	10.8	6.6	9.0	6.6	6.8	9.7	8.5	11.9	9.4
LANDING FOOT SPLAY #2 (CM)	6.9	9.7	7.8	8.5	4.5	6.7	9.6	9.2	12.2	9.6
BODY WEIGHT (G)	441	505	494	472	459	563	506	538	481	473

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

a. Chromodacryorrhea - right eye and incisors misaligned - upper bilateral.

b. Vocalization and aggression observed during air righting response.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B24 (PAGE 5): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP V	10 MG/KG/DAY									
RAT #	19111	19117	19124	19126	19127	19128	19140	19145	19149	19152
HOME CAGE BEHAVIOR	2	2	2	1	2	2	2	2	2	1
ALTERATIONS (HOME CAGE)	1	1	1	1	1	1	1	1	1	1
REACTION TO REMOVAL	1	1	1	1	1	1	1	1	1	1
REACTION TO HANDLING	1	1	1	1	1	1	1	1	1	1
REARS IN OPEN FIELD	6	6	2	8	2	0	6	5	9	1
DEFECATION IN OPEN FIELD	1	1	1	1	2	1	1	1	1	1
URINATION IN OPEN FIELD	2	2	1	2	2	1	2	2	2	1
LEVEL OF AROUSAL	3	3	3	3	3	3	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1	1	1	1	1	1	1
GAIT PATTERN	1	1	1	1	1	1	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1	1	1	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1	1	1	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1	1	1	1	1	1	1
LACRIMATION	1	1	1	1	1	1	1	1	1	1
SALIVATION	1	1	1	1	1	1	1	1	1	1
PILOERECTION	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0	0	0	0	0	0	0
APPEARANCE	1	1	1	1	1	1	1	1	1	1
VISUAL REACTION	2	2	2	2	2	2	2	2	2	2
TACTILE REACTION	2	2	2	2	2	2	2	2	2	2
AUDITORY REACTION	3	3	3	3	3	3	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2	2	2	2	2	2	2
AIR RIGHTING RESPONSE	1	1	1	1	1	1	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1	1	1	1	1	1	1
FORELIMB GRIP TEST #1 (G)	355	335	320	580	415	300	285	165	165	510
FORELIMB GRIP TEST #2 (G)	365	450	350	470	470	450	450	155	275	320
HINDLIMB GRIP TEST #1 (G)	500	420	510	485	440	430	430	500	250	305
HINDLIMB GRIP TEST #2 (G)	485	660	555	400	450	505	440	480	215	330
LANDING FOOT SPLAY #1 (CM)	8.1	7.5	8.1	8.8	9.1	5.3	13.0	8.1	5.8	8.5
LANDING FOOT SPLAY #2 (CM)	7.6	6.8	8.3	7.6	9.7	5.0	12.7	6.5	6.2	7.6
BODY WEIGHT (G)	458	475	440	439	463	470	462	473	466	473

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B25 (PAGE 1): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP I — 0 MG/KG/DAY

RAT NUMBER	19109	19115	19116	19119	19122	19125	19131	19132	19134	19135
NUMBER OF MOVEMENTS										
BLOCK 1	71	60	64	68	67	72	58	62	73	53
BLOCK 2	78	74	56	64	56	61	83	67	71	59
BLOCK 3	59	66	58	72	76	66	76	76	73	69
BLOCK 4	68	80	71	66	70	55	83	70	93	67
BLOCK 5	61	46	56	71	72	75	55	47	73	45
BLOCK 6	64	0	55	62	55	61	78	52	5	51
BLOCK 7	29	9	69	45	50	29	56	50	4	53
BLOCK 8	50	0	76	9	7	97	24	62	0	54
BLOCK 9	3	1	33	1	44	70	0	40	30	54
BLOCK 10	1	1	12	1	5	59	0	31	73	67
BLOCK 11	0	0	2	36	7	71	0	47	20	59
BLOCK 12	33	55	0	0	71	72	3	46	43	55
BLOCK 13	6	58	61	0	59	82	20	73	0	62
BLOCK 14	0	72	15	0	56	44	68	50	0	71
BLOCK 15	0	7	0	0	37	61	61	12	5	50
BLOCK 16	0	0	6	1	56	83	60	25	0	5
BLOCK 17	5	0	0	1	47	49	72	44	16	2
BLOCK 18	0	0	7	36	35	71	14	53	8	4
TOTAL	528	529	641	533	870	1178	811	907	587	880

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B25 (PAGE 2): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP I — 0 MG/KG/DAY

RAT NUMBER	19109	19115	19116	19119	19122	19125	19131	19132	19134	19135
TIME (SECONDS) SPENT IN MOVEMENT										
BLOCK 1	185	217	193	169	161	194	229	219	224	220
BLOCK 2	182	182	133	186	191	201	188	184	217	210
BLOCK 3	161	115	110	181	149	162	183	178	173	143
BLOCK 4	144	127	106	166	190	88	139	129	134	191
BLOCK 5	106	54	113	132	129	140	92	69	94	78
BLOCK 6	91	0	125	111	71	158	133	135	1	87
BLOCK 7	70	6	140	82	125	48	65	80	2	84
BLOCK 8	99	0	87	8	10	124	18	165	0	102
BLOCK 9	0	0	31	0	113	118	0	53	50	75
BLOCK 10	0	0	11	1	4	122	0	43	122	186
BLOCK 11	0	0	0	36	6	169	0	58	12	121
BLOCK 12	38	91	0	0	84	114	1	72	62	119
BLOCK 13	9	90	60	0	95	116	21	126	0	152
BLOCK 14	0	67	9	0	151	127	104	90	0	108
BLOCK 15	0	5	0	0	105	118	99	10	3	51
BLOCK 16	0	0	5	0	79	102	106	24	0	3
BLOCK 17	4	0	0	0	100	57	72	70	16	1
BLOCK 18	0	0	6	46	44	125	23	56	2	3
TOTAL	1089	954	1129	1118	1807	2283	1473	1761	1112	1934

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B25 (PAGE 3): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP II — 0.3 MG/KG/DAY

RAT NUMBER	19102	19106	19108	19110	19113	19120	19129	19136	19138	19139
NUMBER OF MOVEMENTS										
BLOCK 1	64	55	64	64	71	69	52	64	74	66
BLOCK 2	69	55	61	60	56	94	58	57	61	65
BLOCK 3	68	59	47	66	24	82	67	72	50	63
BLOCK 4	63	68	65	73	15	93	67	47	60	61
BLOCK 5	44	60	61	59	0	93	61	55	51	63
BLOCK 6	32	24	51	70	0	86	77	70	55	63
BLOCK 7	5	54	71	65	0	59	70	62	63	51
BLOCK 8	3	45	60	57	2	74	59	67	48	52
BLOCK 9	34	77	37	64	0	70	48	45	70	47
BLOCK 10	6	75	60	37	51	65	56	48	56	77
BLOCK 11	0	53	3	0	16	64	72	63	40	40
BLOCK 12	1	64	0	51	1	45	66	51	35	37
BLOCK 13	5	58	65	0	12	0	74	54	78	84
BLOCK 14	14	61	64	22	0	8	59	61	81	68
BLOCK 15	51	53	39	20	0	17	27	78	25	45
BLOCK 16	36	81	51	65	0	2	2	57	33	49
BLOCK 17	64	78	52	46	0	0	3	63	22	64
BLOCK 18	63	58	41	40	0	38	6	53	1	44
TOTAL	622	1078	892	859	248	959	924	1067	903	1039

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B25 (PAGE 4): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP II — 0.3 MG/KG/DAY

RAT NUMBER	19102	19106	19108	19110	19113	19120	19129	19136	19138	19139
TIME (SECONDS) SPENT IN MOVEMENT										
BLOCK 1	215	201	192	192	176	197	240	216	191	198
BLOCK 2	133	164	152	182	138	160	238	209	170	198
BLOCK 3	150	126	71	150	24	211	223	203	144	101
BLOCK 4	116	140	162	201	16	144	209	129	143	123
BLOCK 5	35	147	166	116	0	171	214	197	83	182
BLOCK 6	40	31	103	142	0	135	157	125	76	88
BLOCK 7	1	125	136	98	0	148	153	102	71	68
BLOCK 8	1	77	81	55	0	162	117	146	69	129
BLOCK 9	33	105	99	85	0	117	116	63	125	66
BLOCK 10	4	114	78	42	94	94	137	95	75	133
BLOCK 11	0	117	4	0	49	135	177	123	58	51
BLOCK 12	0	72	0	60	0	90	146	181	62	60
BLOCK 13	1	88	86	0	7	0	190	135	207	155
BLOCK 14	26	90	120	29	0	2	114	152	122	102
BLOCK 15	113	59	60	17	0	26	28	146	15	67
BLOCK 16	57	125	63	84	0	0	1	121	28	76
BLOCK 17	93	151	66	56	0	0	0	117	21	121
BLOCK 18	111	54	37	41	0	43	2	139	1	46
TOTAL	1129	1986	1676	1550	504	1835	2462	2599	1661	1964

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B25 (PAGE 5): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP III — 1 MG/KG/DAY

RAT NUMBER	19101	19105	19107	19112	19114	19121	19123	19130	19137	19146
NUMBER OF MOVEMENTS										
BLOCK 1	67	57	63	79	60	74	60	51	56	68
BLOCK 2	55	57	63	76	57	67	69	55	81	66
BLOCK 3	76	72	52	71	56	70	59	57	71	67
BLOCK 4	80	68	63	73	61	71	79	43	84	60
BLOCK 5	62	63	66	61	66	75	60	71	72	60
BLOCK 6	72	57	52	60	47	78	64	52	74	86
BLOCK 7	74	57	52	47	65	71	69	28	76	59
BLOCK 8	57	68	51	6	66	78	49	43	68	54
BLOCK 9	59	86	64	22	31	69	22	31	74	39
BLOCK 10	56	73	66	14	35	75	17	47	85	2
BLOCK 11	21	44	52	2	69	74	84	73	50	43
BLOCK 12	71	8	37	14	12	79	60	60	59	55
BLOCK 13	109	5	54	49	8	70	22	37	81	5
BLOCK 14	29	17	81	0	29	55	0	53	57	44
BLOCK 15	27	69	71	1	2	85	0	65	75	3
BLOCK 16	50	72	5	0	0	66	3	47	64	5
BLOCK 17	72	55	1	18	0	54	5	13	27	46
BLOCK 18	73	65	0	55	5	57	1	42	2	59
TOTAL	1110	993	893	648	669	1268	723	868	1156	821

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B25 (PAGE 6): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP III — 1 MG/KG/DAY

RAT NUMBER	19101	19105	19107	19112	19114	19121	19123	19130	19137	19146
TIME (SECONDS) SPENT IN MOVEMENT										
BLOCK 1	212	226	218	207	194	201	228	236	219	207
BLOCK 2	219	224	129	144	197	198	220	230	202	195
BLOCK 3	145	156	92	160	177	197	203	187	202	206
BLOCK 4	127	125	109	138	169	138	141	167	188	122
BLOCK 5	148	191	147	134	160	157	115	151	166	134
BLOCK 6	65	110	87	93	91	164	139	99	201	135
BLOCK 7	164	79	104	60	175	112	146	29	141	92
BLOCK 8	103	139	151	2	160	161	73	51	132	127
BLOCK 9	116	154	102	18	39	208	25	82	116	76
BLOCK 10	98	120	97	6	59	153	11	99	131	0
BLOCK 11	36	76	77	0	134	170	125	99	81	62
BLOCK 12	165	8	37	11	48	180	138	109	111	110
BLOCK 13	103	1	87	54	5	113	34	24	98	2
BLOCK 14	18	20	104	0	30	95	0	136	65	73
BLOCK 15	47	135	79	0	1	139	0	140	138	1
BLOCK 16	52	100	11	0	0	152	5	71	211	1
BLOCK 17	90	81	0	16	0	162	3	18	23	76
BLOCK 18	100	156	0	76	5	85	0	43	1	97
TOTAL	2008	2101	1631	1119	1644	2785	1606	1971	2426	1716

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B25 (PAGE 7): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP IV 3 MG/KG/DAY

RAT NUMBER	19100	19103	19104	19118	19133	19141	19142	19144	19148	19150
NUMBER OF MOVEMENTS										
BLOCK 1	80	55	61	54	47	63	73	66	54	68
BLOCK 2	84	74	72	73	69	69	76	75	70	73
BLOCK 3	54	69	87	87	81	69	67	54	74	74
BLOCK 4	57	57	75	86	78	71	55	48	63	64
BLOCK 5	67	43	85	71	37	74	77	71	42	64
BLOCK 6	29	67	62	79	41	66	59	64	74	58
BLOCK 7	47	60	66	62	71	56	49	70	66	59
BLOCK 8	62	43	64	44	12	63	71	80	69	62
BLOCK 9	55	53	69	27	14	69	83	60	63	60
BLOCK 10	32	69	65	85	0	51	50	49	58	41
BLOCK 11	1	50	76	74	8	58	65	70	68	47
BLOCK 12	1	46	89	60	18	54	66	57	69	31
BLOCK 13	3	14	77	77	54	73	56	62	53	35
BLOCK 14	58	69	63	10	71	69	80	53	61	58
BLOCK 15	75	63	71	3	40	54	54	49	67	37
BLOCK 16	54	74	61	70	0	57	56	67	45	25
BLOCK 17	72	62	63	72	20	48	66	65	67	0
BLOCK 18	67	16	57	61	5	47	34	74	63	0
TOTAL	898	984	1263	1095	666	1111	1137	1134	1126	856

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B25 (PAGE 8): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP IV — 3 MG/KG/DAY

RAT NUMBER	19100	19103	19104	19118	19133	19141	19142	19144	19148	19150
TIME (SECONDS) SPENT IN MOVEMENT										
BLOCK 1	198	244	235	219	171	200	206	182	211	180
BLOCK 2	136	202	171	163	200	206	184	182	183	175
BLOCK 3	83	105	159	138	138	143	153	160	175	152
BLOCK 4	120	193	156	139	181	114	86	125	174	121
BLOCK 5	120	90	131	137	55	145	120	144	145	105
BLOCK 6	30	129	109	128	57	154	65	146	187	92
BLOCK 7	59	186	187	87	141	142	65	122	113	84
BLOCK 8	87	223	108	59	43	131	120	123	161	106
BLOCK 9	82	196	114	27	9	93	152	151	109	103
BLOCK 10	30	155	94	120	0	126	55	107	77	67
BLOCK 11	0	83	155	92	3	143	158	143	148	52
BLOCK 12	0	114	136	101	14	71	84	125	128	38
BLOCK 13	0	18	100	102	87	105	118	124	76	72
BLOCK 14	106	136	102	14	107	106	163	96	153	95
BLOCK 15	113	111	97	1	43	60	69	107	82	59
BLOCK 16	58	134	100	61	0	114	112	134	110	49
BLOCK 17	146	127	95	91	13	109	111	143	79	0
BLOCK 18	108	36	88	78	2	65	58	115	119	0
TOTAL	1476	2482	2337	1757	1264	2227	2079	2429	2430	1550

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B25 (PAGE 9): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP V — 10 MG/KG/DAY

RAT NUMBER	19111	19117	19124	19126	19127	19128	19140	19145	19149	19152
NUMBER OF MOVEMENTS										
BLOCK 1	62	69	57	61	72	68	64	49	77	61
BLOCK 2	68	66	67	72	63	75	87	63	65	70
BLOCK 3	67	56	63	76	61	78	72	60	77	65
BLOCK 4	58	50	73	63	68	37	41	48	59	63
BLOCK 5	62	49	65	42	25	51	62	76	76	61
BLOCK 6	39	50	59	51	67	56	55	66	57	74
BLOCK 7	59	63	62	62	30	49	54	52	68	69
BLOCK 8	55	74	24	61	12	54	78	44	67	28
BLOCK 9	46	37	42	35	75	41	87	56	47	56
BLOCK 10	73	40	47	51	64	23	47	67	52	32
BLOCK 11	44	0	45	50	33	23	82	54	43	41
BLOCK 12	28	39	57	37	67	39	43	64	44	58
BLOCK 13	44	31	64	30	86	42	21	62	39	11
BLOCK 14	77	0	29	64	66	62	16	56	68	0
BLOCK 15	75	0	39	62	57	41	61	39	56	0
BLOCK 16	43	0	66	61	3	49	69	64	68	2
BLOCK 17	71	0	72	49	56	34	6	68	14	3
BLOCK 18	65	1	58	31	63	38	1	31	35	19
TOTAL	1036	625	989	958	968	860	946	1019	1012	713

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B25 (PAGE 10): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

DOSAGE GROUP V — 10 MG/KG/DAY

RAT NUMBER	19111	19117	19124	19126	19127	19128	19140	19145	19149	19152
TIME (SECONDS) SPENT IN MOVEMENT										
BLOCK 1	206	161	173	169	212	192	181	243	230	181
BLOCK 2	170	174	143	116	149	205	176	233	158	177
BLOCK 3	141	110	118	141	109	128	197	231	146	166
BLOCK 4	175	169	118	115	103	42	86	220	126	155
BLOCK 5	153	75	124	111	30	65	108	158	173	141
BLOCK 6	64	67	97	96	87	134	64	196	94	128
BLOCK 7	98	81	112	102	39	104	107	195	121	120
BLOCK 8	74	101	36	64	7	116	90	100	98	34
BLOCK 9	51	63	47	47	107	81	125	196	129	90
BLOCK 10	140	64	80	47	67	27	49	165	87	42
BLOCK 11	87	0	98	102	33	17	126	80	60	69
BLOCK 12	37	94	59	65	105	37	42	138	57	95
BLOCK 13	75	54	107	40	163	48	29	135	38	16
BLOCK 14	150	0	32	66	106	90	14	155	120	0
BLOCK 15	103	0	60	74	68	66	100	95	76	0
BLOCK 16	54	0	77	95	0	132	142	203	68	0
BLOCK 17	93	0	98	86	70	42	5	108	6	2
BLOCK 18	110	0	91	21	106	69	0	69	55	20
TOTAL	1981	1213	1670	1557	1561	1595	1641	2920	1842	1436

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B26 (PAGE 1): SPERM MOTILITY, COUNT AND DENSITY - INDIVIDUAL DATA - Fo GENERATION MALE RATS
(See footnotes on the last page of this table.)

RAT NUMBER	NUMBER MOTILE	MOTILE PERCENT	STATIC COUNT (NONMOTILE)	TOTAL COUNT a	SPERM COUNT b	SPERM DENSITY c
DOSAGE GROUP I		0 MG/KG/DAY				
19109	276	89	33	309	166	1701.6
19115	254	97	8	262	190	1598.6
19116	323	92	27	350	159	1433.3
19119	328	90	38	366	178	1475.8
19122	210	91	21	231	126	978.7
19125	256	91	25	281	121	1073.7
19131	375	94	23	398	271	2496.6
19132	302	88	41	343	222	1743.2
19134	235	97	7	242	156	1339.9
19135	332	92	29	361	112	1101.2
DOSAGE GROUP II		0.3 MG/KG/DAY				
19102	232	93	17	249	139	1402.5
19106	367	89	47	414	149	1455.1
19108	333	93	25	358	232	1916.4
19110	257	97	7	264	101	1051.3
19113	334	90	37	371	177	1515.3
19120	469	92	39	508	220	1983.2
19129	293	95	15	308	231	2100.6
19136	338	92	30	368	95	853.7
19138	223	98	4	227	148	1187.9
19139	228	94	14	242	90	836.0

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B26 (PAGE 2): SPERM MOTILITY, COUNT AND DENSITY - INDIVIDUAL DATA - Fo GENERATION MALE RATS
(See footnotes on the last page of this table.)

RAT NUMBER	NUMBER MOTILE	MOTILE PERCENT	STATIC COUNT (NONMOTILE)	TOTAL COUNT a	SPERM COUNT b	SPERM DENSITY c
DOSAGE GROUP III		1 MG/KG/DAY				
19101	198	89	25	223	163	1575.4
19105	265	87	38	303	186	1593.3
19107	265	90	31	296	121	1312.4
19112	341	95	19	360	173	1564.4
19114	475	97	16	491	130	1290.1
19121	319	96	12	331	248	2163.4
19123	246	90	26	272	164	1401.9
19130	309	93	23	332	190	1564.5
19137	298	92	25	323	114	951.2
19146	404	96	16	420	121	1002.3
DOSAGE GROUP IV		3 MG/KG/DAY				
19100	301	91	28	329	141	1215.7
19103	372	86	60	432	171	1700.4
19104	244	95	14	258	131	1279.8
19118	286	95	16	302	86	823.2
19133	552	97	46	598	143	1397.0
19141	313	23	17	330	217	2026.2
19142	15	90	49	64	33	716.1
19144	298	92	32	330	88	1006.6
19148	495	88	36	531	119	893.9
19150	197	98	29	226	117	1087.9

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B26 (PAGE 3): SPERM MOTILITY, COUNT AND DENSITY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT NUMBER	NUMBER MOTILE	MOTILE PERCENT	STATIC COUNT (NONMOTILE)	TOTAL COUNT a	SPERM COUNT b	SPERM DENSITY c
DOSAGE GROUP V			10 MG/KG/DAY			
19111	304	94	21	325	229	2354.1
19117	286	90	33	319	189	1871.7
19124	461	91	38	499	174	1490.0
19126	264	93	12	276	91	1032.3
19127	339	72	26	365	190	1805.0
19128	231	95	92	323	163	1730.3
19140	464	95	27	491	161	1578.2
19145	360	96	30	390	146	1194.1
19149	289	87	39	328	198	1789.9
19152	256	98	6	262	204	1794.7

a. Sum of number motile and static count. Groups of five fields were evaluated until a sperm count of at least 200 was achieved or 20 fields were evaluated.

b. Sperm count used in the calculation of sperm density. Ten fields were evaluated.

c. The sperm density was calculated by dividing the sperm count by the volume in the image area (34.3×10^{-6} mL), multiplying by 2 (dilution factor) and multiplying by 10^{-6} to obtain the sperm concentration. The calculated sperm concentration value (rounded to 1 decimal place) was multiplied by 50 (volume) and divided by the weight of the left cauda epididymis (see Table B19 for the weight of the left cauda epididymis) to obtain the sperm density. The calculated value will vary by approximately 0.8% from the Computer Automated Sperm Analysis because the digital image evaluated is slightly smaller (4 pixels) than the actual field causing a slight underestimate of the actual volume and an overestimate of the concentration.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B27 (PAGE 1): SPERM MORPHOLOGY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT NUMBER	NORMAL	DETACHED HEAD	NO HEAD	BROKEN FLAGELLUM	BENT FLAGELLUM	PERCENT ABNORMAL
DOSAGE GROUP I		0 MG/KG/DAY				
19109	186	6	7	1	0	7.0
19115	194	2	4	0	0	3.0
19116	189	7	4	0	0	5.5
19119	190	8	2	0	0	5.0
19122	192	3	5	0	0	4.0
19125	195	2	2	1	0	2.5
19131	194	3	2	0	1	3.0
19132	193	2	4	0	1	3.5
19134	196	1	2	1	0	2.0
19135	194	3	2	1	0	3.0
DOSAGE GROUP II		0.3 MG/KG/DAY				
19102	189	5	4	2	0	5.5
19106	196	1	1	1	1	2.0
19108	195	1	2	1	1	2.5
19110	192	3	3	2	0	4.0
19113	196	3	1	0	0	2.0
19120	190	8	2	0	0	5.0
19129	189	6	4	1	0	5.5
19136	196	3	1	0	0	2.0
19138	195	3	1	1	0	2.5
19139	195	3	2	0	0	2.5

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B27 (PAGE 2): SPERM MORPHOLOGY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT NUMBER	NORMAL	DETACHED HEAD	NO HEAD	BROKEN FLAGELLUM	BENT FLAGELLUM	PERCENT ABNORMAL
DOSAGE GROUP III		1 MG/KG/DAY				
19101	198	1	1	0	0	1.0
19105	197	1	1	1	0	1.5
19107	189	5	3	1	2	5.5
19112	197	1	1	1	0	1.5
19114	191	6	3	0	0	4.5
19121	196	2	2	0	0	2.0
19123	192	2	5	1	0	4.0
19130	188	5	4	2	1	6.0
19137	192	3	4	1	0	4.0
19146	193	5	2	0	0	3.5
DOSAGE GROUP IV		3 MG/KG/DAY				
19100	196	0	3	1	0	2.0
19103	192	4	4	0	0	4.0
19104	198	2	0	0	0	1.0
19118	188	4	7	1	0	6.0
19133	192	3	3	2	0	4.0
19141	192	5	2	1	0	4.0
19142	4	37	76	79	4	98.0
19144	184	10	6	0	0	8.0
19148	194	3	2	1	0	3.0
19150	198	0	2	0	0	1.0

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE B27 (PAGE 3): SPERM MORPHOLOGY - INDIVIDUAL DATA - Fo GENERATION MALE RATS

RAT NUMBER	NORMAL	DETACHED HEAD	NO HEAD	BROKEN FLAGELLUM	BENT FLAGELLUM	PERCENT ABNORMAL
DOSAGE GROUP V		10 MG/KG/DAY				
19111	198	1	1	0	0	1.0
19117	197	1	1	1	0	1.5
19124	192	6	1	1	0	4.0
19126	196	2	2	0	0	2.0
19127	189	6	2	3	0	5.5
19128	191	2	5	2	0	4.5
19140	191	8	1	0	0	4.5
19145	196	2	1	1	0	2.0
19149	192	3	3	1	1	4.0
19152	191	7	1	1	0	4.5

APPENDIX C

REPORT TABLES - Fo GENERATION FEMALE RATS

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C1 (PAGE 1): CLINICAL OBSERVATIONS - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP	I	II	III	IV	V
DOSAGE (MG/KG/DAY)	0	0.3	1	3	10
PRECOHABITATION (DAY 1 OF STUDY TO THE DAY OF COHABITATION):					
MAXIMUM POSSIBLE INCIDENCE	210/ 15	210/ 15	210/ 15	210/ 15	210/ 15
MORTALITY	0	0	0	0	0
BROWN PERIORAL SUBSTANCE	0/ 0	0/ 0	0/ 0	0/ 0	7/ 1
RALES	0/ 0	0/ 0	0/ 0	0/ 0	7/ 1
LOCALIZED ALOPECIA: TOTAL	0/ 0	0/ 0	0/ 0	4/ 1	4/ 1
HEAD	0/ 0	0/ 0	0/ 0	0/ 0	4/ 1
LIMBS	0/ 0	0/ 0	0/ 0	4/ 1	0/ 0
URINE-STAINED ABDOMINAL FUR	0/ 0	0/ 0	0/ 0	0/ 0	3/ 1
MIOSIS	0/ 0	0/ 0	0/ 0	0/ 0	2/ 1
ABDOMINAL DISTENTION	0/ 0	0/ 0	0/ 0	0/ 0	2/ 1
EMACIATION	0/ 0	0/ 0	0/ 0	0/ 0	2/ 1
COLD TO TOUCH	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1

STATISTICAL ANALYSES OF CLINICAL OBSERVATION DATA WERE RESTRICTED TO THE NUMBER OF RATS WITH OBSERVATIONS.
MAXIMUM POSSIBLE INCIDENCE = (DAYS x RATS)/NUMBER OF RATS EXAMINED PER GROUP.
N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF RATS WITH OBSERVATION.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C1 (PAGE 2): CLINICAL OBSERVATIONS - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
PRESUMED GESTATION: a						
MAXIMUM POSSIBLE INCIDENCE		330/ 15	329/ 15	338/ 15	312/ 14	330/ 15
MORTALITY		0	0	0	0	0
LOCALIZED ALOPECIA:	TOTAL	0/ 0	0/ 0	2/ 1	30/ 2	21/ 1
	LIMBS	0/ 0	0/ 0	2/ 1	30/ 2	14/ 1
	HEAD	0/ 0	0/ 0	0/ 0	0/ 0	7/ 1
NOSE: SWOLLEN		0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
BACK: SCAB		13/ 1	0/ 0	0/ 0	0/ 0	0/ 0
BACK: ULCERATION		1/ 1	0/ 0	0/ 0	0/ 0	0/ 0

STATISTICAL ANALYSES OF CLINICAL OBSERVATION DATA WERE RESTRICTED TO THE NUMBER OF RATS WITH OBSERVATIONS.
MAXIMUM POSSIBLE INCIDENCE = (DAYS x RATS)/NUMBER OF RATS EXAMINED PER GROUP.
N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF RATS WITH OBSERVATION.
a. Restricted to rats with a confirmed mating date.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C1 (PAGE 3): CLINICAL OBSERVATIONS - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
MAXIMUM POSSIBLE INCIDENCE		330/ 15	330/ 15	286/ 13	286/ 13	330/ 15
LACTATION:						
MORTALITY		0	0	0	0	0
LOCALIZED ALOPECIA:	TOTAL	39/ 3	20/ 1	28/ 2	32/ 3	27/ 2
	LIMBS	30/ 2	20/ 1	22/ 1	28/ 2	21/ 1
	HEAD	9/ 1	0/ 0	7/ 2	0/ 0	6/ 1
	BACK	0/ 0	0/ 0	0/ 0	4/ 1	0/ 0
ABDOMINAL DISTENTION		0/ 0	0/ 0	0/ 0	0/ 0	16/ 1
RALES		0/ 0	0/ 0	0/ 0	0/ 0	9/ 1
EMACIATION		0/ 0	0/ 0	0/ 0	0/ 0	7/ 1
BACK OR HEAD: SCAB		13/ 3	23/ 2	0/ 0	0/ 0	6/ 1
DEHYDRATION		0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
TIP OF TAIL MISSING		0/ 0	0/ 0	0/ 0	6/ 1	0/ 0

STATISTICAL ANALYSES OF CLINICAL OBSERVATION DATA WERE RESTRICTED TO THE NUMBER OF RATS WITH OBSERVATIONS.
MAXIMUM POSSIBLE INCIDENCE = (DAYS x RATS)/NUMBER OF RATS EXAMINED PER GROUP.
N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF RATS WITH OBSERVATION.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C2 (PAGE 1): NECROPSY OBSERVATIONS - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS EXAMINED a	N	15	15	15	15	15
MORTALITY	N	0	0	0	0	0
APPEARED NORMAL	N	15	15	14	13	14
KIDNEYS: RIGHT, CORTEX ADHERED TO RIGHT LATERAL LIVER LOBE	N	0	0	1	0	0
OVARIES: LEFT, SMALL	N	0	0	0	1	0
SPLEEN: OMENTUM ADHERED TO THE LENGTH OF THE OUTER CAPSULE	N	0	0	0	1	0
LARGE AND SMALL INTESTINES: DISTENDED WITH GAS	N	0	0	0	0	1
THYMUS: SMALL	N	0	0	0	0	1
SPLEEN: SMALL	N	0	0	0	0	1
ADRENALS: BILATERAL, LARGE	N	0	0	0	0	1
STOMACH: FUNDIC MUCOSAL SURFACE CONTAINED APPROXIMATELY 12 BLACK AREAS	N	0	0	0	0	1

a. Refer to the individual clinical observations table (Table C27) for external observations confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C3 (PAGE 1): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS AND PRIMORDIAL FOLLICLE COUNT - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS						
RATS TESTED	N	15	15	15	15	15
PREGNANT	N	15	15	13	13	15
TERMINAL BODY WEIGHT	MEAN±S.D.	306.3 ± 26.0	324.3 ± 27.1	311.2 ± 35.0	319.6 ± 40.4	303.5 ± 37.9
BRAIN	MEAN±S.D.	2.16 ± 0.08 [10]a	2.11 ± 0.09 [10]a	2.10 ± 0.09 [10]a	2.08 ± 0.18 [10]a	2.12 ± 0.10 [10]a
LIVER	MEAN±S.D.	14.38 ± 2.24 [10]a	15.98 ± 2.71 [10]a	14.70 ± 2.92 [10]a	15.11 ± 3.28 [10]a	13.64 ± 3.18 [10]a
KIDNEY LEFT	MEAN±S.D.	1.39 ± 0.14 [10]a	1.47 ± 0.14 [10]a	1.38 ± 0.14 [10]a	1.49 ± 0.19 [10]a	1.39 ± 0.10 [10]a
KIDNEY RIGHT	MEAN±S.D.	1.47 ± 0.12 [10]a	1.52 ± 0.16 [10]a	1.45 ± 0.13 [10]a	1.52 ± 0.13 [10]a	1.41 ± 0.15 [10]a
ADRENAL LEFT	MEAN±S.D.	0.052 ± 0.009 [10]a	0.051 ± 0.009 [10]a	0.051 ± 0.009 [10]a	0.053 ± 0.012 [10]a	0.053 ± 0.009 [10]a
ADRENAL RIGHT	MEAN±S.D.	0.043 ± 0.007 [10]a	0.041 ± 0.010 [10]a	0.050 ± 0.011 [10]a	0.049 ± 0.006 [10]a	0.046 ± 0.008 [10]a
SPLEEN	MEAN±S.D.	0.63 ± 0.08 [10]a	0.65 ± 0.09 [10]a	0.60 ± 0.11 [10]a	0.75 ± 0.31 [10]a	0.54 ± 0.10 [10]a
THYMUS	MEAN±S.D.	0.21 ± 0.07 [10]a	0.21 ± 0.06 [10]a	0.18 ± 0.04 [10]a	0.20 ± 0.10 [10]a	0.18 ± 0.04 [10]a
OVARY LEFT	MEAN±S.D.	0.055 ± 0.014	0.056 ± 0.020	0.053 ± 0.014	0.053 ± 0.012	0.054 ± 0.015
OVARY RIGHT	MEAN±S.D.	0.062 ± 0.015	0.060 ± 0.019	0.060 ± 0.021	0.054 ± 0.012	0.054 ± 0.018
UTERUS WITH CERVIX	MEAN±S.D.	0.53 ± 0.09	0.56 ± 0.12	0.50 ± 0.13	0.62 ± 0.15	0.56 ± 0.16
HEART	MEAN±S.D.	1.40 ± 0.17 [10]a	1.26 ± 0.13 [10]a	1.35 ± 0.11 [10]a	1.40 ± 0.13 [10]a	1.33 ± 0.25 [10]a

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
[ ] = NUMBER OF VALUES AVERAGED
a. Only ten rats were tested.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C3 (PAGE 2): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS AND PRIMORDIAL FOLLICLE COUNT - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
PRIMORDIAL FOLLICLE COUNT						
RATS TESTED	N	15				15
PREGNANT	N	15				15
OVARY #1	MEAN±S.D.	12.58 ± 11.01 [10]a				12.40 ± 6.24 [10]a
OVARY #2	MEAN±S.D.	12.94 ± 9.01 [10]a				10.14 ± 2.29 [10]a

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
[ ] = NUMBER OF VALUES AVERAGED
a. Only ten rats were tested.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C4 (PAGE 1): RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	15	15	15	15	15
PREGNANT	N	15	15	13	13	15
TERMINAL BODY WEIGHT	MEAN±S.D.	306.3 ± 26.0	324.3 ± 27.1	311.2 ± 35.0	319.6 ± 40.4	303.5 ± 37.9
BRAIN	MEAN±S.D.	0.711 ± 0.062 [10]a	0.659 ± 0.055 [10]a	0.684 ± 0.082 [10]a	0.675 ± 0.099 [10]a	0.732 ± 0.102 [10]a
LIVER	MEAN±S.D.	4.703 ± 0.450 [10]a	4.947 ± 0.703 [10]a	4.697 ± 0.512 [10]a	4.795 ± 0.517 [10]a	4.582 ± 0.541 [10]a
KIDNEY LEFT	MEAN±S.D.	0.459 ± 0.049 [10]a	0.460 ± 0.053 [10]a	0.446 ± 0.054 [10]a	0.479 ± 0.070 [10]a	0.477 ± 0.040 [10]a
KIDNEY RIGHT	MEAN±S.D.	0.482 ± 0.043 [10]a	0.472 ± 0.052 [10]a	0.467 ± 0.042 [10]a	0.492 ± 0.058 [10]a	0.484 ± 0.043 [10]a
ADRENAL LEFT b	MEAN±S.D.	17.095 ± 2.132 [10]a	15.856 ± 2.913 [10]a	16.799 ± 4.091 [10]a	16.867 ± 3.532 [10]a	18.402 ± 4.737 [10]a
ADRENAL RIGHT b	MEAN±S.D.	13.984 ± 1.612 [10]a	12.842 ± 3.379 [10]a	16.479 ± 4.381 [10]a	15.743 ± 2.727 [10]a	15.959 ± 4.763 [10]a
SPLEEN	MEAN±S.D.	0.208 ± 0.024 [10]a	0.205 ± 0.028 [10]a	0.194 ± 0.035 [10]a	0.238 ± 0.076 [10]a	0.181 ± 0.026 [10]a
THYMUS	MEAN±S.D.	0.070 ± 0.022 [10]a	0.065 ± 0.018 [10]a	0.059 ± 0.016 [10]a	0.065 ± 0.037 [10]a	0.059 ± 0.016 [10]a
OVARY LEFT b	MEAN±S.D.	18.005 ± 4.064	17.632 ± 6.782	17.053 ± 3.559	16.883 ± 4.629	17.611 ± 3.620
OVARY RIGHT b	MEAN±S.D.	20.307 ± 4.390	18.514 ± 5.844	19.152 ± 6.400	17.025 ± 3.632	17.529 ± 5.247
UTERUS WITH CERVIX	MEAN±S.D.	0.175 ± 0.031	0.175 ± 0.042	0.162 ± 0.046	0.198 ± 0.063	0.185 ± 0.055
HEART	MEAN±S.D.	0.459 ± 0.067 [10]a	0.392 ± 0.057 [10]a	0.436 ± 0.054 [10]a	0.457 ± 0.073 [10]a	0.453 ± 0.056 [10]a

ALL WEIGHTS WERE RECORDED IN GRAMS (G). RATIOS (%) = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.
[ ] = NUMBER OF VALUES AVERAGED
a. Only ten rats were tested.
b. Value was multiplied by 1000.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C5 (PAGE 1): RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	10	10	10	10	10
BRAIN WEIGHT	MEAN±S.D.	2.16 ± 0.08	2.11 ± 0.09	2.10 ± 0.09	2.08 ± 0.18	2.12 ± 0.10
LIVER	MEAN±S.D.	664.58 ± 96.72	757.16 ±127.78	701.88 ±155.49	729.66 ±165.57	641.86 ±141.49
KIDNEY LEFT	MEAN±S.D.	64.31 ± 5.18	69.72 ± 4.89	65.73 ± 6.72	71.48 ± 6.75*	65.57 ± 3.88
KIDNEY RIGHT	MEAN±S.D.	67.75 ± 4.49	71.72 ± 6.50	68.95 ± 7.09	73.35 ± 5.96	66.53 ± 5.96
ADRENAL LEFT	MEAN±S.D.	2.42 ± 0.42	2.40 ± 0.35	2.44 ± 0.39	2.54 ± 0.58	2.49 ± 0.40
ADRENAL RIGHT	MEAN±S.D.	1.98 ± 0.31	1.95 ± 0.46	2.39 ± 0.48	2.36 ± 0.40	2.15 ± 0.40
SPLEEN	MEAN±S.D.	29.20 ± 3.42	30.95 ± 4.47	28.56 ± 5.09	36.15 ± 15.02	25.16 ± 4.18
THYMUS	MEAN±S.D.	9.72 ± 3.12	9.96 ± 2.95	8.43 ± 1.96	9.68 ± 4.96	8.35 ± 2.13
OVARY LEFT	MEAN±S.D.	2.68 ± 0.75	2.85 ± 0.84	2.47 ± 0.43	2.55 ± 0.58	2.58 ± 0.78
OVARY RIGHT	MEAN±S.D.	2.83 ± 0.72	3.09 ± 0.93	2.82 ± 0.98	2.55 ± 0.57	2.37 ± 0.89
UTERUS WITH CERVIX	MEAN±S.D.	26.20 ± 4.17	28.44 ± 4.18	24.14 ± 6.72	31.96 ± 7.43	27.71 ± 6.59
HEART	MEAN±S.D.	64.52 ± 7.00	59.50 ± 6.15	64.03 ± 5.41	67.44 ± 6.68	62.58 ± 10.73

ALL WEIGHTS WERE RECORDED IN GRAMS (G). RATIOS (%) = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.

* Significantly different from the Group I value ($p \leq 0.05$).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C6 (PAGE 1): HEMATOLOGY - SUMMARY - Fo GENERATION FEMALE RATS
(See abbreviations on the last page of this table.)

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	10	10	10	10	10
WBC (THSN/CU MM)	MEAN ± S.D.	9.0 ± 3.09	13.8 ± 5.73*	11.1 ± 2.98	10.8 ± 3.14	8.9 ± 3.48
RBC (MILL/CU MM)	MEAN ± S.D.	6.51 ± 0.461	6.22 ± 0.423	6.40 ± 0.554	6.39 ± 0.532	6.42 ± 0.538
HGB (GRAMS/DL)	MEAN ± S.D.	15.5 ± 0.95	15.0 ± 0.77	15.2 ± 0.91	15.2 ± 0.90	15.3 ± 0.77
HCT (%)	MEAN ± S.D.	40.5 ± 2.93	39.3 ± 2.72	39.5 ± 3.24	40.1 ± 3.02	40.4 ± 3.15
MCV (CU MICRONS)	MEAN ± S.D.	62.2 ± 1.19	63.3 ± 2.01	61.8 ± 1.50	62.9 ± 2.04	63.0 ± 1.60
MCH (PICO GRAMS)	MEAN ± S.D.	23.9 ± 0.55	24.2 ± 0.76	23.9 ± 0.88	23.8 ± 1.25	23.8 ± 1.05
MCHC (%)	MEAN ± S.D.	38.4 ± 0.76	38.3 ± 0.94	38.7 ± 1.29	37.8 ± 1.22	37.8 ± 1.37
PLAT (THSN/CU MM)	MEAN ± S.D.	1419 ± 153.0	1240 ± 208.1	1274 ± 226.3	1305 ± 207.2	1355 ± 176.8
MPV (CU MICRONS)	MEAN ± S.D.	8.3 ± 0.49	8.0 ± 0.84	8.3 ± 0.82	8.0 ± 0.63	7.7 ± 0.74

* Significantly different from the Group I value ($p \leq 0.05$).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C6 (PAGE 2): HEMATOLOGY - SUMMARY - Fo GENERATION FEMALE RATS
(See abbreviations on the last page of this table.)

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	10	10	10	10	10
PT (SECONDS)	MEAN ± S.D.	13.2 ± 0.41	13.4 ± 0.29	13.2 ± 0.37	13.5 ± 0.42	13.8 ± 1.12
APTT (SECONDS)	MEAN ± S.D.	21.7 ± 2.36	23.9 ± 3.19	23.5 ± 2.35	25.2 ± 2.45	25.2 ± 3.81
NRBC COUNT	MEAN ± S.D.	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.6
Lymphocytes (THSN/CU MM)	MEAN ± S.D.	6.6 ± 2.44	9.8 ± 3.44*	8.4 ± 2.60	8.2 ± 2.52	6.0 ± 2.77
Segmented (THSN/CU MM)	MEAN ± S.D.	2.2 ± 0.90	3.6 ± 3.69	2.4 ± 0.93	2.4 ± 0.96	2.6 ± 0.82
Bands (THSN/CU MM)	MEAN ± S.D.	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.09	0.0 ± 0.00
Monocytes (THSN/CU MM)	MEAN ± S.D.	0.1 ± 0.15	0.3 ± 0.49	0.2 ± 0.13	0.2 ± 0.11	0.2 ± 0.14
Eosinophils (THSN/CU MM)	MEAN ± S.D.	0.1 ± 0.10	0.1 ± 0.13	0.1 ± 0.13	0.1 ± 0.10	0.1 ± 0.15
Basophils (THSN/CU MM)	MEAN ± S.D.	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00
Abnormal L (THSN/CU MM)	MEAN ± S.D.	0.0 ± 0.05	0.0 ± 0.00	0.1 ± 0.07	0.0 ± 0.10	0.0 ± 0.05
Other (THSN/CU MM)	MEAN ± S.D.	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00

* Significantly different from the Group I value ($p \leq 0.05$).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C6 (PAGE 3): HEMATOLOGY - SUMMARY - Fo GENERATION FEMALE RATS

KEY TO HEMATOLOGY TABLE

ABBREVIATION	TERMINOLOGY
WBC	White Blood Cells (Leukocytes)
RBC	Red Blood Cells (Erythrocytes)
HGB	Hemoglobin
HCT	Hematocrit (Packed Cell Volume)
MCV	Mean Corpuscular Volume
MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hemoglobin Concentration
PLAT	Platelet Count
MPV	Mean Platelet Volume
PT	Prothrombin Time
APTT	Activated Partial Thromboplastin
NRBC	Nucleated Red Blood Cell Count
Segmented	Segmented Neutrophils
Abnormal L	Abnormal Lymphocytes
Other	Other Cells

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C7 (PAGE 1): CLINICAL CHEMISTRY - SUMMARY - Fo GENERATION FEMALE RATS
(See abbreviations on the last page of this table.)

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	10	10	10	10	10
TP (G/DL)	MEAN ± S.D.	6.1 ± 0.52	5.5 ± 0.50	5.9 ± 0.41	5.8 ± 0.32	5.8 ± 0.29
A (G/DL)	MEAN ± S.D.	4.1 ± 0.42	4.0 ± 0.34	4.1 ± 0.24	4.0 ± 0.29	4.0 ± 0.31
GLU (MG/DL)	MEAN ± S.D.	152 ± 19.8	162 ± 20.0	155 ± 18.7	146 ± 16.2	140 ± 35.5
CHOL (MG/DL)	MEAN ± S.D.	77 ± 27.8	72 ± 14.0	71 ± 20.0	62 ± 14.2	61 ± 19.8
TBILI (MG/DL)	MEAN ± S.D.	0.2 ± 0.07	0.2 ± 0.03	0.2 ± 0.05	0.1 ± 0.05	0.1 ± 0.05
BUN (MG/DL)	MEAN ± S.D.	28 ± 4.4	24 ± 4.7	28 ± 6.7	25 ± 4.4	30 ± 15.4
CREAT (MG/DL)	MEAN ± S.D.	0.4 ± 0.05	0.4 ± 0.05	0.3 ± 0.05	0.4 ± 0.08	0.3 ± 0.06
CK (U/L)	MEAN ± S.D.	202 ± 54.1	250 ± 85.6	192 ± 21.7	213 ± 80.4	252 ± 101.6
ALT (U/L)	MEAN ± S.D.	129 ± 31.7	133 ± 23.0	142 ± 34.2	127 ± 24.7	145 ± 20.0

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C7 (PAGE 2): CLINICAL CHEMISTRY - SUMMARY - Fo GENERATION FEMALE RATS
(See abbreviations on the last page of this table.)

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	10	10	10	10	10
AST (U/L)	MEAN ± S.D.	142 ± 22.8	135 ± 21.6	137 ± 11.8	124 ± 12.1	156 ± 40.7
ALK (U/L)	MEAN ± S.D.	145 ± 88.7	159 ± 81.7	136 ± 107.3	178 ± 131.0	128 ± 44.7
CA (MG/DL)	MEAN ± S.D.	10.6 ± 0.72	11.2 ± 0.63	10.4 ± 0.87	10.4 ± 0.46	10.4 ± 0.82
PHOS (MG/DL)	MEAN ± S.D.	8.8 ± 1.33	7.9 ± 1.94	9.0 ± 2.80	8.7 ± 2.88	10.1 ± 1.64
TRI (MG/DL)	MEAN ± S.D.	54 ± 19.9	50 ± 10.2	49 ± 29.4	45 ± 19.5	44 ± 18.3
NA (MMOL/L)	MEAN ± S.D.	143 ± 6.3	143 ± 2.4	142 ± 2.5	142 ± 2.6	142 ± 2.6
K (MMOL/L)	MEAN ± S.D.	5.8 ± 0.67	5.6 ± 0.58	5.6 ± 0.32	6.1 ± 0.70	6.2 ± 0.90
CL (MMOL/L)	MEAN ± S.D.	96 ± 3.4	94 ± 2.7	95 ± 3.8	95 ± 3.4	94 ± 3.1
G (G/DL)	MEAN ± S.D.	1.9 ± 0.22	1.6 ± 0.26**	1.8 ± 0.21	1.7 ± 0.13	1.8 ± 0.21
A/G (NONE)	MEAN ± S.D.	2.2 ± 0.28	2.6 ± 0.43**	2.2 ± 0.21	2.4 ± 0.26	2.3 ± 0.37

** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C7 (PAGE 3): CLINICAL CHEMISTRY - SUMMARY - Fo GENERATION FEMALE RATS

KEY TO CLINICAL CHEMISTRY TABLE

ABBREVIATION	TERMINOLOGY
TP	Total Protein
A	Albumin
GLU	Glucose
CHOL	Cholesterol
TBILI	Total Bilirubin
BUN	Blood Urea Nitrogen
CREAT	Creatinine
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
ALK	Alkaline Phosphatase
CA	Calcium
PHOS	Phosphorus
TRI	Triglycerides
NA	Sodium
K	Potassium
CL	Chloride
G	Globulin
A/G	Albumin/Globulin Ratio

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C8 (PAGE 1): BODY WEIGHTS - PRECOHABITATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP			I	II	III	IV	V
DOSAGE (MG/KG/DAY)			0	0.3	1	3	10
RATS TESTED		N	15	15	15	15	15
BODY WEIGHT (G)							
DAY	1	MEAN±S.D.	228.6 ± 8.0	224.7 ± 8.1	226.3 ± 7.7	226.8 ± 7.9	226.9 ± 8.0
DAY	2	MEAN±S.D.	228.2 ± 8.7	226.2 ± 9.1	227.3 ± 9.2	227.3 ± 7.6	228.3 ± 10.0
DAY	3	MEAN±S.D.	233.5 ± 7.2	228.5 ± 9.5	231.1 ± 10.1	231.5 ± 8.0	231.5 ± 10.0
DAY	4	MEAN±S.D.	236.6 ± 7.7	233.8 ± 9.4	234.2 ± 9.8	234.5 ± 8.3	235.7 ± 10.5
DAY	5	MEAN±S.D.	239.0 ± 10.0	234.6 ± 11.0	236.9 ± 9.8	235.3 ± 9.3	235.1 ± 12.3
DAY	6	MEAN±S.D.	241.2 ± 10.8	235.4 ± 11.2	241.0 ± 10.8	237.7 ± 9.1	236.3 ± 14.9
DAY	7	MEAN±S.D.	245.3 ± 10.4	238.5 ± 10.7	244.3 ± 10.8	241.0 ± 9.4	238.4 ± 15.2
DAY	8	MEAN±S.D.	250.5 ± 11.5	243.4 ± 10.6	246.5 ± 11.6	245.8 ± 9.6	243.5 ± 18.4
DAY	9	MEAN±S.D.	250.4 ± 12.1	244.1 ± 10.8	248.3 ± 11.8	245.8 ± 10.5	242.3 ± 20.8
DAY	10	MEAN±S.D.	251.6 ± 14.3	243.4 ± 12.6	250.0 ± 12.8	246.3 ± 12.5	243.3 ± 20.9
DAY	11	MEAN±S.D.	256.4 ± 14.6	246.1 ± 12.2	254.9 ± 13.3	248.6 ± 11.5	248.3 ± 19.3
DAY	12	MEAN±S.D.	256.9 ± 14.0	250.8 ± 12.4	254.8 ± 12.5	252.1 ± 11.3	252.0 ± 18.4
DAY	13	MEAN±S.D.	256.3 ± 16.3	250.4 ± 12.8	255.0 ± 13.2	252.9 ± 12.8	251.9 ± 17.9
DAY	14a	MEAN±S.D.	258.5 ± 16.1	250.7 ± 12.6	257.9 ± 13.6	253.0 ± 13.2	251.1 ± 18.0

DAY = DAY OF STUDY
a. Last value recorded before cohabitation.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C9 (PAGE 1): BODY WEIGHT CHANGES - PRECOHABITATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	15	15	15	15	15
BODY WEIGHT CHANGE (G)						
DAYS 1 - 8	MEAN±S.D.	+21.9 ± 8.3	+18.7 ± 6.3	+20.3 ± 5.7	+19.0 ± 4.3	+16.7 ± 16.0
DAYS 8 - 14a	MEAN±S.D.	+7.9 ± 7.4	+7.3 ± 4.2	+11.3 ± 6.1	+7.2 ± 6.4	+7.5 ± 8.9
DAYS 1 - 14a	MEAN±S.D.	+29.9 ± 13.7	+25.9 ± 7.2	+31.6 ± 8.4	+26.2 ± 8.3	+24.2 ± 14.4

DAYS = DAYS OF STUDY
a. Last value recorded before cohabitation.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C10 (PAGE 1): MATERNAL BODY WEIGHTS - GESTATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP			I	II	III	IV	V
DOSAGE (MG/KG/DAY)			0	0.3	1	3	10
RATS TESTED		N	15	15	15	15	15
PREGNANT		N	15	15	13	13	15
MATERNAL BODY WEIGHT (G)							
DAY	0	MEAN±S.D.	270.1 ± 14.3	259.4 ± 12.0	270.9 ± 15.6	265.6 ± 15.4	260.9 ± 18.2
DAY	1	MEAN±S.D.	273.7 ± 19.9	264.7 ± 11.5	274.6 ± 13.4	270.9 ± 14.5	266.9 ± 19.2
DAY	2	MEAN±S.D.	280.5 ± 20.2	269.9 ± 12.8	278.2 ± 14.7	275.4 ± 15.6	269.1 ± 18.1
DAY	3	MEAN±S.D.	283.4 ± 20.6	274.3 ± 12.4	284.5 ± 14.0	278.8 ± 16.0	275.7 ± 18.0
DAY	4	MEAN±S.D.	286.5 ± 22.2	278.9 ± 12.9	285.7 ± 16.6	282.7 ± 17.7	277.7 ± 20.8
DAY	5	MEAN±S.D.	291.3 ± 20.3	283.1 ± 13.9	290.2 ± 17.3	286.3 ± 16.8	280.9 ± 19.4
DAY	6	MEAN±S.D.	294.1 ± 18.7	287.3 ± 14.2	292.2 ± 18.0	288.5 ± 18.1	283.7 ± 19.8
DAY	7	MEAN±S.D.	298.0 ± 16.1	290.4 ± 14.9	295.2 ± 18.4	291.3 ± 19.1	287.7 ± 20.6
DAY	8	MEAN±S.D.	303.3 ± 18.0	294.6 ± 13.2	300.5 ± 18.6	296.2 ± 22.1	292.2 ± 21.0
DAY	9	MEAN±S.D.	307.9 ± 16.8	299.3 ± 15.3	305.3 ± 20.1	301.0 ± 22.3	295.9 ± 20.6
DAY	10	MEAN±S.D.	314.1 ± 17.2	304.2 ± 15.5	311.7 ± 20.5	306.3 ± 22.6	302.1 ± 22.1

DAY = DAY OF GESTATION

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C10 (PAGE 2): MATERNAL BODY WEIGHTS - GESTATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	15	15	15	15	15
PREGNANT	N	15	15	13	13	15
MATERNAL BODY WEIGHT (G)						
DAY 11	MEAN±S.D.	320.7 ± 19.6	311.7 ± 16.5	318.5 ± 20.6	313.6 ± 22.0	308.6 ± 23.3
DAY 12	MEAN±S.D.	325.6 ± 19.8	318.3 ± 16.8	325.1 ± 19.8	319.6 ± 26.0	315.0 ± 23.9
DAY 13	MEAN±S.D.	331.1 ± 19.0	321.3 ± 16.9	328.3 ± 21.6	323.2 ± 25.8	319.3 ± 23.3
DAY 14	MEAN±S.D.	338.8 ± 17.9	328.5 ± 16.8	334.2 ± 20.7	329.2 ± 26.1	324.1 ± 23.1
DAY 15	MEAN±S.D.	345.7 ± 18.4	336.1 ± 17.7	342.5 ± 20.6	335.2 ± 26.3	331.2 ± 24.1
DAY 16	MEAN±S.D.	353.1 ± 23.8	345.1 ± 17.8	350.1 ± 20.8	342.8 ± 29.0	337.7 ± 24.6
DAY 17	MEAN±S.D.	365.3 ± 26.7	357.7 ± 19.8	364.8 ± 19.4	356.0 ± 30.6	353.3 ± 24.6
DAY 18	MEAN±S.D.	383.5 ± 27.1	370.3 ± 21.5	380.4 ± 20.8	365.2 ± 25.2	365.0 ± 25.9
DAY 19	MEAN±S.D.	398.1 ± 31.0	380.3 ± 27.4	393.0 ± 22.7	380.4 ± 24.7	378.0 ± 27.8
DAY 20	MEAN±S.D.	412.0 ± 35.0	397.4 ± 27.8	412.1 ± 21.7	398.8 ± 27.6	395.1 ± 28.1

DAY = DAY OF GESTATION

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C11 (PAGE 1): MATERNAL BODY WEIGHT CHANGES - GESTATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0	II 0.3	III 1	IV 3	V 10
RATS TESTED	N	15	15	15	15	15
PREGNANT	N	15	15	13	13	15
MATERNAL BODY WEIGHT CHANGE (G)						
DAYS 0 - 7	MEAN±S.D.	+27.9 ± 6.7	+31.0 ± 7.4	+24.3 ± 6.3	+25.7 ± 10.3	+26.9 ± 5.8
DAYS 7 - 10	MEAN±S.D.	+16.1 ± 4.9	+13.8 ± 3.4	+16.5 ± 5.3	+15.0 ± 6.1	+14.4 ± 3.7
DAYS 10 - 12	MEAN±S.D.	+11.5 ± 4.2	+14.1 ± 3.3	+13.4 ± 4.2	+13.3 ± 5.8	+12.9 ± 6.2
DAYS 12 - 15	MEAN±S.D.	+20.1 ± 4.3	+17.7 ± 3.6	+17.4 ± 4.0	+15.5 ± 5.5	+16.2 ± 4.1
DAYS 15 - 18	MEAN±S.D.	+37.9 ± 10.6	+34.2 ± 7.9	+37.9 ± 5.2	+30.0 ± 12.5	+33.8 ± 5.7
DAYS 18 - 20	MEAN±S.D.	+28.5 ± 16.6	+27.1 ± 13.2	+31.7 ± 6.7	+33.6 ± 9.2	+30.1 ± 8.9
DAYS 0 - 20	MEAN±S.D.	+141.9± 29.0	+138.0± 27.4	+141.2± 14.1	+133.2± 21.9	+134.2± 16.9

DAYS = DAYS OF GESTATION

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C12 (PAGE 1): MATERNAL BODY WEIGHTS - LACTATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP			I	II	III	IV	V
DOSAGE (MG/KG/DAY)			0	0.3	1	3	10
RATS TESTED		N	15	15	15	15	15
PREGNANT		N	15	15	13	13	15
DELIVERED A LITTER		N	15	15	13	13	15
MATERNAL BODY WEIGHT (G)							
DAY 1		MEAN±S.D.	313.1 ± 22.6	302.2 ± 16.8	309.5 ± 20.6	304.7 ± 23.2	296.3 ± 19.9
DAY 2		MEAN±S.D.	313.1 ± 24.6	300.1 ± 17.2	305.4 ± 18.9	304.2 ± 22.2	298.9 ± 19.8
DAY 3		MEAN±S.D.	316.1 ± 22.6	300.2 ± 18.6 [13]a	310.4 ± 18.1 [11]a	305.0 ± 23.1 [12]a	300.3 ± 20.0 [14]a
DAY 4		MEAN±S.D.	321.5 ± 22.7	303.4 ± 17.2* [13]a	314.2 ± 19.8 [12]a	310.2 ± 22.5 [12]a	299.3 ± 19.7* [13]a
DAY 5		MEAN±S.D.	326.0 ± 20.5	307.3 ± 14.2	314.9 ± 21.1 [12]a	311.5 ± 23.0 [12]a	308.4 ± 15.7 [13]a
DAY 6		MEAN±S.D.	332.7 ± 26.1	312.9 ± 11.9*	323.9 ± 18.2 [12]a	316.9 ± 16.1 [11]a	306.0 ± 26.9**
DAY 7		MEAN±S.D.	340.4 ± 20.8	321.4 ± 12.6*	331.2 ± 18.3	317.7 ± 21.6** [12]a	315.2 ± 25.4**
DAY 8		MEAN±S.D.	342.3 ± 19.8	320.7 ± 12.6*	333.6 ± 19.6 [12]a	322.2 ± 21.5*	318.1 ± 26.0**
DAY 9		MEAN±S.D.	349.9 ± 25.6 [14]a	331.7 ± 11.9 [14]a	337.4 ± 17.3	331.8 ± 21.2	324.7 ± 29.7**
DAY 10		MEAN±S.D.	353.6 ± 17.9 [13]a	334.9 ± 17.5	345.5 ± 18.2	333.5 ± 23.0 [12]a	327.4 ± 38.3
DAY 11		MEAN±S.D.	354.4 ± 18.5 [14]a	331.9 ± 25.7*	349.2 ± 20.3 [12]a	336.4 ± 24.6 [12]a	330.2 ± 30.8*

DAY = DAY OF LACTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Excludes values that appeared incorrectly recorded, as well as those associated with interrupted water access.
* Significantly different from the Group I value ($p \leq 0.05$).
** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C12 (PAGE 2): MATERNAL BODY WEIGHTS - LACTATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	15	15	15	15	15
PREGNANT	N	15	15	13	13	15
DELIVERED A LITTER	N	15	15	13	13	15
MATERNAL BODY WEIGHT (G)						
DAY 12	MEAN±S.D.	355.7 ± 20.2	344.2 ± 13.6 [14]a	352.6 ± 20.1 [12]a	347.5 ± 24.4 [12]a	334.2 ± 32.5 [14]a
DAY 13	MEAN±S.D.	364.1 ± 18.5 [14]a	342.9 ± 17.2* [14]a	353.5 ± 20.2 [12]a	352.0 ± 21.8 [12]a	340.1 ± 30.8*
DAY 14	MEAN±S.D.	359.8 ± 21.5	342.7 ± 14.5 [14]a	353.1 ± 17.3	345.1 ± 19.5	335.2 ± 32.2** [13]a
DAY 15	MEAN±S.D.	355.3 ± 31.2	342.4 ± 10.4 [14]a	343.2 ± 17.2 [12]a	348.7 ± 21.4 [12]a	333.4 ± 33.6 [14]a
DAY 16	MEAN±S.D.	360.7 ± 22.0	345.7 ± 12.9	353.2 ± 18.0	348.4 ± 21.3	337.8 ± 34.3 [14]a
DAY 17	MEAN±S.D.	351.7 ± 21.4	341.1 ± 16.9	346.5 ± 17.8 [12]a	339.3 ± 26.4	333.0 ± 33.4
DAY 18	MEAN±S.D.	360.3 ± 21.5	346.4 ± 15.6	352.2 ± 21.5	352.2 ± 21.8	340.6 ± 34.3
DAY 19	MEAN±S.D.	360.1 ± 21.4	347.9 ± 15.1	355.0 ± 19.6	357.5 ± 25.1	339.5 ± 32.3 [14]a
DAY 20	MEAN±S.D.	359.6 ± 19.0	344.6 ± 16.1	348.8 ± 20.6	352.9 ± 24.0	338.9 ± 34.9
DAY 21	MEAN±S.D.	350.1 ± 26.9 [14]a	335.7 ± 18.7 [14]a	343.4 ± 19.8	344.4 ± 25.8	334.4 ± 35.9
DAY 22	MEAN±S.D.	306.3 ± 26.0	324.3 ± 27.1	311.2 ± 35.0	319.6 ± 40.4	303.5 ± 37.9

DAY = DAY OF LACTATION .
[ ] = NUMBER OF VALUES AVERAGED
a. Excludes values that appeared incorrectly recorded, as well as those associated with interrupted water access.
* Significantly different from the Group I value ($p \leq 0.05$).
** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C13 (PAGE 1): MATERNAL BODY WEIGHT CHANGES - LACTATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	15	15	15	15	15
PREGNANT	N	15	15	13	13	15
DELIVERED A LITTER	N	15	15	13	13	15
MATERNAL BODY WEIGHT CHANGE (G)						
DAYS 1 - 5	MEAN±S.D.	+12.9 ± 10.2	+5.1 ± 10.7	+7.2 ± 12.7 [12]a	+7.7 ± 14.8 [12]a	+7.8 ± 15.1 [13]a
DAYS 5 - 8	MEAN±S.D.	+16.3 ± 9.6	+13.5 ± 7.4	+17.3 ± 7.6 [11]a	+11.0 ± 11.0 [12]a	+16.5 ± 10.1 [13]a
DAYS 8 - 11	MEAN±S.D.	+13.9 ± 7.1 [14]a	+11.1 ± 19.2	+14.4 ± 5.6 [11]a	+13.6 ± 10.6 [12]a	+12.1 ± 10.8
DAYS 11 - 15	MEAN±S.D.	-0.7 ± 22.4 [14]a	+12.8 ± 19.9 [14]a	-3.7 ± 13.2 [11]a	+13.8 ± 9.7 [11]a	+3.7 ± 11.2 [14]a
DAYS 15 - 18	MEAN±S.D.	+4.9 ± 21.8	+2.2 ± 11.9 [14]a	+7.9 ± 18.0 [12]a	+4.1 ± 6.3 [12]a	+7.4 ± 11.4 [14]a
DAYS 18 - 22	MEAN±S.D.	-54.0 ± 25.3	-22.1 ± 26.7	-41.1 ± 33.6	-32.5 ± 28.2	-37.1 ± 29.8
DAYS 1 - 22	MEAN±S.D.	-6.9 ± 28.4	+22.1 ± 26.0	+1.7 ± 28.0	+14.9 ± 31.8	+7.3 ± 29.3

DAYS = DAYS OF LACTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Excludes values that appeared incorrectly recorded, as well as those associated with interrupted water access.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C14 (PAGE 1): ABSOLUTE FEED CONSUMPTION VALUES (G/DAY) - PRECOHABITATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	15	15	15	15	15
FEED CONSUMPTION (G/DAY)						
DAYS 1 - 8	MEAN±S.D.	20.4 ± 1.8 [13]a	19.5 ± 1.6	20.7 ± 2.0	19.5 ± 1.8	19.6 ± 3.0

DAYS = DAYS OF STUDY
[ ] = NUMBER OF VALUES AVERAGED
a. Excludes values that were not recorded, as well as those associated with spillage.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C15 (PAGE 1): RELATIVE FEED CONSUMPTION VALUES (G/KG/DAY) - PRECOHABITATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	15	15	15	15	15
FEED CONSUMPTION (G/KG/DAY)						
DAYS 1 - 8	MEAN±S.D.	86.1 ± 5.5 [13]a	83.4 ± 5.6	87.9 ± 7.0	83.0 ± 5.2	83.3 ± 10.0

DAYS = DAYS OF STUDY
[ ] = NUMBER OF VALUES AVERAGED
a. Excludes values that were not recorded, as well as those associated with spillage.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C16 (PAGE 1): MATERNAL ABSOLUTE FEED CONSUMPTION VALUES (G/DAY) - GESTATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	15	15	15	15	15
PREGNANT	N	15	15	13	13	15
MATERNAL FEED CONSUMPTION (G/DAY)						
DAYS 0 - 7	MEAN±S.D.	25.4 ± 3.3	25.0 ± 2.5	24.3 ± 2.7	25.2 ± 3.6	24.0 ± 2.7
DAYS 7 - 10	MEAN±S.D.	27.7 ± 2.8	26.8 ± 2.8	26.3 ± 3.4	26.3 ± 5.0	25.8 ± 2.5
DAYS 10 - 12	MEAN±S.D.	32.0 ± 10.5 [14]a	27.0 ± 3.2	28.0 ± 3.2	26.6 ± 3.9	27.0 ± 2.8
DAYS 12 - 15	MEAN±S.D.	28.4 ± 2.8	27.5 ± 2.4	27.5 ± 2.1	26.7 ± 3.9	27.5 ± 2.6
DAYS 15 - 18	MEAN±S.D.	25.4 ± 4.0	26.7 ± 3.1	25.9 ± 2.1	25.3 ± 3.6	26.0 ± 3.3
DAYS 18 - 20	MEAN±S.D.	26.6 ± 5.7	22.8 ± 6.2	25.8 ± 3.2	25.0 ± 3.7	26.1 ± 4.8
DAYS 0 - 20	MEAN±S.D.	26.9 ± 3.2	25.9 ± 2.4	25.8 ± 2.0	25.7 ± 3.0	25.6 ± 2.3

DAYS = DAYS OF GESTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Excludes values that were associated with spillage.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C17 (PAGE 1): MATERNAL RELATIVE FEED CONSUMPTION VALUES (G/KG/DAY) - GESTATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	15	15	15	15	15
PREGNANT	N	15	15	13	13	15
MATERNAL FEED CONSUMPTION (G/KG/DAY)						
DAYS 0 - 7	MEAN±S.D.	88.8 ± 8.4	90.4 ± 7.1	85.6 ± 6.9	89.8 ± 9.3	86.8 ± 5.5
DAYS 7 - 10	MEAN±S.D.	90.5 ± 7.4	90.0 ± 7.0	86.4 ± 7.4	87.7 ± 12.7	87.6 ± 5.4
DAYS 10 - 12	MEAN±S.D.	99.0 ± 28.7 [14]a	86.5 ± 8.0	87.9 ± 6.1	84.8 ± 7.0	87.3 ± 4.3
DAYS 12 - 15	MEAN±S.D.	84.9 ± 7.3	84.4 ± 5.8	82.7 ± 4.9	81.5 ± 6.9	85.6 ± 7.2
DAYS 15 - 18	MEAN±S.D.	70.0 ± 8.5	75.6 ± 6.9	72.3 ± 6.2	72.2 ± 7.4	75.1 ± 8.3
DAYS 18 - 20	MEAN±S.D.	66.4 ± 12.4	59.3 ± 15.4	65.4 ± 7.9	66.1 ± 11.8	68.7 ± 10.7
DAYS 0 - 20	MEAN±S.D.	83.3 ± 6.6	82.6 ± 5.6	80.5 ± 3.1	81.6 ± 5.4	82.5 ± 4.0

DAYS = DAYS OF GESTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Excludes values that were associated with spillage.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C18 (PAGE 1): MATERNAL ABSOLUTE FEED CONSUMPTION VALUES (G/DAY) - LACTATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	15	15	15	15	15
PREGNANT	N	15	15	13	13	15
DELIVERED A LITTER	N	15	15	13	13	15
MATERNAL FEED CONSUMPTION (G/DAY)						
DAYS 1 - 5	MEAN±S.D.	38.5 ± 7.1	27.6 ± 8.7** [14]a	33.2 ± 4.0 [12]a	31.4 ± 5.5*	34.4 ± 7.9 [14]a
DAYS 5 - 8	MEAN±S.D.	61.2 ± 6.4	53.7 ± 6.6	55.9 ± 4.4	49.4 ± 10.2	52.3 ± 9.0
DAYS 8 - 15	MEAN±S.D.	71.6 ± 8.6	68.3 ± 8.3*	69.2 ± 4.0	69.6 ± 9.5**	68.2 ± 9.4**
DAYS 1 - 15	MEAN±S.D.	59.9 ± 7.0	54.3 ± 7.1	56.9 ± 4.9	54.4 ± 7.2	55.7 ± 8.2

DAYS = DAYS OF LACTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Excludes values that were associated with spillage.
* Significantly different from the Group I value ($p \leq 0.05$).
** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C19 (PAGE 1): MATERNAL RELATIVE FEED CONSUMPTION VALUES (G/KG/DAY) - LACTATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS TESTED	N	15	15	15	15	15
PREGNANT	N	15	15	13	13	15
DELIVERED A LITTER	N	15	15	13	13	15
MATERNAL FEED CONSUMPTION (G/KG/DAY)						
DAYS 1 - 5	MEAN±S.D.	121.1 ± 21.3	91.8 ± 27.8** [14]a	107.6 ± 15.0 [12]a	102.7 ± 21.2 [12]a	118.7 ± 22.1 [12]a
DAYS 5 - 8	MEAN±S.D.	183.0 ± 20.6	170.4 ± 23.5	170.6 ± 12.2 [11]a	155.2 ± 32.4** [12]a	168.2 ± 20.0 [12]a
DAYS 8 - 11	MEAN±S.D.	176.1 ± 134.6 [14]a	176.1 ± 109.9	101.9 ± 97.9 [11]a	155.4 ± 134.0 [12]a	138.4 ± 127.0
DAYS 11 - 15	MEAN±S.D.	222.6 ± 97.5 [14]a	225.3 ± 64.3 [14]a	276.0 ± 76.3 [11]a	245.4 ± 89.7 [11]a	248.7 ± 81.6 [14]a
DAYS 1 - 15	MEAN±S.D.	176.7 ± 19.5	166.9 ± 22.6 [14]a	172.4 ± 11.5 [12]a	166.6 ± 20.2 [12]a	175.1 ± 14.9 [14]a

DAYS = DAYS OF LACTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Excludes values that appeared incorrectly recorded, as well as those associated with interrupted water access or spillage.
** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C20 (PAGE 1): MATING AND FERTILITY, ESTROUS CYCLING AND DAYS IN COHABITATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
ESTROUS CYCLING OBSERVATIONS						
RATS EVALUATED	N	15	15	15	15	15
ESTROUS STAGES/ 13 DAYS	MEAN±S.D.	2.7 ± 0.9	2.8 ± 0.9	3.3 ± 0.6	2.9 ± 0.8	2.1 ± 1.2
RATS WITH 6 OR MORE CONSECUTIVE DAYS OF DIESTRUS	N	1	0	0	0	1
RATS WITH 6 OR MORE CONSECUTIVE DAYS OF ESTRUS	N	0	0	0	1	0

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C20 (PAGE 2): MATING AND FERTILITY, ESTROUS CYCLING AND DAYS IN COHABITATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0	II 0.3	III 1	IV 3	V 10
RATS IN COHABITATION	N	15	15	15	15	15
DAYS IN COHABITATION a	MEAN±S.D.	3.7 ± 3.0	1.9 ± 1.2	2.8 ± 1.2	4.0 ± 4.0	2.5 ± 1.4
RATS THAT MATED	N(%)	15(100.0)	15(100.0)	15(100.0)	14(93.3)	15(100.0)
FERTILITY INDEX b	N/N (%)	15/ 15 (100.0)	15/ 15 (100.0)	13/ 15 (86.7)	13/ 14 (92.8)	15/ 15 (100.0)
RATS WITH CONFIRMED MATING DATES	N	15	15	15	14	15
MATED BY FIRST MALE c DAYS 1-7	N(%)	14(93.3)	15(100.0)	15(100.0)	13(92.8)	15(100.0)
MATED BY SECOND MALE c DAYS 8-14	N(%)	1(6.7)	0(0.0)	0(0.0)	1(7.2)	0(0.0)
RATS PREGNANT/RATS IN COHABITATION	N/N (%)	15/ 15 (100.0)	15/ 15 (100.0)	13/ 15 (86.7)	13/ 15 (86.7)	15/ 15 (100.0)

a. Restricted to rats with a confirmed mating date and rats that did not mate.
b. Number of pregnancies/number of rats that mated.
c. Restricted to rats with a confirmed mating date.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C21 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
FEMALE RATS	N	10	10	10	10	10
HOME CAGE BEHAVIOR						
1: Sleeping	N	1	4	4	4	1
2: Awake, Immobile	N	1	2	1	3	4
3: Normal movement	N	8	4	5	3	5
4: Unusual posture	N	0	0	0	0	0
5: Unusual behavior	N	0	0	0	0	0
ALTERATIONS (HOME CAGE)						
1: None	N	10	10	10	10	10
2: Stereotyped behavior	N	0	0	0	0	0
3: Bizarre behavior	N	0	0	0	0	0
4: Limb twitches/tremor	N	0	0	0	0	0
5: Whole body tremor/spasm	N	0	0	0	0	0
6: Unusual posture	N	0	0	0	0	0
7: Tonic-clonic seizure	N	0	0	0	0	0
REACTION TO REMOVAL						
(1) Sits quietly	N	10	10	10	10	10
(2) Vocalization	N	0	0	0	0	0
(3) Runs or freezes	N	0	0	0	0	0
(4) Tail or throat rattles	N	0	0	0	0	0
	MEAN SCORE	1.0	1.0	1.0	1.0	1.0
REACTION TO HANDLING						
(1) No resistance	N	10	10	10	10	10
(2) Vocalization	N	0	0	0	0	0
(3) Tense	N	0	0	0	0	0
(4) Squirming	N	0	0	0	0	0
	MEAN SCORE	1.0	1.0	1.0	1.0	1.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C21 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
FEMALE RATS	N	10	10	10	10	10
REARS IN OPEN FIELD	MEAN±S.D.	12.0 ± 3.6	13.0 ± 2.7	11.6 ± 3.5	10.7 ± 2.3	10.9 ± 2.6
DEFECATION IN OPEN FIELD						
1: None	N	8	10	8	8	8
2: Feces normal	N	2	0	1	1	2
3: Soft or liquid feces	N	0	0	1	1	0
URINATION IN OPEN FIELD						
(1) None	N	6	7	7	10	8
(2) Normal urination	N	4	3	3	0	2
(3) Excess urination	N	0	0	0	0	0
	MEAN SCORE	1.4	1.3	1.3	1.0	1.2
LEVEL OF AROUSAL						
(1) Stuporous	N	0	0	0	0	0
(2) Sluggish	N	0	0	0	0	0
(3) Apparently normal	N	10	10	10	10	10
(4) Sudden darting	N	0	0	0	0	0
(5) Freezing, vocalization	N	0	0	0	0	0
	MEAN SCORE	3.0	3.0	3.0	3.0	3.0
ALTERATIONS (OPEN FIELD)						
1: None	N	10	10	10	10	10
2: Stereotyped behavior	N	0	0	0	0	0
3: Bizarre behavior	N	0	0	0	0	0
4: Limb twitches/tremor	N	0	0	0	0	0
5: Whole body tremor/spasm	N	0	0	0	0	0
6: Unusual posture	N	0	0	0	0	0
7: Tonic-clonic seizure	N	0	0	0	0	0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C21 (PAGE 3): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
FEMALE RATS	N	10	10	10	10	10
GAIT PATTERN						
1: Apparently normal	N	10	10	10	10	8
2: Ataxic	N	0	0	0	0	0
3: Limbs splay or drag	N	0	0	0	0	0
4: Spastic, tip-toe	N	0	0	0	0	2
5: Duck-walk	N	0	0	0	0	0
6: Scissors gait	N	0	0	0	0	0
GAIT ABNORMALITY, SEVERITY						
(1) Normal gait	N	10	10	10	10	8
(2) Slight	N	0	0	0	0	2
(3) Moderate	N	0	0	0	0	0
(4) Extreme	N	0	0	0	0	0
	MEAN SCORE	1.0	1.0	1.0	1.0	1.2
PALPEBRAL CLOSURE						
(1) Wide open	N	10	10	10	10	10
(2) Slightly drooping	N	0	0	0	0	0
(3) Half-closed	N	0	0	0	0	0
(4) Completely shut	N	0	0	0	0	0
	MEAN SCORE	1.0	1.0	1.0	1.0	1.0
PROMINENCE OF THE EYE						
1: Normal	N	10	10	10	10	10
2: Exophthalmos	N	0	0	0	0	0
3: Enophthalmos	N	0	0	0	0	0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C21 (PAGE 4): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
FEMALE RATS	N	10	10	10	10	10
LACRIMATION						
(1) No excess	N	10	10	10	10	10
(2) Excess at eyelid margin	N	0	0	0	0	0
(3) Margin persistently damp	N	0	0	0	0	0
(4) Extends beyond margin	N	0	0	0	0	0
	MEAN SCORE	1.0	1.0	1.0	1.0	1.0
SALIVATION						
(1) No excess	N	10	10	10	10	10
(2) Margin of mouth wet	N	0	0	0	0	0
(3) 1/4 to 1/2 submandibular	N	0	0	0	0	0
(4) Entire submandibular	N	0	0	0	0	0
	MEAN SCORE	1.0	1.0	1.0	1.0	1.0
PILOERECTION	N	0	0	0	0	0
ABNORMAL RESPIRATION	N	0	0	0	0	1
APPEARANCE						
(1) Clean and groomed	N	10	10	9	9	10
(2) Unkempt	N	0	0	1	0	0
(3) Urine and/or fecal stain	N	0	0	0	1	0
	MEAN SCORE	1.0	1.0	1.1	1.2	1.0
VISUAL REACTION						
(1) None	N	0	0	0	0	0
(2) Orienting	N	10	10	10	10	10
(3) Startle	N	0	0	0	0	0
(4) More energetic reaction	N	0	0	0	0	0
(5) Attacks	N	0	0	0	0	0
	MEAN SCORE	2.0	2.0	2.0	2.0	2.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C21 (PAGE 5): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
FEMALE RATS	N	10	10	10	10	10
TACTILE REACTION						
(1) None	N	0	0	0	0	0
(2) Orienting	N	10	10	10	10	10
(3) Startle	N	0	0	0	0	0
(4) More energetic reaction	N	0	0	0	0	0
(5) Attacks	N	0	0	0	0	0
	MEAN SCORE	2.0	2.0	2.0	2.0	2.0
AUDITORY REACTION						
(1) None	N	0	0	0	0	0
(2) Orienting	N	0	0	0	1	1
(3) Startle	N	10	10	10	9	9
(4) More energetic reaction	N	0	0	0	0	0
(5) Intense vocalization	N	0	0	0	0	0
	MEAN SCORE	3.0	3.0	3.0	2.9	2.9
TAIL-PINCH REACTION						
(1) None	N	0	0	0	0	0
(2) Orienting	N	8	9	8	10	9
(3) Startle	N	2	1	2	0	1
(4) More energetic reaction	N	0	0	0	0	0
(5) Attacks	N	0	0	0	0	0
	MEAN SCORE	2.2	2.1	2.2	2.0	2.1

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C21 (PAGE 6): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
FEMALE RATS	N	10	10	10	10	10
AIR RIGHTING RESPONSE						
(1) All feet land on ground	N	10	10	10	10	10
(2) Lands on side	N	0	0	0	0	0
(3) Lands on back	N	0	0	0	0	0
	MEAN SCORE	1.0	1.0	1.0	1.0	1.0
PUPIL RESPONSE TO LIGHT	N	10	10	10	10	10
FORELIMB GRIP TEST						
Maximum (G)	MEAN±S.D.	509.5 ± 161.7	396.5 ± 125.7	492.5 ± 257.7	493.0 ± 112.3	518.5 ± 161.9
Average (G)	MEAN±S.D.	455.9 ± 136.7	319.8 ± 100.6	423.9 ± 207.3	452.5 ± 103.4	460.3 ± 166.4
HINDLIMB GRIP TEST						
Maximum (G)	MEAN±S.D.	462.0 ± 111.3	412.5 ± 104.7	455.5 ± 87.7	397.0 ± 67.5	485.5 ± 71.5
Average (G)	MEAN±S.D.	423.0 ± 113.7	366.5 ± 77.3	418.3 ± 79.4	362.8 ± 79.8	427.3 ± 52.2
LANDING FOOT SPLAY						
Average (CM)	MEAN±S.D.	7.7 ± 1.8	6.7 ± 1.0	7.7 ± 1.5	7.1 ± 1.4	8.1 ± 1.7
BODY WEIGHT (G)	MEAN±S.D.	353.4 ± 22.0	347.2 ± 14.8	350.6 ± 22.8	345.2 ± 20.0	328.3 ± 44.7

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C22 (PAGE 1): MOTOR ACTIVITY - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
NUMBER OF FEMALE RATS	N	10	10	10	10	10
NUMBER OF MOVEMENTS						
BLOCK 1	MEAN ±	72.0 ± 6.9	67.1 ± 7.6	68.3 ± 6.8	65.7 ± 9.7	68.4 ± 9.8
BLOCK 2	MEAN ±	53.8 ± 25.7	53.6 ± 20.8	66.6 ± 12.4	57.1 ± 18.2	42.5 ± 19.9
BLOCK 3	MEAN ±	50.4 ± 26.5	41.2 ± 34.2	50.2 ± 17.0	49.3 ± 21.4	31.1 ± 24.6
BLOCK 4	MEAN ±	28.6 ± 34.7	30.7 ± 25.5	43.9 ± 26.8	39.0 ± 25.1	20.5 ± 22.9
BLOCK 5	MEAN ±	27.5 ± 24.0	21.2 ± 23.6	43.6 ± 26.4	33.9 ± 24.2	18.6 ± 22.4
BLOCK 6	MEAN ±	23.9 ± 26.5	19.4 ± 20.7	42.6 ± 29.5	35.0 ± 26.8	19.7 ± 18.0
BLOCK 7	MEAN ±	11.6 ± 16.0	17.8 ± 23.2	44.5 ± 21.3	38.3 ± 29.4	14.0 ± 17.3
BLOCK 8	MEAN ±	19.3 ± 18.1	13.2 ± 18.6	38.0 ± 20.5	44.5 ± 18.0	32.6 ± 26.2
BLOCK 9	MEAN ±	21.4 ± 21.0	10.5 ± 24.3	28.1 ± 25.4	34.0 ± 19.0	27.9 ± 24.6
BLOCK 10	MEAN ±	19.6 ± 22.1	6.5 ± 7.2	29.4 ± 29.3	25.9 ± 23.5	15.5 ± 16.5
BLOCK 11	MEAN ±	9.2 ± 10.6	7.0 ± 16.6	26.9 ± 28.2	23.5 ± 22.7	19.7 ± 22.6
BLOCK 12	MEAN ±	18.1 ± 25.5	5.9 ± 5.3	21.1 ± 26.2	21.8 ± 20.4	29.7 ± 21.4
BLOCK 13	MEAN ±	12.1 ± 18.3	15.0 ± 22.1	24.3 ± 26.3	19.8 ± 25.0	22.1 ± 25.5
BLOCK 14	MEAN ±	16.0 ± 19.0	19.0 ± 19.6	24.4 ± 30.8	24.4 ± 26.2	16.8 ± 18.3
BLOCK 15	MEAN ±	22.2 ± 30.6	13.0 ± 15.7	23.6 ± 25.9	19.8 ± 24.9	15.1 ± 20.2
BLOCK 16	MEAN ±	23.2 ± 27.2	15.0 ± 16.7	24.5 ± 28.2	27.2 ± 29.0	19.2 ± 18.9
BLOCK 17	MEAN ±	32.2 ± 33.8	11.7 ± 18.6	24.7 ± 27.9	21.9 ± 23.2	18.3 ± 25.6
BLOCK 18	MEAN ±	25.9 ± 28.5	10.8 ± 14.7	17.9 ± 18.9	19.0 ± 25.3	22.6 ± 20.9
TOTAL	MEAN ±	487.0 ± 244.9	378.6 ± 202.4	642.6 ± 295.6	600.1 ± 292.0	454.3 ± 261.4

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C22 (PAGE 2): MOTOR ACTIVITY - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
NUMBER OF FEMALE RATS	N	10	10	10	10	10
TIME (SECONDS) SPENT IN MOVEMENT						
BLOCK 1	MEAN ±	154.8 ± 27.4	141.5 ± 46.3	154.4 ± 32.2	181.0 ± 36.4	146.2 ± 26.1
BLOCK 2	MEAN ±	95.3 ± 50.4	94.0 ± 54.4	114.4 ± 24.2	119.5 ± 56.0	96.6 ± 63.6
BLOCK 3	MEAN ±	65.7 ± 36.2	60.1 ± 48.0	88.5 ± 56.9	94.4 ± 55.9	52.3 ± 51.5
BLOCK 4	MEAN ±	30.6 ± 41.4	48.0 ± 48.9	70.2 ± 52.2	73.0 ± 61.1	34.6 ± 45.9
BLOCK 5	MEAN ±	33.6 ± 36.5	27.5 ± 30.6	63.4 ± 42.7	52.0 ± 47.4	27.6 ± 35.5
BLOCK 6	MEAN ±	27.5 ± 37.9	31.0 ± 41.8	56.1 ± 41.1	56.7 ± 47.1	31.0 ± 30.6
BLOCK 7	MEAN ±	11.7 ± 18.4	21.4 ± 31.9	69.0 ± 46.5	65.3 ± 59.7	16.5 ± 29.0
BLOCK 8	MEAN ±	25.4 ± 29.0	15.5 ± 26.5	60.7 ± 36.2	70.1 ± 26.6	41.7 ± 38.3
BLOCK 9	MEAN ±	25.5 ± 28.6	13.8 ± 37.1	37.9 ± 41.2	66.6 ± 58.8	40.1 ± 38.6
BLOCK 10	MEAN ±	25.2 ± 30.0	6.2 ± 9.6	38.7 ± 44.1	41.6 ± 49.9	14.1 ± 16.3
BLOCK 11	MEAN ±	11.8 ± 14.7	8.3 ± 21.8	39.7 ± 44.2	37.2 ± 46.8	24.6 ± 33.0
BLOCK 12	MEAN ±	22.9 ± 35.7	4.2 ± 3.7	34.4 ± 48.6	26.6 ± 25.8	38.7 ± 34.5
BLOCK 13	MEAN ±	14.0 ± 23.3	14.7 ± 21.0	38.4 ± 52.5	33.4 ± 49.6	32.7 ± 43.3
BLOCK 14	MEAN ±	14.8 ± 20.2	24.1 ± 27.9	34.5 ± 48.1	33.1 ± 42.5	25.6 ± 30.6
BLOCK 15	MEAN ±	30.1 ± 46.0	15.5 ± 23.7	36.4 ± 44.5	33.0 ± 54.3	17.3 ± 25.7
BLOCK 16	MEAN ±	27.0 ± 33.9	17.6 ± 24.1	36.1 ± 42.1	38.6 ± 40.7	18.5 ± 23.1
BLOCK 17	MEAN ±	40.7 ± 46.3	13.7 ± 27.6	37.8 ± 48.8	34.9 ± 46.8	21.7 ± 33.6
BLOCK 18	MEAN ±	38.2 ± 45.8	9.6 ± 14.8	18.1 ± 23.2	29.3 ± 48.7	27.6 ± 30.1
TOTAL	MEAN ±	694.8 ± 331.8	566.7 ± 350.6	1028.7 ± 477.6	1086.3 ± 711.3	707.4 ± 442.6

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C23 (PAGE 1): NATURAL DELIVERY OBSERVATIONS - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
RATS ASSIGNED TO NATURAL DELIVERY	N	15	15	15	15	15
PREGNANT	N(%)	15(100.0)	15(100.0)	13(88.7)	13(88.7)	15(100.0)
DELIVERED LITTERS	N(%)	15(100.0)	15(100.0)	13(100.0)	13(100.0)	15(100.0)
DURATION OF GESTATION a	MEAN±S.D.	22.5 ± 0.5	22.7 ± 0.4	22.7 ± 0.5	22.8 ± 0.4	22.6 ± 0.5
IMPLANTATION SITES	N	251	230	206	192	231
PER DELIVERED LITTER	MEAN±S.D.	16.7 ± 1.3	15.3 ± 2.9	15.8 ± 1.3	14.8 ± 2.8	15.4 ± 2.3
DAMS WITH STILLBORN PUPS	N(%)	0(0.0)	0(0.0)	1(7.7)	3(23.1)	2(13.3)
DAMS WITH NO LIVEBORN PUPS	N	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
GESTATION INDEX b	%	100.0	100.0	100.0	100.0	100.0
	N/N	15/ 15	15/ 15	13/ 13	13/ 13	15/ 15
DAMS WITH ALL PUPS DYING DAYS 1-4 POSTPARTUM	N(%)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
DAMS WITH ALL PUPS DYING DAYS 5-22 POSTPARTUM	N(%)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)

a. Calculated as the time (in days) elapsed between confirmed mating (arbitrarily defined as day 0) and the time (in days) the first pup was delivered.
b. Number of rats with live offspring/number of pregnant rats.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C24 (PAGE 1): LITTER OBSERVATIONS (NATURALLY DELIVERED PUPS) - SUMMARY - F1 GENERATION LITTERS

MATERNAL DOSAGE GROUP		I	II	III	IV	V
MATERNAL DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
DELIVERED LITTERS WITH ONE OR MORE LIVEBORN PUPS	N	15	15	13	13	15
PUPS DELIVERED (TOTAL)	N	235	214	201	181	220
	MEAN±S.D.	15.7 ± 1.7	14.3 ± 3.2	15.5 ± 1.4	13.9 ± 3.1	14.7 ± 2.5
LIVEBORN	MEAN±S.D.	15.7 ± 1.7	14.3 ± 3.2	15.4 ± 1.6	13.6 ± 3.2	14.5 ± 2.4
	N(%)	235(100.0)	214(100.0)	200(99.5)	177(97.8)	218(99.1)
STILLBORN	MEAN±S.D.	0.0 ± 0.0	0.0 ± 0.0	0.1 ± 0.3	0.2 ± 0.4	0.1 ± 0.4
	N(%)	0(0.0)	0(0.0)	1(0.5)	3(1.6)	2(0.9)
UNKNOWN VITAL STATUS	N	0	0	0	1	0
PUPS FOUND DEAD OR PRESUMED CANNIBALIZED						
DAY 1	N/N(%)	1/235(0.4)	2/214(0.9)	0/200(0.0)	2/177(1.1)	3/218(1.4)
DAYS 2- 8	N/N(%)	6/234(2.6)	6/212(2.8)	3/200(1.5)	2/175(1.1)	3/215(1.4)
DAYS 9-15	N/N(%)	0/228(0.0)	2/206(1.0)	1/197(0.5)	1/173(0.6)	1/212(0.5)
DAYS 16-22	N/N(%)	0/228(0.0)	0/204(0.0)	0/196(0.0)	0/172(0.0)	0/211(0.0)
VIABILITY INDEX a	%	97.0	96.3	98.5	97.7	97.2
	N/N	228/235	206/214	197/200	173/177	212/218
LACTATION INDEX b	%	100.0	99.0	99.5	99.4	99.5
	N/N	228/228	204/206	196/197	172/173	211/212

DAY(S) = DAY(S) POSTPARTUM

a. Number of live pups on day 8 postpartum/number of liveborn pups on day 1 postpartum.

b. Number of live pups on day 22 postpartum/number of live pups on day 8 postpartum.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C24 (PAGE 2): LITTER OBSERVATIONS (NATURALLY DELIVERED PUPS) - SUMMARY - F1 GENERATION LITTERS

MATERNAL DOSAGE GROUP		I	II	III	IV	V
MATERNAL DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
DELIVERED LITTERS WITH ONE OR MORE LIVEBORN PUPS	N	15	15	13	13	15
SURVIVING PUPS/LITTER a						
DAY 1	MEAN±S.D.	15.7 ± 1.7	14.3 ± 3.2	15.4 ± 1.6	13.6 ± 3.2	14.5 ± 2.4
DAY 8	MEAN±S.D.	15.2 ± 1.8	13.7 ± 2.9	15.2 ± 1.5	13.3 ± 3.3	14.1 ± 2.1
DAY 15	MEAN±S.D.	15.2 ± 1.8	13.6 ± 2.8	15.1 ± 1.3	13.2 ± 3.2	14.1 ± 2.2
DAY 22	MEAN±S.D.	15.2 ± 1.8	13.6 ± 2.8	15.1 ± 1.3	13.2 ± 3.2	14.1 ± 2.2
PERCENT MALE PUPS PER NUMBER OF PUPS SEXED						
DAY 1	MEAN±S.D.	45.2 ± 12.4	51.9 ± 13.1	51.6 ± 6.8	43.6 ± 13.4	51.4 ± 13.4
DAY 8	MEAN±S.D.	45.2 ± 13.0	52.7 ± 12.0	51.8 ± 6.3	42.9 ± 13.1	51.4 ± 13.9
DAY 15	MEAN±S.D.	45.2 ± 13.0	53.1 ± 11.8	52.0 ± 6.2	43.1 ± 13.0	51.8 ± 14.2
DAY 22	MEAN±S.D.	45.2 ± 13.0	53.1 ± 11.8	52.0 ± 6.2	43.1 ± 13.0	51.8 ± 14.2

DAY = DAY POSTPARTUM
a. Average number of live pups per litter, including litters with no surviving pups.
b. Includes pups born alive, found dead day 1 postpartum.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C24 (PAGE 3): LITTER OBSERVATIONS (NATURALLY DELIVERED PUPS) - SUMMARY - F1 GENERATION LITTERS

MATERNAL DOSAGE GROUP		I	II	III	IV	V
MATERNAL DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
DELIVERED LITTERS WITH ONE OR MORE LIVEBORN PUPS	N	15	15	13	13	15
LIVE LITTER SIZE AT WEIGHING						
DAY 1	MEAN±S.D.	15.6 ± 1.8	14.1 ± 3.1	15.4 ± 1.6	13.5 ± 3.3	14.3 ± 2.2
DAY 8	MEAN±S.D.	15.2 ± 1.8	13.7 ± 2.9	15.2 ± 1.5	13.3 ± 3.3	14.1 ± 2.1
DAY 15	MEAN±S.D.	15.2 ± 1.8	13.6 ± 2.8	15.1 ± 1.3	13.2 ± 3.2	14.1 ± 2.2
DAY 22	MEAN±S.D.	15.2 ± 1.8	13.6 ± 2.8	15.1 ± 1.3	13.2 ± 3.2	14.1 ± 2.2
PUP WEIGHT/LITTER (GRAMS)						
DAY 1	MEAN±S.D.	6.3 ± 0.3	6.3 ± 0.5	6.4 ± 0.3	6.5 ± 0.7	6.3 ± 0.5
DAY 8	MEAN±S.D.	14.3 ± 1.6	13.3 ± 1.7	13.8 ± 1.0	14.1 ± 3.1	13.1 ± 1.5
DAY 15	MEAN±S.D.	26.2 ± 2.8	26.3 ± 3.9	25.9 ± 2.6	27.4 ± 5.7	25.1 ± 3.3
DAY 22	MEAN±S.D.	37.4 ± 4.7	39.3 ± 6.9	38.0 ± 5.7	40.0 ± 7.9	36.2 ± 7.7

DAY = DAY POSTPARTUM

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C25 (PAGE 1): CLINICAL OBSERVATIONS FROM BIRTH TO DAY 22 POSTPARTUM - SUMMARY - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP		I	II	III	IV	V
MATERNAL DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
LITTERS EXAMINED (N)		15	15	13	13	15
TRANSIENT CLINICAL OBSERVATIONS: a		TOTAL FREQUENCY (DAYS X PUPS)/LITTERS WITH OBSERVATIONS				
NOT NURSING	N/N	0/0	1/1	0/0	0/0	13/1
EMACIATION	N/N	0/0	0/0	0/0	0/0	13/1
DEHYDRATION	N/N	0/0	4/1	2/2	0/0	13/1
WHOLE BODY, EXCLUDING HEAD, DISCOLORATION, PURPLE	N/N	0/0	0/0	0/0	0/0	6/1
SCAB b	N/N	0/0	0/0	0/0	6/1	3/1
COLD TO TOUCH	N/N	0/0	2/2	0/0	0/0	1/1
LEFT EYE, PERIORBITAL DISCOLORATION, PURPLE	N/N	0/0	0/0	0/0	8/1	0/0
RIGHT EYE, ENLARGED	N/N	0/0	0/0	0/0	3/1	0/0
RIGHT HINDLIMB, LACERATION	N/N	0/0	0/0	0/0	1/1	0/0
BACK, BRUISE	N/N	2/1	4/1	0/0	0/0	0/0
NOT NESTING	N/N	0/0	1/1	0/0	0/0	0/0
PALE IN APPEARANCE	N/N	3/2	0/0	0/0	0/0	0/0
RIGHT EYE, CORNEAL OPACITY	N/N	5/1	0/0	0/0	0/0	0/0

a. Tabulation restricted to adverse observations; all other pups appeared normal.
b. Right hindlimb or head.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C26 (PAGE 1): NECROPSY OBSERVATIONS - SUMMARY - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP		I	II	III	IV	V
MATERNAL DOSAGE (MG/KG/DAY)		0	0.3	1	3	10
LITTERS EXAMINED (N)		15	15	13	13	15
TOTAL PUPS STILLBORN, OR FOUND DEAD a,b	N	6	5	2	4	3
STILLBORN	N	0	0	1	2	2
FOUND DEAD	N	6	5	1	2	1
NO MILK IN STOMACH c	N(%)	2(33.3)	5(100.0)	0(0.0)	1(50.0)	0(0.0)
PUPS SACRIFICED AND NECROPSIED ON DAYS 5 AND 22 POSTPARTUM c						
LITTERS EVALUATED	N	15	15	13	13	15
PUPS EVALUATED	N	228	204	196	172	211
APPEARED NORMAL						
LITTER INCIDENCE	N(%)	15(100.0)	14(93.3)	13(100.0)	13(100.0)	15(100.0)
PUP INCIDENCE	N(%)	228(100.0)	203(99.5)	196(100.0)	172(100.0)	211(100.0)
KIDNEYS: RIGHT, PELVIS, MODERATE DILATION						
LITTER INCIDENCE	N(%)	0(0.0)	1(6.7)	0(0.0)	0(0.0)	0(0.0)
PUP INCIDENCE	N(%)	0(0.0)	1(0.5)	0(0.0)	0(0.0)	0(0.0)

a. Restricted to pups in which complete necropsies were performed. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation.
b. Refer to the individual pup clinical observations table (Table C44) for external clinical observations confirmed at necropsy.
c. Analysis restricted to pups found dead and necropsied.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C27 (PAGE 1): PUP LIVER WEIGHTS - SUMMARY - F1 GENERATION PUPS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0	II 0.3	III 1	IV 3	V 10
LITTERS EXAMINED	N	10	10	10	10	10
TERMINAL BODY WEIGHT						
WEIGHT/LITTER	MEAN±S.D.	37.42 ± 4.53	40.00 ± 8.08	38.56 ± 4.78	40.11 ± 8.35	34.70 ± 8.26
MALE PUPS	MEAN±S.D.	38.17 ± 4.72	41.57 ± 8.53	40.27 ± 4.60	41.04 ± 8.18	35.33 ± 8.27
FEMALE PUPS	MEAN±S.D.	36.67 ± 4.44	38.35 ± 7.94	36.86 ± 5.30	39.22 ± 8.57	34.07 ± 8.30
LIVER						
WEIGHT/LITTER	MEAN±S.D.	1.54 ± 0.24	1.65 ± 0.41	1.60 ± 0.28	1.70 ± 0.38	1.40 ± 0.40
MALE PUPS	MEAN±S.D.	1.48 ± 0.26	1.64 ± 0.43	1.62 ± 0.31	1.65 ± 0.40	1.37 ± 0.40
FEMALE PUPS	MEAN±S.D.	1.59 ± 0.24	1.65 ± 0.40	1.58 ± 0.31	1.75 ± 0.39	1.44 ± 0.40
RATIOS (%) OF LIVER TO TERMINAL BODY WEIGHT						
WEIGHT/LITTER	MEAN±S.D.	4.10 ± 0.24	4.10 ± 0.28	4.14 ± 0.33	4.23 ± 0.37	3.98 ± 0.34
MALE PUPS	MEAN±S.D.	3.86 ± 0.27	3.91 ± 0.33	4.02 ± 0.44	4.01 ± 0.47	3.79 ± 0.37
FEMALE PUPS	MEAN±S.D.	4.33 ± 0.24	4.28 ± 0.26	4.26 ± 0.34	4.46 ± 0.35	4.17 ± 0.36

ALL WEIGHTS WERE RECORDED IN GRAMS (G). RATIOS (%) = (LIVER WEIGHT/TERMINAL BODY WEIGHT) X 100.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C28 (PAGE 1): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP I		0 MG/KG/DAY
RAT #		DESCRIPTION
19010		NO ADVERSE FINDINGS
19012	DG(9)	BACK: ULCERATION (1.5 CM X 1.0 CM)
	DG(9- 21)	BACK: SCAB (DID NOT EXCEED 2.0 CM X 1.0 CM)
	DL(1- 2)	BACK: SCAB (2.0 CM X 1.0 CM)
	DL(9- 13)	BACK: SCAB (2.0 CM X 0.5 CM)
	DL(9- 22)	LOCALIZED ALOPECIA: LIMBS a
19019		NO ADVERSE FINDINGS
19021	DL(9- 13)	HEAD: SCAB (0.2 CM IN DIAMETER)
	DL(14- 22)	LOCALIZED ALOPECIA: HEAD a
	DL(22)	HEAD: SCAB (0.2 CM X 0.4 CM)b
19023		NO ADVERSE FINDINGS
19041	DL(7- 22)	LOCALIZED ALOPECIA: LIMBS a
19042		NO ADVERSE FINDINGS
19044		NO ADVERSE FINDINGS
19050		NO ADVERSE FINDINGS
19053		NO ADVERSE FINDINGS
19065		NO ADVERSE FINDINGS
19068		NO ADVERSE FINDINGS
19072		NO ADVERSE FINDINGS
19074		NO ADVERSE FINDINGS
19075		NO ADVERSE FINDINGS

DS = DAY OF STUDY DG = DAY OF PRESUMED GESTATION DL = DAY OF LACTATION

a. Observation confirmed at necropsy.

b. First observed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C28 (PAGE 2): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP II		0.3 MG/KG/DAY
RAT #		DESCRIPTION
19004		NO ADVERSE FINDINGS
19009		NO ADVERSE FINDINGS
19016	DL(5- 21)	HEAD: SCAB (0.3 CM X 1.0 CM)
19018		NO ADVERSE FINDINGS
19026		NO ADVERSE FINDINGS
19036		NO ADVERSE FINDINGS
19037		NO ADVERSE FINDINGS
19043		NO ADVERSE FINDINGS
19047		NO ADVERSE FINDINGS
19048		NO ADVERSE FINDINGS
19052		NO ADVERSE FINDINGS
19055	DL(3- 22)	LOCALIZED ALOPECIA: LIMBS a
	DL(17- 22)	TAIL: SCAB (3.0 CM X 0.8 CM)a
19061		NO ADVERSE FINDINGS
19067		NO ADVERSE FINDINGS
19071		NO ADVERSE FINDINGS

DS = DAY OF STUDY DG = DAY OF PRESUMED GESTATION DL = DAY OF LACTATION

a. Observation confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C28 (PAGE 3): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP III		1 MG/KG/DAY	
RAT #		DESCRIPTION	
19003		NO ADVERSE FINDINGS	
19007		NO ADVERSE FINDINGS	
19008		NO ADVERSE FINDINGS	
19013		NO ADVERSE FINDINGS	
19014		NO ADVERSE FINDINGS	
19015	DL(17- 22)	LOCALIZED ALOPECIA:	HEAD a
19017		NO ADVERSE FINDINGS	
19024		NO ADVERSE FINDINGS	
19029	DG(20- 21)	LOCALIZED ALOPECIA:	LIMBS
	DL(1- 22)	LOCALIZED ALOPECIA:	LIMBS a
	DL(22)	LOCALIZED ALOPECIA:	HEAD b
19034		NO ADVERSE FINDINGS	
19038		NO ADVERSE FINDINGS	
19056		NO ADVERSE FINDINGS	
19057		NO ADVERSE FINDINGS	
19060		NO ADVERSE FINDINGS	
19064		NO ADVERSE FINDINGS	

DS = DAY OF STUDY DG = DAY OF PRESUMED GESTATION DL = DAY OF LACTATION

a. Observation confirmed at necropsy.

b. First observed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C28 (PAGE 4): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP IV		3 MG/KG/DAY
RAT #		DESCRIPTION
19002	DL(19- 22)	LOCALIZED ALOPECIA: BACK a
19005		NO ADVERSE FINDINGS
19035		NO ADVERSE FINDINGS
19039		NO ADVERSE FINDINGS
19040	DG(14)	NOSE: SWOLLEN
19045	DG(18- 21)	LOCALIZED ALOPECIA: LIMBS
	DL(1- 22)	LOCALIZED ALOPECIA: LIMBS a
19046	DS(11- 14)	LOCALIZED ALOPECIA: LIMBS
	DG(0- 25)	LOCALIZED ALOPECIA: LIMBS a
19051		NO ADVERSE FINDINGS
19054	DL(17- 22)	LOCALIZED ALOPECIA: LIMBS a
19058		NO ADVERSE FINDINGS
19062	DL(17- 22)	TIP OF TAIL MISSING a
19063		NO ADVERSE FINDINGS
19066		NO ADVERSE FINDINGS
19069		NO ADVERSE FINDINGS
19073		NO ADVERSE FINDINGS

DS = DAY OF STUDY DG = DAY OF PRESUMED GESTATION DL = DAY OF LACTATION

a. Observation confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C28 (PAGE 5): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP V		10 MG/KG/DAY
RAT #		DESCRIPTION
19001		NO ADVERSE FINDINGS
19006		NO ADVERSE FINDINGS
19011		NO ADVERSE FINDINGS
19020	DS(6- 12)	BROWN PERIORAL SUBSTANCE
	DS(6- 12)	RALES
	DS(10- 12)	URINE-STAINED ABDOMINAL FUR
	DS(11)	COLD TO TOUCH
	DS(11- 12)	MIOSIS
	DS(11- 12)	ABDOMINAL DISTENTION
	DS(11- 12)	EMACIATION
	DS(11- 17)	LOCALIZED ALOPECIA: HEAD
	DG(0- 6)	LOCALIZED ALOPECIA: HEAD
	DG(7- 20)	LOCALIZED ALOPECIA: LIMBS
	DL(2- 22)	LOCALIZED ALOPECIA: LIMBS a
	DL(7- 22)	ABDOMINAL DISTENTION a
	DL(14- 15)	EMACIATION
	DL(14- 22)	RALES
	DL(17)	DEHYDRATION
	DL(18- 22)	EMACIATION a
19022		NO ADVERSE FINDINGS
19025		NO ADVERSE FINDINGS
19027		NO ADVERSE FINDINGS
19028		NO ADVERSE FINDINGS
19030	DL(17- 22)	HEAD: SCAB (0.3 CM X 0.3 CM)a
	DL(17- 22)	LOCALIZED ALOPECIA: HEAD a
19031		NO ADVERSE FINDINGS
19032		NO ADVERSE FINDINGS
19033		NO ADVERSE FINDINGS
19049		NO ADVERSE FINDINGS
19059		NO ADVERSE FINDINGS
19070		NO ADVERSE FINDINGS

DS = DAY OF STUDY DG = DAY OF PRESUMED GESTATION DL = DAY OF LACTATION
a. Observation confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C29 (PAGE 1): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSES ADMINISTERED	OBSERVATIONS a
I					
0	19010	DL 22	P	70	ALL TISSUES APPEARED NORMAL.
	19012	DL 22	P	58	ALL TISSUES APPEARED NORMAL.
	19019	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19021	DL 22	P	58	ALL TISSUES APPEARED NORMAL.
	19023	DL 22	P	60	ALL TISSUES APPEARED NORMAL.
	19041	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19042	DL 22	P	58	ALL TISSUES APPEARED NORMAL.
	19044	DL 22	P	56	ALL TISSUES APPEARED NORMAL.
	19050	DL 22	P	60	ALL TISSUES APPEARED NORMAL.
	19053	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19065	DL 22	P	58	ALL TISSUES APPEARED NORMAL.
	19068	DL 22	P	57	ALL TISSUES APPEARED NORMAL.
	19072	DL 22	P	58	ALL TISSUES APPEARED NORMAL.
	19074	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19075	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
II					
0.3	19004	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19009	DL 22	P	57	ALL TISSUES APPEARED NORMAL.
	19016	DL 22	P	57	ALL TISSUES APPEARED NORMAL.
	19018	DL 22	P	57	ALL TISSUES APPEARED NORMAL.
	19026	DL 22	P	60	ALL TISSUES APPEARED NORMAL.
	19036	DL 22	P	57	ALL TISSUES APPEARED NORMAL.
	19037	DL 22	P	58	ALL TISSUES APPEARED NORMAL.
	19043	DL 22	P	57	ALL TISSUES APPEARED NORMAL.
	19047	DL 22	P	57	ALL TISSUES APPEARED NORMAL.
	19048	DL 22	P	60	ALL TISSUES APPEARED NORMAL.
	19052	DL 22	P	56	ALL TISSUES APPEARED NORMAL.
	19055	DL 22	P	57	ALL TISSUES APPEARED NORMAL.
	19061	DL 22	P	56	ALL TISSUES APPEARED NORMAL.
	19067	DL 22	P	58	ALL TISSUES APPEARED NORMAL.
	19071	DL 22	P	57	ALL TISSUES APPEARED NORMAL.

DG = DAY OF PRESUMED GESTATION DL = DAY OF LACTATION
P = PREGNANT NP = NOT PREGNANT
a. Refer to the individual clinical observations table (Table C27) for external observations confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C29 (PAGE 2): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSES ADMINISTERED	OBSERVATIONS a
III					
1	19003	DL 22	P	58	ALL TISSUES APPEARED NORMAL.
	19007	DL 22	P	59	KIDNEYS: RIGHT, CORTEX ADHERED TO RIGHT LATERAL LIVER LOBE. ALL OTHER TISSUES APPEARED NORMAL.
	19008	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19013	DL 22	P	58	ALL TISSUES APPEARED NORMAL.
	19014	DG 25	NP	39	ALL TISSUES APPEARED NORMAL.
	19015	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19017	DL 22	P	57	ALL TISSUES APPEARED NORMAL.
	19024	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19029	DL 22	P	58	ALL TISSUES APPEARED NORMAL.
	19034	DL 22	P	58	ALL TISSUES APPEARED NORMAL.
	19038	DG 25	NP	39	ALL TISSUES APPEARED NORMAL.
	19056	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19057	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19060	DL 22	P	57	ALL TISSUES APPEARED NORMAL.
	19064	DL 22	P	60	ALL TISSUES APPEARED NORMAL.

DG = DAY OF PRESUMED GESTATION DL = DAY OF LACTATION
P = PREGNANT NP = NOT PREGNANT
a. Refer to the individual clinical observations table (Table C27) for external observations confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C29 (PAGE 3): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSES ADMINISTERED	OBSERVATIONS a
IV					
3	19002	DL 22	P	69	ALL TISSUES APPEARED NORMAL.
	19005	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19035	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19039	DL 22	P	57	ALL TISSUES APPEARED NORMAL.
	19040	DL 22	P	58	ALL TISSUES APPEARED NORMAL.
	19045	DL 22	P	57	ALL TISSUES APPEARED NORMAL.
	19046	DG 25	NP	39	ALL TISSUES APPEARED NORMAL.
	19051	DG 25	NP	52	OVARIES: LEFT, SMALL (0.003 G). ALL OTHER TISSUES APPEARED NORMAL.
	19054	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19058	DL 22	P	57	ALL TISSUES APPEARED NORMAL.
	19062	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19063	DL 22	P	58	SPLEEN: OMENTUM ADHERED TO THE LENGTH OF THE OUTER CAPSULE. ALL OTHER TISSUES APPEARED NORMAL.
	19066	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19069	DL 22	P	58	ALL TISSUES APPEARED NORMAL.
	19073	DL 22	P	57	ALL TISSUES APPEARED NORMAL.

DG = DAY OF PRESUMED GESTATION DL = DAY OF LACTATION
P = PREGNANT NP = NOT PREGNANT
a. Refer to the individual clinical observations table (Table C27) for external observations confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C29 (PAGE 4): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSES ADMINISTERED	OBSERVATIONS a
V					
10	19001	DL 22	P	57	ALL TISSUES APPEARED NORMAL.
	19006	DL 22	P	58	ALL TISSUES APPEARED NORMAL.
	19011	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19020	DL 22	P	59	LARGE AND SMALL INTESTINES: DISTENDED WITH GAS. THYMUS: SMALL. SPLEEN: SMALL. ADRENALS: BILATERAL, LARGE. STOMACH: FUNDIC MUCOSAL SURFACE CONTAINED APPROXIMATELY 12 BLACK AREAS (PINPOINT TO 0.3 CM IN DIAMETER). ALL OTHER TISSUES APPEARED NORMAL.
	19022	DL 22	P	60	ALL TISSUES APPEARED NORMAL.
	19025	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19027	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19028	DL 22	P	57	ALL TISSUES APPEARED NORMAL.
	19030	DL 22	P	60	ALL TISSUES APPEARED NORMAL.
	19031	DL 22	P	56	ALL TISSUES APPEARED NORMAL.
	19032	DL 22	P	59	ALL TISSUES APPEARED NORMAL.
	19033	DL 22	P	56	ALL TISSUES APPEARED NORMAL.
	19049	DL 22	P	57	ALL TISSUES APPEARED NORMAL.
	19059	DL 22	P	56	ALL TISSUES APPEARED NORMAL.
	19070	DL 22	P	57	ALL TISSUES APPEARED NORMAL.

DG = DAY OF PRESUMED GESTATION DL = DAY OF LACTATION
P = PREGNANT NP = NOT PREGNANT
a. Refer to the individual clinical observations table (Table C27) for external observations confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C30 (PAGE 1): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP I — 0 MG/KG/DAY

RAT NUMBER		TERMINAL BODY WEIGHT	BRAIN ABS. WT.	BRAIN REL. % TBW	LIVER ABS. WT.	LIVER REL. % TBW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % TBW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % TBW	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % TBW a	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % TBW a
19012	P	335.	2.22	0.66	16.17	4.83	1.53	0.46	1.66	0.50	0.050	14.92	0.047	14.03
19019	P	309.	2.22	0.72	15.21	4.92	1.43	0.46	1.46	0.47	0.055	17.80	0.047	15.21
19021	P	270.	2.21	0.82	14.21	5.26	1.50	0.56	1.55	0.57	0.045	16.67	0.040	14.81
19023	P	280.	2.11	0.75	13.09	4.68	1.23	0.44	1.39	0.50	0.054	19.28	0.028	10.00
19041	P	305.	2.09	0.68	12.15	3.98	1.24	0.41	1.35	0.44	0.048	15.74	0.044	14.43
19042	P	302.	2.25	0.74	14.31	4.74	1.60	0.53	1.57	0.52	0.056	18.54	0.046	15.23
19044	P	360.	2.17	0.60	19.73	5.48	1.51	0.42	1.60	0.44	0.076	21.11	0.053	14.72
19050	P	290.	2.11	0.73	12.84	4.43	1.32	0.46	1.41	0.49	0.048	16.55	0.036	12.41
19053	P	299.	2.25	0.75	13.17	4.40	1.26	0.42	1.34	0.45	0.049	16.39	0.043	14.38
19065	P	301.	2.00	0.66	12.97	4.31	1.30	0.43	1.33	0.44	0.042	13.95	0.044	14.62

RAT NUMBER		TERMINAL BODY WEIGHT	SPLEEN ABS. WT.	SPLEEN REL. % TBW	THYMUS ABS. WT.	THYMUS REL. % TBW	OVARY LEFT ABS. WT.	OVARY LEFT REL. % TBW a	OVARY RIGHT ABS. WT.	OVARY RIGHT REL. % TBW a	UTERUS WITH CERVIX ABS. WT.	UTERUS WITH CERVIX REL. % TBW	HEART ABS. WT.	HEART REL. % TBW
19010	P	299.					0.035	11.70	0.042	14.05	0.48	0.16		
19012	P	335.	0.78	0.23	0.23	0.07	0.092	27.46	0.073	21.79	0.57	0.17	1.32	0.39
19019	P	309.	0.64	0.21	0.31	0.10	0.044	14.24	0.064	20.71	0.51	0.16	1.55	0.50
19021	P	270.	0.58	0.21	0.11	0.04	0.044	16.30	0.040	14.81	0.53	0.20	1.31	0.48
19023	P	280.	0.58	0.21	0.16	0.06	0.039	13.93	0.062	22.14	0.62	0.22	1.62	0.58
19041	P	305.	0.54	0.18	0.16	0.05	0.062	20.33	0.037	12.13	0.46	0.15	1.35	0.44
19042	P	302.	0.64	0.21	0.33	0.11	0.059	19.54	0.057	18.87	0.68	0.22	1.64	0.54
19044	P	360.	0.67	0.19	0.27	0.08	0.070	19.44	0.081	22.50	0.56	0.16	1.45	0.40
19050	P	290.	0.74	0.26	0.20	0.07	0.044	15.17	0.048	16.55	0.56	0.19	1.19	0.41
19053	P	299.	0.61	0.20	0.17	0.06	0.058	19.40	0.085	28.43	0.47	0.16	1.41	0.47
19065	P	301.	0.54	0.18	0.17	0.06	0.068	22.59	0.066	21.93	0.69	0.23	1.13	0.38
19068	P	360.					0.048	13.33	0.075	20.83	0.55	0.15		
19072	P	292.					0.051	17.46	0.060	20.55	0.36	0.12		
19074	P	297.					0.057	19.19	0.073	24.58	0.53	0.18		
19075	P	295.					0.059	20.00	0.073	24.74	0.44	0.15		

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.
P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
a. Value was multiplied by 1000.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C30 (PAGE 2): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP II 0.3 MG/KG/DAY

RAT NUMBER		TERMINAL BODY WEIGHT	BRAIN ABS. WT.	BRAIN REL. % TBW	LIVER ABS. WT.	LIVER REL. % TBW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % TBW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % TBW	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % TBW a	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % TBW a
19004	P	276.	1.99	0.72	11.23	4.07	1.34	0.48	1.40	0.51	0.043	15.58	0.049	17.75
19009	P	346.	2.11	0.61	16.15	4.67	1.38	0.40	1.37	0.40	0.038	10.98	0.033	9.54
19016	P	314.	2.17	0.69	18.06	5.75	1.41	0.45	1.43	0.46	0.059	18.79	0.048	15.29
19018	P	338.	2.04	0.60	19.18	5.67	1.41	0.42	1.42	0.42	0.052	15.38	0.041	12.13
19026	P	296.	2.12	0.72	15.44	5.22	1.65	0.56	1.70	0.57	0.054	18.24	0.045	15.20
19036	P	359.	2.13	0.59	16.63	4.63	1.45	0.40	1.54	0.43	0.042	11.70	0.044	12.26
19037	P	309.	2.09	0.68	18.25	5.91	1.43	0.46	1.53	0.50	0.056	18.12	0.047	15.21
19043	P	356.	2.23	0.63	18.19	5.11	1.77	0.50	1.87	0.52	0.065	18.26	0.053	14.89
19047	P	325.	2.00	0.62	14.85	4.57	1.35	0.42	1.47	0.45	0.044	13.54	0.027	8.31
19048	P	306.	2.24	0.73	11.85	3.87	1.55	0.51	1.42	0.46	0.055	17.97	0.024	7.84

RAT NUMBER		TERMINAL BODY WEIGHT	SPLEEN ABS. WT.	SPLEEN REL. % TBW	THYMUS ABS. WT.	THYMUS REL. % TBW	OVARY LEFT ABS. WT.	OVARY LEFT REL. % TBW a	OVARY RIGHT ABS. WT.	OVARY RIGHT REL. % TBW a	UTERUS WITH CERVIX ABS. WT.	UTERUS WITH CERVIX REL. % TBW	HEART ABS. WT.	HEART REL. % TBW
19004	P	276.	0.60	0.22	0.24	0.09	0.083	30.07	0.071	25.72	0.65	0.24	1.35	0.49
19009	P	346.	0.61	0.18	0.31	0.09	0.067	19.36	0.072	20.81	0.51	0.15	1.51	0.44
19016	P	314.	0.53	0.17	0.16	0.05	0.063	20.06	0.081	25.80	0.70	0.22	1.23	0.39
19018	P	338.	0.74	0.22	0.21	0.06	0.064	18.93	0.068	20.12	0.64	0.19	1.16	0.34
19026	P	296.	0.70	0.24	0.18	0.06	0.048	16.22	0.075	25.34	0.73	0.25	1.35	0.46
19036	P	359.	0.74	0.21	0.28	0.08	0.077	21.45	0.095	26.46	0.58	0.16	1.20	0.33
19037	P	309.	0.74	0.24	0.21	0.07	0.062	20.06	0.046	14.89	0.45	0.14	1.15	0.37
19043	P	356.	0.77	0.22	0.10	0.03	0.052	14.61	0.056	15.73	0.63	0.18	1.31	0.37
19047	P	325.	0.55	0.17	0.21	0.06	0.057	17.54	0.059	18.15	0.55	0.17	1.05	0.32
19048	P	306.	0.55	0.18	0.19	0.06	0.024	7.84	0.026	8.50	0.56	0.18	1.25	0.41
19052	P	320.					0.093	29.06	0.055	17.19	0.45	0.14		
19055	P	336.					0.032	9.52	0.052	15.48	0.28	0.08		
19061	P	315.					0.038	12.06	0.025	7.94	0.53	0.17		
19067	P	294.					0.061	20.75	0.059	20.07	0.50	0.17		
19071	P	374.					0.026	6.95	0.058	15.51	0.71	0.19		

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.
P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
a. Value was multiplied by 1000.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C30 (PAGE 3): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP III — 1 MG/KG/DAY

RAT NUMBER		TERMINAL BODY WEIGHT	BRAIN ABS. WT.	BRAIN REL. % TBW	LIVER ABS. WT.	LIVER REL. % TBW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % TBW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % TBW	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % TBW a	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % TBW a
19003	P	284.	2.13	0.75	12.51	4.40	1.31	0.46	1.37	0.48	0.054	19.01	0.060	21.13
19007	P	303.	2.16	0.71	13.07	4.31	1.62	0.53	1.66b	0.55	0.067	22.11	0.071	23.43
19008	P	292.	2.01	0.69	12.76	4.37	1.24	0.42	1.31	0.45	0.045	15.41	0.041	14.04
19013	P	389.	2.05	0.53	19.40	4.99	1.44	0.37	1.64	0.42	0.050	12.85	0.049	12.60
19015	P	274.	2.21	0.81	12.50	4.56	1.14	0.42	1.24	0.45	0.066	24.09	0.058	21.17
19017	P	350.	2.15	0.61	16.49	4.71	1.45	0.41	1.45	0.41	0.039	11.14	0.038	10.86
19024	P	309.	2.23	0.72	14.95	4.84	1.53	0.50	1.45	0.47	0.053	17.15	0.042	13.59
19029	P	332.	1.98	0.60	19.93	6.00	1.28	0.38	1.45	0.44	0.049	14.76	0.049	14.76
19034	P	287.	2.10	0.73	12.83	4.47	1.34	0.47	1.41	0.49	0.051	17.77	0.056	19.51
19056	P	292.	2.02	0.69	12.62	4.32	1.47	0.50	1.50	0.51	0.040	13.70	0.040	13.70

RAT NUMBER		TERMINAL BODY WEIGHT	SPLEEN ABS. WT.	SPLEEN REL. % TBW	THYMUS ABS. WT.	THYMUS REL. % TBW	OVARY LEFT ABS. WT.	OVARY LEFT REL. % TBW a	OVARY RIGHT ABS. WT.	OVARY RIGHT REL. % TBW a	UTERUS WITH CERVIX ABS. WT.	UTERUS WITH CERVIX REL. % TBW	HEART ABS. WT.	HEART REL. % TBW
19003	P	284.	0.62	0.22	0.14	0.05	0.054	19.01	0.079	27.82	0.48	0.17	1.29	0.45
19007	P	303.	0.82	0.27	0.12	0.04	0.053	17.49	0.086	28.38	0.79	0.26	1.30	0.43
19008	P	292.	0.49	0.17	0.17	0.06	0.050	17.12	0.055	18.84	0.53	0.18	1.17	0.40
19013	P	389.	0.65	0.17	0.22	0.06	0.068	17.48	0.080	20.56	0.58	0.15	1.35	0.35
19015	P	274.	0.42	0.15	0.24	0.09	0.043	15.69	0.048	17.52	0.48	0.18	1.51	0.55
19017	P	350.	0.60	0.17	0.13	0.04	0.053	15.14	0.048	13.71	0.35	0.10	1.36	0.39
19024	P	309.	0.61	0.20	0.19	0.06	0.043	13.92	0.020	6.47	0.42	0.14	1.40	0.45
19029	P	332.	0.60	0.18	0.16	0.05	0.041	12.35	0.058	17.47	0.34	0.10	1.48	0.44
19034	P	287.	0.54	0.19	0.18	0.06	0.062	21.60	0.074	25.78	0.44	0.15	1.21	0.42
19056	P	292.	0.65	0.22	0.22	0.08	0.051	17.46	0.043	14.73	0.66	0.23	1.39	0.48
19057	P	287.					0.034	11.85	0.041	14.28	0.35	0.12		
19060	P	357.					0.089	24.93	0.092	25.77	0.61	0.17		
19064	P	289.					0.051	17.65	0.051	17.65	0.44	0.15		

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.
P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
a. Value was multiplied by 1000.
b. Dam 19007 had the cortex of the right kidney adhered to the right lateral lobe of the liver . See the individual necropsy observations table (Table C28).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C30 (PAGE 4): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP IV — 3 MG/KG/DAY

RAT NUMBER		TERMINAL BODY WEIGHT	BRAIN ABS. WT.	BRAIN REL. % TBW	LIVER ABS. WT.	LIVER REL. % TBW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % TBW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % TBW	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % TBW a	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % TBW a
19005	P	285.	1.81	0.64	13.80	4.84	1.16	0.41	1.26	0.44	0.044	15.44	0.046	16.14
19035	P	261.	2.04	0.78	12.06	4.62	1.54	0.59	1.56	0.60	0.064	24.52	0.055	21.07
19039	P	315.	2.09	0.66	16.01	5.08	1.27	0.40	1.40	0.44	0.055	17.46	0.055	17.46
19040	P	294.	2.05	0.70	13.33	4.53	1.54	0.52	1.48	0.50	0.052	17.69	0.051	17.35
19045	P	385.	2.15	0.56	17.71	4.60	1.63	0.42	1.66	0.43	0.063	16.36	0.042	10.91
19054	P	287.	2.49	0.87	11.54	4.02	1.65	0.57	1.55	0.54	0.041	14.28	0.038	13.24
19058	P	350.	2.15	0.61	19.11	5.46	1.61	0.46	1.57	0.45	0.064	18.28	0.049	14.00
19062	P	290.	2.13	0.73	13.59	4.69	1.58	0.54	1.61	0.56	0.046	15.86	0.046	15.86
19063	P	369.	2.03	0.55	21.27	5.76	1.67	0.45	1.69	0.46	0.067	18.16	0.059	15.99
19066	P	292.	1.91	0.65	12.70	4.35	1.26	0.43	1.47	0.50	0.031	10.62	0.045	15.41

RAT NUMBER		TERMINAL BODY WEIGHT	SPLEEN ABS. WT.	SPLEEN REL. % TBW	THYMUS ABS. WT.	THYMUS REL. % TBW	OVARY LEFT ABS. WT.	OVARY LEFT REL. % TBW a	OVARY RIGHT ABS. WT.	OVARY RIGHT REL. % TBW a	UTERUS WITH CERVIX ABS. WT.	UTERUS WITH CERVIX REL. % TBW	HEART ABS. WT.	HEART REL. % TBW
19002	P	302.					0.058	19.20	0.052	17.22	0.46	0.15		
19005	P	285.	0.54	0.19	0.14	0.05	0.049	17.19	0.056	19.65	0.80	0.28	1.16	0.41
19035	P	261.	0.66	0.25	0.16	0.06	0.051	19.54	0.055	21.07	0.71	0.27	1.45	0.56
19039	P	315.	0.71	0.22	0.25	0.08	0.079	25.08	0.062	19.68	0.46	0.15	1.20	0.38
19040	P	294.	0.64	0.22	0.24	0.08	0.058	19.73	0.046	15.65	0.50	0.17	1.55	0.53
19045	P	385.	0.61	0.16	0.13	0.03	0.046	11.95	0.057	14.80	0.53	0.14	1.47	0.38
19054	P	287.	0.84	0.29	0.36	0.12	0.064	22.30	0.048	16.72	0.75	0.26	1.48	0.52
19058	P	350.	0.77	0.22	0.12	0.03	0.052	14.86	0.066	18.86	0.74	0.21	1.39	0.40
19062	P	290.	0.62	0.21	0.14	0.05	0.058	20.00	0.058	20.00	0.78	0.27	1.41	0.49
19063	P	369.	1.59b	0.43	0.09	0.02	0.049	13.28	0.057	15.45	0.56	0.15	1.39	0.38
19066	P	292.	0.55	0.19	0.39	0.13	0.028	9.59	0.025	8.56	0.78	0.27	1.51	0.52
19069	P	362.					0.057	15.74	0.076	20.99	0.57	0.16		
19073	P	363.					0.040	11.02	0.046	12.67	0.37	0.10		

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.
P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
a. Value was multiplied by 1000.
b. Dam 19063 had omentum adhered to the entire length of the outer capsule of the spleen. See the individual necropsy observations table (Table C28).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C30 (PAGE 5): TERMINAL BODY WEIGHTS AND ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP V — 10 MG/KG/DAY

RAT NUMBER		TERMINAL BODY WEIGHT	BRAIN ABS. WT.	BRAIN REL. % TBW	LIVER ABS. WT.	LIVER REL. % TBW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % TBW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % TBW	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % TBW a	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % TBW a
19001	P	278.	2.00	0.72	12.11	4.36	1.36	0.49	1.35	0.48	0.041	14.75	0.031	11.15
19006	P	304.	2.13	0.70	14.39	4.73	1.44	0.47	1.55	0.51	0.057	18.75	0.055	18.09
19011	P	283.	2.05	0.72	14.24	5.03	1.41	0.50	1.36	0.48	0.045	15.90	0.045	15.90
19020	P	210.	2.00	0.95	7.01	3.34	1.14	0.54	1.09	0.52	0.058b	27.62	0.056	26.67
19022	P	294.	2.18	0.74	12.61	4.29	1.45	0.49	1.63	0.55	0.064	21.77	0.041	13.94
19025	P	291.	2.13	0.73	13.99	4.81	1.36	0.47	1.40	0.48	0.061	20.96	0.055	18.90
19027	P	266.	2.27	0.85	12.11	4.55	1.38	0.52	1.35	0.51	0.053	19.92	0.047	17.67
19028	P	339.	2.02	0.60	15.89	4.69	1.38	0.41	1.41	0.42	0.044	12.98	0.041	12.09
19030	P	314.	2.18	0.69	14.52	4.62	1.46	0.46	1.50	0.48	0.062	19.74	0.046	14.65
19031	P	361.	2.24	0.62	19.51	5.40	1.52	0.42	1.47	0.41	0.042	11.63	0.038	10.53

RAT NUMBER		TERMINAL BODY WEIGHT	SPLEEN ABS. WT.	SPLEEN REL. % TBW	THYMUS ABS. WT.	THYMUS REL. % TBW	OVARY LEFT ABS. WT.	OVARY LEFT REL. % TBW a	OVARY RIGHT ABS. WT.	OVARY RIGHT REL. % TBW a	UTERUS WITH CERVIX ABS. WT.	UTERUS WITH CERVIX REL. % TBW	HEART ABS. WT.	HEART REL. % TBW
19001	P	278.	0.57	0.20	0.18	0.06	0.048	17.27	0.047	16.91	0.64	0.23	0.92	0.33
19006	P	304.	0.54	0.18	0.15	0.05	0.056	18.42	0.074	24.34	0.46	0.15	1.57	0.52
19011	P	283.	0.50	0.18	0.15	0.05	0.046	16.25	0.036	12.72	0.68	0.24	1.24	0.44
19020	P	210.	0.28b	0.13	0.11b	0.05	0.036	17.14	0.047	22.38	0.50	0.24	0.90	0.43
19022	P	294.	0.53	0.18	0.14	0.05	0.060	20.41	0.035	11.90	0.74	0.25	1.54	0.52
19025	P	291.	0.56	0.19	0.25	0.08	0.053	18.21	0.058	19.93	0.53	0.18	1.38	0.47
19027	P	266.	0.61	0.23	0.23	0.09	0.039	14.66	0.018	6.77	0.44	0.16	1.32	0.50
19028	P	339.	0.54	0.16	0.23	0.07	0.087	25.66	0.053	15.63	0.37	0.11	1.56	0.46
19030	P	314.	0.58	0.18	0.17	0.05	0.045	14.33	0.048	15.29	0.78	0.25	1.37	0.44
19031	P	361.	0.64	0.18	0.16	0.04	0.076	21.05	0.087	24.10	0.74	0.20	1.50	0.42
19032	P	287.					0.031	10.80	0.043	14.98	0.33	0.11		
19033	P	328.					0.069	21.04	0.076	23.17	0.82	0.25		
19049	P	330.					0.050	15.15	0.073	22.12	0.50	0.15		
19059	P	317.					0.061	19.24	0.063	19.87	0.39	0.12		
19070	P	351.					0.051	14.53	0.045	12.82	0.47	0.13		

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.
P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
a. Value was multiplied by 1000.
b. Dam 19020 had a large left adrenal, small spleen, and small thymus. See the individual necropsy observations table (Table C28).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C31 (PAGE 1): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP I — 0 MG/KG/DAY

RAT NUMBER		BRAIN WEIGHT	LIVER ABS. WT.	LIVER REL. % BRW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % BRW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % BRW	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % BRW	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % BRW	SPLEEN ABS. WT.	SPLEEN REL. % BRW
19012	P	2.22	16.17	728.38	1.53	68.92	1.66	74.77	0.050	2.25	0.047	2.12	0.78	35.14
19019	P	2.22	15.21	685.14	1.43	64.41	1.46	65.76	0.055	2.48	0.047	2.12	0.64	28.83
19021	P	2.21	14.21	642.99	1.50	67.87	1.55	70.14	0.045	2.04	0.040	1.81	0.58	26.24
19023	P	2.11	13.09	620.38	1.23	58.29	1.39	65.88	0.054	2.56	0.028	1.33	0.58	27.49
19041	P	2.09	12.15	581.34	1.24	59.33	1.35	64.59	0.048	2.30	0.044	2.10	0.54	25.84
19042	P	2.25	14.31	636.00	1.60	71.11	1.57	69.78	0.056	2.49	0.046	2.04	0.64	28.44
19044	P	2.17	19.73	909.22	1.51	69.58	1.60	73.73	0.076	3.50	0.053	2.44	0.67	30.88
19050	P	2.11	12.84	608.53	1.32	62.56	1.41	66.82	0.048	2.27	0.036	1.71	0.74	35.07
19053	P	2.25	13.17	585.33	1.26	56.00	1.34	59.56	0.049	2.18	0.043	1.91	0.61	27.11
19065	P	2.00	12.97	648.50	1.30	65.00	1.33	66.50	0.042	2.10	0.044	2.20	0.54	27.00

RAT NUMBER		BRAIN WEIGHT	THYMUS ABS. WT.	THYMUS REL. % BRW	OVARY LEFT ABS. WT.	OVARY LEFT REL. % BRW	OVARY RIGHT ABS. WT.	OVARY RIGHT REL. % BRW	UTERUS WITH CERVIX ABS. WT.	UTERUS WITH CERVIX REL. % BRW	HEART ABS. WT.	HEART REL. % BRW
19012	P	2.22	0.23	10.36	0.092	4.14	0.073	3.29	0.57	25.68	1.32	59.46
19019	P	2.22	0.31	13.96	0.044	1.98	0.064	2.88	0.51	22.97	1.55	69.82
19021	P	2.21	0.11	4.98	0.044	1.99	0.040	1.81	0.53	23.98	1.31	59.28
19023	P	2.11	0.16	7.58	0.039	1.85	0.062	2.94	0.62	29.38	1.62	76.78
19041	P	2.09	0.16	7.66	0.062	2.97	0.037	1.77	0.46	22.01	1.35	64.59
19042	P	2.25	0.33	14.67	0.059	2.62	0.057	2.53	0.68	30.22	1.64	72.89
19044	P	2.17	0.27	12.44	0.070	3.22	0.081	3.73	0.56	25.81	1.45	66.82
19050	P	2.11	0.20	9.48	0.044	2.08	0.048	2.27	0.56	26.54	1.19	56.40
19053	P	2.25	0.17	7.56	0.058	2.58	0.085	3.78	0.47	20.89	1.41	62.67
19065	P	2.00	0.17	8.50	0.068	3.40	0.066	3.30	0.69	34.50	1.13	56.50

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.
P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C31 (PAGE 2): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP II — 0.3 MG/KG/DAY

RAT NUMBER		BRAIN WEIGHT	LIVER ABS. WT.	LIVER REL. % BRW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % BRW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % BRW	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % BRW	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % BRW	SPLEEN ABS. WT.	SPLEEN REL. % BRW
19004	P	1.99	11.23	564.32	1.34	67.34	1.40	70.35	0.043	2.16	0.049	2.46	0.60	30.15
19009	P	2.11	16.15	765.40	1.38	65.40	1.37	64.93	0.038	1.80	0.033	1.56	0.61	28.91
19016	P	2.17	18.06	832.26	1.41	64.98	1.43	65.90	0.059	2.72	0.048	2.21	0.53	24.42
19018	P	2.04	19.18	940.20	1.41	69.12	1.42	69.61	0.052	2.55	0.041	2.01	0.74	36.27
19026	P	2.12	15.44	728.30	1.65	77.83	1.70	80.19	0.054	2.55	0.045	2.12	0.70	33.02
19036	P	2.13	16.63	780.75	1.45	68.08	1.54	72.30	0.042	1.97	0.044	2.06	0.74	34.74
19037	P	2.09	18.25	873.20	1.43	68.42	1.53	73.20	0.056	2.68	0.047	2.25	0.74	35.41
19043	P	2.23	18.19	815.70	1.77	79.37	1.87	83.86	0.065	2.91	0.053	2.38	0.77	34.53
19047	P	2.00	14.85	742.50	1.35	67.50	1.47	73.50	0.044	2.20	0.027	1.35	0.55	27.50
19048	P	2.24	11.85	529.02	1.55	69.20	1.42	63.39	0.055	2.46	0.024	1.07	0.55	24.55

RAT NUMBER		BRAIN WEIGHT	THYMUS ABS. WT.	THYMUS REL. % BRW	OVARY LEFT ABS. WT.	OVARY LEFT REL. % BRW	OVARY RIGHT ABS. WT.	OVARY RIGHT REL. % BRW	UTERUS WITH CERVIX ABS. WT.	UTERUS WITH CERVIX REL. % BRW	HEART ABS. WT.	HEART REL. % BRW
19004	P	1.99	0.24	12.06	0.083	4.17	0.071	3.57	0.65	32.66	1.35	67.84
19009	P	2.11	0.31	14.69	0.067	3.18	0.072	3.41	0.51	24.17	1.51	71.56
19016	P	2.17	0.16	7.37	0.063	2.90	0.081	3.73	0.70	32.26	1.23	56.68
19018	P	2.04	0.21	10.29	0.064	3.14	0.068	3.33	0.64	31.37	1.16	56.86
19026	P	2.12	0.18	8.49	0.048	2.26	0.075	3.54	0.73	34.43	1.35	63.68
19036	P	2.13	0.28	13.14	0.077	3.62	0.095	4.46	0.58	27.23	1.20	56.34
19037	P	2.09	0.21	10.05	0.062	2.97	0.046	2.20	0.45	21.53	1.15	55.02
19043	P	2.23	0.10	4.48	0.052	2.33	0.056	2.51	0.63	28.25	1.31	58.74
19047	P	2.00	0.21	10.50	0.057	2.85	0.059	2.95	0.55	27.50	1.05	52.50
19048	P	2.24	0.19	8.48	0.024	1.07	0.026	1.16	0.56	25.00	1.25	55.80

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.
P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C31 (PAGE 3): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP III — 1 MG/KG/DAY

RAT NUMBER		BRAIN WEIGHT	LIVER ABS. WT.	LIVER REL. % BRW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % BRW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % BRW	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % BRW	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % BRW	SPLEEN ABS. WT.	SPLEEN REL. % BRW
19003	P	2.13	12.51	587.32	1.31	61.50	1.37	64.32	0.054	2.54	0.060	2.82	0.62	29.11
19007	P	2.16	13.07	605.09	1.62	75.00	1.66a	76.85	0.067	3.10	0.071	3.29	0.82	37.96
19008	P	2.01	12.76	634.82	1.24	61.69	1.31	65.17	0.045	2.24	0.041	2.04	0.49	24.38
19013	P	2.05	19.40	946.34	1.44	70.24	1.64	80.00	0.050	2.44	0.049	2.39	0.65	31.71
19015	P	2.21	12.50	565.61	1.14	51.58	1.24	56.11	0.066	2.99	0.058	2.62	0.42	19.00
19017	P	2.15	16.49	766.98	1.45	67.44	1.45	67.44	0.039	1.81	0.038	1.77	0.60	27.91
19024	P	2.23	14.95	670.40	1.53	68.61	1.45	65.02	0.053	2.38	0.042	1.88	0.61	27.35
19029	P	1.98	19.93	1006.56	1.28	64.65	1.45	73.23	0.049	2.47	0.049	2.47	0.60	30.30
19034	P	2.10	12.83	610.95	1.34	63.81	1.41	67.14	0.051	2.43	0.056	2.67	0.54	25.71
19056	P	2.02	12.62	624.75	1.47	72.77	1.50	74.26	0.040	1.98	0.040	1.98	0.65	32.18

RAT NUMBER		BRAIN WEIGHT	THYMUS ABS. WT.	THYMUS REL. % BRW	OVARY LEFT ABS. WT.	OVARY LEFT REL. % BRW	OVARY RIGHT ABS. WT.	OVARY RIGHT REL. % BRW	UTERUS WITH CERVIX ABS. WT.	UTERUS WITH CERVIX REL. % BRW	HEART ABS. WT.	HEART REL. % BRW
19003	P	2.13	0.14	6.57	0.054	2.54	0.079	3.71	0.48	22.54	1.29	60.56
19007	P	2.16	0.12	5.56	0.053	2.45	0.086	3.98	0.79	36.57	1.30	60.18
19008	P	2.01	0.17	8.46	0.050	2.49	0.055	2.74	0.53	26.37	1.17	58.21
19013	P	2.05	0.22	10.73	0.068	3.32	0.080	3.90	0.58	28.29	1.35	65.85
19015	P	2.21	0.24	10.86	0.043	1.94	0.048	2.17	0.48	21.72	1.51	68.32
19017	P	2.15	0.13	6.05	0.053	2.46	0.048	2.23	0.35	16.28	1.36	63.26
19024	P	2.23	0.19	8.52	0.043	1.93	0.020	0.90	0.42	18.83	1.40	62.78
19029	P	1.98	0.16	8.08	0.041	2.07	0.058	2.93	0.34	17.17	1.48	74.75
19034	P	2.10	0.18	8.57	0.062	2.95	0.074	3.52	0.44	20.95	1.21	57.62
19056	P	2.02	0.22	10.89	0.051	2.52	0.043	2.13	0.66	32.67	1.39	68.81

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.
P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
a. Dam 19007 had the cortex of the right kidney adhered to the right lateral lobe of the liver . See the individual necropsy observations table (Table C28).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C31 (PAGE 4): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP IV — 3 MG/KG/DAY

RAT NUMBER		BRAIN WEIGHT	LIVER ABS. WT.	LIVER REL. % BRW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % BRW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % BRW	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % BRW	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % BRW	SPLEEN ABS. WT.	SPLEEN REL. % BRW
19005	P	1.81	13.80	762.43	1.16	64.09	1.26	69.61	0.044	2.43	0.046	2.54	0.54	29.83
19035	P	2.04	12.06	591.18	1.54	75.49	1.56	76.47	0.064	3.14	0.055	2.70	0.66	32.35
19039	P	2.09	16.01	766.03	1.27	60.76	1.40	66.98	0.055	2.63	0.055	2.63	0.71	33.97
19040	P	2.05	13.33	650.24	1.54	75.12	1.48	72.20	0.052	2.54	0.051	2.49	0.64	31.22
19045	P	2.15	17.71	823.72	1.63	75.81	1.66	77.21	0.063	2.93	0.042	1.95	0.61	28.37
19054	P	2.49	11.54	463.45	1.65	66.26	1.55	62.25	0.041	1.65	0.038	1.53	0.84	33.73
19058	P	2.15	19.11	888.84	1.61	74.88	1.57	73.02	0.064	2.98	0.049	2.28	0.77	35.81
19062	P	2.13	13.59	638.03	1.58	74.18	1.61	75.59	0.046	2.16	0.046	2.16	0.62	29.11
19063	P	2.03	21.27	1047.78	1.67	82.27	1.69	83.25	0.067	3.30	0.059	2.91	1.59a	78.32
19066	P	1.91	12.70	664.92	1.26	65.97	1.47	76.96	0.031	1.62	0.045	2.36	0.55	28.80

RAT NUMBER		BRAIN WEIGHT	THYMUS ABS. WT.	THYMUS REL. % BRW	OVARY LEFT ABS. WT.	OVARY LEFT REL. % BRW	OVARY RIGHT ABS. WT.	OVARY RIGHT REL. % BRW	UTERUS WITH CERVIX ABS. WT.	UTERUS WITH CERVIX REL. % BRW	HEART ABS. WT.	HEART REL. % BRW
19005	P	1.81	0.14	7.73	0.049	2.71	0.056	3.09	0.80	44.20	1.16	64.09
19035	P	2.04	0.16	7.84	0.051	2.50	0.055	2.70	0.71	34.80	1.45	71.08
19039	P	2.09	0.25	11.96	0.079	3.78	0.062	2.97	0.46	22.01	1.20	57.42
19040	P	2.05	0.24	11.71	0.058	2.83	0.046	2.24	0.50	24.39	1.55	75.61
19045	P	2.15	0.13	6.05	0.046	2.14	0.057	2.65	0.53	24.65	1.47	68.37
19054	P	2.49	0.36	14.46	0.064	2.57	0.048	1.93	0.75	30.12	1.48	59.44
19058	P	2.15	0.12	5.58	0.052	2.42	0.066	3.07	0.74	34.42	1.39	64.65
19062	P	2.13	0.14	6.57	0.058	2.72	0.058	2.72	0.78	36.62	1.41	66.20
19063	P	2.03	0.09	4.43	0.049	2.41	0.057	2.81	0.56	27.59	1.39	68.47
19066	P	1.91	0.39	20.42	0.028	1.46	0.025	1.31	0.78	40.84	1.51	79.06

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.
P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
a. Dam 19063 had omentum adhered to the entire length of the outer capsule of the spleen. See the individual necropsy observations table (Table C28).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C31 (PAGE 5): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP V — 10 MG/KG/DAY

RAT NUMBER		BRAIN WEIGHT	LIVER ABS. WT.	LIVER REL. % BRW	KIDNEY LEFT ABS. WT.	KIDNEY LEFT REL. % BRW	KIDNEY RIGHT ABS. WT.	KIDNEY RIGHT REL. % BRW	ADRENAL LEFT ABS. WT.	ADRENAL LEFT REL. % BRW	ADRENAL RIGHT ABS. WT.	ADRENAL RIGHT REL. % BRW	SPLEEN ABS. WT.	SPLEEN REL. % BRW
19001	P	2.00	12.11	605.50	1.36	68.00	1.35	67.50	0.041	2.05	0.031	1.55	0.57	28.50
19006	P	2.13	14.39	675.59	1.44	67.60	1.55	72.77	0.057	2.68	0.055	2.58	0.54	25.35
19011	P	2.05	14.24	694.63	1.41	68.78	1.36	66.34	0.045	2.20	0.045	2.20	0.50	24.39
19020	P	2.00	7.01	350.50	1.14	57.00	1.09	54.50	0.058a	2.90	0.056	2.80	0.28a	14.00
19022	P	2.18	12.61	578.44	1.45	66.51	1.63	74.77	0.064	2.94	0.041	1.88	0.53	24.31
19025	P	2.13	13.99	656.81	1.36	63.85	1.40	65.73	0.061	2.86	0.055	2.58	0.56	26.29
19027	P	2.27	12.11	533.48	1.38	60.79	1.35	59.47	0.053	2.33	0.047	2.07	0.61	26.87
19028	P	2.02	15.89	786.63	1.38	68.32	1.41	69.80	0.044	2.18	0.041	2.03	0.54	26.73
19030	P	2.18	14.52	666.06	1.46	66.97	1.50	68.81	0.062	2.84	0.046	2.11	0.58	26.60
19031	P	2.24	19.51	870.98	1.52	67.86	1.47	65.62	0.042	1.88	0.038	1.70	0.64	28.57

RAT NUMBER		BRAIN WEIGHT	THYMUS ABS. WT.	THYMUS REL. % BRW	OVARY LEFT ABS. WT.	OVARY LEFT REL. % BRW	OVARY RIGHT ABS. WT.	OVARY RIGHT REL. % BRW	UTERUS WITH CERVIX ABS. WT.	UTERUS WITH CERVIX REL. % BRW	HEART ABS. WT.	HEART REL. % BRW
19001	P	2.00	0.18	9.00	0.048	2.40	0.047	2.35	0.64	32.00	0.92	46.00
19006	P	2.13	0.15	7.04	0.056	2.63	0.074	3.47	0.46	21.60	1.57	73.71
19011	P	2.05	0.15	7.32	0.046	2.24	0.036	1.76	0.68	33.17	1.24	60.49
19020	P	2.00	0.11a	5.50	0.036	1.80	0.047	2.35	0.50	25.00	0.90	45.00
19022	P	2.18	0.14	6.42	0.060	2.75	0.035	1.60	0.74	33.94	1.54	70.64
19025	P	2.13	0.25	11.74	0.053	2.49	0.058	2.72	0.53	24.88	1.38	64.79
19027	P	2.27	0.23	10.13	0.039	1.72	0.018	0.79	0.44	19.38	1.32	58.15
19028	P	2.02	0.23	11.39	0.087	4.31	0.053	2.62	0.37	18.32	1.56	77.23
19030	P	2.18	0.17	7.80	0.045	2.06	0.048	2.20	0.78	35.78	1.37	62.84
19031	P	2.24	0.16	7.14	0.076	3.39	0.087	3.88	0.74	33.04	1.50	66.96

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.
P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
a. Dam 19020 had a large left adrenal, small spleen, and small thymus. See the individual necropsy observations table (Table C28).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C32 (PAGE 1): PRIMORDIAL FOLLICLE COUNT - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP I		0 MG/KG/DAY			
RAT #	OVARY #1	OVARY #2	RAT #	OVARY #1	OVARY #2
19012	31	21	19042	1	18
	37	46		0	9
	46	34		1	9
	33	36		6	16
	34	36		3	13
AVERAGE	36.2	34.6	AVERAGE	2.2	13.0
19019	4	0	19044	3	5
	1	5		11	8
	2	2		9	8
	0	2		13	9
	1	7		51	17
AVERAGE	1.6	3.2	AVERAGE	17.4	9.4
19021	16	4	19050	3	1
	16	4		5	5
	21	12		2	3
	20	17		4	6
	14	30		3	10
AVERAGE	17.4	13.4	AVERAGE	3.4	5.0
19023	7	22	19053	24	3
	14	11		11	11
	10	13		27	16
	14	27		27	20
	11	6		25	38
AVERAGE	11.2	15.8	AVERAGE	22.8	17.6
19041	7	4	19065	4	7
	14	3		3	15
	2	4		9	11
	5	6		3	12
	7	9		14	16
AVERAGE	7.0	5.2	AVERAGE	6.6	12.2

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C32 (PAGE 2): PRIMORDIAL FOLLICLE COUNT - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP V		10 MG/KG/DAY			
RAT #	OVARY #1	OVARY #2	RAT #	OVARY #1	OVARY #2
19001	3	6	19025	11	4
	4	5		12	6
	9	6		6	15
	6	17		6	25
	23	20		7	12
AVERAGE	9.0	10.8	AVERAGE	8.4	12.4
19006	27	5	19027	6	0
	11	6		6	5
	23	19		17	8
	26	20		13	12
	21	20		43	8
AVERAGE	21.6	14.0	AVERAGE	17.0	6.6
19011	6	1	19028	3	1
	16	0		2	7
	8	12		2	13
	16	24		5	13
	37	8		7	10
AVERAGE	16.6	9.0	AVERAGE	3.8	8.8
19020	5	2	19030	9	3
	4	1		21	13
	15	2		24	6
	8	12		22	7
	20	20		26	20
AVERAGE	10.4	7.4	AVERAGE	20.4	9.8
19022	9	9	19031	11	7
	2	4		15	4
	5	11		11	14
	1	17		9	11
	7	19		14	17
AVERAGE	4.8	12.0	AVERAGE	12.0	10.6

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C33 (PAGE 1): BODY WEIGHTS - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DAY	1	2	3	4	5	6	7	8	9	10	11	12	13	14a
RAT #	DOSAGE GROUP I						0 MG/KG/DAY							
19010	213.	218.	223.	225.	224.	229.	235.	237.	238.	239.	246.	251.	246.	249.
19012	235.	239.	238.	236.	247.	246.	250.	251.	261.	261.	267.	258.	270.	267.
19019	230.	232.	240.	242.	244.	251.	254.	261.	256.	263.	269.	269.	272.	277.
19021	231.	236.	237.	240.	244.	248.	245.	250.	253.	258.	258.	260.	264.	266.
19023	219.	213.	222.	227.	223.	222.	228.	232.	229.	224.	233.	235.	235.	234.
19041	245.	239.	247.	252.	252.	249.	258.	264.	266.	260.	268.	272.	268.	264.
19042	227.	225.	232.	236.	238.	236.	236.	244.	247.	248.	248.	242.	249.	250.
19044	231.	230.	233.	235.	242.	238.	240.	247.	249.	243.	246.	245.	249.	250.
19050	220.	222.	226.	229.	229.	232.	236.	245.	243.	240.	245.	251.	246.	247.
19053	234.	238.	243.	244.	246.	255.	260.	262.	262.	269.	272.	274.	271.	277.
19065	223.	223.	230.	232.	234.	241.	245.	247.	244.	250.	255.	255.	254.	261.
19068	232.	229.	236.	247.	256.	260.	265.	277.	275.	281.	291.	288.	288.	293.
19072	222.	217.	228.	229.	228.	228.	239.	244.	238.	238.	247.	250.	242.	240.
19074	235.	238.	238.	241.	244.	247.	246.	253.	251.	254.	254.	258.	263.	260.
19075	232.	224.	229.	234.	234.	236.	242.	244.	244.	246.	247.	246.	227.	242.
RAT #	DOSAGE GROUP II						0.3 MG/KG/DAY							
19004	205.	203.	214.	215.	214.	216.	220.	226.	222.	219.	226.	228.	226.	223.
19009	231.	234.	236.	246.	248.	252.	252.	263.	257.	260.	260.	265.	264.	265.
19016	222.	224.	225.	227.	231.	232.	234.	234.	240.	238.	239.	247.	243.	244.
19018	222.	228.	228.	233.	232.	230.	240.	239.	244.	241.	241.	246.	246.	247.
19026	221.	227.	232.	236.	231.	233.	237.	239.	236.	241.	246.	251.	249.	249.
19036	230.	235.	239.	243.	247.	249.	249.	255.	260.	262.	263.	269.	271.	268.
19037	217.	217.	222.	228.	228.	227.	236.	241.	244.	237.	240.	240.	242.	249.
19043	227.	228.	233.	237.	238.	237.	245.	248.	246.	244.	253.	253.	252.	252.
19047	219.	213.	207.	217.	211.	212.	213.	223.	224.	217.	219.	229.	228.	227.
19048	228.	230.	235.	240.	239.	240.	246.	244.	245.	245.	253.	255.	252.	253.
19052	228.	228.	226.	235.	240.	234.	236.	245.	246.	244.	247.	254.	255.	251.
19055	235.	231.	228.	239.	249.	243.	241.	253.	258.	253.	255.	264.	266.	262.
19061	219.	225.	225.	227.	233.	238.	237.	241.	244.	248.	242.	241.	246.	250.
19067	237.	238.	245.	246.	240.	246.	251.	252.	245.	250.	258.	259.	254.	259.
19071	230.	232.	232.	238.	238.	242.	241.	248.	251.	252.	250.	261.	262.	261.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C33 (PAGE 2): BODY WEIGHTS - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DAY	1	2	3	4	5	6	7	8	9	10	11	12	13	14a
RAT #	DOSAGE GROUP III						1 MG/KG/DAY							
19003	213.	218.	220.	218.	219.	227.	230.	229.	227.	234.	234.	229.	232.	236.
19007	244.	248.	254.	258.	256.	262.	269.	273.	270.	274.	280.	276.	281.	285.
19008	224.	222.	223.	233.	239.	244.	242.	243.	250.	254.	261.	254.	254.	264.
19013	229.	233.	237.	240.	243.	251.	249.	256.	262.	261.	264.	264.	271.	272.
19014	221.	219.	226.	228.	229.	231.	237.	241.	240.	240.	246.	250.	245.	250.
19015	228.	227.	227.	231.	235.	239.	237.	236.	237.	239.	241.	244.	239.	240.
19017	226.	221.	231.	234.	236.	233.	239.	246.	246.	243.	249.	257.	259.	250.
19024	234.	242.	241.	244.	253.	259.	262.	265.	267.	276.	282.	278.	269.	273.
19029	219.	219.	214.	221.	229.	233.	234.	234.	242.	246.	250.	246.	250.	256.
19034	231.	234.	239.	239.	243.	250.	252.	250.	255.	257.	261.	264.	266.	266.
19038	219.	220.	223.	227.	227.	230.	237.	238.	237.	236.	243.	244.	240.	244.
19056	230.	229.	238.	240.	240.	240.	245.	250.	251.	249.	257.	258.	256.	258.
19057	224.	226.	234.	234.	236.	238.	242.	245.	246.	246.	251.	251.	253.	253.
19060	233.	233.	236.	238.	240.	247.	252.	250.	253.	254.	256.	256.	260.	270.
19064	219.	218.	224.	228.	228.	231.	237.	242.	241.	241.	249.	251.	250.	251.
RAT #	DOSAGE GROUP IV						3 MG/KG/DAY							
19002	224.	220.	228.	232.	238.	241.	246.	251.	251.	250.	255.	257.	258.	256.
19005	239.	238.	248.	250.	246.	248.	251.	255.	252.	256.	260.	260.	256.	259.
19035	225.	226.	233.	237.	230.	231.	242.	243.	243.	240.	248.	251.	247.	249.
19039	224.	222.	223.	227.	233.	234.	230.	236.	241.	242.	242.	242.	245.	248.
19040	218.	220.	226.	227.	226.	231.	234.	240.	236.	238.	243.	251.	245.	246.
19045	231.	227.	230.	236.	240.	237.	243.	250.	250.	250.	256.	261.	262.	262.
19046	214.	217.	221.	227.	227.	228.	232.	235.	237.	237.	237.	237.	247.	242.
19051	237.	234.	240.	244.	249.	255.	258.	262.	265.	270.	271.	276.	281.	283.
19054	219.	223.	224.	223.	229.	241.	234.	236.	241.	244.	245.	244.	244.	246.
19058	224.	233.	231.	235.	228.	229.	238.	241.	239.	232.	235.	240.	248.	242.
19062	222.	220.	229.	229.	224.	229.	235.	241.	234.	237.	242.	246.	240.	242.
19063	240.	241.	244.	248.	249.	248.	254.	265.	260.	264.	263.	266.	269.	268.
19066	223.	223.	226.	227.	225.	226.	227.	236.	230.	227.	230.	238.	232.	232.
19069	235.	237.	240.	241.	248.	250.	251.	252.	261.	264.	258.	261.	268.	269.
19073	227.	229.	229.	234.	238.	237.	240.	244.	247.	243.	244.	251.	252.	251.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C33 (PAGE 3): BODY WEIGHTS - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DAY	1	2	3	4	5	6	7	8	9	10	11	12	13	14a
RAT #	DOSAGE GROUP V						10 MG/KG/DAY							
19001	215.	214.	217.	217.	208.	212.	218.	220.	215.	214.	218.	221.	218.	213.
19006	231.	234.	238.	235.	236.	241.	242.	246.	250.	258.	258.	257.	259.	266.
19011	228.	230.	234.	238.	236.	243.	244.	248.	242.	241.	249.	249.	245.	243.
19020	226.	224.	222.	229.	231.	203.	199.	192.	186.	188.	203.	212.	220.	221.
19022	221.	221.	227.	230.	226.	230.	239.	240.	236.	236.	247.	247.	241.	243.
19025	229.	236.	240.	244.	239.	249.	259.	267.	271.	272.	283.	285.	280.	282.
19027	218.	220.	224.	228.	226.	229.	231.	235.	231.	235.	238.	240.	238.	238.
19028	232.	232.	232.	241.	242.	244.	243.	250.	253.	251.	252.	258.	259.	259.
19030	220.	220.	227.	230.	228.	232.	237.	242.	238.	241.	249.	253.	249.	251.
19031	245.	252.	255.	262.	264.	262.	255.	263.	264.	266.	268.	272.	277.	269.
19032	227.	229.	234.	240.	239.	243.	251.	258.	255.	256.	262.	266.	263.	264.
19033	225.	224.	228.	231.	234.	231.	233.	245.	244.	241.	246.	250.	256.	252.
19049	226.	228.	234.	237.	237.	240.	245.	254.	254.	252.	257.	262.	264.	257.
19059	240.	242.	243.	246.	250.	252.	250.	254.	256.	258.	256.	262.	263.	260.
19070	220.	218.	218.	227.	231.	233.	230.	239.	239.	241.	238.	246.	246.	248.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C34 (PAGE 1): MATERNAL BODY WEIGHTS - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP I												0 MG/KG/DAY
PREGNANCY STATUS	DAY 0	1	2	3	4	5	6	7	8	9	10	11	12
19010 P	293.	304.	309.	312.	313.	312.	310.	313.	313.	324.	328.	336.	339.
19012 P	273.	281.	281.	291.	295.	301.	300.	308.	312.	315.	321.	327.	333.
19019 P	267.	284.	286.	293.	301.	310.	309.	304.	308.	311.	316.	324.	331.
19021 P	276.	279.	283.	285.	291.	291.	296.	302.	304.	301.	314.	320.	330.
19023 P	250.	244.	257.	261.	262.	267.	265.	271.	273.	280.	283.	286.	287.
19041 P	291.	290.	304.	312.	308.	314.	318.	320.	324.	332.	337.	343.	347.
19042 P	259.	265.	271.	270.	276.	285.	293.	294.	306.	314.	320.	329.	337.
19044 P	256.	265.	270.	280.	277.	283.	288.	291.	297.	303.	306.	312.	321.
19050 P	258.	248.	270.	269.	272.	274.	280.	282.	290.	292.	300.	305.	307.
19053 P	284.	299.	300.	303.	310.	309.	311.	313.	323.	318.	329.	342.	338.
19065 P	279.	286.	289.	289.	293.	300.	298.	300.	314.	318.	325.	334.	340.
19068 P	287.	290.	302.	297.	307.	312.	320.	320.	331.	333.	338.	345.	352.
19072 P	254.	257.	268.	272.	272.	273.	268.	280.	289.	291.	301.	307.	308.
19074 P	268.	273.	285.	284.	290.	294.	295.	300.	298.	306.	311.	319.	326.
19075 P	257.	240.	232.	233.	230.	244.	261.	272.	268.	280.	282.	281.	288.

	DAY 13	14	15	16	17	18	19	20	21	22	23	24	25
19010 P	344.	350.	358.	365.	378.	398.	416.	436.	453.				
19012 P	338.	343.	350.	355.	369.	386.	408.	424.	445.				
19019 P	336.	348.	357.	365.	379.	396.	420.	426.	445.				
19021 P	331.	337.	347.	354.	365.	373.	352.	344.	385.				
19023 P	299.	305.	314.	318.	298.	325.	341.	357.	366.				
19041 P	354.	358.	366.	371.	392.	416.	425.	449.					
19042 P	338.	348.	354.	374.	378.	397.	414.	430.	443.				
19044 P	325.	340.	337.	349.	362.	380.	392.	420.					
19050 P	316.	320.	328.	305.	338.	360.	374.	388.	403.				
19053 P	350.	359.	366.	373.	391.	415.	429.	449.	458.				
19065 P	346.	348.	360.	376.	386.	411.	432.	446.					
19068 P	354.	359.	365.	382.	394.	410.	434.	441.					
19072 P	310.	321.	327.	335.	350.	369.	384.	403.					
19074 P	332.	340.	345.	356.	370.	377.	397.	408.	424.	419.			
19075 P	294.	306.	311.	318.	329.	340.	353.	359.	382.				

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C34 (PAGE 2): MATERNAL BODY WEIGHTS - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II					0.3 MG/KG/DAY							
PREGNANCY STATUS	DAY 0	1	2	3	4	5	6	7	8	9	10	11	12
19004 P	239.	245.	252.	262.	265.	269.	270.	276.	280.	288.	292.	301.	306.
19009 P	269.	275.	278.	281.	283.	286.	291.	294.	298.	299.	304.	310.	315.
19016 P	249.	250.	258.	260.	266.	260.	269.	270.	281.	277.	282.	291.	296.
19018 P	255.	262.	266.	269.	278.	281.	286.	292.	295.	299.	309.	318.	322.
19026 P	268.	259.	273.	273.	285.	288.	290.	298.	296.	302.	311.	327.	329.
19036 P	271.	281.	288.	292.	296.	301.	304.	313.	321.	324.	330.	332.	342.
19037 P	260.	268.	274.	272.	280.	287.	290.	292.	296.	301.	302.	310.	319.
19043 P	255.	265.	275.	274.	278.	285.	295.	292.	295.	305.	310.	318.	328.
19047 P	232.	244.	241.	248.	248.	251.	255.	256.	264.	264.	270.	274.	279.
19048 P	271.	273.	282.	287.	288.	291.	295.	303.	299.	306.	309.	312.	317.
19052 P	259.	269.	262.	274.	272.	285.	288.	288.	293.	299.	305.	309.	318.
19055 P	267.	277.	284.	289.	294.	300.	306.	307.	305.	318.	322.	334.	339.
19061 P	259.	259.	266.	264.	271.	278.	278.	279.	288.	291.	290.	296.	306.
19067 P	273.	270.	268.	283.	288.	289.	289.	294.	299.	300.	308.	312.	321.
19071 P	264.	274.	281.	286.	292.	295.	304.	302.	309.	316.	319.	331.	338.

	DAY 13	14	15	16	17	18	19	20	21	22	23	24	25
19004 P	310.	320.	325.	334.	349.	361.	383.	396.					
19009 P	321.	321.	330.	335.	343.	349.	326.	334.	361.				
19016 P	299.	310.	312.	325.	338.	348.	361.	380.	395.				
19018 P	326.	332.	339.	348.	363.	373.	391.	408.	422.				
19026 P	336.	349.	346.	361.	378.	394.	418.	432.	452.				
19036 P	343.	348.	357.	367.	383.	398.	410.	424.	422.				
19037 P	321.	325.	328.	342.	351.	364.	377.	393.	399.				
19043 P	329.	338.	346.	357.	372.	387.	389.	405.	417.				
19047 P	280.	289.	297.	304.	314.	329.	334.	364.	380.				
19048 P	321.	329.	336.	336.	348.	358.	358.	375.	382.				
19052 P	322.	330.	338.	350.	366.	377.	391.	409.					
19055 P	341.	349.	358.	371.	384.	401.	411.	433.	452.				
19061 P	308.	315.	325.	338.	345.	351.	367.	382.					
19067 P	324.	325.	340.	344.	351.	370.	379.	395.	414.				
19071 P	339.	348.	364.	365.	380.	394.	409.	431.	444.				

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C34 (PAGE 3): MATERNAL BODY WEIGHTS - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP III												
						1 MG/KG/DAY							
PREGNANCY STATUS	DAY 0	1	2	3	4	5	6	7	8	9	10	11	12
19003 P	244.	252.	252.	258.	258.	260.	262.	264.	267.	269.	271.	287.	286.
19007 P	293.	297.	302.	304.	312.	310.	315.	318.	324.	332.	340.	345.	350.
19008 P	283.	282.	293.	296.	302.	310.	312.	317.	323.	327.	335.	344.	345.
19013 P	291.	289.	294.	296.	304.	311.	310.	310.	320.	317.	328.	333.	341.
19014 NP	250.	259.	263.	264.	270.	276.	281.	280.	290.	291.	295.	295.	299.
19015 P	250.	259.	262.	264.	266.	265.	259.	264.	275.	275.	287.	291.	298.
19017 P	258.	262.	261.	275.	269.	275.	278.	283.	288.	292.	298.	301.	316.
19024 P	291.	294.	292.	304.	305.	311.	309.	318.	316.	329.	330.	340.	342.
19029 P	266.	267.	278.	275.	277.	283.	284.	284.	280.	285.	290.	294.	306.
19034 P	266.	274.	280.	284.	289.	292.	294.	300.	308.	313.	321.	334.	339.
19038 NP	237.	243.	254.	262.	261.	265.	273.	278.	281.	282.	285.	291.	296.
19056 P	272.	277.	282.	285.	290.	287.	292.	293.	299.	308.	313.	315.	318.
19057 P	269.	271.	269.	281.	279.	282.	289.	290.	296.	301.	307.	310.	318.
19060 P	276.	271.	278.	288.	277.	295.	301.	302.	306.	314.	320.	329.	334.
19064 P	263.	275.	274.	288.	286.	291.	294.	295.	305.	307.	312.	317.	333.

	DAY 13	14	15	16	17	18	19	20	21	22	23	24	25
19003 P	291.	301.	308.	320.	335.	354.	365.	386.					
19007 P	354.	360.	369.	380.	391.	412.	431.	444.	420.				
19008 P	352.	358.	368.	370.	389.	411.	423.	439.					
19013 P	350.	358.	361.	372.	386.	398.	409.	432.	450.				
19014 NP	297.	298.	303.	306.	312.	310.	310.	310.	316.	313.	305.	293.	287.
19015 P	290.	298.	310.	315.	329.	346.	360.	374.	386.				
19017 P	314.	323.	332.	338.	358.	364.	385.	406.	421.				
19024 P	341.	345.	355.	358.	374.	388.	368.	416.	400.				
19029 P	317.	317.	323.	336.	355.	363.	376.	393.	403.				
19034 P	340.	346.	359.	364.	369.	390.	400.	413.	432.				
19038 NP	294.	294.	288.	284.	287.	288.	281.	282.	281.	286.	288.	288.	302.
19056 P	324.	326.	338.	342.	355.	368.	384.	395.	420.				
19057 P	318.	328.	333.	337.	357.	375.	388.	402.	424.				
19060 P	346.	347.	353.	371.	379.	392.	409.	425.					
19064 P	331.	337.	343.	348.	366.	384.	411.	432.	445.				

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C34 (PAGE 4): MATERNAL BODY WEIGHTS - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP IV					3 MG/KG/DAY						
PREGNANCY STATUS	DAY 0	1	2	3	4	5	6	7	8	9	10	11	12
19002 P	295.	294.	299.	299.	305.	306.	307.	310.	316.	320.	325.	323.	333.
19005 P	276.	276.	286.	284.	284.	285.	284.	287.	290.	292.	297.	303.	300.
19035 P	264.	270.	273.	272.	273.	280.	281.	282.	273.	277.	282.	296.	293.
19039 P	249.	253.	253.	256.	256.	260.	264.	264.	267.	269.	274.	281.	287.
19040 P	266.	270.	274.	277.	281.	283.	288.	292.	294.	298.	306.	313.	317.
19045 P	269.	279.	282.	288.	293.	294.	290.	296.	313.	313.	320.	324.	340.
19046 NP	247.	254.	258.	269.	267.	268.	273.	275.	281.	274.	282.	280.	296.
19051 NP	MATING NOT CONFIRMED												
19054 P	248.	260.	260.	258.	262.	267.	264.	268.	276.	280.	284.	291.	296.
19058 P	258.	266.	271.	280.	283.	293.	293.	300.	303.	313.	320.	322.	328.
19062 P	256.	266.	268.	274.	278.	279.	289.	292.	292.	304.	307.	316.	320.
19063 P	284.	289.	294.	300.	308.	310.	314.	318.	326.	330.	335.	345.	355.
19066 P	246.	244.	254.	258.	262.	267.	266.	264.	268.	274.	278.	290.	290.
19069 P	284.	289.	298.	304.	311.	314.	322.	324.	336.	341.	346.	358.	370.
19073 P	258.	266.	268.	275.	279.	284.	288.	290.	296.	302.	308.	315.	326.

	DAY 13	14	15	16	17	18	19	20	21	22	23	24	25
19002 P	338.	341.	352.	350.	371.	380.	394.	406.	429.				
19005 P	306.	316.	319.	326.	338.	357.	372.	389.	400.				
19035 P	296.	297.	306.	307.	323.	336.	354.	383.	390.				
19039 P	291.	296.	303.	314.	324.	329.	348.	362.					
19040 P	320.	329.	337.	343.	357.	370.	390.	412.					
19045 P	336.	342.	347.	363.	382.	392.	402.	423.	441.				
19046 NP	290.	294.	293.	288.	284.	283.	284.	279.	274.	281.	280.	284.	274.
19051 NP	MATING NOT CONFIRMED												
19054 P	296.	302.	299.	307.	304.	316.	328.	337.	344.				
19058 P	329.	340.	346.	350.	365.	383.	396.	414.	424.				
19062 P	322.	332.	336.	340.	356.	376.	391.	415.		304.			
19063 P	362.	368.	369.	383.	392.	393.	407.	424.	440.				
19066 P	301.	302.	314.	321.	335.	351.	368.	381.	394.				
19069 P	375.	378.	387.	404.	413.	384.	408.	436.	454.				
19073 P	330.	336.	342.	349.	368.	380.	387.	402.	420.				

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C34 (PAGE 5): MATERNAL BODY WEIGHTS - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP V					10 MG/KG/DAY							
PREGNANCY STATUS	DAY 0	1	2	3	4	5	6	7	8	9	10	11	12
19001 P	223.	229.	233.	237.	235.	242.	239.	243.	251.	250.	251.	255.	266.
19006 P	268.	280.	281.	282.	292.	293.	296.	298.	306.	311.	318.	323.	333.
19011 P	254.	261.	260.	263.	264.	264.	275.	278.	275.	287.	297.	289.	292.
19020 P	236.	234.	249.	254.	256.	259.	257.	263.	269.	276.	283.	311.	293.
19022 P	267.	271.	266.	282.	290.	293.	293.	294.	298.	303.	311.	316.	320.
19025 P	293.	303.	303.	307.	314.	313.	316.	324.	329.	333.	342.	351.	352.
19027 P	248.	252.	251.	260.	256.	260.	269.	270.	272.	274.	282.	287.	290.
19028 P	265.	271.	278.	283.	283.	288.	292.	289.	297.	301.	304.	308.	318.
19030 P	273.	271.	272.	286.	278.	284.	284.	288.	286.	292.	299.	307.	315.
19031 P	281.	290.	285.	297.	298.	303.	303.	313.	322.	318.	327.	337.	346.
19032 P	281.	279.	292.	292.	299.	300.	301.	309.	310.	315.	323.	331.	341.
19033 P	249.	260.	258.	263.	262.	267.	272.	278.	279.	285.	288.	292.	304.
19049 P	256.	267.	278.	281.	287.	284.	295.	296.	302.	307.	309.	312.	329.
19059 P	267.	276.	271.	278.	286.	289.	291.	297.	301.	299.	308.	314.	325.
19070 P	252.	259.	259.	270.	266.	275.	272.	276.	286.	287.	290.	296.	301.

	DAY 13	14	15	16	17	18	19	20	21	22	23	24	25
19001 P	271.	278.	283.	289.	303.	309.	320.	334.	343.				
19006 P	336.	347.	353.	366.	379.	397.	422.	436.	451.				
19011 P	308.	305.	309.	320.	340.	354.	375.	386.	406.				
19020 P	293.	300.	303.	306.	321.	332.	349.	362.					
19022 P	321.	328.	337.	345.	361.	369.	389.	416.	391.				
19025 P	359.	354.	364.	372.	384.	401.	409.	413.	425.				
19027 P	296.	299.	303.	308.	326.	341.	353.	373.	386.				
19028 P	324.	327.	338.	344.	354.	365.	377.	394.	411.				
19030 P	314.	321.	328.	332.	345.	354.	368.	382.	397.				
19031 P	348.	357.	366.	371.	389.	398.	414.	436.					
19032 P	344.	350.	355.	355.	375.	390.	404.	417.	447.				
19033 P	303.	312.	324.	328.	344.	358.	370.	390.					
19049 P	332.	338.	338.	346.	369.	373.	386.	410.	425.				
19059 P	329.	333.	344.	352.	363.	376.	383.	405.	427.				
19070 P	311.	313.	323.	332.	347.	358.	351.	372.	404.				

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C35 (PAGE 1): MATERNAL BODY WEIGHTS - LACTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP I												0 MG/KG/DAY
	DAY 1	2	3	4	5	6	7	8	9	10	11	12	13
19010	334.	330.	332.	334.	341.	344.	351.	351.	368.	353.	360.	356.	345.
19012	316.	319.	322.	327.	323.	331.	347.	346.	349.	295.a	353.	359.	366.
19019	324.	309.	320.	337.	337.	342.	343.	340.	360.	360.	365.	352.	374.
19021	302.	266.	289.	288.	310.	272.	324.	320.	291.	326.	328.	316.	350.
19023	279.	294.	299.	302.	310.	319.	316.	318.	331.	338.	345.	336.	340.
19041	337.	347.	346.	352.	358.	371.	363.	367.	383.	371.	381.	380.	390.
19042	335.	334.	329.	340.	338.	346.	346.	344.	350.	354.	354.	362.	362.
19044	301.	300.	303.	312.	321.	319.	330.	340.	339.	341.	352.	352.	356.
19050	285.	285.	285.	290.	300.	305.	304.	313.	330.	327.	335.	335.	342.
19053	324.	327.	338.	336.	339.	359.	367.	367.	374.	377.	312.a	380.	392.
19065	332.	340.	337.	345.	343.	351.	362.	361.	364.	377.	377.	365.	391.
19068	338.	344.	349.	348.	347.	360.	362.	371.	381.	366.	377.	379.	380.
19072	311.	298.	300.	305.	299.	324.	334.	337.	288.a	340.	345.	360.	359.
19074	313.	319.	313.	320.	336.	345.	352.	348.	358.	367.	369.	378.	350.
19075	266.	284.	279.	287.	288.	303.	305.	311.	321.	297.a	321.	325.	280.a

	DAY 14	15	16	17	18	19	20	21	22b
19010	352.	353.	362.	359.	360.	349.	347.	353.	299.
19012	365.	381.	386.	362.	378.	356.	354.	373.	335.
19019	388.	371.	384.	363.	394.	379.	384.	372.	309.
19021	347.	352.	355.	331.	344.	346.	354.	307.a	270.
19023	335.	331.	323.	322.	329.	338.	332.	317.	280.
19041	378.	396.	385.	376.	359.	367.	375.	362.	305.
19042	370.	370.	371.	346.	382.	365.	365.	355.	302.
19044	368.	354.	367.	327.	354.	359.	376.	366.	360.
19050	337.	339.	343.	329.	338.	337.	336.	341.	290.
19053	374.	378.	360.	367.	381.	377.	366.	285.	299.
19065	385.	393.	376.	346.	370.	371.	356.	345.	301.
19068	382.	382.	386.	398.	382.	403.	388.	386.	360.
19072	363.	294.	348.	355.	351.	364.	354.	367.	292.
19074	337.	338.	346.	365.	363.	376.	380.	359.	297.
19075	316.	298.	318.	330.	319.	314.	327.	320.	295.

DAY = DAY OF LACTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Value appeared incorrectly recorded and was excluded from group averages and statistical analyses.
b. Dams were fasted prior to sacrifice.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C35 (PAGE 2): MATERNAL BODY WEIGHTS - LACTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II					0.3 MG/KG/DAY							
	DAY 1	2	3	4	5	6	7	8	9	10	11	12	13
19004	290.	293.	296.	301.	303.	317.	310.	316.	330.	331.	333.	334.	330.
19009	286.	306.	273.	251.a	301.	312.	324.	318.	325.	331.	329.	342.	343.
19016	295.	297.	298.	306.	310.	320.	323.	321.	323.	318.	324.	328.	329.
19018	302.	308.	311.	311.	318.	320.	325.	327.	336.	347.	339.	332.	342.
19026	318.	296.	273.a	320.	314.	311.	326.	331.	333.	347.	341.	338.	355.
19036	304.	294.	297.	296.	296.	309.	319.	303.	318.	334.	335.	347.	352.
19037	267.	272.	277.	269.	288.	292.	296.	301.	318.	321.	251.	230.a	298.
19043	314.	314.	311.	316.	316.	321.	332.	325.	342.	349.	346.	354.	352.
19047	281.	269.	271.	276.	287.	284.	304.	296.	311.	312.	318.	318.	264.a
19048	306.	300.	305.	302.	307.	315.	320.	327.	336.	343.	336.	351.	345.
19052	302.	297.	261.a	264.a	285.	315.	316.	317.	331.	330.	339.	350.	340.
19055	320.	326.	320.	332.	332.	332.	348.	332.	353.	363.	354.	364.	360.
19061	309.	290.	297.	293.	309.	307.	315.	323.	277.a	297.	319.	340.	332.
19067	305.	306.	311.	310.	314.	319.	331.	335.	346.	352.	350.	356.	367.
19071	334.	334.	335.	312.	329.	320.	332.	339.	342.	348.	364.	365.	356.

	DAY 14	15	16	17	18	19	20	21	22b
19004	349.	337.	345.	317.	332.	344.	325.	304.	276.
19009	349.	348.	343.	341.	345.	349.	342.	336.	346.
19016	342.	341.	336.	330.	327.	329.	324.	308.	314.
19018	336.	337.	341.	341.	353.	349.	340.	343.	338.
19026	360.	354.	356.	355.	341.	353.	358.	360.	296.
19036	344.	355.	356.	343.	345.	358.	344.	351.	359.
19037	310.	326.	332.	312.	332.	326.	342.	321.	309.
19043	355.	342.	338.	333.	344.	349.	344.	348.	356.
19047	323.	321.	330.	318.	324.	317.	319.	308.	325.
19048	355.	346.	349.	338.	356.	365.	368.	350.	306.
19052	315.c	352.	353.	349.	345.	351.	346.	346.	320.
19055	331.	348.	363.	366.	372.	367.	368.	350.	336.
19061	338.	335.	322.	348.	338.	337.	334.	327.	315.
19067	344.	352.	352.	360.	371.	358.	343.	308.a	294.
19071	362.	316.a	369.	365.	371.	367.	372.	348.	374.

DAY = DAY OF LACTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Value appeared incorrectly recorded and was excluded from group averages and statistical analyses.
b. Dams were fasted prior to sacrifice.
c. Water access was interrupted; value excluded from group averages and statistical analyses.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C35 (PAGE 3): MATERNAL BODY WEIGHTS - LACTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP III												1 MG/KG/DAY
DAY	1	2	3	4	5	6	7	8	9	10	11	12	13
19003	285.	284.	287.	293.	300.	308.	312.	317.	316.	330.	274.a	281.a	320.
19007	303.	309.	316.	316.	316.	337.	339.	348.	347.	354.	364.	363.	373.
19008	331.	326.	328.	335.	316.a	341.	350.	355.	351.	361.	368.	361.	358.
19013	346.	334.	315.a	348.	349.	354.	350.	357.	359.	372.	372.	389.	390.
19014	NOT PREGNANT												
19015	281.	266.	283.	288.	277.	295.	302.	296.	313.	321.	311.	310.	344.
19017	320.	307.	310.	312.	313.	322.	324.	339.	341.	352.	350.	356.	363.
19024	295.	312.	321.	327.	332.	332.	342.	344.	354.	361.	368.	369.	348.
19029	282.	284.	281.	283.	290.	301.	305.	309.	309.	309.	318.	326.	323.
19034	311.	320.	323.	322.	328.	309.a	354.	345.	338.	345.	349.	351.	355.
19038	NOT PREGNANT												
19056	317.	311.	316.	282.a	321.	319.	331.	311.a	339.	339.	346.	352.	343.
19057	305.	294.	278.a	300.	311.	320.	324.	324.	321.	339.	336.	350.	352.
19060	336.	318.	330.	328.	342.	345.	353.	348.	358.	366.	369.	360.	373.
19064	311.	305.	319.	318.	300.	313.	319.	321.	340.	342.	340.	344.	302.a

DAY	14	15	16	17	18	19	20	21	22b
19003	344.	336.	335.	333.	330.	335.	315.	338.	284.
19007	369.	331.	359.	354.	377.	369.	352.	355.	303.
19008	361.	370.	358.	340.	360.	356.	350.	350.	292.
19013	391.	379.	387.	369.	380.	386.	381.	374.	389.
19014	NOT PREGNANT								
19015	339.	323.	322.	304.	312.	323.	316.	312.	274.
19017	336.	343.	366.	343.	363.	373.	358.	360.	350.
19024	364.	326.a	368.	351.	366.	369.	367.	354.	309.
19029	323.	326.	332.	299.a	321.	332.	317.	322.	332.
19034	359.	352.	358.	339.	371.	356.	358.	352.	287.
19038	NOT PREGNANT								
19056	347.	341.	343.	346.	348.	329.	350.	338.	292.
19057	351.	337.	343.	352.	337.	356.	354.	305.	287.
19060	362.	350.	371.	373.	351.	372.	351.	352.	357.
19064	344.	330.	349.	354.	363.	359.	366.	352.	289.

DAY = DAY OF LACTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Value appeared incorrectly recorded and was excluded from group averages and statistical analyses.
b. Dams were fasted prior to sacrifice.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C35 (PAGE 4): MATERNAL BODY WEIGHTS - LACTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP IV												3 MG/KG/DAY
DAY	1	2	3	4	5	6	7	8	9	10	11	12	13
19002	335.	330.	328.	337.	338.	340.	345.	356.	338.	348.	357.	368.	367.
19005	284.	295.	297.	307.	317.	322.	320.	325.	328.	328.	328.	340.	336.
19035	271.	267.	276.	285.	289.	286.	292.	292.	309.	309.	305.	316.	332.
19039	271.	269.	265.	270.	272.	254.a	283.	278.	292.	288.	293.	300.	306.
19040	321.	299.	299.	314.	315.	323.	328.	339.	350.	350.	348.	356.	356.
19045	315.	315.	315.	318.	304.a	315.	310.	318.	352.	346.	348.	368.	376.
19046	NOT PREGNANT												
19051	NOT PREGNANT; MATING NOT CONFIRMED												
19054	280.	296.	291.	296.	297.	304.	303.	312.	312.	313.	306.	290.a	333.
19058	309.	320.	276.a	268.a	300.	309.	313.	319.	329.	340.	337.	351.	353.
19062	304.	308.	318.	317.	326.	322.	332.	334.	347.	351.	348.	349.	368.
19063	331.	332.	341.	348.	354.	341.	357.	351.	370.	368.	378.	385.	381.
19066	290.	280.	288.	292.	297.	303.	301.	314.	313.	315.	304.a	322.	351.
19069	332.	329.	332.	332.	330.	288.a	275.a	320.	333.	288.a	337.	353.	365.
19073	318.	315.	310.	306.	303.	321.	328.	330.	340.	346.	352.	362.	290.a

DAY	14	15	16	17	18	19	20	21	22b
19002	361.	358.	360.	369.	358.	376.	378.	359.	302.
19005	341.	342.	351.	320.	344.	352.	350.	333.	285.
19035	315.	322.	314.	306.	322.	326.	315.	312.	261.
19039	311.	310.	310.	296.	320.	317.	313.	317.	315.
19040	360.	355.	350.	334.	365.	361.	367.	356.	294.
19045	349.	377.	361.	353.	380.	402.	386.	398.	385.
19046	NOT PREGNANT								
19051	NOT PREGNANT; MATING NOT CONFIRMED								
19054	335.	332.	333.	313.	328.	326.	322.	323.	287.
19058	331.	302.c	345.	350.	345.	364.	363.	324.	350.
19062	369.	358.	356.	335.	352.	355.	354.	342.	290.
19063	377.	380.	383.	370.	384.	388.	377.	385.	369.
19066	338.	332.	332.	325.	336.	341.	340.	328.	292.
19069	349.	361.	366.	365.	373.	375.	358.	352.	362.
19073	350.	357.	368.	375.	371.	364.	365.	348.	363.

DAY = DAY OF LACTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Value appeared incorrectly recorded and was excluded from group averages and statistical analyses.
b. Dams were fasted prior to sacrifice.
c. Water access was interrupted; value excluded from group averages and statistical analyses.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C35 (PAGE 5): MATERNAL BODY WEIGHTS - LACTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP V					10 MG/KG/DAY							
	DAY 1	2	3	4	5	6	7	8	9	10	11	12	13
19001	256.	257.	254.	254.	234.a	262.	261.	265.	259.	273.	281.	278.	286.
19006	308.	308.	313.	317.	322.	324.	328.	330.	331.	346.	344.	339.	348.
19011	291.	286.	290.	302.	303.	308.	302.	321.	321.	331.	338.	326.	345.
19020	260.	268.	279.	274.	271.	243.	269.	266.	268.	262.	253.	268.	259.
19022	278.	300.	310.	314.	317.	322.	335.	343.	344.	361.	341.	360.	355.
19025	310.	318.	326.	315.a	331.	349.	358.	347.	361.	365.	368.	381.	379.
19027	281.	283.	278.	274.	242.a	276.	294.	283.	291.	238.	296.	304.	322.
19028	313.	302.	307.	310.	310.	311.	315.	315.	325.	331.	334.	331.	338.
19030	307.	301.	304.	309.	318.	320.	327.	331.	348.	340.	346.	346.	348.
19031	316.	324.	289.a	286.a	319.	329.	340.	340.	354.	362.	366.	371.	371.
19032	317.	330.	327.	319.	309.	307.	326.	335.	339.	343.	328.	284.a	354.
19033	295.	292.	292.	299.	305.	308.	320.	326.	329.	342.	339.	335.	344.
19049	310.	304.	308.	305.	286.a	302.	318.	320.	326.	339.	335.	331.	348.
19059	312.	313.	314.	312.	313.	317.	322.	327.	338.	348.	347.	352.	350.
19070	290.	297.	302.	302.	305.	312.	313.	323.	337.	330.	337.	357.	355.

	DAY 14	15	16	17	18	19	20	21	22b
19001	287.	288.	286.	278.	304.	302.	296.	292.	278.
19006	367.	366.	366.	356.	373.	373.	378.	373.	304.
19011	332.	294.a	318.	326.	338.	350.	330.	330.	283.
19020	270.	246.	252.	246.	252.	251.	246.	228.	210.
19022	360.	348.	352.	352.	359.	363.	349.	349.	294.
19025	384.	373.	358.	355.	392.	363.	358.	346.	291.
19027	317.	312.	309.	306.	302.	321.	315.	315.	266.
19028	318.	335.	294.c	329.	340.	348.	330.	346.	339.
19030	357.	355.	353.	344.	346.	346.	365.	355.	314.
19031	316.c	362.	365.	364.	375.	373.	381.	371.	361.
19032	351.	336.	359.	343.	356.	319.a	341.	344.	287.
19033	347.	341.	338.	332.	329.	332.	323.	323.	328.
19049	348.	346.	358.	341.	347.	334.	349.	349.	330.
19059	320.	322.	357.	358.	345.	339.	360.	343.	317.
19070	303.c	337.	358.	365.	351.	358.	363.	352.	351.

DAY = DAY OF LACTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Value appeared incorrectly recorded and was excluded from group averages and statistical analyses.
b. Dams were fasted prior to sacrifice.
c. Water access was interrupted; value excluded from group averages and statistical analyses.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C36 (PAGE 1): FEED CONSUMPTION VALUES - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DAYS	1- 8a
RAT #	DOSAGE GROUP I 0 MG/KG/DAY
19010	140.
19012	142.
19019	162.
19021	147.
19023	124.
19041	b
19042	138.
19044	144.
19050	123.
19053	c
19065	151.
19068	167.
19072	132.
19074	146.
19075	138.
RAT #	DOSAGE GROUP II 0.3 MG/KG/DAY
19004	132.
19009	156.
19016	126.
19018	137.
19026	144.
19036	136.
19037	138.
19043	153.
19047	110.
19048	131.
19052	123.
19055	147.
19061	134.
19067	139.
19071	139.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.
b. Spilled feed precluded the calculation of this value.
c. Value was not recorded.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C36 (PAGE 2): FEED CONSUMPTION VALUES - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DAYS 1- 8a		
RAT #	DOSAGE GROUP III	1 MG/KG/DAY
19003	124.	
19007	150.	
19008	155.	
19013	150.	
19014	136.	
19015	142.	
19017	127.	
19024	169.	
19029	153.	
19034	149.	
19038	130.	
19056	141.	
19057	143.	
19060	174.	
19064	138.	
RAT #	DOSAGE GROUP IV	3 MG/KG/DAY
19002	145.	
19005	150.	
19035	125.	
19039	118.	
19040	133.	
19045	134.	
19046	132.	
19051	160.	
19054	135.	
19058	128.	
19062	129.	
19063	153.	
19066	124.	
19069	153.	
19073	134.	

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C36 (PAGE 3): FEED CONSUMPTION VALUES - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DAYS 1- 8a		
RAT #	DOSAGE GROUP V	10 MG/KG/DAY
19001	107.	
19006	119.	
19011	139.	
19020	92.	
19022	133.	
19025	151.	
19027	135.	
19028	163.	
19030	136.	
19031	180.	
19032	147.	
19033	148.	
19049	141.	
19059	138.	
19070	132.	

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C37 (PAGE 1): MATERNAL FEED CONSUMPTION VALUES - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

PREGNANCY STATUS	DAYS 0 - 7	7 - 10	10 - 12	12 - 15	15 - 18	18 - 20
RAT #	DOSAGE GROUP I				0 MG/KG/DAY	
19010 P	184.	85.	50.	77.	76.	53.
19012 P	178.	82.	55.	83.	81.	59.
19019 P	188.	90.	82.	95.	75.	56.
19021 P	182.	85.	58.	93.	78.	21.
19023 P	140.	66.	44.	76.	47.	51.
19041 P	190.	82.	127.	81.	83.	58.
19042 P	192.	91.	69.	101.	88.	66.
19044 P	189.	91.	59.	93.	90.	54.
19050 P	158.	70.	49.	73.	56.	53.
19053 P	188.	77.	64.	84.	76.	58.
19065 P	203.	92.	73.	94.	88.	68.
19068 P	191.	93.	57.	86.	86.	55.
19072 P	171.	75.	a	77.	74.	58.
19074 P	193.	89.	63.	90.	82.	51.
19075 P	117.	78.	46.	77.	65.	36.
RAT #	DOSAGE GROUP II				0.3 MG/KG/DAY	
19004 P	186.	83.	58.	86.	81.	60.
19009 P	178.	79.	49.	91.	82.	17.
19016 P	137.	65.	45.	70.	71.	42.
19018 P	176.	85.	59.	90.	85.	55.
19026 P	179.	81.	58.	90.	86.	59.
19036 P	193.	93.	56.	82.	78.	40.
19037 P	185.	83.	59.	77.	67.	39.
19043 P	170.	84.	57.	84.	95.	54.
19047 P	150.	67.	43.	70.	72.	46.
19048 P	164.	67.	44.	76.	69.	46.
19052 P	162.	79.	49.	77.	79.	46.
19055 P	198.	91.	63.	90.	97.	49.
19061 P	170.	80.	51.	86.	81.	52.
19067 P	173.	79.	58.	80.	69.	22.
19071 P	203.	90.	60.	90.	88.	57.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAYS = DAYS OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Spilled feed precluded the calculation of this value.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C37 (PAGE 2): MATERNAL FEED CONSUMPTION VALUES - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

PREGNANCY STATUS	DAYS 0 - 7	7 - 10	10 - 12	12 - 15	15 - 18	18 - 20
RAT #	DOSAGE GROUP III				1 MG/KG/DAY	
19003 P	144.	65.	49.	77.	66.	50.
19007 P	179.	83.	60.	86.	78.	53.
19008 P	213.	94.	64.	86.	79.	60.
19013 P	160.	78.	64.	85.	86.	54.
19014 NP	175.	83.	50.	73.	78.	41.
19015 P	142.	71.	49.	73.	79.	55.
19017 P	149.	70.	50.	74.	86.	51.
19024 P	181.	91.	56.	84.	75.	46.
19029 P	175.	63.	49.	89.	80.	45.
19034 P	182.	87.	65.	90.	76.	36.
19038 NP	153.	76.	53.	68.	71.	65.
19056 P	167.	76.	53.	77.	71.	54.
19057 P	174.	80.	53.	79.	80.	53.
19060 P	172.	92.	64.	92.	86.	59.
19064 P	177.	74.	53.	79.	69.	55.
RAT #	DOSAGE GROUP IV				3 MG/KG/DAY	
19002 P	167.	62.	49.	70.	79.	47.
19005 P	165.	68.	48.	75.	70.	55.
19035 P	155.	56.	44.	63.	62.	51.
19039 P	142.	65.	44.	71.	70.	54.
19040 P	187.	79.	57.	87.	77.	59.
19045 P	186.	91.	59.	83.	94.	52.
19046 NP	170.	72.	52.	73.	54.	27.
19051 NP	MATING NOT CONFIRMED					
19054 P	160.	75.	49.	68.	56.	52.
19058 P	196.	92.	51.	81.	88.	49.
19062 P	181.	80.	56.	81.	72.	55.
19063 P	224.	95.	63.	97.	81.	48.
19066 P	149.	66.	47.	76.	74.	51.
19069 P	220.	106.	70.	104.	74.	28.
19073 P	164.	91.	56.	86.	90.	49.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAYS = DAYS OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C37 (PAGE 3): MATERNAL FEED CONSUMPTION VALUES - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

PREGNANCY STATUS DAYS	0 - 7	7 - 10	10 - 12	12 - 15	15 - 18	18 - 20
RAT #	DOSAGE GROUP V				10 MG/KG/DAY	
19001 P	127.	63.	42.	71.	70.	41.
19006 P	165.	74.	55.	85.	72.	61.
19011 P	146.	69.	48.	69.	75.	56.
19020 P	162.	77.	53.	79.	64.	51.
19022 P	185.	75.	57.	88.	81.	69.
19025 P	202.	88.	65.	73.	64.	50.
19027 P	144.	73.	47.	81.	65.	41.
19028 P	184.	82.	56.	93.	84.	55.
19030 P	175.	71.	54.	78.	73.	57.
19031 P	182.	91.	59.	94.	89.	54.
19032 P	180.	84.	59.	93.	94.	62.
19033 P	164.	82.	57.	89.	85.	55.
19049 P	176.	83.	54.	81.	81.	52.
19059 P	169.	75.	54.	84.	86.	50.
19070 P	156.	75.	50.	82.	88.	30.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAYS = DAYS OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C38 (PAGE 1): MATERNAL FEED CONSUMPTION VALUES - LACTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DAY	1 - 5	5 - 8	8 - 15
RAT #	DOSAGE GROUP I		0 MG/KG/DAY
19010	131.	158.	387.
19012	155.	178.	498.
19019	137.	186.	540.
19021	99.	181.	478.
19023	158.	168.	488.
19041	176.	183.	549.
19042	137.	150.	468.
19044	196.	207.	628.
19050	144.	182.	506.
19053	165.	206.	511.
19065	191.	203.	579.
19068	149.	184.	502.
19072	125.	161.	427.
19074	202.	216.	521.
19075	144.	191.	433.
RAT #	DOSAGE GROUP II		0.3 MG/KG/DAY
19004	158.	165.	513.
19009	85.	141.	400.
19016	140.	167.	495.
19018	120.	167.	486.
19026	25.	173.	374.
19036	101.	145.	533.
19037	85.	211.	561.
19043	138.	180.	516.
19047	114.	154.	460.
19048	114.	137.	447.
19052	82.	154.	497.
19055	145.	172.	493.
19061	99.	138.	366.
19067	142.	170.	520.
19071	a	142.	512.

DAY = DAY OF LACTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Spilled feed precluded the calculation of this value.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C38 (PAGE 2): MATERNAL FEED CONSUMPTION VALUES - LACTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DAY	1 - 5	5 - 8	8 - 15
RAT #	DOSAGE GROUP III		1 MG/KG/DAY
19003	155.	164.	439.
19007	156.	181.	508.
19008	a	183.	527.
19013	120.	183.	517.
19014	NOT PREGNANT		
19015	117.	158.	474.
19017	114.	166.	475.
19024	135.	163.	461.
19029	138.	148.	473.
19034	149.	143.	470.
19038	NOT PREGNANT		
19056	113.	169.	513.
19057	117.	168.	471.
19060	138.	185.	513.
19064	143.	168.	455.
RAT #	DOSAGE GROUP IV		3 MG/KG/DAY
19002	113.	132.	427.
19005	175.	159.	497.
19035	108.	112.	438.
19039	146.	145.	436.
19040	140.	189.	542.
19045	130.	160.	584.
19046	NOT PREGNANT		
19051	NOT PREGNANT; MATING NOT CONFIRMED		
19054	113.	125.	360.
19058	98.	184.	496.
19062	147.	175.	560.
19063	131.	160.	568.
19066	110.	139.	453.
19069	106.	81.	451.
19073	114.	167.	523.

DAY = DAY OF LACTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Spilled feed precluded the calculation of this value.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C38 (PAGE 3): MATERNAL FEED CONSUMPTION VALUES - LACTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

	DAY 1 - 5	5 - 8	8 - 15
RAT #	DOSAGE GROUP V		10 MG/KG/DAY
19001	87.	119.	381.
19006	154.	178.	558.
19011	114.	157.	445.
19020	137.	91.	319.
19022	191.	184.	520.
19025	187.	195.	553.
19027	99.	132.	427.
19028	126.	143.	454.
19030	154.	158.	503.
19031	92.	178.	559.
19032	147.	149.	481.
19033	143.	166.	499.
19049	a	169.	474.
19059	144.	167.	494.
19070	150.	167.	492.

DAY = DAY OF LACTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Spilled feed precluded the calculation of this value.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C39 (PAGE 1): MATING AND FERTILITY, ESTROUS CYCLING AND DAYS IN COHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	ESTROUS STAGES/ 13 DAYS	DAYS IN COHABITATION	MATING STATUS	MATING DATE	PREGNANCY STATUS
DOSAGE GROUP I		0 MG/KG/DAY			
19010	2	14	M	C	P
19012	2	2	M	C	P
19019	3	3	M	C	P
19021	3	2	M	C	P
19023	4	4	M	C	P
19041	4	4	M	C	P
19042	1	3	M	C	P
19044	2	1	M	C	P
19050	4	4	M	C	P
19053	2	3	M	C	P
19065	3	3	M	C	P
19068	2a	2	M	C	P
19072	2	4	M	C	P
19074	3	2	M	C	P
19075	3	4	M	C	P
DOSAGE GROUP II		0.3 MG/KG/DAY			
19004	4	4	M	C	P
19009	3	1	M	C	P
19016	3	1	M	C	P
19018	3	2	M	C	P
19026	1	4	M	C	P
19036	2	1	M	C	P
19037	3	2	M	C	P
19043	4	1	M	C	P
19047	2	1	M	C	P
19048	4	4	M	C	P
19052	2	1	M	C	P
19055	2	1	M	C	P
19061	3	2	M	C	P
19067	3	3	M	C	P
19071	3	1	M	C	P

M = MATED C = CONFIRMED P = PREGNANT NP = NOT PREGNANT

a. Six or more consecutive days of diestrus were observed.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C39 (PAGE 2): MATING AND FERTILITY, ESTROUS CYCLING AND DAYS IN COHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	ESTROUS STAGES/ 13 DAYS	DAYS IN COHABITATION	MATING STATUS	MATING DATE	PREGNANCY STATUS
DOSAGE GROUP III		1 MG/KG/DAY			
19003	3	3	M	C	P
19007	3	3	M	C	P
19008	3	4	M	C	P
19013	3	2	M	C	P
19014	4	1	M	C	NP
19015	2	4	M	C	P
19017	3	1	M	C	P
19024	3	4	M	C	P
19029	3	2	M	C	P
19034	3	3	M	C	P
19038	3	1	M	C	NP
19056	4	4	M	C	P
19057	4	4	M	C	P
19060	4	2	M	C	P
19064	4	4	M	C	P
DOSAGE GROUP IV		3 MG/KG/DAY			
19002	4	13	M	C	P
19005	3	4	M	C	P
19035	3	4	M	C	P
19039	3	2	M	C	P
19040	4	4	M	C	P
19045	3	1	M	C	P
19046	2	1	M	C	NP
19051	1a	14	DID NOT MATE	-	-
19054	3	3	M	C	P
19058	2	1	M	C	P
19062	4	4	M	C	P
19063	3	2	M	C	P
19066	3	4	M	C	P
19069	3	2	M	C	P
19073	3	1	M	C	P

M = MATED C = CONFIRMED P = PREGNANT NP = NOT PREGNANT
a. Six or more consecutive days of estrus were observed.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C39 (PAGE 3): MATING AND FERTILITY, ESTROUS CYCLING AND DAYS IN COHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	ESTROUS STAGES/ 13 DAYS	DAYS IN COHABITATION	MATING STATUS	MATING DATE	PREGNANCY STATUS
DOSAGE GROUP V		10 MG/KG/DAY			
19001	3	1	M	C	P
19006	2	3	M	C	P
19011	3	4	M	C	P
19020	0	4	M	C	P
19022	3	4	M	C	P
19025	1a	3	M	C	P
19027	3	4	M	C	P
19028	1	1	M	C	P
19030	0	4	M	C	P
19031	1	1	M	C	P
19032	3	4	M	C	P
19033	3	1	M	C	P
19049	2	1	M	C	P
19059	3	1	M	C	P
19070	3	1	M	C	P

M = MATED C = CONFIRMED P = PREGNANT NP = NOT PREGNANT

a. Six or more consecutive days of diestrus were observed.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C40 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP I	0 MG/KG/DAY									
RAT #	19012	19019	19021	19023	19041	19042	19044	19050	19053	19065
HOME CAGE BEHAVIOR	3	2	3	3	3	3	3	3	3	1
ALTERATIONS (HOME CAGE)	1	1	1	1	1	1	1	1	1	1
REACTION TO REMOVAL	1	1	1	1	1	1	1	1	1	1
REACTION TO HANDLING	1	1	1	1	1	1	1	1	1	1
REARS IN OPEN FIELD	10	12	12	19	7	13	15	7	14	11
DEFECATION IN OPEN FIELD	1	1	1	2	1	1	2	1	1	1
URINATION IN OPEN FIELD	1	1	2	2	1	2	2	1	1	1
LEVEL OF AROUSAL	3	3	3	3	3	3	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1	1	1	1	1	1	1
GAIT PATTERN	1	1	1	1	1	1	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1	1	1	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1	1	1	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1	1	1	1	1	1	1
LACRIMATION	1	1	1	1	1	1	1	1	1	1
SALIVATION	1	1	1	1	1	1	1	1	1	1
PILOERECTION	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0	0	0	0	0	0	0
APPEARANCE	1	1	1a	1	1b	1	1	1	1	1c
VISUAL REACTION	2	2	2	2	2	2	2	2	2	2
TACTILE REACTION	2	2	2	2	2	2	2	2	2	2
AUDITORY REACTION	3	3	3	3	3	3	3	3	3	3
TAIL-PINCH REACTION	2	2	2	3	2	3	2	2	2	2
AIR RIGHTING RESPONSE	1	1	1	1	1	1	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1	1	1	1	1	1	1
FORELIMB GRIP TEST #1 (G)	410	325	240	550	370	655	330	275	505	430
FORELIMB GRIP TEST #2 (G)	465	650	345	500	355	845	375	350	545	600
HINDLIMB GRIP TEST #1 (G)	245	365	450	335	675	565	520	295	405	315
HINDLIMB GRIP TEST #2 (G)	335	445	420	300	670	475	350	350	530	415
LANDING FOOT SPLAY #1 (CM)	12.1	8.8	8.0	4.4	6.4	6.5	9.5	4.0	9.3	7.0
LANDING FOOT SPLAY #2 (CM)	9.6	8.0	8.3	6.0	5.7	5.7	8.0	6.4	9.4	7.7
BODY WEIGHT (G)	372	374	314	327	382	366	342	342	351	364

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

a. Localized alopecia: head (1.0 cm x 0.4 cm).

b. Localized alopecia: left forepaw and forelimb (1.5 cm x 0.6 cm) and right forelimb (0.6 cm x 0.7 cm).

c. Ears torn: both pinnae.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C40 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP II	0.3 MG/KG/DAY									
RAT #	19004	19009	19016	19018	19026	19036	19037	19043	19047	19048
HOME CAGE BEHAVIOR	3	1	3	2	1	3	2	1	3	1
ALTERATIONS (HOME CAGE)	1	1	1	1	1	1	1	1	1	1
REACTION TO REMOVAL	1	1	1	1	1	1	1	1	1	1
REACTION TO HANDLING	1	1	1	1	1	1	1	1	1	1
REARS IN OPEN FIELD	10	12	12	9	11	14	14	15	18	15
DEFECATION IN OPEN FIELD	1	1	1	1	1	1	1	1	1	1
URINATION IN OPEN FIELD	1	2	1	1	1	1	1	2	1	2
LEVEL OF AROUSAL	3	3	3	3	3	3	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1	1	1	1	1	1	1
GAIT PATTERN	1	1	1	1	1	1	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1	1	1	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1	1	1	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1	1	1	1	1	1	1
LACRIMATION	1	1	1	1	1	1	1	1	1	1
SALIVATION	1	1	1	1	1	1	1	1	1	1
PILOERECTION	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0	0	0	0	0	0	0
APPEARANCE	1	1	1a	1	1	1	1	1	1	1
VISUAL REACTION	2	2	2	2	2	2	2	2	2	2
TACTILE REACTION	2	2	2	2	2	2	2	2	2	2
AUDITORY REACTION	3	3	3	3	3	3	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2	2	2	2	2	3	2
AIR RIGHTING RESPONSE	1	1	1	1	1	1	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1	1	1	1	1	1	1
FORELIMB GRIP TEST #1 (G)	165	510	285	275	325	155	120	400	220	305
FORELIMB GRIP TEST #2 (G)	390	333	140	450	530	145	475	535	325	310
HINDLIMB GRIP TEST #1 (G)	335	365	375	385	365	270	420	255	320	410
HINDLIMB GRIP TEST #2 (G)	315	380	525	355	285	365	665	375	240	325
LANDING FOOT SPLAY #1 (CM)	6.0	8.7	7.9	5.2	6.3	6.2	6.5	5.2	6.2	5.8
LANDING FOOT SPLAY #2 (CM)	7.9	9.0	6.9	6.8	7.4	6.7	7.0	5.4	5.7	6.5
BODY WEIGHT (G)	317	356	352	350	334	362	335	356	345	365

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

a. Localized alopecia: head (0.4 cm x 0.5 cm).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C40 (PAGE 3): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP III	1 MG/KG/DAY									
RAT #	19003	19007	19008	19013	19015	19017	19024	19029	19034	19056
HOME CAGE BEHAVIOR	3	3	1	3	1	3	3	1	2	1
ALTERATIONS (HOME CAGE)	1	1	1	1	1	1	1	1	1	1
REACTION TO REMOVAL	1	1	1	1	1	1	1	1	1	1
REACTION TO HANDLING	1	1	1	1	1	1	1	1	1	1
REARS IN OPEN FIELD	14	9	10	8	6	13	14	10	16	16
DEFECATION IN OPEN FIELD	1	1	1	1	1	1	1	3	1	2
URINATION IN OPEN FIELD	1	1	1	1	2	1	1	1	2	2
LEVEL OF AROUSAL	3	3	3	3	3	3	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1	1	1	1	1	1	1
GAIT PATTERN	1	1	1	1	1	1	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1	1	1	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1	1	1	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1	1	1	1	1	1	1
LACRIMATION	1	1	1	1	1	1	1	1	1	1
SALIVATION	1	1	1	1	1	1	1	1	1	1
PILOERECTION	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0	0	0	0	0	0	0
APPEARANCE	1	1	1a	1	1b	2	1	1c	1	1
VISUAL REACTION	2	2	2	2	2	2	2	2	2	2
TACTILE REACTION	2	2	2	2	2	2	2	2	2	2
AUDITORY REACTION	3	3	3	3	3	3	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2	2	3	2	2	2	3
AIR RIGHTING RESPONSE	1	1	1	1	1	1	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1	1	1	1	1	1	1
FORELIMB GRIP TEST #1 (G)	325	975	85	200	420	330	695	320	610	255
FORELIMB GRIP TEST #2 (G)	245	535	75	365	455	720	665	395	505	300
HINDLIMB GRIP TEST #1 (G)	295	280	370	495	445	450	465	435	455	290
HINDLIMB GRIP TEST #2 (G)	445	315	320	470	375	530	440	520	605	365
LANDING FOOT SPLAY #1 (CM)	5.4	7.0	6.2	10.8	6.8	7.7	8.8	6.2	7.4	8.3
LANDING FOOT SPLAY #2 (CM)	6.3	8.5	5.8	10.6	7.2	6.4	10.4	8.0	7.5	8.4
BODY WEIGHT (G)	323	365	360	386	325	369	359	316	344	359

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

a. Chromorhinorrhea.

b. Localized alopecia: head (0.3 cm in diameter).

c. Localized alopecia: both forepaws and forelimbs (2.8 cm x 0.5 cm) and head (0.3 cm x 0.5 cm).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C40 (PAGE 4): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP IV	3 MG/KG/DAY									
RAT #	19005	19035	19039	19040	19045	19054	19058	19062	19063	19066
HOME CAGE BEHAVIOR	3	1	2	3	1	2	3	2	1	1
ALTERATIONS (HOME CAGE)	1	1	1	1	1	1	1	1	1	1
REACTION TO REMOVAL	1	1	1	1	1	1	1	1	1	1
REACTION TO HANDLING	1	1	1	1	1	1	1	1	1	1
REARS IN OPEN FIELD	11	7	15	12	13	10	10	11	8	10
DEFECATION IN OPEN FIELD	3	1	1	1	2	1	1	1	1	1
URINATION IN OPEN FIELD	1	1	1	1	1	1	1	1	1	1
LEVEL OF AROUSAL	3	3	3	3	3	3	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1	1	1	1	1	1	1
GAIT PATTERN	1	1	1	1	1	1	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1	1	1	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1	1	1	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1	1	1	1	1	1	1
LACRIMATION	1	1	1	1	1	1	1	1	1	1
SALIVATION	1	1	1	1	1	1	1	1	1	1
PILOERECTION	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0	0	0	0	0	0	0
APPEARANCE	1	1	1	1	1a	3b	1	1c	1	1
VISUAL REACTION	2	2	2	2	2	2	2	2	2	2
TACTILE REACTION	2	2	2	2	2	2	2	2	2	2
AUDITORY REACTION	3	3	3	2	3	3	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2	2	2	2	2	2	2
AIR RIGHTING RESPONSE	1	1	1	1	1	1	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1	1	1	1	1	1	1
FORELIMB GRIP TEST #1 (G)	415	355	445	490	560	525	260	310	545	495
FORELIMB GRIP TEST #2 (G)	685	360	395	465	555	605	435	225	530	390
HINDLIMB GRIP TEST #1 (G)	465	255	190	355	340	350	220	400	465	270
HINDLIMB GRIP TEST #2 (G)	470	295	315	430	435	325	365	460	485	365
LANDING FOOT SPLAY #1 (CM)	8.0	5.5	5.4	6.5	8.0	7.5	7.4	7.5	7.0	4.0
LANDING FOOT SPLAY #2 (CM)	8.3	5.8	6.3	7.2	9.4	9.6	9.0	7.0	7.5	5.0
BODY WEIGHT (G)	330	322	317	353	380	339	355	351	368	337

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

a. Localized alopecia: left axilla (4.0 cm x 3.0 cm).

b. Localized alopecia: right forepaw and forelimb (1.7 cm x 0.6 cm).

c. Tip of tail missing.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN RATS (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C40 (PAGE 5): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP V	10 MG/KG/DAY									
RAT #	19001	19006	19011	19020	19022	19025	19027	19028	19030	19031
HOME CAGE BEHAVIOR	2	2	2	3	2	3	1	3	3	3
ALTERATIONS (HOME CAGE)	1	1	1	1	1	1	1	1	1	1
REACTION TO REMOVAL	1	1	1	1	1	1	1	1	1	1
REACTION TO HANDLING	1	1	1	1	1	1	1	1	1	1
REARS IN OPEN FIELD	12	9	9	9	9	10	14	8	15	14
DEFECATION IN OPEN FIELD	1	1	1	1	1	1	1	2	1	2
URINATION IN OPEN FIELD	1	1	1	1	1	1	2	2	1	1
LEVEL OF AROUSAL	3	3	3	3	3	3	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1	1	1	1	1	1	1
GAIT PATTERN	4a	1	1	4a	1	1	1	1	1	1
GAIT ABNORMALITY, SEVERITY	2	1	1	2	1	1	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1	1	1	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1	1	1	1	1	1	1
LACRIMATION	1	1	1	1	1	1	1	1	1	1
SALIVATION	1	1	1	1	1	1	1	1	1	1
PILOERECTION	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	1c	0	0	0	0	0	0
APPEARANCE	1	1b	1	1d	1	1	1	1	1e	1
VISUAL REACTION	2	2	2	2	2	2	2	2	2	2
TACTILE REACTION	2	2	2	2	2	2	2	2	2	2
AUDITORY REACTION	2	3	3	3	3	3	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2	2	2	2	2	2	3
AIR RIGHTING RESPONSE	1	1	1	1	1	1	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1	1	1	1	1	1	1
FORELIMB GRIP TEST #1 (G)	170	785	525	205	560	535	315	270	595	270
FORELIMB GRIP TEST #2 (G)	290	735	465	240	645	540	600	525	495	440
HINDLIMB GRIP TEST #1 (G)	385	410	330	435	385	520	265	305	405	410
HINDLIMB GRIP TEST #2 (G)	380	530	490	370	630	430	410	480	530	445
LANDING FOOT SPLAY #1 (CM)	4.8	6.3	9.0	8.8	10.5	10.0	6.3	8.7	6.2	10.4
LANDING FOOT SPLAY #2 (CM)	5.8	7.0	9.4	8.7	8.5	9.0	6.5	9.2	7.0	9.2
BODY WEIGHT (G)	250	365	320	254	366	362	318	343	332	373

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

a. Tip-toe walk.

b. Ear torn: right pinna.

c. Rales.

d. Localized alopecia: both forepaws and forelimbs (1.0 cm x 0.4 cm); Dehydration; Abdominal distention.

e. Scab: head (0.3 cm in diameter); Localized alopecia: head (0.5 cm in diameter).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C41 (PAGE 1): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP I — 0 MG/KG/DAY

RAT NUMBER	19012	19019	19021	19023	19041	19042	19044	19050	19053	19065
NUMBER OF MOVEMENTS										
BLOCK 1	84	77	76	63	74	73	73	69	60	71
BLOCK 2	86	17	67	0	66	52	61	59	65	65
BLOCK 3	83	30	65	0	72	64	18	64	63	45
BLOCK 4	70	7	25	2	23	3	33	9	108	6
BLOCK 5	65	3	43	2	49	4	54	9	33	13
BLOCK 6	76	3	11	0	57	2	34	10	6	40
BLOCK 7	39	41	20	0	4	1	3	4	4	0
BLOCK 8	32	53	23	0	0	11	24	1	10	39
BLOCK 9	12	37	7	0	13	55	54	29	1	6
BLOCK 10	20	41	4	20	1	5	71	8	1	25
BLOCK 11	17	4	10	1	2	0	30	0	23	5
BLOCK 12	71	5	10	2	1	1	19	9	59	4
BLOCK 13	57	4	21	1	1	1	2	2	27	5
BLOCK 14	40	1	9	0	37	2	8	4	8	51
BLOCK 15	67	2	2	1	75	6	3	3	7	56
BLOCK 16	83	2	3	0	47	5	1	39	22	30
BLOCK 17	81	4	5	37	79	4	0	70	39	3
BLOCK 18	59	12	10	0	36	4	0	59	74	5
TOTAL	1042	343	411	129	637	293	488	448	610	469

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C41 (PAGE 2): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP I — 0 MG/KG/DAY

RAT NUMBER	19012	19019	19021	19023	19041	19042	19044	19050	19053	19065
TIME (SECONDS) SPENT IN MOVEMENT										
BLOCK 1	191	138	161	108	167	180	157	185	125	136
BLOCK 2	157	34	147	0	116	84	100	147	85	83
BLOCK 3	119	41	75	0	96	98	29	81	71	47
BLOCK 4	113	7	25	3	17	2	27	10	101	1
BLOCK 5	83	4	48	0	43	1	105	8	31	13
BLOCK 6	111	1	6	0	75	1	37	12	1	31
BLOCK 7	37	50	23	0	1	1	2	1	2	0
BLOCK 8	35	93	28	0	0	8	31	0	12	47
BLOCK 9	5	60	6	0	14	67	62	41	0	0
BLOCK 10	26	50	5	36	0	4	95	7	0	29
BLOCK 11	22	6	10	2	4	0	29	0	43	2
BLOCK 12	74	3	10	3	0	1	18	12	103	5
BLOCK 13	68	2	21	0	2	0	0	0	42	5
BLOCK 14	42	1	9	0	36	1	5	1	1	52
BLOCK 15	77	1	0	0	119	5	1	4	5	89
BLOCK 16	71	1	0	0	74	4	0	79	17	24
BLOCK 17	100	2	3	38	92	3	0	113	56	0
BLOCK 18	114	21	7	0	40	6	0	106	84	4
TOTAL	1445	515	584	190	896	466	698	807	779	568

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C41 (PAGE 3): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP II — 0.3 MG/KG/DAY

RAT NUMBER	19004	19009	19016	19018	19026	19036	19037	19043	19047	19048
NUMBER OF MOVEMENTS										
BLOCK 1	65	68	53	60	75	73	73	65	77	62
BLOCK 2	36	75	61	55	55	64	68	27	16	79
BLOCK 3	31	104	3	6	57	58	50	3	22	78
BLOCK 4	49	41	7	1	54	20	27	16	10	82
BLOCK 5	29	46	0	9	30	12	8	5	0	73
BLOCK 6	22	45	1	7	3	0	30	28	0	58
BLOCK 7	3	18	4	22	3	29	9	12	0	78
BLOCK 8	13	59	2	2	0	2	29	8	0	17
BLOCK 9	0	79	0	1	1	3	10	5	2	4
BLOCK 10	1	22	4	12	5	2	14	2	0	3
BLOCK 11	0	1	6	1	54	0	1	4	0	3
BLOCK 12	7	1	5	11	10	0	7	2	0	16
BLOCK 13	4	6	1	7	38	12	4	6	2	70
BLOCK 14	40	2	14	8	41	0	30	0	4	51
BLOCK 15	30	3	0	6	17	5	50	2	10	7
BLOCK 16	42	32	1	6	3	4	42	3	9	8
BLOCK 17	4	63	13	13	0	4	6	2	10	2
BLOCK 18	6	41	3	1	0	27	25	0	4	1
TOTAL	382	706	178	228	446	315	483	190	166	692

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C41 (PAGE 4): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP II — 0.3 MG/KG/DAY

RAT NUMBER	19004	19009	19016	19018	19026	19036	19037	19043	19047	19048
TIME (SECONDS) SPENT IN MOVEMENT										
BLOCK 1	131	213	85	76	152	181	120	120	133	204
BLOCK 2	41	168	93	49	96	136	140	41	19	157
BLOCK 3	47	135	3	7	82	92	91	1	35	108
BLOCK 4	67	56	4	0	116	12	60	18	8	139
BLOCK 5	32	55	0	9	51	15	19	1	0	93
BLOCK 6	20	76	0	7	0	0	60	25	0	122
BLOCK 7	1	11	3	31	3	46	8	9	0	102
BLOCK 8	12	84	2	1	0	2	36	4	0	14
BLOCK 9	0	119	0	0	1	1	12	3	0	2
BLOCK 10	0	29	1	11	4	1	15	0	0	1
BLOCK 11	0	0	6	3	70	0	2	0	0	2
BLOCK 12	6	0	4	7	9	0	6	1	0	9
BLOCK 13	2	3	0	4	42	19	3	10	2	62
BLOCK 14	33	0	17	13	72	0	36	0	1	69
BLOCK 15	43	1	0	3	22	1	71	1	8	5
BLOCK 16	62	36	0	4	1	2	55	0	9	7
BLOCK 17	2	91	12	11	0	3	11	0	6	1
BLOCK 18	4	40	0	0	0	28	22	0	1	1
TOTAL	503	1117	230	236	721	539	767	234	222	1098

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C41 (PAGE 5): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP III — 1 MG/KG/DAY

RAT NUMBER	19003	19007	19008	19013	19015	19017	19024	19029	19034	19056
NUMBER OF MOVEMENTS										
BLOCK 1	76	74	55	71	69	70	74	69	58	67
BLOCK 2	61	40	63	70	68	59	85	81	68	71
BLOCK 3	65	65	70	19	30	37	59	48	48	61
BLOCK 4	40	60	48	3	61	19	61	56	6	85
BLOCK 5	18	27	89	5	64	25	60	70	43	35
BLOCK 6	37	49	78	1	84	36	58	65	9	9
BLOCK 7	46	50	70	1	74	40	55	44	22	43
BLOCK 8	49	57	64	2	40	38	53	38	34	5
BLOCK 9	9	53	57	2	8	51	24	65	10	2
BLOCK 10	5	85	74	0	2	27	24	38	27	12
BLOCK 11	0	57	64	1	1	29	58	53	1	5
BLOCK 12	3	1	71	10	3	16	59	41	2	5
BLOCK 13	45	9	78	0	3	27	26	50	1	4
BLOCK 14	58	1	77	0	2	32	6	64	1	3
BLOCK 15	52	7	59	1	1	61	10	39	4	2
BLOCK 16	43	1	85	19	6	39	1	46	0	5
BLOCK 17	51	7	60	0	8	43	1	70	1	6
BLOCK 18	47	4	42	1	5	10	28	39	1	2
TOTAL	705	647	1204	206	529	659	742	976	336	422

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C41 (PAGE 6): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP III — 1 MG/KG/DAY

RAT NUMBER	19003	19007	19008	19013	19015	19017	19024	19029	19034	19056
TIME (SECONDS) SPENT IN MOVEMENT										
BLOCK 1	180	153	118	150	153	201	174	97	186	132
BLOCK 2	96	69	139	109	138	129	123	85	119	137
BLOCK 3	128	109	143	19	21	66	176	30	136	57
BLOCK 4	64	99	85	2	78	22	98	66	9	179
BLOCK 5	23	27	136	11	123	49	84	88	53	40
BLOCK 6	59	75	102	0	119	53	81	59	2	11
BLOCK 7	65	55	140	0	154	63	70	61	24	58
BLOCK 8	69	90	123	0	78	65	56	49	69	8
BLOCK 9	13	68	109	0	7	87	14	71	10	0
BLOCK 10	4	122	112	0	1	36	27	47	26	12
BLOCK 11	0	77	100	1	0	41	93	84	0	1
BLOCK 12	3	0	93	10	1	22	136	73	4	2
BLOCK 13	71	7	158	0	2	29	24	90	0	3
BLOCK 14	60	0	125	0	1	47	4	106	0	2
BLOCK 15	80	9	109	0	0	97	11	56	2	0
BLOCK 16	69	0	116	24	9	57	0	83	0	3
BLOCK 17	91	9	138	0	12	47	0	77	0	4
BLOCK 18	56	1	52	0	0	7	22	42	1	0
TOTAL	1131	970	2098	326	897	1118	1193	1264	641	649

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C41 (PAGE 7): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP IV					3 MG/KG/DAY					
RAT NUMBER	19005	19035	19039	19040	19045	19054	19058	19062	19063	19066
NUMBER OF MOVEMENTS										
BLOCK 1	59	82	75	62	55	68	67	49	71	69
BLOCK 2	63	77	58	18	66	75	48	69	37	60
BLOCK 3	52	51	63	11	67	75	27	41	32	74
BLOCK 4	51	33	64	2	79	62	13	40	32	14
BLOCK 5	54	37	73	1	50	52	5	33	6	28
BLOCK 6	64	7	15	15	56	56	2	54	12	69
BLOCK 7	78	5	4	57	66	48	2	57	11	55
BLOCK 8	66	34	28	29	44	75	22	49	36	62
BLOCK 9	57	27	9	1	52	43	39	55	33	24
BLOCK 10	55	0	9	0	59	43	18	49	22	4
BLOCK 11	50	6	5	0	59	35	3	47	26	4
BLOCK 12	54	3	3	32	53	6	16	35	14	2
BLOCK 13	68	1	0	3	55	37	3	21	7	3
BLOCK 14	60	0	9	11	53	52	3	53	3	0
BLOCK 15	46	5	3	1	69	25	1	44	1	3
BLOCK 16	58	4	39	2	50	4	1	31	81	2
BLOCK 17	54	19	17	4	57	2	0	10	52	4
BLOCK 18	50	3	2	0	76	0	14	24	17	4
TOTAL	1039	394	476	249	1066	758	284	761	493	481

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C41 (PAGE 8): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP IV — 3 MG/KG/DAY

RAT NUMBER	19005	19035	19039	19040	19045	19054	19058	19062	19063	19066
TIME (SECONDS) SPENT IN MOVEMENT										
BLOCK 1	241	163	158	215	236	181	154	143	150	169
BLOCK 2	167	129	110	23	188	184	67	158	63	106
BLOCK 3	106	63	100	26	196	155	45	69	41	143
BLOCK 4	130	42	89	1	192	133	23	52	43	25
BLOCK 5	108	29	87	0	140	58	16	60	4	18
BLOCK 6	120	5	29	22	131	64	5	82	20	89
BLOCK 7	117	2	2	79	150	73	1	149	12	68
BLOCK 8	108	42	45	37	76	73	60	98	56	106
BLOCK 9	112	31	14	0	194	65	56	109	68	17
BLOCK 10	83	0	10	0	154	39	29	79	21	1
BLOCK 11	83	2	3	0	137	31	5	77	31	3
BLOCK 12	63	1	2	38	66	2	24	47	22	1
BLOCK 13	135	0	0	0	112	33	11	36	5	2
BLOCK 14	100	0	4	6	101	40	6	73	1	0
BLOCK 15	58	4	0	0	150	9	1	107	0	1
BLOCK 16	83	2	54	1	81	1	2	62	98	2
BLOCK 17	105	23	13	1	119	0	0	10	77	1
BLOCK 18	73	1	1	0	152	0	24	27	14	1
TOTAL	1992	539	721	449	2575	1141	529	1438	726	753

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C41 (PAGE 9): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP V					10 MG/KG/DAY					
RAT NUMBER	19001	19006	19011	19020	19022	19025	19027	19028	19030	19031
NUMBER OF MOVEMENTS										
BLOCK 1	72	76	61	75	63	83	52	78	65	59
BLOCK 2	30	4	59	28	59	45	27	45	64	64
BLOCK 3	20	8	63	3	63	9	41	7	58	39
BLOCK 4	7	2	52	0	56	5	42	1	5	35
BLOCK 5	5	1	64	0	46	27	31	2	4	6
BLOCK 6	6	18	59	0	39	29	17	6	10	13
BLOCK 7	6	1	57	1	23	7	23	16	3	3
BLOCK 8	61	1	61	48	63	49	19	3	3	18
BLOCK 9	57	4	61	3	44	54	0	9	14	33
BLOCK 10	43	2	30	35	28	4	4	7	2	0
BLOCK 11	43	4	65	1	41	1	7	24	5	6
BLOCK 12	52	7	64	48	38	1	34	30	9	14
BLOCK 13	46	4	62	5	46	1	1	51	2	3
BLOCK 14	16	4	38	1	47	2	0	40	3	17
BLOCK 15	7	3	44	0	40	3	0	48	0	6
BLOCK 16	5	1	52	39	36	32	2	17	6	2
BLOCK 17	1	2	67	50	46	10	0	2	2	3
BLOCK 18	6	24	52	44	39	47	1	5	4	4
TOTAL	483	166	1011	381	817	409	301	391	259	325

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C41 (PAGE 10): MOTOR ACTIVITY - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP V — 10 MG/KG/DAY

RAT NUMBER	19001	19006	19011	19020	19022	19025	19027	19028	19030	19031
TIME (SECONDS) SPENT IN MOVEMENT										
BLOCK 1	162	128	132	104	152	151	148	147	134	204
BLOCK 2	17	1	120	16	157	119	121	104	123	188
BLOCK 3	13	14	122	0	125	6	58	4	107	74
BLOCK 4	6	1	60	0	126	1	66	0	2	84
BLOCK 5	3	3	87	0	86	29	55	0	2	11
BLOCK 6	6	25	100	0	49	56	35	6	14	19
BLOCK 7	1	1	94	0	21	2	25	20	1	0
BLOCK 8	52	0	84	54	106	76	23	1	2	19
BLOCK 9	78	5	94	2	81	72	0	3	16	50
BLOCK 10	34	0	39	19	35	1	2	11	0	0
BLOCK 11	54	2	98	0	53	0	5	17	4	13
BLOCK 12	90	7	81	65	68	0	39	20	4	13
BLOCK 13	49	4	121	4	86	0	0	55	1	7
BLOCK 14	28	2	51	0	89	0	0	47	1	38
BLOCK 15	3	2	58	0	54	0	0	51	0	5
BLOCK 16	1	0	65	27	34	45	0	9	3	1
BLOCK 17	0	1	86	61	61	4	0	2	1	1
BLOCK 18	1	34	78	35	50	69	0	3	3	3
TOTAL	598	230	1570	387	1433	631	577	500	418	730

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C42 (PAGE 1): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS/F1 GENERATION LITTERS

RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) N	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	NUMBER OF LIVE PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	8 M	8 F	15 M	15 F	22 M	22 F	TOTAL IMPLAN-TATIONS N
MATERNAL DOSAGE GROUP I					0 MG/KG/DAY								
19010	23	14	0	14	4	10	4	9	4	9	4	9	15
19012	23	16	0	16	5	11	5	11	5	11	5	11	17
19019	23	15	0	15	8	7	8	7	8	7	8	7	17
19021	23	14	0	14	9	5	9	5	9	5	9	5	16
19023	22	13	0	13	7	6	7	5	7	5	7	5	16
19041	22	18	0	18	6	12	6	12	6	12	6	12	18
19042	23	15	0	15	6	9	6	9	6	9	6	9	17
19044	22	17	0	17	8	9	8	8	8	8	8	8	18
19050	22	15	0	15	5	10	5	10	5	10	5	10	17
19053	23	16	0	16	9	7	8	7	8	7	8	7	16
19065	22	20	0	20	9	11	9	10	9	10	9	10	20
19068	22	15	0	15	6	9	5	9	5	9	5	9	15
19072	22	16	0	16	8	8	8	8	8	8	8	8	16
19074	23	15(1)	0	15	4	10	4	10	4	10	4	10	17
19075	23	16	0	16	11	5	11	5	11	5	11	5	16
MATERNAL DOSAGE GROUP II					0.3 MG/KG/DAY								
19004	22	18	0	18	8	10	8	9	8	9	8	9	19
19009	23	7	0	7	2	5	2	5	2	5	2	5	8
19016	23	15	0	15	12	3	12	3	12	3	12	3	15
19018	23	14	0	14	8	6	8	6	8	6	8	6	16
19026	23	19	0	19	10	9	10	8	10	8	10	8	20
19036	22	16(1)	0	16	6	9	6	8	6	7	6	7	16
19037	23	16	0	16	8	8	8	8	8	7	8	7	17
19043	23	13	0	13	7	6	7	6	7	6	7	6	15
19047	23	13	0	13	7	6	7	6	7	6	7	6	14
19048	23	9	0	9	5	4	5	4	5	4	5	4	12
19052	22	17	0	17	6	11	6	10	6	10	6	10	18
19055	23	16(1)	0	16	10	5	10	5	10	5	10	5	16
19061	22	13	0	13	8	5	7	5	7	5	7	5	13
19067	23	14	0	14	6	8	6	7	6	7	6	7	16
19071	23	14	0	14	8	6	8	6	8	6	8	6	15

M = MALE F = FEMALE
( ) = NUMBER OF PUPS DYING PRIOR TO WEIGHING ON DAY 1 POSTPARTUM.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C42 (PAGE 2): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS/F1 GENERATION LITTERS

RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) N	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	NUMBER OF LIVE PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	8 M	8 F	15 M	15 F	22 M	22 F	TOTAL IMPLAN-TATIONS N
MATERNAL DOSAGE GROUP III					1 MG/KG/DAY								
19003	22	16	0	16	8	8	8	8	8	8	8	8	17
19007	22	18	0	18	7	11	7	10	7	10	7	10	18
19008	22	15	0	15	7	8	7	7	7	7	7	7	16
19013	23	15	0	15	9	6	9	6	9	6	9	6	15
19014	NOT PREGNANT												
19015	23	15	0	15	9	6	9	6	9	6	9	6	15
19017	23	14	0	14	6	8	6	8	6	8	6	8	14
19024	23	15	0	15	9	6	9	6	9	6	9	6	16
19029	23	16	0	16	9	7	8	7	8	7	8	7	17
19034	23	13	1	14	6	7	6	7	6	7	6	7	15
19038	NOT PREGNANT												
19056	23	14	0	14	7	7	7	7	7	7	7	7	14
19057	23	17	0	17	9	8	9	8	9	8	9	8	17
19060	22	14	0	14	8	6	8	6	8	6	8	6	15
19064	23	18	0	18	9	9	9	9	9	8	9	8	17
MATERNAL DOSAGE GROUP IV					3 MG/KG/DAY								
19002	23	10(1)	1	11	3	6	3	6	3	6	3	6	14
19005	23	16	0	16	6	10	6	10	6	10	6	10	16
19035	23	14	0	14	6	8	6	8	6	8	6	8	16
19039	22	15	0	15	6	9	5	9	5	9	5	9	15
19040	22	17	0	17	7	10	7	10	7	10	7	10	17
19045	23	15	0	16[1]	6	9	6	9	6	9	6	9	16
19046	NOT PREGNANT												
19051	NOT PREGNANT; MATING NOT CONFIRMED												
19054	23	5	0	5	3	2	3	2	3	2	3	2	6
19058	23	13	0	13	8	5	8	5	8	5	8	5	14
19062	22	15	0	15	9	6	9	6	9	6	9	6	15
19063	23	13	1	14	2	11	2	11	2	11	2	11	16
19066	23	13(1)	1	14	5	7	5	7	5	7	5	7	15
19069	23	17	0	17	6	11	6	11	6	10	6	10	17
19073	23	14	0	14	8	6	7	6	7	6	7	6	15

M = MALE F = FEMALE
( ) = NUMBER OF PUPS DYING PRIOR TO WEIGHING ON DAY 1 POSTPARTUM.
[ ] = NUMBER OF PUPS IN WHICH CANNIBALIZATION AND/OR AUTOLYSIS PRECLUDED THE DETERMINATION OF VIABILITY.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C42 (PAGE 3): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS/F1 GENERATION LITTERS

RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) N	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	NUMBER OF LIVE PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	8 M	8 F	15 M	15 F	22 M	22 F	TOTAL IMPLAN-TATIONS N
MATERNAL DOSAGE GROUP V					10 MG/KG/DAY								
19001	23	11	0	11	4	7	4	7	4	7	4	7	11
19006	23	19(1)	1	20	6	12	5	12	5	12	5	12	20
19011	23	13	0	13	7	6	7	6	7	6	7	6	14
19020	22	13	0	13	8	5	8	5	8	5	8	5	14
19022	23	16(1)	0	16	9	6	9	5	9	5	9	5	16
19025	22	20	0	20	13	7	13	7	13	7	13	7	20
19027	23	14	0	14	4	10	4	10	4	10	4	10	14
19028	23	12	1	13	5	7	5	7	5	7	5	7	15
19030	22	13	0	13	6	7	6	7	6	7	6	7	16
19031	22	15	0	15	8	7	7	7	7	7	7	7	15
19032	23	14	0	14	7	7	7	7	7	7	7	7	17
19033	22	14	0	14	6	8	6	8	6	8	6	8	14
19049	23	15	0	15	11	4	11	4	11	4	11	4	16
19059	23	15	0	15	10	5	10	5	10	5	10	5	15
19070	22	14(1)	0	14	8	5	8	5	8	4	8	4	14

M = MALE F = FEMALE
( ) = NUMBER OF PUPS DYING PRIOR TO WEIGHING ON DAY 1 POSTPARTUM.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C43 (PAGE 1): PUP BODY WEIGHT LITTER AVERAGES FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

RAT/ LITTER NUMBER	DAY 1			DAY 8			DAY 15			DAY 22		
	M	F	T	M	F	T	M	F	T	M	F	T
MATERNAL DOSAGE GROUP I						0 MG/KG/DAY						
19010	6.8	6.6	6.6	16.4	15.9	16.1	28.4	27.7	27.9	41.9	40.0	40.6
19012	6.6	6.4	6.5	13.8	13.6	13.7	26.5	25.5	25.8	42.7	40.6	41.2
19019	6.6	6.2	6.4	15.4	14.4	14.9	28.6	26.5	27.6	40.0	37.2	38.7
19021	6.4	5.9	6.2	12.7	11.9	12.4	23.4	22.1	22.9	35.8	33.8	35.1
19023	6.3	6.2	6.2	16.8	16.5	16.7	32.8	32.1	32.5	46.1	44.4	45.4
19041	6.2	6.0	6.1	13.0	13.0	13.0	24.1	23.8	23.9	32.6	32.5	32.5
19042	6.5	6.4	6.4	14.1	13.6	13.8	26.4	26.3	26.4	36.4	35.6	35.9
19044	5.7	6.0	5.8	13.8	13.0	13.4	26.8	25.2	26.0	42.6	40.5	41.5
19050	6.6	6.2	6.3	14.6	13.7	14.0	27.1	25.7	26.2	36.4	35.1	35.6
19053	6.4	6.4	6.4	15.6	15.4	15.5	29.3	28.2	28.8	35.9	35.5	35.7
19065	6.0	5.7	5.8	13.2	12.2	12.7	24.8	23.4	24.0	32.4	30.8	31.6
19068	6.8	6.4	6.6	17.2	15.8	16.3	29.7	27.4	28.2	47.7	45.1	46.0
19072	5.9	5.5	5.7	12.3	11.9	12.1	22.7	21.6	22.2	31.7	30.0	30.8
19074	7.1	6.7	6.8	17.7	16.8	17.0	27.4	27.4	27.4	35.2	34.0	34.4
19075	6.2	6.3	6.2	12.9	13.0	12.9	22.3	23.1	22.6	36.1	36.1	36.1
MATERNAL DOSAGE GROUP II						0.3 MG/KG/DAY						
19004	5.7	5.4	5.5	13.5	11.9	12.7	24.5	22.3	23.3	31.1	28.8	29.9
19009	7.2	7.0	7.0	15.4	15.5	15.5	34.4	33.5	33.8	56.4	53.2	54.1
19016	6.4	6.1	6.4	14.6	12.9	14.2	27.7	23.1	26.8	46.3	38.1	44.6
19018	7.1	6.5	6.8	15.3	14.4	14.9	28.3	25.6	27.2	45.6	41.6	43.8
19026	7.1	6.5	6.8	13.7	12.1	13.0	25.0	22.7	24.0	31.8	29.4	30.7
19036	6.2	5.6	5.8	11.6	9.6	10.4	26.9	24.1	25.4	41.1	36.8	38.8
19037	5.6	5.4	5.5	11.5	11.2	11.4	18.3	18.0	18.2	31.2	29.2	30.3
19043	6.6	6.2	6.4	14.0	13.4	13.7	29.4	28.3	28.9	46.4	43.7	45.2
19047	7.2	6.8	7.0	15.3	14.4	14.9	28.2	27.0	27.6	38.2	37.3	37.8
19048	6.4	6.2	6.3	16.1	16.2	16.1	33.1	32.4	32.8	49.0	46.4	47.8
19052	6.2	5.9	6.0	11.0	10.8	10.8	22.6	22.8	22.8	35.8	35.9	35.9
19055	6.7	6.4	6.6	14.3	13.1	13.9	26.4	25.1	26.0	39.8	37.2	38.9
19061	5.8	5.6	5.7	13.8	12.8	13.4	24.8	24.6	24.8	32.2	33.8	32.8
19067	7.0	6.5	6.7	13.7	13.3	13.5	29.4	28.1	28.7	40.2	38.8	39.4
19071	6.5	6.7	6.6	11.4	11.7	11.5	24.8	24.5	24.7	40.0	39.7	39.9

M = MALE F = FEMALE T = TOTAL (SUM OF PUP WEIGHTS/NUMBER OF LIVE PUPS) DAY = DAY POSTPARTUM
ALL WEIGHTS WERE RECORDED IN GRAMS (G). MEAN LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C43 (PAGE 2): PUP BODY WEIGHT LITTER AVERAGES FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

RAT/ LITTER NUMBER	DAY 1			DAY 8			DAY 15			DAY 22		
	M	F	T	M	F	T	M	F	T	M	F	T
MATERNAL DOSAGE GROUP III							1 MG/KG/DAY					
19003	6.6	6.0	6.3	13.5	12.1	12.8	23.2	21.3	22.2	30.4	28.1	29.2
19007	6.3	5.8	6.0	13.7	12.3	12.9	24.5	21.7	22.9	33.6	30.5	31.8
19008	6.2	5.7	6.0	14.7	14.1	14.4	29.2	28.1	28.6	41.5	39.0	40.2
19013	7.0	6.4	6.8	15.2	13.9	14.7	27.9	25.1	26.8	47.0	42.3	45.1
19014	NOT PREGNANT											
19015	6.7	6.2	6.5	14.0	13.1	13.7	26.3	24.9	25.8	38.4	35.9	37.4
19017	7.4	6.9	7.1	14.8	14.4	14.5	27.6	25.8	26.6	45.8	44.2	44.9
19024	6.2	5.8	6.1	14.5	13.4	14.1	27.4	25.4	26.6	40.0	37.5	39.0
19029	6.3	5.8	6.1	14.1	12.2	13.2	26.3	22.2	24.4	43.7	34.6	39.5
19034	6.8	6.4	6.6	15.3	14.3	14.8	30.4	28.6	29.4	41.2	39.0	40.0
19038	NOT PREGNANT											
19056	6.8	6.6	6.7	15.1	14.8	14.9	29.6	28.8	29.2	41.4	39.8	40.6
19057	6.6	6.4	6.5	13.1	12.9	13.0	23.6	23.2	23.4	32.7	32.0	32.4
19060	6.9	6.4	6.7	14.8	13.4	14.2	29.2	26.4	28.0	46.6	42.8	45.0
19064	6.7	6.2	6.5	12.1	11.5	11.8	22.8	22.2	22.5	27.8	30.2	28.9
MATERNAL DOSAGE GROUP IV							3 MG/KG/DAY					
19002	7.6	7.1	7.3	19.1	17.9	18.3	35.5	33.1	33.9	48.0	45.4	46.3
19005	6.5	5.8	6.0	13.2	13.0	13.1	24.2	23.7	23.9	33.2	31.7	32.2
19035	7.2	6.7	6.9	12.9	12.5	12.6	23.3	22.5	22.8	33.8	32.3	32.9
19039	5.9	5.4	5.6	11.1	10.2	10.6	22.9	21.2	21.8	35.1	32.4	33.4
19040	5.4	5.1	5.2	11.6	10.9	11.2	25.2	23.4	24.1	31.7	29.3	30.3
19045	6.5	6.6	6.6	11.7	12.0	11.9	24.0	23.6	23.8	37.6	36.2	36.7
19046	NOT PREGNANT											
19051	NOT PREGNANT; MATING NOT CONFIRMED											
19054	7.4	7.5	7.4	20.1	21.2	20.6	41.2	40.4	40.9	57.1	56.6	56.9
19058	6.6	6.5	6.6	14.9	14.6	14.8	27.8	27.2	27.6	46.4	45.1	45.9
19062	6.9	6.6	6.8	16.7	15.8	16.3	30.7	29.4	30.2	42.4	40.1	41.4
19063	7.0	6.9	6.9	14.6	15.2	15.1	29.8	30.0	29.9	47.6	46.2	46.4
19066	6.5	6.3	6.4	15.8	15.9	15.9	30.9	30.8	30.8	43.8	43.0	43.3
19069	5.9	5.7	5.8	10.3	9.7	9.9	19.3	20.4	20.0	30.1	33.4	32.2
19073	7.2	6.8	7.0	13.9	12.8	13.4	27.7	25.6	26.8	44.3	40.9	42.8

M = MALE F = FEMALE T = TOTAL (SUM OF PUP WEIGHTS/NUMBER OF LIVE PUPS) DAY = DAY POSTPARTUM
ALL WEIGHTS WERE RECORDED IN GRAMS (G). MEAN LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C43 (PAGE 3): PUP BODY WEIGHT LITTER AVERAGES FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

RAT/ LITTER NUMBER	DAY 1			DAY 8			DAY 15			DAY 22		
	M	F	T	M	F	T	M	F	T	M	F	T
MATERNAL DOSAGE GROUP V						10 MG/KG/DAY						
19001	6.8	6.6	6.6	14.0	14.3	14.2	26.6	26.6	26.6	44.1	44.0	44.1
19006	6.5	6.1	6.2	13.8	13.1	13.3	25.4	23.7	24.2	35.2	32.7	33.4
19011	6.9	6.6	6.8	13.9	13.6	13.8	26.2	25.5	25.9	36.4	35.5	36.0
19020	5.8	5.5	5.7	9.2	9.1	9.2	15.7	15.4	15.6	15.4	15.5	15.5
19022	6.0	5.7	5.9	15.3	14.9	15.2	29.0	27.0	28.3	36.3	34.5	35.7
19025	5.4	5.0	5.3	12.9	11.0	12.3	24.2	20.4	22.9	30.8	26.8	29.4
19027	7.3	6.5	6.8	12.6	12.1	12.2	23.6	21.9	22.4	33.0	31.1	31.6
19028	6.7	6.3	6.4	13.1	13.2	13.2	25.9	25.9	25.9	39.8	40.1	40.0
19030	6.4	6.1	6.2	15.0	14.3	14.6	29.5	28.1	28.7	40.1	38.2	39.1
19031	5.9	5.7	5.8	12.3	11.9	12.1	27.6	25.7	26.6	44.8	41.1	43.0
19032	7.3	6.9	7.1	14.6	13.2	13.9	25.9	24.4	25.2	35.9	34.2	35.1
19033	6.6	6.0	6.2	13.8	12.6	13.1	27.4	25.2	26.2	44.1	41.0	42.4
19049	6.7	6.2	6.6	12.6	11.0	12.2	25.4	22.8	24.7	36.8	32.9	35.7
19059	7.0	6.5	6.9	12.3	11.0	11.9	24.9	21.3	23.7	34.6	30.4	33.2
19070	6.5	6.3	6.4	15.4	14.8	15.2	29.8	28.0	29.2	49.6	46.8	48.7

M = MALE F = FEMALE T = TOTAL (SUM OF PUP WEIGHTS/NUMBER OF LIVE PUPS) DAY = DAY POSTPARTUM
ALL WEIGHTS WERE RECORDED IN GRAMS (G). MEAN LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C44 (PAGE 1): PUP BODY WEIGHTS FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP I							0 MG/KG/DAY				POSTPARTUM DAY 1								
19010	6.8	7.0	7.4	6.0	6.9	6.8	7.3	6.9	5.1	6.5	6.8	7.0	6.3	6.0						
19012	6.5	6.3	6.5	6.9	7.0	6.4	6.1	6.5	6.8	6.2	6.6	6.2	6.7	6.6	6.1	6.4				
19019	6.8	6.2	6.5	6.6	6.4	6.9	6.7	6.8	6.3	6.4	6.3	6.0	6.2	6.3	6.0					
19021	6.7	6.4	6.5	6.7	6.7	6.1	6.4	6.4	6.2	5.6	5.5	6.1	6.2	6.0						
19023	6.9	6.2	6.2	5.8	6.1	6.2	6.5	6.0	6.1	6.2	6.1	6.2	6.3							
19041	6.3	5.8	6.1	6.3	6.1	6.6	6.5	5.9	6.0	6.6	6.4	6.3	5.9	5.8	6.0	6.0	5.4	5.6		
19042	6.2	7.2	6.9	6.3	6.5	6.1	6.3	6.4	6.4	7.0	6.5	6.1	6.3	6.5	6.1					
19044	5.8	5.0	5.7	5.8	5.9	6.1	6.1	5.3	5.4	6.3	6.1	6.7	6.0	6.6	6.3	5.4	5.1			
19050	6.9	6.6	6.9	6.5	6.2	5.9	6.3	5.7	6.2	6.5	6.0	6.1	6.1	6.4	6.5					
19053	6.5	6.6	6.5	6.1	6.2	6.9	6.5	6.8	6.0	6.2	6.5	6.4	6.3	6.6	6.3	6.3				
19065	5.9	5.8	5.6	5.9	6.0	5.9	6.1	6.0	6.7	5.2	5.7	6.0	6.2	5.8	5.4	5.4	5.9	5.7	5.6	5.7
19068	7.0	6.6	6.6	7.0	6.8	7.0	6.2	6.8	6.7	6.3	6.5	6.0	6.0	6.6	6.7					
19072	5.9	5.7	6.1	6.0	5.5	6.0	6.1	6.0	5.5	5.7	5.5	5.4	5.6	5.6	5.2	5.5				
19074	6.9	7.2	7.3	7.0	MD 1	7.0	6.8	7.1	6.6	7.1	7.0	6.0	6.6	6.3	6.7					
19075	6.4	6.1	5.5	6.4	5.8	6.4	6.4	6.3	6.5	6.5	6.2	6.4	6.3	6.3	6.0	6.3				
RAT/ LITTER #	MATERNAL DOSAGE GROUP II							0.3 MG/KG/DAY				POSTPARTUM DAY 1								
19004	5.6	5.9	5.9	5.8	5.9	5.2	5.5	5.8	5.0	5.5	5.7	5.3	6.1	5.2	5.3	4.9	5.8	5.4		
19009	7.5	7.0	6.7	6.9	7.1	6.8	7.4													
19016	6.6	6.3	6.5	6.1	6.9	6.7	6.4	6.7	6.3	6.0	5.9	6.8	5.7	6.2	6.5					
19018	7.2	6.7	7.2	6.9	7.2	7.2	7.7	6.9	6.1	6.6	6.4	6.4	6.9	6.5						
19026	6.7	7.1	7.3	7.3	6.9	6.7	7.4	7.1	7.4	7.0	6.7	6.9	6.6	6.4	6.1	6.7	5.7	6.6	6.5	
19036	6.1	6.4	6.6	6.0	6.2	5.6	6.6	5.7	4.9	5.8	4.6	5.5	5.6	5.9	5.7	FD 1				
19037	5.7	5.9	5.6	5.6	5.9	5.6	5.6	4.9	5.1	5.8	5.9	5.3	5.0	5.4	5.3	5.4				
19043	6.8	6.7	6.1	6.9	6.8	6.7	6.6	6.3	5.8	6.2	6.4	6.2	6.0							
19047	7.1	7.7	7.9	7.6	6.6	6.5	7.1	6.8	6.5	6.8	6.7	6.7	7.5							
19048	6.7	6.6	6.4	6.3	5.9	6.2	6.2	6.4	5.9											
19052	6.0	6.1	6.3	6.3	6.3	6.1	6.1	5.6	5.8	6.5	5.4	6.3	6.1	5.6	6.0	5.7	5.7			
19055	6.8	6.5	7.2	6.6	7.0	6.8	6.4	6.6	6.7	6.4	MD 1	6.8	6.6	6.2	6.3	6.0				
19061	5.9	5.9	5.8	5.6	5.7	6.3	5.7	5.6	5.8	5.6	5.7	5.6	5.3							
19067	7.2	6.8	7.3	6.9	7.1	7.0	6.5	7.0	6.2	6.2	6.6	6.8	6.5	6.2						
19071	6.6	6.3	5.4	7.4	6.6	6.9	6.7	6.4	7.0	6.5	6.5	6.5	6.9	6.9						

ALL WEIGHTS WERE RECORDED IN GRAMS (G). MEAN LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.
FIRST LETTER -- M-MALE, F-FEMALE, U-SEX UNDETERMINABLE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C44 (PAGE 2): PUP BODY WEIGHTS FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP III							1 MG/KG/DAY				POSTPARTUM DAY 1								
19003	7.2	7.0	6.8	6.5	6.5	6.6	6.3	5.8	6.7	6.0	6.1	6.3	5.8	5.1	5.7	5.9				
19007	6.4	6.3	6.5	5.8	6.3	6.6	6.2	6.6	5.6	5.6	5.6	5.9	5.7	6.1	5.4	5.9	5.6	5.6		
19008	6.4	6.0	6.0	6.5	5.9	6.3	6.6	6.1	5.6	6.2	6.2	6.1	6.3	5.7	3.5					
19013	7.4	7.1	6.8	7.3	7.3	7.0	6.5	7.0	6.8	6.5	7.3	5.9	6.1	6.5	6.4					
19014	NOT PREGNANT																			
19015	6.5	7.2	6.6	6.5	6.4	6.7	6.9	6.8	6.5	6.2	6.3	6.2	6.3	6.3	5.9					
19017	7.1	7.2	7.8	7.7	7.3	7.2	6.7	7.1	6.7	7.2	6.5	8.1	7.4	5.7						
19024	5.7	6.4	6.2	5.8	6.5	6.2	6.3	6.4	6.8	5.4	5.6	6.3	5.7	5.6	6.4					
19029	6.6	6.2	6.4	6.5	6.1	6.4	6.8	6.1	5.8	6.0	5.9	6.0	5.7	5.4	6.3	5.7				
19034	7.1	6.9	6.6	6.8	6.8	6.6	6.4	6.4	6.9	7.1	5.9	6.2	6.3	FS						
19038	NOT PREGNANT																			
19056	6.8	6.9	6.4	6.9	6.7	6.7	7.5	6.7	6.1	6.3	6.4	6.9	6.9	6.6						
19057	6.8	6.5	6.5	6.9	6.6	6.7	6.1	6.6	6.6	6.1	6.3	6.8	6.5	6.8	6.2	5.8	6.6			
19060	7.0	6.8	6.4	6.5	7.1	7.3	7.2	6.8	6.1	5.8	6.6	6.8	6.5	6.4						
19064	6.8	6.9	6.6	6.9	6.8	6.1	6.5	6.9	7.0	6.0	6.5	6.2	6.4	6.7	6.1	5.9	6.4	6.1		
RAT/ LITTER #	MATERNAL DOSAGE GROUP IV							3 MG/KG/DAY				POSTPARTUM DAY 1								
19002	7.7	7.6	7.5	MS	7.2	7.1	6.9	7.2	7.3	7.1	FD 1									
19005	6.9	6.2	7.0	5.9	6.4	6.4	6.2	5.9	5.6	5.4	5.6	6.0	5.7	6.0	6.0	5.7				
19035	7.3	7.3	7.4	7.2	6.9	6.9	6.6	6.6	6.6	7.0	6.7	6.5	6.7	6.8						
19039	6.4	5.8	5.4	5.9	5.7	6.4	5.4	5.9	5.5	5.5	5.5	4.8	5.4	6.0	5.1					
19040	5.5	5.1	5.8	4.9	5.7	5.3	5.3	5.2	5.1	5.2	5.3	5.4	5.4	5.4	4.8	4.8	4.5			
19045	6.5	7.1	6.5	7.1	5.4	6.5	6.2	6.7	6.5	6.8	6.8	6.3	6.3	6.4	7.2	UU				
19046	NOT PREGNANT																			
19051	NOT PREGNANT; MATING NOT CONFIRMED																			
19054	7.0	7.5	7.7	7.6	7.4															
19058	6.2	7.0	6.9	6.3	6.6	6.6	6.3	7.1	6.7	6.4	6.1	6.8	6.6							
19062	7.2	6.9	6.9	6.9	6.9	6.9	7.0	7.3	6.4	6.1	6.6	6.6	6.6	6.7	6.7					
19063	6.7	7.3	7.6	6.8	6.5	6.5	6.8	6.6	6.5	7.3	6.7	7.1	7.4	FS						
19066	6.4	7.2	6.6	6.1	6.2	6.3	MD 1	6.2	5.9	6.0	6.7	6.3	6.5	FS						
19069	6.1	5.8	6.1	5.1	6.1	6.0	6.3	5.7	5.2	5.8	5.7	6.2	4.5	5.8	5.8	5.8	5.8			
19073	7.2	7.0	6.8	7.8	6.9	7.2	7.7	7.4	7.0	6.7	6.4	6.6	7.1	6.7						

ALL WEIGHTS WERE RECORDED IN GRAMS (G). MEAN LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.
FIRST LETTER -- M-MALE, F-FEMALE, U-SEX UNDETERMINABLE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
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TABLE C44 (PAGE 3): PUP BODY WEIGHTS FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP V							10 MG/KG/DAY				POSTPARTUM DAY 1								
19001	6.9	6.4	6.8	7.0	6.7	6.1	6.5	6.6	6.8	6.5	6.7									
19006	7.0	6.3	6.6	7.0	6.1	5.8	5.9	6.1	6.4	6.5	5.6	6.5	6.2	6.0	6.7	5.9	6.0	5.9	FD 1	FS
19011	7.4	7.3	6.3	7.0	6.9	6.7	6.8	7.1	6.7	6.5	6.2	6.6	6.3							
19020	6.3	6.0	6.1	6.7	4.5	5.4	5.7	5.6	4.9	5.2	5.5	5.4	6.3							
19022	6.2	6.0	5.8	6.1	5.7	6.5	5.9	6.0	6.1	MD 1	5.4	5.5	5.4	5.9	5.9	6.0				
19025	5.1	5.0	5.2	5.4	5.4	5.4	5.6	6.1	5.1	5.6	5.7	5.5	4.8	5.2	4.8	5.2	5.2	4.9	5.0	5.0
19027	7.3	6.9	8.1	6.9	7.2	6.0	6.4	6.8	6.8	6.6	5.9	6.3	6.9	6.5						
19028	6.8	7.1	6.1	6.8	6.6	6.2	5.9	6.6	6.5	6.5	6.5	5.9	FS							
19030	6.6	5.9	6.8	6.9	6.0	6.4	5.9	6.3	4.9	6.5	6.3	6.1	6.7							
19031	6.2	6.3	6.2	5.0	5.9	5.8	5.9	5.9	6.1	5.7	5.5	5.5	5.5	5.9	5.9					
19032	7.6	7.4	7.2	7.4	7.2	7.1	7.4	6.9	6.9	7.2	7.0	7.1	6.7	6.7						
19033	6.4	6.7	6.5	6.9	6.4	6.6	6.0	5.9	5.9	6.1	6.0	5.8	6.4	5.9						
19049	7.0	6.4	7.0	6.4	7.3	6.6	6.8	6.4	6.7	6.3	7.2	6.8	6.0	6.1	5.9					
19059	7.2	7.0	6.6	6.8	7.2	7.0	7.4	7.0	7.3	6.8	6.5	6.5	6.4	6.5	6.8					
19070	6.8	6.6	6.0	6.5	6.5	6.4	6.3	6.7	6.2	5.7	6.6	6.7	6.4	FD 1						

ALL WEIGHTS WERE RECORDED IN GRAMS (G). MEAN LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.
FIRST LETTER -- M-MALE, F-FEMALE, U-SEX UNDETERMINABLE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

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TABLE C44 (PAGE 4): PUP BODY WEIGHTS FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP I								0 MG/KG/DAY				POSTPARTUM DAY 8							
19010	15.9	16.5	15.9	17.3	17.0	14.7	18.2	12.1	16.2	16.0	16.7	16.1	16.3	FD 3						
19012	14.2	14.2	13.3	14.4	12.9	13.7	13.1	13.4	13.3	13.9	13.7	14.1	12.1	14.1	13.4	14.8				
19019	15.2	15.1	15.7	15.1	16.2	15.9	14.7	15.0	13.8	14.5	15.3	14.9	12.9	14.7	14.8					
19021	13.3	13.2	13.1	13.5	12.0	13.0	13.3	11.8	11.4	12.5	12.0	11.8	11.6	11.7						
19023	16.5	18.1	17.2	16.9	15.7	17.2	16.0	16.3	15.8	16.1	17.3	17.1	FD 4							
19041	10.5	14.9	12.5	13.5	13.9	12.8	12.7	14.1	13.7	14.1	12.9	11.6	11.4	13.4	15.8	11.8	11.6	13.5		
19042	13.9	15.7	13.8	12.9	14.9	13.5	13.7	14.9	13.5	13.9	12.9	12.7	13.2	13.4	13.9					
19044	14.5	13.2	15.2	13.5	15.1	15.6	12.2	10.9	12.1	13.4	11.7	13.8	14.2	14.0	10.7	13.8	FM 2			
19050	13.8	13.9	14.6	15.2	15.7	12.6	11.6	12.6	15.1	15.0	15.6	13.4	14.4	12.8	13.6					
19053	15.6	14.6	15.7	16.5	14.9	16.0	15.6	16.0	MD 5	15.3	15.7	16.6	14.8	15.2	15.5	14.8				
19065	14.7	14.8	13.4	12.4	11.8	15.1	13.2	13.0	10.0	12.9	12.6	14.9	10.6	11.7	10.4	12.7	12.1	11.3	13.2	FD 5
19068	17.7	17.0	17.0	16.9	17.4	MD 2	16.9	15.7	16.4	15.6	15.6	15.3	15.0	15.8	16.1					
19072	10.9	11.8	12.4	13.2	13.2	11.2	12.8	13.1	11.6	11.1	12.0	12.6	11.8	12.5	11.9	11.4				
19074	16.7	18.1	18.2	17.8	MD 1	17.5	16.2	16.6	17.8	15.3	17.4	17.5	15.9	18.2	15.4					
19075	14.1	13.3	13.3	10.8	13.0	14.2	10.8	13.5	12.5	14.2	11.9	10.7	13.4	13.5	13.8	13.5				
RAT/ LITTER #	MATERNAL DOSAGE GROUP II								0.3 MG/KG/DAY				POSTPARTUM DAY 8							
19004	15.2	11.5	14.9	11.8	13.6	14.5	13.8	13.0	12.3	12.6	12.4	13.3	12.3	10.0	13.6	10.6	10.3	FM 6		
19009	15.3	15.5	16.9	15.4	15.3	15.4	14.6													
19016	15.9	15.2	15.5	13.2	14.5	15.0	14.8	13.0	13.8	14.3	14.8	15.0	14.0	14.7	10.1					
19018	15.9	15.6	14.5	15.2	15.5	15.0	15.4	15.2	15.7	13.1	13.8	15.8	13.9	13.8						
19026	14.4	12.8	14.3	13.2	15.8	13.4	13.3	13.9	12.1	13.4	13.9	12.0	12.1	11.7	11.4	12.6	11.2	11.6	FD 8	
19036	12.1	11.3	12.5	10.1	11.5	11.8	10.5	7.5	11.3	13.3	6.4	8.6	7.6	11.5	FD 2	FD 1				
19037	12.0	9.3	11.2	12.2	12.5	11.7	10.7	12.7	12.1	10.8	11.8	10.7	11.4	9.3	11.7	12.0				
19043	13.5	14.1	13.0	14.7	13.9	14.0	14.6	14.2	13.6	13.2	13.6	12.3	13.3							
19047	14.5	16.0	14.0	15.5	16.1	15.3	15.7	11.4	14.5	14.3	15.6	16.0	14.5							
19048	16.6	17.2	16.3	15.4	15.2	16.4	15.8	16.2	16.2											
19052	11.5	10.3	10.2	11.9	11.1	10.8	10.7	11.4	11.6	10.5	10.4	11.0	11.0	10.6	11.6	9.0	FD 5			
19055	14.0	13.4	14.3	13.8	13.8	14.2	16.1	14.3	15.4	13.7	MD 1	11.4	14.2	14.2	12.9	13.0				
19061	14.3	13.7	13.5	12.8	13.9	13.9	14.3	MD 3	13.2	12.1	13.0	12.7	12.8							
19067	13.5	14.6	14.3	12.6	13.8	13.4	12.5	13.5	13.3	13.2	13.1	13.5	14.1	FD 8						
19071	10.1	9.2	11.6	10.8	12.0	11.3	13.4	12.9	12.1	10.4	12.5	13.2	9.5	12.5						

ALL WEIGHTS WERE RECORDED IN GRAMS (G). MEAN LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.
FIRST LETTER -- M-MALE, F-FEMALE, U-SEX UNDETERMINABLE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C44 (PAGE 5): PUP BODY WEIGHTS FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP III								1 MG/KG/DAY					POSTPARTUM DAY 8						
19003	13.9	13.6	14.3	11.1	13.5	14.1	13.5	13.7	11.7	12.9	12.3	11.1	10.9	11.5	14.2	12.5				
19007	14.1	13.7	13.3	13.7	12.5	14.8	13.9	11.7	13.5	11.2	12.7	11.9	12.2	12.9	11.7	12.8	12.5	FD 2		
19008	13.7	14.8	15.4	15.6	15.1	14.7	13.7	14.8	14.0	13.6	14.6	15.2	14.0	12.5	FM 2					
19013	15.8	14.9	14.0	15.1	15.1	15.3	15.9	15.4	15.6	14.2	12.6	15.3	12.7	13.4	15.0					
19014	NOT PREGNANT																			
19015	13.9	14.5	14.3	14.2	15.2	13.5	14.1	12.9	13.9	11.1	13.2	13.8	13.8	13.3	13.2					
19017	14.1	15.7	15.7	14.4	15.0	13.6	13.6	15.3	12.3	15.3	15.1	15.2	14.2	13.8						
19024	14.6	14.2	14.7	13.8	14.3	14.9	14.0	15.1	14.9	13.6	12.7	13.3	15.5	13.5	12.1					
19029	14.3	14.1	13.5	14.3	14.4	13.7	13.8	14.9	MM 2	12.7	10.9	12.6	11.7	13.0	11.8	12.7				
19034	15.1	15.0	15.5	15.4	15.7	15.0	14.1	12.7	14.6	14.8	15.2	14.0	14.8	FS						
19038	NOT PREGNANT																			
19056	15.0	14.9	16.0	14.6	15.4	14.3	15.4	14.1	15.4	14.5	15.5	15.2	14.5	14.3						
19057	13.2	13.1	12.6	13.5	12.8	13.0	13.2	12.4	13.8	14.0	14.2	12.1	11.9	12.1	12.0	13.9	12.8			
19060	16.1	14.9	16.2	14.9	13.2	14.1	14.0	14.6	12.9	12.2	14.5	13.0	15.8	12.0						
19064	11.1	11.6	14.3	10.1	10.8	10.9	13.8	11.7	14.9	9.7	11.5	10.7	11.3	13.8	9.3	13.6	10.3	13.4		
RAT/ LITTER #	MATERNAL DOSAGE GROUP IV								3 MG/KG/DAY					POSTPARTUM DAY 8						
19002	19.8	19.2	18.4	MS	18.3	17.9	17.3	17.9	17.9	18.2	FD 1									
19005	13.6	11.9	14.8	12.2	12.5	14.0	13.4	12.2	12.8	13.9	13.3	13.9	13.1	12.9	12.3	12.7				
19035	13.0	13.2	12.9	13.2	12.3	12.6	12.2	11.0	13.5	12.7	12.1	13.6	12.9	11.8						
19039	10.4	11.2	12.1	11.6	10.1	MD 2	9.0	8.9	11.5	9.8	9.9	9.9	10.8	11.2	11.3					
19040	12.5	10.5	11.8	13.0	9.7	12.0	11.8	9.8	11.3	8.5	11.2	12.8	9.9	12.7	12.0	11.1	10.1			
19045	12.0	12.8	11.5	11.7	9.8	12.4	12.3	12.7	11.9	11.1	11.3	13.1	12.9	11.8	11.0	UU				
19046	NOT PREGNANT																			
19051	NOT PREGNANT; MATING NOT CONFIRMED																			
19054	20.7	20.4	19.2	21.5	21.0															
19058	14.4	13.9	14.8	14.6	16.6	14.8	14.6	15.2	15.9	14.2	14.2	13.7	15.1							
19062	16.2	17.3	17.3	17.1	16.7	17.4	16.4	15.0	16.7	15.7	16.9	16.2	15.5	15.6	15.2					
19063	15.7	13.4	15.3	14.0	16.3	15.9	16.7	13.4	14.8	15.3	15.1	16.1	13.8	FS						
19066	16.6	15.7	15.5	15.9	15.5	16.5	MD 1	15.7	17.1	16.3	15.3	15.0	15.4	FS						
19069	10.6	10.2	11.4	10.1	8.3	11.0	9.8	10.1	10.4	8.4	10.8	10.3	10.7	6.2	9.4	10.0	10.4			
19073	15.4	13.4	13.6	13.5	13.5	14.5	13.6	MM 3	12.9	13.3	12.4	13.3	12.7	11.9						

ALL WEIGHTS WERE RECORDED IN GRAMS (G). MEAN LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.
FIRST LETTER -- M-MALE, F-FEMALE, U-SEX UNDETERMINABLE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C44 (PAGE 6): PUP BODY WEIGHTS FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP V							10 MG/KG/DAY				POSTPARTUM DAY 8								
19001	14.3	13.6	13.2	14.8	14.4	14.3	14.0	15.3	14.1	14.3	13.7									
19006	12.9	13.5	13.8	14.8	14.2	MD 2	13.4	14.0	13.0	12.7	12.8	12.1	13.7	11.5	12.8	15.4	12.8	13.4	FD 1	FS
19011	13.9	14.2	13.8	14.3	13.3	14.1	13.7	13.0	13.4	13.2	14.9	13.2	14.1							
19020	8.5	9.3	9.1	8.8	8.6	8.4	10.8	9.8	7.7	8.3	9.4	9.5	10.8							
19022	15.8	15.3	16.2	14.8	15.3	15.2	14.8	15.6	14.5	MD 1	14.5	15.7	14.1	14.3	16.0	FM 2				
19025	12.5	10.6	14.5	12.7	12.3	13.7	12.6	15.0	9.9	12.1	12.4	15.3	14.4	11.5	11.9	12.3	10.5	10.5	10.3	10.2
19027	12.0	13.2	13.1	12.2	10.8	11.8	11.8	11.6	12.2	13.5	12.6	12.8	12.6	10.9						
19028	13.1	13.7	13.3	11.7	13.8	13.2	12.9	13.7	12.6	14.5	13.4	12.4	FS							
19030	15.6	14.5	14.9	15.7	13.7	15.3	15.0	14.4	14.5	11.9	13.3	15.5	15.4							
19031	12.7	10.7	12.4	11.3	13.6	12.9	12.6	MM 2	13.1	11.8	11.0	13.8	12.4	10.3	10.8					
19032	13.6	15.2	15.0	14.6	15.2	13.4	14.9	12.5	14.0	14.1	13.0	12.5	13.4	13.1						
19033	13.5	13.9	13.5	14.7	14.0	13.3	12.7	12.3	13.5	12.2	12.6	12.1	13.0	12.4						
19049	11.5	13.7	13.1	11.0	14.1	12.8	12.5	12.1	14.8	12.7	10.4	12.5	12.7	9.3	9.4					
19059	10.3	11.5	12.8	13.1	12.5	13.0	12.3	13.0	12.1	12.4	9.9	11.5	11.4	11.9	10.5					
19070	15.8	13.2	14.3	15.2	16.1	16.4	15.8	16.0	14.7	16.9	14.8	14.9	12.9	FD 1						

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FIRST LETTER -- M-MALE, F-FEMALE, U-SEX UNDETERMINABLE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C44 (PAGE 7): PUP BODY WEIGHTS FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP I							0 MG/KG/DAY				POSTPARTUM DAY 15								
19010	28.0	28.9	26.7	29.8	28.3	30.1	27.6	27.1	27.0	28.6	28.2	28.9	23.5	FD 3						
19012	26.2	25.8	26.8	27.4	26.2	26.1	26.2	22.3	26.7	25.2	23.7	25.9	28.9	23.9	23.3	28.0				
19019	28.9	29.3	25.2	30.6	28.4	29.1	27.7	29.7	27.2	25.4	22.9	28.6	25.5	28.8	27.0					
19021	23.3	23.1	24.8	22.8	21.4	23.5	23.2	24.0	24.1	21.3	22.8	21.8	22.6	22.2						
19023	31.0	31.6	34.7	33.2	32.3	34.8	31.8	31.0	32.8	32.8	32.6	31.1	FD 4							
19041	26.0	21.6	22.9	26.1	23.7	24.3	24.3	27.1	25.4	20.5	25.6	25.0	25.8	23.6	23.4	23.2	19.6	22.4		
19042	26.9	26.5	28.3	26.1	23.4	27.3	26.3	29.4	28.3	26.2	27.0	22.5	26.2	24.8	26.1					
19044	23.6	30.7	22.2	26.1	26.2	29.8	29.8	25.9	25.6	27.2	21.6	25.3	26.1	25.8	26.9	23.1	FM 2			
19050	26.3	26.8	28.3	28.3	25.8	26.9	25.0	24.8	23.1	27.5	25.5	26.4	26.0	27.7	23.9					
19053	29.0	31.0	28.4	28.6	27.1	31.1	29.6	29.5	MD 5	27.1	26.9	27.7	28.7	28.8	28.1	30.4				
19065	29.2	25.1	23.3	25.1	22.5	24.2	19.6	27.8	26.8	27.2	25.0	24.6	22.9	25.8	19.9	20.8	25.5	22.2	19.6	FD 5
19068	29.4	29.5	28.3	30.0	31.3	MD 2	29.2	26.5	28.2	27.6	28.4	25.6	26.7	27.3	27.5					
19072	20.6	23.4	21.2	23.3	24.0	25.6	20.0	23.8	23.1	20.4	21.3	22.3	20.7	21.4	21.9	21.5				
19074	29.1	28.3	27.6	24.0	MD 1	28.2	26.2	28.2	27.6	26.3	26.8	27.2	25.8	28.2	29.0					
19075	23.7	23.8	21.6	20.5	23.0	19.4	23.1	24.0	21.9	22.2	22.6	24.5	22.7	22.2	21.0	24.9				
RAT/ LITTER #	MATERNAL DOSAGE GROUP II							0.3 MG/KG/DAY				POSTPARTUM DAY 15								
19004	22.4	25.9	25.7	24.5	20.9	26.3	23.6	26.5	18.7	21.1	19.0	21.5	26.8	23.0	22.6	23.2	24.6	FM 6		
19009	34.4	34.4	32.6	32.8	33.2	35.0	33.9													
19016	27.5	29.1	27.8	23.7	28.5	29.6	30.0	27.1	28.2	26.3	26.1	29.0	25.4	17.1	26.7					
19018	29.6	27.0	28.1	30.5	26.6	27.1	28.8	28.8	26.3	23.1	28.4	26.4	24.9	24.6						
19026	29.2	24.0	23.0	27.3	26.1	24.3	22.3	24.0	23.9	25.8	24.9	22.2	23.6	22.9	21.3	21.8	23.2	21.7	FD 8	
19036	25.4	27.0	28.0	27.2	27.1	26.8	25.0	18.3	25.6	29.0	20.2	27.3	23.3	FM11	FD 2	FD 1				
19037	18.8	18.6	16.8	19.2	15.6	19.5	20.2	17.9	19.3	19.7	15.9	17.8	19.6	17.5	15.9	FD15				
19043	29.4	30.6	28.6	28.3	29.7	29.1	30.2	27.8	27.9	27.5	28.3	28.9	29.3							
19047	29.5	28.7	29.2	29.5	26.9	28.0	25.8	26.5	23.3	29.0	28.8	29.3	24.8							
19048	31.8	33.9	31.9	33.8	34.0	30.9	31.9	33.9	33.1											
19052	23.4	21.5	22.0	24.4	25.7	18.7	23.3	24.8	24.3	21.1	24.9	22.7	23.3	23.3	19.3	21.5	FD 5			
19055	26.2	27.8	27.4	26.5	24.7	26.1	28.0	26.5	23.7	27.5	MD 1	25.0	24.4	23.6	26.8	25.6				
19061	24.5	24.8	25.5	25.1	24.5	25.0	24.6	MD 3	24.9	24.3	24.8	24.1	25.1							
19067	29.5	29.9	29.9	29.4	29.0	28.9	29.4	27.9	26.8	27.7	28.6	27.5	28.6	FD 8						
19071	26.1	24.7	24.9	27.3	26.0	22.2	22.8	24.7	25.0	18.1	27.0	26.7	22.7	27.4						

ALL WEIGHTS WERE RECORDED IN GRAMS (G). MEAN LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.
FIRST LETTER -- M-MALE, F-FEMALE, U-SEX UNDETERMINABLE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C44 (PAGE 8): PUP BODY WEIGHTS FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP III							1 MG/KG/DAY				POSTPARTUM DAY 15								
19003	24.4	21.2	23.5	25.1	23.5	24.8	24.5	18.8	21.2	19.1	23.3	19.6	21.9	20.3	21.3	23.4				
19007	24.8	25.5	25.5	25.1	25.3	24.1	21.5	23.4	21.4	23.6	23.9	21.3	19.6	20.2	21.0	21.1	21.4	FD 2		
19008	31.1	28.7	29.9	26.9	28.3	29.2	30.5	29.2	27.8	26.8	29.8	26.9	29.9	26.2	FM 2					
19013	29.0	27.3	27.4	28.4	28.8	29.4	28.3	27.9	25.0	24.3	24.1	26.6	28.0	25.8	22.0					
19014	NOT PREGNANT																			
19015	27.5	25.0	29.2	23.2	25.9	24.7	27.7	26.7	27.2	28.2	25.0	20.5	24.9	26.5	24.2					
19017	27.1	28.9	28.4	27.9	27.8	25.7	28.2	28.1	26.4	26.4	28.4	26.4	18.1	24.8						
19024	26.0	27.7	28.8	29.8	26.4	26.3	26.7	25.7	28.9	27.9	25.2	24.7	26.1	24.9	23.8					
19029	26.9	27.4	23.1	26.1	27.0	25.8	26.7	27.4	MM 2	20.1	20.6	20.9	22.4	24.5	23.3	23.8				
19034	30.5	30.5	30.8	29.8	30.9	29.8	27.6	28.2	27.8	29.8	29.9	26.9	29.8	FS						
19038	NOT PREGNANT																			
19056	28.7	30.6	30.8	29.5	27.8	31.3	28.2	29.7	27.6	27.7	30.1	30.1	27.9	28.3						
19057	21.9	24.4	22.8	24.6	22.2	24.6	24.1	24.3	23.3	22.8	23.5	24.2	24.3	22.9	21.9	22.9	22.8			
19060	27.7	31.8	29.9	30.3	27.2	29.0	28.5	29.3	28.7	29.5	25.1	23.5	27.1	24.6						
19064	21.6	25.0	21.1	23.9	26.5	21.9	22.6	20.8	22.0	21.9	26.4	16.8	17.4	21.6	24.3	26.7	22.1	FM11		
RAT/ LITTER #	MATERNAL DOSAGE GROUP IV							3 MG/KG/DAY				POSTPARTUM DAY 15								
19002	34.5	36.4	35.7	MS	33.1	33.6	32.9	32.4	33.7	33.0	FD 1									
19005	23.1	26.5	23.4	24.8	22.1	25.2	24.8	23.7	24.2	24.0	24.0	25.1	21.1	24.7	22.5	23.0				
19035	23.6	23.5	23.2	23.0	22.4	24.1	23.3	22.5	21.3	22.7	23.1	23.4	21.6	21.9						
19039	24.7	19.3	24.0	23.5	23.0	MD 2	18.8	20.6	19.4	23.6	17.0	21.8	22.6	22.1	24.8					
19040	26.1	26.1	26.3	27.4	22.4	24.2	23.9	22.4	27.3	24.6	22.6	21.4	27.5	25.6	24.4	20.1	18.1			
19045	23.4	24.9	21.7	25.4	24.5	24.0	23.0	22.7	26.3	25.0	21.9	24.6	23.7	22.0	23.2	UU				
19046	NOT PREGNANT																			
19051	NOT PREGNANT; MATING NOT CONFIRMED																			
19054	39.0	41.2	43.5	40.1	40.8															
19058	30.7	26.7	29.1	27.6	24.9	27.1	28.4	28.0	26.5	26.3	26.2	28.0	29.0							
19062	31.4	31.3	30.4	31.2	31.2	30.0	31.3	28.9	30.3	30.3	30.0	29.9	29.0	28.7	28.7					
19063	28.3	31.3	31.6	29.9	29.2	32.0	30.0	27.6	29.2	31.9	30.7	26.8	30.8	FS						
19066	31.4	31.2	30.0	32.0	30.1	30.0	MD 1	30.8	30.2	31.9	30.9	29.5	32.1	FS						
19069	16.8	21.7	19.4	19.6	18.2	19.9	19.5	21.8	17.0	21.4	22.3	21.5	20.9	20.0	19.8	19.9	FD10			
19073	26.7	27.5	29.3	27.1	28.0	28.1	27.3	MM 3	25.3	26.1	26.3	25.6	25.2	25.3						

ALL WEIGHTS WERE RECORDED IN GRAMS (G). MEAN LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.
FIRST LETTER -- M-MALE, F-FEMALE, U-SEX UNDETERMINABLE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C44 (PAGE 9): PUP BODY WEIGHTS FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP V							10 MG/KG/DAY				POSTPARTUM DAY 15								
19001	27.5	26.3	26.2	26.2	26.6	26.2	26.1	28.0	26.4	25.8	27.3									
19006	23.2	26.7	26.2	25.7	25.4	MD 2	22.5	25.2	27.5	23.6	24.9	26.3	22.1	22.0	25.1	23.2	21.3	21.2	FD 1	FS
19011	27.0	25.9	27.1	26.2	25.8	24.3	27.5	25.8	24.2	25.7	25.1	24.6	27.5							
19020	17.0	13.8	15.3	14.8	16.6	15.1	17.0	15.9	14.9	15.8	15.2	16.2	15.1							
19022	30.9	27.6	30.0	29.7	28.7	25.7	29.3	27.5	31.4	MD 1	25.6	27.0	29.2	25.1	28.3	FM 2				
19025	25.6	24.5	24.4	23.7	26.2	23.4	18.7	24.0	23.8	21.4	25.3	26.8	27.4	23.6	20.8	20.0	22.4	17.7	19.2	19.1
19027	23.5	24.2	25.0	21.9	21.7	23.2	22.1	21.6	22.2	20.0	22.7	21.4	24.0	20.5						
19028	28.5	22.7	27.8	25.5	25.1	26.3	26.6	25.8	27.4	25.1	24.6	25.5	FS							
19030	29.1	29.3	29.7	30.9	29.3	28.5	29.4	28.8	24.0	29.7	29.0	28.0	28.0							
19031	25.3	24.6	30.7	28.8	27.8	26.9	29.2	MM 2	26.4	23.6	26.5	26.2	27.0	25.1	25.1					
19032	25.9	26.9	26.4	23.9	26.7	26.2	25.3	25.5	24.5	26.5	24.6	23.4	23.7	22.9						
19033	27.4	28.2	27.1	27.0	27.1	27.9	25.8	25.3	25.4	24.8	26.6	24.3	24.7	24.5						
19049	27.2	26.1	25.8	26.1	24.5	26.6	20.8	25.2	24.0	27.6	25.1	26.1	20.3	24.5	20.1					
19059	26.4	24.3	28.1	25.6	23.8	25.5	23.3	22.7	24.1	25.2	22.1	17.4	22.2	20.4	24.3					
19070	30.1	29.4	31.0	30.4	29.7	28.5	29.5	30.1	30.5	25.1	27.3	29.3	FD13	FD 1						

ALL WEIGHTS WERE RECORDED IN GRAMS (G). MEAN LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.
FIRST LETTER -- M-MALE, F-FEMALE, U-SEX UNDETERMINABLE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C44 (PAGE 10): PUP BODY WEIGHTS FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP I								0 MG/KG/DAY				POSTPARTUM DAY 22							
19010	43.0	44.2	41.1	39.4	39.0	39.5	40.7	33.4	42.7	40.0	41.6	41.6	41.4	FD 3						
19012	43.0	43.7	40.3	44.2	42.2	37.9	41.6	41.1	39.0	36.9	41.8	36.7	42.6	41.0	42.1	45.4				
19019	39.6	41.8	36.2	39.0	39.9	42.5	41.2	39.7	37.6	35.4	38.6	39.6	36.3	37.6	35.4					
19021	34.5	34.4	39.4	35.8	35.0	35.6	38.3	36.0	33.2	34.1	34.9	32.1	34.5	33.4						
19023	44.0	45.6	47.2	44.0	48.9	46.4	46.9	44.6	44.2	45.4	44.6	43.1	FD 4							
19041	37.0	31.1	34.9	29.4	32.6	30.4	31.4	33.3	33.9	33.4	35.4	37.9	29.6	35.7	26.8	35.8	25.3	31.8		
19042	38.7	37.4	37.5	36.4	35.0	33.1	34.6	37.6	35.3	35.7	34.4	37.2	35.7	32.8	36.7					
19044	48.1	48.4	25.8	43.9	45.5	43.1	36.4	49.3	43.6	41.6	41.1	37.8	36.6	40.0	43.1	40.2	FM 2			
19050	37.9	37.4	37.1	35.0	34.7	34.5	38.4	34.3	32.4	37.1	38.5	34.3	34.5	32.6	34.6					
19053	34.8	39.9	37.9	33.8	39.2	32.3	35.3	34.1	MD 5	34.7	35.2	34.3	38.3	37.1	31.7	37.1				
19065	41.2	25.4	30.1	36.9	33.3	30.9	31.5	33.6	29.0	32.8	30.9	31.5	32.4	35.7	31.7	28.9	23.9	33.0	26.8	FD 5
19068	47.9	46.2	48.8	50.0	45.5	MD 2	45.4	45.9	45.9	46.8	42.5	44.2	47.1	45.0	43.1					
19072	34.0	33.7	27.0	29.9	33.7	33.5	32.9	28.6	28.0	28.9	33.0	33.7	30.3	28.6	28.6	29.1				
19074	35.4	37.2	38.8	29.2	MD 1	32.9	35.1	32.5	33.6	33.5	34.7	35.2	34.7	33.0	35.1					
19075	34.4	38.5	35.5	37.1	30.8	35.5	38.5	35.4	40.7	36.0	34.5	33.8	37.4	36.0	38.6	34.5				
RAT/ LITTER #	MATERNAL DOSAGE GROUP II								0.3 MG/KG/DAY				POSTPARTUM DAY 22							
19004	33.4	34.4	26.5	33.6	29.0	30.4	33.2	28.5	33.3	26.3	32.4	24.0	28.9	29.9	26.4	29.4	29.1	FM 6		
19009	57.1	55.6	51.3	51.4	57.7	53.8	51.8													
19016	46.5	47.4	48.5	44.5	44.2	44.4	45.8	47.6	49.3	50.3	41.3	45.4	45.1	25.8	43.4					
19018	48.4	47.0	45.9	46.3	44.8	43.4	44.6	44.0	45.6	45.0	39.2	38.1	41.0	40.6						
19026	32.3	32.5	39.1	30.7	30.1	34.9	29.3	29.6	28.7	30.7	29.1	31.2	29.3	27.6	34.6	28.6	27.1	27.5	FD 8	
19036	39.7	40.9	43.1	42.9	42.1	38.1	29.1	35.7	42.7	43.2	39.2	30.5	37.0	FM11	FD 2	FD 1				
19037	33.1	25.3	30.5	31.8	31.6	34.6	31.0	31.9	30.8	29.1	32.9	27.9	31.9	27.0	24.9	FD15				
19043	46.0	46.4	47.2	46.2	48.4	44.9	45.8	43.2	44.6	43.7	45.2	42.9	42.6							
19047	38.9	39.1	34.4	37.1	39.3	39.5	39.5	41.3	39.7	36.9	40.5	33.0	32.2							
19048	46.5	51.0	49.7	47.1	50.5	47.0	48.0	45.8	45.0											
19052	38.6	38.6	31.7	33.6	37.3	35.2	40.1	35.4	31.1	34.0	37.8	40.5	36.9	37.5	29.9	36.2	FD 5			
19055	40.7	40.1	41.3	40.2	39.6	38.1	42.9	38.5	36.3	40.3	MD 1	38.9	39.4	34.5	37.8	35.6				
19061	33.8	30.7	32.2	31.1	34.4	30.2	32.7	MD 3	35.9	31.5	34.2	32.7	34.6							
19067	41.4	39.9	40.2	40.8	39.6	39.3	40.5	39.4	37.5	39.1	37.0	40.2	37.7	FD 8						
19071	40.7	42.3	42.1	40.5	44.4	34.9	40.0	35.3	36.9	41.3	43.3	42.6	43.1	31.1						

ALL WEIGHTS WERE RECORDED IN GRAMS (G). MEAN LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.
FIRST LETTER -- M-MALE, F-FEMALE, U-SEX UNDETERMINABLE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C44 (PAGE 11): PUP BODY WEIGHTS FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP III							1 MG/KG/DAY				POSTPARTUM DAY 22								
19003	35.4	31.5	30.7	26.0	32.3	31.9	24.2	31.3	28.4	30.2	25.0	28.6	26.6	31.6	28.2	26.1				
19007	34.7	35.5	35.5	30.4	27.9	36.0	35.0	31.2	29.3	28.0	31.0	29.0	31.8	30.1	33.8	27.4	33.8	FD 2		
19008	43.6	40.5	42.9	41.5	40.8	38.6	42.5	37.2	41.3	38.4	38.4	42.5	39.9	35.5	FM 2					
19013	45.7	45.8	49.6	42.0	49.1	46.6	50.2	45.5	48.4	41.8	39.5	42.8	46.1	37.9	45.5					
19014	NOT PREGNANT																			
19015	39.1	39.8	41.8	40.0	37.1	33.5	38.6	37.3	38.4	38.8	36.2	38.1	35.8	30.1	36.4					
19017	49.7	42.2	45.8	47.5	48.8	40.5	47.3	48.8	44.4	45.0	47.1	41.9	30.8	48.3						
19024	39.0	39.8	39.7	38.5	38.2	43.4	37.3	42.8	41.4	37.1	41.3	35.6	35.6	38.5	36.8					
19029	46.5	41.8	44.0	41.8	46.1	47.6	44.3	37.7	MM 2	38.6	32.0	31.7	38.0	37.6	34.2	30.3				
19034	41.4	40.9	41.2	41.4	40.6	41.9	38.9	40.2	40.4	40.4	38.7	37.5	37.0	FS						
19038	NOT PREGNANT																			
19056	39.3	41.4	41.4	39.5	42.6	41.6	44.1	38.5	41.5	41.2	39.6	41.6	38.0	38.1						
19057	34.2	33.7	32.2	33.7	30.9	32.3	32.1	32.5	33.0	31.5	34.6	31.1	33.9	30.7	33.9	29.7	30.3			
19060	47.4	47.0	49.2	45.8	48.8	46.4	45.5	42.8	46.7	42.7	48.8	40.6	39.5	38.5						
19064	3.0	34.7	28.0	36.4	29.4	33.0	29.4	28.2	28.4	36.9	28.4	30.3	34.2	35.6	27.5	24.0	24.6	FM11		
RAT/ LITTER #	MATERNAL DOSAGE GROUP IV							3 MG/KG/DAY				POSTPARTUM DAY 22								
19002	47.2	47.4	49.4	MS	44.4	46.3	45.3	46.0	45.4	45.0	FD 1									
19005	31.3	36.4	34.3	31.3	32.7	33.1	28.9	32.0	32.7	31.5	29.6	33.0	33.2	33.4	28.1	34.5				
19035	32.8	35.2	33.6	33.2	34.6	33.3	32.2	30.6	33.9	30.6	34.7	29.9	34.4	32.1						
19039	36.0	39.4	36.2	34.0	30.1	MD 2	32.8	35.6	31.7	36.8	31.7	28.5	32.7	33.7	27.8					
19040	32.8	30.6	32.9	32.0	33.6	31.6	28.3	26.9	27.1	28.3	31.7	30.0	32.9	35.5	32.1	24.7	23.7			
19045	37.1	41.2	37.1	33.5	39.4	37.1	38.3	35.8	36.0	37.8	36.4	30.6	36.0	39.9	34.8	UU				
19046	NOT PREGNANT																			
19051	NOT PREGNANT; MATING NOT CONFIRMED																			
19054	57.5	59.1	54.8	55.5	57.6															
19058	51.3	44.7	41.2	47.9	45.6	47.6	47.5	45.7	44.1	47.5	45.8	42.7	45.3							
19062	43.0	43.6	41.0	42.9	41.0	40.1	44.0	42.9	42.7	41.3	40.4	41.2	38.2	39.9	39.5					
19063	48.7	46.5	46.1	48.6	45.9	49.4	48.4	44.0	42.8	50.1	47.2	39.7	46.2	FS						
19066	43.5	44.3	43.8	44.3	42.9	45.7	MD 1	43.5	43.5	40.9	42.5	41.4	43.2	FS						
19069	31.7	28.5	28.1	30.5	32.5	29.3	33.2	33.4	35.7	27.5	33.0	37.2	36.8	32.3	33.8	31.4	FD10			
19073	44.5	44.2	44.0	43.8	45.6	46.2	42.0	MM 3	39.5	38.6	42.7	41.3	42.2	41.2						

ALL WEIGHTS WERE RECORDED IN GRAMS (G). MEAN LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.
FIRST LETTER -- M-MALE, F-FEMALE, U-SEX UNDETERMINABLE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

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TABLE C44 (PAGE 12): PUP BODY WEIGHTS FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP V							10 MG/KG/DAY				POSTPARTUM DAY 22								
19001	43.5	45.6	43.0	44.3	45.4	43.3	44.0	43.0	42.9	44.2	45.6									
19006	33.2	36.3	35.4	34.5	36.6	MD 2	31.6	32.2	31.7	32.0	30.9	36.9	34.9	34.8	34.4	28.9	29.9	34.2	FD 1	FS
19011	37.9	38.1	33.7	35.8	38.9	34.9	35.5	35.6	37.9	35.7	35.0	33.7	34.9							
19020	15.1	15.8	16.0	16.2	14.4	16.0	15.3	14.8	14.5	18.1	14.9	15.9	14.2							
19022	32.3	33.5	37.9	39.1	39.3	35.4	35.3	37.0	37.2	MD 1	34.6	36.3	35.6	32.5	33.3	FM 2				
19025	31.2	30.6	29.9	30.5	27.0	35.9	25.0	31.7	30.2	34.5	30.6	31.8	31.5	30.5	24.4	27.6	26.8	31.0	23.8	23.8
19027	34.8	33.3	32.3	31.8	29.3	32.4	32.5	29.0	31.1	30.6	31.1	31.7	30.1	33.0						
19028	39.9	43.1	38.4	44.4	33.2	39.6	40.4	40.6	39.5	35.6	42.5	42.4	FS							
19030	39.1	38.9	40.8	43.3	40.0	38.4	39.8	42.0	39.6	32.2	38.7	37.6	37.9							
19031	43.4	45.6	45.0	50.8	40.4	40.9	47.8	MM 2	44.3	39.5	41.2	39.2	44.0	38.4	40.9					
19032	37.3	34.6	36.4	33.5	36.7	37.4	35.6	32.4	34.5	33.8	35.2	36.1	32.9	34.9						
19033	45.7	40.7	43.6	45.8	45.1	43.8	41.2	44.2	42.6	39.1	41.0	41.0	40.2	39.0						
19049	37.8	34.6	35.3	37.1	36.1	39.9	39.6	33.9	39.1	31.2	39.9	36.2	38.6	32.4	24.4					
19059	35.2	33.3	33.8	37.4	37.4	33.6	35.5	33.7	35.0	31.0	33.8	27.5	25.6	32.2	32.9					
19070	48.6	51.7	54.1	47.6	49.5	52.1	46.9	46.5	47.5	46.8	43.9	48.8	FD13	FD 1						

ALL WEIGHTS WERE RECORDED IN GRAMS (G). MEAN LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.
FIRST LETTER -- M-MALE, F-FEMALE, U-SEX UNDETERMINABLE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C45 (PAGE 1): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
RAT/ LITTER #	MATERNAL DOSAGE GROUP I																						0 MG/KG/DAY
19010	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	FD 3									
19012	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A							
19019	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A							
19021	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A								
19023	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	FD 4									
19041	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A				
19042	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A						
19044	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	FM 2					
19050	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A								
19053	M A	M A	M A	M A	M A	M A	M A	M A	MD 5	F A	F A	F A	F A	F A	F A	F A							
19065	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	FD 5		
19068	M A	M A	M A	M A	M A	MD 2	F A	F A	F A	F A	F A	F A	F A	F A	F A								
19072	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A						
19074	M A	M A	M A	M A	MD 1	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A							
19075	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A							
RAT/ LITTER #	MATERNAL DOSAGE GROUP II																						0.3 MG/KG/DAY
19004	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	FM 6					
19009	M A	M A	F A	F A	F A	F A	F A																
19016	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A								
19018	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A									
19026	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	FD 8					
19036	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	FM11	FD 2	FD 1							
19037	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	FD15							
19043	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A									
19047	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A									
19048	M A	M A	M A	M A	M A	F A	F A	F A	F A														
19052	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	FD 5								
19055	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	MD 1	F A	F A	F A	F A	F A							
19061	M A	M A	M A	M A	M A	M A	M A	MD 3	F A	F A	F A	F A	F A	F A									
19067	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	FD 8									
19071	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A								

FIRST LETTER -- M-MALE, F-FEMALE, U-SEX UNDETERMINABLE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C45 (PAGE 2): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
RAT/ LITTER #	MATERNAL DOSAGE GROUP III										1 MG/KG/DAY												
19003	M	A	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A	F	A	F	A	
19007	M	A	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A	F	A	F	A	FD 2
19008	M	A	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A	FM 2				
19013	M	A	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A	F	A			
19014	NOT PREGNANT																						
19015	M	A	M	A	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A			
19017	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A	F	A					
19024	M	A	M	A	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A			
19029	M	A	M	A	M	A	M	A	M	A	M	A	MM 2		F	A	F	A	F	A	F	A	F	A	F	A	
19034	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A	F	S					
19038	NOT PREGNANT																						
19056	M	A	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A					
19057	M	A	M	A	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A	F	A	
19060	M	A	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A					
19064	M	A	M	A	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A	F	A	FM11
RAT/ LITTER #	MATERNAL DOSAGE GROUP IV										3 MG/KG/DAY												
19002	M	A	M	A	M	S	F	A	F	A	F	A	F	A	FD 1								
19005	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A	F	A	F	A			
19035	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A							
19039	M	A	M	A	M	A	M	A	MD 2		F	A	F	A	F	A	F	A	F	A	F	A					
19040	M	A	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A	F	A	F	A	
19045	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A	F	A	U	U			
19046	NOT PREGNANT																						
19051	NOT PREGNANT; MATING NOT CONFIRMED																						
19054	M	A	M	A	M	A	F	A	F	A													
19058	M	A	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A			
19062	M	A	M	A	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A			
19063	M	A	M	A	F	A	F	A	F	A	F	A	F	A	F	A	F	A	F	A	F	S					
19066	M	A	M	A	M	A	M	A	F	A	MD 1		F	A	F	A	F	A	F	A	F	A	F	S			
19069	M	A	M	A	M	A	M	A	M	A	F	A	F	A	F	A	F	A	F	A	F	A	F	A	F	A	FD10
19073	M	A	M	A	M	A	M	A	M	A	M	A	MM 3		F	A	F	A	F	A	F	A					

FIRST LETTER -- M-MALE, F-FEMALE, U-SEX UNDETERMINABLE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
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PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C45 (PAGE 3): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
RAT/ LITTER #	MATERNAL DOSAGE GROUP V										10 MG/KG/DAY												
19001	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A													
19006	M A	M A	M A	M A	M A	MD 2	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	FD 1	F S				
19011	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A										
19020	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A										
19022	M A	M A	M A	M A	M A	M A	M A	M A	M A	MD 1	F A	F A	F A	F A	F A	FM 2							
19025	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A			
19027	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A									
19028	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F S										
19030	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A										
19031	M A	M A	M A	M A	M A	M A	M A	MM 2	F A	F A	F A	F A	F A	F A	F A								
19032	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A									
19033	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A									
19049	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A								
19059	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A								
19070	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	FD13	FD 1									

FIRST LETTER -- M-MALE, F-FEMALE, U-SEX UNDETERMINABLE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C46 (PAGE 1): CLINICAL OBSERVATIONS FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP MATERNAL DOSAGE (MG/KG/DAY)	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
I 0	19010	1- 2	1/14 PUPS: PALE IN APPEARANCE.
	19044	1- 2	1/17 PUPS: BACK, BRUISE (2.5 CM X 2.0 CM).
	19050	1	1/15 PUPS: PALE IN APPEARANCE.
	19072	18-22	1/16 PUPS: RIGHT EYE, CORNEAL OPACITY.b
II 0.3	19004	8	1/17 PUPS: COLD TO TOUCH; NOT NESTING OR NURSING.
	19036	1- 4	1/14 PUPS: BACK, BRUISE (2.0 CM IN DIAMETER).
	19037	18	4/15 PUPS: DEHYDRATION.
	19071	11	1/14 PUPS: COLD TO TOUCH.
III 1	19003	17	1/16 PUPS: DEHYDRATION.
	19064	9	1/18 PUPS: DEHYDRATION.

a. Tabulation restricted to adverse observations; all other pups appeared normal.
b. Confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C46 (PAGE 2): CLINICAL OBSERVATIONS FROM BIRTH TO DAY 22 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP MATERNAL DOSAGE (MG/KG/DAY)	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
IV 3	19039	9- 16	1/14 PUPS: LEFT EYE, PERIORBITAL DISCOLORATION, PURPLE.
	19054	1	1/15 PUPS: RIGHT HINDLIMB, LACERATION.
		2- 7	1/ 5 PUPS: RIGHT HINDLIMB, SCAB (0.1 CM X 1.0 CM).
	19058	20-22	1/13 PUPS: RIGHT EYE, ENLARGED.b
V 10	19006	11	1/17 PUPS: COLD TO TOUCH.
	19020	22	13/13 PUPS: NOT NURSING; DEHYDRATION b; EMACIATION b.
	19049	2- 4	2/15 PUPS: WHOLE BODY, EXCLUDING HEAD, DISCOLORATION, PURPLE.
	19070	8- 10	1/13 PUPS: HEAD, SCAB (DID NOT EXCEED 0.1 CM X 0.5 CM).

a. Tabulation restricted to adverse observations; all other pups appeared normal.
b. Confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C47 (PAGE 1): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP MATERNAL DOSAGE (MG/KG/DAY)	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
I 0	19010	3	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		22	13 PUPS: APPEARED NORMAL.
	19012	22	16 PUPS: APPEARED NORMAL.
	19019	22	15 PUPS: APPEARED NORMAL.
	19021	22	14 PUPS: APPEARED NORMAL.
	19023	4	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		22	12 PUPS: APPEARED NORMAL.
	19041	22	18 PUPS: APPEARED NORMAL.
	19042	22	15 PUPS: APPEARED NORMAL.
	19044	22	16 PUPS: APPEARED NORMAL.
	19050	22	15 PUPS: APPEARED NORMAL.
	19053	5	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		22	15 PUPS: APPEARED NORMAL.
	19065	5	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		22	19 PUPS: APPEARED NORMAL.
	19068	2	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		22	14 PUPS: APPEARED NORMAL.
	19072	22	16 PUPS: APPEARED NORMAL.
	19074	1	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		22	14 PUPS: APPEARED NORMAL.
	19075	22	16 PUPS: APPEARED NORMAL.

a. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation. Refer to the individual pup clinical observations table (Table C44) for external clinical observations confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C47 (PAGE 2): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP MATERNAL DOSAGE (MG/KG/DAY)	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
II 0.3	19004	22	17 PUPS: APPEARED NORMAL.
	19009	22	7 PUPS: APPEARED NORMAL.
	19016	22	15 PUPS: APPEARED NORMAL.
	19018	22	14 PUPS: APPEARED NORMAL.
	19026	8	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		22	18 PUPS: APPEARED NORMAL.
	19036	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		22	13 PUPS: APPEARED NORMAL.
	19037	15	1 PUP: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		22	1 PUP: KIDNEYS: RIGHT, PELVIS, MODERATE DILATION. ALL OTHER TISSUES APPEARED NORMAL.
			14 PUPS: APPEARED NORMAL.
	19043	22	13 PUPS: APPEARED NORMAL.
	19047	22	13 PUPS: APPEARED NORMAL.
	19048	22	9 PUPS: APPEARED NORMAL.
	19052	5	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		22	16 PUPS: APPEARED NORMAL.

a. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation. Refer to the individual pup clinical observations table (Table C44) for external clinical observations confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C47 (PAGE 3): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP MATERNAL DOSAGE (MG/KG/DAY)	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
II 0.3 cont.	19055	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		22	15 PUPS: APPEARED NORMAL.
	19061	3	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		22	12 PUPS: APPEARED NORMAL.
	19067	8	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		22	13 PUPS: APPEARED NORMAL.
	19071	22	14 PUPS: APPEARED NORMAL.

a. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation. Refer to the individual pup clinical observations table (Table C44) for external clinical observations confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C47 (PAGE 4): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP MATERNAL DOSAGE (MG/KG/DAY)	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
III			
1	19003	22	16 PUPS: APPEARED NORMAL.
	19007	2	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		22	17 PUPS: APPEARED NORMAL.
	19008	22	14 PUPS: APPEARED NORMAL.
	19013	22	15 PUPS: APPEARED NORMAL.
	19015	22	15 PUPS: APPEARED NORMAL.
	19017	22	14 PUPS: APPEARED NORMAL.
	19024	22	15 PUPS: APPEARED NORMAL.
	19029	22	15 PUPS: APPEARED NORMAL.
	19034	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		22	13 PUPS: APPEARED NORMAL.
	19056	22	14 PUPS: APPEARED NORMAL.
	19057	22	17 PUPS: APPEARED NORMAL.
	19060	22	14 PUPS: APPEARED NORMAL.
	19064	22	17 PUPS: APPEARED NORMAL.

a. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation. Refer to the individual pup clinical observations table (Table C44) for external clinical observations confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C47 (PAGE 5): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP MATERNAL DOSAGE (MG/KG/DAY)	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
IV 3	19002	1	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
			1 PUP: STILLBORN. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		22	9 PUPS: APPEARED NORMAL.
	19005	22	16 PUPS: APPEARED NORMAL.
	19035	22	14 PUPS: APPEARED NORMAL.
	19039	2	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		22	14 PUPS: APPEARED NORMAL.
	19040	22	17 PUPS: APPEARED NORMAL.
	19045	22	15 PUPS: APPEARED NORMAL.
	19054	22	5 PUPS: APPEARED NORMAL.
	19058	22	13 PUPS: APPEARED NORMAL.
	19062	22	15 PUPS: APPEARED NORMAL.
	19063	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		22	13 PUPS: APPEARED NORMAL.
	19066	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
			1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		22	12 PUPS: APPEARED NORMAL.
	19069	10	1 PUP: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		22	16 PUPS: APPEARED NORMAL.
	19073	22	13 PUPS: APPEARED NORMAL.

a. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation. Refer to the individual pup clinical observations table (Table C44) for external clinical observations confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C47 (PAGE 6): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP MATERNAL DOSAGE (MG/KG/DAY)	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
V 10	19001	22	11 PUPS: APPEARED NORMAL.
	19006	1	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
			1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		2	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		22	17 PUPS: APPEARED NORMAL.
	19011	22	13 PUPS: APPEARED NORMAL.
	19020	22	13 PUPS: APPEARED NORMAL.
	19022	1	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		22	14 PUPS: APPEARED NORMAL.
	19025	22	20 PUPS: APPEARED NORMAL.
	19027	22	14 PUPS: APPEARED NORMAL.
	19028	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		22	12 PUPS: APPEARED NORMAL.
	19030	22	13 PUPS: APPEARED NORMAL.
	19031	22	14 PUPS: APPEARED NORMAL.
	19032	22	14 PUPS: APPEARED NORMAL.
	19033	22	14 PUPS: APPEARED NORMAL.
	19049	22	15 PUPS: APPEARED NORMAL.
	19059	22	15 PUPS: APPEARED NORMAL.
	19070	1	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		13	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		22	12 PUPS: APPEARED NORMAL.

a. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation. Refer to the individual pup clinical observations table (Table C44) for external clinical observations confirmed at necropsy.

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C48 (PAGE 1): PUP LIVER WEIGHTS - INDIVIDUAL DATA - F1 GENERATION PUPS

RAT/ LITTER NUMBER	LIVER M	LIVER F	LIVER T	TERMINAL BODY WEIGHT M	TERMINAL BODY WEIGHT F	TERMINAL BODY WEIGHT T
DOSAGE GROUP I			0 MG/KG/DAY			
19012	1.864	2.008	1.936	42.68	42.24	42.46
19019	1.436	1.636	1.536	39.70	37.50	38.60
19021	1.360	1.558	1.459	34.74	33.80	34.27
19023	1.814	1.878	1.846	46.02	44.38	45.20
19041	1.114	1.232	1.173	33.00	31.02	32.01
19042	1.390	1.552	1.471	36.12	36.16	36.14
19044	1.798	1.736	1.767	44.30	39.82	42.06
19050	1.336	1.406	1.371	36.42	34.86	35.64
19053	1.438	1.562	1.500	35.60	35.92	35.76
19065	1.266	1.354	1.310	33.08	31.00	32.04
DOSAGE GROUP II			0.3 MG/KG/DAY			
19004	1.138	1.246	1.192	30.78	30.12	30.45
19009	2.350	2.356	2.354	56.35	53.20	54.10
19016	1.874	1.633	1.784	45.32	38.10	42.61
19018	1.768	1.752	1.760	45.50	41.70	43.60
19026	1.062	1.214	1.138	32.30	30.04	31.17
19036	1.596	1.596	1.596	40.74	34.30	37.52
19037	1.170	1.182	1.176	30.66	29.16	29.91
19043	2.098	2.074	2.086	46.34	43.80	45.07
19047	1.510	1.462	1.486	38.78	36.62	37.70
19048	1.826	1.985	1.897	48.96	46.45	47.84
DOSAGE GROUP III			1 MG/KG/DAY			
19003	1.268	0.998	1.133	30.78	27.58	29.18
19007	1.324	1.278	1.301	35.34	29.70	32.52
19008	1.516	1.732	1.624	41.82	40.10	40.96
19013	1.976	1.736	1.856	46.36	42.36	44.36
19015	1.416	1.510	1.463	38.06	35.84	36.95
19017	2.102	2.188	2.145	44.96	43.88	44.42
19024	1.504	1.550	1.524	40.04	37.62	38.83
19029	2.076	1.456	1.766	43.22	33.24	38.23
19034	1.550	1.670	1.610	41.24	38.76	40.00
19056	1.500	1.646	1.573	40.88	39.48	40.18
19005	1.296	1.312	1.304	33.56	30.84	32.20

M = MALE F = FEMALE T = TOTAL

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST (SPONSOR'S STUDY NUMBER: T-7706.1)

TABLE C48 (PAGE 2): PUP LIVER WEIGHTS - INDIVIDUAL DATA - F1 GENERATION PUPS

RAT/ LITTER NUMBER	LIVER M	LIVER F	LIVER T	TERMINAL BODY WEIGHT M	TERMINAL BODY WEIGHT F	TERMINAL BODY WEIGHT T
DOSAGE GROUP IV			3 MG/KG/DAY			
19035	1.192	1.316	1.254	33.82	32.04	32.93
19039	1.540	1.380	1.460	35.14	31.46	33.30
19040	1.226	1.582	1.404	31.48	30.28	30.88
19045	1.624	1.730	1.677	37.66	37.18	37.42
19054	2.137	2.495	2.280	57.13	56.55	56.90
19058	2.364	2.110	2.237	47.80	45.08	46.44
19062	1.470	1.702	1.586	42.50	39.86	41.18
19063	2.040	2.132	2.106	47.60	46.10	46.53
19066	1.582	1.702	1.642	43.76	42.82	43.29
DOSAGE GROUP V			10 MG/KG/DAY			
19001	1.855	1.902	1.881	44.10	44.24	44.18
19006	1.358	1.512	1.435	35.20	32.84	34.02
19011	1.290	1.434	1.362	36.28	35.44	35.86
19020	0.454	0.540	0.497	15.30	15.52	15.41
19022	1.336	1.286	1.311	36.60	34.46	35.53
19025	1.098	1.160	1.129	30.00	26.70	28.35
19027	1.283	1.286	1.284	33.05	31.46	32.17
19028	1.550	1.742	1.646	39.80	40.10	39.95
19030	1.594	1.632	1.613	39.94	39.16	39.55
19031	1.842	1.870	1.856	43.06	40.80	41.93

APPENDIX D

PROTOCOL AND AMENDMENTS

905 Sheehy Drive, Bldg. A
Horsham, PA 19044
Telephone: (215) 443-8710
Telefax: (215) 443-8587



ARGUS RESEARCH
Charles River Laboratories
Discovery and Development Services

PROTOCOL 418-028

SPONSOR'S STUDY NUMBER: T-7706.1

STUDY TITLE: Oral (Gavage) Combined Repeated Dose Toxicity Study of T-7706 with the Reproduction/Developmental Toxicity Screening Test

PURPOSE: The purpose of this study is to provide information on the possible health hazards that may result from repeated exposure of Crl:CD®(SD)IGS BR VAF/Plus® male and female rats to a test substance beginning before cohabitation, through mating and continuing for at least 42 days (male rats) or through parturition until day 21 of lactation (female rats). This repeated dose study incorporates a reproduction/developmental toxicity screening test that can be used to provide initial information on possible effects on male and female reproductive performance (e.g., gonadal function, mating behavior, conception, development of the conceptus and parturition). The study also places emphasis on neurological effects as a specific endpoint and should identify the neurotoxic potential of a test substance, which may warrant further in-depth investigation.

Because of the selectivity of the endpoints and the short duration of the study, the screening test will not provide evidence for definitive claims of no reproduction/developmental effects. In particular, it offers only limited means of detecting postnatal manifestations of prenatal exposure or effects that may be induced during postnatal exposure.

TESTING FACILITY:
Argus Research
905 Sheehy Drive, Building A
Horsham, Pennsylvania 19044-1297
Telephone: (215) 443-8710
Telefax: (215) 443-8587

STUDY DIRECTOR:
Raymond G. York, Ph.D., DABT
Associate Director of Research
Email: raymond.york@criver.com
Address as cited above for Testing Facility

SPONSOR:
3M Corporate Toxicology
3M Center, Building 220-2E-02
St. Paul, Minnesota 55144-1000

STUDY MONITOR:

John Butenhoff, Ph.D., DABT, CIH
3M Corporate Toxicology
3M Medical Department
Telephone: (651) 733-1962
Telefax: (651) 733-1773
Email: jlbutenhoff@mmm.com

REGULATORY CITATIONS:

Organisation for Economic Co-operation and Development (1996). *OECD Guideline for Testing of Chemicals*. Section 4, No. 422: Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test, adopted 22 March 1996.

Organisation for Economic Co-operation and Development (1998). The Revised OECD Principles of Good Laboratory Practices [C(97)186/Final].

U.S. Food and Drug Administration. Good Laboratory Practice Regulations; Final Rule. 21 CFR Part 58.

Japanese Ministry of Health and Welfare (1997). *Good Laboratory Practice Standard for Safety Studies on Drugs*, MHW Ordinance Number 21, March 26, 1997.

REGULATORY COMPLIANCE:

This study will be conducted in compliance with the Good Laboratory Practice (GLP) regulations cited above.

All changes or revisions of this protocol shall be documented, signed by the Study Director and the Sponsor, dated and maintained with the protocol.

The Testing Facility's Quality Assurance Unit (QAU) will audit the protocol, the raw data and the report, and will inspect critical phases of those portions of the study conducted at the Testing Facility in accordance with the Standard Operating Procedures of the Testing Facility.

The final report will include a compliance statement signed by the Study Director that the report accurately reflects the raw data obtained during the performance of the study and that all applicable GLP regulations were followed in the conduct of the study. Should significant deviations from GLP regulations occur, each will be described in detail, together with how the deviation might affect the quality or integrity of the study.

Should any portion of the study be conducted by a subcontractor or by the Sponsor, the Study Director will ensure that a qualified Principal Investigator is identified by the facility conducting that portion of the study. The QAU for this facility will conduct critical phase inspections and audit respective results and reports for that study portion according to the SOPs of that facility. Such critical phase inspection reports and report audits will be submitted by the facility to the Principal Investigator and the Study Director. The dates of the inspections and report submissions will be incorporated into a QAU Statement generated by that facility and provided

to the Testing Facility for inclusion in the final report. In addition, this facility will provide a statement of GLP compliance, as described above, signed by the Principal Investigator for inclusion in the final report.

SCHEMATIC OF STUDY DESIGN AND STUDY SCHEDULE:

See ATTACHMENT 1 to the protocol.

TEST SUBSTANCE AND VEHICLE:

Identification:

Test Substance:

T-7706 [Perfluorohexane Sulfonate Potassium Salt (PFHS)] Lot identification will be documented in the raw data.

The Sponsor will provide to the Testing Facility documentation or certification of the identity, composition, method of synthesis, strength and activity/purity of the test substance. This documentation will be included in the final report.

Vehicle:

Aqueous 0.5% carboxymethlycellulose (CMC) (medium viscosity) prepared using reverse osmosis membrane processed deionized water (R.O. deionized water). Lot identification and Supplier will be documented in the raw data.

Neither the Sponsor nor the Study Director is aware of any potential contaminants likely to be present in the vehicle that would interfere with the results of this study. Therefore, no analyses other than those mentioned in this protocol will be conducted.

Safety Precautions:

Gloves, dust-mist/HEPA-filtered mask, appropriate eye protection and uniform/lab coat to be worn during formulation preparation and dosage. The Material Safety Data Sheet (MSDS) is attached to the protocol (ATTACHMENT 2).

Storage:

Bulk Test Substance:	Room temperature.
Bulk Vehicle Components:	Room temperature.
Prepared Test Substance and Vehicle Formulations:	Refrigerated (2°C to 8°C).

All test substance shipments should be addressed to the attention of Julian Gulbinski, Manager of Formulation Laboratory, at the previously cited Testing Facility address and telephone number.

Shipments should include information concerning storage conditions and shipping cartons should be labeled appropriately. The recipient should be notified in advance of shipment.

FORMULATION:

Frequency of Preparation:

Formulations (suspensions) will be prepared weekly at the Testing Facility.

Detailed preparation procedures will be attached to this protocol (ATTACHMENT 3).

Adjustment for Purity:

The test substance will be considered 100% pure for the purpose of dosage calculations.

Testing Facility Reserve Samples:

The Testing Facility will reserve a sample of each lot of bulk test substance (approximately 1 g) and bulk vehicle components (approximately 1 g or 5 mL) used during the course of the study. Samples will be stored under the previously cited conditions.

ANALYSES:

Results of required analyses will be provided to the Testing Facility for inclusion in the study report.

Samples additional to those described below may be taken if deemed necessary during the course of the study. Additional analyses, if required, will be documented by protocol amendment.

Bulk Test Substance Sampling:

A sample of approximately 1 g of the test substance will be taken on the last day of treatment and sent (ambient conditions) to:

Principal Investigator: Lisa Clemen
3M Environmental Technology and Safety Services
Building 2-3E-09
St. Paul, Minnesota 55133-3331
Telephone: (651) 778-5568
Telefax: (651) 778-6176
Email: laclemen@mmm.com

The recipient will be notified in advance of sample shipment.

Analyses of Prepared Formulations:

Concentration and Homogeneity:

Concentration and homogeneity of the prepared formulations will be verified during the course of this study. Quadruplicate samples (2 mL each) will be taken from the top, middle and bottom of each concentration on the first day of preparation. Two samples from each quadruplicate set will be shipped for analysis; the remaining samples will be retained at the Testing Facility as backup samples. Quadruplicate samples will be taken from each concentration on the last day of preparation. Two samples from each quadruplicate set will be shipped for analysis; the remaining samples will be retained as backup samples. Backup samples will be stored under the previously cited conditions and discarded at the Testing Facility upon the request of the Sponsor.

Stability:

Stability of the prepared formulations will be documented during this study. Two sets of duplicate samples (2 mL each) from each concentration will be taken on the first day of preparation. One sample of each duplicate set will be shipped on the day of preparation. These samples will be analyzed at the following time points: as soon after preparation as possible and ten days after the first analysis. The remaining samples will be retained at the Testing Facility as backup samples. Backup samples will be stored under the previously cited conditions and discarded at the Testing Facility upon the request of the Sponsor.

Shipping Instructions:

Samples to be analyzed will be shipped (refrigerated) to:

Principal Investigator: Lisa Clemen
3M Environmental Technology and Safety Services
Building 2-3E-09
St. Paul, Minnesota 55133-3331
Telephone: (651) 778-5568
Telefax: (651) 778-6176
Email: laclemen@mmm.com

The recipient will be notified in advance of sample shipment.

DISPOSITION:

Prepared formulations will be discarded at the Testing Facility. All remaining bulk test substance will be returned to:

Dan Hakes
3M EHSR - Auto & Chem Grp
3M Center, Building 236-1B-10
St. Paul, Minnesota 55144-1000
Telephone: (651) 733-2392

TEST SYSTEM:

Species/Strain and Reason for Selection:

The Crl:CD®(SD)IGS BR VAF/Plus® rat was selected as the Test System because: 1) it is one mammalian species accepted for use in toxicity studies and it has been widely used throughout industry; 2) this strain of rat has been demonstrated to be sensitive to reproductive and developmental toxins; and 3) historical data and experience exist at the Testing Facility[1-3].

Number:

Initial population acclimated:	100 male and 100 virgin female rats.
Population selected for main study:	75 male and 75 virgin female rats (15 per sex per dosage group).
Population selected for toxicokinetic study:	15 male and 15 female rats (three per sex per dosage group).

Body Weight and Age:

Male rats will be ordered to weigh from 275 g to 300 g each at receipt, at which time they will be expected to be at least 60 days of age. Female rats will be ordered to weigh from 200 g to 225 g each at receipt, at which time they will be expected to be at least 56 days of age. Actual body weights will be recorded the day after receipt and will be documented in the raw data. The weight ranges will be included in the final report. At study initiation, the weight variation of the rats will not exceed ±20% of the mean weight of each sex.

Sex:

Both male and female rats will be evaluated.

Source:

Charles River Laboratories, Inc.

The rats will be shipped in filtered cartons by air freight and/or truck from Charles River Laboratories, Inc., to the Testing Facility.

Identification:

Rats are permanently identified using Monel® self-piercing ear tags (Gey Band and Tag Co., Inc., No. MSPT 20101). Male and female rats are assigned temporary numbers at receipt and given unique permanent identification numbers when assigned to the study before administration of the first dosage. Pups will not be individually identified during lactation; all parameters will be evaluated in terms of the litter.

ANIMAL HUSBANDRY:

All cage sizes and housing conditions are in compliance with the *Guide for the Care and Use of Laboratory Animals*[4]. Argus Research is an AAALAC-accredited facility.

Housing:

Fo generation rats will be individually housed in stainless steel wire-bottomed cages except during the cohabitation and postpartum periods. During cohabitation, each pair of rats will be housed in the male rat's cage. Beginning no later than day 20 of presumed gestation, Fo generation female rats will be individually housed in nesting boxes. Each dam and delivered litter will be housed in a common nesting box during the postpartum period.

Nesting Material:

Nesting material (bed-o'cobs®) will be provided.

Bedding will be changed as often as necessary to keep the animals dry and clean. Analyses for possible contamination are conducted semi-annually and documented in the raw data.

Room Air, Temperature and Humidity:

The animal room is independently supplied with at least ten changes per hour of 100% fresh air that has been passed through 99.97% HEPA filters. Room temperature will be maintained at 64°F to 79°F (18°C to 26°C) and monitored constantly. Room humidity will also be monitored constantly and maintained at 30% to 70%.

Light:

An automatically controlled 12-hour light:12-hour dark fluorescent light cycle will be maintained. Each dark period will begin at 1900 hours EST. The light cycle may be adjusted by the Study Director or designee if deemed necessary to accommodate scheduled laboratory activities. Any such adjustment will be documented in the raw data.

Diet:

Rats will be given Certified Rodent Diet® #5002 (PMI Nutrition International) available *ad libitum* from individual feeders. Feed will be removed the evening prior to the scheduled sacrifice.

Water:

Water will be available *ad libitum* from individual bottles attached to the cages or from an automatic watering access system. All water will be from a local source and passed through a reverse osmosis membrane before use. Chlorine will be added to the processed water as a bacteriostat; processed water is expected to contain no more than 1.2 ppm chlorine at the time of analysis. Water is analyzed monthly for possible bacterial contamination and twice annually for possible chemical contamination.

Contaminants:

Neither the Sponsor nor the Study Director is aware of any potential contaminants likely to be present in the certified diet, in the drinking water or in the nesting materials at levels that would interfere with the results of this study. Therefore, no analyses other than those routinely performed by the feed supplier or those mentioned in this protocol will be conducted.

DAY NUMBERING SYSTEM:

Gestation day 0 is defined as the day spermatozoa are observed in a smear of the vaginal contents and/or a copulatory plug observed *in situ*.

The day of birth is designated lactation day 0 (postpartum day 0) in the Health Effects Test Guidelines - Reproduction and Fertility Effects (Office of Prevention, Pesticides and Toxic Substances 870.3800, August, 1998) and in the OECD Guideline for the Testing of Chemicals - Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (Section 4, No. 422, 22 March 1966). This same day is designated day 1 postpartum (day 1 of lactation) in the Standard Operating Procedures of the Testing Facility. Throughout this protocol, the day of birth will be designated day 1 postpartum (day 1 of lactation) and all subsequent ages of the F1 generation rats and days of the lactation period will be determined and cited accordingly.

RANDOMIZATION AND COHABITATION:

Upon arrival, rats will be assigned to individual housing on the basis of computer-generated random units. During an acclimation period of at least five days, male and female rats will be selected for study on the basis of physical appearance and body weights recorded during acclimation. The rats will be assigned to dosage groups based on computer-generated (weight-ordered) randomization procedures.

Within each dosage group, consecutive order will be used to assign rats to cohabitation, one male rat per female rat. The cohabitation period will consist of a maximum of 14 days. Female rats with spermatozoa observed in a smear of the vaginal contents and/or a copulatory plug observed *in situ* will be considered to be at day 0 of presumed gestation and assigned to individual housing. Female rats not mated within the first seven days of cohabitation will be assigned alternate male rats that have mated (same dosage group) and will remain in cohabitation for a maximum of seven additional days.

Day 1 of lactation (postpartum) is defined as the day of birth and is also the first day on which all pups in a litter are individually weighed (pup body weights will be recorded after all pups in a litter are delivered and groomed by the dam).

Litters will not be culled during the lactation period, because random selection of pups for culling could result in potential biases in pup viabilities and body weight gains over this period.

Within each dosage group, consecutive order will be used to assign the first 10 male and the first 10 female rats to a functional observational battery (FOB) and motor activity assessment, blood sample collection for clinical chemistry and hematology (CC&H), and histological evaluations.

On day 22 postpartum, a table of random units will be used to select five male and five female pups per litter for blood sample and liver collection; these pups will only be selected from the ten dams selected for FOB, motor activity, CC&H and histological evaluation.

ADMINISTRATION:

Route and Reason for Choice:

The oral (gavage) route was selected for use because: 1) in comparison with the dietary route, the exact dosage can be accurately administered; and 2) it is one of the possible routes for environmental exposure.

Method and Frequency:

Dosages will be adjusted daily for body weight changes and given at approximately the same time each day. The first day of dosage is designated as day 1 of study.

Male rats will be given the test substance once daily beginning 14 days before a cohabitation period that consists of a maximum 14 days. Dosage will continue through the day before sacrifice, after completion of the cohabitation period, after a minimum of 42 days of administration.

Female rats will be given the test substance once daily beginning 14 days before a cohabitation period that consists of a maximum of 14 days. Dosage will continue through the day before scheduled sacrifice (day 21 of lactation).

Rationale for Dosage Selection:

Dosages were selected by the Sponsor based on previous studies conducted with the test substance, taking into account possible differences in sensitivity between pregnant and nonpregnant rats. The highest dosage will be expected to cause toxic effects but not mortality or obvious suffering. The descending sequence of the lower dosage levels will be selected for the purpose of demonstrating any dosage-related response, with no adverse effects expected at the lowest level.

Dosage Levels, Concentrations and Volumes:

Dosage Group	Number of Rats Per Sex	Dosage (mg/kg/day)	Concentration[a] (mg/mL)	Dosage Volume (mL/kg)	Argus Batch Number
I	15 + 3[b]	0	0	10	B-418-028-A(Day.Month.Year)
II	15 + 3[b]	0.3	0.03	10	B-418-028-B(Day.Month.Year)
III	15 + 3[b]	1	0.1	10	B-418-028-C(Day.Month.Year)
IV	15 + 3[b]	3	0.3	10	B-418-028-D(Day.Month.Year)
V	15 + 3[b]	10	1	10	B-418-028-E(Day.Month.Year)

a. The test substance will be considered 100% pure for the purpose of dosage calculations.
b. Three additional rats per sex per dosage group will be assigned to toxicokinetic sample collection.

TESTS, ANALYSES AND MEASUREMENTS - Fo GENERATION:

Viability - Male and Female Rats:

All Periods: At least twice daily.

Clinical Observations and/or General Appearance - Male and Female Rats:

Acclimation Period: Weekly.

Dosage Period: Daily before dosage. On the first day of dosage, postdosage observations will be recorded at approximately hourly intervals for the first four hours and at the end of the normal working day. Subsequent postdosage observations will be recorded at intervals deemed appropriate by the Study Director or designee after determination of peak toxicologic effects.

Maternal Behavior: Days 1, 5, 8, 15 and 22 postpartum. Observed abnormal behavior recorded daily.

Clinical observations may be recorded more frequently than cited above, if deemed appropriate by the Study Director and/or Study Monitor.

Data collected for rats assigned to toxicokinetic sample collection will not be summarized or analyzed statistically.

Detailed Clinical Observations - Male and Female Rats:

Once before the first dosage and at least once weekly thereafter, detailed clinical observations will be conducted for all male and female rats. These observations will be made outside the cage in a standard arena at the same time each day of conduct. Effort will be made to ensure that variations in the test conditions are minimal and that observations are conducted by observers unaware of treatment groups. Signs noted should include, but not be limited to: changes in skin, fur, eyes, mucous membranes, occurrence of secretions and excretions and autonomic activity (e.g., lacrimation, piloerection, pupil size, unusual respiratory pattern). Changes in gait, posture

and response to handling as well as the presence of clonic or tonic movements, sterotypic behavior (e.g., excessive grooming, repetitive circling), difficult or prolonged parturition or bizarre behavior (e.g., self-mutilation, walking backwards) should also be recorded.

Body Weights - Male and Female Rats:

Acclimation Period:	Weekly.
Dosage Period:	Daily.
Sacrifice:	Terminal weight.

Feed Consumption Values - Male Rats (recorded and tabulated):

Dosage Period:	Weekly.

Feed Consumption Values - Female Rats (recorded and tabulated):

Dosage Period:	Weekly to cohabitation.
Gestation Period:	Days 0, 7, 10, 12, 15, 18, 20 and 25 (if necessary).
Postpartum Period:	Days 1, 5, 8 and 15.

Feed consumption not tabulated after day 15 postpartum, when it is expected that pups will begin to consume maternal feed.

Feed Consumption Values - Male and Female Rats:

Feed consumption values may be recorded more frequently than cited above if it is necessary to replenish the feed. During cohabitation, when two rats occupy the same cage with one feed jar, replenishment of the feed jars will be documented. Individual values will not be recorded or tabulated.

Toxicokinetic Sample Collection:

On day 14 and 42 of study, blood samples (approximately 1 mL each) will be collected from each male rat assigned to the toxicokinetic sample collection portion of the study (3 per group).

On day 14 of study and day 21 of presumed gestation, blood samples (approximately 1 mL each) will be collected from each female rat assigned to the toxicokinetic sample collection portion of the study (3 per group). Samples will be collected prior to dosage on day 14 of study. The time of each blood collection will be recorded in the raw data.

Blood will be collected from the orbital sinus. If necessary, blood may be collected from an alternate site; if so, the alternate site will be documented in the raw data.) The samples will be transferred into EDTA-coated (purple top) tubes and spun in a centrifuge. The resulting serum will be transferred into polypropylene tubes labeled with the protocol number, Sponsor study number, animal number, sex, group number, dosage level, day of study, collection interval, date of collection, species, generation and storage conditions. All samples will be immediately frozen on dry ice and maintained frozen (≤-70°C) until shipment for analysis.

After the last blood sample collection, rats will be sacrificed and samples of the liver will be collected for analysis.

Shipping Instructions:

Samples to be analyzed will be shipped on dry ice to:

Principal Investigator: Lisa Clemen
3M Environmental Technology and Safety Services
Building 2-3E-09
St. Paul, Minnesota 55133-3331
Telephone: (651) 778-5568
Telefax: (651) 778-6176
Email: laclemen@mmm.com

The recipient will be notified in advance of sample shipment.

Estrous Cycling and Mating:

Estrous cycling will be evaluated by examination of vaginal cytology beginning with the day after the first administration and then until spermatozoa are observed in a smear of the vaginal contents and/or a copulatory plug is observed *in situ* during the cohabitation period.

Caesarean-Sectioning - Toxicokinetic Study:

On day 21 of presumed gestation, blood and liver samples will be collected from all female rats designated for toxicokinetic sample collection.

Blood samples will be collected from the rats as previously described. After sacrifice, the liver of each rat will be excised and the liver weight will be recorded. The median liver lobe will be frozen and stored (≤-20°C) until shipment for possible analysis.

The fetuses will be removed from the uterus and blood samples will be collected from each fetus via decapitation. Blood will be placed into tubes, pooled per litter, allowed to clot and spun in a centrifuge; the resulting serum will be transferred into labeled polypropylene tubes. All samples will be immediately frozen on dry ice and maintained frozen (≤-70°C) until shipment for analysis.

The liver from each fetus will be collected, pooled per litter and placed into labeled tubes. The samples will be frozen and stored (≤-20°C) until shipment for analysis.

Samples will be shipped on dry ice to Lisa Clemen at the previously cited address.

Natural Delivery:

Female rats will be evaluated for:

Adverse Clinical Signs Observed During Parturition.

Duration of Gestation (day 0 of presumed gestation to the time the first pup is observed).

Litter Size (defined as all pups delivered).

Pup Viability at Birth.

Functional Observational Battery:

On one occasion during the course of the study, a functional observational battery (FOB)[5-8] will be conducted on 10 male and 10 female rats per group. For male rats, this assessment will be conducted shortly before scheduled sacrifice, but prior to blood sample collection for hematology and clinical chemistry evaluations. Female rats should be tested during the lactation period, shortly before scheduled sacrifice.

The FOB, to be conducted by an observer unaware of the group assignment of the rat, will assess the following parameters:

1. Lacrimation, salivation, palpebral closure, prominence of the eye, pupillary reaction to light, piloerection, respiration, and urination and defecation (autonomic functions).

2. Sensorimotor responses to visual, auditory, tactile and painful stimuli (reactivity and sensitivity).

3. Reactions to handling and behavior in the open field (excitability).

4. Gait pattern in the open field, severity of gait abnormalities, air righting reaction, and landing foot splay (gait and sensorimotor coordination).

5. Forelimb and hindlimb grip strength.

6. Abnormal clinical signs including but not limited to convulsions, tremors and other unusual behavior, hypotonia or hypertonia, emaciation, dehydration, unkempt appearance and deposits around the eyes, nose or mouth.

Evidence of the ability of this battery to detect the effects of positive control substances will be provided (Testing Facility Positive Control Data). Data will also be provided to document interobserver reliability if more than one observer is involved in the testing.

Motor Activity Test:

Motor activity will be evaluated on 10 male and 10 female rats per group once during the course of the study. This assessment will be conducted shortly before scheduled sacrifice, but prior to blood sample collection.

The movements of each rat will be monitored by a passive infrared sensor mounted outside a stainless-steel wire-bottomed cage (40.6 x 25.4 x 17.8 cm). Each test session will be 1.5 hours in duration with the number of movements and time spent in movement tabulated at each five-minute interval. The apparatus will monitor a rack of up to 32 cages and sensors during each session, with each rat tested in the same location on the rack across test sessions. Groups will be counterbalanced across testing sessions and cages.

Data will be provided to demonstrate that the test system is capable of detecting increases in activity produced by positive control substances (Testing Facility Positive Control Data).

HEMATOLOGY AND CLINICAL CHEMISTRY:

At scheduled sacrifice, the rats (fasted) assigned to hematology and clinical chemistry (H&CC) sample collection will be exsanguinated from the inferior vena cava following sacrifice by carbon dioxide asphyxiation. Approximately 5 mL of blood will be collected and processed as described below. Determinations additional to those described below may be conducted if the known properties of the test substance may, or are suspected to, affect related metabolic profiles (e.g., calcium, phosphate, fasting triglycerides and fasting glucose, specific hormones, and cholinesterase).

Hematology:

Approximately 1 mL of blood will be collected into EDTA-coated tubes and maintained on wet ice or refrigerated until shipment for analysis of the following hematologic parameters:

Erythrocyte Count (RBC)
Hematocrit (HCT)
Hemoglobin (HGB)
Mean Corpuscular Hemoglobin (MCH)
Mean Corpuscular Hemoglobin Concentration (MCHC)
Mean Corpuscular Volume (MCV)
Leukocyte Count, Total (WBC)
Leukocyte Count, Differential
Platelet Count (PLAT)
Mean Platelet Volume (MPV)
Cell Morphology

Two blood smear slides will be prepared at the Testing Facility for each sample for measurements of differential leukocyte count. All samples (on wet ice) and slides (ambient conditions) will be shipped to Redfield Laboratories at the following address.

Approximately 1.8 mL of blood will be added to a tube containing 0.2 mL of sodium citrate (0.129 M). The contents will be mixed and maintained on wet ice until the tubes are centrifuged

(within 30 minutes of the collection time). The resulting plasma will be transferred 2.0 mL polypropylene tubes labeled with study number, Sponsor's study number, rat number, dosage level, day of study, collection interval, date of collection, species, generation and storage. All samples will be frozen on dry ice and maintained frozen (≤-70°C) until shipment on dry ice by overnight courier for measurement of prothrombin time (PT) and activated partial thromboplastin time (APTT).

Clinical Chemistry:

Approximately 2 mL of blood will be collected into serum separator tubes and centrifuged. The resulting sera samples will be immediately frozen on dry ice and maintained frozen (≤-70°C) until shipment for analysis of the following parameters:

Total Protein (TP)	Creatinine Kinase (CK)
Triglycerides (TRI)	Alanine Aminotransferase (ALT)
Albumin (A)	Aspartate Aminotransferase (AST)
Globulin (G)	Alkaline Phosphatase (ALK)
Albumin/Globulin Ratio (A/G)	Calcium (CA)
Glucose (GLU)	Phosphorus (PHOS)
Cholesterol (CHOL)	Sodium (NA)
Total Bilirubin (TBILI)	Potassium (K)
Urea Nitrogen (BUN)	Chloride (CL)
Creatinine (CREAT)	

Samples will be shipped (on dry ice) to Redfield Laboratories at the following address.

Shipping Instructions:

Samples will be shipped to arrive on Monday through Friday according to the conditions described above to:

Principal Investigator: Ms. Phyllis Powell
Redfield Laboratories
A Division of CRL-DDS
100 East Boone Street
P.O. Box 308
Redfield, Arkansas 72132
Telephone: (501) 397-2540
Telefax: (501) 397-2002

The recipient will be notified in advance of sample shipment.

URINALYSIS:

Urinalysis will not be conducted unless indicated based on expected or observed toxicity of the test substance.

METHOD OF SACRIFICE:

Fo generation rats will be sacrificed by carbon dioxide asphyxiation.

GROSS NECROPSY AND HISTOPATHOLOGY - Fo GENERATION RATS:

Scheduled Sacrifice - Toxicokinetic Study:

Scheduled sacrifice of male rats will be conducted on day 42 of study. Scheduled sacrifice of female rats will be conducted on day 21 of presumed gestation.

Blood samples will be collected from the rats as previously described. After sacrifice, the liver of each rat will be excised and the liver weight will be recorded. The median liver lobe will be frozen and stored (≤-20°C) until shipment for analysis. Fetal samples will be collected as previously described.

Carcasses will be discarded without further evaluation.

Samples will be shipped on dry ice to Lisa Clemen at the previously cited address.

Scheduled Sacrifice - Main Study:

Scheduled sacrifice of male rats will be conducted on the day following the last dosage administration, after a minimum of 42 days of dosage. Scheduled sacrifice of female rats will be conducted on day 22 of lactation.

Gross necropsy of all male and female rats will include an initial physical examination of external surfaces and all orifices, as well as the cranial, thoracic and abdominal cavities and their contents. Special attention will be paid to the organs of the reproductive system. The number of implantation sites and corpora lutea will be recorded.

Male and female rats will be examined for gross lesions. Gross lesions will be retained in neutral buffered 10% formalin and examined histologically. Tissue trimming and histopathology will be performed under the supervision of or by a Board-Certified Veterinary Pathologist.

The ovaries and the uterus with cervix of each female rat will be weighed, and ovaries, uterus, vagina and a mammary gland will be retained in neutral buffered 10% formalin. Uteri of apparently nonpregnant rats will be examined after being pressed between glass plates to confirm the absence of implantation sites, and retained in neutral buffered 10% formalin.

Sperm Evaluations of Male Rats:

To assess the potential toxicity of the test article on the male reproductive system, the endpoints listed below will be evaluated from the first 10 male rats in each dosage group.

> Organ Weights: The following organs will be individually weighed: right testis, left testis, left epididymis (whole and cauda), right epididymis, seminal vesicles (with and without fluid) and prostate.
>
> Sperm Evaluations: Sperm concentration and motility will be evaluated using computer-assisted sperm analysis (CASA). Motility will be evaluated by the Hamilton Thorne IVOS by collection of a sample from the left vas deferens. A homogenate will be prepared from the left cauda epididymis for evaluation by the Hamilton Thorne IVOS to determine sperm concentration (sperm per gram of tissue weight). The remaining portion of the left cauda epididymis will be used to manually evaluate sperm morphology. Sperm morphology evaluations will include the following: 1) determination of the percentage of normal sperm in a sample of at least 200; and 2) qualitative evaluation of abnormal sperm, including such categories as abnormal head, abnormal tail, and abnormal head and tail.

See ATTACHMENT 4 for additional tissues to be weighed and retained from the ten rats per sex per group assigned to histological sample collection and evaluation.

All other tissues will be discarded.

Scheduled Sacrifice of Female Rats that Do Not Deliver Litters:

Rats that do not deliver a litter will be sacrificed on day 25 of presumed gestation. Gross necropsy, examination and tissue retention will be conducted as described previously for rats at scheduled sacrifice.

Dams with No Surviving Pups:

Dams with no surviving pups will be sacrificed after the last pup is found dead, missing or presumed cannibalized. Gross necropsy, examination and tissue retention will be conducted as described above for rats at scheduled sacrifice.

Rats Found Dead or Moribund:

Rats that die or are sacrificed because of moribund condition, abortion or premature delivery will be examined for the cause of death or moribund condition on the day the observation is made. The rats will be examined for gross lesions. Testes and epididymides of male rats will be excised and paired organ weights will be recorded. The epididymides will be retained in neutral buffered 10% formalin. The testes will be fixed in Bouin's solution for 48 to 96 hours and then retained in neutral buffered 10% formalin. Pregnancy status and uterine contents of female rats will be recorded. Aborted fetuses and/or delivered pups will be examined to the extent possible. Uteri of apparently nonpregnant rats will be examined after being pressed between glass plates to confirm the absence of implantation sites. Ovaries and uteri will be retained in neutral buffered 10% formalin.

TESTS, ANALYSES AND MEASUREMENTS - F1 GENERATION:

Viability:

Preweaning Period: Litters will be observed for dead pups at least twice daily. The pups in each litter will be counted once daily.

Clinical Observations and/or General Appearance:

Preweaning Period: Once daily.

Pups will be observed if they are warm and clean, for evidence of a nest and if pups are grouped together and nursing or have milk in stomach. Each pup will be examined for general shape of the head, trunk, limbs, tail and presence of anus.

Clinical observations may be recorded more frequently than cited above, if deemed appropriate by the Study Director and/or the Study Monitor.

Body Weights:

Preweaning Period: Days 1 (birth), 8, 15 and 22 postpartum.

Sacrifice: Terminal weight.

Feed Consumption Values (recorded and tabulated):

Preweaning Period: Not recorded.

METHOD OF SACRIFICE - F1 GENERATION PUPS:

F1 generation pups will be sacrificed by carbon dioxide asphyxiation.

NECROPSY - F1 GENERATION:

Gross lesions will be retained in neutral buffered 10% formalin for possible future evaluation. Unless specifically cited below, all other tissues will be discarded.

Pups Found Dead on Day 1 Postpartum:

Pups that die before examination of the litter for pup viability will be evaluated for vital status at birth. The lungs will be removed and immersed in water. Pups with lungs that sink will be identified as stillborn; pups with lungs that float will be identified as liveborn, and to have died shortly after birth. Pups with gross lesions will be preserved in Bouin's solution for possible future evaluation.

Pups Found Dead or Moribund on Days 2 to 4 Postpartum:

Pups found dead or sacrificed because of moribundity will be examined for gross lesions and for the cause of death or the moribund condition. Pups with gross lesions will be preserved in Bouin's solution for possible future evaluation.

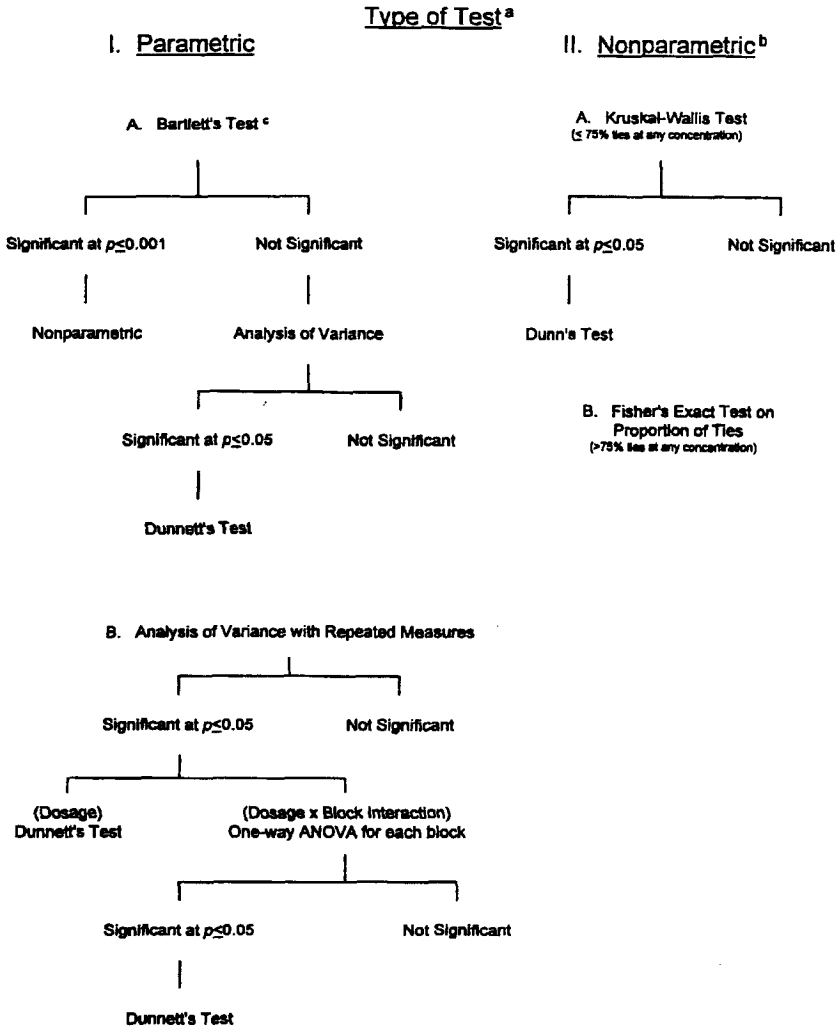
Scheduled Sacrifice:

On day 22 postpartum, pups will be will be sacrificed and examined for gross lesions; gross lesions will be preserved in neutral buffered 10% formalin. Necropsy will include a single cross-section of the head at the level of the frontal-parietal suture and examination of the cross-sectioned brain for apparent hydrocephaly.

Blood samples will be collected from each selected pup (5 per sex per litter from the 10 females per group selected for FOB and motor activity assessment, blood sample collection for H&CC, and histological evaluations) from the vena cava. The blood will be placed into tubes, pooled per litter, allowed to clot and spun in a centrifuge; the resulting serum will be transferred into labeled polypropylene tubes. All samples will be immediately frozen on dry ice and maintained frozen ($\leq$-70°C) until shipment for analysis. The liver from each selected pup will be collected excised and the organ weight recorded. The median lobe will be frozen and stored ($\leq$-20°C) until shipment for possible analysis. Frozen samples will be shipped to Lisa Clemen at the previously cited address. The remaining portion of each liver will be retained in neutral buffered 10% formalin for possible histological evaluation. The livers will be processed and evaluated histologically as described for the Fo generation rats in Histological Evaluation in ATTACHMENT 4.

PROPOSED STATISTICAL TESTS[9-16]:

The following schematic represents statistical analyses of the data.



---

a. Statistically significant probabilities are reported as either $p \leq 0.05$ or $p \leq 0.01$.
b. Proportion data are not included in this category.
c. Test for homogeneity of variance.

Test items in the FOB using interval scales, such as the grip-strength tests and the landing foot splay test, as well as body weight data and feed consumption values will be analyzed as described under the Parametric heading of the schematic. Bartlett's Test of Homogeneity of Variances[9] will be used to estimate the probability that the groups had different variances. A nonsignificant result ($p>0.001$) will indicate that an assumption of homogeneity of variance is not inappropriate, and the data will be compared using the Analysis of Variance Test[10]. If that test is significant ($p\leq0.05$), the groups exposed to the test article/substance will be compared with the control group using Dunnett's Test[11]. If Bartlett's Test is significant ($p\leq0.001$), the Analysis of Variance Test is not appropriate, and the data will be analyzed as described under the Nonparametric heading of the schematic. When 75% or fewer of the scores in all the groups are tied, the Kruskal-Wallis Test[12] will be used to analyze the data, and in the event of a significant result ($p\leq0.05$), Dunn's Test[13] will be used to compare the groups exposed to the test article/substance with the control group. When more than 75% of the scores in any group are tied, Fisher's Exact Test[14] will be used to compare the proportion of ties in the groups.

Data from the motor activity test, with repeated measurements within a session, will be analyzed using an Analysis of Variance with Repeated Measures[15], as described under that heading in the schematic. A significant effect ($p\leq0.05$) in that test can appear as effect of Concentration (a difference between groups in the total across all measurements in a session) or as an interaction between Concentration and Block (a difference between groups at specific measurement periods). If the Concentration effect is significant, the totals for the control group and the groups given the test article/substance will be compared using Dunnett's Test. If the Concentration x Block interaction is significant, an Analysis of Variance Test will be used to evaluate the data at each measurement period, and a significant result ($p\leq0.05$) will be followed by a comparison of the groups using Dunnett's Test.

Test items in the FOB having graded or count scores will be analyzed using the procedures described under the Nonparametric heading of the schematic.

Clinical observation incidence data, as well as the descriptive and quantal data from the FOB, will be analyzed as contingency tables using the Variance Test for Homogeneity of the Binomial Distribution[16].

Alternate or additional statistical evaluations may be performed if deemed necessary or appropriate.

DATA ACQUISITION, VERIFICATION AND STORAGE:

Data generated during the course of this study will be recorded either by hand or using the *Argus Automated Data Collection and Management System*, the *Vivarium Temperature and Relative Humidity Monitoring System*, the *Coulbourn Instruments Passive Infrared Motor Activity System*, the *Coulbourn Instruments Auditory Startle System*, the *Coulbourn Instruments Spatial Delayed Alternation System*, and/or the passive avoidance software. All data will be tabulated, summarized and/or statistically analyzed using the *Argus Automated Data Collection and Management System*, the *Vivarium Temperature and Relative Humidity Monitoring System, Microsoft Excel* [part of Microsoft Office 97 (version SR-2)] and/or *The SAS System* (version 6.12).

Records will be reviewed by the Study Director and/or appropriate management personnel within 21 days after generation. All original records will be stored in the archives of the Testing Facility. All original data will be bound and indexed. A copy of all raw data will be supplied to the Sponsor upon request. Preserved tissues will be stored at the Testing Facility at no charge for one year after mailing of the draft final report, after which time the Sponsor will be contacted to determine the disposition of these materials.

KEY PERSONNEL:

Executive Director of Research: Mildred S. Christian, Ph.D., Fellow, ATS
Director of Research: Alan M. Hoberman, Ph.D., DABT
Associate Director of Research and Study Director: Raymond G. York, Ph.D., DABT
Director of Operations and Compliance: Barbara J. Patterson, B.A.
Director of Laboratory Operations: John F. Barnett, B.S.
Director of Study Management: Valerie A. Sharper, M.S.
Manager of Animal Operations: Dena C. Lebo, V.M.D.
Chairperson, Institutional Animal Care and Use Committee: Douglas B. Learn, Ph.D.
Consultant, Veterinary Pathology: W. Ray Brown, D.V.M., Ph.D., ACVP

RECORDS TO BE MAINTAINED:

Protocol and Amendments.
Test Substance, Vehicle and/or Reagent Receipt, Preparation and Use.
Animal Acquisition.
Randomization Schedules.
Mating History.
Treatment (if prescribed by Staff Veterinarian).
General Comments.
Clinical Observations and/or General Appearance.
Body Weights.
Feed Consumption Values.
Natural Delivery Observations.
FOB and Motor Activity Observations.
Blood Sample Collection, Processing and Shipment.
Gross Necropsy Observations.
Organ Weights.
Photographs (if required).
Study Maintenance (room and environmental records).
Feed and Water Analyses.
Packing and/or Shipment Lists.

FINAL REPORT:

The Study Director will provide periodic updates of study progress to the Sponsor. Draft summary tables of unaudited computer-recorded data may accompany these updates. Statistical analyses will not be performed on these interim data.

A comprehensive draft final report will be prepared on completion of the study and will be finalized following consultation with the Sponsor. The report will include the following:

> Summary and Conclusion.
> Experimental Design and Method.
> Evaluation of Test Results.
> Appendices: Figures, Summary and Individual Tables Summarizing the Above Data, Protocol and Associated Amendments and Deviations, Study Director's GLP Compliance Statement, Reports of Supporting Data (if appropriate) and QAU Statement.

The Sponsor will receive one copy of the draft report and two copies of the final report. Data will be hand- and/or computer-recorded. Records will be reviewed by the Study Director and/or appropriate management personnel within 21 days after generation. All original records will be stored in the archives of the Testing Facility. All original data will be bound and indexed. A copy of all raw data will be supplied to the Sponsor upon request. Preserved tissues will be stored at the Testing Facility at no charge for one year after mailing of the draft final report, after which time the Sponsor will be contacted to determine the disposition of these materials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE STATEMENT:

The procedures described in this protocol have been reviewed by the Testing Facility's Institutional Animal Care and Use Committee. All procedures described in this protocol that involve study animals will be conducted in a manner to avoid or minimize discomfort, distress or pain to the animals.

The Sponsor's signature below documents the fact that information concerning the necessity for conducting this study and the fact that this is not an unnecessarily duplicative study may be obtained from the Sponsor. No alternative (*in vitro*) procedures were available for meeting the stated purposes of the study.

REFERENCES:

1. Christian, M.S. and Voytek, P.E. (1982). *In Vivo Reproductive and Mutagenicity Tests.* Environmental Protection Agency, Washington, D.C. National Technical Information Service, U.S. Department of Commerce, Springfield, VA 22161.

2. Christian, M.S. (1984). Reproductive toxicity and teratology evaluations of naltrexone (Proceedings of Naltrexone Symposium, New York Academy of Sciences, November 7, 1983), J. Clin. Psychiat. 45(9):7-10.

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11. Dunnett, C.W. (1955). A multiple comparison procedure for comparing several treatments with a control. J. Amer. Stat. Assoc. 50:1096-1121.

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15. SAS Institute, Inc. (1988). Repeated measures analysis of variance. *SAS/STAT™ User's Guide*, Release 6.03 Edition, Cary, NC, pp. 602-609.

16. Snedecor, G.W. and Cochran, W.G. (1967). Variance test for homogeneity of the binomial distribution. *Statistical Methods*, 6th Edition, Iowa State University Press, Ames, pp. 240-241.

PROTOCOL APPROVAL:

FOR THE TESTING FACILITY

Alan M. Hoberman, Ph.D., DABT
Director of Research

26 MARCH 2002
Date

Raymond G. York, Ph.D., DABT
Associate Director of Research
Study Director

26 MAR 2002
Date

for Theresa H. Woodard, D.V.M.
Member, Institutional Animal Care and
Use Committee

26 Mar 2002
Date

FOR THE SPONSOR

John Butenhoff, Ph.D., DABT, CIH
Study Monitor and
Sponsor's Representative

1 April, 2002
Date

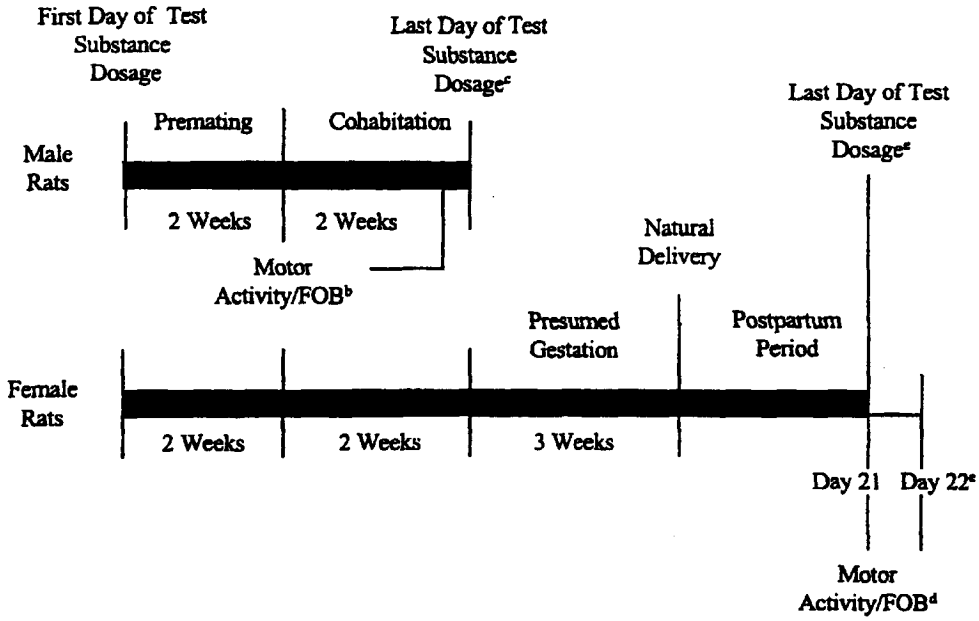
ATTACHMENT 1

SCHEMATIC OF STUDY DESIGN AND STUDY SCHEDULE

ATTACHMENT 1

STUDY SCHEMATIC

COMBINED REPEAT DOSE AND REPRODUCTIVE/DEVELOPMENTAL TOXICITY SCREEN[a]



Dosage Period

a. For additional details see "Tests, Analyses and Measurements" section of the protocol.
b. FOB and motor activity evaluations conducted on ten males per group.
c. Male rats sacrificed after completion of at least 42 days of dosage; necropsy and retention of male reproductive organs. Hematology, clinical biochemistry and histological samples collected from ten male rats per group.
d. Ten female rats per group assigned to FOB evaluation and motor activity evaluation.
e. Ten female rats per group and their litters sacrificed on day 22 postpartum; necropsy and retention of female reproductive organs. Hematology, clinical biochemistry and histological samples collected. Remaining female rats sacrificed on day 22 postpartum and discarded.

SCHEDULE[a]

26 MAR 02	Animal Receipt - Acclimation Begins.
01 APR 02	Start of Dosage Period - Male Rats (14 days before cohabitation and through a 14-day cohabitation period until the day before sacrifice after at least 42 days of dosage).
01 APR 02 - 12 JUN 02	Dosage Period - Female Rats (14 days before cohabitation through Day 22 of lactation).
	Cohabitation Period (Maximum of 14 days).
14 APR 02 PM - 21 APR 02 AM	Male 1 (7 days)
21 APR 02 PM - 28 APR 02 AM	Male 2 (7 days)
14 APR 02	Day 14 Toxicokinetic Sample Collection
15 APR 02	First Possible Day 0 of Presumed Gestation.
28 APR 02	Last Possible Day 0 of Presumed Gestation.
06 MAY 02	First Possible Day 21 of Presumed Gestation Toxicokinetic Sample Collection and Sacrifice - Toxicokinetic Study Female Rats
19 MAY 02	Last Possible Day 21 of Presumed Gestation Toxicokinetic Sample Collection and Sacrifice - Toxicokinetic Study Female Rats
06 MAY 02 - 07 MAY 02	FOB and Motor Activity Evaluation - 10 Male Rats per Group

---

a. The start date of the study is the day the Study Director signs the protocol.
b. Throughout this schedule, the day of birth is designated day 1 postpartum (day 1 of lactation) and all subsequent ages of the F1 generation rats and days of the lactation period will be determined and cited accordingly, as described above the protocol section, "Day Numbering System."

06 MAY 02	First Possible Delivery (Day 21 of presumed gestation).
23 MAY 02	Last Possible Delivery (Day 25 of presumed gestation).
10 MAY 02	First Possible Day 25 of Presumed Gestation Female Sacrifice.
23 MAY 02	Last Possible Day 25 of Presumed Gestation Female Sacrifice.
12 MAY 02	Day 42 Toxicokinetic Sample Collection and Scheduled Sacrifice - Toxicokinetic Study Male Rats
13 MAY 02	Scheduled Sacrifice - Main Study Male Rats (Earliest possible date). Hematology, Clinical Biochemistry and Histological Sample Collection of Selected Male Rats.
23 MAY 02 - 09 JUN 02	FOB and Motor Activity Evaluation - 10 Female Rats per Group.
27 MAY 02 - 13 JUN 02	Day 22 Postpartum - Sacrifice Female Rats and Pups. Hematology, Clinical Chemistry and Histological Sample Collection of Selected Female Rats and Pups.
24 SEP 02	Draft Final Report

ATTACHMENT 2

MATERIAL SAFETY DATA SHEET

MATERIAL SAFETY DATA SHEET (Experimental)

3M
3M Center
St. Paul, Minnesota
55144-1000
1-800-364-3577 or (651) 737-6501 (24 hours)

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1) the information is copied in full with no changes unless prior agreement is obtained from 3M, and
2) neither the copy nor the original is resold or otherwise distributed with the intention of earning a profit thereon.

DIVISION: 3M SPECIALTY MATERIALS
MATERIAL:
L-9051 DEVELOPMENTAL PRODUCT
ISSUED: December 07, 1999
SUPERSEDES: May 17, 1999
DOCUMENT: 04-5470-2

1. INGREDIENT

INGREDIENT	C.A.S. NO.	PERCENT
POTASSIUM PERFLUOROHEXANE SULFONATE.....	3871-99-6	100.0
RESIDUAL ORGANIC FLUOROCHEMICALS.....	Mixture	Unknown

This material is not listed on the TSCA inventory and should be used for research and development purposes only under the direct supervision of a technically qualified individual.

2. PHYSICAL DATA

BOILING POINT:..... N/A
VAPOR PRESSURE:..... Negligible
VAPOR DENSITY:..... N/A
EVAPORATION RATE:..... Negligible
SOLUBILITY IN WATER:..... slight
SPECIFIC GRAVITY:..... ca. 1.0 Water=1 (Bulk)
PERCENT VOLATILE:..... Negligible
pH:..... N/A
VISCOSITY:..... N/D
MELTING POINT:..... N/D

APPEARANCE AND ODOR:
Off-white crystalline solid, sharp odor.

Abbreviations: N/D - Not Determined N/A - Not Applicable CA - Approximately

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3. FIRE AND EXPLOSION HAZARD DATA

FLASH POINT:..... > 212 F Setaflash
Setaflash Closed Cup
FLAMMABLE LIMITS - LEL:..... N/A
FLAMMABLE LIMITS - UEL:..... N/A
AUTOIGNITION TEMPERATURE:..... N/D

EXTINGUISHING MEDIA:
Water, Carbon dioxide, Dry chemical, Foam

SPECIAL FIRE FIGHTING PROCEDURES:
Wear full protective clothing, including helmet, self-contained, positive pressure or pressure demand breathing apparatus, bunker coat and pants, bands around arms, waist and legs, face mask, and protective covering for exposed areas of the head.

UNUSUAL FIRE AND EXPLOSION HAZARDS:
See Hazardous Decomposition section for products of combustion.

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4. REACTIVITY DATA

STABILITY: Stable

INCOMPATIBILITY - MATERIALS/CONDITIONS TO AVOID:
None known.

HAZARDOUS POLYMERIZATION: Hazardous polymerization will not occur.

HAZARDOUS DECOMPOSITION PRODUCTS:
May produce fluorocarbon gases if exposed to very high temperatures (over 300 C).

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5. ENVIRONMENTAL INFORMATION

SPILL RESPONSE:
Observe precautions from other sections. Collect spilled material. Use wet sweeping compound or water to avoid dusting. Clean up residue. Place in a closed container.

RECOMMENDED DISPOSAL:
Incinerate in an industrial or commercial facility in the presence of a combustible material. Combustion products will include HF. Disposal alternative: Dispose of waste product in a facility permitted to accept chemical waste.

Abbreviations: N/D - Not Determined N/A - Not Applicable CA - Approximately

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5. ENVIRONMENTAL INFORMATION (continued)

ENVIRONMENTAL DATA:
Not determined.

REGULATORY INFORMATION:
Volatile Organic Compounds: N/D.
VOC Less H2O & Exempt Solvents: N/D.

Since regulations vary, consult applicable regulations or authorities before disposal. U.S. EPA Hazardous Waste Number = None (Not U.S. EPA Hazardous).

OTHER ENVIRONMENTAL INFORMATION:
This product may contain one or more organic fluorochemicals that have the potential to resist degradation and persist in the environment.

EPCRA HAZARD CLASS:
FIRE HAZARD: No PRESSURE: No REACTIVITY: No ACUTE: Yes CHRONIC: No

---

6. SUGGESTED FIRST AID

EYE CONTACT:
Immediately flush eyes with large amounts of water. Get immediate medical attention.

SKIN CONTACT:
Flush skin with large amounts of water. If irritation persists, get medical attention.

INHALATION:
If signs/symptoms occur, remove person to fresh air. If signs/symptoms continue, call a physician.

IF SWALLOWED:
If swallowed, call a physician immediately. Only induce vomiting at the instruction of a physician. Never give anything by mouth to an unconscious person.

---

7. PRECAUTIONARY INFORMATION

EYE PROTECTION:
Avoid eye contact. Avoid eye contact with vapor, spray, or mist. The following should be worn alone or in combination, as appropriate, to prevent eye contact: Wear vented goggles.

Abbreviations: N/D - Not Determined N/A - Not Applicable CA - Approximately

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7. PRECAUTIONARY INFORMATION (continued)

SKIN PROTECTION:
Avoid skin contact. Wear appropriate gloves when handling this material. A pair of gloves made from the following material(s) are recommended: butyl rubber, polyethylene/polyvinylidene chloride (Saranex). Use one or more of the following personal protection items as necessary to prevent skin contact: head covering, coveralls. Protective garments (other than gloves) should be made of either of the following materials: polyethylene/polyvinylidene chloride (Saranex).

RECOMMENDED VENTILATION:
Use with appropriate local exhaust ventilation. Provide appropriate local exhaust ventilation at transfer points. Use in a well-ventilated area. Provide sufficient ventilation to maintain emissions below recommended exposure limits. If exhaust ventilation is not adequate, use appropriate respiratory protection. Provide ventilation adequate to control vapor concentrations below recommended exposure limits and/or control spray or mist.

Local exhaust ventilation is recommended where the material becomes airborne.

RESPIRATORY PROTECTION:
Avoid breathing of airborne material. Select one of the following NIOSH approved respirators based on airborne concentration of contaminants and in accordance with OSHA regulations: half-mask supplied air respirator, full-face supplied air respirator.

PREVENTION OF ACCIDENTAL INGESTION:
Do not eat, drink or smoke when using this product. Wash exposed areas thoroughly with soap and water. Wash hands after handling and before eating.

RECOMMENDED STORAGE:
Store at room temperature. Keep container dry. Keep container closed when not in use.

FIRE AND EXPLOSION AVOIDANCE:
Not determined.

EXPOSURE LIMITS

INGREDIENT	VALUE	UNIT	TYPE	AUTH	SKIN*
POTASSIUM PERFLUOROHEXANE SULFONATE.....	0.1	MG/M3	TWA	3M	Y
RESIDUAL ORGANIC FLUOROCHEMICALS.....	0.1	MG/M3	TWA	3M	Y

* SKIN NOTATION: Listed substances indicated with 'Y' under SKIN refer to

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Abbreviations: N/D - Not Determined N/A - Not Applicable CA - Approximately

EXPOSURE LIMITS (continued)

INGREDIENT	VALUE	UNIT	TYPE	AUTH	SKIN*

the potential contribution to the overall exposure by the cutaneous route including mucous membrane and eye, either by airborne or, more particularly, by direct contact with the substance. Vehicles can alter skin absorption.

SOURCE OF EXPOSURE LIMIT DATA:
- 3M: 3M Recommended Exposure Guidelines

8. HEALTH HAZARD DATA

EYE CONTACT:
No information was found regarding effects from eye contact.

Single exposure may cause:

Mild Eye Irritation: signs/symptoms can include redness, swelling, pain, and tearing.

SKIN CONTACT:
No information was found regarding effects from skin contact.

May be absorbed through the skin and persist in the body for an extended time.

Single exposure may cause:

Moderate Skin Irritation: signs/symptoms can include redness, swelling, itching, and dryness.

INHALATION:
No information was found regarding effects from inhalation exposure.

May be absorbed by inhalation and persist in the body for an extended time.

Single overexposure, above recommended guidelines, may cause:

Irritation (upper respiratory): signs/symptoms can include soreness of the nose and throat, coughing and sneezing.

IF SWALLOWED:
Ingestion is not a likely route of exposure to this product.

No information was found regarding effects from swallowing.

Animal studies conducted on organic fluorochemicals which may be present in this product indicate effects including liver disturbances, weight loss, loss of appetite, lethargy, and neurological, pancreatic, adrenal and hematologic effects. There are no known human health

8. HEALTH HAZARD DATA (continued)

effects from anticipated exposure to these organic fluorochemicals when used as intended and instructed.

OTHER HEALTH HAZARD INFORMATION:
This product may contain one or more organic fluorochemicals that have the potential to be absorbed and remain in the body for long periods of time, either as the parent molecule or as metabolites, and may accumulate with repeated exposures. There are no known human health effects from anticipated exposure to these organic fluorochemicals when used as intended and instructed.

The presence of organic fluorochemicals in the blood of the general population and subpopulations, such as workers, has been published dating back to the 1970's. 3M's epidemiological study of its own workers indicates no adverse effects.

SECTION CHANGE DATES

PRECAUTIONARY INFO. SECTION CHANGED SINCE May 17, 1999 ISSUE

Abbreviations: N/D - Not Determined N/A - Not Applicable CA - Approximately

The information in this Material Safety Data Sheet (MSDS) is believed to be correct as of the date issued. 3M MAKES NO WARRANTIES, EXPRESSED OR IMPLIED, INCLUDING, BUT NOT LIMITED TO, ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OR COURSE OF PERFORMANCE OR USAGE OF TRADE. User is responsible for determining whether the 3M product is fit for a particular purpose and suitable for user's method of use or application. Given the variety of factors that can affect the use and application of a 3M product, some of which are uniquely within the user's knowledge and control, it is essential that the user evaluate the 3M product to determine whether it is fit for a particular purpose and suitable for user's method of use or application.

3M provides information in electronic form as a service to its customers. Due to the remote possibility that electronic transfer may have resulted in errors, omissions or alterations in this information, 3M makes no representations as to its completeness or accuracy. In addition, information obtained from a database may not be as current as the information in the MSDS available directly from 3M.

ATTACHMENT 3

TEST SUBSTANCE PREPARATION PROCEDURE

ATTACHMENT 3

TEST SUBSTANCE PREPARATION PROCEDURE

Test Substance: T-7706
Vehicle: Aqueous 0.5% CMC (medium viscosity)

A. Purpose:

The purpose of this procedure is to provide a method for the preparation of dosage suspensions of T-7706 for oral (gavage) administration to rats on Argus Research Study number 418-028.

B. General Information:

1. All suspension containers will be labeled and color-coded. Each label will specify the protocol number, test substance identification, Argus batch number, concentration, dosage level, preparation date, expiration date and storage conditions.

2. Suspensions will be prepared:
   __ Daily X Weekly _ For_ days of use
   _ Approximately every ten days __ By Sponsor

3. Suspensions will be administered at a final dosage volume of 10 mL/kg.

4. Safety:
   X Gloves, uniform/lab coat, goggles or safety glasses with side shields
   X Dust-mist/HEPA-filtered Mask
   __ Half-Face Respirator if not used in a chemical fume hood
   __ Full-Face Respirator/Positive Pressure Hood
   ___ Tyvek Suit or tyvek apron and sleeves

5. Dosage suspensions adjusted for % Activity/Purity or Correction Factor:
   __ Yes X No (Calculations based on 100%)
   __ % Activity __ % Purity __ Correction Factor

6. Sampling requirements: Cited in protocol

7. Storage: Cited in protocol

ATTACHMENT 3

TEST SUBSTANCE PREPARATION PROCEDURE

NOTE: Prior to test substance preparation accurately measure the required amount of the appropriate vehicle (R.O. deionized water should be used for calibration purposes) in a graduated cylinder, pour the required amount of vehicle into a beaker. Carefully mark each beaker at the meniscus. This mark will be used during the preparation to bring the test substance slurry up to volume.

C. Dosage Suspension Preparation:

1. Weigh the required amount of test substance on a piece of weigh paper or into an appropriately sized mortar (see PREPARATION CALCULATIONS).

2. If weigh paper is used, transfer the test substance to an appropriately sized mortar. If necessary, grind the test substance into a fine powder. Slowly add a small amount of vehicle and grind. Continue to add vehicle slowly and grind the vehicle and the test substance together to form a fine slurry. Transfer the vehicle/test substance slurry to a marked beaker.

3. Rinse the mortar and pestle with additional vehicle to remove any remaining test substance. Transfer rinse to beaker.

4. Add additional vehicle to the beaker to bring volume up to the mark. Place on magnetic stir plate and agitate prior to and during sampling, aliquotting and/or administration.

5. Repeat steps (1) through (4) for each concentration.

Written By: Michael D. Brenner

Approved by: [signature] Date: 26 MAR 02

Clarification: ✓ No ___ Yes [see attached clarification form]

Initial/Date : CR 7/31/03

ATTACHMENT 4

TISSUES TO BE WEIGHED, RETAINED AND EXAMINED HISTOLOGICALLY

TISSUES TO WEIGHED AND RETAINED FOR POSSIBLE EXAMINATION FROM TEN RATS PER SEX PER GROUP

The ten rats per sex per group assigned to functional observational battery and motor activity tests will be assigned to hematology, clinical biochemistry and histological evaluations.

Tissues to be Weighed:

The following organs will be excised, trimmed and individually weighed as soon as possible after excision to avoid drying.

liver	spleen
kidneys	brain
adrenals	heart
thymus	ovaries
testes	uterus (with cervix)
right epididymis	prostate
left epididymis (whole and cauda)	
seminal vesicles (with and without fluid)	

Tissues to be Retained:

The following tissues or representative samples will be retained in neutral buffered 10% formalin.

brain (representative regions including cerebrum, cerebellum, pons)	
small and large intestines (including Peyer's patches)	
lungs (perfused with neutral buffered 10% formalin)	
lymph nodes (submandiblar and mediastinal)	
peripheral nerve (sciatic or tibial)	
gross lesions	spinal cord (cervical, thoracic and lumbar)
stomach	liver
kidneys	adrenals
spleen	heart
thymus	thyroid/parathyroid
trachea	uterus
urinary bladder	bone marrow (sternum)
testes*	ovaries
prostate	uterus
seminal vesicles (with coagulating gland)	vagina
mammary gland (female rats only)	

* Testes will be fixed in Bouin's solution for 48 to 96 hours before being retained in neutral buffered 10% formalin.

Additionally, the remaining portion of the left epididymis (corpus and caput), as well as the right epididymis will be fixed in neutral buffered 10% formalin.

Histological Examination:

Histological examination of retained tissues, including reproductive organs, will be conducted for the assigned ten rats per sex from the control and high dosage groups and from the F1 generation pups (livers) from the control and high dosage groups. If lesions attributed to the test substance are observed in the rats exposed to the high test substance concentration, the same tissues will be examined from the assigned ten rats per sex exposed to the lower test substance concentrations. Should results warrant examination of the lower dosage groups and conduct of quantitative evaluation, scheduled report date and prices will be adjusted accordingly.

The postlactional ovary should contain primordial and growing follicles as well as the large corpora lutea of lactation. Histopathological examination may detect qualitative depletion of the primordial follicle population. A quantitative evaluation of primordial follicles will be conducted for Fo generation female rats; the number of rats, ovarian section selection and section sample size will be statistically appropriate for the evaluation procedure used. Examination will include enumeration of the number of primordial follicles, which can be combined with small growing follicles, for comparison of ovaries of rats assigned to treated and control groups.

Shipping Instructions:

Tissues to be examined histologically will be shipped (ambient conditions) to:

Principal Investigator: W. Ray Brown, D.V.M., Ph.D., ACVP
Veterinary Pathologist
Research Pathology Services, Inc.
438 E. Butler Avenue
New Britain, Pennsylvania 18901
Telephone: (215) 345-7070
Telefax: (215) 345-4326
Email: WRBRPS@concentric.net

The recipient will be notified in advance of sample shipment.

905 Sheehy Drive, Bldg. A
Horsham, PA 19044
Telephone: (215) 443-8710
Telefax: (215) 443-8587

ARGUS RESEARCH
Charles River Laboratories
Discovery and Development Services

PROTOCOL 418-028

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST

SPONSOR'S STUDY NUMBER: T-7706.1

Amendment 1 - 17 April 2002

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1. Detailed Clinical Observations - Male and Female Rats (page 10 of the protocol):

   [Effective Date: 1 April 2002] Detailed ciinical observations will not be recorded for male and female rats assigned to toxicokinetic sampling.

   Reason for Change:

   This change was made because sufficient data for evaluation of detailed clinical observations will be available from the rats assigned to the main study.

2. Feed Consumption Values - Male Rats and Female Rats (page 11 of the protocol):

   [Effective Date: 1 April 2002] Feed consumption values will not be recorded or tabulated for male and female rats assigned to toxicokinetic sampling.

   Reason for Change:

   This change was made because sufficient data for evaluation of feed consumption will be available from the rats assigned to the main study.

Any revisions made to this finalized amendment must be made by subsequent amendment.

3. Estrous Cycling and Mating (page 12 of the protocol):

   [Effective Date: 1 April 2002] For the rats assigned to toxicokinetic sampling, estrous cycling will be evaluated during the cohabitation period until spermatozoa are observed in a smear of the vaginal contents and/or a copulatory plug is observed *in situ*, but not during the dosage period, prior to cohabitation.

   Reason for Change:

   This change was made because sufficient data for evaluation of estrous cycling will be available from the rats assigned to the main study.

4. Scheduled Sacrifice - Toxicokinetic Study (page 16 of the protocol):

   [Effective Date: 5 April 2002] The number of implantation sites and corpora lutea will be recorded. Carcasses will be discarded without further evaluation.

   Reason of Change:

   This change was made in order to provide more information about possible toxicity of the test substance in pregnant rats.

5. Scheduled Sacrifice - Main Study (page 16 of the protocol):

   [Effective Date: 27 March 2002] The number of implantation sites will be recorded, rather than the number of implantation sites and corpora lutea will be recorded.

   Reason of Change:

   The number of corpora lutea will not be recorded because corpora lutea regress at a rapid rate and are not counted on studies at weaning.

6. Scheduled Sacrifice (page 19 of the protocol):

   [Effective Date: 4 April 2002] The liver from each selected pup will be excised and the organ weight recorded, rather than the liver from each selected pup will be collected excised and the organ weight recorded.

Any revisions made to this finalized amendment must be made by subsequent amendment.

Reason for Change:

This change clarifies the protocol by removing an extraneous word.

C Hoberman 4-17-02

Alan M. Hoberman, Ph.D., DABT Date
Director of Research

Raymond G. York 4-17-02

Raymond G. York, Ph.D., DABT Date
Associate Director of Research
Study Director

Theresa H. Woodard 4-17-02

Theresa H. Woodard, D.V.M. Date
Member, Institutional Animal Care
and Use Committee

John L. Butenhoff 4-18-02

John Butenhoff, Ph.D., DABT, CIH Date
Study Monitor and
Sponsor's Representative

Any revisions made to this finalized amendment must be made by subsequent amendment.

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PROTOCOL 418-028

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST

SPONSOR'S STUDY NUMBER: T-7706.1

Amendment 2 - 15 July 2002

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1. Safety Precautions (page 3 of the protocol and Attachment 3 page 1 of the protocol):

   [Effective Date: 29 April 2002] A half face respirator will be worn in addition to gloves, appropriate eye protection and a uniform/lab coat during formulation preparation of the bulk test substance.

   Reason for Change:

   This change was made to match the bulk test substance text with the text located within the Material Safety Data Sheet.

2. Study Schedule (Attachment 1 page 2 of the protocol):

   [Effective Date: 29 April 2002] The dates for FOB and motor activity evaluations have been extended to four days (06 MAY 02 - 09 MAY 02) rather than two days (06 MAY 02 - 07 MAY 02).

Any revisions to this finalized amendment must be made by subsequent amendment.

Reason for Change:

This change was made because more time is needed to evaluate animals assigned to FOB and motor activity evaluations.

for Alan M. Hoberman, Ph.D., DABT — Date
Director of Research

Raymond G. York, Ph.D., DABT — 15 JUL 2002 — Date
Associate Director of Research
Study Director

for Theresa H. Woodard, D.V.M. — 15 July 2002 — Date
Member, Institutional Animal Care
and Use Committee

John Butenhoff, Ph.D., DABT, CIH — 17 JUL 2002 — Date
Study Monitor and
Sponsor's Representative

Any revisions to this finalized amendment must be made by subsequent amendment.

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PROTOCOL 418-028

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST

SPONSOR'S STUDY NUMBER: T-7706.1

Amendment 3 - 17 July 2002

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1. Bulk Test Substance Sampling, Shipping Instructions, Shipping Instructions, Caesarean-Sectioning - Toxicokinetic Study, Scheduled Sacrifice - Toxicokinetic Study, and Scheduled Sacrifice, (pages 4, 5, 12, 13, 16 and 19, respectively of the protocol)

   [Effective Date: 29 May 2002] Samples for perfluorohexanesulfonate (PFHS) analysis shipped to Lisa Clemen at 3M Environmental Technology and Safety Services will be reshipped and remaining samples, that were to be shipped to Lisa Clemen and have not yet been shipped, will be shipped to:

   John Flaherty, Ph.D. (Principal Investigator)
   Exygen Research
   3058 Research Drive
   State College, Pennsylvania 16801
   Telephone: (814) 272-1039, ext. 122
   Telefax: (814) 231-1580
   Email: john.flaherty@exygen.com

Any revisions to this finalized amendment must be made by subsequent amendment.

These samples include:

Bulk test substance sampling (page 4 of the protocol)
Concentration and homogeneity (page 5 of the protocol)
Stability (page 5 of the protocol)
Plasma toxicokinetic samples (page 11 to 12 and page 16 of the protocol)
Plasma samples, rather than serum samples, were retained.
Liver toxicokinetic samples (pages 12 and 16 of the protocol)
Pooled fetal serum toxicokinetic samples (pages 12 and 16 of the protocol)
Pooled fetal liver toxicokinetic samples (pages 13 and 16 of the protocol)
Pooled pup serum toxicokinetic samples (page 19 of the protocol)
Pup liver toxicokinetic samples (page 19 of the protocol)

The analyses will be subcontracted to Exygen by the Sponsor and the Quality Assurance Unit for Exygen Research will conduct critical phase inspections and audit the respective results and reports according to the Standard Operating procedures of that facility. Such critical phase inspection reports and audit reports will be submitted by that facility to the Study Director, Raymond G. York. The date of the inspections and report submissions will be incorporated into a QAU statement generated by Exygen Research for inclusion in the final report for Protocol 418-028.

Reason for Change:

This change was made at the request of the Sponsor because 3M is not able to complete the formulation analysis with their current staffing.

for Alan M. Hoberman, Ph.D., DABT Date
Director of Research

Raymond G. York, Ph.D., DABT Date
Associate Director of Research
Study Director

for Theresa H. Woodard, D.V.M. Date
Member, Institutional Animal Care
and Use Committee

John Butenhoff, Ph.D., DABT, CIH Date
Study Monitor and
Sponsor's Representative

Any revisions to this finalized amendment must be made by subsequent amendment.

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ARGUS RESEARCH
Charles River Laboratories
Discovery and Development Services

PROTOCOL 418-028

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST

SPONSOR'S STUDY NUMBER: T-7706.1

Amendment 4 - 20 March 2003

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1. Bulk Test Substance Sampling, Shipping Instructions, Shipping Instructions, Caesarean-Sectioning - Toxicokinetic Study, Scheduled Sacrifice - Toxicokinetic Study, and Scheduled Sacrifice, (pages 4, 5, 12, 13, 16 and 19, respectively of the protocol) and Amendment 3, Item 1: Bulk Test Substance Sampling, Shipping Instructions, Shipping Instructions, Caesarean-Sectioning - Toxicokinetic Study, Scheduled Sacrifice - Toxicokinetic Study, and Scheduled Sacrifice (page 1 of Amendment 3)

   [Effective Date: 27 February 2003] The analyses performed by Exygen Research will be done according to Exygen Method ExM-023-071 Revision 1, entitled "Method of Analysis for the Determination of Perfluorohexanesulfonate (PFHS), Perfluorooctanesulfonate (PFOS) and Pentadecafluorooctanoic Acid (PFOA) in Rat Liver, Serum and Urine Revision 1".

Any revisions to this finalized amendment must be made by subsequent amendment.

Reason for Change:

This change was made at the request of the Exygen Research in order to clarify the method of analysis.

Alan M. Hoberman, Ph.D., DABT Date
Director of Research

Raymond G. York, Ph.D., DABT Date
Associate Director of Research
Study Director

Douglas B. Learn, Ph.D. Date
Chair, Institutional Animal Care
and Use Committee

John Butenhoff, Ph.D., DABT, CIH Date
Study Monitor and
Sponsor's Representative

Any revisions to this finalized amendment must be made by subsequent amendment.

APPENDIX E

DEVIATIONS FROM THE PROTOCOL AND THE STANDARD OPERATING PROCEDURES OF THE TESTING FACILITY

DEVIATIONS FROM THE PROTOCOL AND THE STANDARD OPERATING PROCEDURES OF THE TESTING FACILITY

1. The following rats were not fasted overnight prior to necropsy.

Dosage Group	Dosage (mg/kg/day)	Date of Necropsy	Sex	Rat Numbers
I	0	28 MAY 02	Female	19044
		29 MAY 02	Female	19012, 19021, 19068
II	0.3	28 MAY 02	Female	19009, 19016, 19036, 19043, 19047, 19052, 19055, 19061, 19071
		29 MAY 02	Female	19018, 19037
III	1	28 MAY 02	Female	19017
		29 MAY 02	Female	19013, 19029, 19060
IV	3	28 MAY 02	Female	19045, 19058, 19073
		29 MAY 02	Female	19039, 19063, 19069
V	10	28 MAY 02	Female	19001, 19028, 19031, 19033, 19049, 19059, 19070

This deviation did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter and there were no indications of toxicity in clinical chemistry parameters for the female rats.

2. Postdosage observations were performed out of the range of 60 ± 10 minutes on the following dates.

Dosage Group	Dosage (mg/kg/day)	Date	Number of Rats		Range of Time Deviated (minutes)
			Male Rats	Female Rats	
I	0	09 APR 02	4	-	+1 to +2
		03 JUN 02	-	1	+8
IV	3	03 JUN 02	-	1	+7

These deviations did not adversely affect the outcome or interpretation of the study because the extent of the deviation was less than 10 minutes.

3. On day 39 of study (DS 39) (9 May 2002), a postdosage clinical observation was not recorded for one male rat in the 0.3 mg/kg/day dosage group (19153). This deviation did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.

4. On DS 44 (14 May 2002), dosage volume was not recorded for one male rat in the 3 mg/kg/day dosage group (19156). This deviation did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.

5. On DS 46 (16 May 2002), postdosage clinical observations and dosage volumes were not recorded for two male rats in the 0 mg/kg/day dosage group (19161 and 19167). These deviations did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.

6. Detailed clinical observations were not recorded weekly for the following rats.

Dosage Group	Dosage (mg/kg/day)	Date	Sex	Rat Numbers
I	0	09 MAY 02	Female	19023, 19041, 19050
II	0.3	09 MAY 02	Female	19004
III	1	09 MAY 02	Female	19008
IV	3	09 MAY 02	Female	19054, 19062
V	10	09 MAY 02	Female	19020, 19030

These deviations did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.

7. On DS 13 (13 April 2002), feed left values were not recorded for all rats before they were placed into cohabitation. This deviation did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.

8. On days 1 and 2 of lactation (DLs 1 and 2) (10 May 2002 and 11 May 2002, respectively), one pup in the 0 mg/g/day dosage group (litter 19050) was recorded as having an adverse clinical observation without the sex being recorded. This deviation did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.

9. On DL 3 (12 May 2002), one litter in the 10 mg/kg/day dosage group (19022) was not recorded as having been observed. All pups appeared normal on DL 4. This deviation did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.

10. On DL 5 (12 May 2002), maternal observation was not recorded for one rat in the 0.3 mg/kg/day dosage group (19018). Maternal behavior on DL 8 was normal for this rat. This deviation did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.

11. On 19 May 2002, the frozen liver sample for one female rat with a non-confirmed date of mating in the 0 mg/kg/day dosage group (19077) was lost before sample shipment. This deviation did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.

12. On DL 22 (31 May 2002) the liver weight of one pup in the 1 mg/kg/day dosage group (pup 9 in litter 19024) was not recorded. This deviation did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.

All deviations are documented in the raw data.

31 JUL 2003

Raymond G. York, Ph.D., DABT Date
Associate Director of Research
Study Director

APPENDIX F

CERTIFICATE OF ANALYSIS

Certificate of Analysis

Nominal Product: Potassium perfluorohexanesulfonate: $C_6F_{13}SO_3^{(-)}\ K^{(+)}$

Product Code: PFHS; 127498-80

April 15, 2002

Tom Kestner and Joel Miller

The sample of 127498-80 PFHS was analyzed using LCMS, ^{19}F-NMR and ^{1}H-NMR analysis techniques. The overall qualitative and quantitative compositional results that were derived from these combined analyses are summarized below in TABLE-1.

TABLE-1

Sample: 127498-80: PFHS

Overall Quantitative Compositional Results by LCMS, ^{19}F-NMR, and ^{1}H-NMR Analyses

Component Identities *	**Relative** Wt.% Concentrations (single trial measurements, excluding any water)
$CF_3CF_2CF_2CF_2CF_2CF_2SO_3^{(-)}\ K^{(+)}$	88.93% (NMR)
$(CF_3)_2$-CF-$(CF_2)_3$-$SO_3^{(-)}\ K^{(+)}$	6.83% (NMR)
CF_3CF_2-CF(CF_3)-CF_2CF_2-$SO_3^{(-)}\ K^{(+)}$	2.75% (NMR)
$CF_3CF_2CF_2CF_2$-CF(CF_3)-$SO_3^{(-)}\ K^{(+)}$	0.83% (NMR)
$CF_3CF_2CF_2$CF(CF_3)-CF_2-$SO_3^{(-)}\ K^{(+)}$	0.56% (NMR)
$(CF_3)_3$-C-CF_2-$CF_2SO_3^{(-)}\ K^{(+)}$	0.078% (NMR)
$C_6F_{12}HSO_3^{(-)}\ K^{(+)}$	0.009% (LCMS)
$C_7F_{15}SO_3^{(-)}\ K^{(+)}$	0.006% (LCMS)
$C_4F_9SO_3^{(-)}\ K^{(+)}$	0.004% (LCMS)
Probable C_nH_{2n+2} hydrocarbons	0.0034% (NMR)
Other components	<0.001% (LCMS)
Sum of $C_6F_{13}SO_3^{(-)}\ K^{(+)}$ Isomers	**99.98%**
Sum of Known Impurities	**0.021%**

* Trace amounts of other unassigned components were also detected.

File Reference: CofA_PFHS_127498-80.doc

3M SPECIALTY MATERIALS MANUFACTURING DIVISION ANALYTICAL LABORATORY

Request No. **GID:32537**

To: Dan Hakes - (3-2392) – EHSR – Auto & Chem Group – 236-1B-10

From: Tom Kestner - (3-5633) - SMMD Analytical Lab - 236-2B-11

Subject: **Chemical Characterization of PFHS (127498-80) by ^{1}H-NMR & ^{19}F-NMR Spectroscopy**

Date: April 15, 2002

SAMPLE DESCRIPTION:

- 127498-80: PFHS made by George Moore and to be used for toxicological testing. Nominal product =C_6F_{13}-$SO_3^{(-)}$ $K^{(+)}$ (white powder).

OBJECTIVE:

This sample was subjected to ^{1}H-NMR and ^{19}F-NMR spectral analyses to determine the purity of the nominal product and to characterize as many impurity components as possible. Joel Miller also performed an LC/MS analysis and his results were reported to you previously.

EXPERIMENTAL:

A portion of the sample (~400 mg) was totally dissolved in deuterated dimethylsulfoxide (DMSO-d_6) and then the solution was spiked with a small amount of 1,4-bis(trifluoromethyl)benzene (p-HFX) for NMR analysis. A 400 MHz ^{1}H-NMR spectrum (# h32537.GID.401) and a 376 MHz ^{19}F-NMR spectrum (# f32537.GID.401) were acquired at room temperature using a Varian UNITYplus 400 FT-NMR spectrometer. The p-HFX was used as a ^{1}H/^{19}F-NMR cross integration standard to permit the cross correlation of the relative ^{1}H and ^{19}F signal intensities for evaluation of the overall sample composition.

RESULTS:

The combined NMR spectral data indicated the sample of 127498-80 consisted of a high purity form of the nominal isomeric product mixture, C_nF_{2n+1}-$SO_3^{(-)}$ $M^{(+)}$, where 'n' was mainly 6 and where the metal cation ['$M^{(+)}$'] was assumed to be $K^{(+)}$. Trace-levels of probable aliphatic hydrocarbon impurity components were also observed and quantified.

The qualitative and quantitative compositional results that were derived from the single trial ^{1}H/^{19}F-NMR cross integration analysis are summarized in **TABLE-1** on the following page. Any water that may have been present in the sample was ignored for calculation purposes. The relative weight percent concentrations shown in TABLE-1 should be very close to their respective absolute weight percent values. Trace amounts of other unidentified impurity components were also detected in the NMR spectra, but additional work would be needed in an effort to assign or quantify the unassigned impurities.

Copies of the NMR spectra are attached with the paper copy of this report for your reference. If you have any questions about these results, or if any further work is needed, please let me know.

Tom Kestner

c: Joel Miller
George Moore
Rick Payfer

File Reference: dh32537.GID.doc/93

April 15, 2002 3M SMMD Analytical Lab Request # GID:32537

TABLE-1

Sample: 127498-80: PFHS made by George Moore and to be used for toxicological testing.
Overall Quantitative Compositional Results by $^{1}H/^{19}F$-NMR Cross Integration Analysis

Identified Components *	$^{19}F/^{1}H$-NMR **Relative** Wt.% Concentrations (single trial measurement)
$CF_3CF_2CF_2CF_2CF_2CF_2SO_3^{(-)}\ K^{(+)}$	88.94%
$(CF_3)_2$-CF-$(CF_2)_3$-$SO_3^{(-)}\ K^{(+)}$	6.83%
CF_3CF_2-CF(CF_3)-CF_2CF_2-$SO_3^{(-)}\ K^{(+)}$	2.75%
$CF_3CF_2CF_2CF_2$-CF(CF_3)-$SO_3^{(-)}\ K^{(+)}$	0.83%
$CF_3CF_2CF_2CF(CF_3)$-CF_2-$SO_3^{(-)}\ K^{(+)}$	0.56%
$(CF_3)_3$-C-CF_2-$CF_2SO_3^{(-)}\ K^{(+)}$	0.078%
Probable C_nH_{2n+2} hydrocarbons	0.0034%

* Trace amounts of other unassigned components were also detected in the NMR spectra.

APPENDIX G

ANALYTICAL AND BIOANALYTICAL REPORT

ANALYTICAL PHASE

STUDY TITLE
Oral (Gavage) Combined Repeated Dose Toxicity Study of T-7706 with the Reproduction/Developmental Toxicity Screening Test

DATA REQUIREMENTS
OECD Principles on Good Laboratory Practice. ENV/MC/CHEM(98)17,
U.S. Food and Drug Administration 21 CFR Part 58,
MHW Good Laboratory Practice Standard for Safety Studies on Drugs Ordinance Number 21, March 26, 1997

STUDY DIRECTOR
Raymond G. York

ANALYTICAL REPORT COMPLETION DATE
July 21, 2003

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STUDY SPONSOR
3M Corporate Toxicology
Building 220-2E-02
St. Paul, MN 55144-1000

PROJECT
Protocol Number: 418-028
Sponsor's Study Number: T-7706.1
Exygen Study Number: 023-072

Total Pages: 153

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

Exgyen Study Number 023-072, entitled "Oral (Gavage) Combined Repeated Dose Toxicity Study of T-7706 with the Reproduction/Developmental Toxicity Screening Test," conducted for 3M Corporate Toxicology, was performed in compliance with U.S. Food and Drug Administration Good Laboratory Practice Regulations 21 CFR Part 58, OECD Principles on Good Laboratory Practice. ENV/MC/CHEM(98)17 and MHW Good Laboratory Practice Standards for Safety Studies on Drugs Ordinance Number 21 by Exygen Research.

John M Flaherty — 7/31/03

John Flaherty
Principal Investigator
Exygen Research

Date

Raymond G. York — 24 JUL 2003

Raymond G. York
Study Director
Argus Research

Date

John R. Butenhoff — 28 JUL 2003

John Butenhoff
Study Monitor
3M Corporate Toxicology

Date

QUALITY ASSURANCE STATEMENT

Exygen Research's Quality Assurance Unit reviewed Exygen Study Number 023-072, entitled, "Oral (Gavage) Combined Repeated Dose Toxicity Study of T-7706 with the Reproduction/Developmental Toxicity Screening Test". All reviewed phases were inspected for conduct according to Exygen Research's Standard Operating Procedures, the Study Protocol, and all applicable Good Laboratory Practice Standards. All findings were reported to the Exygen Principal Investigator and Management and to the Study Director.

Phase	Date Inspected	Date Reported to Principal Investigator	Date Reported to Exygen Management	Date Reported to Study Director
1. Protocol Review	09/24/02	11/20/02	11/22/02	01/20/03
2. Extraction, Fortification	09/24/02	11/21/02	12/18/02	01/20/03
3. Raw Data Review and Draft Analytical Report Review	02/03-07/03 and 02/10-11/03	02/24/03	02/28/03	03/07/03
4. Final Analytical Report Review	07/21/03	07/21/03	07/21/03	07/21/03

Lydia Shaffer
Quality Assurance Auditor

07/21/03
Date

CERTIFICATION OF AUTHENTICITY

This report, for Exygen Study Number 023-072, is a true and complete representation of the raw data for the study.

Submitted by: Exygen Research
3058 Research Drive
State College, PA 16801
(814) 272-1039

Principal Investigator, Exygen:

John M Flaherty — 7/21/03
John Flaherty
Vice President
Exygen Research
Date

Exygen Research Facility Management:

R A Grazzini — 21-JUL-03
Richard A. Grazzini
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Study Director, Argus Research:

Raymond G York — 24 JUL 2003
Raymond G. York
Associate Director of Research
Argus Research
Date

Study Monitor, 3M:

John L Butenhoff — 28 JUL 2003
John Butenhoff
3M Corporate Toxicology
Date

STUDY IDENTIFICATION

Oral (Gavage) Combined Repeated Dose Toxicity Study of T-7706 with the Reproduction/Developmental Toxicity Screening Test

PROTOCOL NUMBER:	418-028
SPONSOR'S STUDY NUMBER:	T-7706.1
EXYGEN STUDY NUMBER:	023-072
TYPE OF STUDY:	Residue
SAMPLE MATRIX:	Rat Liver, Serum, and Plasma
TEST SUBSTANCE:	Perfluorohexanesulfonate (PFHS)
SPONSOR:	3M Corporate Toxicology Building 220-2E-02 St. Paul, MN 55144-1000
STUDY DIRECTOR:	Raymond G. York Argus Research 905 Sheehy Drive, Building A Horsham, PA 19044-1297
TESTING FACILITY:	Argus Research 905 Sheehy Drive, Building A Horsham, PA 19044-1297
STUDY MONITOR:	John Butenhoff 3M Corporate Toxicology Building 220-2E-02 St. Paul, MN 55144-1000
PERFORMING LABORATORY:	Exygen Research 3058 Research Drive State College, PA 16801
ANALYTICAL PHASE TIMETABLE:	Study Initiation Date: 03/26/02 Analytical Start Date: 09/16/02 Analytical Termination Date: 11/13/02 Analytical Report Completion Date: 07/21/03

PROJECT PERSONNEL

The Study Director for this project was Raymond G. York at Argus Research. The following personnel from Exygen Research were associated with various phases of the study:

Name	Title
John Flaherty	Vice President
Karen Risha	Scientist
Paul Connolly	Technical Lead-LC/MS
Xiaoming Zhu	Technician
Lawrence Ord	Sample Custodian
Rickey Kelley	Sample Custodian
Amy Sheehan	Technician
Emily Decker	Scientist
Mark Neeley	Scientist

TABLE OF CONTENTS

Page
TITLE PAGE 1
GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT 2
QUALITY ASSURANCE STATEMENT 3
CERTIFICATION OF AUTHENTICITY 4
STUDY IDENTIFICATION 5
PROJECT PERSONNEL 6
TABLE OF CONTENTS 7
LIST OF TABLES 8
LIST OF FIGURES 9
LIST OF APPENDICES 10
1.0 SUMMARY 11
2.0 OBJECTIVE 11
3.0 INTRODUCTION 11
4.0 ANALYTICAL TEST SAMPLES 12
5.0 REFERENCE MATERIAL 13
6.0 DESCRIPTION OF ANALYTICAL METHOD 13
6.1. Extraction Procedure 13
6.2 Preparation of Standards and Fortification Solutions 14
6.3 Chromatography 14
6.4 Instrument Sensitivity 14
6.5 Description of LC/MS/MS Instrument and Operating Conditions 15
6.6 Quantitation and Example Calculation 15
7.0 EXPERIMENTAL DESIGN 17
8.0 RESULTS 18
9.0 CONCLUSIONS 18
10.0 RETENTION OF DATA AND SAMPLES 19

LIST OF TABLES

Page

Table I. Summary of PFHS in Control Rat Plasma Samples....21
Table II. Summary of PFHS in Control Rat Serum Samples....21
Table III. Summary of PFHS in Control Rat Liver Samples....21
Table IV. Summary of PFHS Fortification Recoveries in Rat Plasma....22
Table V. Summary of PFHS Fortification Recoveries in Rat Serum....22
Table VI. Summary of PFHS Fortification Recoveries in Rat Liver....23
Table VII. Summary of PFHS Residues in Rat Plasma Samples....24
Table VIII. Summary of PFHS Residues in Rat Serum Samples....26
Table IX. Summary of PFHS Residues in Rat Liver Samples....28
Table X. Summary of PFHS Residues in Dosing Solutions....40
Table XI. Summary of PFHS Residues in Stability Samples....41
Table XII. Summary of PFHS Residues in Homogeneity Samples....42

LIST OF FIGURES

Page

Figure 1. Typical Calibration Curve for PFHS 44

Figure 2. Chromatogram Representing a 0.1 ng/mL standard for PFHS 45

Figure 3. Chromatogram Representing a Control Rat Plasma Sample for PFHS (Exygen ID 0202913 Control, Data Set: 091602B) 46

Figure 4. Chromatogram Representing a Control Rat Serum Sample for PFHS (Exygen ID: 0202987 Control, Data Set: 091902B) 47

Figure 5. Chromatogram Representing a Control Rat Liver Sample for PFHS, (Exygen ID: 0202877 Control , Data Set: 100202A) 48

Figure 6. Chromatogram Representing Control Rat Plasma Sample Fortified with 10 ppb of PFHS (Exygen ID: 0202913 Spk A, Data Set: 091602B) 49

Figure 7. Chromatogram Representing Control Rat Serum Sample Fortified with 10 ppb of PFHS (Exygen ID: 0202987 Spk A, Data Set: 091902B) 50

Figure 8. Chromatogram Representing Control Rat Liver Sample Fortified with 10 ppb of PFHS (Exygen ID: 0202877 Spk A, Data Set: 100202A) 51

Figure 9. Chromatogram Representing Rat Plasma Sample Analyzed for PFHS (Exygen ID: 0201816, Sponsor ID: 19176 GROUP I, Data Set: 091602B) ..52

Figure 10. Chromatogram Representing Rat Serum Sample Analyzed for PFHS, DF=10 (Exygen ID: 0201863, Sponsor ID: 19079 GROUP II, Data Set: 091902BR) 53

Figure 11. Chromatogram Representing Rat Liver Sample Analyzed for PFHS (Exygen ID: 0202050, Sponsor ID: 19018 GROUP II Male 1, Data Set: 100202A) 54

LIST OF APPENDICES

Page

Appendix A Study Protocol 418-028 (Exygen Study No. 023-072) and Amendments, Deviation and Note to File.....55

Appendix B Analytical Method: Method of Analysis for the Determination of Perfluorohexanesulfonate (PFHS), Perfluorooctanesulfonate (PFOS) and Pentadecafluorooctanoic Acid (PFOA) in Rat Liver, Serum and Urine Revision 1 (Exygen Method No. ExM-023-071 Revision 1) 110

1.0 SUMMARY

Exygen Resarch extracted and analyzed rat liver, serum, and plasma samples for the determination of perfluorohexanesulfonate (PFHS) according to Exygen Method ExM-023-071 Revision 1 (**Appendix B**).

The limit of quantitation for PFHS in rat liver was 10 ng/g and 10 ng/mL in rat serum and plasma. The LOQ for each matrix was determined in a method validation study performed at Exygen (Exygen Study No: 023-073).

PFHS in the rat plasma samples ranged from non-detected levels to 237,000 ng/mL. PFHS in the rat serum samples ranged from non-detected levels to 189,000 ng/mL. PFHS in the rat liver samples ranged from non-detected levels to 675,000 ng/g.

The average percent recoveries ± standard deviations for PFHS in rat plasma, serum, and liver samples were 84% ± 7%, 95% ± 12%, and 86% ± 13%, respectively.

PFHS residues in the dosing solutions, stability samples and homogeneity samples were all within 70% to 125% of their known concentrations.

2.0 OBJECTIVE

The objective of the analytical part of this study was to determine levels of perfluorohexanesulfonate (PFHS) in specimens of rat liver, serum and plasma samples, bulk test substance, concentration and homogeneity formulations, and stability solutions according to Protocol 418-028 (**Appendix A**).

3.0 INTRODUCTION

This report details the results of the analysis for the determination of PFHS in rat liver, serum and plasma samples, bulk test substance, concentration and homogeneity formulations, and stability solutions using the analytical method entitled, "Method of Analysis for the Determination of Perfluorohexanesulfonate (PFHS), Perfluorooctanesulfonate (PFOS) and Pentadecafluorooctanoic Acid (PFOA) in Rat Liver, Serum and Urine Revision 1."

The study was initiated on March 26, 2002, when the study director signed protocol number 418-028. The analytical start date was September 16, 2002, and the analytical termination date was November 13, 2002.

4.0 ANALYTICAL TEST SAMPLES

The control rat liver (Exygen ID 0202877) used for the matrix blanks and matrix fortifications was received frozen on dry ice on August 7, 2002 from Pel-Freez Biologicals, Rogers, Arkansas. The control rat plasma (Exygen ID 0202912 and 0202913) used for the matrix blanks and matrix fortifications was received frozen on dry ice on August 8, 2002 from Pel-Freez Biologicals, Rogers, Arkansas. The control rat serum (Exygen ID 0202987) used for the matrix blanks and matrix fortifications was received frozen on dry ice on August 15, 2002 from Pel-Freez Biologicals, Rogers, Arkansas.

Dosage solution/suspension samples (Exygen ID 0201753-0201755) were received refrigerated at Exygen from Argus Research on May 29, 2002. Dosage solution/suspension samples (Exygen ID 0201757-0201758) were received refrigerated at Exygen from Argus Research on June 11, 2002. These samples were logged in by Exygen personnel and placed in refrigerated storage.

Bulk TA/S sample (Exygen ID 0201756) was received ambient at Exygen from Argus Research on June 11, 2002. This sample was logged in by Exygen personnel and placed in refrigerated storage.

Median liver lobe (Exygen ID 0201759-0201787), pooled fetal liver (Exygen ID 0201788-0201800), plasma (Exygen ID 0201801-0201860), pooled fetal serum (Exygen ID 0201861-0201874), pooled pup serum (Exygen ID 0201875-0201924), and pup livers (Exygen ID 0201925-0202408) were received frozen on dry ice at Exygen from Argus Research on June 18, 2002. These samples were logged in by Exygen personnel and placed in frozen storage.

Median liver lobe (Exygen ID 0203650) and pooled fetal liver (Exygen ID 0203651) were received frozen on dry ice at Exygen from Argus Research on September 11, 2002 and logged in by Exygen personnel and placed in frozen storage.

Prepared formulations (Exygen ID 0203923-0203962) were received frozen from 3M on September 19, 2002 and logged in by Exygen personnel and placed in frozen storage.

Sample log-in and chain of custody information can be found in the raw data package associated with this study. Storage records will be kept at Exygen Research.

5.0 REFERENCE MATERIAL

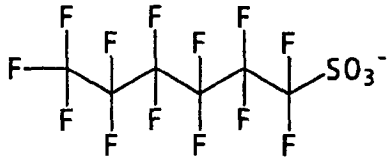
The analytical standard PFHS was received at Exygen on January 26, 2000 from 3M Environmental Technology and Services.

The available information for the reference material is listed below. The reference material was stored frozen.

Compound	Exygen Inventory No..	TCR No.	Purity (%)	Expiration Date
PFHS	SP244	SE036	99.99	01/01/10

The molecular structures of test substance is given below:

Name: PFHS
Chemical Name: Perfluorohexanesulfonate
Molecular Weight: 399



6.0 DESCRIPTION OF ANALYTICAL METHOD

The analytical method ExM-023-071 Revision 1 was used for this study.

6.1. Extraction Procedure

A 1 mL aliquot of the serum and plasma and 1 g of liver were used for the extraction procedure for the laboratory controls and fortifications. Due to insufficient sample size, a 100 µL aliquot of the serum and plasma and 0.1 g of the liver were used for the extraction procedure for the study samples. After fortification of appropriate samples, the serum samples were brought up to 20 mL with Type I Water and the liver samples were brought up to 10 mL with Type I Water. The serum samples were vortexed for ~ 1 minute and the liver samples were homogenized with a tissuemizer for ~ 1 minute. An aliquot of one milliliter was transferred from each sample and 5 mL of acetonitrile was added and the samples were shaken for ~ 20 minutes. The samples were centrifuged and the supernatant was decanted onto a conditioned SPE column. Then the samples were eluted with 2 mL of methanol. Each sample was analyzed by LC/MS/MS electrospray.

An extraction procedure was not necessary for the bulk test substance, concentration and homogeneity formulations, and the stability solutions. 10 mg of the bulk test substance was weighed and brought to volume with methanol in a 100-mL volumetric flask. The

sample was then diluted 100000 times with methanol to fit in the range of the analytical curve and analyzed by LC/MS/MS electrospray. The concentration and homogeneity formulations and the stability solutions were all diluted appropriately with methanol and analyzed by LC/MS/MS electrospray.

6.2 Preparation of Standards and Fortification Solutions

A stock standard solution of PFHS was prepared on August 20, 2002 as specified in Exygen method ExM-023-071 Revision 1. The stock standard solution was prepared at a concentration of 100 µg/mL by dissolving 10 mg of each standard (corrected for purity only) in methanol. From this solution, a 1.0 µg/mL fortification standard solution was prepared by taking 1 mL of the stock and bringing the volume up to 100 mL with methanol.

A 0.1 µg/mL fortification standard was prepared by taking 10 mL of the 1.0 µg/mL fortification standard and bringing the volume up to 100 mL with methanol.

A set of standards containing PFHS was prepared via dilution of the 0.1 µg/mL and various calibration solutions in the following manner:

Initial Conc. (µg/mL)[1]	Volume (mL)	Diluted to (mL)	Final Conc. (µg/mL)
0.1	5	100	0.005
0.1	2	100	0.002
0.1	1	100	0.001
0.005	10	100	0.0005
0.002	10	100	0.0002
0.001	10	100	0.0001

[1] of PFHS

The stock standard solution and all fortification and calibration standard solutions were stored in a refrigerator (4° ± 2°C) when not in use. Documentation of standard preparation can be found in the raw data associated with this report.

6.3 Chromatography

Quantification of PFHS was accomplished by LC/MS/MS electrospray. The retention time of PFHS was ~ 8.3 min. Peaks above the LOQ were not detected in any of the control samples corresponding to the analyte retention time.

6.4 Instrument Sensitivity

The smallest standard amount injected during the chromatographic run had a concentration of 0.0001 µg/mL of PFHS.

6.5 Description of LC/MS/MS Instrument and Operating Conditions

Instrument: Micromass Quattro Ultima (Micromass)

Interface: Electrospray (Micromass)

Computer: COMPAQ Professional Workstation AP200

Software: Windows NT, Masslynx 3.3

HPLC: Hewlett Packard (HP) Series 1100
HP Quat Pump
HP Vacuum Degasser
HP Autosampler
HP Column Oven

HPLC Column:Genesis C_8 (Jones Chromatography), 2.1 mm x 50 mm, 4µ
Column Temp.: 35° C
Injection Vol.: 15 µL
Mobile Phase (A): 2 mM Ammonium Acetate in type I water
Mobile Phase (B): Methanol

Time	% A	% B	Flow Rate (mL/min)
0.0	90	10	0.3
2.0	90	10	0.3
5.0	10	90	0.3
9.0	10	90	0.3
9.5	0	100	0.3
14.0	0	100	0.3
14.5	90	10	0.3
20.0	90	10	0.3

Ions monitored:

Analyte	Mode	Transition Monitored	Approximate Retention Time (min)
PFHS	Negative	399 → 80	~8.3 min.

6.6 Quantitation and Example Calculation

Fifteen microliters of sample or calibration standard were injected into the LC/MS/MS. The peak area was measured and the standard curve was generated (using 1/x fit weighted linear regression) by Masslynx software using six concentrations of standards. The concentration was determined from the equations below.

Equation 1 calculated the amount of analyte found (in ng/mL, based on peak area) using the standard curve (linear regression parameters) generated by the Masslynx software

program. Then Equation 2 calculated the amount of analyte found in ng/g for liver and ng/mL for serum and plasma.

Equation 1:

$$\text{Analyte found (ng/mL)} = \frac{(\text{Peak area - intercept})}{\text{slope}} \times DF \times AF$$

Where: AF = Aliquot Factor
DF = Dilution Factor

Equation 2:
Analyte found (ppb, ng/g for liver and ng/mL for serum and plasma) =

$$\frac{\text{analyte found (ng/mL)} \times FV\ (mL)}{\text{sample volume (mL) or sample weight (g)}}$$

Where: FV = Final Volume

For samples fortified with known amounts of PFHS prior to extraction, Equation 3 calculated the percent recovery.

Equation 3:
Recovery (%) =

$$\frac{(\text{analyte found (ppb)} - \text{analyte in control (ppb)})}{\text{amount added (ppb)}} \times 100\%$$

To find the total analyte found corrected for the salt content Equation 4 was used.

Equation 4:

Total Analyte Found Corrected (ppb) = analyte found (ppb) × salt correction factor

Where the salt correction factor = 0.91.

An example of a calculation using an actual sample follows:
Rat liver sample Exygen ID 0202877 Spk A (Set: 100202A), fortified at 10 ng/g where:

peak area	=	2125
intercept	=	41.0365
slope	=	4728.12
dilution factor	=	1
ppb added (fort level)	=	10
avg. amt in controls	=	0 (Not Detected)
final volume	=	2 mL
aliquot factor	=	10
sample weight	=	1.0 g

From equation 1:

Analyte found (ng/mL) = $\frac{[2125 - 41.0365] \times 1 \times 10}{4728.12}$

= 4.41 ng/mL

From equation 2:

Analyte found (ppb) = $\frac{(4.41 \text{ ng/mL} \times 2 \text{ mL})}{(1.0 \text{ g})}$

= 8.82 ppb

From equation 3:

% Recovery = $\frac{((8.82 \text{ ppb} - 0 \text{ ppb})}{10 \text{ ppb}} \times 100\%$

= 88%

From equation 4:

Analyte Found Corrected (ppb) = 8.82 ppb × 0.91

= 8.03 ppb

7.0 EXPERIMENTAL DESIGN

Each set of samples (liver, serum or plasma) consisted of one matrix blank, two matrix blanks fortified at known concentrations, and ~ 20 samples. Each sample was extracted using the method and then analyzed in duplicate.

8.0 RESULTS

The PFHS found in the control rat plasma, serum, and liver samples are listed in **Tables I-III.** Peaks were not detected in any of the control plasma or serum samples corresponding to the analyte retention time. Some peaks were detected in the control liver samples corresponding to the analyte retention time; however, the peaks detected were all below the LOQ of 10 ppb.

Fortification recoveries for PFHS in the rat plasma, serum, and liver samples are detailed in **Tables IV-VI.** The average percent recoveries ± standard deviations for PFHS in rat plasma, serum, and liver samples were 84% ± 7%, 95% ± 12%, and 86% ± 13%, respectively.

PFHS in the rat plasma samples ranged from non-detected levels to 237,000 ng/mL. Individual results are listed in **Table VII.** PFHS in the rat serum samples ranged from non-detected levels to 189,000 ng/mL. Individual results are listed in **Table VIII.** PFHS in the rat liver samples ranged from non-detected levels to 675,000 ng/g. Individual results are listed in **Table IX.**

PFHS residues in the dosing solutions ranged from 88% to 125% of their known concentrations. The results are listed in **Table X.**

PFHS residues found in the stability samples ranged from 91% to 122% of their known concentrations. The results are listed in **Table XI.**

PFHS residues found in the homogeneity samples ranged from 70% to 116% of their known concentrations. The results are listed in **Table XII.**

9.0 CONCLUSIONS

The rat liver, serum, and plasma samples were successfully extracted and analyzed for PFHS according to analytical method ExM-023-071 Revision 1. The bulk test substance, concentration and homogeneity formulations, and stability solutions were also successfully analyzed for PFHS according to analytical method ExM-023-071 Revision 1.

10.0 RETENTION OF DATA AND SAMPLES

When the final analytical report is complete, all original paper data generated by Exygen Research will be shipped to the sponsor. This does not include facility-specific raw data such as instrument or temperature logs. Exact copies of all raw data, as well as a signed copy of the final analytical report and all original facility-specific raw data, will be retained in the Exygen Research archives for the period of time specified in 21 CFR Part 58, OECD ENV/MC/CHEM(98)17, and MHW Ordinance Number 21. Retained samples of reference substances are archived by the sponsor.

TABLES

Table I. Summary of PFHS in Control Rat Plasma Samples

Sponsor ID	Exygen ID	Set Number	PFHS Found (ppb)
LOT 17824	0202913 Control	091602AR	ND
LOT 17824	0202913 Control	091602B	ND
LOT 05024	0202912 Control	091802A	ND
LOT 17824	0202913 Control	091902A	ND

Table II. Summary of PFHS in Control Rat Serum Samples

Sponsor ID	Exygen ID	Set Number	PFHS Found (ppb)
36119-3	0202987 Control	091902B	ND
36119-3	0202987 Control	092002A	ND
36119-3	0202987 Control	092002B	ND
36119-3	0202987 Control	092302A	ND
36119-3	0202987 Control	101102A	ND

Table III. Summary of PFHS in Control Rat Liver Samples

Sponsor ID	Exygen ID	Set Number	PFHS Found (ppb)
LOT 21824	0202877 Control	092802A	ND
LOT 21824	0202877 Control A	092602A	ND
LOT 21824	0202877 Control A	092602B	2.32 (NQ)
LOT 21824	0202877 Control	092702A	3.84 (NQ)
LOT 21824	0202877 Control	092702B	3.85 (NQ)
LOT 21824	0202877 Control	100202A	ND
LOT 21824	0202877 Control	100102A	ND
LOT 21824	0202877 Control	100302A	ND
LOT 21824	0202877 Control	100402A	ND
LOT 21824	0202877 Control	100402BR	2.09 (NQ)
LOT 21824	0202877 Control	100902AR	3.95 (NQ)
LOT 21824	0202877 Control	100902BR	2.01 (NQ)
LOT 21824	0202877 Control	101002A	1.85 (NQ)
LOT 21824	0202877 Control	101002B	3.95 (NQ)
LOT 21824	0202877 Control	101102AR	4.73 (NQ)
LOT 21824	0202877 Control	101402A	3.37 (NQ)

ND = Not Detected (Area less than the lowest concentration of the calibration standards (0.1 ng/mL))
NQ = Not Quantifiable (Area is greater than 0.1 ng/mL but less than LOQ (10 ng/mL))

Table IV. Summary of PFHS Fortification Recoveries in Rat Plasma

Sponsor ID	Exygen ID	Set Number	Amount Added (ppb)	% Recovery
LOT 17824	0202913 Spk A	091602A	10	91
LOT 17824	0202913 Spk B	091602A	50	84
19176 GROUP 1	0201801 Spk C	091602A	5000	77
LOT 17824	0202913 Spk A	091602B	10	86
LOT 17824	0202913 Spk B	091602B	50	84
19176 GROUP I	0201816 Spk C	091602B	5000	78
LOT 05024	0202912 Spk A	091802A	10	88
LOT 05024	0202912 Spk B	091802A	50	86
19076 GROUP I	0201846 Spk C	091802A	5000	89
LOT 17824	0202913 Spk A	091902A	10	71
LOT 17824	0202913 Spk B	091902A	50	96
19076 GROUP I	0201831 Spk C	091902A	5000	82
			Average:	**84**
			Standard Deviation:	**7**
			Relative Standard Deviation:	**8**

Table V. Summary of PFHS Fortification Recoveries in Rat Serum

Sponsor ID	Exygen ID	Set Number	Amount Added (ppb)	% Recovery
36119-3	0202987 Spk A	091902B	10	92
36119-3	0202987 Spk B	091902B	50	96
19076 GROUP I	0201861 Spk C	091902B	5000	94
36119-3	0202987 Spk A	092002A	10	106
36119-3	0202987 Spk B	092002A	50	105
19012 GROUP I	0201875 Spk C	092002A	5000	90
36119-3	0202987 Spk A	092002B	10	97
36119-3	0202987 Spk B	092002B	50	97
19036 GROUP II	0201890 Spk C	092002BR	5000	120
36119-3	0202987 Spk A	092302A	10	90
36119-3	0202987 Spk B	092302A	50	101
19005 GROUP IV	0201905 Spk C	101102A	200000	88
36119-3	0202987 Spk A	101102A	10	78
36119-3	0202987 Spk B	101102A	50	72
			Average:	**95**
			Standard Deviation:	**12**
			Relative Standard Deviation:	**12**

Table VI. Summary of PFHS Fortification Recoveries in Rat Liver

Sponsor ID	Exygen ID	Set Number	Amount Added (ppb)	% Recovery
LOT 21824	0202877 Spk A	092802A	10	83
LOT 21824	0202877 Spk B	092802A	50	87
19176 GROUP I	0201759 Spk C	092802A	5000	96
LOT 21824	0202877 Spk A	092602A	10	125
LOT 21824	0202877 Spk B	092602A	50	110
19076 GROUP I	0201774 Spk C	092602A	5000	100
LOT 21824	0202877 Spk A	092602B	10	104
LOT 21824	0202877 Spk B	092602B	50	87
19076 GROUP I	0201788 Spk C	092602B	5000	111
LOT 21824	0202877 Spk A	092702A	10	75
LOT 21824	0202877 Spk B	092702A	50	93
19012 GROUP I, Male 1	0201925 Spk C	092702A	5000	94
LOT 21824	0202877 Spk A	092702B	10	83
LOT 21824	0202877 Spk B	092702B	50	100
19021 GROUP I, Male 1	0201945 Spk C	092702B	5000	109
LOT 21824	0202877 Spk A	100202A	10	88
LOT 21824	0202877 Spk B	100202A	50	71
19018 GROUP II, Male 1	0202050 Spk C	100202A	5000	76
LOT 21824	0202877 Spk A	100102A	10	74
LOT 21824	0202877 Spk B	100102A	50	77
19041 GROUP I, Male 1	0201965 Spk C	100102A	5000	76
LOT 21824	0202877 Spk A	100302A	10	98
LOT 21824	0202877 Spk B	100302A	50	81
19036 GROUP II, Male 1	0202070 Spk C	100302A	5000	77
LOT 21824	0202877 Spk A	100402A	10	81
LOT 21824	0202877 Spk B	100402A	50	79
19003 GROUP III, Male 1	0202119 Spk C	100402A	5000	62
LOT 21824	0202877 Spk A	100402BR	10	70
LOT 21824	0202877 Spk B	100402BR	50	78
19008 GROUP III, Male 1	0202139 Spk C	100402BR	5000	86
LOT 21824	0202877 Spk A	100902AR	10	72
LOT 21824	0202877 Spk B	100902AR	50	81
19015 GROUP III, Male 1	0202159 Spk C	100902AR	5000	79
LOT 21824	0202877 Spk A	100902BR	10	72
LOT 21824	0202877 Spk B	100902BR	50	70
19035 GROUP IV, Male 1	0202229 Spk C	100902BR	5000	72
LOT 21824	0202877 Spk A	101002A	10	96
LOT 21824	0202877 Spk B	101002A	50	93
19040 GROUP IV, Male 2	0202249 Spk C	101002AR	5000	84
LOT 21824	0202877 Spk A	101002B	10	97
LOT 21824	0202877 Spk B	101002B	50	72
19006 GROUP V, Male 1	0202320 Spk C	101002BR	5000	90
LOT 21824	0202877 Spk A	101102AR	10	88
LOT 21824	0202877 Spk B	101102AR	50	75
19020 GROUP V, Male 2	0202340 Spk C	101102AR	25000	83
LOT 21824	0202877 Spk A	101402A	10	95
LOT 21824	0202877 Spk B	101402A	50	77
19025 GROUP V, Male 1	0202360 Spk C	101402ARR	5000	110
			Average:	**86**
			Standard Deviation:	**13**
			Relative Standard Deviation:	**16**

Table VII. Summary of PFHS Residues in Rat Plasma Samples

Sponsor ID	Exygen ID	Matrix	Collection Date	Set Number	PFHS Found (ng/mL)
19176 GROUP I	0201801	PD 14 PLASMA	4/14/02	091602A	182
19176 GROUP I*	0201801 Dup Inj.	PD 14 PLASMA	4/14/02	091602A	172
19177 GROUP I	0201802	PD 14 PLASMA	4/14/02	091602A	103
19177 GROUP I*	0201802 Dup Inj.	PD 14 PLASMA	4/14/02	091602A	108
19178 GROUP I	0201803	PD 14 PLASMA	4/14/02	091602A	46.5^^
19178 GROUP I*	0201803 Dup Inj.	PD 14 PLASMA	4/14/02	091602A	43.3^^
19179 GROUP II	0201804	PD 14 PLASMA	4/14/02	091602AR	18300
19179 GROUP II*	0201804 Dup Inj.	PD 14 PLASMA	4/14/02	091602AR	19400
19180 GROUP II	0201805	PD 14 PLASMA	4/14/02	091602AR	15700
19180 GROUP II*	0201805 Dup Inj.	PD 14 PLASMA	4/14/02	091602AR	15300
19181 GROUP II	0201806	PD 14 PLASMA	4/14/02	091602AR	20000
19181 GROUP II*	0201806 Dup Inj.	PD 14 PLASMA	4/14/02	091602AR	20400
19182 GROUP III	0201807	PD 14 PLASMA	4/14/02	091602AR	58000
19182 GROUP III*	0201807 Dup Inj.	PD 14 PLASMA	4/14/02	091602AR	58000
19183 GROUP III	0201808	PD 14 PLASMA	4/14/02	091602AR	68300
19183 GROUP III*	0201808 Dup Inj.	PD 14 PLASMA	4/14/02	091602AR	69500
19184 GROUP III	0201809	PD 14 PLASMA	4/14/02	091602AR	117000
19184 GROUP III*	0201809 Dup Inj.	PD 14 PLASMA	4/14/02	091602AR	115000
19185 GROUP IV	0201810	PD 14 PLASMA	4/14/02	091602AR	70400
19185 GROUP IV*	0201810 Dup Inj.	PD 14 PLASMA	4/14/02	091602AR	71900
19186 GROUP IV	0201811	PD 14 PLASMA	4/14/02	091602AR	126000
19186 GROUP IV*	0201811 Dup Inj.	PD 14 PLASMA	4/14/02	091602AR	125000
19187 GROUP IV	0201812	PD 14 PLASMA	4/14/02	091602AR	237000
19187 GROUP IV*	0201812 Dup Inj.	PD 14 PLASMA	4/14/02	091602AR	228000
19188 GROUP V	0201813	PD 14 PLASMA	4/14/02	091602AR	197000
19188 GROUP V*	0201813 Dup Inj.	PD 14 PLASMA	4/14/02	091602AR	182000
19189 GROUP V	0201814	PD 14 PLASMA	4/14/02	091602AR	187000
19189 GROUP V*	0201814 Dup Inj.	PD 14 PLASMA	4/14/02	091602AR	183000
19190 GROUP V	0201815	PD 14 PLASMA	4/14/02	091602AR	177000
19190 GROUP V*	0201815 Dup Inj	PD 14 PLASMA	4/14/02	091602AR	170000
19176 GROUP I	0201816	PD 42 PLASMA	5/12/02	091602B	245
19176 GROUP I*	0201816 Dup Inj	PD 42 PLASMA	5/12/02	091602B	256
19177 GROUP I	0201817	PD 42 PLASMA	5/12/02	091602B	382
19177 GROUP I*	0201817 Dup Inj	PD 42 PLASMA	5/12/02	091602B	376
19178 GROUP I	0201818	PD 42 PLASMA	5/12/02	091602B	74.7^^
19178 GROUP I*	0201818 Dup Inj	PD 42 PLASMA	5/12/02	091602B	65.4^^
19179 GROUP II	0201819	PD 42 PLASMA	5/12/02	091602BR	57400
19179 GROUP II*	0201819 Dup Inj	PD 42 PLASMA	5/12/02	091602BR	60200
19180 GROUP II	0201820	PD 42 PLASMA	5/12/02	091602BR	35700
19180 GROUP II*	0201820 Dup Inj	PD 42 PLASMA	5/12/02	091602BR	36400
19181 GROUP II	0201821	PD 42 PLASMA	5/12/02	091602BR	37100
19181 GROUP II*	0201821 Dup Inj	PD 42 PLASMA	5/12/02	091602BR	38500
19182 GROUP III	0201822	PD 42 PLASMA	5/12/02	091602BR	91000
19182 GROUP III*	0201822 Dup Inj	PD 42 PLASMA	5/12/02	091602BR	85900
19183 GROUP III	0201823	PD 42 PLASMA	5/12/02	091602BR	90300
19183 GROUP III*	0201823 Dup Inj	PD 42 PLASMA	5/12/02	091602BR	87500
19184 GROUP III	0201824	PD 42 PLASMA	5/12/02	091602BR	90700
19184 GROUP III*	0201824 Dup Inj	PD 42 PLASMA	5/12/02	091602BR	89300
19185 GROUP IV	0201825	PD 42 PLASMA	5/12/02	091602BR	119000
19185 GROUP IV*	0201825 Dup Inj	PD 42 PLASMA	5/12/02	091602BR	119000
19186 GROUP IV	0201826	PD 42 PLASMA	5/12/02	091602BR	137000
19186 GROUP IV*	0201826 Dup Inj	PD 42 PLASMA	5/12/02	091602BR	142000
19187 GROUP IV	0201827	PD 42 PLASMA	5/12/02	091602BR	128000
19187 GROUP IV*	0201827 Dup Inj	PD 42 PLASMA	5/12/02	091602BR	127000
19188 GROUP V	0201828	PD 42 PLASMA	5/12/02	091602BR	188000
19188 GROUP V*	0201828 Dup Inj	PD 42 PLASMA	5/12/02	091602BR	188000
19189 GROUP V	0201829	PD 42 PLASMA	5/12/02	091602BR	224000
19189 GROUP V*	0201829 Dup Inj	PD 42 PLASMA	5/12/02	091602BR	225000
19190 GROUP V	0201830	PD 42 PLASMA	5/12/02	091602BR	191000
19190 GROUP V*	0201830 Dup Inj	PD 42 PLASMA	5/12/02	091602BR	193000

^^Although the method used allows for alternate sample volumes or weights and all the peak area responses are within the calibration curve limits, the precision for the 0.1 mL or 0.1 g samples below 100 ppb has not been validated.
* Duplicate Injection

Table VII (cont'd). Summary of PFHS Residues in Rat Plasma Samples

Sponsor ID	Exygen ID	Matrix	Collection Date	Set Number	PFHS Found (ng/mL)
19076 GROUP I	0201846	GD 21 PLASMA	5/9/02	091802A	ND
19076 GROUP I*	0201846 Dup Inj	GD 21 PLASMA	5/9/02	091802A	ND
19077 GROUP I	0201847	GD 21 PLASMA	5/19/02	091802A	ND
19077 GROUP I*	0201847 Dup Inj	GD 21 PLASMA	5/19/02	091802A	ND
19078 GROUP I	0201848	GD 21 PLASMA	5/7/02	091802A	ND
19078 GROUP I*	0201848 Dup Inj	GD 21 PLASMA	5/7/02	091802A	ND
19079 GROUP II	0201849	GD 21 PLASMA	5/9/02	091802AR	4150
19079 GROUP II*	0201849 Dup Inj	GD 21 PLASMA	5/9/02	091802AR	4000
19080 GROUP II	0201850	GD 21 PLASMA	5/9/02	091802AR	3240
19080 GROUP II*	0201850 Dup Inj	GD 21 PLASMA	5/9/02	091802AR	3230
19081 GROUP II	0201851	GD 21 PLASMA	5/10/02	091802AR	2640
19081 GROUP II*	0201851 Dup Inj	GD 21 PLASMA	5/10/02	091802AR	2670
19082 GROUP III	0201852	GD 21 PLASMA	5/9/02	091802AR	7150
19082 GROUP III*	0201852 Dup Inj	GD 21 PLASMA	5/9/02	091802AR	7280
19083 GROUP III	0201853	GD 21 PLASMA	5/7/02	091802AR	18000
19083 GROUP III*	0201853 Dup Inj	GD 21 PLASMA	5/7/02	091802AR	18100
19084 GROUP III	0201854	GD 21 PLASMA	5/9/02	091802AR	6490
19084 GROUP III*	0201854 Dup Inj	GD 21 PLASMA	5/9/02	091802AR	6900
19085 GROUP IV	0201855	GD 21 PLASMA	5/6/02	091802AR	24800
19085 GROUP IV*	0201855 Dup Inj	GD 21 PLASMA	5/6/02	091802AR	25400
19086 GROUP IV	0201856	GD 21 PLASMA	5/6/02	091802AR	40700
19086 GROUP IV*	0201856 Dup Inj	GD 21 PLASMA	5/6/02	091802AR	40800
19087 GROUP IV	0201857	GD 21 PLASMA	5/6/02	091802AR	32500
19087 GROUP IV*	0201857 Dup Inj	GD 21 PLASMA	5/6/02	091802AR	32300
19088 GROUP V	0201858	GD 21 PLASMA	5/9/02	091802AR	72600
19088 GROUP V*	0201858 Dup Inj	GD 21 PLASMA	5/9/02	091802AR	73600
19089 GROUP V	0201859	GD 21 PLASMA	5/9/02	091802AR	53200
19089 GROUP V*	0201859 Dup Inj	GD 21 PLASMA	5/9/02	091802AR	54400
19090 GROUP V	0201860	GD 21 PLASMA	5/9/02	091802AR	52200
19090 GROUP V*	0201860 Dup Inj	GD 21 PLASMA	5/9/02	091802AR	52800
19076 GROUP I	0201831	PD 14 PLASMA	4/14/02	091902A	ND
19076 GROUP I*	0201831 Dup Inj	PD 14 PLASMA	4/14/02	091902A	ND
19077 GROUP I	0201832	PD 14 PLASMA	4/14/02	091902A	386
19077 GROUP I*	0201832 Dup Inj	PD 14 PLASMA	4/14/02	091902A	398
19078 GROUP I	0201833	PD 14 PLASMA	4/14/02	091902A	ND
19078 GROUP I*	0201833 Dup Inj	PD 14 PLASMA	4/14/02	091902A	ND
19079 GROUP II	0201834	PD 14 PLASMA	4/14/02	091902AR	3800
19079 GROUP II*	0201834 Dup Inj	PD 14 PLASMA	4/14/02	091902AR	3530
19080 GROUP II	0201835	PD 14 PLASMA	4/14/02	091902AR	2600
19080 GROUP II*	0201835 Dup Inj	PD 14 PLASMA	4/14/02	091902AR	2630
19081 GROUP II	0201836	PD 14 PLASMA	4/14/02	091902AR	2040
19081 GROUP II*	0201836 Dup Inj	PD 14 PLASMA	4/14/02	091902AR	2090
19082 GROUP III	0201837	PD 14 PLASMA	4/14/02	091902AR	10400
19082 GROUP III*	0201837 Dup Inj	PD 14 PLASMA	4/14/02	091902AR	10100
19083 GROUP III	0201838	PD 14 PLASMA	4/14/02	091902AR	13100
19083 GROUP III*	0201838 Dup Inj	PD 14 PLASMA	4/14/02	091902AR	14000
19084 GROUP III	0201839	PD 14 PLASMA	4/14/02	091902AR	5540
19084 GROUP III*	0201839 Dup Inj	PD 14 PLASMA	4/14/02	091902AR	5980
19085 GROUP IV	0201840	PD 14 PLASMA	4/14/02	091902AR	16900
19085 GROUP IV*	0201840 Dup Inj	PD 14 PLASMA	4/14/02	091902AR	17900
19086 GROUP IV	0201841	PD 14 PLASMA	4/14/02	091902AR	24800
19086 GROUP IV*	0201841 Dup Inj	PD 14 PLASMA	4/14/02	091902AR	25200
19087 GROUP IV	0201842	PD 14 PLASMA	4/14/02	091902AR	19200
19087 GROUP IV*	0201842 Dup Inj	PD 14 PLASMA	4/14/02	091902AR	20000
19088 GROUP V	0201843	PD 14 PLASMA	4/14/02	091902AR	43900
19088 GROUP V*	0201843 Dup Inj	PD 14 PLASMA	4/14/02	091902AR	43000
19089 GROUP V	0201844	PD 14 PLASMA	4/14/02	091902AR	47100
19089 GROUP V*	0201844 Dup Inj	PD 14 PLASMA	4/14/02	091902AR	48200
19090 GROUP V	0201845	PD 14 PLASMA	4/14/02	091902AR	34000
19090 GROUP V*	0201845 Dup Inj	PD 14 PLASMA	4/14/02	091902AR	35900

* Duplicate Injection ND = Not Detected (Area less than lowest calibration standard of 0.1 ng/mL)

Table VIII. Summary of PFHS Residues in Rat Serum Samples

Sponsor ID	Exygen ID	Matrix	Collection Date	Set Number	PFHS Found (ng/mL)
19076 GROUP I	0201861	Pooled Fetal Serum	5/9/02	091902B	ND
19076 GROUP I*	0201861 Dup Inj	Pooled Fetal Serum	5/9/02	091902B	ND
19078 GROUP I	0201862	Pooled Fetal Serum	5/7/02	091902B	ND
19078 GROUP I*	0201862 Dup Inj	Pooled Fetal Serum	5/7/02	091902B	ND
19079 GROUP II	0201863	Pooled Fetal Serum	5/9/02	091902BR	6460
19079 GROUP II*	0201863 Dup Inj	Pooled Fetal Serum	5/9/02	091902BR	6800
19080 GROUP II	0201864	Pooled Fetal Serum	5/9/02	091902BR	3940
19080 GROUP II*	0201864 Dup Inj	Pooled Fetal Serum	5/9/02	091902BR	4040
19081 GROUP II	0201865	Pooled Fetal Serum	5/10/02	091902BR	5280
19081 GROUP II*	0201865 Dup Inj	Pooled Fetal Serum	5/10/02	091902BR	5370
19082 GROUP III	0201866	Pooled Fetal Serum	5/9/02	091902BR	12600
19082 GROUP III*	0201866 Dup Inj	Pooled Fetal Serum	5/9/02	091902BR	13500
19083 GROUP III	0201867	Pooled Fetal Serum	5/7/02	091902BR	15700
19083 GROUP III*	0201867 Dup Inj	Pooled Fetal Serum	5/7/02	091902BR	15700
19084 GROUP III	0201868	Pooled Fetal Serum	5/9/02	091902BR	11700
19084 GROUP III*	0201868 Dup Inj	Pooled Fetal Serum	5/9/02	091902BR	11600
19085 GROUP IV	0201869	Pooled Fetal Serum	5/6/02	091902BR	38600
19085 GROUP IV*	0201869 Dup Inj	Pooled Fetal Serum	5/6/02	091902BR	40200
19086 GROUP IV	0201870	Pooled Fetal Serum	5/6/02	091902BR	33000
19086 GROUP IV*	0201870 Dup Inj	Pooled Fetal Serum	5/6/02	091902BR	34700
19087 GROUP IV	0201871	Pooled Fetal Serum	5/6/02	091902BR	36900
19087 GROUP IV*	0201871 Dup Inj	Pooled Fetal Serum	5/6/02	091902BR	39200
19088 GROUP V	0201872	Pooled Fetal Serum	5/9/02	091902BR	35700
19088 GROUP V*	0201872 Dup Inj	Pooled Fetal Serum	5/9/02	091902BR	38400
19089 GROUP V	0201873	Pooled Fetal Serum	5/9/02	091902BR	44900
19089 GROUP V*	0201873 Dup Inj	Pooled Fetal Serum	5/9/02	091902BR	47900
19090 GROUP V	0201874	Pooled Fetal Serum	5/9/02	091902BR	47900
19090 GROUP V*	0201874 Dup Inj	Pooled Fetal Serum	5/9/02	091902BR	51200
19012 GROUP I	0201875	Pooled Pup Serum	5/29/02	092002A	ND
19012 GROUP I*	0201875 Dup Inj	Pooled Pup Serum	5/29/02	092002A	ND
19019 GROUP I	0201876	Pooled Pup Serum	5/30/02	092002A	65.3^^
19019 GROUP I*	0201876 Dup Inj	Pooled Pup Serum	5/30/02	092002A	68.9^^
19021 GROUP I	0201877	Pooled Pup Serum	5/29/02	092002A	81.1^^
19021 GROUP I*	0201877 Dup Inj	Pooled Pup Serum	5/29/02	092002A	86.0^^
19023 GROUP I	0201878	Pooled Pup Serum	5/31/02	092002A	45.6^^
19023 GROUP I*	0201878 Dup Inj	Pooled Pup Serum	5/31/02	092002A	42.7^^
19041 GROUP I	0201879	Pooled Pup Serum	5/31/02	092002A	ND
19041 GROUP I*	0201879 Dup Inj	Pooled Pup Serum	5/31/02	092002A	ND
19042 GROUP I	0201880	Pooled Pup Serum	5/30/02	092002A	ND
19042 GROUP I*	0201880 Dup Inj	Pooled Pup Serum	5/30/02	092002A	ND
19044 GROUP I	0201881	Pooled Pup Serum	5/28/02	092002A	ND
19044 GROUP I*	0201881 Dup Inj	Pooled Pup Serum	5/28/02	092002A	ND
19050 GROUP I	0201882	Pooled Pup Serum	5/31/02	092002A	ND
19050 GROUP I*	0201882 Dup Inj	Pooled Pup Serum	5/31/02	092002A	ND
19053 GROUP I	0201883	Pooled Pup Serum	5/30/02	092002A	ND
19053 GROUP I*	0201883 Dup Inj	Pooled Pup Serum	5/30/02	092002A	ND
19065 GROUP I	0201884	Pooled Pup Serum	5/30/02	092002A	ND
19065 GROUP I*	0201884 Dup Inj	Pooled Pup Serum	5/30/02	092002A	ND
19004 GROUP II	0201885	Pooled Pup Serum	5/31/02	092002AR	9650
19004 GROUP II*	0201885 Dup Inj	Pooled Pup Serum	5/31/02	092002AR	9560
19009 GROUP II	0201886	Pooled Pup Serum	5/28/02	092002AR	7940
19009 GROUP II*	0201886 Dup Inj	Pooled Pup Serum	5/28/02	092002AR	7940
19016 GROUP II	0201887	Pooled Pup Serum	5/28/02	092002AR	8490
19016 GROUP II*	0201887 Dup Inj	Pooled Pup Serum	5/28/02	092002AR	8200
19018 GROUP II	0201888	Pooled Pup Serum	5/29/02	092002AR	8630
19018 GROUP II*	0201888 Dup Inj	Pooled Pup Serum	5/29/02	092002AR	8720
19026 GROUP II	0201889	Pooled Pup Serum	5/31/02	092002AR	5490
19026 GROUP II*	0201889 Dup Inj	Pooled Pup Serum	5/31/02	092002AR	5420
19036 GROUP II	0201890	Pooled Pup Serum	5/28/02	092002BR	6300
19036 GROUP II*	0201890 Dup Inj	Pooled Pup Serum	5/28/02	092002BR	6370

^^Although the method used allows for alternate sample volumes or weights and all the peak area responses are within the calibration curve limits, the precision for the 0.1 mL or 0.1 g samples below 100 ppb has not been validated.

* Duplicate Injection ND = Not Detected (Area less than lowest calibration standard of 0.1 ng/mL)

Table VIII (cont'd). Summary of PFHS Residues in Rat Serum Samples

Sponsor ID	Exygen ID	Matrix	Collection Date	Set Number	PFHS Found (ng/mL)
19037 GROUP II	0201891	Pooled Pup Serum	5/29/02	092002BR	12800
19037 GROUP II*	0201891 Dup Inj	Pooled Pup Serum	5/29/02	092002BR	13000
19043 GROUP II	0201892	Pooled Pup Serum	5/28/02	092002BR	5750
19043 GROUP II*	0201892 Dup Inj	Pooled Pup Serum	5/28/02	092002BR	5970
19047 GROUP II	0201893	Pooled Pup Serum	5/28/02	092002BR	8990
19047 GROUP II*	0201893 Dup Inj	Pooled Pup Serum	5/28/02	092002BR	8810
19048 GROUP II	0201894	Pooled Pup Serum	5/31/02	092002BR	11700
19048 GROUP II*	0201894 Dup Inj	Pooled Pup Serum	5/31/02	092002BR	11700
19003 GROUP III	0201895	Pooled Pup Serum	5/30/02	092002BR	37300
19003 GROUP III*	0201895 Dup Inj	Pooled Pup Serum	5/30/02	092002BR	37400
19007 GROUP III	0201896	Pooled Pup Serum	5/30/02	092002BR	47300
19007 GROUP III*	0201896 Dup Inj	Pooled Pup Serum	5/30/02	092002BR	46300
19008 GROUP III	0201897	Pooled Pup Serum	5/31/02	092002BR	44000
19008 GROUP III*	0201897 Dup Inj	Pooled Pup Serum	5/31/02	092002BR	45400
19013 GROUP III	0201898	Pooled Pup Serum	5/29/02	092002BR	24300
19013 GROUP III*	0201898 Dup Inj	Pooled Pup Serum	5/29/02	092002BR	24600
19015 GROUP III	0201899	Pooled Pup Serum	5/31/02	092002BR	36900
19015 GROUP III*	0201899 Dup Inj	Pooled Pup Serum	5/31/02	092002BR	37000
19017 GROUP III	0201900	Pooled Pup Serum	5/28/02	092002BR	20800
19017 GROUP III*	0201900 Dup Inj	Pooled Pup Serum	5/28/02	092002BR	21200
19024 GROUP III	0201901	Pooled Pup Serum	5/31/02	092002BR	42900
19024 GROUP III*	0201901 Dup Inj	Pooled Pup Serum	5/31/02	092002BR	45000
19029 GROUP III	0201902	Pooled Pup Serum	5/29/02	092002BR	24900
19029 GROUP III*	0201902 Dup Inj	Pooled Pup Serum	5/29/02	092002BR	22600
19034 GROUP III	0201903	Pooled Pup Serum	5/30/02	092002BR	45000
19034 GROUP III*	0201903 Dup Inj	Pooled Pup Serum	5/30/02	092002BR	43700
19056 GROUP III	0201904	Pooled Pup Serum	5/31/02	092002BR	19700
19056 GROUP III*	0201904 Dup Inj	Pooled Pup Serum	5/31/02	092002BR	20500
19005 GROUP IV	0201905	Pooled Pup Serum	5/31/02	092302AR	30900
19005 GROUP IV*	0201905 Dup Inj	Pooled Pup Serum	5/31/02	092302AR	30800
19035 GROUP IV	0201906	Pooled Pup Serum	5/31/02	092302AR	34600
19035 GROUP IV*	0201906 Dup Inj	Pooled Pup Serum	5/31/02	092302AR	33500
19039 GROUP IV	0201907	Pooled Pup Serum	5/29/02	092302AR	22600
19039 GROUP IV*	0201907 Dup Inj	Pooled Pup Serum	5/29/02	092302AR	22800
19040 GROUP IV	0201908	Pooled Pup Serum	5/30/02	092302AR	40700
19040 GROUP IV*	0201908 Dup Inj	Pooled Pup Serum	5/30/02	092302AR	38400
19045 GROUP IV	0201909	Pooled Pup Serum	5/28/02	092302AR	27800
19045 GROUP IV*	0201909 Dup Inj	Pooled Pup Serum	5/28/02	092302AR	29300
19054 GROUP IV	0201910	Pooled Pup Serum	5/31/02	092302AR	42900
19054 GROUP IV*	0201910 Dup Inj	Pooled Pup Serum	5/31/02	092302AR	43800
19058 GROUP IV	0201911	Pooled Pup Serum	5/28/02	092302AR	25800
19058 GROUP IV*	0201911 Dup Inj	Pooled Pup Serum	5/28/02	092302AR	25800
19062 GROUP IV	0201912	Pooled Pup Serum	5/31/02	092302AR	41200
19062 GROUP IV*	0201912 Dup Inj	Pooled Pup Serum	5/31/02	092302AR	41100
19063 GROUP IV	0201913	Pooled Pup Serum	5/29/02	092302AR	19800
19063 GROUP IV*	0201913 Dup Inj	Pooled Pup Serum	5/29/02	092302AR	19100
19066 GROUP IV	0201914	Pooled Pup Serum	5/31/02	092302AR	36800
19066 GROUP IV*	0201914 Dup Inj	Pooled Pup Serum	5/31/02	092302AR	39300
19001 GROUP V	0201915	Pooled Pup Serum	5/13/02	092302AR	29000
19001 GROUP V*	0201915 Dup Inj	Pooled Pup Serum	5/13/02	092302AR	32700
19006 GROUP V	0201916	Pooled Pup Serum	5/13/02	092302AR	47900
19006 GROUP V*	0201916 Dup Inj	Pooled Pup Serum	5/13/02	092302AR	52400
19011 GROUP V	0201917	Pooled Pup Serum	5/13/02	092302AR	162000
19011 GROUP V*	0201917 Dup Inj	Pooled Pup Serum	5/13/02	092302AR	164000
19020 GROUP V	0201918	Pooled Pup Serum	5/14/02	092302AR	72800
19020 GROUP V*	0201918 Dup Inj	Pooled Pup Serum	5/14/02	092302AR	76200
19022 GROUP V	0201919	Pooled Pup Serum	5/31/02	092302AR	84100
19022 GROUP V*	0201919 Dup Inj	Pooled Pup Serum	5/31/02	092302AR	89400
19025 GROUP V	0201920	Pooled Pup Serum	5/30/02	092302AR	50200
19025 GROUP V*	0201920 Dup Inj	Pooled Pup Serum	5/30/02	092302AR	53900
19027 GROUP V	0201921	Pooled Pup Serum	5/31/02	092302AR	57200
19027 GROUP V*	0201921 Dup Inj	Pooled Pup Serum	5/31/02	092302AR	53700
19028 GROUP V	0201922	Pooled Pup Serum	5/28/02	092302AR	162000
19028 GROUP V*	0201922 Dup Inj	Pooled Pup Serum	5/28/02	092302AR	163000
19030 GROUP V	0201923	Pooled Pup Serum	5/31/02	092302AR	184000
19030 GROUP V*	0201923 Dup Inj	Pooled Pup Serum	5/31/02	092302AR	189000
19031 GROUP V	0201924	Pooled Pup Serum	5/28/02	092302AR	71200
19031 GROUP V*	0201924 Dup Inj	Pooled Pup Serum	5/28/02	092302AR	76200

* Duplicate Injection

Table IX. Summary of PFHS Residues in Rat Liver Samples

Sponsor ID	Exygen ID	Matrix	Collection Date	Set Number	PFHS Found (ng/mL)
19176 GROUP I	0201759	Median Liver Lobe	5/12/02	092802A	606
19176 GROUP I*	0201759 Dup Inj	Median Liver Lobe	5/12/02	092802A	576
19177 GROUP I	0201760	Median Liver Lobe	5/12/02	092802A	138
19177 GROUP I*	0201760 Dup Inj	Median Liver Lobe	5/12/02	092802A	141
19178 GROUP I	0201761	Median Liver Lobe	5/12/02	092802A	326
19178 GROUP I*	0201761 Dup Inj	Median Liver Lobe	5/12/02	092802A	335
19179 GROUP II	0201762	Median Liver Lobe	5/12/02	092802A	40100
19179 GROUP II*	0201762 Dup Inj	Median Liver Lobe	5/12/02	092802A	42300
19180 GROUP II	0201763	Median Liver Lobe	5/12/02	092802A	36800
19180 GROUP II*	0201763 Dup Inj	Median Liver Lobe	5/12/02	092802A	37900
19181 GROUP II	0201764	Median Liver Lobe	5/12/02	092802A	52900
19181 GROUP II*	0201764 Dup Inj	Median Liver Lobe	5/12/02	092802A	52800
19182 GROUP III	0201765	Median Liver Lobe	5/12/02	092802A	149000
19182 GROUP III*	0201765 Dup Inj	Median Liver Lobe	5/12/02	092802A	154000
19183 GROUP III	0201766	Median Liver Lobe	5/12/02	092802A	124000
19183 GROUP III*	0201766 Dup Inj	Median Liver Lobe	5/12/02	092802A	121000
19184 GROUP III	0201767	Median Liver Lobe	5/12/02	092802A	172000
19184 GROUP III*	0201767 Dup Inj	Median Liver Lobe	5/12/02	092802A	177000
19185 GROUP IV	0201768	Median Liver Lobe	5/12/02	092802A	194000
19185 GROUP IV*	0201768 Dup Inj	Median Liver Lobe	5/12/02	092802A	187000
19186 GROUP IV	0201769	Median Liver Lobe	5/12/02	092802A	408000
19186 GROUP IV*	0201769 Dup Inj	Median Liver Lobe	5/12/02	092802A	407000
19187 GROUP IV	0201770	Median Liver Lobe	5/12/02	092802A	416000
19187 GROUP IV*	0201770 Dup Inj	Median Liver Lobe	5/12/02	092802A	420000
19188 GROUP V	0201771	Median Liver Lobe	5/12/02	092802A	501000
19188 GROUP V*	0201771 Dup Inj	Median Liver Lobe	5/12/02	092802A	511000
19189 GROUP V	0201772	Median Liver Lobe	5/12/02	092802A	659000
19189 GROUP V*	0201772 Dup Inj	Median Liver Lobe	5/12/02	092802A	675000
19190 GROUP V	0201773	Median Liver Lobe	5/12/02	092802A	612000
19190 GROUP V*	0201773 Dup Inj	Median Liver Lobe	5/12/02	092802A	603000
19076 GROUP I	0201774	Median Liver Lobe	5/9/02	092602A	ND
19076 GROUP I*	0201774 Dup Inj	Median Liver Lobe	5/9/02	092602A	ND
19077 GROUP I	0201775	Median Liver Lobe	5/19/02	092602A	82.2^^
19077 GROUP I*	0201775 Dup Inj	Median Liver Lobe	5/19/02	092602A	82.4^^
19078 GROUP I	0201776	Median Liver Lobe	5/7/02	092602A	ND
19078 GROUP I*	0201776 Dup Inj	Median Liver Lobe	5/7/02	092602A	ND
19081 GROUP II Female 1	0203650	Median Liver Lobe	5/10/02	092602A	628
19081 GROUP II Female 1*	0203650 Dup Inj	Median Liver Lobe	5/10/02	092602A	633
19079 GROUP II	0201777	Median Liver Lobe	5/9/02	092602AR	1040
19079 GROUP II*	0201777 Dup Inj	Median Liver Lobe	5/9/02	092602AR	974
19080 GROUP II	0201778	Median Liver Lobe	5/9/02	092602AR	762
19080 GROUP II*	0201778 Dup Inj	Median Liver Lobe	5/9/02	092602AR	725
19082 GROUP III	0201779	Median Liver Lobe	5/9/02	092602AR	1960
19082 GROUP III*	0201779 Dup Inj	Median Liver Lobe	5/9/02	092602AR	2080
19083 GROUP III	0201780	Median Liver Lobe	5/7/02	092602AR	3070
19083 GROUP III*	0201780 Dup Inj	Median Liver Lobe	5/7/02	092602AR	3090
19084 GROUP III	0201781	Median Liver Lobe	5/9/02	092602AR	2700
19084 GROUP III*	0201781 Dup Inj	Median Liver Lobe	5/9/02	092602AR	2750
19085 GROUP IV	0201782	Median Liver Lobe	5/6/02	092602AR	6360
19085 GROUP IV*	0201782 Dup Inj	Median Liver Lobe	5/6/02	092602AR	6640
19086 GROUP IV	0201783	Median Liver Lobe	5/6/02	092602AR	9740
19086 GROUP IV*	0201783 Dup Inj	Median Liver Lobe	5/6/02	092602AR	9370

^^Although the method used allows for alternate sample volumes or weights and all the peak area responses are within the calibration curve limits, the precision for the 0.1 mL or 0.1 g samples below 100 ppb has not been validated.

* Duplicate Injection ND = Not Detected (Area less than lowest calibration standard of 0.1 ng/mL)

Table IX. (cont'd). Summary of PFHS Residues in Rat Liver Samples

Sponsor ID	Exygen ID	Matrix	Collection Date	Set Number	PFHS Found (ng/mL)
19087 GROUP IV	0201784	Median Liver Lobe	5/6/02	092602AR	7500
19087 GROUP IV*	0201784 Dup Inj	Median Liver Lobe	5/6/02	092602AR	7210
19088 GROUP V	0201785	Median Liver Lobe	5/9/02	092602AR	19000
19088 GROUP V*	0201785 Dup Inj	Median Liver Lobe	5/9/02	092602AR	20000
19089 GROUP V	0201786	Median Liver Lobe	5/9/02	092602AR	15100
19089 GROUP V*	0201786 Dup Inj	Median Liver Lobe	5/9/02	092602AR	15300
19090 GROUP V	0201787	Median Liver Lobe	5/9/02	092602AR	14700
19090 GROUP V*	0201787 Dup Inj	Median Liver Lobe	5/9/02	092602AR	15100
19076 GROUP I	0201788	Pooled Fetal Liver	5/9/02	092602B	27.7^^
19076 GROUP I*	0201788 Dup Inj	Pooled Fetal Liver	5/9/02	092602B	25.7^^
19078 GROUP I	0201789	Pooled Fetal Liver	5/7/02	092602B	ND
19078 GROUP I*	0201789 Dup Inj	Pooled Fetal Liver	5/7/02	092602B	ND
19081 GROUP II Female 2	0203651	Pooled Fetal Liver	5/10/02	092602B	789
19081 GROUP II Female 2*	0203651 Dup Inj	Pooled Fetal Liver	5/10/02	092602B	821
19079 GROUP II	0201790	Pooled Fetal Liver	5/9/02	092602BR	1460
19079 GROUP II*	0201790 Dup Inj	Pooled Fetal Liver	5/9/02	092602BR	1480
19080 GROUP II	0201791	Pooled Fetal Liver	5/9/02	092602BR	1810
19080 GROUP II*	0201791 Dup Inj	Pooled Fetal Liver	5/9/02	092602BR	1880
19082 GROUP III	0201792	Pooled Fetal Liver	5/9/02	092602BR	2180
19082 GROUP III*	0201792 Dup Inj	Pooled Fetal Liver	5/9/02	092602BR	2290
19083 GROUP III	0201793	Pooled Fetal Liver	5/7/02	092602BR	4560
19083 GROUP III*	0201793 Dup Inj	Pooled Fetal Liver	5/7/02	092602BR	4550
19084 GROUP III	0201794	Pooled Fetal Liver	5/9/02	092602BR	3020
19084 GROUP III*	0201794 Dup Inj	Pooled Fetal Liver	5/9/02	092602BR	3150
19085 GROUP IV	0201795	Pooled Fetal Liver	5/6/02	092602BR	7320
19085 GROUP IV*	0201795 Dup Inj	Pooled Fetal Liver	5/6/02	092602BR	7170
19086 GROUP IV	0201796	Pooled Fetal Liver	5/6/02	092602BR	8510
19086 GROUP IV*	0201796 Dup Inj	Pooled Fetal Liver	5/6/02	092602BR	8590
19087 GROUP IV	0201797	Pooled Fetal Liver	5/6/02	092602BR	5630
19087 GROUP IV*	0201797 Dup Inj	Pooled Fetal Liver	5/6/02	092602BR	5920
19088 GROUP V	0201798	Pooled Fetal Liver	5/9/02	092602BR	22200
19088 GROUP V*	0201798 Dup Inj	Pooled Fetal Liver	5/9/02	092602BR	22800
19089 GROUP V	0201799	Pooled Fetal Liver	5/9/02	092602BR	20100
19089 GROUP V*	0201799 Dup Inj	Pooled Fetal Liver	5/9/02	092602BR	19800
19090 GROUP V	0201800	Pooled Fetal Liver	5/9/02	092602BR	14700
19090 GROUP V*	0201800 Dup Inj	Pooled Fetal Liver	5/9/02	092602BR	13600
19012 GROUP I, Male 1	0201925	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Male 1*	0201925 Dup Inj	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Male 2	0201926	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Male 2*	0201926 Dup Inj	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Male 3	0201927	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Male 3*	0201927 Dup Inj	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Male 4	0201928	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Male 4*	0201928 Dup Inj	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Male 5	0201929	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Male 5*	0201929 Dup Inj	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Female 7	0201930	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Female 7*	0201930 Dup Inj	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Female 8	0201931	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Female 8*	0201931 Dup Inj	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Female 14	0201932	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Female 14*	0201932 Dup Inj	Pup Livers	5/29/02	092702A	ND

^^Although the method used allows for alternate sample volumes or weights and all the peak area responses are within the calibration curve limits, the precision for the 0.1 mL or 0.1 g samples below 100 ppb has not been validated.

* Duplicate Injection ND = Not Detected (Area less than lowest calibration standard of 0.1 ng/mL)

Table IX. (cont'd). Summary of PFHS Residues in Rat Liver Samples

Sponsor ID	Exygen ID	Matrix	Collection Date	Set Number	PFHS Found (ng/mL)
19012 GROUP I, Female 15	0201933	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Female 15*	0201933 Dup Inj	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Female 16	0201934	Pup Livers	5/29/02	092702A	ND
19012 GROUP I, Female 16*	0201934 Dup Inj	Pup Livers	5/29/02	092702A	ND
19019 GROUP I, Male 1	0201935	Pup Livers	5/30/02	092702A	ND
19019 GROUP I, Male 1*	0201935 Dup Inj	Pup Livers	5/30/02	092702A	ND
19019 GROUP I, Male 2	0201936	Pup Livers	5/30/02	092702A	ND
19019 GROUP I, Male 2*	0201936 Dup Inj	Pup Livers	5/30/02	092702A	ND
19019 GROUP I, Male 3	0201937	Pup Livers	5/30/02	092702A	21.7^^
19019 GROUP I, Male 3*	0201937 Dup Inj	Pup Livers	5/30/02	092702A	18.3^^
19019 GROUP I, Male 7	0201938	Pup Livers	5/30/02	092702A	20.5^^
19019 GROUP I, Male 7*	0201938 Dup Inj	Pup Livers	5/30/02	092702A	18.9^^
19019 GROUP I, Male 8	0201939	Pup Livers	5/30/02	092702A	ND
19019 GROUP I, Male 8*	0201939 Dup Inj	Pup Livers	5/30/02	092702A	ND
19019 GROUP I, Female 11	0201940	Pup Livers	5/30/02	092702A	ND
19019 GROUP I, Female 11*	0201940 Dup Inj	Pup Livers	5/30/02	092702A	ND
19019 GROUP I, Female 12	0201941	Pup Livers	5/30/02	092702A	ND
19019 GROUP I, Female 12*	0201941 Dup Inj	Pup Livers	5/30/02	092702A	ND
19019 GROUP I, Female 13	0201942	Pup Livers	5/30/02	092702A	34.0^^
19019 GROUP I, Female 13*	0201942 Dup Inj	Pup Livers	5/30/02	092702A	30.6^^
19019 GROUP I, Female 14	0201943	Pup Livers	5/30/02	092702A	ND
19019 GROUP I, Female 14*	0201943 Dup Inj	Pup Livers	5/30/02	092702A	ND
19019 GROUP I, Female 15	0201944	Pup Livers	5/30/02	092702A	ND
19019 GROUP I, Female 15*	0201944 Dup Inj	Pup Livers	5/30/02	092702A	ND
19021 GROUP I, Male 1	0201945	Pup Livers	5/29/02	092702B	ND
19021 GROUP I, Male 1*	0201945 Dup Inj	Pup Livers	5/29/02	092702B	ND
19021 GROUP I, Male 2	0201946	Pup Livers	5/29/02	092702B	ND
19021 GROUP I, Male 2*	0201946 Dup Inj	Pup Livers	5/29/02	092702B	ND
19021 GROUP I, Male 6	0201947	Pup Livers	5/29/02	092702B	ND
19021 GROUP I, Male 6*	0201947 Dup Inj	Pup Livers	5/29/02	092702B	ND
19021 GROUP I, Male 8	0201948	Pup Livers	5/29/02	092702B	ND
19021 GROUP I, Male 8*	0201948 Dup Inj	Pup Livers	5/29/02	092702B	ND
19021 GROUP I, Male 9	0201949	Pup Livers	5/29/02	092702B	ND
19021 GROUP I, Male 9*	0201949 Dup Inj	Pup Livers	5/29/02	092702B	ND
19021 GROUP I, Female 11	0201951	Pup Livers	5/29/02	092702B	ND
19021 GROUP I, Female 11*	0201951 Dup Inj	Pup Livers	5/29/02	092702B	ND
19021 GROUP I, Female 12	0201952	Pup Livers	5/29/02	092702B	ND
19021 GROUP I, Female 12*	0201952 Dup Inj	Pup Livers	5/29/02	092702B	ND
19021 GROUP I, Female 13	0201953	Pup Livers	5/29/02	092702B	ND
19021 GROUP I, Female 13*	0201953 Dup Inj	Pup Livers	5/29/02	092702B	ND
19021 GROUP I, Female 14	0201954	Pup Livers	5/29/02	092702B	ND
19021 GROUP I, Female 14*	0201954 Dup Inj	Pup Livers	5/29/02	092702B	ND
19023 GROUP I, Male 1	0201955	Pup Livers	5/31/02	092702B	50.6^^
19023 GROUP I, Male 1*	0201955 Dup Inj	Pup Livers	5/31/02	092702B	53.5^^
19023 GROUP I, Male 2	0201956	Pup Livers	5/31/02	092702B	34.0^^
19023 GROUP I, Male 2*	0201956 Dup Inj	Pup Livers	5/31/02	092702B	37.0^^
19023 GROUP I, Male 3	0201957	Pup Livers	5/31/02	092702B	19.6^^
19023 GROUP I, Male 3*	0201957 Dup Inj	Pup Livers	5/31/02	092702B	24.1^^
19023 GROUP I, Male 6	0201958	Pup Livers	5/31/02	092702B	ND
19023 GROUP I, Male 6*	0201958 Dup Inj	Pup Livers	5/31/02	092702B	ND
19023 GROUP I, Male 7	0201959	Pup Livers	5/31/02	092702B	30.8^^
19023 GROUP I, Male 7*	0201959 Dup Inj	Pup Livers	5/31/02	092702B	34.0^^

^^Although the method used allows for alternate sample volumes or weights and all the peak area responses are within the calibration curve limits, the precision for the 0.1 mL or 0.1 g samples below 100 ppb has not been validated.

* Duplicate Injection ND = Not Detected (Area less than lowest calibration standard of 0.1 ng/mL)

Table IX. (cont'd). Summary of PFHS Residues in Rat Liver Samples

Sponsor ID	Exygen ID	Matrix	Collection Date	Set Number	PFHS Found (ng/mL)
9	0201960	Pup Livers	5/31/02	092702B	ND
19023 GROUP I, Female 8*	0201960 Dup Inj	Pup Livers	5/31/02	092702B	ND
19023 GROUP I, Female 9	0201961	Pup Livers	5/31/02	092702B	ND
19023 GROUP I, Female 9*	0201961 Dup Inj	Pup Livers	5/31/02	092702B	ND
19023 GROUP I, Female 10	0201962	Pup Livers	5/31/02	092702B	ND
19023 GROUP I, Female 10*	0201962 Dup Inj	Pup Livers	5/31/02	092702B	ND
19023 GROUP I, Female 11	0201963	Pup Livers	5/31/02	092702B	ND
19023 GROUP I, Female 11*	0201963 Dup Inj	Pup Livers	5/31/02	092702B	ND
19023 GROUP I, Female 12	0201964	Pup Livers	5/31/02	092702B	ND
19023 GROUP I, Female 12*	0201964 Dup Inj	Pup Livers	5/31/02	092702B	ND
19021 GROUP I, Female 10	0201950	Pup Livers	5/29/02	092702BR	ND
19021 GROUP I, Female 10*	0201950 Dup Inj	Pup Livers	5/29/02	092702BR	ND
19041 GROUP I, Male 1	0201965	Pup Livers	5/31/02	100102A	ND
19041 GROUP I, Male 1*	0201965 Dup Inj	Pup Livers	5/31/02	100102A	ND
19041 GROUP I, Male 2	0201966	Pup Livers	5/31/02	100102A	24.4^^
19041 GROUP I, Male 2*	0201966 Dup Inj	Pup Livers	5/31/02	100102A	26.6^^
19041 GROUP I, Male 3	0201967	Pup Livers	5/31/02	100102A	26.0^^
19041 GROUP I, Male 3*	0201967 Dup Inj	Pup Livers	5/31/02	100102A	24.7^^
19041 GROUP I, Male 4	0201968	Pup Livers	5/31/02	100102A	ND
19041 GROUP I, Male 4*	0201968 Dup Inj	Pup Livers	5/31/02	100102A	ND
19041 GROUP I, Male 5	0201969	Pup Livers	5/31/02	100102A	ND
19041 GROUP I, Male 5*	0201969 Dup Inj	Pup Livers	5/31/02	100102A	ND
19041 GROUP I, Female 8	0201970	Pup Livers	5/31/02	100102A	ND
19041 GROUP I, Female 8*	0201970 Dup Inj	Pup Livers	5/31/02	100102A	ND
19041 GROUP I, Female 9	0201971	Pup Livers	5/31/02	100102A	30.6^^
19041 GROUP I, Female 9*	0201971 Dup Inj	Pup Livers	5/31/02	100102A	30.8^^
19041 GROUP I, Female 15	0201972	Pup Livers	5/31/02	100102A	ND
19041 GROUP I, Female 15*	0201972 Dup Inj	Pup Livers	5/31/02	100102A	ND
19041 GROUP I, Female 16	0201973	Pup Livers	5/31/02	100102A	ND
19041 GROUP I, Female 16*	0201973 Dup Inj	Pup Livers	5/31/02	100102A	ND
19041 GROUP I, Female 17	0201974	Pup Livers	5/31/02	100102A	ND
19041 GROUP I, Female 17*	0201974 Dup Inj	Pup Livers	5/31/02	100102A	ND
19004 GROUP II, Male 2	0202025	Pup Livers	5/31/02	100102AR	1220
19004 GROUP II, Male 2*	0202025 Dup Inj	Pup Livers	5/31/02	100102AR	1160
19004 GROUP II, Male 3	0202026	Pup Livers	5/31/02	100102AR	1160
19004 GROUP II, Male 3*	0202026 Dup Inj	Pup Livers	5/31/02	100102AR	1120
19004 GROUP II, Male 4	0202027	Pup Livers	5/31/02	100102AR	2380
19004 GROUP II, Male 4*	0202027 Dup Inj	Pup Livers	5/31/02	100102AR	2480
19004 GROUP II, Male 5	0202028	Pup Livers	5/31/02	100102AR	1670
19004 GROUP II, Male 5*	0202028 Dup Inj	Pup Livers	5/31/02	100102AR	1670
19004 GROUP II, Male 6	0202029	Pup Livers	5/31/02	100102AR	2070
19004 GROUP II, Male 6*	0202029 Dup Inj	Pup Livers	5/31/02	100102AR	2000
19004 GROUP II, Female 9	0202030	Pup Livers	5/31/02	100102AR	1870
19004 GROUP II, Female 9*	0202030 Dup Inj	Pup Livers	5/31/02	100102AR	1880
19004 GROUP II, Female 11	0202031	Pup Livers	5/31/02	100102AR	1740
19004 GROUP II, Female 11*	0202031 Dup Inj	Pup Livers	5/31/02	100102AR	1710
19004 GROUP II, Female 15	0202032	Pup Livers	5/31/02	100102AR	1070
19004 GROUP II, Female 15*	0202032 Dup Inj	Pup Livers	5/31/02	100102AR	1060
19004 GROUP II, Female 16	0202033	Pup Livers	5/31/02	100102AR	1450
19004 GROUP II, Female 16*	0202033 Dup Inj	Pup Livers	5/31/02	100102AR	1530
19004 GROUP II, Female 17	0202034	Pup Livers	5/31/02	100102AR	946
19004 GROUP II, Female 17*	0202034 Dup Inj	Pup Livers	5/31/02	100102AR	983

^^Although the method used allows for alternate sample volumes or weights and all the peak area responses are within the calibration curve limits, the precision for the 0.1 mL or 0.1 g samples below 100 ppb has not been validated.

* Duplicate Injection ND = Not Detected (Area less than lowest calibration standard of 0.1 ng/mL)

Table IX. (cont'd). Summary of PFHS Residues in Rat Liver Samples

Sponsor ID	Exygen ID	Matrix	Collection Date	Set Number	PFHS Found (ng/mL)
19018 GROUP II, Male 1	0202050	Pup Livers	5/29/02	100202A	839
19018 GROUP II, Male 1*	0202050 Dup Inj	Pup Livers	5/29/02	100202A	816
19018 GROUP II, Male 4	0202051	Pup Livers	5/29/02	100202A	788
19018 GROUP II, Male 4*	0202051 Dup Inj	Pup Livers	5/29/02	100202A	818
19018 GROUP II, Male 5	0202052	Pup Livers	5/29/02	100202A	886
19018 GROUP II, Male 5*	0202052 Dup Inj	Pup Livers	5/29/02	100202A	872
19018 GROUP II, Male 6	0202053	Pup Livers	5/29/02	100202A	868
19018 GROUP II, Male 6*	0202053 Dup Inj	Pup Livers	5/29/02	100202A	888
19018 GROUP II, Male 7	0202054	Pup Livers	5/29/02	100202A	523
19018 GROUP II, Male 7*	0202054 Dup Inj	Pup Livers	5/29/02	100202A	514
19018 GROUP II, Female 9	0202055	Pup Livers	5/29/02	100202A	556
19018 GROUP II, Female 9*	0202055 Dup Inj	Pup Livers	5/29/02	100202A	596
19018 GROUP II, Female 10	0202056	Pup Livers	5/29/02	100202A	804
19018 GROUP II, Female 10*	0202056 Dup Inj	Pup Livers	5/29/02	100202A	785
19018 GROUP II, Female 11	0202057	Pup Livers	5/29/02	100202A	649
19018 GROUP II, Female 11*	0202057 Dup Inj	Pup Livers	5/29/02	100202A	664
19018 GROUP II, Female 12	0202058	Pup Livers	5/29/02	100202A	743
19018 GROUP II, Female 12*	0202058 Dup Inj	Pup Livers	5/29/02	100202A	751
19018 GROUP II, Female 14	0202059	Pup Livers	5/29/02	100202A	788
19018 GROUP II, Female 14*	0202059 Dup Inj	Pup Livers	5/29/02	100202A	815
19026 GROUP II, Male 5	0202063	Pup Livers	5/31/02	100202A	937
19026 GROUP II, Male 5*	0202063 Dup Inj	Pup Livers	5/31/02	100202A	928
19026 GROUP II, Male 1	0202060	Pup Livers	5/31/02	100202AR	1130
19026 GROUP II, Male 1*	0202060 Dup Inj	Pup Livers	5/31/02	100202AR	1130
19026 GROUP II, Male 3	0202061	Pup Livers	5/31/02	100202AR	1170
19026 GROUP II, Male 3*	0202061 Dup Inj	Pup Livers	5/31/02	100202AR	1150
19026 GROUP II, Male 4	0202062	Pup Livers	5/31/02	100202AR	1140
19026 GROUP II, Male 4*	0202062 Dup Inj	Pup Livers	5/31/02	100202AR	1130
19026 GROUP II, Male 7	0202064	Pup Livers	5/31/02	100202AR	1050
19026 GROUP II, Male 7*	0202064 Dup Inj	Pup Livers	5/31/02	100202AR	1010
19026 GROUP II, Female 12	0202065	Pup Livers	5/31/02	100202AR	946
19026 GROUP II, Female 12*	0202065 Dup Inj	Pup Livers	5/31/02	100202AR	956
19026 GROUP II, Female 13	0202066	Pup Livers	5/31/02	100202AR	928
19026 GROUP II, Female 13*	0202066 Dup Inj	Pup Livers	5/31/02	100202AR	919
19026 GROUP II, Female 14	0202067	Pup Livers	5/31/02	100202AR	1040
19026 GROUP II, Female 14*	0202067 Dup Inj	Pup Livers	5/31/02	100202AR	1140
19026 GROUP II, Female 15	0202068	Pup Livers	5/31/02	100202AR	1780
19026 GROUP II, Female 15*	0202068 Dup Inj	Pup Livers	5/31/02	100202AR	1830
19026 GROUP II, Female 18	0202069	Pup Livers	5/31/02	100202AR	1270
19026 GROUP II, Female 18*	0202069 Dup Inj	Pup Livers	5/31/02	100202AR	1310
19036 GROUP II, Male 1	0202070	Pup Livers	5/28/02	100302A	746
19036 GROUP II, Male 1*	0202070 Dup Inj	Pup Livers	5/28/02	100302A	748
19036 GROUP II, Male 2	0202071	Pup Livers	5/28/02	100302A	169
19036 GROUP II, Male 2*	0202071 Dup Inj	Pup Livers	5/28/02	100302A	174
19036 GROUP II, Male 4	0202072	Pup Livers	5/28/02	100302A	707
19036 GROUP II, Male 4*	0202072 Dup Inj	Pup Livers	5/28/02	100302A	693
19036 GROUP II, Male 5	0202073	Pup Livers	5/28/02	100302A	965
19036 GROUP II, Male 5*	0202073 Dup Inj	Pup Livers	5/28/02	100302A	946
19036 GROUP II, Male 6	0202074	Pup Livers	5/28/02	100302A	667
19036 GROUP II, Male 6*	0202074 Dup Inj	Pup Livers	5/28/02	100302A	649
19036 GROUP II, Female 7	0202075	Pup Livers	5/28/02	100302A	622
19036 GROUP II, Female 7*	0202075 Dup Inj	Pup Livers	5/28/02	100302A	620

* Duplicate Injection ND = Not Detected (Area less than lowest calibration standard of 0.1 ng/mL)

Table IX. (cont'd). Summary of PFHS Residues in Rat Liver Samples

Sponsor ID	Exygen ID	Matrix	Collection Date	Set Number	PFHS Found (ng/mL)
19036 GROUP II, Female 8	0202076	Pup Livers	5/28/02	100302A	668
19036 GROUP II, Female 8*	0202076 Dup Inj	Pup Livers	5/28/02	100302A	650
19036 GROUP II, Female 11	0202077	Pup Livers	5/28/02	100302A	554
19036 GROUP II, Female 11*	0202077 Dup Inj	Pup Livers	5/28/02	100302A	543
19036 GROUP II, Female 12	0202078	Pup Livers	5/28/02	100302A	676
19036 GROUP II, Female 12*	0202078 Dup Inj	Pup Livers	5/28/02	100302A	642
19036 GROUP II, Female 13	0202079	Pup Livers	5/28/02	100302A	494
19036 GROUP II, Female 13*	0202079 Dup Inj	Pup Livers	5/28/02	100302A	490
19037 GROUP II, Male 6	0202082	Pup Livers	5/29/02	100302A	906
19037 GROUP II, Male 6*	0202082 Dup Inj	Pup Livers	5/29/02	100302A	900
19037 GROUP II, Female 15	0202089	Pup Livers	5/29/02	100302A	956
19037 GROUP II, Female 15*	0202089 Dup Inj	Pup Livers	5/29/02	100302A	965
19037 GROUP II, Male 2	0202080	Pup Livers	5/29/02	100302AR	1670
19037 GROUP II, Male 2*	0202080 Dup Inj	Pup Livers	5/29/02	100302AR	1670
19037 GROUP II, Male 3	0202081	Pup Livers	5/29/02	100302AR	1430
19037 GROUP II, Male 3*	0202081 Dup Inj	Pup Livers	5/29/02	100302AR	1380
19037 GROUP II, Male 7	20831983	Pup Livers	5/29/02	100302AR	1280
19037 GROUP II, Male 7*	0202083 Dup Inj	Pup Livers	5/29/02	100302AR	1270
19037 GROUP II, Male 8	0202084	Pup Livers	5/29/02	100302AR	1760
19037 GROUP II, Male 8*	0202084 Dup Inj	Pup Livers	5/29/02	100302AR	1770
19037 GROUP II, Female 10	0202085	Pup Livers	5/29/02	100302AR	1150
19037 GROUP II, Female 10*	0202085 Dup Inj	Pup Livers	5/29/02	100302AR	1160
19037 GROUP II, Female 11	0202086	Pup Livers	5/29/02	100302AR	1300
19037 GROUP II, Female 11*	0202086 Dup Inj	Pup Livers	5/29/02	100302AR	1320
19037 GROUP II, Female 13	0202087	Pup Livers	5/29/02	100302AR	1680
19037 GROUP II, Female 13*	0202087 Dup Inj	Pup Livers	5/29/02	100302AR	1670
19037 GROUP II, Female 14	0202088	Pup Livers	5/29/02	100302AR	1330
19037 GROUP II, Female 14*	0202088 Dup Inj	Pup Livers	5/29/02	100302AR	1350
19003 GROUP III, Male 1	0202119	Pup Livers	5/30/02	100402AR	4640
19003 GROUP III, Male 1*	0202119 Dup Inj	Pup Livers	5/30/02	100402AR	4730
19003 GROUP III, Male 3	0202120	Pup Livers	5/30/02	100402AR	6250
19003 GROUP III, Male 3*	0202120 Dup Inj	Pup Livers	5/30/02	100402AR	6320
19003 GROUP III, Male 5	0202121	Pup Livers	5/30/02	100402AR	4490
19003 GROUP III, Male 5*	0202121 Dup Inj	Pup Livers	5/30/02	100402AR	4650
19003 GROUP III, Male 7	0202122	Pup Livers	5/30/02	100402AR	4540
19003 GROUP III, Male 7*	0202122 Dup Inj	Pup Livers	5/30/02	100402AR	4440
19003 GROUP III, Male 8	0202123	Pup Livers	5/30/02	100402AR	5820
19003 GROUP III, Male 8*	0202123 Dup Inj	Pup Livers	5/30/02	100402AR	5840
19003 GROUP III, Female 9	0202124	Pup Livers	5/30/02	100402AR	4100
19003 GROUP III, Female 9*	0202124 Dup Inj	Pup Livers	5/30/02	100402AR	4170
19003 GROUP III, Female 10	0202125	Pup Livers	5/30/02	100402AR	4400
19003 GROUP III, Female 10*	0202125 Dup Inj	Pup Livers	5/30/02	100402AR	4340
19003 GROUP III, Female 11	0202126	Pup Livers	5/30/02	100402AR	3270
19003 GROUP III, Female 11*	0202126 Dup Inj	Pup Livers	5/30/02	100402AR	3240
19003 GROUP III, Female 15	0202127	Pup Livers	5/30/02	100402AR	4810
19003 GROUP III, Female 15*	0202127 Dup Inj	Pup Livers	5/30/02	100402AR	4920
19003 GROUP III, Female 16	0202128	Pup Livers	5/30/02	100402AR	5430
19003 GROUP III, Female 16*	0202128 Dup Inj	Pup Livers	5/30/02	100402AR	5630
19007 GROUP III, Male 1	0202129	Pup Livers	5/30/02	100402AR	3030
19007 GROUP III, Male 1*	0202129 Dup Inj	Pup Livers	5/30/02	100402AR	3090
19007 GROUP III, Male 2	0202130	Pup Livers	5/30/02	100402AR	4310
19007 GROUP III, Male 2*	0202130 Dup Inj	Pup Livers	5/30/02	100402AR	4400

* Duplicate Injection ND = Not Detected (Area less than lowest calibration standard of 0.1 ng/mL)

Table IX. (cont'd). Summary of PFHS Residues in Rat Liver Samples

Sponsor ID	Exygen ID	Matrix	Collection Date	Set Number	PFHS Found (ng/mL)
19007 GROUP III, Male 3	0202131	Pup Livers	5/30/02	100402AR	4450
19007 GROUP III, Male 3*	0202131 Dup Inj	Pup Livers	5/30/02	100402AR	4370
19007 GROUP III, Male 6	0202132	Pup Livers	5/30/02	100402AR	4430
19007 GROUP III, Male 6*	0202132 Dup Inj	Pup Livers	5/30/02	100402AR	4600
19007 GROUP III, Male 7	0202133	Pup Livers	5/30/02	100402AR	5630
19007 GROUP III, Male 7*	0202133 Dup Inj	Pup Livers	5/30/02	100402AR	5720
19007 GROUP III, Female 9	0202134	Pup Livers	5/30/02	100402AR	6340
19007 GROUP III, Female 9*	0202134 Dup Inj	Pup Livers	5/30/02	100402AR	6330
19007 GROUP III, Female 11	0202135	Pup Livers	5/30/02	100402AR	3850
19007 GROUP III, Female 11*	0202135 Dup Inj	Pup Livers	5/30/02	100402AR	3820
19007 GROUP III, Female 12	0202136	Pup Livers	5/30/02	100402AR	5230
19007 GROUP III, Female 12*	0202136 Dup Inj	Pup Livers	5/30/02	100402AR	5130
19007 GROUP III, Female 13	0202137	Pup Livers	5/30/02	100402AR	6630
19007 GROUP III, Female 13*	0202137 Dup Inj	Pup Livers	5/30/02	100402AR	6870
19007 GROUP III, Female 16	0202138	Pup Livers	5/30/02	100402AR	5720
19007 GROUP III, Female 16*	0202138 Dup Inj	Pup Livers	5/30/02	100402AR	5690
19008 GROUP III, Male 1	0202139	Pup Livers	5/31/02	100402BR	3920
19008 GROUP III, Male 1*	0202139 Dup Inj	Pup Livers	5/31/02	100402BR	3810
19008 GROUP III, Male 3	0202140	Pup Livers	5/31/02	100402BR	5080
19008 GROUP III, Male 3*	0202140 Dup Inj	Pup Livers	5/31/02	100402BR	5070
19008 GROUP III, Male 4	0202141	Pup Livers	5/31/02	100402BR	4090
19008 GROUP III, Male 4*	0202141 Dup Inj	Pup Livers	5/31/02	100402BR	4070
19008 GROUP III, Male 6	0202142	Pup Livers	5/31/02	100402BR	4810
19008 GROUP III, Male 6*	0202142 Dup Inj	Pup Livers	5/31/02	100402BR	4750
19008 GROUP III, Male 7	0202143	Pup Livers	5/31/02	100402BR	4690
19008 GROUP III, Male 7*	0202143 Dup Inj	Pup Livers	5/31/02	100402BR	4380
19008 GROUP III, Female 9	0202144	Pup Livers	5/31/02	100402BR	5190
19008 GROUP III, Female 9*	0202144 Dup Inj	Pup Livers	5/31/02	100402BR	5050
19008 GROUP III, Female 10	0202145	Pup Livers	5/31/02	100402BR	3070
19008 GROUP III, Female 10*	0202145 Dup Inj	Pup Livers	5/31/02	100402BR	2770
19008 GROUP III, Female 11	0202146	Pup Livers	5/31/02	100402BR	4120
19008 GROUP III, Female 11*	0202146 Dup Inj	Pup Livers	5/31/02	100402BR	3760
19008 GROUP III, Female 12	0202147	Pup Livers	5/31/02	100402BR	2790
19008 GROUP III, Female 12*	0202147 Dup Inj	Pup Livers	5/31/02	100402BR	2480
19008 GROUP III, Female 13	0202148	Pup Livers	5/31/02	100402BR	2440
19008 GROUP III, Female 13*	0202148 Dup Inj	Pup Livers	5/31/02	100402BR	2340
19013 GROUP III, Male 1	0202149	Pup Livers	5/29/02	100402BR	1590
19013 GROUP III, Male 1*	0202149 Dup Inj	Pup Livers	5/29/02	100402BR	1790
19013 GROUP III, Male 4	0202150	Pup Livers	5/29/02	100402BR	1950
19013 GROUP III, Male 4*	0202150 Dup Inj	Pup Livers	5/29/02	100402BR	2050
19013 GROUP III, Male 5	0202151	Pup Livers	5/29/02	100402BR	2030
19013 GROUP III, Male 5*	0202151 Dup Inj	Pup Livers	5/29/02	100402BR	2090
19013 GROUP III, Male 6	0202152	Pup Livers	5/29/02	100402BR	2420
19013 GROUP III, Male 6*	0202152 Dup Inj	Pup Livers	5/29/02	100402BR	2480
19013 GROUP III, Male 9	0202153	Pup Livers	5/29/02	100402BR	2180
19013 GROUP III, Male 9*	0202153 Dup Inj	Pup Livers	5/29/02	100402BR	2280
19013 GROUP III, Female 11	0202154	Pup Livers	5/29/02	100402BR	2130
19013 GROUP III, Female 11*	0202154 Dup Inj	Pup Livers	5/29/02	100402BR	2150
19013 GROUP III, Female 12	0202155	Pup Livers	5/29/02	100402BR	2000
19013 GROUP III, Female 12*	0202155 Dup Inj	Pup Livers	5/29/02	100402BR	2010
19013 GROUP III, Female 13	0202156	Pup Livers	5/29/02	100402BR	1680
19013 GROUP III, Female 13*	0202156 Dup Inj	Pup Livers	5/29/02	100402BR	1780

* Duplicate Injection ND = Not Detected (Area less than lowest calibration standard of 0.1 ng/mL)

Table IX. (cont'd). Summary of PFHS Residues in Rat Liver Samples

Sponsor ID	Exygen ID	Matrix	Collection Date	Set Number	PFHS Found (ng/mL)
19013 GROUP III, Female 14	0202157	Pup Livers	5/29/02	100402BR	2290
19013 GROUP III, Female 14*	0202157 Dup Inj	Pup Livers	5/29/02	100402BR	2300
19013 GROUP III, Female 15	0202158	Pup Livers	5/29/02	100402BR	2000
19013 GROUP III, Female 15*	0202158 Dup Inj	Pup Livers	5/29/02	100402BR	2070
19015 GROUP III, Male 1	0202159	Pup Livers	5/31/02	100902AR	2950
19015 GROUP III, Male 1*	0202159 Dup Inj	Pup Livers	5/31/02	100902AR	2840
19015 GROUP III, Male 3	0202160	Pup Livers	5/31/02	100902AR	2780
19015 GROUP III, Male 3*	0202160 Dup Inj	Pup Livers	5/31/02	100902AR	2840
19015 GROUP III, Male 6	0202161	Pup Livers	5/31/02	100902AR	2860
19015 GROUP III, Male 6*	0202161 Dup Inj	Pup Livers	5/31/02	100902AR	2940
19015 GROUP III, Male 7	0202162	Pup Livers	5/31/02	100902AR	3150
19015 GROUP III, Male 7*	0202162 Dup Inj	Pup Livers	5/31/02	100902AR	3220
19015 GROUP III, Male 8	0202163	Pup Livers	5/31/02	100902AR	4680
19015 GROUP III, Male 8*	0202163 Dup Inj	Pup Livers	5/31/02	100902AR	4710
19015 GROUP III, Female 10	0202164	Pup Livers	5/31/02	100902AR	3800
19015 GROUP III, Female 10*	0202164 Dup Inj	Pup Livers	5/31/02	100902AR	3800
19015 GROUP III, Female 12	0202165	Pup Livers	5/31/02	100902AR	4280
19015 GROUP III, Female 12*	0202165 Dup Inj	Pup Livers	5/31/02	100902AR	4180
19015 GROUP III, Female 13	0202166	Pup Livers	5/31/02	100902AR	4000
19015 GROUP III, Female 13*	0202166 Dup Inj	Pup Livers	5/31/02	100902AR	3950
19015 GROUP III, Female 14	0202167	Pup Livers	5/31/02	100902AR	3800
19015 GROUP III, Female 14*	0202167 Dup Inj	Pup Livers	5/31/02	100902AR	3890
19015 GROUP III, Female 15	0202168	Pup Livers	5/31/02	100902AR	5330
19015 GROUP III, Female 15*	0202168 Dup Inj	Pup Livers	5/31/02	100902AR	5420
19005 GROUP IV, Male 1	0202219	Pup Livers	5/31/02	100902AR	8860
19005 GROUP IV, Male 1*	0202219 Dup Inj	Pup Livers	5/31/02	100902AR	8800
19005 GROUP IV, Male 2	0202220	Pup Livers	5/31/02	100902AR	9280
19005 GROUP IV, Male 2*	0202220 Dup Inj	Pup Livers	5/31/02	100902AR	9370
19005 GROUP IV, Male 3	0202221	Pup Livers	5/31/02	100902AR	10500
19005 GROUP IV, Male 3*	0202221 Dup Inj	Pup Livers	5/31/02	100902AR	11100
19005 GROUP IV, Male 5	0202222	Pup Livers	5/31/02	100902AR	8340
19005 GROUP IV, Male 5*	0202222 Dup Inj	Pup Livers	5/31/02	100902AR	9100
19005 GROUP IV, Male 6	0202223	Pup Livers	5/31/02	100902AR	11200
19005 GROUP IV, Male 6*	0202223 Dup Inj	Pup Livers	5/31/02	100902AR	10900
19005 GROUP IV, Female 8	0202224	Pup Livers	5/31/02	100902AR	11400
19005 GROUP IV, Female 8*	0202224 Dup Inj	Pup Livers	5/31/02	100902AR	11500
19005 GROUP IV, Female 10	0202225	Pup Livers	5/31/02	100902AR	12300
19005 GROUP IV, Female 10*	0202225 Dup Inj	Pup Livers	5/31/02	100902AR	12800
19005 GROUP IV, Female 11	0202226	Pup Livers	5/31/02	100902AR	12600
19005 GROUP IV, Female 11*	0202226 Dup Inj	Pup Livers	5/31/02	100902AR	12800
19005 GROUP IV, Female 12	0202227	Pup Livers	5/31/02	100902AR	9010
19005 GROUP IV, Female 12*	0202227 Dup Inj	Pup Livers	5/31/02	100902AR	9100
19005 GROUP IV, Female 15	0202228	Pup Livers	5/31/02	100902AR	11800
19005 GROUP IV, Female 15*	0202228 Dup Inj	Pup Livers	5/31/02	100902AR	12000
19035 GROUP IV, Male 1	0202229	Pup Livers	5/31/02	100902BR	11500
19035 GROUP IV, Male 1*	0202229 Dup Inj	Pup Livers	5/31/02	100902BR	12000
19035 GROUP IV, Male 2	0202230	Pup Livers	5/31/02	100902BR	14500
19035 GROUP IV, Male 2*	0202230 Dup Inj	Pup Livers	5/31/02	100902BR	14500
19035 GROUP IV, Male 4	0202231	Pup Livers	5/31/02	100902BR	13700
19035 GROUP IV, Male 4*	0202231 Dup Inj	Pup Livers	5/31/02	100902BR	13600
19035 GROUP IV, Male 5	0202232	Pup Livers	5/31/02	100902BR	11300
19035 GROUP IV, Male 5*	0202232 Dup Inj	Pup Livers	5/31/02	100902BR	10800

* Duplicate Injection ND = Not Detected (Area less than lowest calibration standard of 0.1 ng/mL)

Table IX. (cont'd). Summary of PFHS Residues in Rat Liver Samples

Sponsor ID	Exygen ID	Matrix	Collection Date	Set Number	PFHS Found (ng/mL)
19035 GROUP IV, Male 6	0202233	Pup Livers	5/31/02	100902BR	10600
19035 GROUP IV, Male 6*	0202233 Dup Inj	Pup Livers	5/31/02	100902BR	10500
19035 GROUP IV, Female 8	0202234	Pup Livers	5/31/02	100902BR	12000
19035 GROUP IV, Female 8*	0202234 Dup Inj	Pup Livers	5/31/02	100902BR	13300
19035 GROUP IV, Female 10	0202235	Pup Livers	5/31/02	100902BR	10000
19035 GROUP IV, Female 10*	0202235 Dup Inj	Pup Livers	5/31/02	100902BR	10400
19035 GROUP IV, Female 11	0202236	Pup Livers	5/31/02	100902BR	18500
19035 GROUP IV, Female 11*	0202236 Dup Inj	Pup Livers	5/31/02	100902BR	18400
19035 GROUP IV, Female 12	0202237	Pup Livers	5/31/02	100902BR	12600
19035 GROUP IV, Female 12*	0202237 Dup Inj	Pup Livers	5/31/02	100902BR	12000
19035 GROUP IV, Female 13	0202238	Pup Livers	5/31/02	100902BR	17300
19035 GROUP IV, Female 13*	0202238 Dup Inj	Pup Livers	5/31/02	100902BR	17300
19039 GROUP IV, Male 1	0202239	Pup Livers	5/29/02	100902BR	5320
19039 GROUP IV, Male 1*	0202239 Dup Inj	Pup Livers	5/29/02	100902BR	5200
19039 GROUP IV, Male 2	0202240	Pup Livers	5/29/02	100902BR	6160
19039 GROUP IV, Male 2*	0202240 Dup Inj	Pup Livers	5/29/02	100902BR	6310
19039 GROUP IV, Male 3	0202241	Pup Livers	5/29/02	100902BR	5300
19039 GROUP IV, Male 3*	0202241 Dup Inj	Pup Livers	5/29/02	100902BR	5150
19039 GROUP IV, Male 4	0202242	Pup Livers	5/29/02	100902BR	5870
19039 GROUP IV, Male 4*	0202242 Dup Inj	Pup Livers	5/29/02	100902BR	6130
19039 GROUP IV, Male 5	0202243	Pup Livers	5/29/02	100902BR	6500
19039 GROUP IV, Male 5*	0202243 Dup Inj	Pup Livers	5/29/02	100902BR	6430
19039 GROUP IV, Female 8	0202244	Pup Livers	5/29/02	100902BR	4910
19039 GROUP IV, Female 8*	0202244 Dup Inj	Pup Livers	5/29/02	100902BR	5010
19039 GROUP IV, Female 11	0202245	Pup Livers	5/29/02	100902BR	3510
19039 GROUP IV, Female 11*	0202245 Dup Inj	Pup Livers	5/29/02	100902BR	3710
19039 GROUP IV, Female 12	0202246	Pup Livers	5/29/02	100902BR	4550
19039 GROUP IV, Female 12*	0202246 Dup Inj	Pup Livers	5/29/02	100902BR	4620
19039 GROUP IV, Female 14	0202247	Pup Livers	5/29/02	100902BR	4310
19039 GROUP IV, Female 14*	0202247 Dup Inj	Pup Livers	5/29/02	100902BR	4180
19039 GROUP IV, Female 15	0202248	Pup Livers	5/29/02	100902BR	5110
19039 GROUP IV, Female 15*	0202248 Dup Inj	Pup Livers	5/29/02	100902BR	4920
19040 GROUP IV, Male 2	0202249	Pup Livers	5/30/02	101002AR	6480
19040 GROUP IV, Male 2*	0202249 Dup Inj	Pup Livers	5/30/02	101002AR	7690
19040 GROUP IV, Male 3	0202250	Pup Livers	5/30/02	101002AR	11500
19040 GROUP IV, Male 3*	0202250 Dup Inj	Pup Livers	5/30/02	101002AR	11200
19040 GROUP IV, Male 4	0202251	Pup Livers	5/30/02	101002AR	7540
19040 GROUP IV, Male 4*	0202251 Dup Inj	Pup Livers	5/30/02	101002AR	7750
19040 GROUP IV, Male 5	0202252	Pup Livers	5/30/02	101002AR	13000
19040 GROUP IV, Male 5*	0202252 Dup Inj	Pup Livers	5/30/02	101002AR	12200
19040 GROUP IV, Male 7	0202253	Pup Livers	5/30/02	101002AR	11100
19040 GROUP IV, Male 7*	0202253 Dup Inj	Pup Livers	5/30/02	101002AR	11100
19040 GROUP IV, Female 11	0202254	Pup Livers	5/30/02	101002AR	12100
19040 GROUP IV, Female 11*	0202254 Dup Inj	Pup Livers	5/30/02	101002AR	11200
19040 GROUP IV, Female 12	0202255	Pup Livers	5/30/02	101002AR	10600
19040 GROUP IV, Female 12*	0202255 Dup Inj	Pup Livers	5/30/02	101002AR	10700
19040 GROUP IV, Female 13	0202256	Pup Livers	5/30/02	101002AR	14100
19040 GROUP IV, Female 13*	0202256 Dup Inj	Pup Livers	5/30/02	101002AR	14000
19040 GROUP IV, Female 15	0202257	Pup Livers	5/30/02	101002AR	12400
19040 GROUP IV, Female 15*	0202257 Dup Inj	Pup Livers	5/30/02	101002AR	12300
19040 GROUP IV, Female 16	0202258	Pup Livers	5/30/02	101002AR	14900
19040 GROUP IV, Female 16*	0202258 Dup Inj	Pup Livers	5/30/02	101002AR	15700

* Duplicate Injection ND = Not Detected (Area less than lowest calibration standard of 0.1 ng/mL)

Table IX. (cont'd). Summary of PFHS Residues in Rat Liver Samples

Sponsor ID	Exygen ID	Matrix	Collection Date	Set Number	PFHS Found (ng/mL)
19045 GROUP IV, Male 1	0202259	Pup Livers	5/28/02	101002AR	6200
19045 GROUP IV, Male 1*	0202259 Dup Inj	Pup Livers	5/28/02	101002AR	6210
19045 GROUP IV, Male 2	0202260	Pup Livers	5/28/02	101002AR	4830
19045 GROUP IV, Male 2*	0202260 Dup Inj	Pup Livers	5/28/02	101002AR	4900
19045 GROUP IV, Male 4	0202261	Pup Livers	5/28/02	101002AR	7820
19045 GROUP IV, Male 4*	0202261 Dup Inj	Pup Livers	5/28/02	101002AR	7510
19045 GROUP IV, Male 5	0202262	Pup Livers	5/28/02	101002AR	5700
19045 GROUP IV, Male 5*	0202262 Dup Inj	Pup Livers	5/28/02	101002AR	5750
19045 GROUP IV, Male 6	0202263	Pup Livers	5/28/02	101002AR	4840
19045 GROUP IV, Male 6*	0202263 Dup Inj	Pup Livers	5/28/02	101002AR	4970
19045 GROUP IV, Female 8	0202264	Pup Livers	5/28/02	101002AR	7350
19045 GROUP IV, Female 8*	0202264 Dup Inj	Pup Livers	5/28/02	101002AR	7350
19045 GROUP IV, Female 9	0202265	Pup Livers	5/28/02	101002AR	6510
19045 GROUP IV, Female 9*	0202265 Dup Inj	Pup Livers	5/28/02	101002AR	6740
19045 GROUP IV, Female 10	0202266	Pup Livers	5/28/02	101002AR	8350
19045 GROUP IV, Female 10*	0202266 Dup Inj	Pup Livers	5/28/02	101002AR	8010
19045 GROUP IV, Female 11	0202267	Pup Livers	5/28/02	101002AR	6520
19045 GROUP IV, Female 11*	0202267 Dup Inj	Pup Livers	5/28/02	101002AR	6380
19045 GROUP IV, Female 14	0202268	Pup Livers	5/28/02	101002AR	6030
19045 GROUP IV, Female 14*	0202268 Dup Inj	Pup Livers	5/28/02	101002AR	5870
19006 GROUP V, Male 1	0202320	Pup Livers	5/30/02	101002BR	13500
19006 GROUP V, Male 1*	0202320 Dup Inj	Pup Livers	5/30/02	101002BR	13700
19006 GROUP V, Male 2	0202321	Pup Livers	5/30/02	101002BR	16500
19006 GROUP V, Male 2*	0202321 Dup Inj	Pup Livers	5/30/02	101002BR	16700
19006 GROUP V, Male 3	0202322	Pup Livers	5/30/02	101002BR	25800
19006 GROUP V, Male 3*	0202322 Dup Inj	Pup Livers	5/30/02	101002BR	26100
19006 GROUP V, Male 4	0202323	Pup Livers	5/30/02	101002BR	30100
19006 GROUP V, Male 4*	0202323 Dup Inj	Pup Livers	5/30/02	101002BR	29400
19006 GROUP V, Male 5	0202324	Pup Livers	5/30/02	101002BR	30200
19006 GROUP V, Male 5*	0202324 Dup Inj	Pup Livers	5/30/02	101002BR	29800
19006 GROUP V, Female 8	0202325	Pup Livers	5/30/02	101002BR	23300
19006 GROUP V, Female 8*	0202325 Dup Inj	Pup Livers	5/30/02	101002BR	22500
19006 GROUP V, Female 10	0202326	Pup Livers	5/30/02	101002BR	17700
19006 GROUP V, Female 10*	0202326 Dup Inj	Pup Livers	5/30/02	101002BR	16400
19006 GROUP V, Female 11	0202327	Pup Livers	5/30/02	101002BR	25000
19006 GROUP V, Female 11*	0202327 Dup Inj	Pup Livers	5/30/02	101002BR	25000
19006 GROUP V, Female 13	0202328	Pup Livers	5/30/02	101002BR	16700
19006 GROUP V, Female 13*	0202328 Dup Inj	Pup Livers	5/30/02	101002BR	16500
19006 GROUP V, Female 18	0202329	Pup Livers	5/30/02	101002BR	20700
19006 GROUP V, Female 18*	0202329 Dup Inj	Pup Livers	5/30/02	101002BR	20200
19011 GROUP V, Male 2	0202330	Pup Livers	5/31/02	101002BR	19200
19011 GROUP V, Male 2*	0202330 Dup Inj	Pup Livers	5/31/02	101002BR	20000
19011 GROUP V, Male 3	0202331	Pup Livers	5/31/02	101002BR	18700
19011 GROUP V, Male 3*	0202331 Dup Inj	Pup Livers	5/31/02	101002BR	19900
19011 GROUP V, Male 4	0202332	Pup Livers	5/31/02	101002BR	19300
19011 GROUP V, Male 4*	0202332 Dup Inj	Pup Livers	5/31/02	101002BR	19000
19011 GROUP V, Male 5	0202333	Pup Livers	5/31/02	101002BR	18600
19011 GROUP V, Male 5*	0202333 Dup Inj	Pup Livers	5/31/02	101002BR	19300
19011 GROUP V, Male 6	0202334	Pup Livers	5/31/02	101002BR	14000
19011 GROUP V, Male 6*	0202334 Dup Inj	Pup Livers	5/31/02	101002BR	14100
19011 GROUP V, Female 9	0202335	Pup Livers	5/31/02	101002BR	20800
19011 GROUP V, Female 9*	0202335 Dup Inj	Pup Livers	5/31/02	101002BR	21100

* Duplicate Injection ND = Not Detected (Area less than lowest calibration standard of 0.1 ng/mL)

Table IX. (cont'd). Summary of PFHS Residues in Rat Liver Samples

Sponsor ID	Exygen ID	Matrix	Collection Date	Set Number	PFHS Found (ng/mL)
19011 GROUP V, Female 10	0202336	Pup Livers	5/31/02	101002BRR	18700
19011 GROUP V, Female 10*	0202336 Dup Inj	Pup Livers	5/31/02	101002BRR	20000
19011 GROUP V, Female 11	0202337	Pup Livers	5/31/02	101002BRR	23500
19011 GROUP V, Female 11*	0202337 Dup Inj	Pup Livers	5/31/02	101002BRR	22400
19011 GROUP V, Female 12	0202338	Pup Livers	5/31/02	101002BRR	21900
19011 GROUP V, Female 12*	0202338 Dup Inj	Pup Livers	5/31/02	101002BRR	22500
19011 GROUP V, Female 13	0202339	Pup Livers	5/31/02	101002BRR	21000
19011 GROUP V, Female 13*	0202339 Dup Inj	Pup Livers	5/31/02	101002BRR	21400
19020 GROUP V, Male 2	0202340	Pup Livers	5/31/02	101102AR	11800
19020 GROUP V, Male 2*	0202340 Dup Inj	Pup Livers	5/31/02	101102AR	11300
19020 GROUP V, Male 4	0202341	Pup Livers	5/31/02	101102AR	9460
19020 GROUP V, Male 4*	0202341 Dup Inj	Pup Livers	5/31/02	101102AR	9190
19020 GROUP V, Male 5	0202342	Pup Livers	5/31/02	101102AR	8130
19020 GROUP V, Male 5*	0202342 Dup Inj	Pup Livers	5/31/02	101102AR	8510
19020 GROUP V, Male 7	0202343	Pup Livers	5/31/02	101102AR	9280
19020 GROUP V, Male 7*	0202343 Dup Inj	Pup Livers	5/31/02	101102AR	9050
19020 GROUP V, Male 8	0202344	Pup Livers	5/31/02	101102AR	8750
19020 GROUP V, Male 8*	0202344 Dup Inj	Pup Livers	5/31/02	101102AR	8750
19020 GROUP V, Female 9	02021345	Pup Livers	5/31/02	101102AR	14800
19020 GROUP V, Female 9*	0202345 Dup Inj	Pup Livers	5/31/02	101102AR	14300
19020 GROUP V, Female 10	0202346	Pup Livers	5/31/02	101102AR	12200
19020 GROUP V, Female 10*	0202346 Dup Inj	Pup Livers	5/31/02	101102AR	12600
19020 GROUP V, Female 11	0202347	Pup Livers	5/31/02	101102AR	14400
19020 GROUP V, Female 11*	0202347 Dup Inj	Pup Livers	5/31/02	101102AR	14300
19020 GROUP V, Female 12	0202348	Pup Livers	5/31/02	101102AR	15600
19020 GROUP V, Female 12*	0202348 Dup Inj	Pup Livers	5/31/02	101102AR	15300
19020 GROUP V, Female 13	0202349	Pup Livers	5/31/02	101102AR	20900
19020 GROUP V, Female 13*	0202349 Dup Inj	Pup Livers	5/31/02	101102AR	21300
19022 GROUP V, Male 1	0202350	Pup Livers	5/31/02	101102AR	11100
19022 GROUP V, Male 1*	0202350 Dup Inj	Pup Livers	5/31/02	101102AR	11000
19022 GROUP V, Male 4	0202351	Pup Livers	5/31/02	101102AR	12700
19022 GROUP V, Male 4*	0202351 Dup Inj	Pup Livers	5/31/02	101102AR	12400
19022 GROUP V, Male 5	0202352	Pup Livers	5/31/02	101102AR	12500
19022 GROUP V, Male 5*	0202352 Dup Inj	Pup Livers	5/31/02	101102AR	12800
19022 GROUP V, Male 7	0202353	Pup Livers	5/31/02	101102AR	11800
19022 GROUP V, Male 7*	0202353 Dup Inj	Pup Livers	5/31/02	101102AR	11600
19022 GROUP V, Male 8	0202354	Pup Livers	5/31/02	101102AR	14400
19022 GROUP V, Male 8*	0202354 Dup Inj	Pup Livers	5/31/02	101102AR	14300
19022 GROUP V, Female 11	0202355	Pup Livers	5/31/02	101102AR	13700
19022 GROUP V, Female 11*	0202355 Dup Inj	Pup Livers	5/31/02	101102AR	14100
19022 GROUP V, Female 12	0202356	Pup Livers	5/31/02	101102AR	17400
19022 GROUP V, Female 12*	0202356 Dup Inj	Pup Livers	5/31/02	101102AR	17500
19022 GROUP V, Female 13	0202357	Pup Livers	5/31/02	101102AR	12200
19022 GROUP V, Female 13*	0202357 Dup Inj	Pup Livers	5/31/02	101102AR	11600
19022 GROUP V, Female 14	0202358	Pup Livers	5/31/02	101102AR	15700
19022 GROUP V, Female 14*	0202358 Dup Inj	Pup Livers	5/31/02	101102AR	15300
19022 GROUP V, Female 15	0202359	Pup Livers	5/31/02	101102AR	14100
19022 GROUP V, Female 15*	0202359 Dup Inj	Pup Livers	5/31/02	101102AR	14200
19025 GROUP V, Male 2	0202361	Pup Livers	5/30/02	101402AR	21700
19025 GROUP V, Male 2*	0202361 Dup Inj	Pup Livers	5/30/02	101402AR	21900
19025 GROUP V, Male 7	0202362	Pup Livers	5/30/02	101402AR	18600
19025 GROUP V, Male 7*	0202362 Dup Inj	Pup Livers	5/30/02	101402AR	18600

* Duplicate Injection ND = Not Detected (Area less than lowest calibration standard of 0.1 ng/mL)

Table IX. (cont'd). Summary of PFHS Residues in Rat Liver Samples

Sponsor ID	Exygen ID	Matrix	Collection Date	Set Number	PFHS Found (ng/mL)
19025 GROUP V, Male 8	0202363	Pup Livers	5/30/02	101402AR	21400
19025 GROUP V, Male 8*	0202363 Dup Inj	Pup Livers	5/30/02	101402AR	21800
19025 GROUP V, Male 13	0202364	Pup Livers	5/30/02	101402AR	18300
19025 GROUP V, Male 13*	0202364 Dup Inj	Pup Livers	5/30/02	101402AR	19400
19025 GROUP V, Female 14	02021365	Pup Livers	5/30/02	101402AR	14700
19025 GROUP V, Female 14*	0202365 Dup Inj	Pup Livers	5/30/02	101402AR	15300
19025 GROUP V, Female 15	0202366	Pup Livers	5/30/02	101402AR	26400
19025 GROUP V, Female 15*	0202366 Dup Inj	Pup Livers	5/30/02	101402AR	26500
19025 GROUP V, Female 18	0202367	Pup Livers	5/30/02	101402AR	19800
19025 GROUP V, Female 18*	0202367 Dup Inj	Pup Livers	5/30/02	101402AR	19500
19025 GROUP V, Female 19	0202368	Pup Livers	5/30/02	101402AR	18900
19025 GROUP V, Female 19*	0202368 Dup Inj	Pup Livers	5/30/02	101402AR	18800
19025 GROUP V, Female 20	0202369	Pup Livers	5/30/02	101402AR	16800
19025 GROUP V, Female 20*	0202369 Dup Inj	Pup Livers	5/30/02	101402AR	17600
19025 GROUP V, Male 1	0202360	Pup Livers	5/30/02	101402ARR	13300
19025 GROUP V, Male 1*	0202360 Dup Inj	Pup Livers	5/30/02	101402ARR	14400

* Duplicate Injection ND = Not Detected (Area less than lowest calibration standard of 0.1 ng/mL)

Table X. Summary of PFHS Residues in Dosing Solutions

Sample Description	Set Number	PFHS Known Concentration (ng/mL)	PFHS Found (ng/mL)	PFHS Recovery (%)
B-418-028-A (07.Jun.02) 0 mg/mL 1 of 4	110702C	0	ND	-
B-418-028-A (07.Jun.02) 0 mg/mL 1 of 4	110702C	0	ND	-
B-418-028-B (24.May.02) 0.03 mg/mL 1 of 4	110702C	30000	26500	88
B-418-028-B (24.May.02) 0.03 mg/mL 1 of 4	110702C	30000	27300	91
B-418-028-C (24.May.02) 0.1 mg/mL 1 of 4	110702C	100000	88900	89
B-418-028-C (24.May.02) 0.1 mg/mL 1 of 4	110702C	100000	91000	91
B-418-028-D (07.Jun.02) 0.3 mg/mL 1 of 4	110702C	300000	268000	89
B-418-028-D (07.Jun.02) 0.3 mg/mL 1 of 4	110702C	300000	278000	93
B-418-028-E (24.May.02) 1 mg/mL 1 of 4	110702CR	1000000	1010000	101
B-418-028-E (24.May.02) 1 mg/mL 1 of 4	110702CR	1000000	1000000	100
Bulk TA/S Sample (09.Jun.02)	110702C	100000	125000	125
Bulk TA/S Sample (09.Jun.02)	110702C	100000	122000	122

ND = Not Detected (Area less than lowest calibration standard of 0.1 ng/mL)

Table XI. Summary of PFHS Residues in Stability Samples

3M ID	Exygen ID	Sample Description	Set Number	PFHS Known Conc. (ng/mL)	PFHS Found (ng/mL)	PFHS Recovery (%)
E02-0514-38611	0203923	B-418-028 A (29 Mar 02) 0 mg/mL 1 of 4	110502A	0	ND	-
E02-0514-38611*	0203923 Dup Inj	B-418-028 A (29 Mar 02) 0 mg/mL 1 of 4	110502A	0	ND	-
E02-0514-38612	0203924	B-418-028 A (29 Mar 02) 0 mg/mL 2 of 4	110502A	0	ND	-
E02-0514-38612*	0203924 Dup Inj	B-418-028 A (29 Mar 02) 0 mg/mL 2 of 4	110502A	0	ND	-
E02-0514-38613	0203925	B-418-028 B (29 Mar 02) 0.03 mg/mL 1 of 4	110502A	30000	29700	99
E02-0514-38613*	0203925 Dup Inj	B-418-028 B (29 Mar 02) 0.03 mg/mL 1 of 4	110502A	30000	29600	99
E02-0514-38614	0203926	B-418-028 B (29 Mar 02) 0.03 mg/mL 2 of 4	110502A	30000	29700	99
E02-0514-38614*	0203926 Dup Inj	B-418-028 B (29 Mar 02) 0.03 mg/mL 2 of 4	110502A	30000	29500	98
E02-0514-38615	0203927	B-418-028 C (29 Mar 02) 0.1 mg/mL 1 of 4	110502A	100000	122000	122
E02-0514-38615*	0203927 Dup Inj	B-418-028 C (29 Mar 02) 0.1 mg/mL 1 of 4	110502A	100000	117000	117
E02-0514-38616	0203928	B-418-028 C (29 Mar 02) 0.1 mg/mL 2 of 4	110502A	100000	100000	100
E02-0514-38616*	0203928 Dup Inj	B-418-028 C (29 Mar 02) 0.1 mg/mL 2 of 4	110502A	100000	100000	100
E02-0514-38617	0203929	B-418-028 D (29 Mar 02) 0.3 mg/mL 1 of 4	110502A	300000	308000	103
E02-0514-38617*	0203929 Dup Inj	B-418-028 D (29 Mar 02) 0.3 mg/mL 1 of 4	110502A	300000	316000	105
E02-0514-38618	0203930	B-418-028 D (29 Mar 02) 0.3 mg/mL 2 of 4	110502A	300000	326000	109
E02-0514-38618*	0203930 Dup Inj	B-418-028 D (29 Mar 02) 0.3 mg/mL 2 of 4	110502A	300000	324000	108
E02-0514-38619	0203931	B-418-028 E (29 Mar 02) 1 mg/mL 1 of 4	110702AR	1000000	910000	91
E02-0514-38619*	0203931 Dup Inj	B-418-028 E (29 Mar 02) 1 mg/mL 1 of 4	110702AR	1000000	919000	92
E02-0514-38620	0203932	B-418-028 E (29 Mar 02) 1 mg/mL 2 of 4	110702AR	1000000	1030000	103
E02-0514-38620*	0203932 Dup Inj	B-418-028 E (29 Mar 02) 1 mg/mL 2 of 4	110702AR	1000000	1010000	101

* Duplicate Injection ND = Not Detected (Area less than lowest calibration standard of 0.1 ng/mL)

Table XII. Summary of PFHS Residues in Homogeneity Samples

3M ID	Exygen ID	Sample Description	Set Number	PFHS Known Conc. (ng/mL)	PFHS Found (ng/mL)	PFHS Recovery (%)
E02-0514-38621	0203933	B-418-028-A (29Mar02) 0 mg/mL 1 of 12T	110702A	0	ND	-
E02-0514-38621*	0203933 Dup Inj	B-418-028-A (29Mar02) 0 mg/mL 1 of 12T	110702A	0	ND	-
E02-0514-38622	0203934	B-418-028-A (29Mar02) 0 mg/mL 2 of 12T	110702A	0	ND	-
E02-0514-38622*	0203934 Dup Inj	B-418-028-A (29Mar02) 0 mg/mL 2 of 12T	110702A	0	ND	-
E02-0514-38623	0203935	B-418-028-A (29Mar02) 0 mg/mL 5 of 12M	110702A	0	ND	-
E02-0514-38623*	0203935 Dup Inj	B-418-028-A (29Mar02) 0 mg/mL 5 of 12M	110702A	0	ND	-
E02-0514-38624	0203936	B-418-028-A (29Mar02) 0 mg/mL 6 of 12M	110702A	0	ND	-
E02-0514-38624*	0203936 Dup Inj	B-418-028-A (29Mar02) 0 mg/mL 6 of 12M	110702A	0	ND	-
E02-0514-38625	0203937	B-418-028-A (29Mar02) 0 mg/mL 9 of 12B	110702A	0	ND	-
E02-0514-38625*	0203937 Dup Inj	B-418-028-A (29Mar02) 0 mg/mL 9 of 12B	110702A	0	ND	-
E02-0514-38626	0203938	B-418-028-A (29Mar02) 0 mg/mL 10 of 12B	110702A	0	ND	-
E02-0514-38626*	0203938 Dup Inj	B-418-028-A (29Mar02) 0 mg/mL 10 of 12B	110702A	0	ND	-
E02-0514-38627	0203939	B-418-028-B (29Mar02) 0.03 mg/mL 1 of 12T	110702A	30000	24400	81
E02-0514-38627*	0203939 Dup Inj	B-418-028-B (29Mar02) 0.03 mg/mL 1 of 12T	110702A	30000	23700	79
E02-0514-38628	0203940	B-418-028-B (29Mar02) 0.03 mg/mL 2 of 12T	110702A	30000	26900	90
E02-0514-38628*	0203940 Dup Inj	B-418-028-B (29Mar02) 0.03 mg/mL 2 of 12T	110702A	30000	25800	86
E02-0514-38629	0203941	B-418-028-B (29Mar02) 0.03 mg/mL 5 of 12M	110702A	30000	25500	85
E02-0514-38629*	0203941 Dup Inj	B-418-028-B (29Mar02) 0.03 mg/mL 5 of 12M	110702A	30000	26100	87
E02-0514-38630	0203942	B-418-028-B (29Mar02) 0.03 mg/mL 6 of 12M	110702A	30000	25800	86
E02-0514-38630*	0203942 Dup Inj	B-418-028-B (29Mar02) 0.03 mg/mL 6 of 12M	110702A	30000	25800	86
E02-0514-38631	0203943	B-418-028-B (29Mar02) 0.03 mg/mL 9 of 12B	110702A	30000	24200	81
E02-0514-38631*	0203943 Dup Inj	B-418-028-B (29Mar02) 0.03 mg/mL 9 of 12B	110702A	30000	24400	81
E02-0514-38632	0203944	B-418-028-B (29Mar02) 0.03 mg/mL 10 of 12B	110702A	30000	24800	83
E02-0514-38632*	0203944 Dup Inj	B-418-028-B (29Mar02) 0.03 mg/mL 10 of 12B	110702A	30000	24500	82
E02-0514-38633	0203945	B-418-028-C (29Mar02) 0.1 mg/mL 1 of 12T	110702A	100000	75400	75
E02-0514-38633*	0203945 Dup Inj	B-418-028-C (29Mar02) 0.1 mg/mL 1 of 12T	110702A	100000	73800	74
E02-0514-38634	0203946	B-418-028-C (29Mar02) 0.1 mg/mL 2 of 12T	110702A	100000	76300	76
E02-0514-38634*	0203946 Dup Inj	B-418-028-C (29Mar02) 0.1 mg/mL 2 of 12T	110702A	100000	74700	75
E02-0514-38635	0203947	B-418-028-C (29Mar02) 0.1 mg/mL 5 of 12M	110702AR	100000	93300	93
E02-0514-38635*	0203947 Dup Inj	B-418-028-C (29Mar02) 0.1 mg/mL 5 of 12M	110702AR	100000	95100	95
E02-0514-38636	0203948	B-418-028-C (29Mar02) 0.1 mg/mL 6 of 12M	110702A	100000	69800	70
E02-0514-38636*	0203948 Dup Inj	B-418-028-C (29Mar02) 0.1 mg/mL 6 of 12M	110702A	100000	72300	72
E02-0514-38637	0203949	B-418-028-C (29Mar02) 0.1 mg/mL 9 of 12B	110702A	100000	84400	84
E02-0514-38637*	0203949 Dup Inj	B-418-028-C (29Mar02) 0.1 mg/mL 9 of 12B	110702A	100000	83700	84
E02-0514-38638	0203950	B-418-028-C (29Mar02) 0.1 mg/mL 10 of 12B	110702AR	100000	95700	96
E02-0514-38638*	0203950 Dup Inj	B-418-028-C (29Mar02) 0.1 mg/mL 10 of 12B	110702AR	100000	92800	93
E02-0514-38639	0203951	B-418-028-D (29Mar02) 0.3 mg/mL 1 of 12T	110702A	300000	270000	90
E02-0514-38639*	0203951 Dup Inj	B-418-028-D (29Mar02) 0.3 mg/mL 1 of 12T	110702A	300000	268000	89
E02-0514-38640	0203952	B-418-028-D (29Mar02) 0.3 mg/mL 2 of 12T	110702A	300000	270000	90
E02-0514-38640*	0203952 Dup Inj	B-418-028-D (29Mar02) 0.3 mg/mL 2 of 12T	110702A	300000	279000	93
E02-0514-38641	0203953	B-418-028-D (29Mar02) 0.3 mg/mL 5 of 12M	110702B	300000	254000	85
E02-0514-38641*	0203953 Dup Inj	B-418-028-D (29Mar02) 0.3 mg/mL 5 of 12M	110702B	300000	266000	89
E02-0514-38642	0203954	B-418-028-D (29Mar02) 0.3 mg/mL 6 of 12M	110702B	300000	241000	80
E02-0514-38642*	0203954 Dup Inj	B-418-028-D (29Mar02) 0.3 mg/mL 6 of 12M	110702B	300000	239000	80
E02-0514-38643	0203955	B-418-028-D (29Mar02) 0.3 mg/mL 9 of 12B	110702B	300000	255000	85
E02-0514-38643*	0203955 Dup Inj	B-418-028-D (29Mar02) 0.3 mg/mL 9 of 12B	110702B	300000	250000	83
E02-0514-38644	0203956	B-418-028-D (29Mar02) 0.3 mg/mL 10 of 12B	110702B	300000	280000	93
E02-0514-38644*	0203956 Dup Inj	B-418-028-D (29Mar02) 0.3 mg/mL 10 of 12B	110702B	300000	293000	98
E02-0514-38645	0203957	B-418-028-E (29Mar02) 1 mg/mL 1 of 12T	110702B	1000000	1020000	102
E02-0514-38645*	0203957 Dup Inj	B-418-028-E (29Mar02) 1 mg/mL 1 of 12T	110702B	1000000	1090000	109
E02-0514-38646	0203958	B-418-028-E (29Mar02) 1 mg/mL 2 of 12T	110702B	1000000	987000	99
E02-0514-38646*	0203958 Dup Inj	B-418-028-E (29Mar02) 1 mg/mL 2 of 12T	110702B	1000000	980000	98
E02-0514-38647	0203959	B-418-028-E (29Mar02) 1 mg/mL 5 of 12M	110702B	1000000	1160000	116
E02-0514-38647*	0203959 Dup Inj	B-418-028-E (29Mar02) 1 mg/mL 5 of 12M	110702B	1000000	1170000	117
E02-0514-38648	0203960	B-418-028-E (29Mar02) 1 mg/mL 6 of 12M	110702B	1000000	1040000	104
E02-0514-38648*	0203960 Dup Inj	B-418-028-E (29Mar02) 1 mg/mL 6 of 12M	110702B	1000000	994000	99
E02-0514-38649	0203961	B-418-028-E (29Mar02) 1 mg/mL 9 of 12B	110702B	1000000	1090000	109
E02-0514-38649*	0203961 Dup Inj	B-418-028-E (29Mar02) 1 mg/mL 9 of 12B	110702B	1000000	1100000	110
E02-0514-38650	0203962	B-418-028-E (29Mar02) 1 mg/mL 10 of 12B	110702B	1000000	1110000	111
E02-0514-38650*	0203962 Dup Inj	B-418-028-E (29Mar02) 1 mg/mL 10 of 12B	110702B	1000000	1070000	107

* Duplicate Injection ND = Not Detected (Area less than lowest calibration standard of 0.1 ng/mL)

FIGURES

Figure 1. Typical Calibration Curve for PFHS

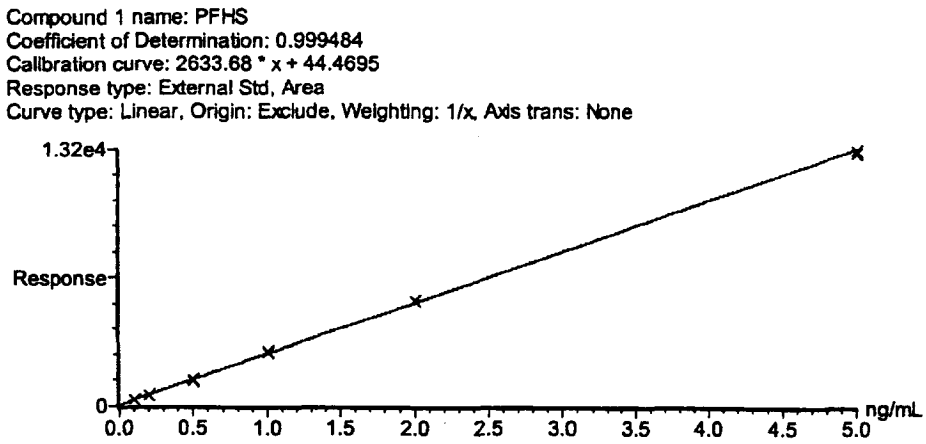


Figure 2. Chromatogram Representing a 0.1 ng/mL standard for PFHS

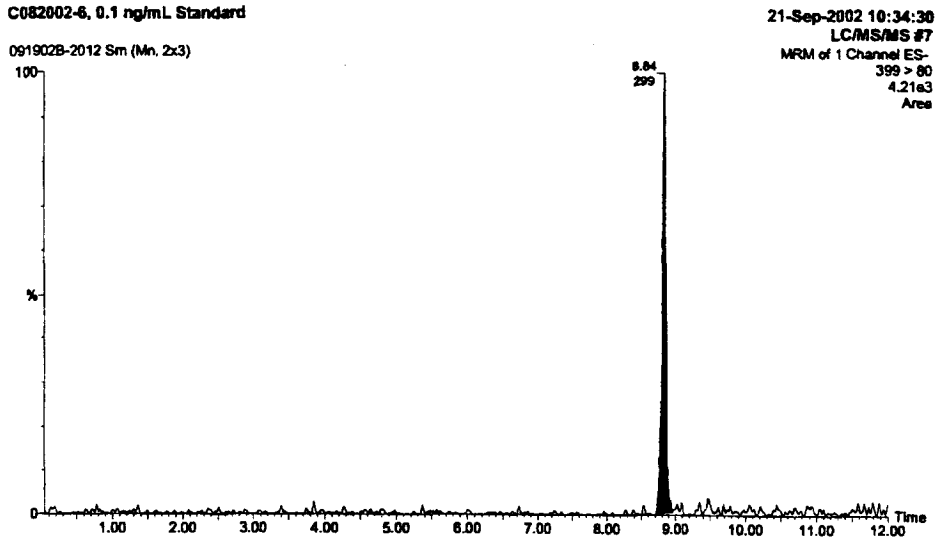


Figure 3. Chromatogram Representing a Control Rat Plasma Sample for PFHS (Exygen ID 0202913 Control, Data Set: 091602B)

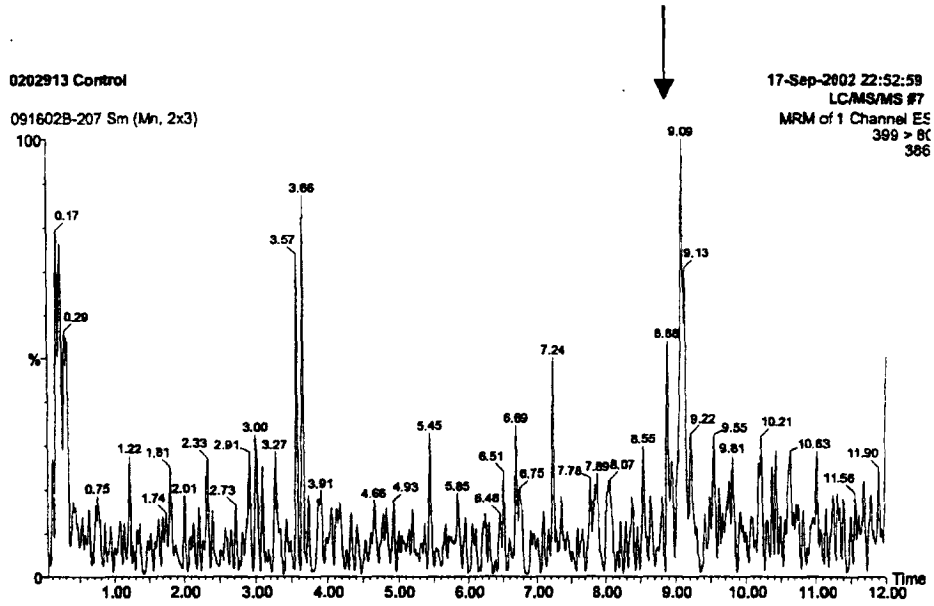


Figure 4. Chromatogram Representing a Control Rat Serum Sample for PFHS (Exygen ID: 0202987 Control, Data Set: 091902B)

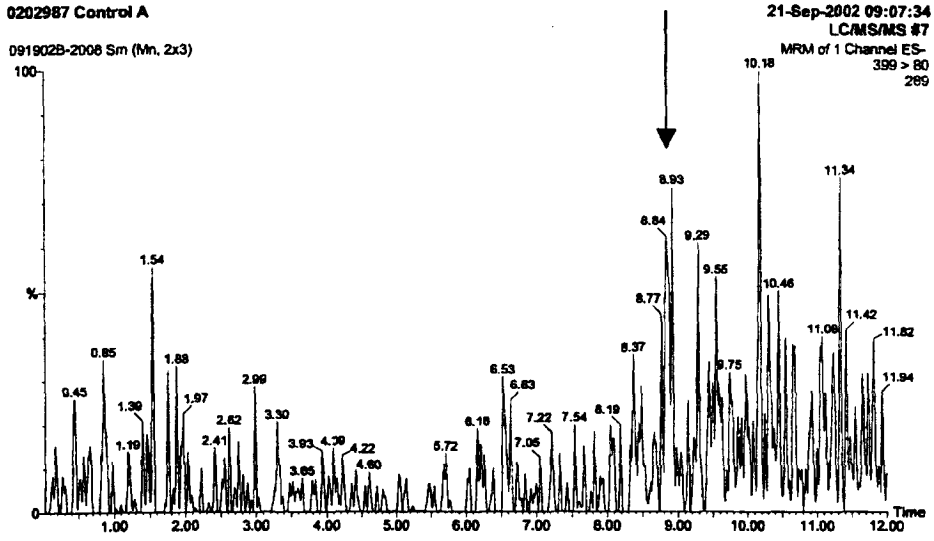


Figure 5. Chromatogram Representing a Control Rat Liver Sample for PFHS, (Exygen ID: 0202877 Control , Data Set: 100202A)

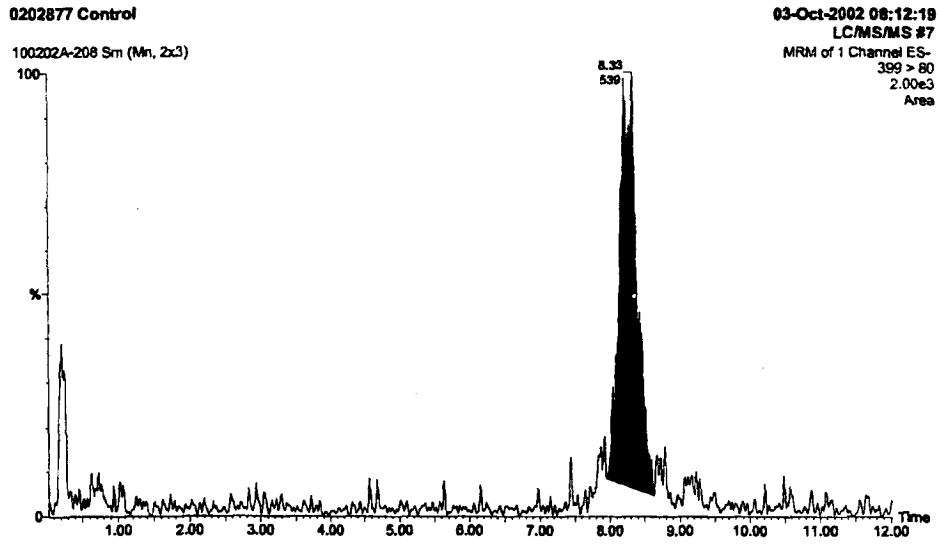


Figure 6. Chromatogram Representing Control Rat Plasma Sample Fortified with 10 ppb of PFHS (Exygen ID: 0202913 Spk A, Data Set: 091602B)

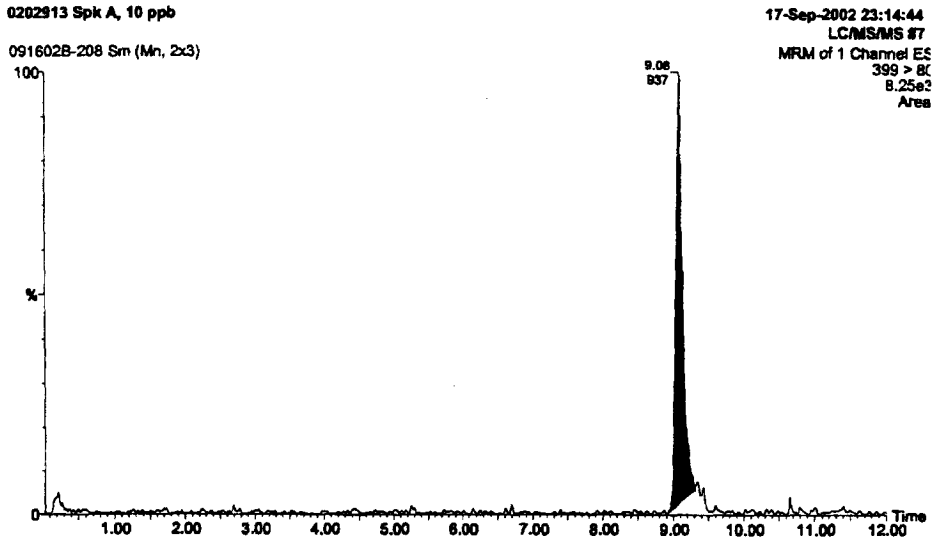


Figure 7. Chromatogram Representing Control Rat Serum Sample Fortified with 10 ppb of PFHS (Exygen ID: 0202987 Spk A, Data Set: 091902B)

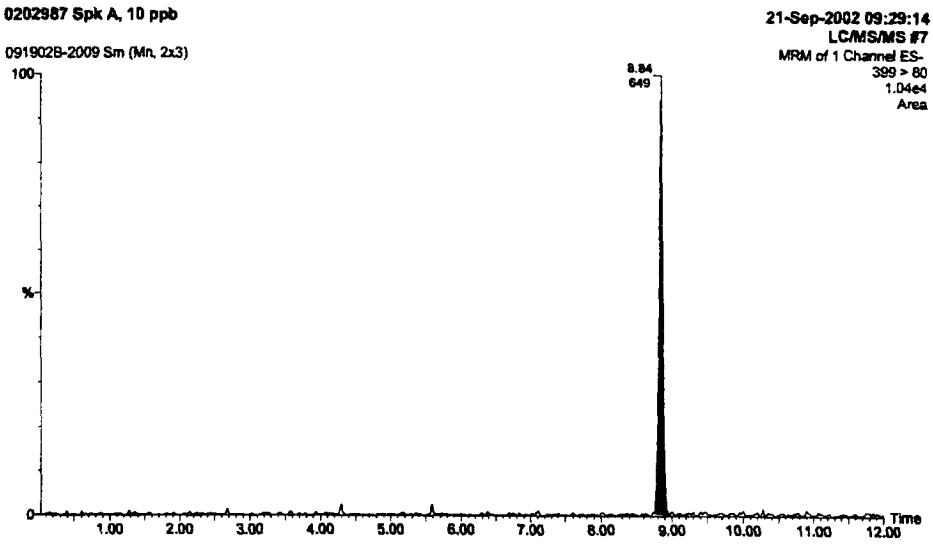


Figure 8. Chromatogram Representing Control Rat Liver Sample Fortified with 10 ppb of PFHS (Exygen ID: 0202877 Spk A, Data Set: 100202A)

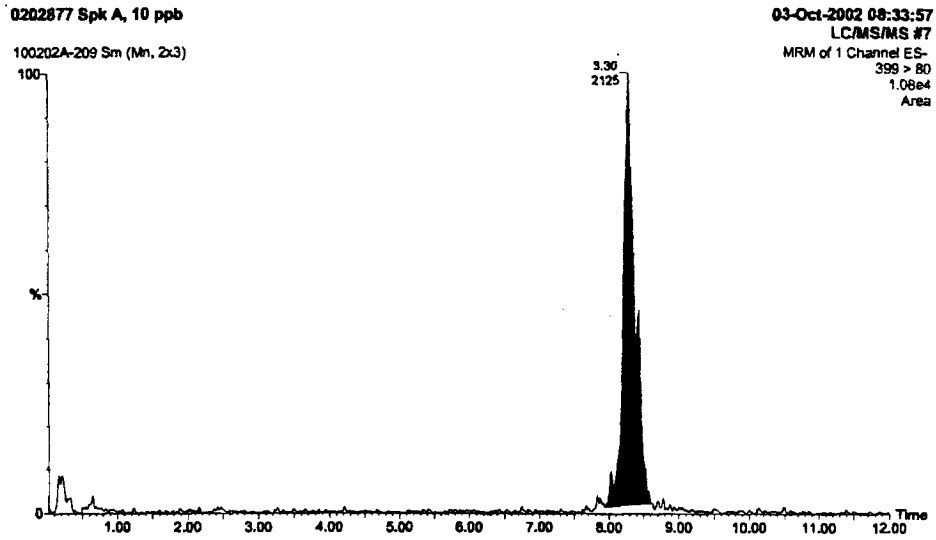


Figure 9. Chromatogram Representing Rat Plasma Sample Analyzed for PFHS (Exygen ID: 0201816, Sponsor ID: 19176 GROUP I, Data Set: 091602B)

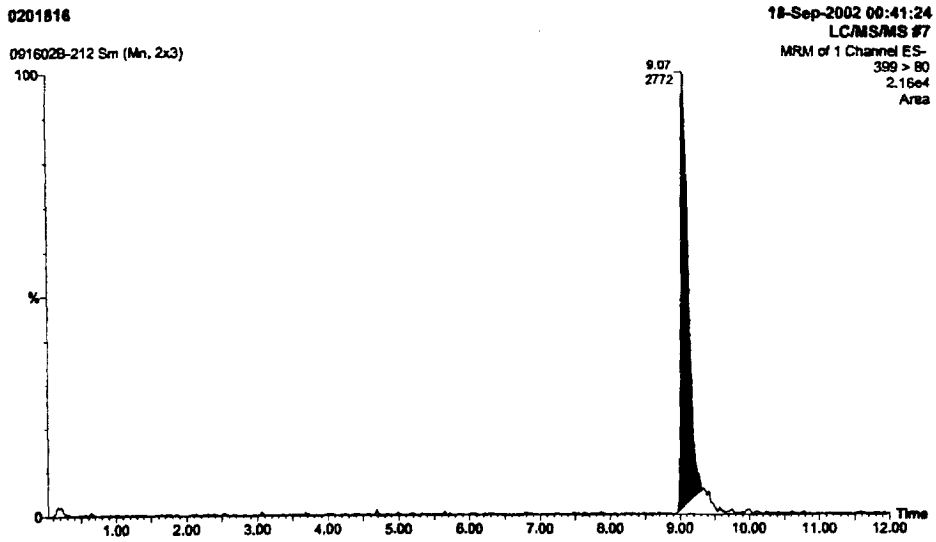


Figure 10. Chromatogram Representing Rat Serum Sample Analyzed for PFHS, DF=10 (Exygen ID: 0201863, Sponsor ID: 19079 GROUP II, Data Set: 091902BR)

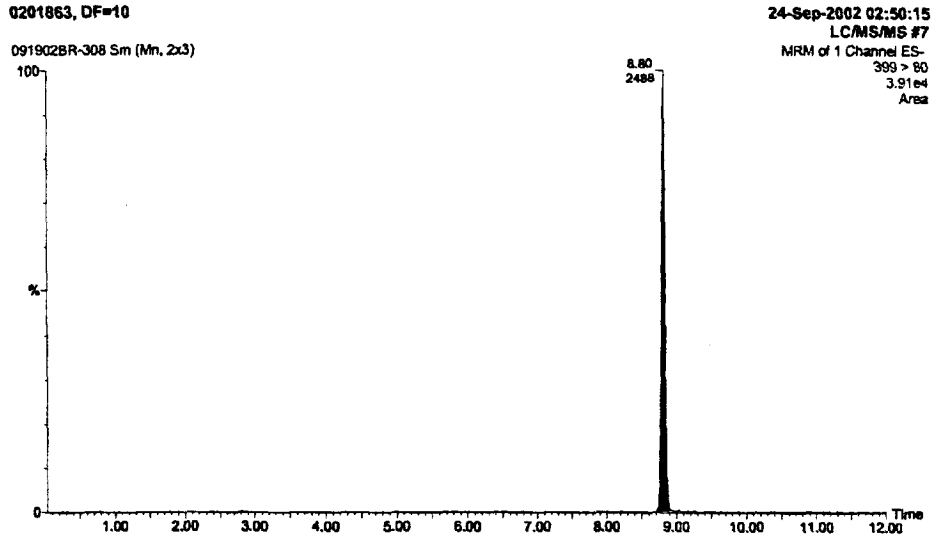
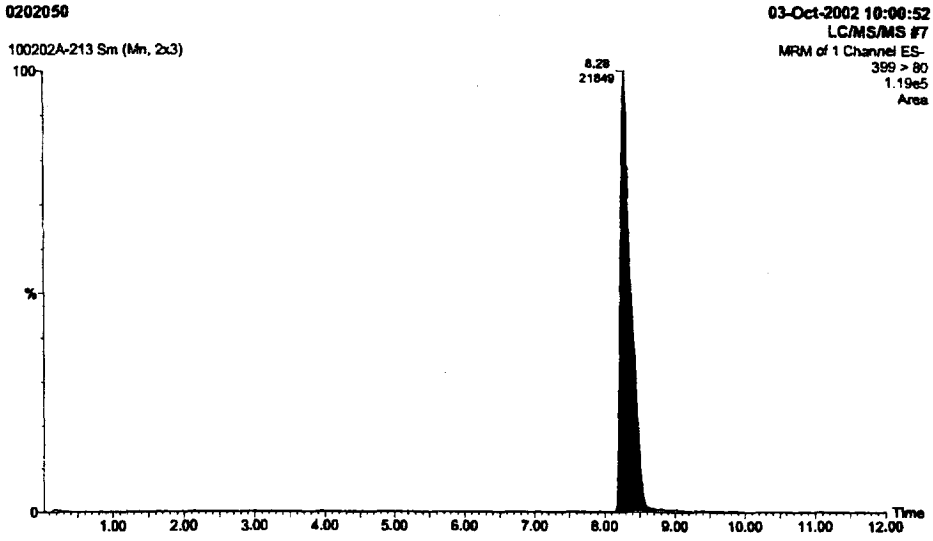


Figure 11. Chromatogram Representing Rat Liver Sample Analyzed for PFHS (Exygen ID: 0202050, Sponsor ID: 19018 GROUP II Male 1, Data Set: 100202A)



APPENDIX A

Study Protocol
418-028
(Exygen Study No. 023-072)
and
Amendments, Deviation
and
Note to File

905 Sheehy Drive, Bldg. A
Horsham, PA 19044
Telephone: (215) 443-8710
Telefax: (215) 443-8587



ARGUS RESEARCH
Charles River Laboratories
Discovery and Development Services

PROTOCOL 418-028

SPONSOR'S STUDY NUMBER: T-7706.1

STUDY TITLE: Oral (Gavage) Combined Repeated Dose Toxicity Study of T-7706 with the Reproduction/Developmental Toxicity Screening Test

PURPOSE: The purpose of this study is to provide information on the possible health hazards that may result from repeated exposure of Crl:CD®(SD)IGS BR VAF/Plus® male and female rats to a test substance beginning before cohabitation, through mating and continuing for at least 42 days (male rats) or through parturition until day 21 of lactation (female rats). This repeated dose study incorporates a reproduction/developmental toxicity screening test that can be used to provide initial information on possible effects on male and female reproductive performance (e.g., gonadal function, mating behavior, conception, development of the conceptus and parturition). The study also places emphasis on neurological effects as a specific endpoint and should identify the neurotoxic potential of a test substance, which may warrant further in-depth investigation.

Because of the selectivity of the endpoints and the short duration of the study, the screening test will not provide evidence for definitive claims of no reproduction/developmental effects. In particular, it offers only limited means of detecting postnatal manifestations of prenatal exposure or effects that may be induced during postnatal exposure.

TESTING FACILITY:
Argus Research
905 Sheehy Drive, Building A
Horsham, Pennsylvania 19044-1297
Telephone: (215) 443-8710
Telefax: (215) 443-8587

STUDY DIRECTOR:
Raymond G. York, Ph.D., DABT
Associate Director of Research
Email: raymond.york@criver.com
Address as cited above for Testing Facility

SPONSOR:
3M Corporate Toxicology
3M Center, Building 220-2E-02
St. Paul, Minnesota 55144-1000

STUDY MONITOR: John Butenhoff, Ph.D., DABT, CIH
3M Corporate Toxicology
3M Medical Department
Telephone: (651) 733-1962
Telefax: (651) 733-1773
Email: jlbutenhoff@mmm.com

REGULATORY CITATIONS:

Organisation for Economic Co-operation and Development (1996). *OECD Guideline for Testing of Chemicals*. Section 4, No. 422: Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test, adopted 22 March 1996.

Organisation for Economic Co-operation and Development (1998). The Revised OECD Principles of Good Laboratory Practices [C(97)186/Final].

U.S. Food and Drug Administration. Good Laboratory Practice Regulations; Final Rule. 21 CFR Part 58.

Japanese Ministry of Health and Welfare (1997). *Good Laboratory Practice Standard for Safety Studies on Drugs*, MHW Ordinance Number 21, March 26, 1997.

REGULATORY COMPLIANCE:

This study will be conducted in compliance with the Good Laboratory Practice (GLP) regulations cited above.

All changes or revisions of this protocol shall be documented, signed by the Study Director and the Sponsor, dated and maintained with the protocol.

The Testing Facility's Quality Assurance Unit (QAU) will audit the protocol, the raw data and the report, and will inspect critical phases of those portions of the study conducted at the Testing Facility in accordance with the Standard Operating Procedures of the Testing Facility.

The final report will include a compliance statement signed by the Study Director that the report accurately reflects the raw data obtained during the performance of the study and that all applicable GLP regulations were followed in the conduct of the study. Should significant deviations from GLP regulations occur, each will be described in detail, together with how the deviation might affect the quality or integrity of the study.

Should any portion of the study be conducted by a subcontractor or by the Sponsor, the Study Director will ensure that a qualified Principal Investigator is identified by the facility conducting that portion of the study. The QAU for this facility will conduct critical phase inspections and audit respective results and reports for that study portion according to the SOPs of that facility. Such critical phase inspection reports and report audits will be submitted by the facility to the Principal Investigator and the Study Director. The dates of the inspections and report submissions will be incorporated into a QAU Statement generated by that facility and provided

to the Testing Facility for inclusion in the final report. In addition, this facility will provide a statement of GLP compliance, as described above, signed by the Principal Investigator for inclusion in the final report.

SCHEMATIC OF STUDY DESIGN AND STUDY SCHEDULE:

See ATTACHMENT 1 to the protocol.

TEST SUBSTANCE AND VEHICLE:

Identification:

Test Substance:

T-7706 [Perfluorohexane Sulfonate Potassium Salt (PFHS)] Lot identification will be documented in the raw data.

The Sponsor will provide to the Testing Facility documentation or certification of the identity, composition, method of synthesis, strength and activity/purity of the test substance. This documentation will be included in the final report.

Vehicle:

Aqueous 0.5% carboxymethlycellulose (CMC) (medium viscosity) prepared using reverse osmosis membrane processed deionized water (R.O. deionized water). Lot identification and Supplier will be documented in the raw data.

Neither the Sponsor nor the Study Director is aware of any potential contaminants likely to be present in the vehicle that would interfere with the results of this study. Therefore, no analyses other than those mentioned in this protocol will be conducted.

Safety Precautions:

Gloves, dust-mist/HEPA-filtered mask, appropriate eye protection and uniform/lab coat to be worn during formulation preparation and dosage. The Material Safety Data Sheet (MSDS) is attached to the protocol (ATTACHMENT 2).

Storage:

Bulk Test Substance:	Room temperature.
Bulk Vehicle Components:	Room temperature.
Prepared Test Substance and Vehicle Formulations:	Refrigerated (2°C to 8°C).

All test substance shipments should be addressed to the attention of Julian Gulbinski, Manager of Formulation Laboratory, at the previously cited Testing Facility address and telephone number.

Shipments should include information concerning storage conditions and shipping cartons should be labeled appropriately. The recipient should be notified in advance of shipment.

FORMULATION:

Frequency of Preparation:

Formulations (suspensions) will be prepared weekly at the Testing Facility.

Detailed preparation procedures will be attached to this protocol (ATTACHMENT 3).

Adjustment for Purity:

The test substance will be considered 100% pure for the purpose of dosage calculations.

Testing Facility Reserve Samples:

The Testing Facility will reserve a sample of each lot of bulk test substance (approximately 1 g) and bulk vehicle components (approximately 1 g or 5 mL) used during the course of the study. Samples will be stored under the previously cited conditions.

ANALYSES:

Results of required analyses will be provided to the Testing Facility for inclusion in the study report.

Samples additional to those described below may be taken if deemed necessary during the course of the study. Additional analyses, if required, will be documented by protocol amendment.

Bulk Test Substance Sampling:

A sample of approximately 1 g of the test substance will be taken on the last day of treatment and sent (ambient conditions) to:

Principal Investigator: Lisa Clemen
3M Environmental Technology and Safety Services
Building 2-3E-09
St. Paul, Minnesota 55133-3331
Telephone: (651) 778-5568
Telefax: (651) 778-6176
Email: laclemen@mmm.com

The recipient will be notified in advance of sample shipment.

Analyses of Prepared Formulations:

Concentration and Homogeneity:

Concentration and homogeneity of the prepared formulations will be verified during the course of this study. Quadruplicate samples (2 mL each) will be taken from the top, middle and bottom of each concentration on the first day of preparation. Two samples from each quadruplicate set will be shipped for analysis; the remaining samples will be retained at the Testing Facility as backup samples. Quadruplicate samples will be taken from each concentration on the last day of preparation. Two samples from each quadruplicate set will be shipped for analysis; the remaining samples will be retained as backup samples. Backup samples will be stored under the previously cited conditions and discarded at the Testing Facility upon the request of the Sponsor.

Stability:

Stability of the prepared formulations will be documented during this study. Two sets of duplicate samples (2 mL each) from each concentration will be taken on the first day of preparation. One sample of each duplicate set will be shipped on the day of preparation. These samples will be analyzed at the following time points: as soon after preparation as possible and ten days after the first analysis. The remaining samples will be retained at the Testing Facility as backup samples. Backup samples will be stored under the previously cited conditions and discarded at the Testing Facility upon the request of the Sponsor.

Shipping Instructions:

Samples to be analyzed will be shipped (refrigerated) to:

Principal Investigator: Lisa Clemen
3M Environmental Technology and Safety Services
Building 2-3E-09
St. Paul, Minnesota 55133-3331
Telephone: (651) 778-5568
Telefax: (651) 778-6176
Email: laclemen@mmm.com

The recipient will be notified in advance of sample shipment.

DISPOSITION:

Prepared formulations will be discarded at the Testing Facility. All remaining bulk test substance will be returned to:

Dan Hakes
3M EHSR - Auto & Chem Grp
3M Center, Building 236-1B-10
St. Paul, Minnesota 55144-1000
Telephone: (651) 733-2392

TEST SYSTEM:

Species/Strain and Reason for Selection:

The Crl:CD®(SD)IGS BR VAF/Plus® rat was selected as the Test System because: 1) it is one mammalian species accepted for use in toxicity studies and it has been widely used throughout industry; 2) this strain of rat has been demonstrated to be sensitive to reproductive and developmental toxins; and 3) historical data and experience exist at the Testing Facility[1-3].

Number:

Initial population acclimated:	100 male and 100 virgin female rats.
Population selected for main study:	75 male and 75 virgin female rats (15 per sex per dosage group).
Population selected for toxicokinetic study:	15 male and 15 female rats (three per sex per dosage group).

Body Weight and Age:

Male rats will be ordered to weigh from 275 g to 300 g each at receipt, at which time they will be expected to be at least 60 days of age. Female rats will be ordered to weigh from 200 g to 225 g each at receipt, at which time they will be expected to be at least 56 days of age. Actual body weights will be recorded the day after receipt and will be documented in the raw data. The weight ranges will be included in the final report. At study initiation, the weight variation of the rats will not exceed ±20% of the mean weight of each sex.

Sex:

Both male and female rats will be evaluated.

Source:

Charles River Laboratories, Inc.

The rats will be shipped in filtered cartons by air freight and/or truck from Charles River Laboratories, Inc., to the Testing Facility.

Identification:

Rats are permanently identified using Monel® self-piercing ear tags (Gey Band and Tag Co., Inc., No. MSPT 20101). Male and female rats are assigned temporary numbers at receipt and given unique permanent identification numbers when assigned to the study before administration of the first dosage. Pups will not be individually identified during lactation; all parameters will be evaluated in terms of the litter.

ANIMAL HUSBANDRY:

All cage sizes and housing conditions are in compliance with the *Guide for the Care and Use of Laboratory Animals*[4]. Argus Research is an AAALAC-accredited facility.

Housing:

Fo generation rats will be individually housed in stainless steel wire-bottomed cages except during the cohabitation and postpartum periods. During cohabitation, each pair of rats will be housed in the male rat's cage. Beginning no later than day 20 of presumed gestation, Fo generation female rats will be individually housed in nesting boxes. Each dam and delivered litter will be housed in a common nesting box during the postpartum period.

Nesting Material:

Nesting material (bed-o'cobs®) will be provided.

Bedding will be changed as often as necessary to keep the animals dry and clean. Analyses for possible contamination are conducted semi-annually and documented in the raw data.

Room Air, Temperature and Humidity:

The animal room is independently supplied with at least ten changes per hour of 100% fresh air that has been passed through 99.97% HEPA filters. Room temperature will be maintained at 64°F to 79°F (18°C to 26°C) and monitored constantly. Room humidity will also be monitored constantly and maintained at 30% to 70%.

Light:

An automatically controlled 12-hour light:12-hour dark fluorescent light cycle will be maintained. Each dark period will begin at 1900 hours EST. The light cycle may be adjusted by the Study Director or designee if deemed necessary to accommodate scheduled laboratory activities. Any such adjustment will be documented in the raw data.

Diet:

Rats will be given Certified Rodent Diet® #5002 (PMI Nutrition International) available *ad libitum* from individual feeders. Feed will be removed the evening prior to the scheduled sacrifice.

Water:

Water will be available *ad libitum* from individual bottles attached to the cages or from an automatic watering access system. All water will be from a local source and passed through a reverse osmosis membrane before use. Chlorine will be added to the processed water as a bacteriostat; processed water is expected to contain no more than 1.2 ppm chlorine at the time of analysis. Water is analyzed monthly for possible bacterial contamination and twice annually for possible chemical contamination.

Contaminants:

Neither the Sponsor nor the Study Director is aware of any potential contaminants likely to be present in the certified diet, in the drinking water or in the nesting materials at levels that would interfere with the results of this study. Therefore, no analyses other than those routinely performed by the feed supplier or those mentioned in this protocol will be conducted.

DAY NUMBERING SYSTEM:

Gestation day 0 is defined as the day spermatozoa are observed in a smear of the vaginal contents and/or a copulatory plug observed *in situ*.

The day of birth is designated lactation day 0 (postpartum day 0) in the Health Effects Test Guidelines - Reproduction and Fertility Effects (Office of Prevention, Pesticides and Toxic Substances 870.3800, August, 1998) and in the OECD Guideline for the Testing of Chemicals - Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (Section 4, No. 422, 22 March 1966). This same day is designated day 1 postpartum (day 1 of lactation) in the Standard Operating Procedures of the Testing Facility. Throughout this protocol, the day of birth will be designated day 1 postpartum (day 1 of lactation) and all subsequent ages of the F1 generation rats and days of the lactation period will be determined and cited accordingly.

RANDOMIZATION AND COHABITATION:

Upon arrival, rats will be assigned to individual housing on the basis of computer-generated random units. During an acclimation period of at least five days, male and female rats will be selected for study on the basis of physical appearance and body weights recorded during acclimation. The rats will be assigned to dosage groups based on computer-generated (weight-ordered) randomization procedures.

Within each dosage group, consecutive order will be used to assign rats to cohabitation, one male rat per female rat. The cohabitation period will consist of a maximum of 14 days. Female rats with spermatozoa observed in a smear of the vaginal contents and/or a copulatory plug observed *in situ* will be considered to be at day 0 of presumed gestation and assigned to individual housing. Female rats not mated within the first seven days of cohabitation will be assigned alternate male rats that have mated (same dosage group) and will remain in cohabitation for a maximum of seven additional days.

Day 1 of lactation (postpartum) is defined as the day of birth and is also the first day on which all pups in a litter are individually weighed (pup body weights will be recorded after all pups in a litter are delivered and groomed by the dam).

Litters will not be culled during the lactation period, because random selection of pups for culling could result in potential biases in pup viabilities and body weight gains over this period.

Within each dosage group, consecutive order will be used to assign the first 10 male and the first 10 female rats to a functional observational battery (FOB) and motor activity assessment, blood sample collection for clinical chemistry and hematology (CC&H), and histological evaluations.

On day 22 postpartum, a table of random units will be used to select five male and five female pups per litter for blood sample and liver collection; these pups will only be selected from the ten dams selected for FOB, motor activity, CC&H and histological evaluation.

ADMINISTRATION:

Route and Reason for Choice:

The oral (gavage) route was selected for use because: 1) in comparison with the dietary route, the exact dosage can be accurately administered; and 2) it is one of the possible routes for environmental exposure.

Method and Frequency:

Dosages will be adjusted daily for body weight changes and given at approximately the same time each day. The first day of dosage is designated as day 1 of study.

Male rats will be given the test substance once daily beginning 14 days before a cohabitation period that consists of a maximum 14 days. Dosage will continue through the day before sacrifice, after completion of the cohabitation period, after a minimum of 42 days of administration.

Female rats will be given the test substance once daily beginning 14 days before a cohabitation period that consists of a maximum of 14 days. Dosage will continue through the day before scheduled sacrifice (day 21 of lactation).

Rationale for Dosage Selection:

Dosages were selected by the Sponsor based on previous studies conducted with the test substance, taking into account possible differences in sensitivity between pregnant and nonpregnant rats. The highest dosage will be expected to cause toxic effects but not mortality or obvious suffering. The descending sequence of the lower dosage levels will be selected for the purpose of demonstrating any dosage-related response, with no adverse effects expected at the lowest level.

Dosage Levels, Concentrations and Volumes:

Dosage Group	Number of Rats Per Sex	Dosage (mg/kg/day)	Concentration[a] (mg/mL)	Dosage Volume (mL/kg)	Argus Batch Number
I	15 + 3[b]	0	0	10	B-418-028-A(Day.Month.Year)
II	15 + 3[b]	0.3	0.03	10	B-418-028-B(Day.Month.Year)
III	15 + 3[b]	1	0.1	10	B-418-028-C(Day.Month.Year)
IV	15 + 3[b]	3	0.3	10	B-418-028-D(Day.Month.Year)
V	15 + 3[b]	10	1	10	B-418-028-E(Day.Month.Year)

a. The test substance will be considered 100% pure for the purpose of dosage calculations.
b. Three additional rats per sex per dosage group will be assigned to toxicokinetic sample collection.

TESTS, ANALYSES AND MEASUREMENTS - Fo GENERATION:

Viability - Male and Female Rats:

All Periods: At least twice daily.

Clinical Observations and/or General Appearance - Male and Female Rats:

Acclimation Period: Weekly.

Dosage Period: Daily before dosage. On the first day of dosage, postdosage observations will be recorded at approximately hourly intervals for the first four hours and at the end of the normal working day. Subsequent postdosage observations will be recorded at intervals deemed appropriate by the Study Director or designee after determination of peak toxicologic effects.

Maternal Behavior: Days 1, 5, 8, 15 and 22 postpartum. Observed abnormal behavior recorded daily.

Clinical observations may be recorded more frequently than cited above, if deemed appropriate by the Study Director and/or Study Monitor.

Data collected for rats assigned to toxicokinetic sample collection will not be summarized or analyzed statistically.

Detailed Clinical Observations - Male and Female Rats:

Once before the first dosage and at least once weekly thereafter, detailed clinical observations will be conducted for all male and female rats. These observations will be made outside the cage in a standard arena at the same time each day of conduct. Effort will be made to ensure that variations in the test conditions are minimal and that observations are conducted by observers unaware of treatment groups. Signs noted should include, but not be limited to: changes in skin, fur, eyes, mucous membranes, occurrence of secretions and excretions and autonomic activity (e.g., lacrimation, piloerection, pupil size, unusual respiratory pattern). Changes in gait, posture

and response to handling as well as the presence of clonic or tonic movements, sterotypic behavior (e.g., excessive grooming, repetitive circling), difficult or prolonged parturition or bizarre behavior (e.g., self-mutilation, walking backwards) should also be recorded.

Body Weights - Male and Female Rats:

Acclimation Period:	Weekly.
Dosage Period:	Daily.
Sacrifice:	Terminal weight.

Feed Consumption Values - Male Rats (recorded and tabulated):

Dosage Period:	Weekly.

Feed Consumption Values - Female Rats (recorded and tabulated):

Dosage Period:	Weekly to cohabitation.
Gestation Period:	Days 0, 7, 10, 12, 15, 18, 20 and 25 (if necessary).
Postpartum Period:	Days 1, 5, 8 and 15.

Feed consumption not tabulated after day 15 postpartum, when it is expected that pups will begin to consume maternal feed.

Feed Consumption Values - Male and Female Rats:

Feed consumption values may be recorded more frequently than cited above if it is necessary to replenish the feed. During cohabitation, when two rats occupy the same cage with one feed jar, replenishment of the feed jars will be documented. Individual values will not be recorded or tabulated.

Toxicokinetic Sample Collection:

On day 14 and 42 of study, blood samples (approximately 1 mL each) will be collected from each male rat assigned to the toxicokinetic sample collection portion of the study (3 per group).

On day 14 of study and day 21 of presumed gestation, blood samples (approximately 1 mL each) will be collected from each female rat assigned to the toxicokinetic sample collection portion of the study (3 per group). Samples will be collected prior to dosage on day 14 of study. The time of each blood collection will be recorded in the raw data.

Blood will be collected from the orbital sinus. If necessary, blood may be collected from an alternate site; if so, the alternate site will be documented in the raw data.) The samples will be transferred into EDTA-coated (purple top) tubes and spun in a centrifuge. The resulting serum will be transferred into polypropylene tubes labeled with the protocol number, Sponsor study number, animal number, sex, group number, dosage level, day of study, collection interval, date of collection, species, generation and storage conditions. All samples will be immediately frozen on dry ice and maintained frozen (≤-70°C) until shipment for analysis.

After the last blood sample collection, rats will be sacrificed and samples of the liver will be collected for analysis.

Shipping Instructions:

Samples to be analyzed will be shipped on dry ice to:

Principal Investigator: Lisa Clemen
3M Environmental Technology and Safety Services
Building 2-3E-09
St. Paul, Minnesota 55133-3331
Telephone: (651) 773-5568
Telefax: (651) 778-6176
Email: laclemen@mmm.com

The recipient will be notified in advance of sample shipment.

Estrous Cycling and Mating:

Estrous cycling will be evaluated by examination of vaginal cytology beginning with the day after the first administration and then until spermatozoa are observed in a smear of the vaginal contents and/or a copulatory plug is observed *in situ* during the cohabitation period.

Caesarean-Sectioning - Toxicokinetic Study:

On day 21 of presumed gestation, blood and liver samples will be collected from all female rats designated for toxicokinetic sample collection.

Blood samples will be collected from the rats as previously described. After sacrifice, the liver of each rat will be excised and the liver weight will be recorded. The median liver lobe will be frozen and stored (≤-20°C) until shipment for possible analysis.

The fetuses will be removed from the uterus and blood samples will be collected from each fetus via decapitation. Blood will be placed into tubes, pooled per litter, allowed to clot and spun in a centrifuge; the resulting serum will be transferred into labeled polypropylene tubes. All samples will be immediately frozen on dry ice and maintained frozen (≤-70°C) until shipment for analysis.

The liver from each fetus will be collected, pooled per litter and placed into labeled tubes. The samples will be frozen and stored (≤-20°C) until shipment for analysis.

Samples will be shipped on dry ice to Lisa Clemen at the previously cited address.

Natural Delivery:

Female rats will be evaluated for:

Adverse Clinical Signs Observed During Parturition.

Duration of Gestation (day 0 of presumed gestation to the time the first pup is observed).

Litter Size (defined as all pups delivered).

Pup Viability at Birth.

Functional Observational Battery:

On one occasion during the course of the study, a functional observational battery (FOB)[5-8] will be conducted on 10 male and 10 female rats per group. For male rats, this assessment will be conducted shortly before scheduled sacrifice, but prior to blood sample collection for hematology and clinical chemistry evaluations. Female rats should be tested during the lactation period, shortly before scheduled sacrifice.

The FOB, to be conducted by an observer unaware of the group assignment of the rat, will assess the following parameters:

1. Lacrimation, salivation, palpebral closure, prominence of the eye, pupillary reaction to light, piloerection, respiration, and urination and defecation (autonomic functions).

2. Sensorimotor responses to visual, auditory, tactile and painful stimuli (reactivity and sensitivity).

3. Reactions to handling and behavior in the open field (excitability).

4. Gait pattern in the open field, severity of gait abnormalities, air righting reaction, and landing foot splay (gait and sensorimotor coordination).

5. Forelimb and hindlimb grip strength.

6. Abnormal clinical signs including but not limited to convulsions, tremors and other unusual behavior, hypotonia or hypertonia, emaciation, dehydration, unkempt appearance and deposits around the eyes, nose or mouth.

Evidence of the ability of this battery to detect the effects of positive control substances will be provided (Testing Facility Positive Control Data). Data will also be provided to document interobserver reliability if more than one observer is involved in the testing.

Motor Activity Test:

Motor activity will be evaluated on 10 male and 10 female rats per group once during the course of the study. This assessment will be conducted shortly before scheduled sacrifice, but prior to blood sample collection.

The movements of each rat will be monitored by a passive infrared sensor mounted outside a stainless-steel wire-bottomed cage (40.6 x 25.4 x 17.8 cm). Each test session will be 1.5 hours in duration with the number of movements and time spent in movement tabulated at each five-minute interval. The apparatus will monitor a rack of up to 32 cages and sensors during each session, with each rat tested in the same location on the rack across test sessions. Groups will be counterbalanced across testing sessions and cages.

Data will be provided to demonstrate that the test system is capable of detecting increases in activity produced by positive control substances (Testing Facility Positive Control Data).

HEMATOLOGY AND CLINICAL CHEMISTRY:

At scheduled sacrifice, the rats (fasted) assigned to hematology and clinical chemistry (H&CC) sample collection will be exsanguinated from the inferior vena cava following sacrifice by carbon dioxide asphyxiation. Approximately 5 mL of blood will be collected and processed as described below. Determinations additional to those described below may be conducted if the known properties of the test substance may, or are suspected to, affect related metabolic profiles (e.g., calcium, phosphate, fasting triglycerides and fasting glucose, specific hormones, and cholinesterase).

Hematology:

Approximately 1 mL of blood will be collected into EDTA-coated tubes and maintained on wet ice or refrigerated until shipment for analysis of the following hematologic parameters:

Erythrocyte Count (RBC)	Mean Corpuscular Volume (MCV)
Hematocrit (HCT)	Leukocyte Count, Total (WBC)
Hemoglobin (HGB)	Leukocyte Count, Differential
Mean Corpuscular Hemoglobin (MCH)	Platelet Count (PLAT)
Mean Corpuscular Hemoglobin Concentration (MCHC)	Mean Platelet Volume (MPV)
	Cell Morphology

Two blood smear slides will be prepared at the Testing Facility for each sample for measurements of differential leukocyte count. All samples (on wet ice) and slides (ambient conditions) will be shipped to Redfield Laboratories at the following address.

Approximately 1.8 mL of blood will be added to a tube containing 0.2 mL of sodium citrate (0.129 M). The contents will be mixed and maintained on wet ice until the tubes are centrifuged

(within 30 minutes of the collection time). The resulting plasma will be transferred 2.0 mL polypropylene tubes labeled with study number, Sponsor's study number, rat number, dosage level, day of study, collection interval, date of collection, species, generation and storage. All samples will be frozen on dry ice and maintained frozen (≤-70°C) until shipment on dry ice by overnight courier for measurement of prothrombin time (PT) and activated partial thromboplastin time (APTT).

Clinical Chemistry:

Approximately 2 mL of blood will be collected into serum separator tubes and centrifuged. The resulting sera samples will be immediately frozen on dry ice and maintained frozen (≤-70°C) until shipment for analysis of the following parameters:

Total Protein (TP)	Creatinine Kinase (CK)
Triglycerides (TRI)	Alanine Aminotransferase (ALT)
Albumin (A)	Aspartate Aminotransferase (AST)
Globulin (G)	Alkaline Phosphatase (ALK)
Albumin/Globulin Ratio (A/G)	Calcium (CA)
Glucose (GLU)	Phosphorus (PHOS)
Cholesterol (CHOL)	Sodium (NA)
Total Bilirubin (TBILI)	Potassium (K)
Urea Nitrogen (BUN)	Chloride (CL)
Creatinine (CREAT)	

Samples will be shipped (on dry ice) to Redfield Laboratories at the following address.

Shipping Instructions:

Samples will be shipped to arrive on Monday through Friday according to the conditions described above to:

Principal Investigator: Ms. Phyllis Powell
Redfield Laboratories
A Division of CRL-DDS
100 East Boone Street
P.O. Box 308
Redfield, Arkansas 72132
Telephone: (501) 397-2540
Telefax: (501) 397-2002

The recipient will be notified in advance of sample shipment.

URINALYSIS:

Urinalysis will not be conducted unless indicated based on expected or observed toxicity of the test substance.

METHOD OF SACRIFICE:

Fo generation rats will be sacrificed by carbon dioxide asphyxiation.

GROSS NECROPSY AND HISTOPATHOLOGY - Fo GENERATION RATS:

Scheduled Sacrifice - Toxicokinetic Study:

Scheduled sacrifice of male rats will be conducted on day 42 of study. Scheduled sacrifice of female rats will be conducted on day 21 of presumed gestation.

Blood samples will be collected from the rats as previously described. After sacrifice, the liver of each rat will be excised and the liver weight will be recorded. The median liver lobe will be frozen and stored (≤-20°C) until shipment for analysis. Fetal samples will be collected as previously described.

Carcasses will be discarded without further evaluation.

Samples will be shipped on dry ice to Lisa Clemen at the previously cited address.

Scheduled Sacrifice - Main Study:

Scheduled sacrifice of male rats will be conducted on the day following the last dosage administration, after a minimum of 42 days of dosage. Scheduled sacrifice of female rats will be conducted on day 22 of lactation.

Gross necropsy of all male and female rats will include an initial physical examination of external surfaces and all orifices, as well as the cranial, thoracic and abdominal cavities and their contents. Special attention will be paid to the organs of the reproductive system. The number of implantation sites and corpora lutea will be recorded.

Male and female rats will be examined for gross lesions. Gross lesions will be retained in neutral buffered 10% formalin and examined histologically. Tissue trimming and histopathology will be performed under the supervision of or by a Board-Certified Veterinary Pathologist.

The ovaries and the uterus with cervix of each female rat will be weighed, and ovaries, uterus, vagina and a mammary gland will be retained in neutral buffered 10% formalin. Uteri of apparently nonpregnant rats will be examined after being pressed between glass plates to confirm the absence of implantation sites, and retained in neutral buffered 10% formalin.

Sperm Evaluations of Male Rats:

To assess the potential toxicity of the test article on the male reproductive system, the endpoints listed below will be evaluated from the first 10 male rats in each dosage group.

Organ Weights: The following organs will be individually weighed: right testis, left testis, left epididymis (whole and cauda), right epididymis, seminal vesicles (with and without fluid) and prostate.

Sperm Evaluations: Sperm concentration and motility will be evaluated using computer-assisted sperm analysis (CASA). Motility will be evaluated by the Hamilton Thorne IVOS by collection of a sample from the left vas deferens. A homogenate will be prepared from the left cauda epididymis for evaluation by the Hamilton Thorne IVOS to determine sperm concentration (sperm per gram of tissue weight). The remaining portion of the left cauda epididymis will be used to manually evaluate sperm morphology. Sperm morphology evaluations will include the following: 1) determination of the percentage of normal sperm in a sample of at least 200; and 2) qualitative evaluation of abnormal sperm, including such categories as abnormal head, abnormal tail, and abnormal head and tail.

See ATTACHMENT 4 for additional tissues to be weighed and retained from the ten rats per sex per group assigned to histological sample collection and evaluation.

All other tissues will be discarded.

Scheduled Sacrifice of Female Rats that Do Not Deliver Litters:

Rats that do not deliver a litter will be sacrificed on day 25 of presumed gestation. Gross necropsy, examination and tissue retention will be conducted as described previously for rats at scheduled sacrifice.

Dams with No Surviving Pups:

Dams with no surviving pups will be sacrificed after the last pup is found dead, missing or presumed cannibalized. Gross necropsy, examination and tissue retention will be conducted as described above for rats at scheduled sacrifice.

Rats Found Dead or Moribund:

Rats that die or are sacrificed because of moribund condition, abortion or premature delivery will be examined for the cause of death or moribund condition on the day the observation is made. The rats will be examined for gross lesions. Testes and epididymides of male rats will be excised and paired organ weights will be recorded. The epididymides will be retained in neutral buffered 10% formalin. The testes will be fixed in Bouin's solution for 48 to 96 hours and then retained in neutral buffered 10% formalin. Pregnancy status and uterine contents of female rats will be recorded. Aborted fetuses and/or delivered pups will be examined to the extent possible. Uteri of apparently nonpregnant rats will be examined after being pressed between glass plates to confirm the absence of implantation sites. Ovaries and uteri will be retained in neutral buffered 10% formalin.

TESTS, ANALYSES AND MEASUREMENTS - F1 GENERATION:

Viability:

Preweaning Period: Litters will be observed for dead pups at least twice daily. The pups in each litter will be counted once daily.

Clinical Observations and/or General Appearance:

Preweaning Period: Once daily.

Pups will be observed if they are warm and clean, for evidence of a nest and if pups are grouped together and nursing or have milk in stomach. Each pup will be examined for general shape of the head, trunk, limbs, tail and presence of anus.

Clinical observations may be recorded more frequently than cited above, if deemed appropriate by the Study Director and/or the Study Monitor.

Body Weights:

Preweaning Period: Days 1 (birth), 8, 15 and 22 postpartum.

Sacrifice: Terminal weight.

Feed Consumption Values (recorded and tabulated):

Preweaning Period: Not recorded.

METHOD OF SACRIFICE - F1 GENERATION PUPS:

F1 generation pups will be sacrificed by carbon dioxide asphyxiation.

NECROPSY - F1 GENERATION:

Gross lesions will be retained in neutral buffered 10% formalin for possible future evaluation. Unless specifically cited below, all other tissues will be discarded.

Pups Found Dead on Day 1 Postpartum:

Pups that die before examination of the litter for pup viability will be evaluated for vital status at birth. The lungs will be removed and immersed in water. Pups with lungs that sink will be identified as stillborn; pups with lungs that float will be identified as liveborn, and to have died shortly after birth. Pups with gross lesions will be preserved in Bouin's solution for possible future evaluation.

Pups Found Dead or Moribund on Days 2 to 4 Postpartum:

Pups found dead or sacrificed because of moribundity will be examined for gross lesions and for the cause of death or the moribund condition. Pups with gross lesions will be preserved in Bouin's solution for possible future evaluation.

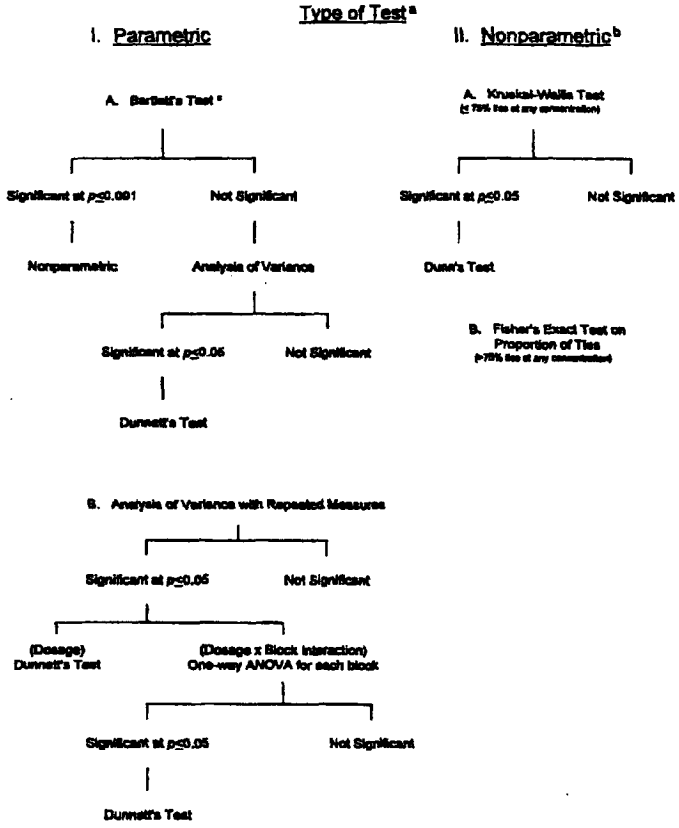
Scheduled Sacrifice:

On day 22 postpartum, pups will be will be sacrificed and examined for gross lesions; gross lesions will be preserved in neutral buffered 10% formalin. Necropsy will include a single cross-section of the head at the level of the frontal-parietal suture and examination of the cross-sectioned brain for apparent hydrocephaly.

Blood samples will be collected from each selected pup (5 per sex per litter from the 10 females per group selected for FOB and motor activity assessment, blood sample collection for H&CC, and histological evaluations) from the vena cava. The blood will be placed into tubes, pooled per litter, allowed to clot and spun in a centrifuge; the resulting serum will be transferred into labeled polypropylene tubes. All samples will be immediately frozen on dry ice and maintained frozen (≤-70°C) until shipment for analysis. The liver from each selected pup will be collected excised and the organ weight recorded. The median lobe will be frozen and stored (≤-20°C) until shipment for possible analysis. Frozen samples will be shipped to Lisa Clemen at the previously cited address. The remaining portion of each liver will be retained in neutral buffered 10% formalin for possible histological evaluation. The livers will be processed and evaluated histologically as described for the Fo generation rats in Histological Evaluation in ATTACHMENT 4.

PROPOSED STATISTICAL TESTS[9-16]:

The following schematic represents statistical analyses of the data.



a. Statistically significant probabilities are reported as either $p \leq 0.05$ or $p \leq 0.01$.
b. Proportion data are not included in this category.
c. Test for homogeneity of variance.

Test items in the FOB using interval scales, such as the grip-strength tests and the landing foot splay test, as well as body weight data and feed consumption values will be analyzed as described under the Parametric heading of the schematic. Bartlett's Test of Homogeneity of Variances[9] will be used to estimate the probability that the groups had different variances. A nonsignificant result ($p>0.001$) will indicate that an assumption of homogeneity of variance is not inappropriate, and the data will be compared using the Analysis of Variance Test[10]. If that test is significant ($p\leq0.05$), the groups exposed to the test article/substance will be compared with the control group using Dunnett's Test[11]. If Bartlett's Test is significant ($p\leq0.001$), the Analysis of Variance Test is not appropriate, and the data will be analyzed as described under the Nonparametric heading of the schematic. When 75% or fewer of the scores in all the groups are tied, the Kruskal-Wallis Test[12] will be used to analyze the data, and in the event of a significant result ($p\leq0.05$), Dunn's Test[13] will be used to compare the groups exposed to the test article/substance with the control group. When more than 75% of the scores in any group are tied, Fisher's Exact Test[14] will be used to compare the proportion of ties in the groups.

Data from the motor activity test, with repeated measurements within a session, will be analyzed using an Analysis of Variance with Repeated Measures[15], as described under that heading in the schematic. A significant effect ($p\leq0.05$) in that test can appear as effect of Concentration (a difference between groups in the total across all measurements in a session) or as an interaction between Concentration and Block (a difference between groups at specific measurement periods). If the Concentration effect is significant, the totals for the control group and the groups given the test article/substance will be compared using Dunnett's Test. If the Concentration x Block interaction is significant, an Analysis of Variance Test will be used to evaluate the data at each measurement period, and a significant result ($p\leq0.05$) will be followed by a comparison of the groups using Dunnett's Test.

Test items in the FOB having graded or count scores will be analyzed using the procedures described under the Nonparametric heading of the schematic.

Clinical observation incidence data, as well as the descriptive and quantal data from the FOB, will be analyzed as contingency tables using the Variance Test for Homogeneity of the Binomial Distribution[16].

Alternate or additional statistical evaluations may be performed if deemed necessary or appropriate.

DATA ACQUISITION, VERIFICATION AND STORAGE:

Data generated during the course of this study will be recorded either by hand or using the *Argus Automated Data Collection and Management System*, the *Vivarium Temperature and Relative Humidity Monitoring System*, the *Coulbourn Instruments Passive Infrared Motor Activity System*, the *Coulbourn Instruments Auditory Startle System*, the *Coulbourn Instruments Spatial Delayed Alternation System*, and/or the passive avoidance software. All data will be tabulated, summarized and/or statistically analyzed using the *Argus Automated Data Collection and Management System*, the *Vivarium Temperature and Relative Humidity Monitoring System*, *Microsoft Excel* [part of Microsoft Office 97 (version SR-2)] and/or *The SAS System* (version 6.12).

Records will be reviewed by the Study Director and/or appropriate management personnel within 21 days after generation. All original records will be stored in the archives of the Testing Facility. All original data will be bound and indexed. A copy of all raw data will be supplied to the Sponsor upon request. Preserved tissues will be stored at the Testing Facility at no charge for one year after mailing of the draft final report, after which time the Sponsor will be contacted to determine the disposition of these materials.

KEY PERSONNEL:

Executive Director of Research: Mildred S. Christian, Ph.D., Fellow, ATS
Director of Research: Alan M. Hoberman, Ph.D., DABT
Associate Director of Research and Study Director: Raymond G. York, Ph.D., DABT
Director of Operations and Compliance: Barbara J. Patterson, B.A.
Director of Laboratory Operations: John F. Barnett, B.S.
Director of Study Management: Valerie A. Sharper, M.S.
Manager of Animal Operations: Dena C. Lebo, V.M.D.
Chairperson, Institutional Animal Care and Use Committee: Douglas B. Learn, Ph.D.
Consultant, Veterinary Pathology: W. Ray Brown, D.V.M., Ph.D., ACVP

RECORDS TO BE MAINTAINED:

Protocol and Amendments.
Test Substance, Vehicle and/or Reagent Receipt, Preparation and Use.
Animal Acquisition.
Randomization Schedules.
Mating History.
Treatment (if prescribed by Staff Veterinarian).
General Comments.
Clinical Observations and/or General Appearance.
Body Weights.
Feed Consumption Values.
Natural Delivery Observations.
FOB and Motor Activity Observations.
Blood Sample Collection, Processing and Shipment.
Gross Necropsy Observations.
Organ Weights.
Photographs (if required).
Study Maintenance (room and environmental records).
Feed and Water Analyses.
Packing and/or Shipment Lists.

FINAL REPORT:

The Study Director will provide periodic updates of study progress to the Sponsor. Draft summary tables of unaudited computer-recorded data may accompany these updates. Statistical analyses will not be performed on these interim data.

A comprehensive draft final report will be prepared on completion of the study and will be finalized following consultation with the Sponsor. The report will include the following:

Summary and Conclusion.
Experimental Design and Method.
Evaluation of Test Results.
Appendices: Figures, Summary and Individual Tables Summarizing the Above Data, Protocol and Associated Amendments and Deviations, Study Director's GLP Compliance Statement, Reports of Supporting Data (if appropriate) and QAU Statement.

The Sponsor will receive one copy of the draft report and two copies of the final report. Data will be hand- and/or computer-recorded. Records will be reviewed by the Study Director and/or appropriate management personnel within 21 days after generation. All original records will be stored in the archives of the Testing Facility. All original data will be bound and indexed. A copy of all raw data will be supplied to the Sponsor upon request. Preserved tissues will be stored at the Testing Facility at no charge for one year after mailing of the draft final report, after which time the Sponsor will be contacted to determine the disposition of these materials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE STATEMENT:

The procedures described in this protocol have been reviewed by the Testing Facility's Institutional Animal Care and Use Committee. All procedures described in this protocol that involve study animals will be conducted in a manner to avoid or minimize discomfort, distress or pain to the animals.

The Sponsor's signature below documents the fact that information concerning the necessity for conducting this study and the fact that this is not an unnecessarily duplicative study may be obtained from the Sponsor. No alternative (*in vitro*) procedures were available for meeting the stated purposes of the study.

REFERENCES:

1. Christian, M.S. and Voytek, P.E. (1982). *In Vivo Reproductive and Mutagenicity Tests.* Environmental Protection Agency, Washington, D.C. National Technical Information Service, U.S. Department of Commerce, Springfield, VA 22161.

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PROTOCOL APPROVAL:

FOR THE TESTING FACILITY

Alan M. Hoberman, Ph.D., DABT
Director of Research — Date: 26 MAR 2002

Raymond G. York, Ph.D., DABT
Associate Director of Research
Study Director — Date: 26 MAR 2002

for Theresa H. Woodard, D.V.M.
Member, Institutional Animal Care and Use Committee — Date: 26 Mar 2002

FOR THE SPONSOR

John Butenhoff, Ph.D., DABT, CIH
Study Monitor and
Sponsor's Representative — Date: 1 April, 2002

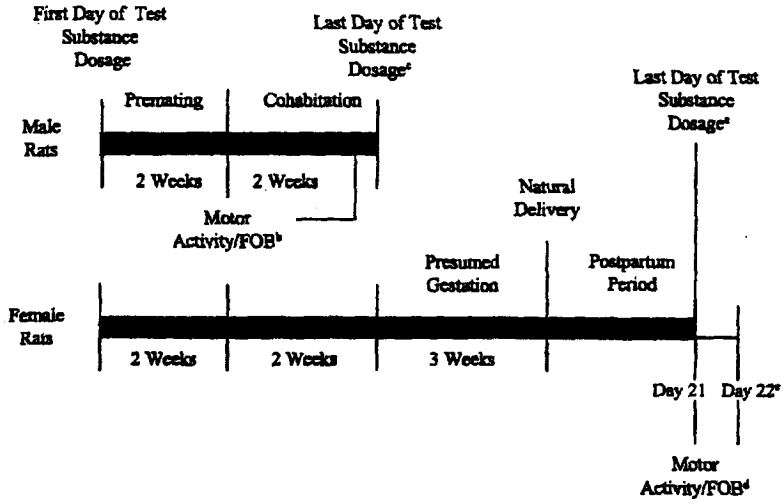
ATTACHMENT 1

SCHEMATIC OF STUDY DESIGN AND STUDY SCHEDULE

ATTACHMENT 1

STUDY SCHEMATIC

COMBINED REPEAT DOSE AND REPRODUCTIVE/DEVELOPMENTAL TOXICITY SCREEN[a]



Dosage Period

a. For additional details see "Tests, Analyses and Measurements" section of the protocol.
b. FOB and motor activity evaluations conducted on ten males per group.
c. Male rats sacrificed after completion of at least 42 days of dosage; necropsy and retention of male reproductive organs. Hematology, clinical biochemistry and histological samples collected from ten male rats per group.
d. Ten female rats per group assigned to FOB evaluation and motor activity evaluation.
e. Ten female rats per group and their litters sacrificed on day 22 postpartum; necropsy and retention of female reproductive organs. Hematology, clinical biochemistry and histological samples collected. Remaining female rats sacrificed on day 22 postpartum and discarded.

SCHEDULE[a]

26 MAR 02	Animal Receipt - Acclimation Begins.
01 APR 02	Start of Dosage Period - Male Rats (14 days before cohabitation and through a 14-day cohabitation period until the day before sacrifice after at least 42 days of dosage).
01 APR 02 - 12 JUN 02	Dosage Period - Female Rats (14 days before cohabitation through Day 22 of lactation).
	Cohabitation Period (Maximum of 14 days).
14 APR 02 PM - 21 APR 02 AM	Male 1 (7 days)
21 APR 02 PM - 28 APR 02 AM	Male 2 (7 days)
14 APR 02	Day 14 Toxicokinetic Sample Collection
15 APR 02	First Possible Day 0 of Presumed Gestation.
28 APR 02	Last Possible Day 0 of Presumed Gestation.
06 MAY 02	First Possible Day 21 of Presumed Gestation Toxicokinetic Sample Collection and Sacrifice - Toxicokinetic Study Female Rats
19 MAY 02	Last Possible Day 21 of Presumed Gestation Toxicokinetic Sample Collection and Sacrifice - Toxicokinetic Study Female Rats
06 MAY 02 - 07 MAY 02	FOB and Motor Activity Evaluation - 10 Male Rats per Group

a. The start date of the study is the day the Study Director signs the protocol.
b. Throughout this schedule, the day of birth is designated day 1 postpartum (day 1 of lactation) and all subsequent ages of the F1 generation rats and days of the lactation period will be determined and cited accordingly, as described above the protocol section, "Day Numbering System."

06 MAY 02	First Possible Delivery (Day 21 of presumed gestation).
23 MAY 02	Last Possible Delivery (Day 25 of presumed gestation).
10 MAY 02	First Possible Day 25 of Presumed Gestation Female Sacrifice.
23 MAY 02	Last Possible Day 25 of Presumed Gestation Female Sacrifice.
12 MAY 02	Day 42 Toxicokinetic Sample Collection and Scheduled Sacrifice - Toxicokinetic Study Male Rats
13 MAY 02	Scheduled Sacrifice - Main Study Male Rats (Earliest possible date). Hematology, Clinical Biochemistry and Histological Sample Collection of Selected Male Rats.
23 MAY 02 - 09 JUN 02	FOB and Motor Activity Evaluation - 10 Female Rats per Group.
27 MAY 02 - 13 JUN 02	Day 22 Postpartum - Sacrifice Female Rats and Pups. Hematology, Clinical Chemistry and Histological Sample Collection of Selected Female Rats and Pups.
24 SEP 02	Draft Final Report

ATTACHMENT 2

MATERIAL SAFETY DATA SHEET

T-7706

MATERIAL SAFETY DATA SHEET (Experimental)

3M
3M Center
St. Paul, Minnesota
55144-1000
1-800-364-3577 or (651) 737-6501 (24 hours)

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1) the information is copied in full with no changes unless prior agreement is obtained from 3M, and
2) neither the copy nor the original is resold or otherwise distributed with the intention of earning a profit thereon.

DIVISION: 3M SPECIALTY MATERIALS
MATERIAL:
L-9051 DEVELOPMENTAL PRODUCT
ISSUED: December 07, 1999
SUPERSEDES: May 17, 1999
DOCUMENT: 04-5470-2

1. INGREDIENT	C.A.S. NO.	PERCENT
POTASSIUM PERFLUOROHEXANE SULFONATE.....	3871-99-6	100.0
RESIDUAL ORGANIC FLUOROCHEMICALS.....	Mixture	Unknown

This material is not listed on the TSCA inventory and should be used for research and development purposes only under the direct supervision of a technically qualified individual.

2. PHYSICAL DATA

BOILING POINT:..... N/A
VAPOR PRESSURE:..... Negligible
VAPOR DENSITY:..... N/A
EVAPORATION RATE:..... Negligible
SOLUBILITY IN WATER:..... slight
SPECIFIC GRAVITY:..... ca. 1.0 Water=1 (Bulk)
PERCENT VOLATILE:..... Negligible
pH:..... N/A
VISCOSITY:..... N/D
MELTING POINT:..... N/D

APPEARANCE AND ODOR:
Off-white crystalline solid, sharp odor.

Abbreviations: N/D - Not Determined N/A - Not Applicable CA - Approximately

---

3. FIRE AND EXPLOSION HAZARD DATA

FLASH POINT:..... > 212 F Setaflash
Setaflash Closed Cup
FLAMMABLE LIMITS - LEL:..... N/A
FLAMMABLE LIMITS - UEL:..... N/A
AUTOIGNITION TEMPERATURE:..... N/D

EXTINGUISHING MEDIA:
Water, Carbon dioxide, Dry chemical, Foam

SPECIAL FIRE FIGHTING PROCEDURES:
Wear full protective clothing, including helmet, self-contained, positive pressure or pressure demand breathing apparatus, bunker coat and pants, bands around arms, waist and legs, face mask, and protective covering for exposed areas of the head.

UNUSUAL FIRE AND EXPLOSION HAZARDS:
See Hazardous Decomposition section for products of combustion.

---

4. REACTIVITY DATA

STABILITY: Stable

INCOMPATIBILITY - MATERIALS/CONDITIONS TO AVOID:
None known.

HAZARDOUS POLYMERIZATION: Hazardous polymerization will not occur.

HAZARDOUS DECOMPOSITION PRODUCTS:
May produce fluorocarbon gases if exposed to very high temperatures (over 300 C).

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5. ENVIRONMENTAL INFORMATION

SPILL RESPONSE:
Observe precautions from other sections. Collect spilled material. Use wet sweeping compound or water to avoid dusting. Clean up residue. Place in a closed container.

RECOMMENDED DISPOSAL:
Incinerate in an industrial or commercial facility in the presence of a combustible material. Combustion products will include HF. Disposal alternative: Dispose of waste product in a facility permitted to accept chemical waste.

Abbreviations: N/D - Not Determined N/A - Not Applicable CA - Approximately

5. ENVIRONMENTAL INFORMATION (continued)

ENVIRONMENTAL DATA:
Not determined.

REGULATORY INFORMATION:
Volatile Organic Compounds: N/D.
VOC Less H2O & Exempt Solvents: N/D.

Since regulations vary, consult applicable regulations or authorities before disposal. U.S. EPA Hazardous Waste Number = None (Not U.S. EPA Hazardous).

OTHER ENVIRONMENTAL INFORMATION:
This product may contain one or more organic fluorochemicals that have the potential to resist degradation and persist in the environment.

EPCRA HAZARD CLASS:
FIRE HAZARD: No PRESSURE: No REACTIVITY: No ACUTE: Yes CHRONIC: No

6. SUGGESTED FIRST AID

EYE CONTACT:
Immediately flush eyes with large amounts of water. Get immediate medical attention.

SKIN CONTACT:
Flush skin with large amounts of water. If irritation persists, get medical attention.

INHALATION:
If signs/symptoms occur, remove person to fresh air. If signs/symptoms continue, call a physician.

IF SWALLOWED:
If swallowed, call a physician immediately. Only induce vomiting at the instruction of a physician. Never give anything by mouth to an unconscious person.

7. PRECAUTIONARY INFORMATION

EYE PROTECTION:
Avoid eye contact. Avoid eye contact with vapor, spray, or mist. The following should be worn alone or in combination, as appropriate, to prevent eye contact: Wear vented goggles.

Abbreviations: N/D - Not Determined N/A - Not Applicable CA - Approximately

7. PRECAUTIONARY INFORMATION (continued)

SKIN PROTECTION:
Avoid skin contact. Wear appropriate gloves when handling this material. A pair of gloves made from the following material(s) are recommended: butyl rubber, polyethylene/polyvinylidene chloride (Saranex). Use one or more of the following personal protection items as necessary to prevent skin contact: head covering, coveralls. Protective garments (other than gloves) should be made of either of the following materials: polyethylene/polyvinylidene chloride (Saranex).

RECOMMENDED VENTILATION:
Use with appropriate local exhaust ventilation. Provide appropriate local exhaust ventilation at transfer points. Use in a well-ventilated area. Provide sufficient ventilation to maintain emissions below recommended exposure limits. If exhaust ventilation is not adequate, use appropriate respiratory protection. Provide ventilation adequate to control vapor concentrations below recommended exposure limits and/or control spray or mist.

Local exhaust ventilation is recommended where the material becomes airborne.

RESPIRATORY PROTECTION:
Avoid breathing of airborne material. Select one of the following NIOSH approved respirators based on airborne concentration of contaminants and in accordance with OSHA regulations: half-mask supplied air respirator, full-face supplied air respirator.

PREVENTION OF ACCIDENTAL INGESTION:
Do not eat, drink or smoke when using this product. Wash exposed areas thoroughly with soap and water. Wash hands after handling and before eating.

RECOMMENDED STORAGE:
Store at room temperature. Keep container dry. Keep container closed when not in use.

FIRE AND EXPLOSION AVOIDANCE:
Not determined.

EXPOSURE LIMITS

INGREDIENT	VALUE	UNIT	TYPE	AUTH	SKIN*
POTASSIUM PERFLUOROHEXANE SULFONATE.....	0.1	MG/M3	TWA	3M	Y
RESIDUAL ORGANIC FLUOROCHEMICALS.....	0.1	MG/M3	TWA	3M	Y

* SKIN NOTATION: Listed substances indicated with 'Y' under SKIN refer to

Abbreviations: N/D - Not Determined N/A - Not Applicable CA - Approximately

EXPOSURE LIMITS (continued)

INGREDIENT	VALUE	UNIT	TYPE	AUTH	SKIN*

the potential contribution to the overall exposure by the cutaneous route including mucous membrane and eye, either by airborne or, more particularly, by direct contact with the substance. Vehicles can alter skin absorption.

SOURCE OF EXPOSURE LIMIT DATA:
- 3M: 3M Recommended Exposure Guidelines

8. HEALTH HAZARD DATA

EYE CONTACT:
No information was found regarding effects from eye contact.

Single exposure may cause:

Mild Eye Irritation: signs/symptoms can include redness, swelling, pain, and tearing.

SKIN CONTACT:
No information was found regarding effects from skin contact.

May be absorbed through the skin and persist in the body for an extended time.

Single exposure may cause:

Moderate Skin Irritation: signs/symptoms can include redness, swelling, itching, and dryness.

INHALATION:
No information was found regarding effects from inhalation exposure.

May be absorbed by inhalation and persist in the body for an extended time.

Single overexposure, above recommended guidelines, may cause:

Irritation (upper respiratory): signs/symptoms can include soreness of the nose and throat, coughing and sneezing.

IF SWALLOWED:
Ingestion is not a likely route of exposure to this product.

No information was found regarding effects from swallowing.

Animal studies conducted on organic fluorochemicals which may be present in this product indicate effects including liver disturbances, weight loss, loss of appetite, lethargy, and neurological, pancreatic, adrenal and hematologic effects. There are no known human health

Abbreviations: N/D - Not Determined N/A - Not Applicable CA - Approximately

8. HEALTH HAZARD DATA (continued)

effects from anticipated exposure to these organic fluorochemicals when used as intended and instructed.

OTHER HEALTH HAZARD INFORMATION:
This product may contain one or more organic fluorochemicals that have the potential to be absorbed and remain in the body for long periods of time, either as the parent molecule or as metabolites, and may accumulate with repeated exposures. There are no known human health effects from anticipated exposure to these organic fluorochemicals when used as intended and instructed.

The presence of organic fluorochemicals in the blood of the general population and subpopulations, such as workers, has been published dating back to the 1970's. 3M's epidemiological study of its own workers indicates no adverse effects.

SECTION CHANGE DATES

PRECAUTIONARY INFO. SECTION CHANGED SINCE May 17, 1999 ISSUE

Abbreviations: N/D - Not Determined N/A - Not Applicable CA - Approximately

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ATTACHMENT 3

TEST SUBSTANCE PREPARATION PROCEDURE

ATTACHMENT 3

TEST SUBSTANCE PREPARATION PROCEDURE

Test Substance: T-7706
Vehicle: Aqueous 0.5% CMC (medium viscosity)

A. Purpose:

The purpose of this procedure is to provide a method for the preparation of dosage suspensions of T-7706 for oral (gavage) administration to rats on Argus Research Study number 418-028.

B. General Information:

1. All suspension containers will be labeled and color-coded. Each label will specify the protocol number, test substance identification, Argus batch number, concentration, dosage level, preparation date, expiration date and storage conditions.

2. Suspensions will be prepared:
   __ Daily X Weekly __ For_ days of use
   __ Approximately every ten days __ By Sponsor

3. Suspensions will be administered at a final dosage volume of 10 mL/kg.

4. Safety:
   X Gloves, uniform/lab coat, goggles or safety glasses with side shields
   X Dust-mist/HEPA-filtered Mask
   __ Half-Face Respirator if not used in a chemical fume hood
   __ Full-Face Respirator/Positive Pressure Hood
   __ Tyvek Suit or tyvek apron and sleeves

5. Dosage suspensions adjusted for % Activity/Purity or Correction Factor:
   __ Yes X No (Calculations based on 100%)
   __ % Activity __ % Purity __ Correction Factor

6. Sampling requirements: Cited in protocol

7. Storage: Cited in protocol

ATTACHMENT 3

TEST SUBSTANCE PREPARATION PROCEDURE

NOTE: Prior to test substance preparation accurately measure the required amount of the appropriate vehicle (R.O. deionized water should be used for calibration purposes) in a graduated cylinder, pour the required amount of vehicle into a beaker. Carefully mark each beaker at the meniscus. This mark will be used during the preparation to bring the test substance slurry up to volume.

C. Dosage Suspension Preparation:

1. Weigh the required amount of test substance on a piece of weigh paper or into an appropriately sized mortar (see PREPARATION CALCULATIONS).

2. If weigh paper is used, transfer the test substance to an appropriately sized mortar. If necessary, grind the test substance into a fine powder. Slowly add a small amount of vehicle and grind. Continue to add vehicle slowly and grind the vehicle and the test substance together to form a fine slurry. Transfer the vehicle/test substance slurry to a marked beaker.

3. Rinse the mortar and pestle with additional vehicle to remove any remaining test substance. Transfer rinse to beaker.

4. Add additional vehicle to the beaker to bring volume up to the mark. Place on magnetic stir plate and agitate prior to and during sampling, aliquotting and/or administration.

5. Repeat steps (1) through (4) for each concentration.

Written By: Michael B. Brennan

Approved by: [signature] Date: 26 MAR 02

(1) Clarification: ___ No ___ Yes [see attached clarification form]

Initial/Date : _____

(1) Please refer to original protocol. [signature] 31-JUL-03

ATTACHMENT 4

TISSUES TO BE WEIGHED, RETAINED AND EXAMINED HISTOLOGICALLY

ATTACHMENT 4

TISSUES TO WEIGHED AND RETAINED FOR POSSIBLE EXAMINATION FROM TEN RATS PER SEX PER GROUP

The ten rats per sex per group assigned to functional observational battery and motor activity tests will be assigned to hematology, clinical biochemistry and histological evaluations.

Tissues to be Weighed:

The following organs will be excised, trimmed and individually weighed as soon as possible after excision to avoid drying.

liver	spleen
kidneys	brain
adrenals	heart
thymus	ovaries
testes	uterus (with cervix)
right epididymis	prostate
left epididymis (whole and cauda)	
seminal vesicles (with and without fluid)	

Tissues to be Retained:

The following tissues or representative samples will be retained in neutral buffered 10% formalin.

brain (representative regions including cerebrum, cerebellum, pons)	
small and large intestines (including Peyer's patches)	
lungs (perfused with neutral buffered 10% formalin)	
lymph nodes (submandiblar and mediastinal)	
peripheral nerve (sciatic or tibial)	
gross lesions	spinal cord (cervical, thoracic and lumbar)
stomach	liver
kidneys	adrenals
spleen	heart
thymus	thyroid/parathyroid
trachea	uterus
urinary bladder	bone marrow (sternum)
testes*	ovaries
prostate	uterus
seminal vesicles (with coagulating gland)	vagina
mammary gland (female rats only)	

* Testes will be fixed in Bouin's solution for 48 to 96 hours before being retained in neutral buffered 10% formalin.

Additionally, the remaining portion of the left epididymis (corpus and caput), as well as the right epididymis will be fixed in neutral buffered 10% formalin.

Histological Examination:

Histological examination of retained tissues, including reproductive organs, will be conducted for the assigned ten rats per sex from the control and high dosage groups and from the F1 generation pups (livers) from the control and high dosage groups. If lesions attributed to the test substance are observed in the rats exposed to the high test substance concentration, the same tissues will be examined from the assigned ten rats per sex exposed to the lower test substance concentrations. Should results warrant examination of the lower dosage groups and conduct of quantitative evaluation, scheduled report date and prices will be adjusted accordingly.

The postlactional ovary should contain primordial and growing follicles as well as the large corpora lutea of lactation. Histopathological examination may detect qualitative depletion of the primordial follicle population. A quantitative evaluation of primordial follicles will be conducted for Fo generation female rats; the number of rats, ovarian section selection and section sample size will be statistically appropriate for the evaluation procedure used. Examination will include enumeration of the number of primordial follicles, which can be combined with small growing follicles, for comparison of ovaries of rats assigned to treated and control groups.

Shipping Instructions:

Tissues to be examined histologically will be shipped (ambient conditions) to:

Principal Investigator: W. Ray Brown, D.V.M., Ph.D., ACVP
Veterinary Pathologist
Research Pathology Services, Inc.
438 E. Butler Avenue
New Britain, Pennsylvania 18901
Telephone: (215) 345-7070
Telefax: (215) 345-4326
Email: WRBRPS@concentric.net

The recipient will be notified in advance of sample shipment.

905 Sheehy Drive, Bldg. A
Horsham, PA 19044
Telephone: (215) 443-8710
Telefax: (215) 443-8587

ARGUS RESEARCH
Charles River Laboratories
Discovery and Development Services

PROTOCOL 418-028

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST

SPONSOR'S STUDY NUMBER: T-7706.1

Amendment 1 - 17 April 2002

---

1. Detailed Clinical Observations - Male and Female Rats (page 10 of the protocol):

   [Effective Date: 1 April 2002] Detailed clinical observations will not be recorded for male and female rats assigned to toxicokinetic sampling.

   Reason for Change:

   This change was made because sufficient data for evaluation of detailed clinical observations will be available from the rats assigned to the main study.

2. Feed Consumption Values - Male Rats and Female Rats (page 11 of the protocol):

   [Effective Date: 1 April 2002] Feed consumption values will not be recorded or tabulated for male and female rats assigned to toxicokinetic sampling.

   Reason for Change:

   This change was made because sufficient data for evaluation of feed consumption will be available from the rats assigned to the main study.

Any revisions made to this finalized amendment must be made by subsequent amendment.

---

3. Estrous Cycling and Mating (page 12 of the protocol):

[Effective Date: 1 April 2002] For the rats assigned to toxicokinetic sampling, estrous cycling will be evaluated during the cohabitation period until spermatozoa are observed in a smear of the vaginal contents and/or a copulatory plug is observed *in situ*, but not during the dosage period, prior to cohabitation.

Reason for Change:

This change was made because sufficient data for evaluation of estrous cycling will be available from the rats assigned to the main study.

4. Scheduled Sacrifice - Toxicokinetic Study (page 16 of the protocol):

[Effective Date: 5 April 2002] The number of implantation sites and corpora lutea will be recorded. Carcasses will be discarded without further evaluation.

Reason of Change:

This change was made in order to provide more information about possible toxicity of the test substance in pregnant rats.

5. Scheduled Sacrifice - Main Study (page 16 of the protocol):

[Effective Date: 27 March 2002] The number of implantation sites will be recorded, rather than the number of implantation sites and corpora lutea will be recorded.

Reason of Change:

The number of corpora lutea will not be recorded because corpora lutea regress at a rapid rate and are not counted on studies at weaning.

6. Scheduled Sacrifice (page 19 of the protocol):

[Effective Date: 4 April 2002] The liver from each selected pup will be excised and the organ weight recorded, rather than the liver from each selected pup will be collected excised and the organ weight recorded.

Any revisions made to this finalized amendment must be made by subsequent amendment.

Reason for Change:

This change clarifies the protocol by removing an extraneous word.

C Hoberman 4-17-02		Raymond G. York 4-17-02	
Alan M. Hoberman, Ph.D., DABT Director of Research	Date	Raymond G. York, Ph.D., DABT Associate Director of Research Study Director	Date
Theresa H. Woodard 4-17-02		John L. Butenhoff 4-18-02	
Theresa H. Woodard, D.V.M. Member, Institutional Animal Care and Use Committee	Date	John Butenhoff, Ph.D., DABT, CIH Study Monitor and Sponsor's Representative	Date

Any revisions made to this finalized amendment must be made by subsequent amendment.

905 Sheehy Drive, Bldg. A
Horsham, PA 19044
Telephone: (215) 443-8710
Telefax: (215) 443-8587

ARGUS RESEARCH
Charles River Laboratories
Discovery and Development Services

PROTOCOL 418-028

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY
OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL
TOXICITY SCREENING TEST

SPONSOR'S STUDY NUMBER: T-7706.1

Amendment 2 - 15 July 2002

---

1. Safety Precautions (page 3 of the protocol and Attachment 3 page 1 of the protocol):

   [Effective Date: 29 April 2002] A half face respirator will be worn in addition to gloves, appropriate eye protection and a uniform/lab coat during formulation preparation of the bulk test substance.

   Reason for Change:

   This change was made to match the bulk test substance text with the text located within the Material Safety Data Sheet.

2. Study Schedule (Attachment 1 page 2 of the protocol):

   [Effective Date: 29 April 2002] The dates for FOB and motor activity evaluations have been extended to four days (06 MAY 02 - 09 MAY 02) rather than two days (06 MAY 02 - 07 MAY 02).

Any revisions to this finalized amendment must be made by subsequent amendment.

Reason for Change:

This change was made because more time is needed to evaluate animals assigned to FOB and motor activity evaluations.

for Alan M. Hoberman, Ph.D., DABT — Date
Director of Research

Raymond G. York, Ph.D., DABT — Date
Associate Director of Research
Study Director

for Theresa H. Woodard, D.V.M. — Date
Member, Institutional Animal Care and Use Committee

John Butenhoff, Ph.D., DABT, CIH — Date
Study Monitor and
Sponsor's Representative

Any revisions to this finalized amendment must be made by subsequent amendment.

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ARGUS RESEARCH
Charles River Laboratories
Discovery and Development Services

PROTOCOL 418-028

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY
OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL
TOXICITY SCREENING TEST

SPONSOR'S STUDY NUMBER: T-7706.1

Amendment 3 - 17 July 2002

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1. Bulk Test Substance Sampling, Shipping Instructions, Shipping Instructions, Caesarean-Sectioning - Toxicokinetic Study, Scheduled Sacrifice - Toxicokinetic Study, and Scheduled Sacrifice, (pages 4, 5, 12, 13, 16 and 19, respectively of the protocol)

   [Effective Date: 29 May 2002] Samples for perfluorohexanesulfonate (PFHS) analysis shipped to Lisa Clemen at 3M Environmental Technology and Safety Services will be reshipped and remaining samples, that were to be shipped to Lisa Clemen and have not yet been shipped, will be shipped to:

   John Flaherty, Ph.D. (Principal Investigator)
   Exygen Research
   3058 Research Drive
   State College, Pennsylvania 16801
   Telephone: (814) 272-1039, ext. 122
   Telefax: (814) 231-1580
   Email: john.flaherty@exygen.com

Any revisions to this finalized amendment must be made by subsequent amendment.

These samples include:

Bulk test substance sampling (page 4 of the protocol)
Concentration and homogeneity (page 5 of the protocol)
Stability (page 5 of the protocol)
Plasma toxicokinetic samples (page 11 to 12 and page 16 of the protocol)
Plasma samples, rather than serum samples, were retained.
Liver toxicokinetic samples (pages 12 and 16 of the protocol)
Pooled fetal serum toxicokinetic samples (pages 12 and 16 of the protocol)
Pooled fetal liver toxicokinetic samples (pages 13 and 16 of the protocol)
Pooled pup serum toxicokinetic samples (page 19 of the protocol)
Pup liver toxicokinetic samples (page 19 of the protocol)

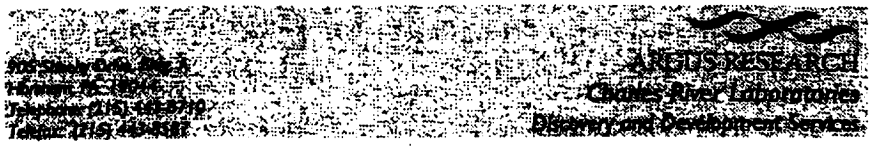
The analyses will be subcontracted to Exygen by the Sponsor and the Quality Assurance Unit for Exygen Research will conduct critical phase inspections and audit the respective results and reports according to the Standard Operating procedures of that facility. Such critical phase inspection reports and audit reports will be submitted by that facility to the Study Director, Raymond G. York. The date of the inspections and report submissions will be incorporated into a QAU statement generated by Exygen Research for inclusion in the final report for Protocol 418-028.

Reason for Change:

This change was made at the request of the Sponsor because 3M is not able to complete the formulation analysis with their current staffing.

for Alan M. Hoberman, Ph.D., DABT Date Director of Research	Raymond G. York, Ph.D., DABT Date Associate Director of Research Study Director
for Theresa H. Woodard, D.V.M. Date Member, Institutional Animal Care and Use Committee	John Butenhoff, Ph.D., DABT, CIH Date Study Monitor and Sponsor's Representative

Any revisions to this finalized amendment must be made by subsequent amendment.



PROTOCOL 418-028

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST

SPONSOR'S STUDY NUMBER: T-7706.1

Amendment 4 - 20 March 2003

1. Bulk Test Substance Sampling, Shipping Instructions, Shipping Instructions, Caesarean-Sectioning - Toxicokinetic Study, Scheduled Sacrifice - Toxicokinetic Study, and Scheduled Sacrifice, (pages 4, 5, 12, 13, 16 and 19, respectively of the protocol) and Amendment 3, Item 1: Bulk Test Substance Sampling, Shipping Instructions, Shipping Instructions, Caesarean-Sectioning - Toxicokinetic Study, Scheduled Sacrifice - Toxicokinetic Study, and Scheduled Sacrifice (page 1 of Amendment 3)

[Effective Date: 27 February 2003] The analyses performed by Exygen Research will be done according to Exygen Method ExM-023-071 Revision 1, entitled "Method of Analysis for the Determination of Perfluorohexanesulfonate (PFHS), Perfluorooctanesulfonate (PFOS) and Pentadecafluorooctanoic Acid (PFOA) in Rat Liver, Serum and Urine Revision 1".

Any revisions to this finalized amendment must be made by subsequent amendment.

Reason for Change:

This change was made at the request of the Exygen Research in order to clarify the method of analysis.

Alan M. Hoberman, Ph.D., DABT Date
Director of Research

Raymond G. York, Ph.D., DABT Date
Associate Director of Research
Study Director

Douglas B. Learn, Ph.D. Date
Chair, Institutional Animal Care
and Use Committee

John Butenhoff, Ph.D., DABT, CIH Date
Study Monitor and
Sponsor's Representative

Any revisions to this finalized amendment must be made by subsequent amendment.

Exygen RESEARCH
Precise Research. Proven Results.

Page 1 of 1

PROTOCOL DEVIATION

Deviation Number: 1
Date of Occurrence: 10/14/02

Exygen Study Number: 023-072 Protocol Number: 418-028

DESCRIPTION OF DEVIATION

A recovery of 62% for PFHS is being accepted for the 5000 ppb spike (02021119 Spk C) in data set 100402A.

ACTIONS TAKEN
for example - deviation issued, SOP revision, etc.

Deviation Issued.

Recorded By: [signature] Date: 07/15/03

IMPACT ON STUDY

The 10 ppb and 50 ppb control matrix spikes included with the set gave acceptable recoveries.

[signature] Principal Investigator Signature	Date 7/15/03
[signature] Study Director Signature	Date 7/16/03
[signature] Management Signature	Date 7/16/03
(Sponsor) John L. Butenhoff Study Monitor	Date 07/17/2003
Exygen QAU Review	Date 7/15/03

U:\Forms\PROTOCOL_DEVIATION.doc 9/25/2002/5

NOTE: THIS DEVIATION IS BEING RE-ISSUED DUE TO SUSPECTED LOSS OF ORIGINAL. KB 07/15/03

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NOTE TO FILE

Date: 01/14/03

Exygen Research Study # 023-072

PROTOCOL # 418-028

NOTE:

The PFHS stock solution was inadvertently not corrected for salt content when prepared. The stock solution was used to make the fortification and calibration standards used for the study. Due to the large amount of data associated with this study, the concentrations of fortification and calibration solutions listed throughout the raw data were left uncorrected for the salt content. The final PFHS values recorded were corrected to reflect the difference in PFHS concentration due to the salt content. The correction was performed by multiplying the final ppb value found by 0.91.

Signature: _____ Date: 01/14/03

July 31, 2001/0

APPENDIX B

Analytical Method:

Method of Analysis for the Determination of Perfluorohexanesulfonate (PFHS), Perfluorooctanesulfonate (PFOS) and Pentadecafluorooctanoic Acid (PFOA) in Rat Liver, Serum and Urine Revision 1 (Exygen Method No. ExM-023-071 Revision 1)

TITLE

Method of Analysis for the Determination of Perfluorohexanesulfonate (PFHS), Perfluorooctanesulfonate (PFOS) and Pentadecafluorooctanoic Acid (PFOA) in Rat Liver, Serum and Urine Revision 1

AUTHORS

John Flaherty, Karen Risha, and Emily Decker

DATE ISSUED

November 20, 2002

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METHOD NUMBER

ExM-023-071 Revision 1

TOTAL NUMBER OF PAGES

43

MANAGEMENT APPROVAL

John M Flaherty 11/20/02

John Flaherty Date
Laboratory Manager
Exygen Research

John L. Butenhoff 11/21/02

John L. Butenhoff Date
Sponsor Representative
3M Medical Department Corporate Toxicology

TABLE OF CONTENTS

TITLE 1
MANAGEMENT APPROVAL 2
TABLE OF CONTENTS 3
LIST OF TABLES 4
LIST OF FIGURES 5
1. SUMMARY 7
2. EXPERIMENTAL COMPOUNDS 8
3. CHEMICALS AND SUPPLIES 9
3.1. CHEMICALS 9
3.2. STANDARDS 9
3.3. EQUIPMENT AND SUPPLIES 9
3.4. SOLUTIONS 10
3.5. PREPARATION OF STANDARD SOLUTIONS 10
3.5.1. Stock solution 11
3.5.2. Fortification Solutions 11
3.5.3. Calibration Standards 11
4. METHOD 12
4.1. FLOW DIAGRAM 12
4.2. SAMPLE PROCESSING 12
4.3. BATCH SET UP 13
4.4. SAMPLE EXTRACTION 13
4.4.1. Liver Extraction 13
4.4.2. Serum and Urine Extraction 13
4.4.3. SPE Column Conditioning 14
4.5. QUANTITATION 14
4.5.1. LC/MS/MS System and Operating Conditions 14
4.5.2. Calibration Curve Procedures 15
4.5.3. Sample Analysis 16
4.6. ACCEPTANCE CRITERIA 17
4.7. PERFORMANCE CRITERIA 17
4.8. TIME REQUIRED FOR ANALYSIS 18
5. CALCULATIONS 18
6. SAFETY 19

LIST OF TABLES

Table 1. Recovery Summary of PFHS in Rat Liver and Serum.....20
Table 2. Recovery Summary of PFOS in Rat Liver, Serum and Urine 21
Table 3. Recovery Summary of PFOA in Rat Liver, Serum and Urine.....22

LIST OF FIGURES

Figure 1. Calibration Curve for PFHS 23
Figure 2. Calibration Curve for PFOS 24
Figure 3. Calibration Curve for PFOA 25
Figure 4. Representative Chromatogram of a 0.1 ng/mL Standard Containing PFHS 26
Figure 5. Representative Chromatogram of a 0.1 ng/mL Standard Containing PFOS 26
Figure 6. Representative Chromatogram of a 0.1 ng/mL Standard Containing PFOA 27
Figure 7. Representative Chromatogram of a 0.5 ng/mL Standard Containing PFHS 27
Figure 8. Representative Chromatogram of a 0.5 ng/mL Standard Containing PFOS 28
Figure 9. Representative Chromatogram of a 0.5 ng/mL Standard Containing PFOA 28
Figure 10. Representative Chromatogram of a 5.0 ng/mL Standard Containing PFHS 29
Figure 11. Representative Chromatogram of a 5.0 ng/mL Standard Containing PFOS 29
Figure 12. Representative Chromatogram of a 5.0 ng/mL Standard Containing PFOA 30
Figure 13. Representative Chromatogram of a Reagent Blank Sample Analyzed for PFHS 30
Figure 14. Representative Chromatogram of a Reagent Blank Sample Analyzed for PFOS 31
Figure 15. Representative Chromatogram of a Reagent Blank Sample Analyzed for PFOA 31
Figure 16. Representative Chromatogram of a Control Liver Sample Analyzed for PFHS 32
Figure 17. Representative Chromatogram of a Control Liver Sample Analyzed for PFOS 32
Figure 18. Representative Chromatogram of a Control Liver Sample Analyzed for PFOA 33
Figure 19. Representative Chromatogram of a Control Serum Sample Analyzed for PFHS 33
Figure 20. Representative Chromatogram of a Control Serum Sample Analyzed for PFOS 34
Figure 21. Representative Chromatogram of a Control Serum Sample Analyzed for PFOA 34
Figure 22. Representative Chromatogram of a Control Urine Sample Analyzed for PFOS 35
Figure 23. Representative Chromatogram of a Control Urine Sample Analyzed for PFOA 35
Figure 24. Representative Chromatogram of a Control Liver Sample Fortified at 10 ng/g with PFHS 36

LIST OF FIGURES (continued)

Figure 25. Representative Chromatogram of a Control Liver Sample Fortified at 10 ng/g with PFOS 36
Figure 26. Representative Chromatogram of a Control Liver Sample Fortified at 10 ng/g with PFOA 37
Figure 27. Representative Chromatogram of a Control Liver Sample Fortified at 50 ng/g with PFHS 37
Figure 28. Representative Chromatogram of a Control Liver Sample Fortified at 50 ng/g with PFOS 38
Figure 29. Representative Chromatogram of a Control Liver Sample Fortified at 50 ng/g with PFOA 38
Figure 30. Representative Chromatogram of a Control Serum Sample Fortified at 10 ng/mL with PFHS 39
Figure 31. Representative Chromatogram of a Control Serum Sample Fortified at 10 ng/mL with PFOS 39
Figure 32. Representative Chromatogram of a Control Serum Sample Fortified at 10 ng/mL with PFOA 40
Figure 33. Representative Chromatogram of a Control Serum Sample Fortified at 50 ng/mL with PFHS 40
Figure 34. Representative Chromatogram of a Control Serum Sample Fortified at 50 ng/mL with PFOS 41
Figure 35. Representative Chromatogram of a Control Serum Sample Fortified at 50 ng/mL with PFOA 41
Figure 36. Representative Chromatogram of a Control Urine Sample Fortified at 10 ng/mL with PFOS 42
Figure 37. Representative Chromatogram of a Control Urine Sample Fortified at 10 ng/mL with PFOA 42
Figure 38. Representative Chromatogram of a Control Urine Sample Fortified at 50 ng/mL with PFOS 43
Figure 39. Representative Chromatogram of a Control Urine Sample Fortified at 50 ng/mL with PFOA 43

1. SUMMARY

This report details a method of analysis for residues of Perfluorohexanesulfonate (PFHS), Perfluorooctanesulfonate (PFOS) and Pentadecafluorooctanoic Acid (PFOA) in Rat Liver, Serum and Urine.

Residues of PFHS, PFOS and PFOA are extracted from each matrix with acetonitrile. The acetonitrile extract is added to water and loaded onto a conditioned C18 solid phase extraction (SPE) cartridge. Analyte residues are eluted with 2 mL of methanol. Quantification of PFHS, PFOS and PFOA is accomplished by liquid chromatography/tandem mass spectrometry (LC/MS/MS) analysis using multiple reaction monitoring (MRM).

The proposed limit of quantitation (LOQ; the lowest fortification specified by the method which gives adequate recovery according to EPA guidelines) for this method is 10 ng/g (parts-per-billion) each for PFHS, PFOS and PFOA.

The theoretical limit of detection (LOD) will be based on the signal to noise ratio and will be at least greater than 3 times the level of noise, based on the instrumentation system used. For all analytes, the lowest analytical standard corresponds to 0.1 ng/mL.

This method was developed using rat liver, serum and urine. Typical percent recoveries ± standard deviations (at 10 and 50 ng/g) are shown below:

Fortification Level (ng/g)	PFHS Recovery in Rat Liver	Fortification Level (ng/mL)	PFHS Recovery in Rat Serum
10	115% ± 9.9% (n=3)	10	108% ± 4.7% (n=3)
50	98% ± 3.5% (n=3)	50	111% ± 9.6% (n=3)

Fortification Level (ng/g)	PFOS Recovery in Rat Liver	Fortification Level (ng/mL)	PFOS Recovery in Rat Serum	PFOS Recovery in Rat Urine
10	96% ± 8.5% (n=3)	10	88% ± 9.8% (n=3)	93% ± 4.7% (n=3)
50	88% ± 1.5% (n=3)	50	120% ± 2.1% (n=3)	79% ± 1.2% (n=3)

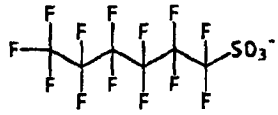
Fortification Level (ng/g)	PFOA Recovery in Rat Liver	Fortification Level (ng/mL)	PFOA Recovery in Rat Serum	PFOA Recovery in Rat Urine
10	98% ± 3.1% (n=3)	10	117% ± 1.5% (n=3)	89% ± 2.5% (n=3)
50	94% ± 2.5% (n=3)	50	111% ± 4.0% (n=3)	87% ± 2.1% (n=3)

Representative calibration curves are shown in **Figures 1-3.** Representative chromatograms are shown in **Figures 4 to 39.**

2. EXPERIMENTAL COMPOUNDS

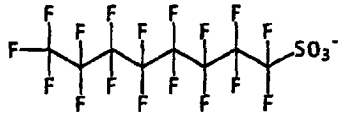
The structures for PFHS, PFOS and PFOA are given below.

PFHS
Chemical Name = Perfluorohexanesulfonate
Molecular weight = 399, as shown



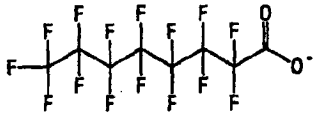
PFHS is supplied as the potassium salt ($C_6F_{13}SO_3^-K^+$), molecular weight = 438

PFOS
Chemical Name = Perfluorooctanesulfonate
Molecular weight = 499, as shown



PFOS is supplied as the potassium salt ($C_8F_{17}SO_3^-K^+$) molecular weight = 538

PFOA
Chemical Name = Pentadecafluorooctanoic Acid
Molecular weight = 413, as shown



3. CHEMICALS AND SUPPLIES

3.1. CHEMICALS

Chemical	Grade	Source	Catalog No.
Methanol (MeOH)	HPLC	EM Science	MX0475-1
Ammonium Acetate	Reagent	JT Baker	0596-01
Water	Type I	Exygen	NA
Acetonitrile	HPLC	EM Science	AX0145-1

Type I water = electrical reaistivity, minimum of 16.67 MΩ/cm at 25 °C, from a Labconco Waterpro™ workstation.

3.2. STANDARDS

Standard	TCR Number	Purity (%)	Source
Perfluorohexanesulfonate (PFHS)	SE-036	99.99 all isomers, 84.36 straight chain	3M
Perfluorooctanesulfonate (PFOS)	SD-018	86.9	3M
Pentadecafluorooctanoic Acid (PFOA)	Lot No: 08316DO	96	Aldrich Chem

3.3. EQUIPMENT AND SUPPLIES

Equipment	Supplier
Balance, analytical (display at least 0.0001 g)	Mettler
125-mL LDPE narrow mouth bottles	Nalgene
Disposable glass micropipets (50-100 & 100-200 µL)	Drummond (VWR)
Tissumizer	Tekmar
Wrist action shaker	Burrell Scientific
Sorvall RC 5C plus Centrifuge	Dupont
50 mL disposable polypropylene centrifuge tubes	VWR
15 mL disposable polypropylene centrifuge tubes	VWR
Visiprep vacuum manifold	Supelco
Sep Pak Vac 6 cc (1g) tC18 cartridges (part # WAT 036795	Waters
2-mL clear HPLC vial Kit (cat # 5181-3400)	Hewlett-Packard
Class A pipets and volumetric flasks	various suppliers
Standard lab equipment (graduated cylinders, disposable tubes etc.)	various suppliers
Stand-alone drop-in guard cartridge holder (part #844017-400)	Keystone Scientific
Hypercarb drop-in guard column (4 mm) (part # 844017-400)	Keystone Scientific
HPLC Pump (LC-10AD)	Shimadzu
LC/MS/MS and HPLC systems	As described in section 4.5.

Notes:

1. In order to avoid contamination, the use of disposable labware (containers, tubes, pipettes, etc.) is highly recommended.
2. Teflon or Teflon-lined containers or equipment should not be used.
3. It may be necessary to check the solvents (acetonitrile, methanol) for the presence of contaminants (especially PFOA) by LC/MS/MS before use. Certain lot numbers have been found to be unsuitable for use.
4. Use disposable micropipettes or pipettes to aliquot standard solutions when preparing standards and samples for extraction.
5. Equivalent materials may be substituted for those specified in this method.

3.4. Solutions

(1) 2 mM ammonium acetate in water is prepared by weighing 0.154 g of ammonium acetate and dissolving in 1 L of water.

(2) Hypercarb filtered type I water is prepared by filtering type I water through a Hypercarb guard column using a HPLC pump at ~2-3 mL/min. Before use, wash the guard cartridge with ~25 mL of HPLC grade acetonitrile, then ~ 25 mL of type I water, then begin collecting the filtered type I water eluate for use in the extraction. Repeat the wash after filtering ~2L of water.

Note: The aforementioned example is provided for guidance, alternative volumes may be prepared as long as the appropriate ratios of the solvent to solute are maintained.

3.5. Preparation of Standard Solutions

Analytical standards are used for three purposes:

1. Calibration Standards – These standards are prepared in methanol and are used to calibrate the response of the detector used in the analysis.
2. Laboratory Control Spikes – These fortifications are prepared at concentrations corresponding to the LOQ and 5x LOQ and are used to determine analytical recovery. Laboratory control spikes are prepared in control matrix.
3. Matrix Spikes – These fortifications are prepared by spiking into the field samples at a known concentration. Matrix spikes are used to evaluate the effect of the sample matrix on analytical recovery and are prepared at the client's request.

The analyst may vary the absolute volumes of the standards as long as the correct proportions of solute to solvent are maintained.

3.5.1. Stock solution

Prepare individual stock solutions at 100 µg/mL for PFHS, PFOS and PFOA by weighing out 10 mg of each analytical standard (corrected for purity and if necessary, salt content) and dilute to 100 mL with methanol in separate 100-mL volumetric flasks. The stock solutions (in 125-mL LDPE bottles) are to be stored in a refrigerator at 2°C to 6°C and are stable for a maximum period of one year from the date of preparation.

3.5.2. Fortification Solutions

a. Prepare a mixed fortification standard at 1.0 µg/mL (1000 ng/mL) of PFHS, PFOS and PFOA by adding 1.0 mL of each of the 100 µg/mL stock solutions into a 100-mL volumetric flask and bring up to volume with methanol.
b. Prepare a mixed fortification standard at 0.1 µg/mL (100 ng/mL) of PFHS, PFOS and PFOA by diluting 10.0 mL of the 1.0 µg/mL mixed fortification solution to 100 mL with methanol in a volumetric flask.

Example: one hundred microliters of the 0.1 µg/mL solution spiked into 1 g of liver or 1 mL of serum/urine is equivalent to a 10 ppb (10 ng/mL or ng/g) fortification.

Store all fortification standard solutions in a refrigerator (in 125-mL LDPE bottles) at 2°C to 6°C for a maximum period of one year from the date of preparation. Note also that additional concentrations may be prepared if necessary.

3.5.3. Calibration Standards

LC/MS/MS calibration standards containing PFHS, PFOS and PFOA are prepared at 0.1, 0.2, 0.5, 1.0, 2.0 and 5.0 ng/mL in methanol via dilution of the 0.1 µg/mL mixed fortification solution (section 3.5.2.b).

The following is a typical example; additional concentrations may be prepared as needed.

Initial Conc. (ng/mL)	Volume (mL)	Diluted to (mL)	Final Conc. (ng/mL)
100	5.0	100	5.0
100	2.0	100	2.0
100	1.0	100	1.0
5.0	10.0	100	0.5
2.0	10.0	100	0.2
1.0	10.0	100	0.1

The standards may be used for a period of one year (in 125-mL LDPE bottles) when stored refrigerated (at 2°C to 6°C).

4. METHOD

4.1. Flow Diagram

The flow diagram of the method is given below, followed by a detailed description of each step.

Method Flow Diagram

Weigh appropriate amount of liver or measure appropriate volume of serum or urine (fortify samples designated as matrix spikes and laboratory control spikes)
↓
Add water to liver for a final volume of 10 mL, add water to serum and urine for a final volume of 20 mL, homogenize
↓
Remove 1 mL and add 5 mL of ACN, shake
↓
Centrifuge
↓
Decant supernatant into 35 mL of water
↓
Load onto conditioned SPE
↓
Elute with 2 mL methanol
↓
LC/MS/MS Analysis

4.2. Sample Processing

For liver samples, place frozen samples in a food processor and homogenize with dry ice. Then place samples in containers and leave open in frozen storage overnight to allow for CO_2 sublimation. Seal and place the samples in frozen storage below −10°C until time of extraction. Alternately, if there is an insufficient amount of sample (~ less than 5 g), then no processing is necessary and the sample can be used as supplied. No sample processing is needed for serum and urine samples. However, frozen serum and urine samples must be allowed to completely thaw to room temperature before use.

4.3. BATCH SET UP

a. A batch of samples should not contain more than 20 field samples.

b. Each batch of samples analyzed must include at least one control (method blank using control matrix) and two matrix controls fortified at known concentrations (typically 10 and 50 ng/g for liver or ng/mL for serum and urine) to verify procedural recovery for the batch.

c. At least one field sample in each batch must also be separately fortified at a known concentration and carried through the procedure to verify recovery. Additional samples in the batch may also be fortified if desired.

d. All samples require duplicate injections.

4.4. SAMPLE EXTRACTION

4.4.1. Liver Extraction

a. Weigh 1 g of liver sample into a 50 mL disposable centrifuge tube and fortify, if appropriate. Note that alternate weights of liver may be measured depending on the sample size available for use.
b. Add water to the sample for a final volume of 10 mL. Cap tightly.
c. Homogenize sample using a tissuemizer for ~1 minute.
d. Transfer 1 mL of the sample using a disposable pipette into 15 mL disposable centrifuge tubes. Add 5 mL of ACN and shake for ~20 minutes on a wrist action shaker.
e. Centrifuge tubes at ~3000 rpm for ~ 5 minutes. Carefully decant supernatant into a 50 mL disposable centrifuge tube and add 35 mL of water.
f. Load the sample onto a conditioned SPE column (for conditioning details, see section 4.4.3.). Discard the eluate. Any analyte residues will be trapped on the SPE column at this point.
g. Elute with 2 mL of methanol. Collect 2 mL of elute into a graduated 15 mL centrifuge tube.
h. Analyze samples using electrospray LC/MS/MS.

4.4.2. Serum and Urine Extraction

a. Measure 1 mL of serum or urine sample into a 50 mL disposable centrifuge tube and fortify, if appropriate. Note that alternate volumes of serum and urine may be measured depending on sample size available for use.

b. Add water to sample for a final volume of 20 mL. Cap tightly and vortex for ~1 minute. Then continue with steps d-h in section 4.4.1.

4.4.3. SPE Column Conditioning

Place the unconditioned SPE columns on the vacuum manifold. Condition the SPE columns by passing ~ 10 mL of methanol through the column followed by ~ 5 mL of water. The washes may be pulled through the SPE column using vacuum at a flow rate of ~1 drop/sec or may be allowed to pass through the column unaided. Discard all washes. Do not allow the column to dry.

4.5. Quantitation

4.5.1. LC/MS/MS System and Operating Conditions

Mass Spec: Micromass Quattro Ultima (Micromass)
Interface: Electrospray (Micromass)
Harvard infusion pump (Harvard Instruments), for tuning
Computer: COMPAQ Professional Workstation AP200
Software: Windows NT, Masslynx 3.3

HPLC: Hewlett Packard (HP) Series 1100
HP Quat Pump
HP Vacuum Degasser
HP Autosampler
HP Column Oven

Note: A 4 x 10 mm hypercarb drop in guard cartridge is attached on-line after the purge valve and before the sample injector port to trap any residue contaminants that may be in the mobile phase and/or HPLC system.

HPLC Column: Genesis C_8 (Jones Chromatography), 2.1 mm x 50 mm, 4µ
Column Temperature: 35° C
Injection Volume: 15 µL
Mobile Phase (A): 2 mM Ammonium Acetate in Type I water
Mobile Phase (B): Methanol

Time	% A	% B	Flow Rate (mL/min)
0.0	90	10	0.3
2.0	90	10	0.3
5.0	10	90	0.3
9.0	10	90	0.3
9.5	0	100	0.3
14.0	0	100	0.3
14.5	90	10	0.3
20.0	90	10	0.3

It may be necessary to adjust the HPLC gradient in order to optimize instrument performance. Columns with different dimensions (e.g. 2.1 x 30) and also columns from different manufacturers (Keystone Betasil C_{18} etc.) could be used, provided equivalent chromatography is obtained.

Ions monitored:

Analyte	Mode	Transition Monitored	Approximate Retention Time
PFHS	Negative	399 → 80	~8.2 min.
PFOS	Negative	499 → 99	~8.8 min
PFOA	Negative	413 → 369	~8.6 min

The retention times may vary, on a day to day basis, depending on the batch of mobile phase etc. Drift in retention times (up to ± 4 %) is acceptable within an analytical run, as long as the drift continues through the entire analysis and the standards are included at the beginning and end of the analytical run.

Note: An alternative LC/MS/MS system may be used once demonstrated to be equivalent.

The mass spectrometer is tuned for each analyte by infusing a ~ 1.0 µg/mL standard solution (at 10 µL/min, using an infusion pump) via a "T" into a stream of mobile phase containing 50% methanol and 50% 2mM ammonium acetate in water at 0.2 mL/min flow rate. Each analyte is initially tuned for the parent ion and then tuned for the product ion. Once the instrument is tuned, the optimized parameters are saved as a tune file. This tune file is then used during routine analysis.

4.5.2. Calibration Curve Procedures

a. Inject the same aliquot (between 10 to 50 µL) of each calibration standard (ranging from the lowest level standard to the highest level prepared), into the LC/MS/MS.

b. Use weighted linear standard curves for quantitation. Linear standard curves are generated for each analyte by linear regression using 1/x weighting of peak area versus calibration standard concentration using Masslynx (or equivalent) software system. Any calibration standard found to be a statistical outlier by using an appropriate outlier test, may be excluded from the calculation of the calibration curve. However, the total number of calibration standards that may be excluded must not exceed 20% of the total number of standards injected.

c. The correlation coefficient (R) for calibration curves generated must be ≥0.9925 (R^2 ≥0.985). If calibration results fall outside these limits, then appropriate steps must be taken to adjust instrument operation, and the standards or the relevant set of samples should be reanalyzed.

Typical calibration curves for PFHS, PFOS and PFOA can be found in Figures 1-3.

4.5.3 Sample Analysis

a. Inject the same aliquot (between 10 to 50 µL) of each standard, sample, recovery, control, etc. into the LC/MS/MS system.

b. Standards corresponding to at least five or more concentration levels (starting with the LOQ level or below) must be included in an analytical set.

c. An entire set of calibration standards should be injected at the beginning of a set followed by calibration standards interspersed approximately every 5-10 samples (to account for a second set of extracted standards). As an alternative, an entire set of calibration standards may be included at the beginning and at the end of a sample set. In either case, calibration standards must be the first and last injection in a sample set.

d. The concentration of each sample/fortification/control is determined from the standard curve, based on the peak area of each analyte. The standard responses should bracket responses of the residue found in each sample set. Results may be quantitated up to 10% outside the curve by extrapolation. If necessary, dilute the samples to give a response within the standard curve range.

e. Fortification recoveries falling within 70 to 130% are considered acceptable.

f. Samples must be stored refrigerated between 2°C to 6°C until analysis.

g. Samples in which either no peaks are detected or peaks less than the lowest concentration of the calibration standards are detected at the corresponding analyte retention time will be reported as ND (not detected). Samples in which peaks are detected at the corresponding analyte retention time that are less than the LOQ and greater than or equal to the lowest concentration of the calibration standards will be reported as NQ (not quantifiable).

The analysis performed during the method development included fortifications at 10 and 50 ng/g of PFHS in rat liver, 10 and 50 ng/mL of PFHS in serum, 10 and 50 ng/g of PFOS and PFOA in rat liver and 10 and 50 ng/mL of PFOS and PFOA in serum and urine. Typical chromatograms can be found in Figures 4-39.

4.6. Acceptance Criteria

The following criteria must be met to ensure the presence of PFHS, PFOS and PFOA:

1. The chromatogram must show a peak of a daughter ion at 80 amu from a parent of 399 amu for PFHS, a daughter ion at 99 amu from a parent of 499 amu for PFOS, and a daughter ion at 369 amu from a parent of 413 amu for PFOA.

2. Method blanks must not contain analyte at levels greater than the LOQ. If a blank contains the analyte at levels greater than 10 ng/mL, then a new blank sample must be obtained and the entire set must be re-extracted.

3. Recoveries of control spikes and matrix spikes (if any) must be between 70-130% of their known values. If a control spike falls outside the acceptable limits, the entire set of samples should be re-extracted. Any matrix spike outside 70-130% should be evaluated by the analyst to determine if re-extraction is warranted.

4. Any calibration standard found to be a statistical outlier by using the Huge Error Test, may be excluded from the calculation of the calibration curve. However, the total number of calibration standards that could be excluded must not exceed 20% of the total number of standards injected.

5. The correlation coefficient (R) for calibration curves generated must be ≥0.9925 (R^2 ≥0.985). If calibration results fall outside these limits, then appropriate steps must be taken to adjust instrument operation, and the standards or the relevant set of samples should be reanalyzed.

6. Retention times between standards and samples must not drift more than ± 4 % within an analytical run. If retention time drift exceeds this limit within an analytical run then the set must be reanalyzed.

4.7. Performance Criteria

The following two criteria must be performed once as a system suitability test, before the commencement of analysis, when using an instrumentation set-up that has not been used for this method.

First Criterion:
Run a standard solution on LC/MS/MS corresponding to the estimated LOQ (10 ng/mL) in matrix and obtain a signal to noise ratio for the analyte transition of at least 9:1, compared to a reagent blank. If this criterion cannot be met, optimize and change instrument operating parameters (or increase the injection volume, if appropriate).

Second Criterion:
Run a set of standards of five or more concentration levels, from at or below the LOQ, up to the highest concentration level to be included in the analysis. Generate a calibration curve for the analyte and obtain a linear regression with a coefficient of determination (R^2) of at least 0.985 for the analyte. Once this criterion is met, samples may be analyzed with standards interspersed.

4.8. Time Required for Analysis

One person can take a set of 20 samples through the sample preparation procedure in approximately 4 hours. The LC/MS/MS analysis of the set (containing 20 field samples, 1 matrix blank, 2 laboratory control spikes, 1 matrix spike and 12 standard injections) will take approximately 14 hours.

5. CALCULATIONS

a. Use Equation 1 to calculate the amount of analyte found (in ng/mL, based on peak area) using the standard curve (1/x weighted linear regression parameters) generated by the Masslynx software program.

Equation 1:

$$\text{Analyte found (ng/mL)} = \frac{(\text{peak area} - \text{intercept})}{\text{slope}} \times \text{DF} \times \text{aliquot factor}$$

DF = factor by which the final volume was diluted, if necessary.
Aliquot factor= 10 for liver, 20 for serum and urine

b. For samples fortified with known amounts of analyte prior to extraction, use Equation 2 to calculate the percent recovery.

Equation 2:

Recovery (%) =

$$\frac{[\text{total analyte found (ng/mL)} - \text{analyte found in control (ng/mL)}]}{\text{analyte added (ng/mL)}} \times 100$$

Note: Subtract analyte found in control (ng/mL) from analyte found (ng/mL), if ng/mL in control is greater than LOQ.

c. Use Equation 3 to calculate the amount of analyte found (in ppb)

Equation 3:

$$\text{Analyte found (ng/g or ng/mL)} = \frac{\text{(analyte found (ng/mL) x FV (mL)}}{\text{sample weight (g) or sample volume (mL)}}$$

FV = final volume

For reporting purposes, samples in which either no peaks are detected or peaks less than the lowest concentration of the calibration standards are detected at the corresponding analyte retention time will be reported as ND (not detected). Samples in which peaks are detected at the corresponding analyte retention time that are less than the LOQ and greater than or equal to the lowest concentration of the calibration standards will be reported as NQ (not quantifiable).

6. SAFETY

The analyst should read the material safety data sheets for all standards and reagents before performing this method. Use universal precautions when handling standards and reagents, including working in fume hoods and wearing laboratory coats, safety glasses, and gloves.

Table 1. Recovery Summary of PFHS in Rat Liver and Serum

Recovery Summary of PFHS in Rat Liver

Sample ID	Analyte Added (ng/g)	Percent Recovery (%)
0201684 Spk A	10	108
0201684 Spk B	10	110
0201684 Spk C	10	126
	Average:	**115**
	Standard Deviation:	**9.9**

Sample ID	Analyte Added (ng/g)	Percent Recovery (%)
0201684 Spk D	50	101
0201684 Spk E	50	98
0201684 Spk F	50	94
	Average:	**98**
	Standard Deviation:	**3.5**

Recovery Summary of PFHS in Rat Serum

Sample ID	Analyte Added (ng/mL)	Percent Recovery (%)
0201682 Spk A	10	112
0201682 Spk B	10	103
0201682 Spk C	10	110
	Average:	**108**
	Standard Deviation:	**4.7**

Sample ID	Analyte Added (ng/mL)	Percent Recovery (%)
0201682 Spk D	50	107
0201682 Spk E	50	104
0201682 Spk F	50	122
	Average:	**111**
	Standard Deviation:	**9.6**

Table 2. Recovery Summary of PFOS in Rat Liver, Serum and Urine

Recovery Summary of PFOS in Rat Liver

Sample ID	Analyte Added (ng/g)	Percent Recovery (%)
0201684 Spk A	10	88
0201684 Spk B	10	95
0201684 Spk C	10	105
	Average:	96
	Standard Deviation:	8.5

Sample ID	Analyte Added (ng/g)	Percent Recovery (%)
0201684 Spk D	50	90
0201684 Spk E	50	88
0201684 Spk F	50	87
	Average:	88
	Standard Deviation:	1.5

Recovery Summary of PFOS in Rat Serum

Sample ID	Analyte Added (ng/mL)	Percent Recovery (%)
0201682 Spk A	10	80
0201682 Spk B	10	85
0201682 Spk C	10	99
	Average:	88
	Standard Deviation:	9.8

Sample ID	Analyte Added (ng/mL)	Percent Recovery (%)
0201682 Spk D	50	118
0201682 Spk E	50	122
0201682 Spk F	50	121
	Average:	120
	Standard Deviation:	2.1

Recovery Summary of PFOS in Rat Urine

Sample ID	Analyte Added (ng/mL)	Percent Recovery (%)
0201682 Spk A	10	98
0201682 Spk B	10	89
0201682 Spk C	10	91
	Average:	93
	Standard Deviation:	4.7

Sample ID	Analyte Added (ng/mL)	Percent Recovery (%)
0201682 Spk D	50	80
0201682 Spk E	50	78
0201682 Spk F	50	78
	Average:	79
	Standard Deviation:	1.2

Table 3. Recovery Summary of PFOA in Rat Liver, Serum and Urine

Recovery Summary of PFOA in Rat Liver

Sample ID	Analyte Added (ng/g)	Percent Recovery (%)
0201684 Spk A	10	95
0201684 Spk B	10	101
0201684 Spk C	10	98
	Average:	98
	Standard Deviation:	3.1

Sample ID	Analyte Added (ng/g)	Percent Recovery (%)
0201684 Spk D	50	97
0201684 Spk E	50	92
0201684 Spk F	50	94
	Average:	94
	Standard Deviation:	2.5

Recovery Summary of PFOA in Rat Serum

Sample ID	Analyte Added (ng/mL)	Percent Recovery (%)
0201682 Spk A	10	118
0201682 Spk B	10	117
0201682 Spk C	10	115
	Average:	117
	Standard Deviation:	1.5

Sample ID	Analyte Added (ng/mL)	Percent Recovery (%)
0201682 Spk D	50	107
0201682 Spk E	50	112
0201682 Spk F	50	115
	Average:	111
	Standard Deviation:	4.0

Recovery Summary of PFOA in Rat Urine

Sample ID	Analyte Added (ng/mL)	Percent Recovery (%)
0201682 Spk A	10	86
0201682 Spk B	10	91
0201682 Spk C	10	89
	Average:	89
	Standard Deviation:	2.5

Sample ID	Analyte Added (ng/mL)	Percent Recovery (%)
0201682 Spk D	50	89
0201682 Spk E	50	88
0201682 Spk F	50	85
	Average:	87
	Standard Deviation:	2.1

Figure 1. Calibration Curve for PFHS

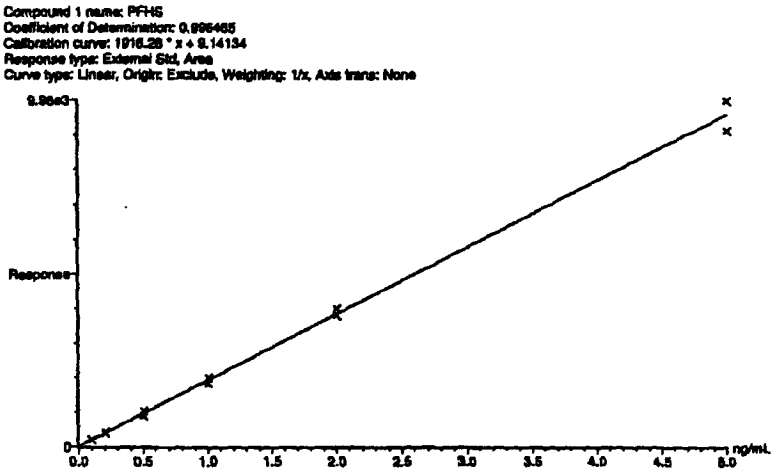


Figure 2. Calibration Curve for PFOS

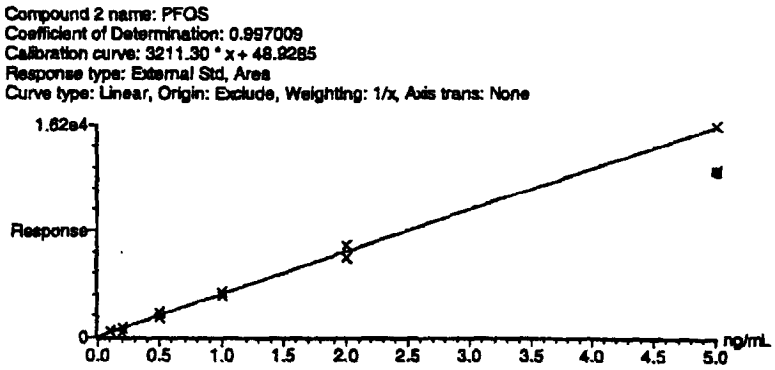


Figure 3. Calibration Curve for PFOA

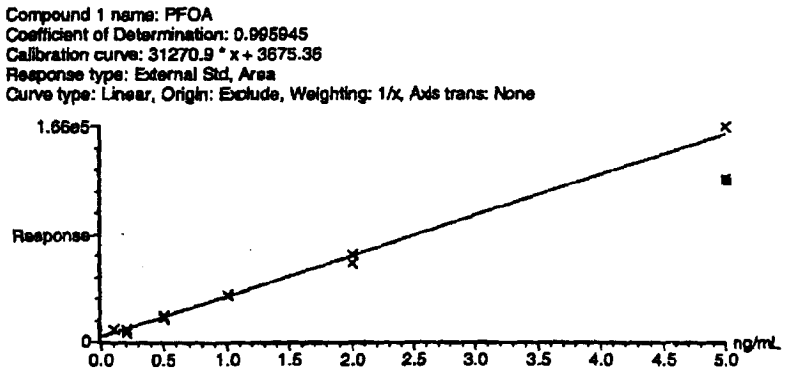


Figure 4. Representative Chromatogram of a 0.1 ng/mL Standard Containing PFHS

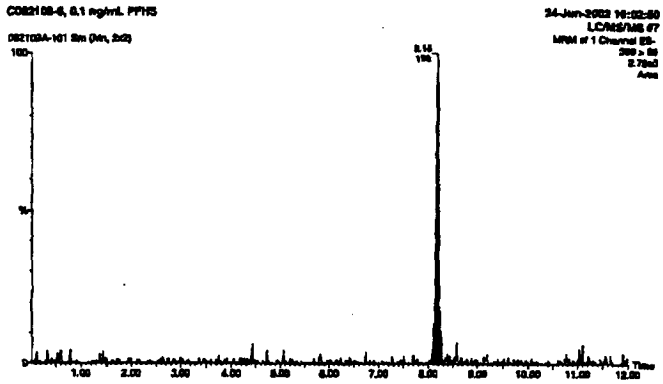


Figure 5. Representative Chromatogram of a 0.1 ng/mL Standard Containing PFOS

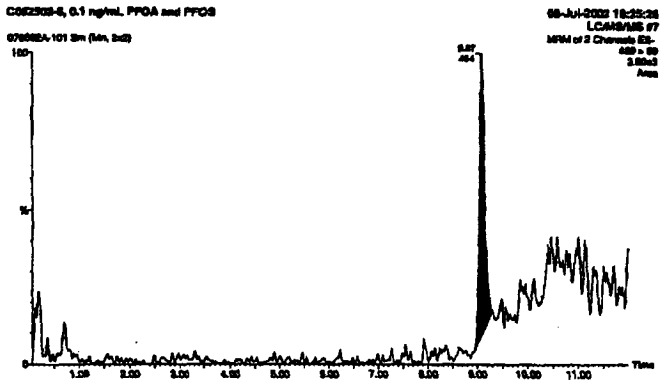


Figure 6. Representative Chromatogram of a 0.1 ng/mL Standard Containing PFOA

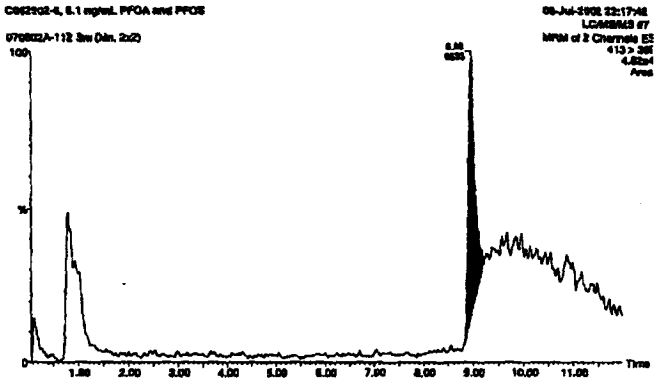


Figure 7. Representative Chromatogram of a 0.5 ng/mL Standard Containing PFHS

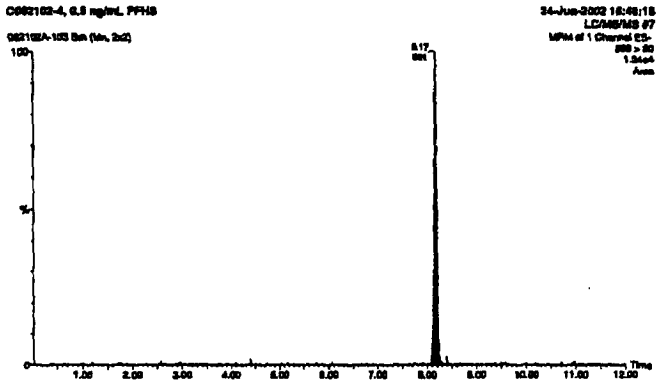


Figure 8. Representative Chromatogram of a 0.5 ng/mL Standard Containing PFOS

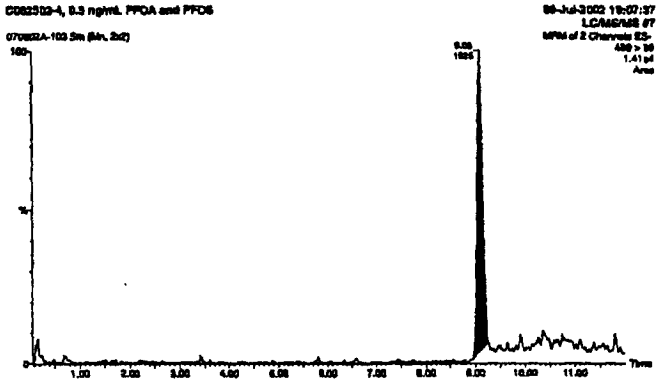


Figure 9. Representative Chromatogram of a 0.5 ng/mL Standard Containing PFOA

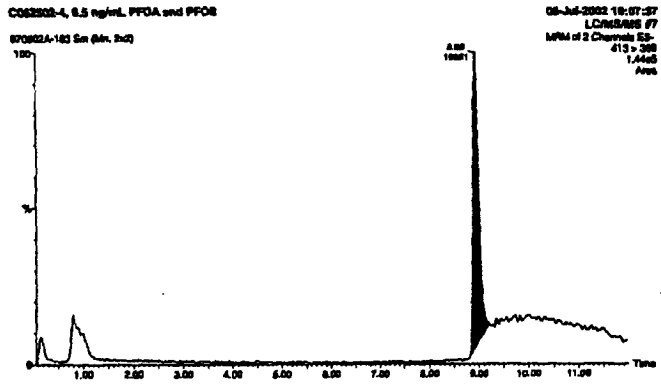


Figure 10. Representative Chromatogram of a 5.0 ng/mL Standard Containing PFHS

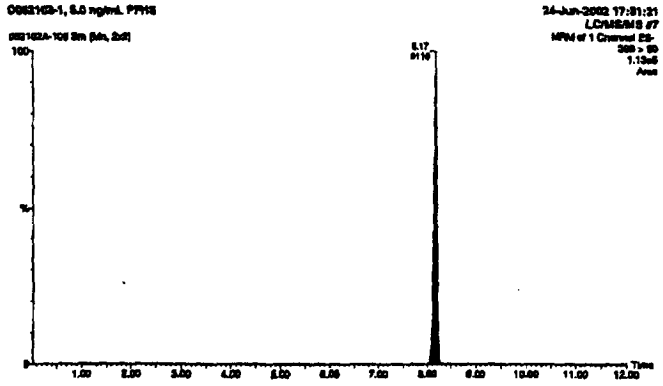


Figure 11. Representative Chromatogram of a 5.0 ng/mL Standard Containing PFOS

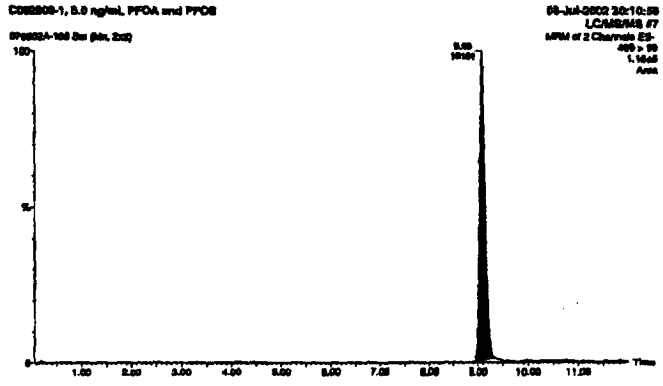


Figure 12. Representative Chromatogram of a 5.0 ng/mL Standard Containing PFOA

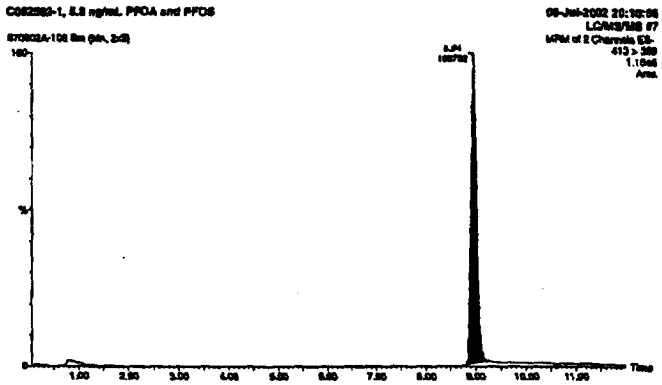


Figure 13. Representative Chromatogram of a Reagent Blank Sample Analyzed for PFHS

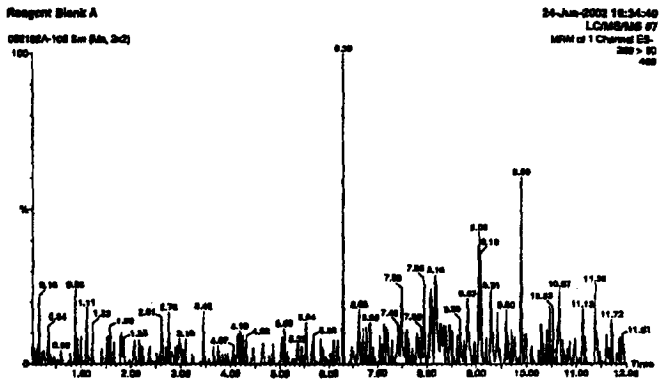


Figure 14. Representative Chromatogram of a Reagent Blank Sample Analyzed for PFOS

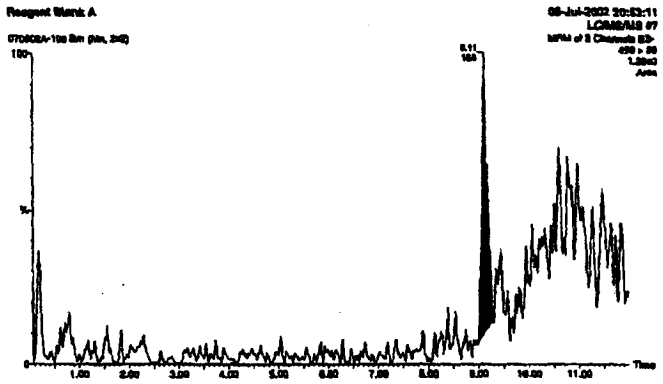


Figure 15. Representative Chromatogram of a Reagent Blank Sample Analyzed for PFOA

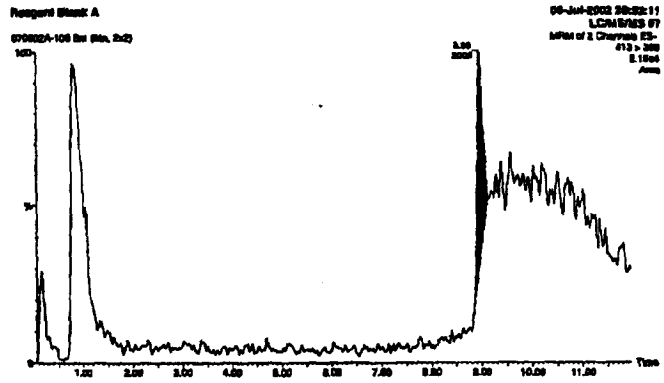


Figure 16. Representative Chromatogram of a Control Liver Sample Analyzed for PFHS

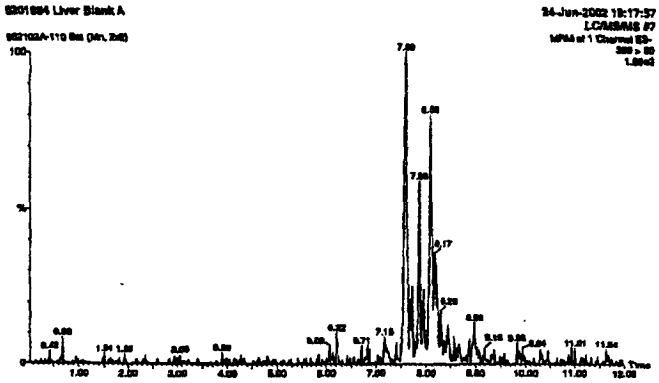


Figure 17. Representative Chromatogram of a Control Liver Sample Analyzed for PFOS

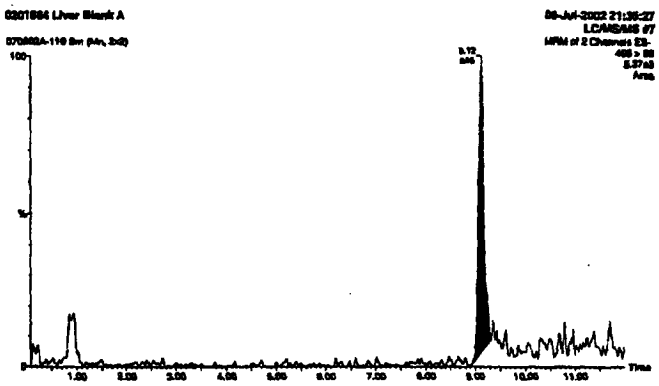


Figure 18. Representative Chromatogram of a Control Liver Sample Analyzed for PFOA

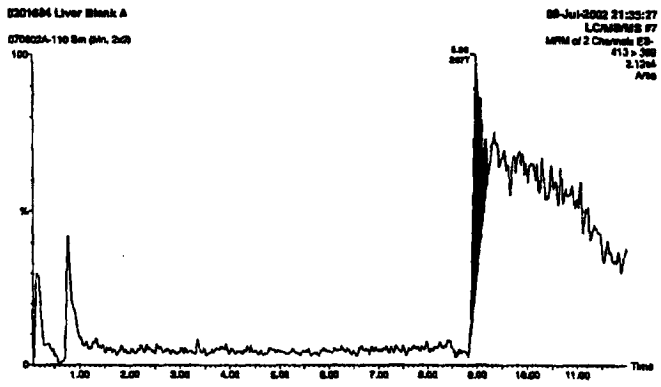


Figure 19. Representative Chromatogram of a Control Serum Sample Analyzed for PFHS

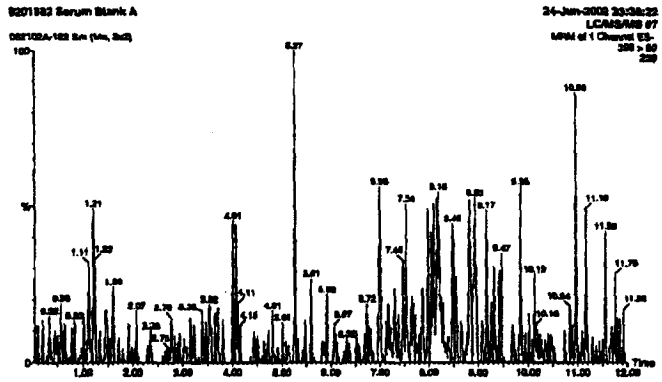


Figure 20. Representative Chromatogram of a Control Serum Sample Analyzed for PFOS

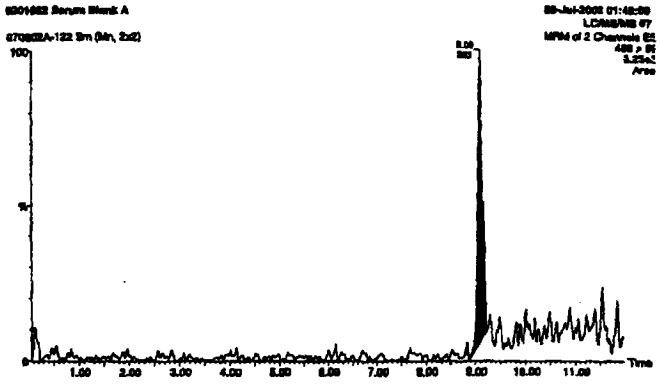


Figure 21. Representative Chromatogram of a Control Serum Sample Analyzed for PFOA

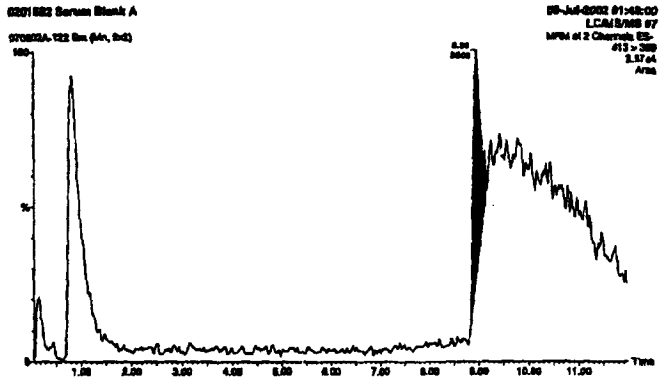


Figure 22. Representative Chromatogram of a Control Urine Sample Analyzed for PFOS

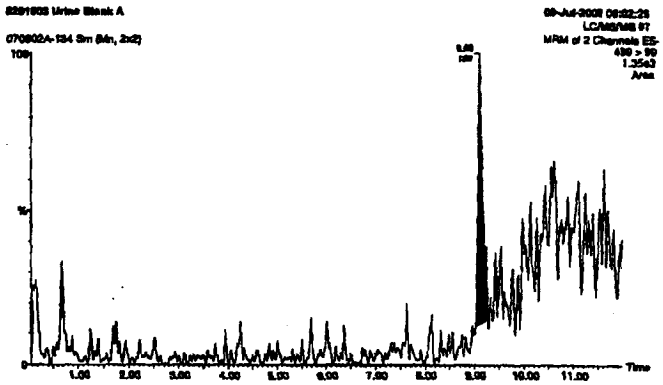


Figure 23. Representative Chromatogram of a Control Urine Sample Analyzed for PFOA

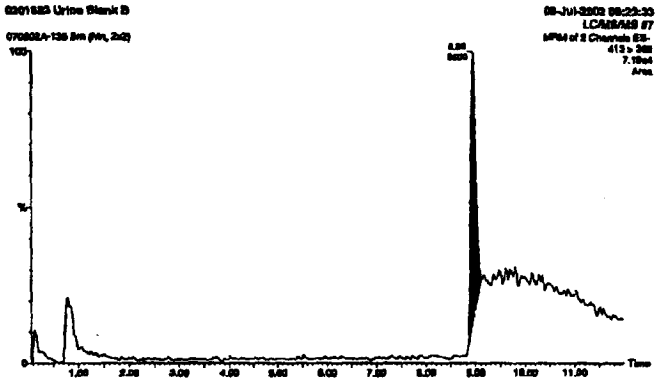


Figure 24. Representative Chromatogram of a Control Liver Sample Fortified at 10 ng/g with PFHS

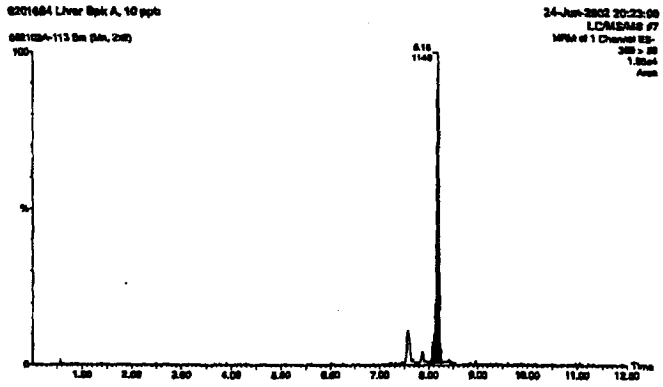


Figure 25. Representative Chromatogram of a Control Liver Sample Fortified at 10 ng/g with PFOS

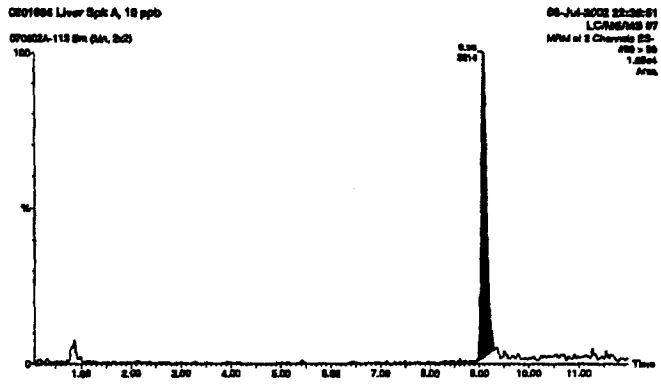


Figure 26. Representative Chromatogram of a Control Liver Sample Fortified at 10 ng/g with PFOA

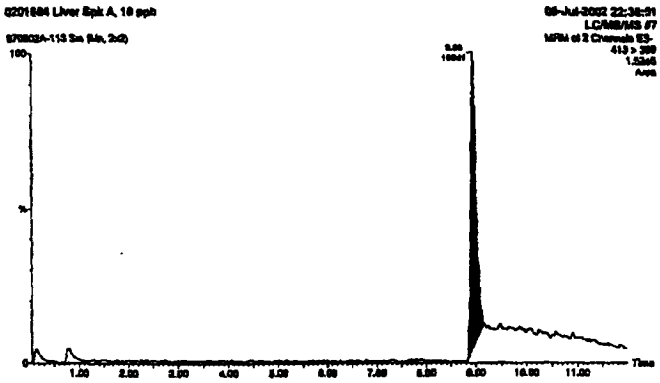


Figure 27. Representative Chromatogram of a Control Liver Sample Fortified at 50 ng/g with PFHS

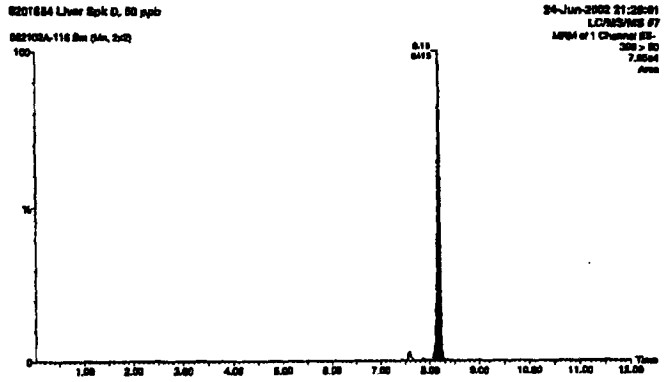


Figure 28. Representative Chromatogram of a Control Liver Sample Fortified at 50 ng/g with PFOS

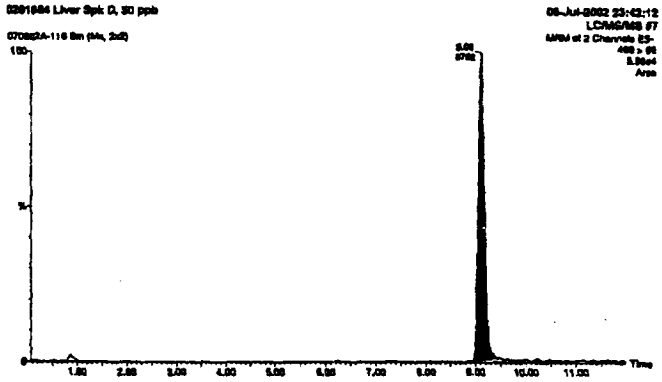


Figure 29. Representative Chromatogram of a Control Liver Sample Fortified at 50 ng/g with PFOA

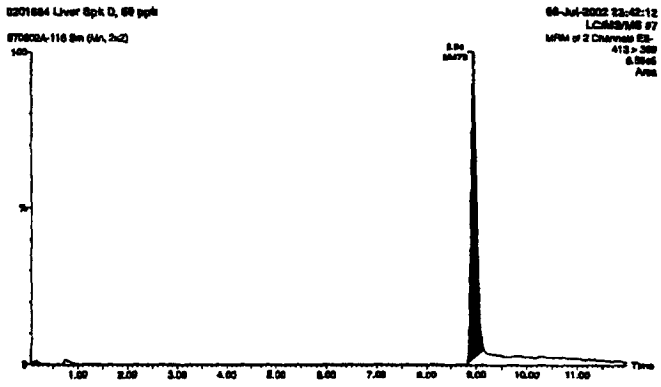


Figure 30. Representative Chromatogram of a Control Serum Sample Fortified at 10 ng/mL with PFHS

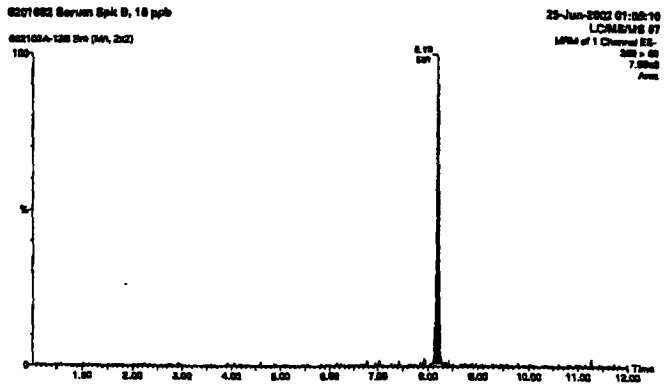


Figure 31. Representative Chromatogram of a Control Serum Sample Fortified at 10 ng/mL with PFOS

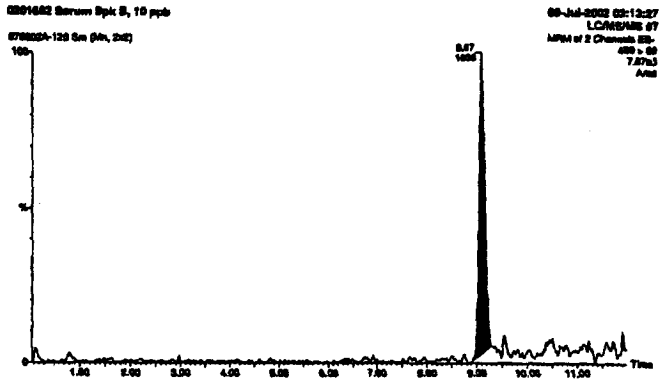


Figure 32. Representative Chromatogram of a Control Serum Sample Fortified at 10 ng/mL with PFOA

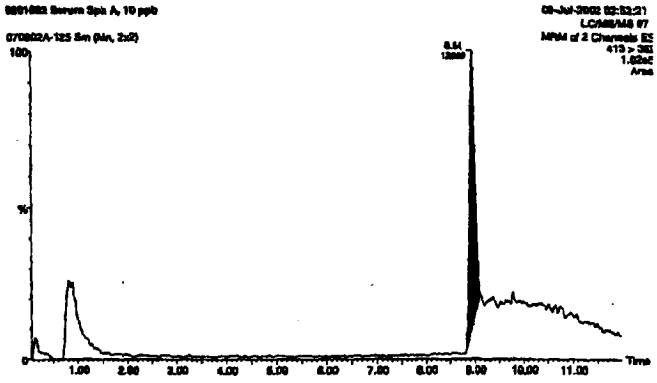


Figure 33. Representative Chromatogram of a Control Serum Sample Fortified at 50 ng/mL with PFHS

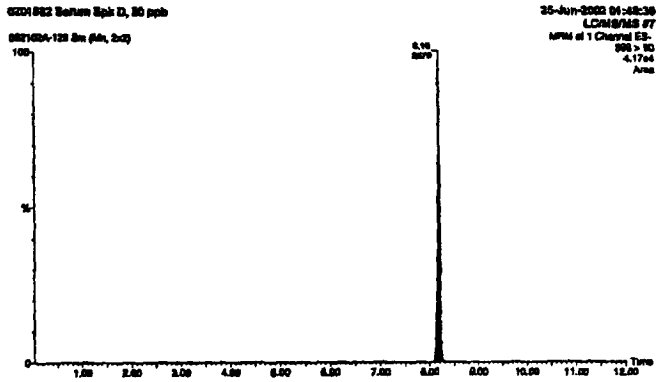


Figure 34. Representative Chromatogram of a Control Serum Sample Fortified at 50 ng/mL with PFOS

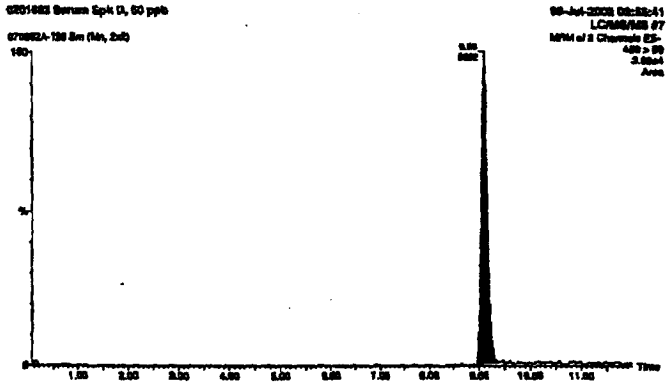


Figure 35. Representative Chromatogram of a Control Serum Sample Fortified at 50 ng/mL with PFOA

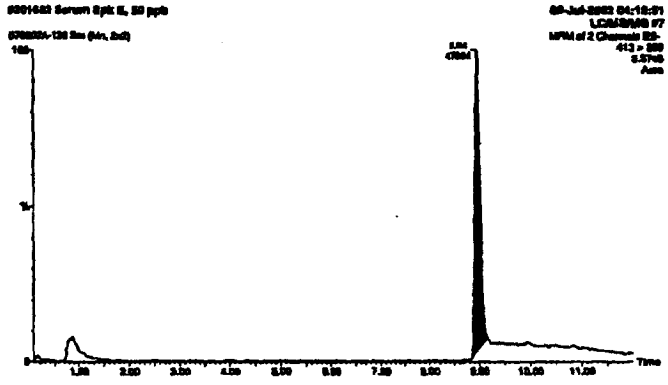


Figure 36. Representative Chromatogram of a Control Urine Sample Fortified at 10 ng/mL with PFOS

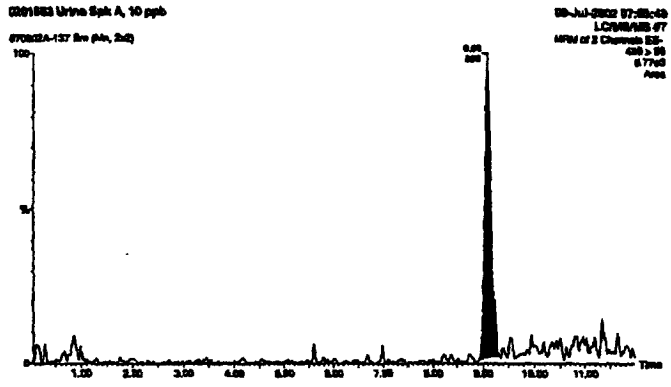


Figure 37. Representative Chromatogram of a Control Urine Sample Fortified at 10 ng/mL with PFOA

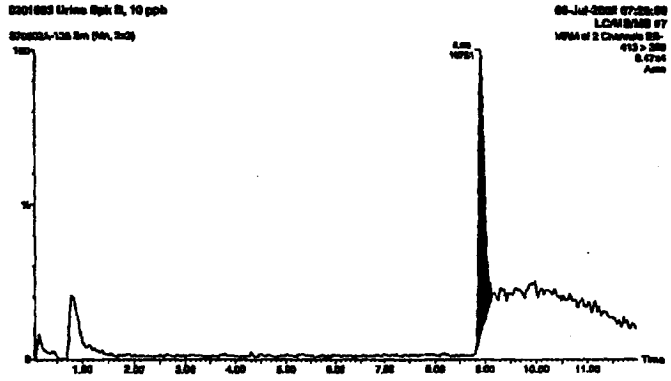


Figure 38. Representative Chromatogram of a Control Urine Sample Fortified at 50 ng/mL with PFOS

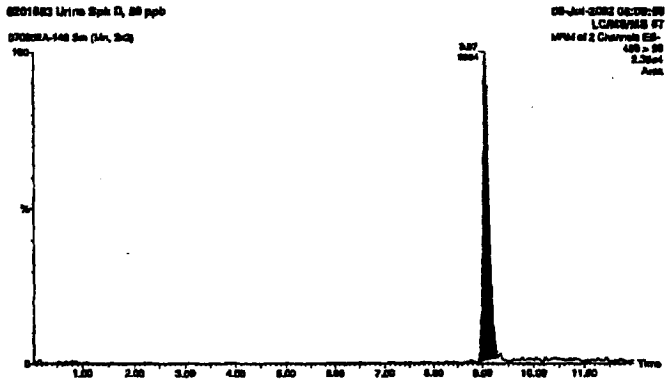
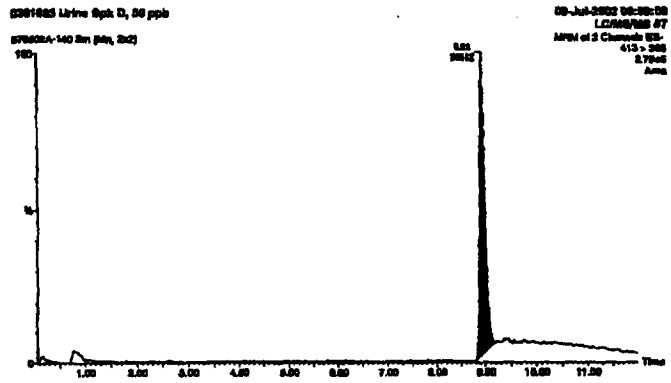


Figure 39. Representative Chromatogram of a Control Urine Sample Fortified at 50 ng/mL with PFOA



APPENDIX H

TEMPERATURE AND RELATIVE HUMIDITY REPORTS

ARGUS

Temperature and Relative Humidity Report
Location: Room 05

Protocol Number: 418-028

Range of Dates: 26-Mar-2002 14:20 to 10-Jun-2002 08:59

	Temperature 64°F to 79°F		Relative Humidity 30% to 70%	
Target Range:				
Species: Rat				
Total Number of Days:	77		77	
Total Number of Hours:	1818.25		1818.25	
Total Number of Data Points:	1817		1817	
Mean (± SD):	69.2	(± 0.7)	54.6	(± 4.4)
Maximum:	71.0		64.5	
Median:	69.2		55.3	
Minimum:	66.0		36.4	
Number of Points in Range (%):	1817	(100.0)	1817	(100.0)
Number of Points High (%):	0	(0.0)	0	(0.0)
Number of Points Low (%):	0	(0.0)	0	(0.0)

Report Generated: 10-Jun-2002 at 13:26

COMMENTS: _____

_____

_____

_____

REVIEWED BY: Krista m. Cole **DATE:** 6.10.02

APPENDIX I

POSITIVE CONTROL DATA

Historical Control Data

This Functional Observation Battery Standard Operating Procedure and Studies conducted to document the training and competency of the technical staff and Motor Activity Negative Control Data and Positive Control Data are available at the Testing Facility.

Summary Information for Functional Observation Battery

Study Number – Title	In-Life Start	Test Substance	Dosage Information mg/kg	mL/kg	Number of Dosages
012-006 – Validation of Functional Observational Battery and Motor Activity Measure Using Positive Test Substances	12/89	acrylamide	50	1	7
		physostigmine	0.75	1.5	1
		DDT	75	1	1
012-014 – Neurotoxicity Evaluation of Positive Control Substances in Crl:CD®BR VAF/Plus® Rats	9/91	acrylamide	40	1	9
		IDPN	200	1	3
		carbaryl	75	5	1
		DDT	75	5	1
		triadimefon	200	5	1
012-015 – Neurotoxicity Evaluation of DDT in Crl:CD®BR VAF/Plus® Rats	3/92	DDT	75	1	1
012-017 – Neurotoxicity Evaluation of Positive Control Substances in Crl:CD®BR VAF/Plus® Rats	5/92	acrylamide	40	1	9
		IDPN	200	1	3
		carbaryl	40	5	1
		DDT	75	1	1
		d-amphetamine	4.0	1	1
012-022 – Neurotoxicity Evaluation of Carbaryl in Crl:CD®BR VAF/Plus® Rats	10/92	carbaryl	40, 200	5	1
012-031 - Neurotoxicity Evaluation of Positive Control Substances in Crl:CD®BR VAF/Plus® Rats	7/93	acrylamide	45	1	10
		IDPN	250	1	4
		carbaryl	40	5	1
		DDT	75	1	1
		d-amphetamine	4	1	1

012-056 – Neurotoxicity Evaluation of Positive Control Substances in Crl:CD®BR VAF/Plus® Rats	11/95	acrylamide	45	1	10
		IDPN	250	1	5
		carbaryl	40	1	1
		DDT	75	1	1
		d-amphetamine	4.0	1	1
012-075 – Neurotoxicity Evaluation of Positive Control Substances in Crl:CD®BR VAF/Plus® Rats	3/98	acrylamide	30	1	17
		trimethyltin	8	1	1
		MK-801	0.3	1	1
		carbaryl	100	4	1
		DDT	100	2	1
012-081 – Neurotoxicity Evaluation of Positive Control Substances in Crl:CD®BR VAF/Plus® Rats	11/01	acrylamide	30	1	10
		IDPN	250	1	1
		d-amphetamine	40	1	1
		carbaryl	100	4	1
		DDT	100	2	5

Summary Information for Motor Activity

Study – Title	In-Life Start	Test Substance	Dosage Information mg/kg	mL/kg	Number of Dosages
012-011 – The Assessment of Motor Activity in Neonatal and Adult Rodents using Passive Infrared Sensors	5/91	d-amphetamine	0.75, 1.5, 4	1	1
		chlorpromazine	1, 2, 4	1	1
012-014 – Neurotoxicity Evaluation of Positive Control Substances in Crl:CD®BR VAF/Plus® Rats	9/91	acrylamide	40	1	9
		IDPN	200	1	3
		carbaryl	75	5	1
		DDT	75	5	1
		triadimefon	200	5	1
012-016 – Motor Activity Evaluation in Crl:CD®BR VAF/Plus® Rats Administered Chlorpromazine and d-Amphetamine (Positive Control Study)		d-amphetamine	0.5, 1, 4	1	1
		chlorpromazine	1, 2, 4	1	1
012-058 – Neurotoxicity Evaluation of Positive Control Substances in Crl:CD®BR VAF/Plus® Rats	4/96	acrylamide	45	1	10
		d-amphetamine	0.75	1	1
		trimethyltin	8	1	1
		MK-801	10	1	1

APPENDIX J

HISTOPATHOLOGY REPORT

RESEARCH PATHOLOGY SERVICES, INC.

438 East Butler Avenue, New Britain, PA 18901
Phone: 215-345-7070 • Fax: 215-345-4326

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCEENING TEST
PROTOCOL 418-028
SPONSOR'S STUDY NUMBER T-7706.1
HISTOPATHOLOGY REPORT

SUBMITTED TO:
Raymond G. York, Ph.D., D.A.B.T.
Argus Research
905 Sheehy Drive
Horsham, PA 19044

SUBMITTED BY:

W. Ray Brown July 3, 2003

W. Ray Brown, D.V.M., Ph.D.
Veterinary Pathologist

July 3, 2003

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL 418-028
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HISTOPATHOLOGY REPORT

TABLE OF CONTENTS

REPORT

Page

Method 1

Results 3

Summary 5

Quality Assurance Unit Statement 6

Good Laboratory Practice Compliance Statement 7

TABLE

1. Incidence and Degree of Severity of Histomorphologic Observations 8

APPENDICES

I. Histomorphologic Observations ..... I-1 to I-12

Key to Histomorphologic Observations I-1

Tables

I-1. Histomorphologic Observations - Group I Male Rats I-2
I-2. Histomorphologic Observations - Group II Male Rats I-4
I-3. Histomorphologic Observations - Group III Male Rats I-5
I-4. Histomorphologic Observations - Group IV Male Rats I-6
I-5. Histomorphologic Observations - Group V Male Rats I-7
I-6. Histomorphologic Observations - Group I Female Rats I-9
I-7. Histomorphologic Observations - Group V Female Rats I-11

II. Individual Animal Gross and Histomorphology Data ..... II-1 to II-70

III. Histomorphologic Observations in the Liver - F1 Generation Pups ..... III-1 to III-2

Tables

III-1. Histomorphologic Observations in the Liver – Group I - F1 Generation Pups III-2
III-2. Histomorphologic Observations in the Liver – Group V - F1 Generation Pups III-3

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL 418-028
SPONSOR'S STUDY NUMBER T-7706.1

HISTOPATHOLOGY REPORT

METHOD

Microscopic examination was made of the specified tissues from 50 adult male and 20 adult female Crl:CD®(SD)IGS BR VAF/Plus® rats from five groups in an oral (gavage) combined repeated dose toxicity study of T-7706 (PFHS) with the reproduction/developmental toxicity screening test. In addition, microscopic examination was made of the liver of 10 pups in each of the control and high dosage groups of the F1 Generation. A brief outline of the study design showing the dose group identification, number of rats per sex per group, and dosage levels of the control and test substances are shown below.

DOSAGE GROUP	NUMBER OF RATS PER SEX[a]	DOSAGE (mg/kg/day)	CONCENTRATION[b] (mg/mL)	DOSE VOLUME (mL/kg)
I	15 + 3[c]	0	0	10
II	15 + 3[c]	0.3	0.03	10
III	15 + 3[c]	1	0.1	10
IV	15 + 3[c]	3	0.3	10
V	15 + 3[c]	10	1	10

[a]Ten male and ten female rats of Groups I and V were assigned for histopathologic evaluation.
[b]The test substance was considered to be 100% active for the purpose of dosage calculations.
[c]Three additional rats per sex per dosage group were assigned to toxicokinetic sample collection.

Male rats were given the test substance once daily beginning 14 days before a cohabitation period that consisted of a maximum of 14 days. Dosing continued through the day before sacrifice, after completion of a cohabitation period, after a minimum of 42 days of administration. Female rats were given the test substance once daily beginning 14 days before a cohabitation period that consisted of a maximum of 14 days. Dosing continued through the day before scheduled sacrifice (Day 22 of lactation). Dosages were adjusted daily for body weight changes and were given at approximately the same time each day. The first day of dosing was desig-

nated as Day 1 of the study. Pups were sacrificed and necropsied on Day 22 post-partum.

All rats were necropsied and the specified tissues were collected and placed in 10% neutral buffered formalin for fixation. The testes were fixed in Bouin's solution for 48 to 96 hours and then retained in 10% neutral buffered formalin. The in-life portion of the study, necropsies, and recording of the gross necropsy observations were performed by the staff of Argus Research, Horsham, PA. The tissue processing, microscopic slide preparation and histopathologic evaluation were performed by Research Pathology Services, Inc.

The tissues specified for microscopic evaluation from 10 male and 10 female rats of Groups I and V included: brain, duodenum, jejunum, ileum, cecum, colon, rectum, Peyer's patch, lung, submandibular and mediastinal lymph nodes, sciatic nerve, stomach, kidneys, spleen, thymus, trachea, urinary bladder, testes, epididymides, seminal vesicles, coagulating gland, prostate, spinal cord (cervical, lumbar and thoracic), liver, adrenal glands, heart, thyroid, parathyroid, uterus, bone marrow (sternum), ovaries, uterus, vagina, mammary gland (female rats) and all other tissues with gross changes. In addition, the liver and thyroid of 10 male and 10 female rats in each of the intermediate dosage groups were examined. The liver of 9 or 10 pups F1 generation pups from each of the 10 selected control and high dosage female rats were also examined. Representative samples of these tissues were routinely processed, embedded in paraffin, sectioned, and stained with hematoxylin and eosin for microscopic evaluation. In addition, sections of the testes from the control and high dosage group male rats were stained with periodic acid-Schiff (PAS) reaction and examined.

The study was initiated on June 24, 2002 and completed on July 3, 2003. Upon completion of the project, all raw data (remaining wet tissue, paraffin blocks, microscopic slides and histology records) will be returned to Argus Research for archiving.

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL 418-028
SPONSOR'S STUDY NUMBER T-7706.1

HISTOPATHOLOGY REPORT

RESULTS

The type, incidence and degree of severity of the histomorphologic changes in the specified tissues for the male and female rats are presented in Table 1. The microscopic observations in each rat are summarized in tabular form in Appendix I (Tables I-1 to I-7). A key to the histomorphologic observations precedes Table I-1. The gross necropsy observations, detailed descriptions of the microscopic observations, and a correlation of the microscopic findings with the gross changes in these rats, when applicable, are contained in Appendix II. The histomorphologic observations in the liver of the F1 Generation pups of the control and high dosage groups are summarized in tabular form in Appendix III (Tables III-1 and III-2). A key to the histomorphologic observations is included on Tables III-1 and III-2.

No treatment-related microscopic changes were observed in any of the male rats given 0.3 or 1 mg/kg/day of the test substance or in female rats given 10 mg/kg/day of T-7706.

Treatment-related microscopic changes were observed in the liver and thyroid gland of male rats of the 3 and 10 mg/kg/day dosage groups.

The treatment-related microscopic change in the liver consisted of minimal to moderate enlargement (hypertrophy) of centrilobular hepatocytes (Table 1). The affected hepatocytes were enlarged with an increased amount of dense eosinophilic granular cytoplasm.

The treatment-related effect in the thyroid gland consisted of an increased incidence of male rats of the 3 and 10 mg/kg/day dosage groups with hypertrophy (enlargement) of follicular cells and hyperplasia (increased follicular cells and small follicles) in male rats (Table 1). Although the incidence in Group IV was minimally increased over the controls, the hypertrophy and hyperplasia in this group of rats could have been associated with the liver-cell changes.

These microscopic changes in the liver and thyroid are consistent with the known effects of compounds that cause microsomal enzyme induction where the hepatocellular hypertrophy results in a compensatory hypertrophy and hyperplasia of

the thyroid due to increased plasma turnover of thyroxine and an associated stimulation of thyroid-stimulating hormone in rats.[1]

There were no compound-related microscopic changes observed in the liver of the F1 generation pups from the dams given 10 mg/kg/day of the test substance.

There were a few other microscopic changes observed in the various organs and tissues which were considered to have occurred spontaneously and to be incidental and unrelated to compound administration. The type, incidence and severity of these changes were not influenced by compound administration. These changes also are listed in the attached histomorphology tables.

[1] Sanders, J.E., Eigenberg, D.A., Bracht, L..J., Wang, W.R., and van Zwieten, M.J., Thyroid and Liver Trophic Changes in Rats Secondary to Liver Microsomal Enzyme Induction Caused by an Experimental Leukotriene Antagonist (L-649,923), Toxicology and Pharmacology 95, 378-387 (1988)

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL 418-028
SPONSOR'S STUDY NUMBER T-7706.1

HISTOPATHOLOGY REPORT

SUMMARY

Microscopic examination was made of the specified tissues from five groups of male and female Crl:CD®(SD)IGS BR VAF/Plus® rats used in an oral (gavage) combined repeated dose toxicity study of T-7706 with the reproduction/developmental toxicity screening test. The five groups of rats had been given the vehicle (aqueous 0.5% carboxymethylcellulose), or 0.3, 1, 3 or 10 mg/kg/day of T-7706, orally by gavage, once daily for the protocol-specified number of days. In addition, the liver was examined microscopically from 9 or 10 pups of the F1 generation from 10 dams each of the control and high dosage groups.

No treatment-related microscopic changes were observed in female rats given 10 mg/kg/day of T-7706 or in male rats given 0.3 or 1 mg/kg/day of T-7706.

Treatment-related microscopic changes were observed in the liver and thyroid of male rats of the 3 and 10 mg/kg/day dosage groups.

The treatment-related change in the liver consisted of minimal to moderate hypertrophy of centrilobular hepatocytes and the effect in the thyroid was an increased incidence of male rats with a compensatory hypertrophy and hyperplasia of the follicular epithelium in these groups of male rats.

No treatment-related microscopic changes were observed in the liver of the F1 generation pups from dams given 10 mg/kg/day of T-7706.

All other microscopic changes were considered to be spontaneous in origin and not treatment-related. The type, incidence or severity of these changes were not considered to be influenced by administration of the test substance.

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL 418-028
SPONSOR'S STUDY NUMBER T-7706.1

HISTOPATHOLOGY REPORT

QUALITY ASSURANCE UNIT STATEMENT

All aspects of the tissue processing, microscopic slide preparation, histopathologic evaluation and report preparation for the study listed above have been performed according to the Standard Operating Procedures of Research Pathology Services, Inc. and were audited in accordance with the procedures established by the Quality Assurance Unit of Research Pathology Services, Inc. in compliance with the Good Laboratory Practice regulations specified in the protocol.

Organisation for Economic Cooperation and Development (1996). *OECD Guideline for Testing of Chemicals.* Section 4, No. 422: Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test, adopted 22 March 1996.

Organisation for Economic Cooperation and Development (1998). The Revised OECD Principles of Good Laboratory Practices [C(97)186/Final].

US Food and Drug Administration. Good Laboratory Practice Regulations: Final Rule. 21 CFR Part 58.

Japanese Ministry of Health and Welfare (1997). *Good Laboratory Practice Standard for Safety Studies on Drugs*, MHW Ordinance Number 21, March 26, 1997.

Quality assurance unit study-based inspections were performed as shown below. There were no deviations from the protocol, standard operating procedures and/or appropriate good laboratory practice regulations noted during the conduct of the study. The summary report of QA inspections is included in the final report submitted to the study director on July 3, 2003.

Dates of Inspection	Study Phase	Dates Reported to Management	Date Reported to Study Director
12/16/02	Master Schedule	12/31/02	02/28/03
12/16/02	Pre-initiation	12/31/02	02/28/03
01/07/03	Trimming	01/30/03	02/28/03
01/09/03	Embedding	01/31/03	02/28/03
01/11/03	Microtomy	01/31/03	02/28/03
01/13/03	Staining	01/31/03	02/28/03
01/13/03	Organization & Review	01/27/03	02/28/03
01/31/03	Histopathology	01/31/03	02/28/03
01/31/03	Data Entry	02/27/03	02/28/03
02/21/03	Data Verification	02/27/03	02/28/03
02/24/03	Data Processing	02/27/03	02/28/03
02/26/03	Report Preparation	02/27/03	02/28/03
02/27/03	Pre-submission Audit	02/27/03	02/28/03
02/28/03	Draft report	02/28/03	02/28/03
07/03/03	Final report	07/03/03	07/03/03

Karen W. Harkins, BS 07-03-03

Karen W. Harkins, BS — Date
Quality Assurance Unit

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL 418-028
SPONSOR'S STUDY NUMBER T-7706.1

HISTOPATHOLOGY REPORT

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

All aspects of the above-referenced study performed by Research Pathology Services, Inc. were conducted according to:

Organisation for Economic Cooperation and Development (1996). *OECD Guideline for Testing of Chemicals.* Section 4, No. 422: Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test, adopted 22 March 1996.

Organisation for Economic Cooperation and Development (1998). The Revised OECD Principles of Good Laboratory Practices [C(97)186/Final].

US Food and Drug Administration. Good Laboratory Practice Regulations: Final Rule. 21 CFR Part 58.

Japanese Ministry of Health and Welfare (1997). *Good Laboratory Practice Standard for Safety Studies on Drugs*, MHW Ordinance Number 21, March 26, 1997.

No deviations were noted that had any significant impact on the validity of the study.

W. Ray Brown 07-03-03

W. Ray Brown, DVM, PhD, DACVP — Date
Veterinary Pathologist

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE 1

Incidence and Degree of Severity of Histomorphologic Observations

Dose Group:	I	II	III	IV	V	I	V
Sex:	M	M	M	M	M	F	F
Number of Animals/Group:	10	10	10	10	10	10	10
ADRENAL GLANDS:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	7	0	0	0	9	8	7
-degeneration, cystic, cortex, multifocal	[0]	[0]	[0]	[0]	[0]	[0]	[1]
mild	0	0	0	0	0	0	1
-hypertrophy/vacuolation, cortex, multifocal	[0]	[0]	[0]	[0]	[0]	[0]	[1]
mild	0	0	0	0	0	0	1
-necrosis, cortex, focal	[0]	[0]	[0]	[0]	[0]	[0]	[1]
mild	0	0	0	0	0	0	1
-vacuolation, cortex, diffuse	[3]	[0]	[0]	[0]	[1]	[0]	[0]
minimal	2	0	0	0	0	0	0
mild	1	0	0	0	1	0	0
-vacuolation, zona glomerulosa	[0]	[0]	[0]	[0]	[0]	[2]	[0]
mild	0	0	0	0	0	2	0
BONE MARROW (STERNUM):							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	10	0	0	0	10	10	10
BRAIN:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	10	0	0	0	10	10	10
CECUM:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	8	0	0	0	9	8	10
-inflammation, mucosa, chronic	[2]	[0]	[0]	[0]	[1]	[2]	[0]
mild	0	0	0	0	1	1	0
moderate	2	0	0	0	0	1	0
COAGULATING GLAND:							
NO. EXAMINED	10	0	0	0	10		
NO. NORMAL	10	0	0	0	10		
COLON:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	9	0	0	0	10	10	10
-inflammation, mucosa, chronic	[1]	[0]	[0]	[0]	[0]	[0]	[0]
mild	1	0	0	0	0	0	0
DUODENUM:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	10	0	0	0	10	10	10
EPIDIDYMIDES:							
NO. EXAMINED	10	0	0	1	10		
NO. NORMAL	6	0	0	0	9		

[ ] = Total incidence of specified lesion, all grades.

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE 1 (Continued)

Incidence and Degree of Severity of Histomorphologic Observations

Dose Group:	I	II	III	IV	V	I	V
Sex:	M	M	M	M	M	F	F
Number of Animals/Group:	10	10	10	10	10	10	10
EPIDIDYMIDES (Continued):							
-exfoliated spermatogenic cells	[0]	[0]	[0]	[1]	[0]		
moderate	0	0	0	1	0		
-hypospermia	[0]	[0]	[0]	[1]	[0]		
marked	0	0	0	1	0		
-infiltration, mononuclear-cell, focal	[4]	[0]	[0]	[0]	[1]		
minimal	4	0	0	0	1		
HEART:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	8	0	0	0	9	10	10
-inflammation, chronic, focal	[2]	[0]	[0]	[0]	[1]	[0]	[0]
minimal	1	0	0	0	1	0	0
mild	1	0	0	0	0	0	0
ILEUM:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	10	0	0	0	10	10	10
JEJUNUM:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	10	0	0	0	9	10	10
-diverticulum	0	0	0	0	1	0	0
KIDNEYS:							
NO. EXAMINED	10	3	0	0	10	10	10
NO. NORMAL	7	1	0	0	7	9	8
-basophilia/degeneration, cortical tubules,							
focal/multifocal	[0]	[0]	[0]	[0]	[1]	[0]	[0]
minimal	0	0	0	0	1	0	0
-cyst(s), medulla	1	0	0	0	2	0	0
-dilatation, pelvis	[0]	[2]	[0]	[0]	[0]	[0]	[0]
minimal	0	1	0	0	0	0	0
mild	0	1	0	0	0	0	0
-infiltration, mononuclear-cell, focal/multifocal	[2]	[0]	[0]	[0]	[2]	[0]	[0]
minimal	2	0	0	0	2	0	0
-mineralization, multifocal	[0]	[0]	[0]	[0]	[0]	[0]	[1]
minimal	0	0	0	0	0	0	1

[ ] = Total incidence of specified lesion, all grades.

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE 1 (Continued)

Incidence and Degree of Severity of Histomorphologic Observations

Dose Group:	I	II	III	IV	V	I	V
Sex:	M	M	M	M	M	F	F
Number of Animals/Group:	10	10	10	10	10	10	10
KIDNEYS (Continued):							
-nephritis, chronic, focal	[0]	[0]	[0]	[0]	[1]	[1]	[1]
minimal	0	0	0	0	1	1	1
LIVER:							
NO. EXAMINED	10	10	10	10	10	10	10
NO. NORMAL	2	3	2	0	0	8	7
-hypertrophy, hepatocellular, centrilobular	[0]	[0]	[0]	[9]	[10]	[0]	[0]
minimal	0	0	0	8	4	0	0
mild	0	0	0	1	5	0	0
moderate	0	0	0	0	1	0	0
-inflammation, chronic, focal/multifocal	[8]	[6]	[7]	[6]	[5]	[2]	[1]
minimal	5	4	7	6	5	2	1
mild	3	2	0	0	0	0	0
-lipidosis, tension, focal	0	2	0	0	0	0	0
-necrosis, focal	[0]	[0]	[0]	[0]	[0]	[0]	[2]
minimal	0	0	0	0	0	0	2
-vacuolation, hepatocellular, midzonal	[0]	[0]	[1]	[0]	[0]	[0]	[0]
mild	0	0	1	0	0	0	0
-vacuolation, hepatocellular, multifocal	[0]	[1]	[1]	[0]	[0]	[0]	[0]
minimal	0	1	0	0	0	0	0
mild	0	0	1	0	0	0	0
LUNG:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	10	0	0	0	10	9	9
-infiltration, polymorphonuclear, perivascular/peribronchial	[0]	[0]	[0]	[0]	[0]	[1]	[0]
mild	0	0	0	0	0	1	0
-inflammation, interstitial, focal	[0]	[0]	[0]	[0]	[0]	[0]	[1]
minimal	0	0	0	0	0	0	1
-macrophages, alveoli, focal	[0]	[0]	[0]	[0]	[0]	[0]	[1]
minimal	0	0	0	0	0	0	1
LYMPH NODE, MEDIASTINAL:							
NO. EXAMINED	8	0	0	0	10	10	10
NO. NORMAL	7	0	0	0	8	7	10
-congestion	[0]	[0]	[0]	[0]	[0]	[2]	[0]
minimal	0	0	0	0	0	2	0

[ ] = Total incidence of specified lesion, all grades.

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE 1 (Continued)

Incidence and Degree of Severity of Histomorphologic Observations

Dose Group:	I	II	III	IV	V	I	V
Sex:	M	M	M	M	M	F	F
Number of Animals/Group:	10	10	10	10	10	10	10
LYMPH NODE, MEDIASTINAL (Continued):							
-hyperplasia, lymphocytic/plasmacytic	[0]	[0]	[0]	[0]	[0]	[1]	[0]
mild	0	0	0	0	0	1	0
-mastocytosis	[1]	[0]	[0]	[0]	[2]	[1]	[0]
minimal	1	0	0	0	2	1	0
LYMPH NODE, SUBMANDIBULAR:							
NO. EXAMINED	10	0	0	0	10	10	9
NO. NORMAL	5	0	0	0	4	4	3
-hyperplasia, lymphocytic/plasmacytic	[5]	[0]	[0]	[0]	[6]	[6]	[6]
minimal	1	0	0	0	2	1	0
mild	2	0	0	0	0	3	5
moderate	2	0	0	0	4	2	1
MAMMARY GLAND:							
NO. EXAMINED						10	10
NO. NORMAL						10	9
-necrosis, focal						[0]	[1]
minimal						0	1
NERVE, SCIATIC:							
NO. EXAMINED	10	0	0	0	10	10	9
NO. NORMAL	10	0	0	0	10	10	9
OVARIES:							
NO. EXAMINED						10	10
NO. NORMAL						9	10
-cyst(s), intraovarian						1	0
PARATHYROID:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	10	0	0	0	10	10	10
PEYER'S PATCH:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	10	0	0	0	9	10	10
-mineralization, focal	[0]	[0]	[0]	[0]	[1]	[0]	[0]
minimal	0	0	0	0	1	0	0
PROSTATE:							
NO. EXAMINED	10	0	0	0	10		
NO. NORMAL	6	0	0	0	6		

[ ] = Total incidence of specified lesion, all grades.

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE 1 (Continued)

Incidence and Degree of Severity of Histomorphologic Observations

Dose Group:	I	II	III	IV	V	I	V
Sex:	M	M	M	M	M	F	F
Number of Animals/Group:	10	10	10	10	10	10	10
PROSTATE (Continued):							
-atrophy, focal/multifocal	[1]	[0]	[0]	[0]	[2]		
minimal	1	0	0	0	1		
moderate	0	0	0	0	1		
-inflammation, chronic, focal/multifocal	[3]	[0]	[0]	[0]	[3]		
minimal	3	0	0	0	3		
RECTUM:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	9	0	0	0	9	10	10
-inflammation, mucosa, chronic	[1]	[0]	[0]	[0]	[1]	[0]	[0]
minimal	0	0	0	0	1	0	0
mild	1	0	0	0	0	0	0
SEMINAL VESICLES:							
NO. EXAMINED	10	0	0	0	10		
NO. NORMAL	10	0	0	0	10		
SKIN (GROSS LESION):							
NO. EXAMINED	0	0	0	0	0	1	1
NO. NORMAL	0	0	0	0	0	0	0
-dermatitis, chronic, focal	[0]	[0]	[0]	[0]	[0]	[1]	[1]
minimal	0	0	0	0	0	0	1
mild	0	0	0	0	0	1	0
SPINAL CORD, CERVICAL:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	10	0	0	0	10	10	10
SPINAL CORD, LUMBAR:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	10	0	0	0	10	10	10
SPINAL CORD, THORACIC:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	10	0	0	0	10	10	10
SPLEEN:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	10	0	0	0	10	10	9
-atrophy	[0]	[0]	[0]	[0]	[0]	[0]	[1]
mild	0	0	0	0	0	0	1
STOMACH:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	8	0	0	0	9	7	6

[ ] = Total incidence of specified lesion, all grades.

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE 1 (Continued)

Incidence and Degree of Severity of Histomorphologic Observations

Dose Group:	I	II	III	IV	V	I	V
Sex:	M	M	M	M	M	F	F
Number of Animals/Group:	10	10	10	10	10	10	10
STOMACH (Continued):							
-dilatation, mucosal glands	[1]	[0]	[0]	[0]	[0]	[1]	[1]
minimal	1	0	0	0	0	1	1
-edema/inflammation, submucosa, forestomach	[1]	[0]	[0]	[0]	[1]	[0]	[1]
mild	1	0	0	0	1	0	1
-edema/inflammation, submucosa, glandular area	[2]	[0]	[0]	[0]	[0]	[2]	[3]
minimal	1	0	0	0	0	0	0
mild	0	0	0	0	0	1	3
moderate	1	0	0	0	0	1	0
-erosion(s), glandular mucosa	[0]	[0]	[0]	[0]	[0]	[0]	[1]
moderate	0	0	0	0	0	0	1
TESTIS (H&E):							
NO. EXAMINED	10	0	0	1	10		
NO. NORMAL	10	0	0	0	10		
-degeneration, multifocal	[0]	[0]	[0]	[1]	[0]		
mild	0	0	0	1	0		
TESTIS (PAS):							
NO. EXAMINED	10	0	0	1	10		
NO. NORMAL	10	0	0	0	10		
-degeneration, multifocal	[0]	[0]	[0]	[1]	[0]		
mild	0	0	0	1	0		
THYMUS:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	10	0	0	0	10	9	9
-atrophy	[0]	[0]	[0]	[0]	[0]	[1]	[1]
moderate	0	0	0	0	0	1	0
marked	0	0	0	0	0	0	1
THYROID:							
NO. EXAMINED	10	10	10	10	10	10	10
NO. NORMAL	5	3	5	5	3	5	5
-hypertrophy/hyperplasia, follicular epithelium	[2]	[3]	[2]	[4]	[7]	[0]	[0]
minimal	0	1	1	2	0	0	0
mild	2	2	1	2	3	0	0
moderate	0	0	0	0	4	0	0
-ultimobranchial body/cyst	3	4	4	2	2	5	5
TRACHEA:							
NO. EXAMINED	10	0	0	0	10	10	10
NO. NORMAL	6	0	0	0	9	10	9

[ ] = Total incidence of specified lesion, all grades.

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE 1 (Continued)

Incidence and Degree of Severity of Histomorphologic Observations

Dose Group:	I	II	III	IV	V	I	V
Sex:	M	M	M	M	M	F	F
Number of Animals/Group:	10	10	10	10	10	10	10
TRACHEA (Continued):							
-inflammation, chronic, focal	[4]	[0]	[0]	[0]	[1]	[0]	[1]
minimal	2	0	0	0	0	0	1
mild	2	0	0	0	1	0	0
URINARY BLADDER:							
NO. EXAMINED	10	0	0	0	10	9	10
NO. NORMAL	10	0	0	0	10	8	10
-inflammation, chronic, focal	[0]	[0]	[0]	[0]	[0]	[1]	[0]
minimal	0	0	0	0	0	1	0
UTERUS:							
NO. EXAMINED						10	10
NO. NORMAL						0	1
-distention, lumen						[0]	[2]
mild						0	1
moderate						0	1
-macrophages, pigmented						[10]	[8]
minimal						1	0
mild						2	2
moderate						7	5
marked						0	1
VAGINA:							
NO. EXAMINED						10	10
NO. NORMAL						10	10

[ ] = Total incidence of specified lesion, all grades.

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL 418-028
SPONSOR'S STUDY NUMBER T-7706.1

HISTOPATHOLOGY REPORT

APPENDIX I

HISTOMORPHOLOGIC OBSERVATIONS

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL 418-028
SPONSOR'S STUDY NUMBER T-7706.1

HISTOPATHOLOGY REPORT

KEY TO HISTOMORPHOLOGIC OBSERVATIONS

-	=	No change (not remarkable, within normal histologic limits or indicated change not present).
*	=	Tissue not available (specified tissue missing, insufficient tissue in plane of section, artifact precludes evaluation, or specified tissue not present in section).
< >	=	Microscopic finding(s) in tissue(s) with gross observation(s).
<->	=	Within normal limits [no microscopic change(s) to correlate with the gross observation(s)].
P	=	Indicated change or lesion present
1	=	Minimal degree or amount of indicated change or lesion.
2	=	Mild degree or amount of indicated change or lesion.
3	=	Moderate degree or amount of indicated change or lesion.
4	=	Marked degree or amount of indicated change or lesion.
SS	=	Scheduled Sacrifice

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE I-1

Histomorphologic Observations

Dose Group:	I	I	I	I	I	I	I	I	I	I
Animal Number:	19109	19115	19116	19119	19122	19125	19131	19132	19134	19135
Sex:	M	M	M	M	M	M	M	M	M	M
Death Type:	SS	SS	SS	SS	SS	SS	SS	SS	SS	SS
ADRENAL GLANDS:										
-vacuolation, cortex, diffuse	-	1	-	1	-	-	2	-	-	-
BONE MARROW (STERNUM):	-	-	-	-	-	-	-	-	-	-
BRAIN:	-	-	-	-	-	-	-	-	-	-
CECUM:										
-inflammation, mucosa, chronic	-	-	-	3	-	3	-	-	-	-
COAGULATING GLAND:	-	-	-	-	-	-	-	-	-	-
COLON:										
-inflammation, mucosa, chronic	-	-	-	2	-	-	-	-	-	-
DUODENUM:	-	-	-	-	-	-	-	-	-	-
EPIDIDYMIDES:										
-infiltration, mononuclear-cell, focal	-	1	-	-	1	-	1	-	1	-
HEART:										
-inflammation, chronic, focal	-	1	-	-	-	-	2	-	-	-
ILEUM:	-	-	-	-	-	-	-	-	-	-
JEJUNUM:	-	-	-	-	-	-	-	-	-	-
KIDNEYS:										
-cyst(s), medulla	-	-	<->	-	-	-	-	-	P	-
-infiltration, mononuclear-cell, focal/multifocal	-	-	<->	1	-	-	-	-	-	1
LIVER:										
-inflammation, chronic, focal/multifocal	-	1	1	2	1	1	2	2	-	1
LUNG:	-	-	-	-	-	-	-	-	-	-
LYMPH NODE, MEDIASTINAL:										
-mastocytosis	1	-	-	-	*	-	-	*	-	-
LYMPH NODE, SUBMANDIBULAR:										
-hyperplasia, lymphocytic/plasmacytic	3	-	2	-	1	3	2	-	-	-
NERVE, SCIATIC:	-	-	-	-	-	-	-	-	-	-
PARATHYROID:	-	-	-	-	-	-	-	-	-	-
PEYER'S PATCH:	-	-	-	-	-	-	-	-	-	-
PROSTATE:										
-atrophy, focal/multifocal	-	-	-	-	-	1	-	-	-	-

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE I-1 (Continued)

Histomorphologic Observations

Dose Group:	I	I	I	I	I	I	I	I	I	I
Animal Number:	19109	19115	19116	19119	19122	19125	19131	19132	19134	19135
Sex:	M	M	M	M	M	M	M	M	M	M
Death Type:	SS	SS	SS	SS	SS	SS	SS	SS	SS	SS
PROSTATE (Continued):										
-inflammation, chronic, focal/multifocal	1	-	-	-	-	-	1	-	-	1
RECTUM:										
-inflammation, mucosa, chronic	-	-	-	2	-	-	-	-	-	-
SEMINAL VESICLES:	-	-	-	-	-	-	-	-	-	-
SPINAL CORD, CERVICAL:	-	-	-	-	-	-	-	-	-	-
SPINAL CORD, LUMBAR:	-	-	-	-	-	-	-	-	-	-
SPINAL CORD, THORACIC:	-	-	-	-	-	-	-	-	-	-
SPLEEN:	-	-	-	-	-	-	-	-	-	-
STOMACH:										
-dilatation, mucosal glands	-	-	-	-	-	-	-	-	1	-
-edema/inflammation, submucosa, forestomach	-	-	-	-	-	-	-	-	2	-
-edema/inflammation, submucosa, glandular area	-	-	-	-	-	-	-	3	1	-
TESTIS (H&E):	-	-	-	-	-	-	-	-	-	-
TESTIS (PAS):	-	-	-	-	-	-	-	-	-	-
THYMUS:	-	-	-	-	-	-	-	-	-	-
THYROID:										
-hypertrophy/hyperplasia, follicular epithelium	2	-	-	-	-	-	-	-	2	-
-ultimobranchial body/cyst	-	P	-	-	-	P	-	P	-	-
TRACHEA:										
-inflammation, chronic, focal	-	2	-	-	1	-	2	-	1	-
URINARY BLADDER:	-	-	-	-	-	-	-	-	-	-

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE I-2

Histomorphologic Observations

Dose Group:	II	II	II	II	II	II	II	II	II	II
Animal Number:	19102	19106	19108	19110	19113	19120	19129	19136	19138	19139
Sex:	M	M	M	M	M	M	M	M	M	M
Death Type:	SS	SS	SS	SS	SS	SS	SS	SS	SS	SS
KIDNEYS:										
-dilatation, pelvis	<->				<2>			<1>		
LIVER:										
-inflammation, chronic, focal/multifocal	2	2	1	1	-	1	1	-	-	-
-lipidosis, tension, focal	-	-	P	-	-	P	-	-	-	-
-vacuolation, hepatocellular, multifocal	-	-	-	-	-	-	-	1	-	-
THYROID:										
-hypertrophy/hyperplasia, follicular epithelium	-	-	-	2	-	-	1	-	-	2
-ultimobranchial body/cyst	P	P	-	-	-	-	-	P	P	-

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE I-3

Histomorphologic Observations

Dose Group:	III	III	III	III	III	III	III	III	III	III
Animal Number:	19101	19105	19107	19112	19114	19121	19123	19130	19137	19146
Sex:	M	M	M	M	M	M	M	M	M	M
Death Type:	SS	SS	SS	SS	SS	SS	SS	SS	SS	SS
LIVER:										
-inflammation, chronic, focal/multifocal	-	1	1	1	1	1	1	1	-	-
-vacuolation, hepatocellular, midzonal	-	-	-	-	-	-	-	-	-	2
-vacuolation, hepatocellular, multifocal	-	-	-	-	-	2	-	-	-	-
THYROID:										
-hypertrophy/hyperplasia, follicular epithelium	-	-	1	-	-	-	-	2	-	-
-ultimobranchial body/cyst	-	-	P	P	P	P	-	-	-	-

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE I-4

Histomorphologic Observations

Dose Group:	IV	IV	IV	IV	IV	IV	IV	IV	IV	IV
Animal Number:	19100	19103	19104	19118	19133	19141	19142	19144	19148	19150
Sex:	M	M	M	M	M	M	M	M	M	M
Death Type:	SS	SS	SS	SS	SS	SS	SS	SS	SS	SS
EPIDIDYMIDES:										
-exfoliated spermatogenic cells							<3>			
-hypospermia							<4>			
LIVER:										
-hypertrophy, hepatocellular, centrilobular	1	1	2	1	1	1	1	-	1	1
-inflammation, chronic, focal/multifocal	1	-	1	1	-	-	1	1	1	-
TESTIS (H&E):										
-degeneration, multifocal							<2>			
TESTIS (PAS):										
-degeneration, multifocal							<2>			
THYROID:										
-hypertrophy/hyperplasia, follicular epithelium	1	-	-	-	1	-	-	-	2	2
-ultimobranchial body/cyst	-	-	-	-	P	P	-	-	-	-

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE I-5

Histomorphologic Observations

Dose Group:	V	V	V	V	V	V	V	V	V	V
Animal Number:	19111	19117	19124	19126	19127	19128	19140	19145	19149	19152
Sex:	M	M	M	M	M	M	M	M	M	M
Death Type:	SS	SS	SS	SS	SS	SS	SS	SS	SS	SS
ADRENAL GLANDS:										
-vacuolation, cortex, diffuse	-	-	-	-	2	-	-	-	-	-
BONE MARROW (STERNUM):	-	-	-	-	-	-	-	-	-	-
BRAIN:	-	-	-	-	-	-	-	-	-	-
CECUM:										
-inflammation, mucosa, chronic	-	-	-	-	-	2	-	-	-	-
COAGULATING GLAND:	-	-	-	-	-	-	-	-	-	-
COLON:	-	-	-	-	-	-	-	-	-	-
DUODENUM:	-	-	-	-	-	-	-	-	-	-
EPIDIDYMIDES:										
-infiltration, mononuclear-cell, focal	-	-	1	-	-	-	-	-	-	-
HEART:										
-inflammation, chronic, focal	-	-	-	-	-	-	-	-	-	1
ILEUM:	-	-	-	-	-	-	-	-	-	-
JEJUNUM:										
-diverticulum	<P>	-	-	-	-	-	-	-	-	-
KIDNEYS:										
-basophilia/degeneration, cortical tubules, focal/multifocal	1	-	-	-	-	-	-	-	-	-
-cyst(s), medulla	P	-	P	-	-	-	-	-	-	-
-infiltration, mononuclear-cell, focal/multifocal	1	-	-	-	-	-	-	1	-	-
-nephritis, chronic, focal	-	-	1	-	-	-	-	-	-	-
LIVER:										
-hypertrophy, hepatocellular, centrilobular	2	1	2	2	3	2	1	2	1	1
-inflammation, chronic, focal/multifocal	1	-	-	1	-	1	1	-	-	1
LUNG:	-	-	-	-	-	-	-	-	-	-
LYMPH NODE, MEDIASTINAL:										
-mastocytosis	-	1	1	-	-	-	-	-	-	-
LYMPH NODE, SUBMANDIBULAR:										
-hyperplasia, lymphocytic/plasmacytic	1	3	-	-	1	3	-	3	-	3
NERVE, SCIATIC:	-	-	-	-	-	-	-	-	-	-
PARATHYROID:	-	-	-	-	-	-	-	-	-	-
PEYER'S PATCH:										
-mineralization, focal	1	-	-	-	-	-	-	-	-	-

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE I-5 (Continued)

Histomorphologic Observations

Dose Group:	V	V	V	V	V	V	V	V	V	V
Animal Number:	19111	19117	19124	19126	19127	19128	19140	19145	19149	19152
Sex:	M	M	M	M	M	M	M	M	M	M
Death Type:	SS	SS	SS	SS	SS	SS	SS	SS	SS	SS
PROSTATE:										
-atrophy, focal/multifocal	-	-	-	-	-	3	-	-	-	1
-inflammation, chronic, focal/multifocal	1	-	-	1	-	-	-	-	-	1
RECTUM:										
-inflammation, mucosa, chronic	-	-	-	-	-	-	-	1	-	-
SEMINAL VESICLES:	-	-	-	-	-	-	-	-	-	-
SPINAL CORD, CERVICAL:	-	-	-	-	-	-	-	-	-	-
SPINAL CORD, LUMBAR:	-	-	-	-	-	-	-	-	-	-
SPINAL CORD, THORACIC:	-	-	-	-	-	-	-	-	-	-
SPLEEN:	-	-	-	-	-	-	-	-	-	-
STOMACH:										
-edema/inflammation, submucosa, forestomach	-	2	-	-	-	-	-	-	-	-
TESTIS (H&E):	-	-	-	-	-	-	-	-	-	-
TESTIS (PAS):	-	-	-	-	-	-	-	-	-	-
THYMUS:	-	-	-	-	-	-	-	-	-	-
THYROID:										
-hypertrophy/hyperplasia, follicular epithelium	3	-	2	-	2	3	3	-	3	2
-ultimobranchial body/cyst	P	-	-	-	-	-	-	-	P	-
TRACHEA:										
-inflammation, chronic, focal	-	-	-	-	-	-	-	2	-	-
URINARY BLADDER:	-	-	-	-	-	-	-	-	-	-

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE I-6

Histomorphologic Observations

Dose Group:	I	I	I	I	I	I	I	I	I	I
Animal Number:	19012	19019	19021	19023	19041	19042	19044	19050	19053	19065
Sex:	F	F	F	F	F	F	F	F	F	F
Death Type:	SS	SS	SS	SS	SS	SS	SS	SS	SS	SS
ADRENAL GLANDS:										
-vacuolation, zona glomerulosa	-	-	-	-	-	-	-	2	2	-
BONE MARROW (STERNUM):	-	-	-	-	-	-	-	-	-	-
BRAIN:	-	-	-	-	-	-	-	-	-	-
CECUM:										
-inflammation, mucosa, chronic	-	-	-	-	-	-	-	-	3	2
COLON:	-	-	-	-	-	-	-	-	-	-
DUODENUM:	-	-	-	-	-	-	-	-	-	-
HEART:	-	-	-	-	-	-	-	-	-	-
ILEUM:	-	-	-	-	-	-	-	-	-	-
JEJUNUM:	-	-	-	-	-	-	-	-	-	-
KIDNEYS:										
-nephritis, chronic, focal	-	-	-	-	-	-	1	-	-	-
LIVER:										
-inflammation, chronic, focal/multifocal	-	-	1	-	-	-	-	-	-	1
LUNG:										
-infiltration, polymorphonuclear, perivascular/peribronchial	-	-	-	2	-	-	-	-	-	-
LYMPH NODE, MEDIASTINAL:										
-congestion	-	-	1	-	-	-	1	-	-	-
-hyperplasia, lymphocytic/plasmacytic	-	-	-	-	-	-	2	-	-	-
-mastocytosis	-	-	-	1	-	-	-	-	-	-
LYMPH NODE, SUBMANDIBULAR:										
-hyperplasia, lymphocytic/plasmacytic	-	2	-	-	3	-	3	1	2	2
MAMMARY GLAND:	-	-	-	-	-	-	-	-	-	-
NERVE, SCIATIC:	-	-	-	-	-	-	-	-	-	-
OVARIES:										
-cyst(s), intraovarian	-	-	-	-	-	P	-	-	-	-
PARATHYROID:	-	-	-	-	-	-	-	-	-	-
PEYER'S PATCH:	-	-	-	-	-	-	-	-	-	-
RECTUM:	-	-	-	-	-	-	-	-	-	-
SKIN (GROSS LESION):										
-dermatitis, chronic, focal			<2>							

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE I-6 (Continued)

Histomorphologic Observations

Dose Group:	I	I	I	I	I	I	I	I	I	I
Animal Number:	19012	19019	19021	19023	19041	19042	19044	19050	19053	19065
Sex:	F	F	F	F	F	F	F	F	F	F
Death Type:	SS	SS	SS	SS	SS	SS	SS	SS	SS	SS
SPINAL CORD, CERVICAL:	-	-	-	-	-	-	-	-	-	-
SPINAL CORD, LUMBAR:	-	-	-	-	-	-	-	-	-	-
SPINAL CORD, THORACIC:	-	-	-	-	-	-	-	-	-	-
SPLEEN:	-	-	-	-	-	-	-	-	-	-
STOMACH:										
-dilatation, mucosal glands	1	-	-	-	-	-	-	-	-	-
-edema/inflammation, submucosa, glandular area	-	-	-	2	3	-	-	-	-	-
THYMUS:										
-atrophy	-	-	-	-	-	-	-	-	3	-
THYROID:										
-ultimobranchial body/cyst	P	-	P	-	P	P	-	-	P	-
TRACHEA:	-	-	-	-	-	-	-	-	-	-
URINARY BLADDER:										
-inflammation, chronic, focal	-	-	*	-	-	-	-	-	-	1
UTERUS:										
-macrophages, pigmented	3	2	3	1	3	3	3	3	3	2
VAGINA:	-	-	-	-	-	-	-	-	-	-

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE I-7

Histomorphologic Observations

Dose Group:	V	V	V	V	V	V	V	V	V	V
Animal Number:	19001	19006	19011	19020	19022	19025	19027	19028	19030	19031
Sex:	F	F	F	F	F	F	F	F	F	F
Death Type:	SS	SS	SS	SS	SS	SS	SS	SS	SS	SS
ADRENAL GLANDS:										
-degeneration, cystic, cortex, multifocal	-	-	-	<2>	-	-	-	-	-	-
-hypertrophy/vacuolation, cortex, multifocal	-	-	-	-	-	2	-	-	-	-
-necrosis, cortex, focal	-	-	2	-	-	-	-	-	-	-
BONE MARROW (STERNUM):	-	-	-	-	-	-	-	-	-	-
BRAIN:	-	-	-	-	-	-	-	-	-	-
CECUM:	-	-	-	<->	-	-	-	-	-	-
COLON:	-	-	-	<->	-	-	-	-	-	-
DUODENUM:	-	-	-	<->	-	-	-	-	-	-
HEART:	-	-	-	-	-	-	-	-	-	-
ILEUM:	-	-	-	<->	-	-	-	-	-	-
JEJUNUM:	-	-	-	<->	-	-	-	-	-	-
KIDNEYS:										
-mineralization, multifocal	-	-	-	-	-	-	1	-	-	-
-nephritis, chronic, focal	-	-	-	-	-	1	-	-	-	-
LIVER:										
-inflammation, chronic, focal/multifocal	-	-	-	-	1	-	-	-	-	-
-necrosis, focal	-	-	-	1	-	-	-	-	-	1
LUNG:										
-inflammation, interstitial, focal	1	-	-	-	-	-	-	-	-	-
-macrophages, alveoli, focal	1	-	-	-	-	-	-	-	-	-
LYMPH NODE, MEDIASTINAL:	-	-	-	-	-	-	-	-	-	-
LYMPH NODE, SUBMANDIBULAR:										
-hyperplasia, lymphocytic/plasmacytic	-	2	-	2	2	-	2	3	*	2
MAMMARY GLAND:										
-necrosis, focal	-	-	-	-	1	-	-	-	-	-
NERVE, SCIATIC:	-	-	-	-	-	-	*	-	-	-
OVARIES:	-	-	-	-	-	-	-	-	-	-
PARATHYROID:	-	-	-	-	-	-	-	-	-	-
PEYER'S PATCH:	-	-	-	-	-	-	-	-	-	-
RECTUM:	-	-	-	<->	-	-	-	-	-	-

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

TABLE I-7 (Continued)

Histomorphologic Observations

Dose Group:	V	V	V	V	V	V	V	V	V	V
Animal Number:	19001	19006	19011	19020	19022	19025	19027	19028	19030	19031
Sex:	F	F	F	F	F	F	F	F	F	F
Death Type:	SS	SS	SS	SS	SS	SS	SS	SS	SS	SS
SKIN (GROSS LESION):										
-dermatitis, chronic, focal									<1>	
SPINAL CORD, CERVICAL:	-	-	-	-	-	-	-	-	-	-
SPINAL CORD, LUMBAR:	-	-	-	-	-	-	-	-	-	-
SPINAL CORD, THORACIC:	-	-	-	-	-	-	-	-	-	-
SPLEEN:										
-atrophy	-	-	-	<2>	-	-	-	-	-	-
STOMACH:										
-dilatation, mucosal glands	-	-	-	-	-	-	-	1	-	-
-edema/inflammation, submucosa, forestomach	-	-	-	<2>	-	-	-	-	-	-
-edema/inflammation, submucosa, glandular area	-	-	-	<2>	-	2	2	-	-	-
-erosion(s), glandular mucosa	-	-	-	<3>	-	-	-	-	-	-
THYMUS:										
-atrophy	-	-	-	<4>	-	-	-	-	-	-
THYROID:										
-ultimobranchial body/cyst	-	P	-	P	P	-	P	-	P	-
TRACHEA:										
-inflammation, chronic, focal	1	-	-	-	-	-	-	-	-	-
URINARY BLADDER:	-	-	-	-	-	-	-	-	-	-
UTERUS:										
-distention, lumen	2	-	-	-	-	-	-	-	-	3
-macrophages, pigmented	3	2	3	4	2	3	-	3	3	-
VAGINA:	-	-	-	-	-	-	-	-	-	-

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL 418-028
SPONSOR'S STUDY NUMBER T-7706.1

HISTOPATHOLOGY REPORT

APPENDIX II

INDIVIDUAL ANIMAL GROSS AND HISTOMORPHOLOGY DATA

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19109 DOSE GROUP: I
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LYMPH NODE, MEDIASTINAL:	mastocytosis (minimal)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (moderate)
PROSTATE:	inflammation, chronic, focal/multifocal (minimal)
THYROID:	hypertrophy/hyperplasia, follicular epithelium (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COAGULATING GLAND	COLON	DUODENUM	EPIDIDYMIDES
HEART	ILEUM	JEJUNUM	KIDNEYS
LIVER	LUNG	NERVE, SCIATIC	PARATHYROID
PEYER'S PATCH	RECTUM	SEMINAL VESICLES	SPINAL CORD, CERVICAL
SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN	STOMACH
TESTIS (H&E)	TESTIS (PAS)	THYMUS	TRACHEA
URINARY BLADDER			

End of Record- 19109

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19115 DOSE GROUP: I
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
GENERAL: No gross changes.	Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

ADRENAL GLANDS:	vacuolation, cortex, diffuse (minimal)
EPIDIDYMIDES:	infiltration, mononuclear-cell, focal (minimal)
HEART:	inflammation, chronic, focal (minimal)
LIVER:	inflammation, chronic, focal/multifocal (minimal)
THYROID:	ultimobranchial body/cyst
TRACHEA:	inflammation, chronic, focal (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

BONE MARROW (STERNUM)	BRAIN	CECUM	COAGULATING GLAND
COLON	DUODENUM	ILEUM	JEJUNUM
KIDNEYS	LUNG	LYMPH NODE, MEDIASTINAL	LYMPH NODE, SUBMANDIBULAR
NERVE, SCIATIC	PARATHYROID	PEYER'S PATCH	PROSTATE
RECTUM	SEMINAL VESICLES	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR
SPINAL CORD, THORACIC	SPLEEN	STOMACH	TESTIS (H&E)
TESTIS (PAS)	THYMUS	URINARY BLADDER	

End of Record- 19115

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19116 DOSE GROUP: I
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
KIDNEYS: Mottled tan and red, bilateral.	No microscopic change to correlate

HISTOMORPHOLOGIC OBSERVATIONS:

KIDNEYS:	No microscopic change to correlate
LIVER:	inflammation, chronic, focal/multifocal (minimal)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COAGULATING GLAND	COLON	DUODENUM	EPIDIDYMIDES
HEART	ILEUM	JEJUNUM	KIDNEYS
LUNG	LYMPH NODE, MEDIASTINAL	NERVE, SCIATIC	PARATHYROID
PEYER'S PATCH	PROSTATE	RECTUM	SEMINAL VESICLES
SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN
STOMACH	TESTIS (H&E)	TESTIS (PAS)	THYMUS
THYROID	TRACHEA	URINARY BLADDER	

End of Record- 19116

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19119 DOSE GROUP: I
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
GENERAL: No gross changes.	Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

ADRENAL GLANDS:	vacuolation, cortex, diffuse (minimal)
CECUM:	inflammation, mucosa, chronic (moderate)
COLON:	inflammation, mucosa, chronic (mild)
KIDNEYS:	infiltration, mononuclear-cell, focal/multifocal (minimal)
LIVER:	inflammation, chronic, focal/multifocal (mild)
RECTUM:	inflammation, mucosa, chronic (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

BONE MARROW (STERNUM)	BRAIN	COAGULATING GLAND	DUODENUM
EPIDIDYMIDES	HEART	ILEUM	JEJUNUM
LUNG	LYMPH NODE, MEDIASTINAL	LYMPH NODE, SUBMANDIBULAR	NERVE, SCIATIC
PARATHYROID	PEYER'S PATCH	PROSTATE	SEMINAL VESICLES
SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN
STOMACH	TESTIS (H&E)	TESTIS (PAS)	THYMUS
THYROID	TRACHEA	URINARY BLADDER	

End of Record- 19119

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19122 DOSE GROUP: I
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

EPIDIDYMIDES:	infiltration, mononuclear-cell, focal (minimal)
LIVER:	inflammation, chronic, focal/multifocal (minimal)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (minimal)
TRACHEA:	inflammation, chronic, focal (minimal)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COAGULATING GLAND	COLON	DUODENUM	HEART
ILEUM	JEJUNUM	KIDNEYS	LUNG
NERVE, SCIATIC	PARATHYROID	PEYER'S PATCH	PROSTATE
RECTUM	SEMINAL VESICLES	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR
SPINAL CORD, THORACIC	SPLEEN	STOMACH	TESTIS (H&E)
TESTIS (PAS)	THYMUS	THYROID	URINARY BLADDER

TISSUE(S) NOT AVAILABLE FOR EVALUATION:

LYMPH NODE, MEDIASTINAL

End of Record- 19122

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19125 DOSE GROUP: I
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

CECUM:	inflammation, mucosa, chronic (moderate)
LIVER:	inflammation, chronic, focal/multifocal (minimal)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (moderate)
PROSTATE:	atrophy, focal/multifocal (minimal)
THYROID:	ultimobranchial body/cyst

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	COAGULATING GLAND
COLON	DUODENUM	EPIDIDYMIDES	HEART
ILEUM	JEJUNUM	KIDNEYS	LUNG
LYMPH NODE, MEDIASTINAL	NERVE, SCIATIC	PARATHYROID	PEYER'S PATCH
RECTUM	SEMINAL VESICLES	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR
SPINAL CORD, THORACIC	SPLEEN	STOMACH	TESTIS (H&E)
TESTIS (PAS)	THYMUS	TRACHEA	URINARY BLADDER

End of Record- 19125

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19131 DOSE GROUP: I
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

ADRENAL GLANDS:	vacuolation, cortex, diffuse (mild)
EPIDIDYMIDES:	infiltration, mononuclear-cell, focal (minimal)
HEART:	inflammation, chronic, focal (mild)
LIVER:	inflammation, chronic, focal/multifocal (mild)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (mild)
PROSTATE:	inflammation, chronic, focal/multifocal (minimal)
TRACHEA:	inflammation, chronic, focal (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

BONE MARROW (STERNUM)	BRAIN	CECUM	COAGULATING GLAND
COLON	DUODENUM	ILEUM	JEJUNUM
KIDNEYS	LUNG	LYMPH NODE, MEDIASTINAL	NERVE, SCIATIC
PARATHYROID	PEYER'S PATCH	RECTUM	SEMINAL VESICLES
SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN
STOMACH	TESTIS (H&E)	TESTIS (PAS)	THYMUS
THYROID	URINARY BLADDER		

End of Record- 19131

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19132 DOSE GROUP: I
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	inflammation, chronic, focal/multifocal (mild)
STOMACH:	edema/inflammation, submucosa, glandular area (moderate)
THYROID:	ultimobranchial body/cyst

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COAGULATING GLAND	COLON	DUODENUM	EPIDIDYMIDES
HEART	ILEUM	JEJUNUM	KIDNEYS
LUNG	LYMPH NODE, SUBMANDIBULAR	NERVE, SCIATIC	PARATHYROID
PEYER'S PATCH	PROSTATE	RECTUM	SEMINAL VESICLES
SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN
TESTIS (H&E)	TESTIS (PAS)	THYMUS	TRACHEA
URINARY BLADDER			

TISSUE(S) NOT AVAILABLE FOR EVALUATION:

LYMPH NODE, MEDIASTINAL

End of Record- 19132

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19134 DOSE GROUP: I
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

EPIDIDYMIDES:	infiltration, mononuclear-cell, focal (minimal)
KIDNEYS:	cyst(s), medulla
STOMACH:	dilatation, mucosal glands (minimal)
	edema/inflammation, submucosa, glandular area (minimal)
	edema/inflammation, submucosa, forestomach (mild)
THYROID:	hypertrophy/hyperplasia, follicular epithelium (mild)
TRACHEA:	inflammation, chronic, focal (minimal)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COAGULATING GLAND	COLON	DUODENUM	HEART
ILEUM	JEJUNUM	LIVER	LUNG
LYMPH NODE, MEDIASTINAL	LYMPH NODE, SUBMANDIBULAR	NERVE, SCIATIC	PARATHYROID
PEYER'S PATCH	PROSTATE	RECTUM	SEMINAL VESICLES
SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN
TESTIS (H&E)	TESTIS (PAS)	THYMUS	URINARY BLADDER

End of Record- 19134

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19135 DOSE GROUP: I
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

KIDNEYS:	infiltration, mononuclear-cell, focal/multifocal (minimal)
LIVER:	inflammation, chronic, focal/multifocal (minimal)
PROSTATE:	inflammation, chronic, focal/multifocal (minimal)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COAGULATING GLAND	COLON	DUODENUM	EPIDIDYMIDES
HEART	ILEUM	JEJUNUM	LUNG
LYMPH NODE, MEDIASTINAL	LYMPH NODE, SUBMANDIBULAR	NERVE, SCIATIC	PARATHYROID
PEYER'S PATCH	RECTUM	SEMINAL VESICLES	SPINAL CORD, CERVICAL
SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN	STOMACH
TESTIS (H&E)	TESTIS (PAS)	THYMUS	THYROID
TRACHEA	URINARY BLADDER		

End of Record- 19135

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19102 DOSE GROUP: II
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
KIDNEYS: Bilateral- mottled.	No microscopic change to correlate

HISTOMORPHOLOGIC OBSERVATIONS:

KIDNEYS:	No microscopic change to correlate
LIVER:	inflammation, chronic, focal/multifocal (mild)
THYROID:	ultimobranchial body/cyst

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

KIDNEYS

End of Record- 19102

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19106 DOSE GROUP: II
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
GENERAL: No gross changes.	Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	inflammation, chronic, focal/multifocal (mild)
THYROID:	ultimobranchial body/cyst

End of Record- 19106

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19108 DOSE GROUP: II
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
GENERAL: No gross changes.	Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	lipidosis, tension, focal inflammation, chronic, focal/multifocal (minimal)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

THYROID

End of Record- 19108

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19110 DOSE GROUP: II
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
GENERAL: No gross changes.	Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	inflammation, chronic, focal/multifocal (minimal)
THYROID:	hypertrophy/hyperplasia, follicular epithelium (mild)

End of Record- 19110

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19113 DOSE GROUP: II
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
KIDNEYS: Left- pelvis, slight dilation.	dilatation, pelvis

HISTOMORPHOLOGIC OBSERVATIONS:

KIDNEYS: dilatation, pelvis (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

LIVER THYROID

End of Record- 19113

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19120 DOSE GROUP: II
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
GENERAL: No gross changes.	Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	inflammation, chronic, focal/multifocal (minimal) lipidosis, tension, focal

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

THYROID

End of Record- 19120

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19129 DOSE GROUP: II
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	inflammation, chronic, focal/multifocal (minimal)
THYROID:	hypertrophy/hyperplasia, follicular epithelium (minimal)

End of Record- 19129

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19136 DOSE GROUP: II
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
KIDNEYS: Bilateral- mottled.	dilatation, pelvis

HISTOMORPHOLOGIC OBSERVATIONS:

KIDNEYS:	dilatation, pelvis (minimal)
LIVER:	vacuolation, hepatocellular, multifocal (minimal)
THYROID:	ultimobranchial body/cyst

End of Record- 19136

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19138 DOSE GROUP: II
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

THYROID: ultimobranchial body/cyst

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

LIVER

End of Record- 19138

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19139 DOSE GROUP: II
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

THYROID: hypertrophy/hyperplasia, follicular epithelium (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

LIVER

End of Record- 19139

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19101 DOSE GROUP: III
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

LIVER THYROID

End of Record- 19101

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19105 DOSE GROUP: III
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER: inflammation, chronic, focal/multifocal (minimal)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

THYROID

End of Record- 19105

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19107 DOSE GROUP: III
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	inflammation, chronic, focal/multifocal (minimal)
THYROID:	hypertrophy/hyperplasia, follicular epithelium (minimal)
	ultimobranchial body/cyst

End of Record- 19107

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19112 DOSE GROUP: III
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
GENERAL: No gross changes.	Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	inflammation, chronic, focal/multifocal (minimal)
THYROID:	ultimobranchial body/cyst

End of Record- 19112

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19114 DOSE GROUP: III
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	inflammation, chronic, focal/multifocal (minimal)
THYROID:	ultimobranchial body/cyst

End of Record- 19114

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19121 DOSE GROUP: III
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
GENERAL: No gross changes.	Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	inflammation, chronic, focal/multifocal (minimal) vacuolation, hepatocellular, multifocal (mild)
THYROID:	ultimobranchial body/cyst

End of Record- 19121

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19123 DOSE GROUP: III
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
GENERAL: No gross changes.	Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER: inflammation, chronic, focal/multifocal (minimal)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

THYROID

End of Record- 19123

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19130 DOSE GROUP: III
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
GENERAL: No gross changes.	Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	inflammation, chronic, focal/multifocal (minimal)
THYROID:	hypertrophy/hyperplasia, follicular epithelium (mild)

End of Record- 19130

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19137 DOSE GROUP: III
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

LIVER THYROID

End of Record- 19137

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19146 DOSE GROUP: III
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER: vacuolation, hepatocellular, midzonal (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

THYROID

End of Record- 19146

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19100 DOSE GROUP: IV
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
GENERAL: No gross changes.	Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	hypertrophy, hepatocellular, centrilobular (minimal) inflammation, chronic, focal/multifocal (minimal)
THYROID:	hypertrophy/hyperplasia, follicular epithelium (minimal)

End of Record- 19100

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19103 DOSE GROUP: IV
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
GENERAL: No gross changes.	Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER: hypertrophy, hepatocellular, centrilobular (minimal)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

THYROID

End of Record- 19103

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19104 DOSE GROUP: IV
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
GENERAL: No gross changes.	Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	inflammation, chronic, focal/multifocal (minimal) hypertrophy, hepatocellular, centrilobular (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

THYROID

End of Record- 19104

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19118 DOSE GROUP: IV
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
GENERAL: No gross changes.	Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	inflammation, chronic, focal/multifocal (minimal) hypertrophy, hepatocellular, centrilobular (minimal)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

THYROID

End of Record- 19118

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19133 DOSE GROUP: IV
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	hypertrophy, hepatocellular, centrilobular (minimal)
THYROID:	hypertrophy/hyperplasia, follicular epithelium (minimal)
	ultimobranchial body/cyst

End of Record- 19133

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19141 DOSE GROUP: IV
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
GENERAL: No gross changes.	Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	hypertrophy, hepatocellular, centrilobular (minimal)
THYROID:	ultimobranchial body/cyst

End of Record- 19141

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19142 DOSE GROUP: IV
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
EPIDIDYMIDES: Bilateral- small; cauda epididymis, left, small.	hypospermia exfoliated spermatogenic cells
TESTES: Bilateral- small.	degeneration, multifocal, TESTIS (PAS) degeneration, multifocal, TESTIS (H&E)

HISTOMORPHOLOGIC OBSERVATIONS:

EPIDIDYMIDES:	hypospermia (marked)
	exfoliated spermatogenic cells (moderate)
LIVER:	inflammation, chronic, focal/multifocal (minimal)
	hypertrophy, hepatocellular, centrilobular (minimal)
TESTIS (H&E):	degeneration, multifocal (mild)
TESTIS (PAS):	degeneration, multifocal (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

THYROID

End of Record- 19142

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19144 DOSE GROUP: IV
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER: inflammation, chronic, focal/multifocal (minimal)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

THYROID

End of Record- 19144

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19148 DOSE GROUP: IV
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	inflammation, chronic, focal/multifocal (minimal) hypertrophy, hepatocellular, centrilobular (minimal)
THYROID:	hypertrophy/hyperplasia, follicular epithelium (mild)

End of Record- 19148

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19150 DOSE GROUP: IV
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	hypertrophy, hepatocellular, centrilobular (minimal)
THYROID:	hypertrophy/hyperplasia, follicular epithelium (mild)

End of Record- 19150

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19111 DOSE GROUP: V
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
GASTROINTESTINAL TRACT: Jejunum- diverticulum, 1.5x0.6x0.4cm.	diverticulum, JEJUNUM

HISTOMORPHOLOGIC OBSERVATIONS:

JEJUNUM:	diverticulum
KIDNEYS:	basophilia/degeneration, cortical tubules, focal/multifocal (minimal)
	cyst(s), medulla
	infiltration, mononuclear-cell, focal/multifocal (minimal)
LIVER:	hypertrophy, hepatocellular, centrilobular (mild)
	inflammation, chronic, focal/multifocal (minimal)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (minimal)
PEYER'S PATCH:	mineralization, focal (minimal)
PROSTATE:	inflammation, chronic, focal/multifocal (minimal)
THYROID:	ultimobranchial body/cyst
	hypertrophy/hyperplasia, follicular epithelium (moderate)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COAGULATING GLAND	COLON	DUODENUM	EPIDIDYMIDES
HEART	ILEUM	LUNG	LYMPH NODE, MEDIASTINAL
NERVE, SCIATIC	PARATHYROID	RECTUM	SEMINAL VESICLES
SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN
STOMACH	TESTIS (H&E)	TESTIS (PAS)	THYMUS
TRACHEA	URINARY BLADDER		

End of Record- 19111

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19117 DOSE GROUP: V
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	hypertrophy, hepatocellular, centrilobular (minimal)
LYMPH NODE, MEDIASTINAL:	mastocytosis (minimal)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (moderate)
STOMACH:	edema/inflammation, submucosa, forestomach (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COAGULATING GLAND	COLON	DUODENUM	EPIDIDYMIDES
HEART	ILEUM	JEJUNUM	KIDNEYS
LUNG	NERVE, SCIATIC	PARATHYROID	PEYER'S PATCH
PROSTATE	RECTUM	SEMINAL VESICLES	SPINAL CORD, CERVICAL
SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN	TESTIS (H&E)
TESTIS (PAS)	THYMUS	THYROID	TRACHEA
URINARY BLADDER			

End of Record- 19117

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19124 DOSE GROUP: V
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

EPIDIDYMIDES:	infiltration, mononuclear-cell, focal (minimal)
KIDNEYS:	nephritis, chronic, focal (minimal)
	cyst(s), medulla
LIVER:	hypertrophy, hepatocellular, centrilobular (mild)
LYMPH NODE, MEDIASTINAL:	mastocytosis (minimal)
THYROID:	hypertrophy/hyperplasia, follicular epithelium (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COAGULATING GLAND	COLON	DUODENUM	HEART
ILEUM	JEJUNUM	LUNG	LYMPH NODE, SUBMANDIBULAR
NERVE, SCIATIC	PARATHYROID	PEYER'S PATCH	PROSTATE
RECTUM	SEMINAL VESICLES	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR
SPINAL CORD, THORACIC	SPLEEN	STOMACH	TESTIS (H&E)
TESTIS (PAS)	THYMUS	TRACHEA	URINARY BLADDER

End of Record- 19124

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19126 DOSE GROUP: V
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	inflammation, chronic, focal/multifocal (minimal) hypertrophy, hepatocellular, centrilobular (mild)
PROSTATE:	inflammation, chronic, focal/multifocal (minimal)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COAGULATING GLAND	COLON	DUODENUM	EPIDIDYMIDES
HEART	ILEUM	JEJUNUM	KIDNEYS
LUNG	LYMPH NODE, MEDIASTINAL	LYMPH NODE, SUBMANDIBULAR	NERVE, SCIATIC
PARATHYROID	PEYER'S PATCH	RECTUM	SEMINAL VESICLES
SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN
STOMACH	TESTIS (H&E)	TESTIS (PAS)	THYMUS
THYROID	TRACHEA	URINARY BLADDER	

End of Record- 19126

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19127 DOSE GROUP: V
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

ADRENAL GLANDS:	vacuolation, cortex, diffuse (mild)
LIVER:	hypertrophy, hepatocellular, centrilobular (moderate)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (minimal)
THYROID:	hypertrophy/hyperplasia, follicular epithelium (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

BONE MARROW (STERNUM)	BRAIN	CECUM	COAGULATING GLAND
COLON	DUODENUM	EPIDIDYMIDES	HEART
ILEUM	JEJUNUM	KIDNEYS	LUNG
LYMPH NODE, MEDIASTINAL	NERVE, SCIATIC	PARATHYROID	PEYER'S PATCH
PROSTATE	RECTUM	SEMINAL VESICLES	SPINAL CORD, CERVICAL
SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN	STOMACH
TESTIS (H&E)	TESTIS (PAS)	THYMUS	TRACHEA
URINARY BLADDER			

End of Record- 19127

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19128 DOSE GROUP: V
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
GENERAL: No gross changes.	Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

CECUM:	inflammation, mucosa, chronic (mild)
LIVER:	inflammation, chronic, focal/multifocal (minimal)
	hypertrophy, hepatocellular, centrilobular (mild)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (moderate)
PROSTATE:	atrophy, focal/multifocal (moderate)
THYROID:	hypertrophy/hyperplasia, follicular epithelium (moderate)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	COAGULATING GLAND
COLON	DUODENUM	EPIDIDYMIDES	HEART
ILEUM	JEJUNUM	KIDNEYS	LUNG
LYMPH NODE, MEDIASTINAL	NERVE, SCIATIC	PARATHYROID	PEYER'S PATCH
RECTUM	SEMINAL VESICLES	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR
SPINAL CORD, THORACIC	SPLEEN	STOMACH	TESTIS (H&E)
TESTIS (PAS)	THYMUS	TRACHEA	URINARY BLADDER

End of Record- 19128

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19140 DOSE GROUP: V
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	inflammation, chronic, focal/multifocal (minimal) hypertrophy, hepatocellular, centrilobular (minimal)
THYROID:	hypertrophy/hyperplasia, follicular epithelium (moderate)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COAGULATING GLAND	COLON	DUODENUM	EPIDIDYMIDES
HEART	ILEUM	JEJUNUM	KIDNEYS
LUNG	LYMPH NODE, MEDIASTINAL	LYMPH NODE, SUBMANDIBULAR	NERVE, SCIATIC
PARATHYROID	PEYER'S PATCH	PROSTATE	RECTUM
SEMINAL VESICLES	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC
SPLEEN	STOMACH	TESTIS (H&E)	TESTIS (PAS)
THYMUS	TRACHEA	URINARY BLADDER	

End of Record- 19140

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19145 DOSE GROUP: V
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

KIDNEYS:	infiltration, mononuclear-cell, focal/multifocal (minimal)
LIVER:	hypertrophy, hepatocellular, centrilobular (mild)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (moderate)
RECTUM:	inflammation, mucosa, chronic (minimal)
TRACHEA:	inflammation, chronic, focal (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COAGULATING GLAND	COLON	DUODENUM	EPIDIDYMIDES
HEART	ILEUM	JEJUNUM	LUNG
LYMPH NODE, MEDIASTINAL	NERVE, SCIATIC	PARATHYROID	PEYER'S PATCH
PROSTATE	SEMINAL VESICLES	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR
SPINAL CORD, THORACIC	SPLEEN	STOMACH	TESTIS (H&E)
TESTIS (PAS)	THYMUS	THYROID	URINARY BLADDER

End of Record- 19145

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19149 DOSE GROUP: V
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	hypertrophy, hepatocellular, centrilobular (minimal)
THYROID:	ultimobranchial body/cyst
	hypertrophy/hyperplasia, follicular epithelium (moderate)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COAGULATING GLAND	COLON	DUODENUM	EPIDIDYMIDES
HEART	ILEUM	JEJUNUM	KIDNEYS
LUNG	LYMPH NODE, MEDIASTINAL	LYMPH NODE, SUBMANDIBULAR	NERVE, SCIATIC
PARATHYROID	PEYER'S PATCH	PROSTATE	RECTUM
SEMINAL VESICLES	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC
SPLEEN	STOMACH	TESTIS (H&E)	TESTIS (PAS)
THYMUS	TRACHEA	URINARY BLADDER	

End of Record- 19149

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19152 DOSE GROUP: V
SEX: M DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

HEART:	inflammation, chronic, focal (minimal)
LIVER:	inflammation, chronic, focal/multifocal (minimal) hypertrophy, hepatocellular, centrilobular (minimal)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (moderate)
PROSTATE:	inflammation, chronic, focal/multifocal (minimal) atrophy, focal/multifocal (minimal)
THYROID:	hypertrophy/hyperplasia, follicular epithelium (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COAGULATING GLAND	COLON	DUODENUM	EPIDIDYMIDES
ILEUM	JEJUNUM	KIDNEYS	LUNG
LYMPH NODE, MEDIASTINAL	NERVE, SCIATIC	PARATHYROID	PEYER'S PATCH
RECTUM	SEMINAL VESICLES	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR
SPINAL CORD, THORACIC	SPLEEN	STOMACH	TESTIS (H&E)
TESTIS (PAS)	THYMUS	TRACHEA	URINARY BLADDER

End of Record- 19152

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19012 DOSE GROUP: I
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

STOMACH:	dilatation, mucosal glands (minimal)
THYROID:	ultimobranchial body/cyst
UTERUS:	macrophages, pigmented (moderate)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COLON	DUODENUM	HEART	ILEUM
JEJUNUM	KIDNEYS	LIVER	LUNG
LYMPH NODE, MEDIASTINAL	LYMPH NODE, SUBMANDIBULAR	MAMMARY GLAND	NERVE, SCIATIC
OVARIES	PARATHYROID	PEYER'S PATCH	RECTUM
SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN
THYMUS	TRACHEA	URINARY BLADDER	VAGINA

End of Record- 19012

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19019 DOSE GROUP: I
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (mild)
UTERUS:	macrophages, pigmented (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COLON	DUODENUM	HEART	ILEUM
JEJUNUM	KIDNEYS	LIVER	LUNG
LYMPH NODE, MEDIASTINAL	MAMMARY GLAND	NERVE, SCIATIC	OVARIES
PARATHYROID	PEYER'S PATCH	RECTUM	SPINAL CORD, CERVICAL
SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN	STOMACH
THYMUS	THYROID	TRACHEA	URINARY BLADDER
VAGINA			

End of Record- 19019

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19021
SEX: F

DOSE GROUP: I
DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

HEAD: Head- scab, 0.2cmx0.4cm.

HISTOMORPHOLOGIC OBSERVATION(S):

dermatitis, chronic, focal, SKIN (GROSS LESION)

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	inflammation, chronic, focal/multifocal (minimal)
LYMPH NODE, MEDIASTINAL:	congestion (minimal)
SKIN (GROSS LESION):	dermatitis, chronic, focal (mild)
THYROID:	ultimobranchial body/cyst
UTERUS:	macrophages, pigmented (moderate)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COLON	DUODENUM	HEART	ILEUM
JEJUNUM	KIDNEYS	LUNG	LYMPH NODE, SUBMANDIBULAR
MAMMARY GLAND	NERVE, SCIATIC	OVARIES	PARATHYROID
PEYER'S PATCH	RECTUM	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR
SPINAL CORD, THORACIC	SPLEEN	STOMACH	THYMUS
TRACHEA	VAGINA		

TISSUE(S) NOT AVAILABLE FOR EVALUATION:

URINARY BLADDER

End of Record- 19021

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19023 DOSE GROUP: I
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LUNG:	infiltration, polymorphonuclear, perivascular/peribronchial (mild)
LYMPH NODE, MEDIASTINAL:	mastocytosis (minimal)
STOMACH:	edema/inflammation, submucosa, glandular area (mild)
UTERUS:	macrophages, pigmented (minimal)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COLON	DUODENUM	HEART	ILEUM
JEJUNUM	KIDNEYS	LIVER	LYMPH NODE, SUBMANDIBULAR
MAMMARY GLAND	NERVE, SCIATIC	OVARIES	PARATHYROID
PEYER'S PATCH	RECTUM	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR
SPINAL CORD, THORACIC	SPLEEN	THYMUS	THYROID
TRACHEA	URINARY BLADDER	VAGINA	

End of Record- 19023

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19041 DOSE GROUP: I
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (moderate)
STOMACH:	edema/inflammation, submucosa, glandular area (moderate)
THYROID:	ultimobranchial body/cyst
UTERUS:	macrophages, pigmented (moderate)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COLON	DUODENUM	HEART	ILEUM
JEJUNUM	KIDNEYS	LIVER	LUNG
LYMPH NODE, MEDIASTINAL	MAMMARY GLAND	NERVE, SCIATIC	OVARIES
PARATHYROID	PEYER'S PATCH	RECTUM	SPINAL CORD, CERVICAL
SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN	THYMUS
TRACHEA	URINARY BLADDER	VAGINA	

End of Record- 19041

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19042 DOSE GROUP: I
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

OVARIES:	cyst(s), intraovarian
THYROID:	ultimobranchial body/cyst
UTERUS:	macrophages, pigmented (moderate)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COLON	DUODENUM	HEART	ILEUM
JEJUNUM	KIDNEYS	LIVER	LUNG
LYMPH NODE, MEDIASTINAL	LYMPH NODE, SUBMANDIBULAR	MAMMARY GLAND	NERVE, SCIATIC
PARATHYROID	PEYER'S PATCH	RECTUM	SPINAL CORD, CERVICAL
SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN	STOMACH
THYMUS	TRACHEA	URINARY BLADDER	VAGINA

End of Record- 19042

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19044 DOSE GROUP: I
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

KIDNEYS:	nephritis, chronic, focal (minimal)
LYMPH NODE, MEDIASTINAL:	congestion (minimal)
	hyperplasia, lymphocytic/plasmacytic (mild)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (moderate)
UTERUS:	macrophages, pigmented (moderate)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COLON	DUODENUM	HEART	ILEUM
JEJUNUM	LIVER	LUNG	MAMMARY GLAND
NERVE, SCIATIC	OVARIES	PARATHYROID	PEYER'S PATCH
RECTUM	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC
SPLEEN	STOMACH	THYMUS	THYROID
TRACHEA	URINARY BLADDER	VAGINA	

End of Record- 19044

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19050 DOSE GROUP: I
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

ADRENAL GLANDS:	vacuolation, zona glomerulosa (mild)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (minimal)
UTERUS:	macrophages, pigmented (moderate)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

BONE MARROW (STERNUM)	BRAIN	CECUM	COLON
DUODENUM	HEART	ILEUM	JEJUNUM
KIDNEYS	LIVER	LUNG	LYMPH NODE, MEDIASTINAL
MAMMARY GLAND	NERVE, SCIATIC	OVARIES	PARATHYROID
PEYER'S PATCH	RECTUM	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR
SPINAL CORD, THORACIC	SPLEEN	STOMACH	THYMUS
THYROID	TRACHEA	URINARY BLADDER	VAGINA

End of Record- 19050

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19053 DOSE GROUP: I
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

ADRENAL GLANDS:	vacuolation, zona glomerulosa (mild)
CECUM:	inflammation, mucosa, chronic (moderate)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (mild)
THYMUS:	atrophy (moderate)
THYROID:	ultimobranchial body/cyst
UTERUS:	macrophages, pigmented (moderate)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

BONE MARROW (STERNUM)	BRAIN	COLON	DUODENUM
HEART	ILEUM	JEJUNUM	KIDNEYS
LIVER	LUNG	LYMPH NODE, MEDIASTINAL	MAMMARY GLAND
NERVE, SCIATIC	OVARIES	PARATHYROID	PEYER'S PATCH
RECTUM	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC
SPLEEN	STOMACH	TRACHEA	URINARY BLADDER
VAGINA			

End of Record- 19053

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19065 DOSE GROUP: I
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

CECUM:	inflammation, mucosa, chronic (mild)
LIVER:	inflammation, chronic, focal/multifocal (minimal)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (mild)
URINARY BLADDER:	inflammation, chronic, focal (minimal)
UTERUS:	macrophages, pigmented (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	COLON
DUODENUM	HEART	ILEUM	JEJUNUM
KIDNEYS	LUNG	LYMPH NODE, MEDIASTINAL	MAMMARY GLAND
NERVE, SCIATIC	OVARIES	PARATHYROID	PEYER'S PATCH
RECTUM	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC
SPLEEN	STOMACH	THYMUS	THYROID
TRACHEA	VAGINA		

End of Record- 19065

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19001 DOSE GROUP: V
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LUNG:	inflammation, interstitial, focal (minimal)
	macrophages, alveoli, focal (minimal)
TRACHEA:	inflammation, chronic, focal (minimal)
UTERUS:	macrophages, pigmented (moderate)
	distention, lumen (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COLON	DUODENUM	HEART	ILEUM
JEJUNUM	KIDNEYS	LIVER	LYMPH NODE, MEDIASTINAL
LYMPH NODE, SUBMANDIBULAR	MAMMARY GLAND	NERVE, SCIATIC	OVARIES
PARATHYROID	PEYER'S PATCH	RECTUM	SPINAL CORD, CERVICAL
SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN	STOMACH
THYMUS	THYROID	URINARY BLADDER	VAGINA

End of Record- 19001

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19006 DOSE GROUP: V
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (mild)
THYROID:	ultimobranchial body/cyst
UTERUS:	macrophages, pigmented (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COLON	DUODENUM	HEART	ILEUM
JEJUNUM	KIDNEYS	LIVER	LUNG
LYMPH NODE, MEDIASTINAL	MAMMARY GLAND	NERVE, SCIATIC	OVARIES
PARATHYROID	PEYER'S PATCH	RECTUM	SPINAL CORD, CERVICAL
SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN	STOMACH
THYMUS	TRACHEA	URINARY BLADDER	VAGINA

End of Record- 19006

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19011 DOSE GROUP: V
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

ADRENAL GLANDS:	necrosis, cortex, focal (mild)
LIVER:	Not remarkable
UTERUS:	macrophages, pigmented (moderate)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

BONE MARROW (STERNUM)	BRAIN	CECUM	COLON
DUODENUM	HEART	ILEUM	JEJUNUM
KIDNEYS	LUNG	LYMPH NODE, MEDIASTINAL	LYMPH NODE, SUBMANDIBULAR
MAMMARY GLAND	NERVE, SCIATIC	OVARIES	PARATHYROID
PEYER'S PATCH	RECTUM	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR
SPINAL CORD, THORACIC	SPLEEN	STOMACH	THYMUS
THYROID	TRACHEA	URINARY BLADDER	VAGINA

End of Record- 19011

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19020 DOSE GROUP: V
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):	HISTOMORPHOLOGIC OBSERVATION(S):
ADRENAL GLANDS: Bilateral- large.	degeneration, cystic, cortex, multifocal
GASTROINTESTINAL TRACT: Abdominal distention, large and small intestines distended with gas.	No microscopic change to correlate, DUODENUM No microscopic change to correlate, JEJUNUM No microscopic change to correlate, ILEUM No microscopic change to correlate, COLON No microscopic change to correlate, CECUM No microscopic change to correlate, RECTUM
SPLEEN: Small.	atrophy
STOMACH: Fundic mucosa surface contains approximately 12 black areas ranging in size from pinpoint to 0.3cm in diameter.	edema/inflammation, submucosa, glandular area edema/inflammation, submucosa, forestomach erosion(s), glandular mucosa
THYMUS: Small.	atrophy

HISTOMORPHOLOGIC OBSERVATIONS:

ADRENAL GLANDS:	degeneration, cystic, cortex, multifocal (mild)
CECUM:	No microscopic change to correlate
COLON:	No microscopic change to correlate
DUODENUM:	No microscopic change to correlate
ILEUM:	No microscopic change to correlate
JEJUNUM:	No microscopic change to correlate
LIVER:	necrosis, focal (minimal)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (mild)
RECTUM:	No microscopic change to correlate
SPLEEN:	atrophy (mild)
STOMACH:	erosion(s), glandular mucosa (moderate)
	edema/inflammation, submucosa, glandular area (mild)
	edema/inflammation, submucosa, forestomach (mild)
THYMUS:	atrophy (marked)
THYROID:	ultimobranchial body/cyst
UTERUS:	macrophages, pigmented (marked)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

BONE MARROW (STERNUM)	BRAIN	CECUM	COLON
DUODENUM	HEART	ILEUM	JEJUNUM
KIDNEYS	LUNG	LYMPH NODE, MEDIASTINAL	MAMMARY GLAND
NERVE, SCIATIC	OVARIES	PARATHYROID	PEYER'S PATCH
RECTUM	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC
TRACHEA	URINARY BLADDER	VAGINA	

End of Record- 19020

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19022 DOSE GROUP: V
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	inflammation, chronic, focal/multifocal (minimal)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (mild)
MAMMARY GLAND:	necrosis, focal (minimal)
THYROID:	ultimobranchial body/cyst
UTERUS:	macrophages, pigmented (mild)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COLON	DUODENUM	HEART	ILEUM
JEJUNUM	KIDNEYS	LUNG	LYMPH NODE, MEDIASTINAL
NERVE, SCIATIC	OVARIES	PARATHYROID	PEYER'S PATCH
RECTUM	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC
SPLEEN	STOMACH	THYMUS	TRACHEA
URINARY BLADDER	VAGINA		

End of Record- 19022

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19025 DOSE GROUP: V
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

ADRENAL GLANDS:	hypertrophy/vacuolation, cortex, multifocal (mild)
KIDNEYS:	nephritis, chronic, focal (minimal)
STOMACH:	edema/inflammation, submucosa, glandular area (mild)
UTERUS:	macrophages, pigmented (moderate)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

BONE MARROW (STERNUM)	BRAIN	CECUM	COLON
DUODENUM	HEART	ILEUM	JEJUNUM
LIVER	LUNG	LYMPH NODE, MEDIASTINAL	LYMPH NODE, SUBMANDIBULAR
MAMMARY GLAND	NERVE, SCIATIC	OVARIES	PARATHYROID
PEYER'S PATCH	RECTUM	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR
SPINAL CORD, THORACIC	SPLEEN	THYMUS	THYROID
TRACHEA	URINARY BLADDER	VAGINA	

End of Record- 19025

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19027 DOSE GROUP: V
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

KIDNEYS:	mineralization, multifocal (minimal)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (mild)
STOMACH:	edema/inflammation, submucosa, glandular area (mild)
THYROID:	ultimobranchial body/cyst

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COLON	DUODENUM	HEART	ILEUM
JEJUNUM	LIVER	LUNG	LYMPH NODE, MEDIASTINAL
MAMMARY GLAND	OVARIES	PARATHYROID	PEYER'S PATCH
RECTUM	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC
SPLEEN	THYMUS	TRACHEA	URINARY BLADDER
UTERUS	VAGINA		

TISSUE(S) NOT AVAILABLE FOR EVALUATION:

NERVE, SCIATIC

End of Record- 19027

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19028 DOSE GROUP: V
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (moderate)
STOMACH:	dilatation, mucosal glands (minimal)
UTERUS:	macrophages, pigmented (moderate)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COLON	DUODENUM	HEART	ILEUM
JEJUNUM	KIDNEYS	LIVER	LUNG
LYMPH NODE, MEDIASTINAL	MAMMARY GLAND	NERVE, SCIATIC	OVARIES
PARATHYROID	PEYER'S PATCH	RECTUM	SPINAL CORD, CERVICAL
SPINAL CORD, LUMBAR	SPINAL CORD, THORACIC	SPLEEN	THYMUS
THYROID	TRACHEA	URINARY BLADDER	VAGINA

End of Record- 19028

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19030 DOSE GROUP: V
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

HEAD: Head- scab, 0.3cm x 0.3cm.

HISTOMORPHOLOGIC OBSERVATION(S):

dermatitis, chronic, focal, SKIN (GROSS LESION)

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	Not remarkable
SKIN (GROSS LESION):	dermatitis, chronic, focal (minimal)
THYROID:	ultimobranchial body/cyst
UTERUS:	macrophages, pigmented (moderate)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COLON	DUODENUM	HEART	ILEUM
JEJUNUM	KIDNEYS	LUNG	LYMPH NODE, MEDIASTINAL
MAMMARY GLAND	NERVE, SCIATIC	OVARIES	PARATHYROID
PEYER'S PATCH	RECTUM	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR
SPINAL CORD, THORACIC	SPLEEN	STOMACH	THYMUS
TRACHEA	URINARY BLADDER	VAGINA	

TISSUE(S) NOT AVAILABLE FOR EVALUATION:

LYMPH NODE, SUBMANDIBULAR

End of Record- 19030

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Appendix II
Individual Animal Gross and Histomorphology Data

ANIMAL NUMBER: 19031 DOSE GROUP: V
SEX: F DEATH TYPE: Sacrifice-Scheduled

GROSS OBSERVATION(S):

GENERAL: No gross changes.

HISTOMORPHOLOGIC OBSERVATION(S):

Not applicable

HISTOMORPHOLOGIC OBSERVATIONS:

LIVER:	necrosis, focal (minimal)
LYMPH NODE, SUBMANDIBULAR:	hyperplasia, lymphocytic/plasmacytic (mild)
UTERUS:	distention, lumen (moderate)

THE FOLLOWING TISSUE(S) WERE WITHIN NORMAL LIMITS:

ADRENAL GLANDS	BONE MARROW (STERNUM)	BRAIN	CECUM
COLON	DUODENUM	HEART	ILEUM
JEJUNUM	KIDNEYS	LUNG	LYMPH NODE, MEDIASTINAL
MAMMARY GLAND	NERVE, SCIATIC	OVARIES	PARATHYROID
PEYER'S PATCH	RECTUM	SPINAL CORD, CERVICAL	SPINAL CORD, LUMBAR
SPINAL CORD, THORACIC	SPLEEN	STOMACH	THYMUS
THYROID	TRACHEA	URINARY BLADDER	VAGINA

End of Record- 19031

ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL 418-028
SPONSOR'S STUDY NUMBER T-7706.1

HISTOPATHOLOGY REPORT

APPENDIX III

HISTOMORPHOLOGIC OBSERVATIONS IN THE LIVER

F1 GENERATION PUPS

ORAL (GAVAGE) COMBINED REPEATED DOSE STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Table III-1
Histomorphologic Observations in the Liver - Group I - F1 Generation Pups

Dose Group:										
Dam Number:	19012	19012	19012	19012	19012	19012	19012	19012	19012	19012
Pup Number:	1	2	3	4	5	7	8	14	15	16
LIVER:	-	-	-	-	-	-	-	-	-	-

Dose Group:										
Dam Number:	19019	19019	19019	19019	19019	19019	19019	19019	19019	19019
Pup Number:	1	2	3	7	8	11	12	13	14	15
LIVER:	-	-	-	-	-	-	-	-	-	-

Dose Group:										
Dam Number:	19021	19021	19021	19021	19021	19021	19021	19021	19021	19021
Pup Number:	1	2	6	8	9	10	11	12	13	14
LIVER:	-	-	-	-	-	-	-	-	-	-

Dose Group:										
Dam Number:	19023	19023	19023	19023	19023	19023	19023	19023	19023	19023
Pup Number:	1	2	3	6	7	8	9	10	11	12
LIVER:	-	-	-	-	-	-	-	-	-	-

Dose Group:										
Dam Number:	19041	19041	19041	19041	19041	19041	19041	19041	19041	19041
Pup Number:	1	2	3	4	5	8	9	15	16	17
LIVER:	-	-	-	-	-	-	-	-	-	-

ORAL (GAVAGE) COMBINED REPEATED DOSE STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Table III-1 (Continued)
Histomorphologic Observations in the Liver – Group I - F1 Generation Pups

Dose Group:	I	I	I	I	I	I	I	I	I	I
Dam Number:	19042	19042	19042	19042	19042	19042	19042	19042	19042	19042
Pup Number:	1	2	4	5	6	7	8	10	12	13
LIVER:	-	-	-	-	-	-	-	-	-	-

Dose Group:	I	I	I	I	I	I	I	I	I	I
Dam Number:	19044	19044	19044	19044	19044	19044	19044	19044	19044	19044
Pup Number:	1	2	5	6	7	9	11	12	13	14
LIVER:	-	-	-	-	-	-	-	-	-	-

Dose Group:	I	I	I	I	I	I	I	I	I	I
Dam Number:	19050	19050	19050	19050	19050	19050	19050	19050	19050	19050
Pup Number:	1	2	3	4	5	6	7	8	13	14
LIVER:	-	-	-	-	-	-	-	-	-	-

Dose Group:	I	I	I	I	I	I	I	I	I	I
Dam Number:	19053	19053	19053	19053	19053	19053	19053	19053	19053	19053
Pup Number:	1	3	4	5	6	10	11	12	13	14
LIVER:	-	-	-	-	-	-	-	-	-	-

Dose Group:	I	I	I	I	I	I	I	I	I	I
Dam Number:	19065	19065	19065	19065	19065	19065	19065	19065	19065	19065
Pup Number:	3	4	5	7	8	10	11	14	15	17
LIVER:	-	-	-	-	-	-	-	-	-	-

ORAL (GAVAGE) COMBINED REPEATED DOSE STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Table III-2
Histomorphologic Observations in the Liver – Group V – F1 Generation Pups

Dose Group:	V	V	V	V	V	V	V	V	V
Dam Number:	19001	19001	19001	19001	19001	19001	19001	19001	19001
Pup Number:	1	2	3	4	5	6	7	9	11
LIVER :	-	-	-	-	-	-	-	-	-

Dose Group:	V	V	V	V	V	V	V	V	V	V
Dam Number:	19006	19006	19006	19006	19006	19006	19006	19006	19006	19006
Pup Number:	1	2	3	4	5	8	10	11	13	18
LIVER :	-	-	-	-	-	-	-	-	-	-

Dose Group:	V	V	V	V	V	V	V	V	V	V
Dam Number:	19011	19011	19011	19011	19011	19011	19011	19011	19011	19011
Pup Number:	2	3	4	5	6	9	10	11	12	13
LIVER :	-	-	-	-	-	-	-	-	-	-

Dose Group:	V	V	V	V	V	V	V	V	V	V
Dam Number:	19020	19020	19020	19020	19020	19020	19020	19020	19020	19020
Pup Number:	2	4	5	7	8	9	10	11	12	13
LIVER :	-	-	-	-	-	-	-	-	-	-

Dose Group:	V	V	V	V	V	V	V	V	V	V
Dam Number:	19022	19022	19022	19022	19022	19022	19022	19022	19022	19022
Pup Number:	1	4	5	7	8	11	12	13	14	15
LIVER :	-	-	-	-	-	-	-	-	-	-

ORAL (GAVAGE) COMBINED REPEATED DOSE STUDY OF T-7706
WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST
PROTOCOL NUMBER 418-028
SPONSOR'S STUDY NUMBER T-7706.1

Table III-2 (Continued)
Histomorphologic Observations in the Liver – Group V – F1 Generation Pups

Dose Group:	V	V	V	V	V	V	V	V	V	V
Dam Number:	19025	19025	19025	19025	19025	19025	19025	19025	19025	19025
Pup Number:	1	2	7	8	13	14	15	18	19	20
LIVER :	-	-	-	-	-	-	-	-	-	-

Dose Group:	V	V	V	V	V	V	V	V	V
Dam Number:	19027	19027	19027	19027	19027	19027	19027	19027	19027
Pup Number:	1	2	3	4	5	6	7	13	14
LIVER :	-	-	-	-	-	-	-	-	-

Dose Group:	V	V	V	V	V	V	V	V	V	V
Dam Number:	19028	19028	19028	19028	19028	19028	19028	19028	19028	19028
Pup Number:	1	2	3	4	5	6	7	10	11	12
LIVER :	-	-	-	-	-	-	-	-	-	-

Dose Group:	V	V	V	V	V	V	V	V	V	V
Dam Number:	19030	19030	19030	19030	19030	19030	19030	19030	19030	19030
Pup Number:	1	2	4	5	6	8	9	11	12	13
LIVER :	-	-	-	-	-	-	-	-	-	-

Dose Group:	V	V	V	V	V	V	V	V	V	V
Dam Number:	19031	19031	19031	19031	19031	19031	19031	19031	19031	19031
Pup Number:	1	2	3	5	6	9	11	12	14	15
LIVER :	-	-	-	-	-	-	-	-	-	-

APPENDIX K

HEMATOLOGY AND CLINICAL CHEMISTRY REPORTS

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: MALE
STUDY NO: 060-069

Animal ID	WBC THSN/CU MM	RBC MILL/CU MM	HGB GRAMS/DL	HCT %	MCV CU MICRONS	MCH PICO GRAMS	MCHC %	PLT THSN/CU MM
GROUP: 1-M								
19109	13.5	7.10	15.4	40.6	57.2	21.7	37.9	1219
19115	15.9	8.58	19.0	50.0	58.3	22.1	38.0	1072
19116	15.1	6.95	16.3	42.6	61.3	23.5	38.3	964
19119	12.7	7.16	16.2	42.1	58.8	22.6	38.5	1354
19122	16.4	6.77	15.7	40.6	59.9	23.2	38.7	1074
19125	17.6	7.61	16.2	41.4	54.4	21.3	39.1	1322
19131	17.7	7.37	16.3	41.6	56.5	22.1	39.2	1049
19132	14.9	7.45	16.3	43.3	58.1	21.9	37.6	1264
19134	15.0	7.43	15.6	42.7	57.5	21.0	36.5	1269
19135	14.3	8.71	18.2	49.7	57.1	20.9	36.6	1203
19143	—	—	—	—	—	—	—	—
19151	—	—	—	—	—	—	—	—
19157	—	—	—	—	—	—	—	—
19161	—	—	—	—	—	—	—	—
19167	—	—	—	—	—	—	—	—
MEAN	15.3	7.51	16.5	43.5	57.9	22.0	38.0	1179
SD	1.63	0.648	1.16	3.48	1.89	0.87	0.93	130.9
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	WBC THSN/CU MM	RBC MILL/CU MM	HGB GRAMS/DL	HCT %	MCV CU MICRONS	MCH PICO GRAMS	MCHC %	PLT THSN/CU MM
GROUP: 2-M								
19102	10.9	7.55	16.2	43.6	57.7	21.5	37.2	926
19106	17.0	6.93	15.2	39.6	57.1	21.9	38.4	970
19108	12.7	7.02	16.1	40.3	57.4	22.9	40.0	959
19110	13.1	8.20	15.9	43.9	53.5	19.4	36.2	1468
19113	15.7	6.80	16.1	42.0	61.8	23.7	38.3	1170
19120	18.4	7.42	16.4	44.4	59.8	22.1	36.9	1382
19129	14.7	7.29	15.9	43.2	59.3	21.8	36.8	1184
19136	10.5	7.32	15.4	41.3	56.4	21.0	37.3	1183
19138	17.2	7.53	16.4	42.2	56.0	21.8	38.9	1069
19139	19.0	7.20	15.5	41.7	57.9	21.5	37.2	994
19147	—	—	—	—	—	—	—	—
19153	—	—	—	—	—	—	—	—
19164	—	—	—	—	—	—	—	—
19165	—	—	—	—	—	—	—	—
19171	—	—	—	—	—	—	—	—
MEAN	14.9	7.33	15.9	42.2	57.7	21.8	37.7	1131
SD	3.03	0.396	0.42	1.57	2.27	1.13	1.15	183.7
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: MALE
STUDY NO: 060-069

Animal ID	WBC THSN/CU MM	RBC MILL/CU MM	HGB GRAMS/DL	HCT %	MCV CU MICRONS	MCH PICO GRAMS	MCHC %	PLT THSN/CU MM
GROUP: 3-M								
19101	13.1	7.38	16.0	42.4	57.4	21.7	37.7	958
19105	11.0	7.28	16.3	43.2	59.3	22.4	37.7	960
19107	12.5	7.59	16.1	44.4	58.5	21.2	36.3	993
19112	13.3	7.20	15.4	40.1	55.7	21.4	38.4	1002
19114	11.2	7.72	15.7	42.6	55.2	20.3	36.9	1253
19121	20.9	7.23	15.4	40.5	56.0	21.3	38.0	1340
19123	14.1	6.69	15.0	39.1	58.4	22.4	38.4	1143
19130	13.9	7.96	16.4	43.8	55.0	20.6	37.4	1123
19137	12.2	7.60	16.3	45.0	59.2	21.4	36.2	1046
19146	15.4	6.54	14.7	38.8	59.4	22.5	37.9	1336
19155	—	—	—	—	—	—	—	—
19159	—	—	—	—	—	—	—	—
19172	—	—	—	—	—	—	—	—
19173	—	—	—	—	—	—	—	—
19174	—	—	—	—	—	—	—	—
MEAN	13.8	7.32	15.7	42.0	57.4	21.5	37.5	1115
SD	2.84	0.441	0.59	2.22	1.78	0.75	0.79	149.2
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: MALE
STUDY NO: 060-069

Animal ID	WBC THSN/CU MM	RBC MILL/CU MM	HGB GRAMS/DL	HCT %	MCV CU MICRONS	MCH PICO GRAMS	MCHC %	PLT THSN/CU MM
GROUP: 4-M								
19100	12.6	6.59	14.6	38.2	57.9	22.2	38.2	1072
19103	21.0	6.73	15.0	39.0	58.0	22.3	38.5	1144
19104	18.1	6.75	15.6	39.3	58.2	23.1	39.7	1029
19118	12.0	6.83	14.8	38.4	56.2	21.7	38.5	1274
19133	22.0	7.50	16.8	45.5	60.7	22.4	36.9	1124
19141	17.4	7.07	15.5	40.3	57.0	21.9	38.5	1125
19142	12.8	6.87	15.0	39.9	58.1	21.8	37.6	998
19144	19.6	7.37	16.1	42.4	57.5	21.8	38.0	962
19148	15.6	6.97	15.6	40.6	58.2	22.4	38.4	1155
19150	11.1	6.62	15.0	38.1	57.6	22.7	39.4	1161
19156	—	—	—	—	—	—	—	—
19160	—	—	—	—	—	—	—	—
19162	—	—	—	—	—	—	—	—
19163	—	—	—	—	—	—	—	—
19166	—	—	—	—	—	—	—	—
MEAN	16.2	6.93	15.4	40.2	57.9	22.2	38.4	1104
SD	3.97	0.305	0.67	2.29	1.15	0.45	0.80	91.4
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	WBC THSN/CU MM	RBC MILL/CU MM	HGB GRAMS/DL	HCT %	MCV CU MICRONS	MCH PICO GRAMS	MCHC %	PLT THSN/CU MM
GROUP: 5-M								
19111	15.7	7.20	16.1	41.7	57.9	22.4	38.6	1013
19117	14.3	6.72	15.7	39.8	59.2	23.4	39.4	1181
19124	10.8	6.68	15.0	39.0	58.4	22.5	38.5	1249
19126	12.5	8.07	17.3	44.4	55.0	21.4	39.0	1142
19127	11.0	6.61	14.7	38.1	57.6	22.2	38.6	1040
19128	14.2	7.09	15.5	41.1	58.0	21.9	37.7	1001
19140	15.2	7.05	16.2	41.9	59.5	23.0	38.7	1059
19145	20.7	7.13	15.7	41.4	58.1	22.0	37.9	1523
19149	18.3	6.66	14.8	39.8	59.8	22.2	37.2	1234
19152	13.9	6.68	14.8	39.5	59.2	22.2	37.5	1041
19154	--	--	--	--	--	--	--	--
19158	--	--	--	--	--	--	--	--
19168	--	--	--	--	--	--	--	--
19169	--	--	--	--	--	--	--	--
19170	--	--	--	--	--	--	--	--
MEAN	14.7	6.99	15.6	40.7	58.3	22.3	38.3	1148
SD	3.07	0.442	0.81	1.81	1.37	0.56	0.70	159.9
N	10	10	10	10	10	10	10	10

(--) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	WBC THSN/CU MM	RBC MILL/CU MM	HGB GRAMS/DL	HCT %	MCV CU MICRONS	MCH PICO GRAMS	MCHC %	PLT THSN/CU MM
GROUP: 1-F								
19010	—	—	—	—	—	—	—	—
19012	15.9	5.60	14.0	35.2	62.9	25.0	39.8	1421
19019	6.6	6.95	16.4	42.5	61.1	23.6	38.6	1344
19021	7.4	7.10	16.7	44.7	63.0	23.5	37.4	1199
19023	7.3	6.62	16.3	42.4	64.1	24.6	38.4	1352
19041	8.0	6.86	16.2	42.4	61.8	23.6	38.2	1529
19042	6.8	6.45	15.1	40.2	62.3	23.4	37.6	1225
19044	10.6	6.09	14.3	37.6	61.7	23.5	38.0	1343
19050	8.2	6.64	16.0	42.2	63.6	24.1	37.9	1629
19053	6.6	6.08	14.7	37.5	61.6	24.2	39.2	1524
19065	12.5	6.67	15.7	40.2	60.2	23.5	39.1	1623
19068	—	—	—	—	—	—	—	—
19072	—	—	—	—	—	—	—	—
19074	—	—	—	—	—	—	—	—
19075	—	—	—	—	—	—	—	—
MEAN	9.0	6.51	15.5	40.5	62.2	23.9	38.4	1419
SD	3.09	0.461	0.95	2.93	1.19	0.55	0.76	153.0
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

LABCAT HE4.43

27-JUN-2002

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	WBC THSN/CU MM	RBC MILL/CU MM	HGB GRAMS/DL	HCT %	MCV CU MICRONS	MCH PICO GRAMS	MCHC %	PLT THSN/CU MM
GROUP: 2-F								
19004	7.8	7.07	16.6	43.8	62.0	23.5	37.9	1540
19009	14.6	5.90	14.8	38.3	64.9	25.1	38.6	1157
19016	17.0	6.32	14.9	38.5	60.9	23.6	38.7	1529
19018	13.3	5.61	14.1	35.3	63.0	25.1	39.9	1057
19026	9.1	6.36	15.5	41.6	65.4	24.4	37.3	1443
19036	18.0	6.30	14.5	38.9	61.7	23.0	37.3	1166
19037	26.3	6.23	14.8	37.8	60.6	23.8	39.2	1257
19043	13.5	5.83	14.7	38.3	65.7	25.2	38.4	942
19047	11.1	5.93	14.5	37.5	63.3	24.5	38.7	1041
19048	7.1	6.60	16.0	43.4	65.8	24.2	36.9	1264
19052	—	—	—	—	—	—	—	—
19055	—	—	—	—	—	—	—	—
19061	—	—	—	—	—	—	—	—
19067	—	—	—	—	—	—	—	—
19071	—	—	—	—	—	—	—	—
MEAN	13.8	6.22	15.0	39.3	63.3	24.2	38.3	1240
SD	5.73	0.423	0.77	2.72	2.01	0.76	0.94	208.1
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

LABCAT HE4.43

27-JUN-2002

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	WBC THSN/CU MM	RBC MILL/CU MM	HGB GRAMS/DL	HCT %	MCV CU MICRONS	MCH PICO GRAMS	MCHC %	PLT THSN/CU MM
GROUP: 3-F								
19003	11.1	6.43	15.7	40.0	62.2	24.4	39.3	1165
19007	7.9	6.31	15.4	39.9	63.3	24.4	38.6	1450
19008	7.0	6.71	15.7	40.5	60.3	23.4	38.8	1319
19013	16.6	5.53	13.8	33.1	59.9	25.0	41.7	1167
19014	--	--	--	--	--	--	--	--
19015	7.4	6.41	15.1	39.8	62.1	23.6	37.9	1671
19017	12.9	6.03	14.4	38.0	63.0	23.9	37.9	866
19024	10.5	6.93	15.6	42.1	60.8	22.5	37.1	1424
19029	12.5	5.69	14.0	35.6	62.6	24.6	39.3	1062
19034	12.1	6.54	16.1	41.9	64.1	24.6	38.4	1231
19038	--	--	--	--	--	--	--	--
19056	12.7	7.38	16.6	44.2	59.9	22.5	37.6	1380
19057	--	--	--	--	--	--	--	--
19060	--	--	--	--	--	--	--	--
19064	--	--	--	--	--	--	--	--
MEAN	11.1	6.40	15.2	39.5	61.8	23.9	38.7	1274
SD	2.98	0.554	0.91	3.24	1.50	0.88	1.29	226.3
N	10	10	10	10	10	10	10	10

(--) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: FEMALE
STUDY NO: 060-069

Animal ID	WBC THSN/CU MM	RBC MILL/CU MM	HGB GRAMS/DL	HCT %	MCV CU MICRONS	MCH PICO GRAMS	MCHC %	PLT THSN/CU MM
GROUP: 4-F								
19002	—	—	—	—	—	—	—	—
19005	9.5	6.51	15.8	42.0	64.5	24.3	37.6	1479
19035	9.6	6.81	16.2	42.4	62.3	23.8	38.2	1527
19039	12.8	6.48	14.8	38.9	60.1	22.8	38.0	1066
19040	10.0	6.48	15.8	41.3	63.8	24.4	38.3	1333
19045	9.7	5.77	13.7	36.7	63.6	23.7	37.3	1148
19046	—	—	—	—	—	—	—	—
19051	—	—	—	—	—	—	—	—
19054	14.9	7.33	15.7	44.1	60.2	21.4	35.6	1497
19058	15.7	5.94	14.2	37.2	62.6	23.9	38.2	1094
19062	6.2	6.86	15.7	43.3	63.1	22.9	36.3	1399
19063	12.9	5.68	14.0	35.2	61.9	24.6	39.8	999
19066	7.1	6.01	15.7	40.3	67.0	26.1	39.0	1506
19069	—	—	—	—	—	—	—	—
19073	—	—	—	—	—	—	—	—
MEAN	10.8	6.39	15.2	40.1	62.9	23.8	37.8	1305
SD	3.15	0.532	0.90	3.02	2.04	1.25	1.22	207.2
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	WBC THSN/CU MM	RBC MILL/CU MM	HGB GRAMS/DL	HCT %	MCV CU MICRONS	MCH PICO GRAMS	MCHC %	PLT THSN/CU MM
GROUP: 5-F								
19001	15.1	5.90	14.3	37.3	63.2	24.2	38.3	1131
19006	7.6	6.33	15.4	39.0	61.6	24.3	39.5	1312
19011	6.4	6.46	15.7	40.5	62.7	24.3	38.8	1254
19020	4.2	7.49	16.1	46.8	62.5	21.5	34.4	1549
19022	5.4	6.79	16.0	43.0	63.4	23.6	37.2	1448
19025	7.3	6.47	15.1	39.7	61.3	23.3	38.0	1391
19027	12.3	6.69	15.9	42.2	63.1	23.8	37.7	1667
19028	10.2	5.76	13.8	35.8	62.2	24.0	38.5	1286
19030	8.1	6.62	15.6	41.4	62.6	23.6	37.7	1417
19031	12.3	5.72	14.7	38.4	67.1	25.7	38.3	1099
19032	—	—	—	—	—	—	—	—
19033	—	—	—	—	—	—	—	—
19049	—	—	—	—	—	—	—	—
19059	—	—	—	—	—	—	—	—
19070	—	—	—	—	—	—	—	—
MEAN	8.9	6.42	15.3	40.4	63.0	23.8	37.8	1355
SD	3.48	0.538	0.77	3.15	1.60	1.05	1.37	176.8
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	MPV CU MICRON	PT seconds	APTT seconds	NRBC COUNT	Lymphocyte THSN/CU MM	Segmented THSN/CU MM	Bands THSN/CU MM	Monocytes THSN/CU MM
GROUP: 1-M								
19109	8.0	13.2	13.2	0	9.7	2.0	0.0	1.1
19115	8.0	13.3	21.5	0	11.4	2.7	0.0	1.6
19116	7.2	13.7	22.4	0	11.6	3.0	0.0	0.3
19119	7.5	13.6	23.0	0	9.1	2.2	0.0	1.3
19122	8.2	13.1	19.8	0	14.1	1.5	0.0	0.2
19125	8.9	13.6	20.8	0	14.3	1.4	0.0	1.1
19131	8.2	13.2	19.8	0	13.1	2.7	0.0	1.6
19132	8.0	13.7	21.8	0	12.7	1.5	0.0	0.4
19134	8.4	13.2	23.9	0	11.0	3.5	0.0	0.5
19135	8.8	13.2	23.6	0	12.2	1.6	0.0	0.3
19143	—	—	—	—	—	—	—	—
19151	—	—	—	—	—	—	—	—
19157	—	—	—	—	—	—	—	—
19161	—	—	—	—	—	—	—	—
19167	—	—	—	—	—	—	—	—
MEAN	8.1	13.4	21.0	0	11.9	2.2	0.0	0.8
SD	0.52	0.24	3.09	0.0	1.72	0.73	0.00	0.56
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	MPV CU MICRON	PT seconds	APTT seconds	NRBC COUNT	Lymphocyte THSN/CU MM	Segmented THSN/CU MM	Bands THSN/CU MM	Monocytes THSN/CU MM
GROUP: 2-M								
19102	7.5	14.0	22.1	0	6.5	2.7	0.0	1.0
19106	7.6	14.0	22.0	0	12.1	2.9	0.0	1.4
19108	8.4	14.6	24.6	0	10.9	1.4	0.0	0.1
19110	8.4	14.2	26.2	0	10.0	2.0	0.0	0.7
19113	7.2	14.4	20.0	0	11.1	3.6	0.0	0.8
19120	7.6	14.4	17.5	0	13.4	3.1	0.0	1.5
19129	7.2	14.3	20.8	0	9.4	4.0	0.0	0.7
19136	8.8	14.2	19.3	0	8.6	1.4	0.0	0.3
19138	8.1	13.7	16.6	0	11.4	5.2	0.0	0.2
19139	7.8	14.5	31.4	0	16.3	2.5	0.0	0.2
19147	—	—	—	—	—	—	—	—
19153	—	—	—	—	—	—	—	—
19164	—	—	—	—	—	—	—	—
19165	—	—	—	—	—	—	—	—
19171	—	—	—	—	—	—	—	—
MEAN	7.9	14.2	22.1	0	11.0	2.9	0.0	0.7
SD	0.54	0.27	4.41	0.0	2.68	1.18	0.00	0.50
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	MPV CU MICRON	PT seconds	APTT seconds	NRBC COUNT	Lymphocyte THSN/CU MM	Segmented THSN/CU MM	Bands THSN/CU MM	Monocytes THSN/CU MM
GROUP: 3-M								
19101	8.0	13.9	18.3	0	10.1	2.1	0.0	0.5
19105	7.4	13.7	24.6	0	8.8	1.9	0.0	0.2
19107	8.0	13.6	22.0	0	9.8	0.6	0.1	1.5
19112	9.9	13.6	22.1	0	11.0	1.3	0.0	0.5
19114	8.3	13.5	19.8	0	7.8	2.7	0.0	0.6
19121	8.3	13.2	21.2	0	14.8	4.0	0.0	1.5
19123	8.1	13.7	18.1	0	10.4	3.4	0.0	0.1
19130	8.9	13.7	22.3	0	11.7	1.7	0.0	0.4
19137	7.8	13.4	20.6	0	10.6	1.1	0.0	0.2
19146	7.6	14.0	16.7	0	13.1	1.4	0.0	0.3
19155	—	—	—	—	—	—	—	—
19159	—	—	—	—	—	—	—	—
19172	—	—	—	—	—	—	—	—
19173	—	—	—	—	—	—	—	—
19174	—	—	—	—	—	—	—	—
MEAN	8.2	13.6	20.6	0	10.8	2.0	0.0	0.6
SD	0.72	0.23	2.38	0.0	2.02	1.06	0.03	0.51
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: MALE
STUDY NO: 060-069

Animal ID	MPV CU MICRON	PT seconds	APTT seconds	NRBC COUNT	Lymphocyte THSN/CU MM	Segmented THSN/CU MM	Bands THSN/CU MM	Monocytes THSN/CU MM
GROUP: 4-M								
19100	7.1	13.5	19.8	0	7.7	4.0	0.0	0.6
19103	8.2	14.6	26.3	0	16.4	2.3	0.0	1.7
19104	7.9	14.0	23.0	0	12.1	3.1	0.0	2.2
19118	8.3	13.9	21.4	0	9.4	1.4	0.0	0.5
19133	7.4	14.0	19.1	0	17.4	2.9	0.0	0.7
19141	8.4	13.6	21.5	0	12.7	3.7	0.0	0.5
19142	7.5	13.5	20.8	0	8.6	2.8	0.1	1.0
19144	9.3	13.9	21.5	0	15.9	2.7	0.0	0.6
19148	8.7	13.8	19.7	0	12.3	3.1	0.0	0.0
19150	9.3	13.1	18.6	0	8.3	2.4	0.0	0.2
19156	—	—	—	—	—	—	—	—
19160	—	—	—	—	—	—	—	—
19162	—	—	—	—	—	—	—	—
19163	—	—	—	—	—	—	—	—
19166	—	—	—	—	—	—	—	—
MEAN	8.2	13.8	21.2	0	12.1	2.8	0.0	0.8
SD	0.76	0.40	2.24	0.0	3.57	0.73	0.03	0.67
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	MPV CU MICRON	PT seconds	APTT seconds	NRBC COUNT	Lymphocyte THSN/CU MM	Segmented THSN/CU MM	Bands THSN/CU MM	Monocytes THSN/CU MM
GROUP: 5-M								
19111	7.7	13.9	23.6	0	13.0	1.4	0.0	0.6
19117	7.5	15.1	23.3	0	11.3	1.7	0.0	0.9
19124	7.3	13.8	20.8	0	10.2	0.3	0.0	0.2
19126	9.0	13.7	21.8	0	10.1	1.1	0.0	0.9
19127	8.8	14.1	20.7	0	8.0	2.4	0.0	0.2
19128	8.6	13.5	21.6	0	12.4	1.4	0.0	0.3
19140	8.0	13.9	19.6	0	12.2	2.1	0.0	0.2
19145	7.5	14.3	21.9	0	17.2	2.5	0.0	0.8
19149	7.8	13.5	19.5	0	16.1	2.2	0.0	0.0
19152	8.2	13.7	20.0	0	13.1	0.4	0.0	0.4
19154	—	—	—	—	—	—	—	—
19158	—	—	—	—	—	—	—	—
19168	—	—	—	—	—	—	—	—
19169	—	—	—	—	—	—	—	—
19170	—	—	—	—	—	—	—	—
MEAN	8.0	14.0	21.3	0	12.4	1.6	0.0	0.5
SD	0.59	0.47	1.43	0.0	2.75	0.78	0.00	0.33
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	MPV CU MICRON	PT seconds	APTT seconds	NRBC COUNT	Lymphocyte THSN/CU MM	Segmented THSN/CU MM	Bands THSN/CU MM	Monocytes THSN/CU MM
GROUP: 1-F								
19010	—	—	—	—	—	—	—	—
19012	7.7	13.9	26.6	0	12.6	2.7	0.0	0.5
19019	8.9	13.0	20.4	0	4.4	2.0	0.0	0.2
19021	7.8	13.8	24.2	0	5.7	1.4	0.0	0.0
19023	7.9	12.9	21.9	0	6.1	0.9	0.0	0.1
19041	9.1	13.4	19.3	0	5.0	2.9	0.0	0.1
19042	8.4	12.8	21.8	0	5.3	1.5	0.0	0.0
19044	8.4	12.8	18.5	0	7.3	3.1	0.0	0.1
19050	8.2	13.1	20.5	0	6.1	1.8	0.0	0.2
19053	8.1	13.3	22.5	0	4.7	1.8	0.0	0.0
19065	8.9	12.8	21.6	0	8.4	3.8	0.0	0.1
19068	—	—	—	—	—	—	—	—
19072	—	—	—	—	—	—	—	—
19074	—	—	—	—	—	—	—	—
19075	—	—	—	—	—	—	—	—
MEAN	8.3	13.2	21.7	0	6.6	2.2	0.0	0.1
SD	0.49	0.41	2.36	0.0	2.44	0.90	0.00	0.15
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: FEMALE
STUDY NO: 060-069

Animal ID	MPV CU MICRON	PT seconds	APTT seconds	NRBC COUNT	Lymphocyte THSN/CU MM	Segmented THSN/CU MM	Bands THSN/CU MM	Monocytes THSN/CU MM
GROUP: 2-F								
19004	9.6	13.3	27.5	0	5.8	2.0	0.0	0.1
19009	7.2	13.8	21.3	0	12.7	1.6	0.0	0.1
19016	8.8	13.3	29.2	0	13.6	3.1	0.0	0.0
19018	8.2	13.7	22.6	0	10.9	2.3	0.0	0.0
19026	8.4	12.8	20.3	0	7.7	1.4	0.0	0.0
19036	7.8	13.5	24.3	0	15.1	2.2	0.0	0.4
19037	8.1	13.3	20.0	0	11.0	13.7	0.0	1.6
19043	8.0	13.2	26.8	0	9.6	3.5	0.0	0.3
19047	6.9	13.5	25.3	0	6.2	4.6	0.0	0.2
19048	7.0	13.1	22.1	0	5.4	1.6	0.0	0.0
19052	--	--	--	--	--	--	--	--
19055	--	--	--	--	--	--	--	--
19061	--	--	--	--	--	--	--	--
19067	--	--	--	--	--	--	--	--
19071	--	--	--	--	--	--	--	--
MEAN	8.0	13.4	23.9	0	9.8	3.6	0.0	0.3
SD	0.84	0.29	3.19	0.0	3.44	3.69	0.00	0.49
N	10	10	10	10	10	10	10	10

(--) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	MPV CU MICRON	PT seconds	APTT seconds	NRBC COUNT	Lymphocyte THSN/CU MM	Segmented THSN/CU MM	Bands THSN/CU MM	Monocytes THSN/CU MM
GROUP: 3-F								
19003	7.2	12.9	22.7	0	6.5	4.0	0.0	0.3
19007	7.3	12.9	21.7	0	5.7	2.0	0.0	0.2
19008	9.3	12.8	22.6	0	5.0	1.9	0.0	0.0
19013	8.5	13.7	22.7	0	12.3	3.8	0.0	0.3
19014	—	—	—	—	—	—	—	—
19015	9.0	13.6	27.6	0	5.7	1.6	0.0	0.1
19017	7.8	13.3	21.9	0	9.8	2.6	0.0	0.1
19024	8.8	12.9	22.1	0	7.4	2.6	0.0	0.2
19029	7.4	13.3	24.4	0	10.3	2.1	0.0	0.0
19034	8.1	12.7	21.2	0	10.9	1.0	0.0	0.1
19038	—	—	—	—	—	—	—	—
19056	9.3	13.6	27.6	0	10.2	2.2	0.0	0.4
19057	—	—	—	—	—	—	—	—
19060	—	—	—	—	—	—	—	—
19064	—	—	—	—	—	—	—	—
MEAN	8.3	13.2	23.5	0	8.4	2.4	0.0	0.2
SD	0.82	0.37	2.35	0.0	2.60	0.93	0.00	0.13
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	MPV CU MICRON	PT seconds	APTT seconds	NRBC COUNT	Lymphocyte THSN/CU MM	Segmented THSN/CU MM	Bands THSN/CU MM	Monocytes THSN/CU MM
GROUP: 4-F								
19002	--	--	--	--	--	--	--	--
19005	7.8	13.1	21.4	0	7.7	1.6	0.0	0.1
19035	9.0	13.4	24.5	0	7.1	2.3	0.0	0.1
19039	7.8	13.4	23.7	0	9.6	2.8	0.0	0.3
19040	8.1	12.9	27.9	0	7.7	2.2	0.0	0.1
19045	7.6	13.0	21.9	0	5.4	3.8	0.3	0.2
19046	--	--	--	--	--	--	--	--
19051	--	--	--	--	--	--	--	--
19054	7.5	14.1	27.1	0	12.2	1.9	0.0	0.4
19058	7.5	13.5	25.7	0	11.5	3.9	0.0	0.2
19062	9.1	13.9	25.2	0	4.8	1.4	0.0	0.1
19063	8.5	14.0	26.2	0	9.8	2.6	0.0	0.3
19066	7.4	13.5	28.9	0	6.0	1.0	0.0	0.1
19069	--	--	--	--	--	--	--	--
19073	--	--	--	--	--	--	--	--
MEAN	8.0	13.5	25.3	0	8.2	2.4	0.0	0.2
SD	0.63	0.42	2.45	0.0	2.52	0.96	0.09	0.11
N	10	10	10	10	10	10	10	10

(--) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	MPV CU MICRON	PT seconds	APTT seconds	NRBC COUNT	Lymphocyte THSN/CU MM	Segmented THSN/CU MM	Bands THSN/CU MM	Monocytes THSN/CU MM
GROUP: 5-F								
19001	6.9	13.8	30.4	0	10.1	4.2	0.0	0.5
19006	9.2	12.8	22.1	0	4.6	2.7	0.0	0.2
19011	7.4	12.9	22.3	0	4.4	1.8	0.0	0.1
19020	7.0	16.8	27.6	2	2.2	1.9	0.0	0.1
19022	7.6	13.7	21.6	0	3.1	2.0	0.0	0.2
19025	8.3	13.5	25.3	0	5.2	2.0	0.0	0.1
19027	7.3	13.2	27.5	0	10.2	2.0	0.0	0.1
19028	8.1	13.6	22.2	0	7.1	2.8	0.0	0.3
19030	7.9	13.7	31.5	0	5.2	2.8	0.0	0.1
19031	6.8	13.5	21.6	0	8.2	3.7	0.0	0.0
19032	--	--	--	--	--	--	--	--
19033	--	--	--	--	--	--	--	--
19049	--	--	--	--	--	--	--	--
19059	--	--	--	--	--	--	--	--
19070	--	--	--	--	--	--	--	--
MEAN	7.7	13.8	25.2	0	6.0	2.6	0.0	0.2
SD	0.74	1.12	3.81	0.6	2.77	0.82	0.00	0.14
N	10	10	10	10	10	10	10	10

(--) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	Eosinophil THSN/CU MM	Basophils THSN/CU MM	Abnormal L THSN/CU MM	Other THSN/CU MM
GROUP: 1-M				
19109	0.7	0.0	0.0	0.0
19115	0.2	0.0	0.0	0.0
19116	0.2	0.0	0.0	0.0
19119	0.1	0.0	0.0	0.0
19122	0.2	0.0	0.5	0.0
19125	0.5	0.0	0.4	0.0
19131	0.2	0.0	0.2	0.0
19132	0.0	0.0	0.3	0.0
19134	0.2	0.0	0.0	0.0
19135	0.3	0.0	0.0	0.0
19143	—	—	—	—
19151	—	—	—	—
19157	—	—	—	—
19161	—	—	—	—
19167	—	—	—	—
MEAN	0.3	0.0	0.1	0.0
SD	0.20	0.00	0.20	0.00
N	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	Eosinophil THSN/CU MM	Basophils THSN/CU MM	Abnormal L THSN/CU MM	Other THSN/CU MM
GROUP: 2-M				
19102	0.3	0.0	0.3	0.0
19106	0.5	0.0	0.2	0.0
19108	0.0	0.0	0.3	0.0
19110	0.3	0.0	0.3	0.0
19113	0.2	0.0	0.0	0.0
19120	0.4	0.0	0.0	0.0
19129	0.6	0.0	0.0	0.0
19136	0.2	0.0	0.0	0.0
19138	0.5	0.0	0.0	0.0
19139	0.0	0.0	0.0	0.0
19147	—	—	—	—
19153	—	—	—	—
19164	—	—	—	—
19165	—	—	—	—
19171	—	—	—	—
MEAN	0.3	0.0	0.1	0.0
SD	0.21	0.00	0.14	0.00
N	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	Eosinophil THSN/CU MM	Basophils THSN/CU MM	Abnormal L THSN/CU MM	Other THSN/CU MM
GROUP: 3-M				
19101	0.3	0.0	0.1	0.0
19105	0.0	0.0	0.1	0.0
19107	0.5	0.0	0.0	0.0
19112	0.3	0.0	0.1	0.0
19114	0.1	0.0	0.0	0.0
19121	0.4	0.0	0.2	0.0
19123	0.0	0.0	0.1	0.0
19130	0.1	0.0	0.0	0.0
19137	0.2	0.0	0.0	0.0
19146	0.6	0.0	0.0	0.0
19155	—	—	—	—
19159	—	—	—	—
19172	—	—	—	—
19173	—	—	—	—
19174	—	—	—	—
MEAN	0.3	0.0	0.1	0.0
SD	0.21	0.00	0.07	0.00
N	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	Eosinophil THSN/CU MM	Basophils THSN/CU MM	Abnormal L THSN/CU MM	Other THSN/CU MM
GROUP: 4-M				
19100	0.1	0.0	0.1	0.0
19103	0.0	0.0	0.6	0.0
19104	0.4	0.0	0.4	0.0
19118	0.2	0.0	0.5	0.0
19133	0.9	0.0	0.2	0.0
19141	0.3	0.0	0.2	0.0
19142	0.1	0.0	0.1	0.0
19144	0.4	0.0	0.0	0.0
19148	0.2	0.0	0.0	0.0
19150	0.1	0.0	0.0	0.0
19156	—	—	—	—
19160	—	—	—	—
19162	—	—	—	—
19163	—	—	—	—
19166	—	—	—	—
MEAN	0.3	0.0	0.2	0.0
SD	0.26	0.00	0.22	0.00
N	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	Eosinophil THSN/CU MM	Basophils THSN/CU MM	Abnormal L THSN/CU MM	Other THSN/CU MM
GROUP: 5-M				
19111	0.2	0.0	0.5	0.0
19117	0.4	0.0	0.0	0.0
19124	0.1	0.0	0.0	0.0
19126	0.4	0.0	0.0	0.0
19127	0.1	0.0	0.2	0.0
19128	0.1	0.0	0.0	0.0
19140	0.3	0.0	0.5	0.0
19145	0.2	0.0	0.0	0.0
19149	0.0	0.0	0.0	0.0
19152	0.0	0.0	0.0	0.0
19154	—	—	—	—
19158	—	—	—	—
19168	—	—	—	—
19169	—	—	—	—
19170	—	—	—	—
MEAN	0.2	0.0	0.1	0.0
SD	0.15	0.00	0.21	0.00
N	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	Eosinophil THSN/CU MM	Basophils THSN/CU MM	Abnormal L THSN/CU MM	Other THSN/CU MM
GROUP: 1-F				
19010	—	—	—	—
19012	0.2	0.0	0.0	0.0
19019	0.0	0.0	0.0	0.0
19021	0.3	0.0	0.0	0.0
19023	0.1	0.0	0.1	0.0
19041	0.0	0.0	0.0	0.0
19042	0.0	0.0	0.0	0.0
19044	0.1	0.0	0.0	0.0
19050	0.1	0.0	0.0	0.0
19053	0.0	0.0	0.1	0.0
19065	0.1	0.0	0.1	0.0
19068	—	—	—	—
19072	—	—	—	—
19074	—	—	—	—
19075	—	—	—	—
MEAN	0.1	0.0	0.0	0.0
SD	0.10	0.00	0.05	0.00
N	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	Eosinophil THSN/CU MM	Basophils THSN/CU MM	Abnormal L THSN/CU MM	Other THSN/CU MM
GROUP: 2-F				
19004	0.0	0.0	0.0	0.0
19009	0.1	0.0	0.0	0.0
19016	0.3	0.0	0.0	0.0
19018	0.1	0.0	0.0	0.0
19026	0.0	0.0	0.0	0.0
19036	0.4	0.0	0.0	0.0
19037	0.0	0.0	0.0	0.0
19043	0.1	0.0	0.0	0.0
19047	0.1	0.0	0.0	0.0
19048	0.1	0.0	0.0	0.0
19052	—	—	—	—
19055	—	—	—	—
19061	—	—	—	—
19067	—	—	—	—
19071	—	—	—	—
MEAN	0.1	0.0	0.0	0.0
SD	0.13	0.00	0.00	0.00
N	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	Eosinophil THSN/CU MM	Basophils THSN/CU MM	Abnormal L THSN/CU MM	Other THSN/CU MM
GROUP: 3-F				
19003	0.1	0.0	0.1	0.0
19007	0.0	0.0	0.1	0.0
19008	0.0	0.0	0.1	0.0
19013	0.0	0.0	0.2	0.0
19014	—	—	—	—
19015	0.0	0.0	0.0	0.0
19017	0.4	0.0	0.0	0.0
19024	0.2	0.0	0.1	0.0
19029	0.1	0.0	0.0	0.0
19034	0.1	0.0	0.0	0.0
19038	—	—	—	—
19056	0.0	0.0	0.0	0.0
19057	—	—	—	—
19060	—	—	—	—
19064	—	—	—	—
MEAN	0.1	0.0	0.1	0.0
SD	0.13	0.00	0.07	0.00
N	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	Eosinophil THSN/CU MM	Basophils THSN/CU MM	Abnormal L THSN/CU MM	Other THSN/CU MM
GROUP: 4-F				
19002	—	—	—	—
19005	0.1	0.0	0.0	0.0
19035	0.0	0.0	0.1	0.0
19039	0.1	0.0	0.0	0.0
19040	0.0	0.0	0.0	0.0
19045	0.0	0.0	0.0	0.0
19046	—	—	—	—
19051	—	—	—	—
19054	0.0	0.0	0.3	0.0
19058	0.2	0.0	0.0	0.0
19062	0.0	0.0	0.0	0.0
19063	0.3	0.0	0.0	0.0
19066	0.0	0.0	0.1	0.0
19069	—	—	—	—
19073	—	—	—	—
MEAN	0.1	0.0	0.1	0.0
SD	0.11	0.00	0.10	0.00
N	10	10	10	10

(—) - Data Unavailable

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	Eosinophil THSN/CU MM	Basophils THSN/CU MM	Abnormal L THSN/CU MM	Other THSN/CU MM
GROUP: 5-F				
19001	0.3	0.0	0.0	0.0
19006	0.0	0.0	0.0	0.0
19011	0.0	0.0	0.1	0.0
19020	0.0	0.0	0.0	0.0
19022	0.1	0.0	0.0	0.0
19025	0.0	0.0	0.1	0.0
19027	0.0	0.0	0.0	0.0
19028	0.0	0.0	0.0	0.0
19030	0.0	0.0	0.1	0.0
19031	0.4	0.0	0.0	0.0
19032	--	--	--	--
19033	--	--	--	--
19049	--	--	--	--
19059	--	--	--	--
19070	--	--	--	--
MEAN	0.1	0.0	0.0	0.0
SD	0.15	0.00	0.05	0.00
N	10	10	10	10

(--) - Data Unavailable

LABCAT HE4.43

27-JUN-2002

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	MPV
UNITS:	THSN/CU MM	MILL/CU MM	GRAMS/DL	%	CU MICRONS	PICO GRAMS	%	THSN/CU MM	CU MICRON
Group: 1-M									
MEAN	15.3	7.51	16.5	43.5	57.9	22.0	38.0	1179	8.1
SD	1.63	0.648	1.16	3.48	1.89	0.87	0.93	130.9	0.52
N	10	10	10	10	10	10	10	10	10
Group: 2-M									
MEAN	14.9	7.33	15.9	42.2	57.7	21.8	37.7	1131	7.9
SD	3.03	0.396	0.42	1.57	2.27	1.13	1.15	183.7	0.54
N	10	10	10	10	10	10	10	10	10
Group: 3-M									
MEAN	13.8	7.32	15.7	42.0	57.4	21.5	37.5	1115	8.2
SD	2.84	0.441	0.59	2.22	1.78	0.75	0.79	149.2	0.72
N	10	10	10	10	10	10	10	10	10
Group: 4-M									
MEAN	16.2	6.93*	15.4**	40.2*	57.9	22.2	38.4	1104	8.2
SD	3.97	0.305	0.67	2.29	1.15	0.45	0.80	91.4	0.76
N	10	10	10	10	10	10	10	10	10
Group: 5-M									
MEAN	14.7	6.99*	15.6*	40.7*	58.3	22.3	38.3	1148	8.0
SD	3.07	0.442	0.81	1.81	1.37	0.56	0.70	159.9	0.59
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05 **-Significant Difference from Control P < .01

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: MALE
STUDY NO: 060-069

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	PT	APTT	NRBC	Lymphocyte	Segmented	Bands	Monocytes	Eosinophil	Basophils
UNITS:	seconds	seconds	COUNT	THSN/CU MM	THSN/CU MM	THSN/CU MM	THSN/CU MM	THSN/CU MM	THSN/CU MM
Group: 1-M									
MEAN	13.4	21.0	0	11.9	2.2	0.0	0.8	0.3	0.0
SD	0.24	3.09	0.0	1.72	0.73	0.00	0.56	0.20	0.00
N	10	10	10	10	10	10	10	10	10
Group: 2-M									
MEAN	14.2**	22.1	0	11.0	2.9	0.0	0.7	0.3	0.0
SD	0.27	4.41	0.0	2.68	1.18	0.00	0.50	0.21	0.00
N	10	10	10	10	10	10	10	10	10
Group: 3-M									
MEAN	13.6	20.6	0	10.8	2.0	0.0	0.6	0.3	0.0
SD	0.23	2.38	0.0	2.02	1.06	0.03	0.51	0.21	0.00
N	10	10	10	10	10	10	10	10	10
Group: 4-M									
MEAN	13.8*	21.2	0	12.1	2.8	0.0	0.8	0.3	0.0
SD	0.40	2.24	0.0	3.57	0.73	0.03	0.67	0.26	0.00
N	10	10	10	10	10	10	10	10	10
Group: 5-M									
MEAN	14.0**	21.3	0	12.4	1.6	0.0	0.5	0.2	0.0
SD	0.47	1.43	0.0	2.75	0.78	0.00	0.33	0.15	0.00
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05 **-Significant Difference from Control P < .01

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	Abnormal L	Other
UNITS:	THSN/CU MM	THSN/CU MM
Group: 1-M		
MEAN	0.1	0.0
SD	0.20	0.00
N	10	10
Group: 2-M		
MEAN	0.1	0.0
SD	0.14	0.00
N	10	10
Group: 3-M		
MEAN	0.1	0.0
SD	0.07	0.00
N	10	10
Group: 4-M		
MEAN	0.2	0.0
SD	0.22	0.00
N	10	10
Group: 5-M		
MEAN	0.1	0.0
SD	0.21	0.00
N	10	10

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: MALE
STUDY NO: 060-069

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

White Blood Count

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	153.1	15.3	1.63						TREATMENTS	4	32.41	8.10
2-M	10	149.2	14.9	3.03	0.29	11.9	18.7	11.1	19.5	ERROR	45	406.23	9.03
3-M	10	137.6	13.8	2.84	1.15	11.9	18.7	11.1	19.5				
4-M	10	162.2	16.2	3.97	0.68	11.9	18.7	11.1	19.5	TOTAL	49	438.64	
5-M	10	146.6	14.7	3.07	0.48	11.9	18.7	11.1	19.5				

F Ratio = 0.90 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 20.065 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Red Blood Count

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	75.13	7.51	0.648						TREATMENTS	4	2.44	0.61
2-M	10	73.26	7.33	0.396	0.91	7.00	8.03	6.87	8.16	ERROR	45	9.54	0.21
3-M	10	73.19	7.32	0.441	0.94	7.00	8.03	6.87	8.16				
4-M	10	69.30	6.93	0.305	2.83	7.00	8.03*	6.87	8.16	TOTAL	49	11.98	
5-M	10	69.89	6.99	0.442	2.54	7.00	8.03*	6.87	8.16				

F Ratio = 2.88 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 6.381 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Hemoglobin

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	165.2	16.5	1.16						TREATMENTS	4	7.40	1.85
2-M	10	159.1	15.9	0.42	1.77	15.7	17.4	15.4	17.6	ERROR	45	26.78	0.60
3-M	10	157.3	15.7	0.59	2.29	15.7	17.4	15.4	17.6				
4-M	10	154.0	15.4	0.67	3.25	15.7	17.4*	15.4	17.6**	TOTAL	49	34.18	
5-M	10	155.8	15.6	0.81	2.72	15.7	17.4*	15.4	17.6				

F Ratio = 3.11 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 4.874 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups
Source-Source of Variation
Treatments-between groups

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069
SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Hematocrit

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	434.6	43.5	3.48						TREATMENTS	4	68.54	17.13
2-M	10	422.2	42.2	1.57	1.17	40.8	46.1	40.2	46.8	ERROR	45	252.15	5.60
3-M	10	419.9	42.0	2.22	1.39	40.8	46.1	40.2	46.8				
4-M	10	401.7	40.2	2.29	3.11	40.8	46.1*	40.2	46.8	TOTAL	49	320.69	
5-M	10	406.7	40.7	1.81	2.64	40.8	46.1*	40.2	46.8				

F Ratio = 3.06 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 5.676 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Mean Corpuscular Volume

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	579.1	57.9	1.89						TREATMENTS	4	4.07	1.02
2-M	10	576.9	57.7	2.27	0.28	56.0	59.9	55.5	60.3	ERROR	45	136.05	3.02
3-M	10	574.1	57.4	1.78	0.64	56.0	59.9	55.5	60.3				
4-M	10	579.4	57.9	1.15	0.04	56.0	59.9	55.5	60.3	TOTAL	49	140.12	
5-M	10	582.7	58.3	1.37	0.46	56.0	59.9	55.5	60.3				

F Ratio = 0.34 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 3.006 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Mean Corpuscular Hemoglobin

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	220.3	22.0	0.87						TREATMENTS	4	4.40	1.10
2-M	10	217.6	21.8	1.13	0.76	21.1	22.9	20.9	23.1	ERROR	45	28.04	0.62
3-M	10	215.2	21.5	0.75	1.44	21.1	22.9	20.9	23.1				
4-M	10	222.3	22.2	0.45	0.57	21.1	22.9	20.9	23.1	TOTAL	49	32.44	
5-M	10	223.2	22.3	0.56	0.82	21.1	22.9	20.9	23.1				

F Ratio = 1.77 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 3.593 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

*-Significant Difference from Control P < .05
Error-within groups
Source-Source of Variation
Treatments-between groups

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: MALE
STUDY NO: 060-069

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Mean Corpuscular Hem. Conc.

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	380.4	38.0	0.93						TREATMENTS	4	5.72	1.43
2-M	10	377.2	37.7	1.15	0.80	37.0	39.0	36.8	39.3	ERROR	45	35.64	0.79
3-M	10	374.9	37.5	0.79	1.38	37.0	39.0	36.8	39.3				
4-M	10	383.7	38.4	0.80	0.83	37.0	39.0	36.8	39.3	TOTAL	49	41.36	
5-M	10	383.1	38.3	0.70	0.68	37.0	39.0	36.8	39.3				

F Ratio = 1.81 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 2.343 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Platelets

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	11790	1179	130.9						TREATMENTS	4	34523	8631
2-M	10	11305	1131	183.7	0.74	1015	1343	975	1383	ERROR	45	963815	21418
3-M	10	11154	1115	149.2	0.97	1015	1343	975	1383				
4-M	10	11044	1104	91.4	1.14	1015	1343	975	1383	TOTAL	49	998339	
5-M	10	11483	1148	159.9	0.47	1015	1343	975	1383				

F Ratio = 0.40 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 12.888 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

MEAN PLATELET VOLUME

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	81.2	8.1	0.52						TREATMENTS	4	0.90	0.23
2-M	10	78.6	7.9	0.54	0.92	7.4	8.8	7.2	9.0	ERROR	45	18.03	0.40
3-M	10	82.3	8.2	0.72	0.39	7.4	8.8	7.2	9.0				
4-M	10	82.1	8.2	0.76	0.32	7.4	8.8	7.2	9.0	TOTAL	49	18.94	
5-M	10	80.4	8.0	0.59	0.28	7.4	8.8	7.2	9.0				

F Ratio = 0.56 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 7.823 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Error-within groups Treatments-between groups
Source-Source of Variation

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: MALE
STUDY NO: 060-069

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Prothrombin

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	133.8	13.4	0.24						TREATMENTS	4	4.13	1.03
2-M	10	142.3	14.2	0.27	5.63	13.0	13.8*	12.9	13.9**	ERROR	45	5.13	0.11
3-M	10	136.3	13.6	0.23	1.66	13.0	13.8	12.9	13.9				
4-M	10	137.9	13.8	0.40	2.71	13.0	13.8*	12.9	13.9	TOTAL	49	9.26	
5-M	10	139.5	14.0	0.47	3.77	13.0	13.8*	12.9	13.9**				

F Ratio = 9.05 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 2.448 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Act. Part. Thromboplastin Time

1-M	10	209.8	21.0	3.09						TREATMENTS	4	11.75	2.94
2-M	10	220.5	22.1	4.41	0.83	17.7	24.2	17.0	25.0	ERROR	45	374.92	8.33
3-M	10	205.7	20.6	2.38	0.32	17.7	24.2	17.0	25.0				
4-M	10	211.7	21.2	2.24	0.15	17.7	24.2	17.0	25.0	TOTAL	49	386.66	
5-M	10	212.8	21.3	1.43	0.23	17.7	24.2	17.0	25.0				

F Ratio = 0.35 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 13.609 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Nucleated Red Cells

1-M	10	0	0	0.0						TREATMENTS	4	0.00000	0.00000
2-M	10	0	0	0.0	0.00	0	0	0	0	ERROR	45	0.00000	0.00000
3-M	10	0	0	0.0	0.00	0	0	0	0				
4-M	10	0	0	0.0	0.00	0	0	0	0	TOTAL	49	0.00000	
5-M	10	0	0	0.0	0.00	0	0	0	0				

F Ratio = 0.00 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069
SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Lymphocytes

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	119.2	11.9	1.72						TREATMENTS	4	19.27	4.82
2-M	10	109.7	11.0	2.68	0.81	9.0	14.9	8.3	15.6	ERROR	45	311.29	6.92
3-M	10	108.1	10.8	2.02	0.94	9.0	14.9	8.3	15.6				
4-M	10	120.8	12.1	3.57	0.14	9.0	14.9	8.3	15.6	TOTAL	49	330.56	
5-M	10	123.6	12.4	2.75	0.37	9.0	14.9	8.3	15.6				

F Ratio = 0.70 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 22.619 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Segmented Neutrophils

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	22.1	2.2	0.73						TREATMENTS	4	12.77	3.19
2-M	10	28.8	2.9	1.18	1.63	1.2	3.2	0.9	3.5	ERROR	45	37.87	0.84
3-M	10	20.2	2.0	1.06	0.46	1.2	3.2	0.9	3.5				
4-M	10	28.4	2.8	0.73	1.54	1.2	3.2	0.9	3.5	TOTAL	49	50.64	
5-M	10	15.5	1.6	0.78	1.61	1.2	3.2	0.9	3.5				

F Ratio = 3.79 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 39.885 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Bands

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	0.0	0.0	0.00						TREATMENTS	4	0.0012	0.0003
2-M	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0	ERROR	45	0.0180	0.0004
3-M	10	0.1	0.0	0.03	1.12	0.0	0.0	0.0	0.0				
4-M	10	0.1	0.0	0.03	1.12	0.0	0.0	0.0	0.0	TOTAL	49	0.0192	
5-M	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0				

F Ratio = 0.75 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 500.000 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Error-within groups
Source-Source of Variation
Treatments-between groups

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: MALE
STUDY NO: 060-069

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Monocytes

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	8.4	0.8	0.56						TREATMENTS	4	1.03	0.26
2-M	10	6.9	0.7	0.50	0.64	0.2	1.4	0.1	1.6	ERROR	45	12.43	0.28
3-M	10	5.8	0.6	0.51	1.11	0.2	1.4	0.1	1.6				
4-M	10	8.0	0.8	0.67	0.17	0.2	1.4	0.1	1.6	TOTAL	49	13.46	
5-M	10	4.5	0.5	0.33	1.66	0.2	1.4	0.1	1.6				

F Ratio = 0.93 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 78.222 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Eosinophils

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	2.6	0.3	0.20						TREATMENTS	4	0.08	0.02
2-M	10	3.0	0.3	0.21	0.43	0.0	0.5	0.0	0.5	ERROR	45	1.93	0.04
3-M	10	2.5	0.3	0.21	0.11	0.0	0.5	0.0	0.5				
4-M	10	2.7	0.3	0.26	0.11	0.0	0.5	0.0	0.5	TOTAL	49	2.00	
5-M	10	1.8	0.2	0.15	0.86	0.0	0.5	0.0	0.5				

F Ratio = 0.46 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 82.096 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Basophils

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	0.0	0.0	0.00						TREATMENTS	4	0.00000	0.00000
2-M	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0	ERROR	45	0.00000	0.00000
3-M	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0				
4-M	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0	TOTAL	49	0.00000	
5-M	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0				

F Ratio = 0.00 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Error-within groups Treatments-between groups
Source-Source of Variation

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069
SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Abnormal Lymphocytes

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	1.4	0.1	0.20						TREATMENTS	4	0.12	0.03
2-M	10	1.1	0.1	0.14	0.38	-.1	0.3	-.1	0.4	ERROR	45	1.40	0.03
3-M	10	0.6	0.1	0.07	1.01	-.1	0.3	-.1	0.4				
4-M	10	2.1	0.2	0.22	0.89	-.1	0.3	-.1	0.4	TOTAL	49	1.52	
5-M	10	1.2	0.1	0.21	0.25	-.1	0.3	-.1	0.4				

F Ratio = 0.95 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 137.898 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Other

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	0.0	0.0	0.00						TREATMENTS	4	0.00000	0.00000
2-M	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0	ERROR	45	0.00000	0.00000
3-M	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0				
4-M	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0	TOTAL	49	0.00000	
5-M	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0				

F Ratio = 0.00 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Error-within groups
Treatments-between groups
Source-Source of Variation

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069
SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	MPV
UNITS:	THSN/CU MM	MILL/CU MM	GRAMS/DL	%	CU MICRONS	PICO GRAMS	%	THSN/CU MM	CU MICRON
Group: 1-F									
MEAN	9.0	6.51	15.5	40.5	62.2	23.9	38.4	1419	8.3
SD	3.09	0.461	0.95	2.93	1.19	0.55	0.76	153.0	0.49
N	10	10	10	10	10	10	10	10	10
Group: 2-F									
MEAN	13.8*	6.22	15.0	39.3	63.3	24.2	38.3	1240	8.0
SD	5.73	0.423	0.77	2.72	2.01	0.76	0.94	208.1	0.84
N	10	10	10	10	10	10	10	10	10
Group: 3-F									
MEAN	11.1	6.40	15.2	39.5	61.8	23.9	38.7	1274	8.3
SD	2.98	0.554	0.91	3.24	1.50	0.88	1.29	226.3	0.82
N	10	10	10	10	10	10	10	10	10
Group: 4-F									
MEAN	10.8	6.39	15.2	40.1	62.9	23.8	37.8	1305	8.0
SD	3.15	0.532	0.90	3.02	2.04	1.25	1.22	207.2	0.63
N	10	10	10	10	10	10	10	10	10
Group: 5-F									
MEAN	8.9	6.42	15.3	40.4	63.0	23.8	37.8	1355	7.7
SD	3.48	0.538	0.77	3.15	1.60	1.05	1.37	176.8	0.74
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: FEMALE
STUDY NO: 060-069

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	PT	APTT	NRBC	Lymphocyte	Segmented	Bands	Monocytes	Eosinophil	Basophils
UNITS:	seconds	seconds	COUNT	THSN/CU MM	THSN/CU MM	THSN/CU MM	THSN/CU MM	THSN/CU MM	THSN/CU MM
Group: 1-F									
MEAN	13.2	21.7	0	6.6	2.2	0.0	0.1	0.1	0.0
SD	0.41	2.36	0.0	2.44	0.90	0.00	0.15	0.10	0.00
N	10	10	10	10	10	10	10	10	10
Group: 2-F									
MEAN	13.4	23.9	0	9.8*	3.6	0.0	0.3	0.1	0.0
SD	0.29	3.19	0.0	3.44	3.69	0.00	0.49	0.13	0.00
N	10	10	10	10	10	10	10	10	10
Group: 3-F									
MEAN	13.2	23.5	0	8.4	2.4	0.0	0.2	0.1	0.0
SD	0.37	2.35	0.0	2.60	0.93	0.00	0.13	0.13	0.00
N	10	10	10	10	10	10	10	10	10
Group: 4-F									
MEAN	13.5	25.3	0	8.2	2.4	0.0	0.2	0.1	0.0
SD	0.42	2.45	0.0	2.52	0.96	0.09	0.11	0.11	0.00
N	10	10	10	10	10	10	10	10	10
Group: 5-F									
MEAN	13.8	25.2	0	6.0	2.6	0.0	0.2	0.1	0.0
SD	1.12	3.81	0.6	2.77	0.82	0.00	0.14	0.15	0.00
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	Abnormal L	Other
UNITS:	THSN/CU MM	THSN/CU MM
Group: 1-F		
MEAN	0.0	0.0
SD	0.05	0.00
N	10	10
Group: 2-F		
MEAN	0.0	0.0
SD	0.00	0.00
N	10	10
Group: 3-F		
MEAN	0.1	0.0
SD	0.07	0.00
N	10	10
Group: 4-F		
MEAN	0.1	0.0
SD	0.10	0.00
N	10	10
Group: 5-F		
MEAN	0.0	0.0
SD	0.05	0.00
N	10	10

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: FEMALE
STUDY NO: 060-069

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

White Blood Count

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	89.9	9.0	3.09						TREATMENTS	4	158.42	39.61
2-F	10	137.8	13.8	5.73	2.80	4.7	13.3*	3.6	14.3	ERROR	45	659.12	14.65
3-F	10	110.7	11.1	2.98	1.22	4.7	13.3	3.6	14.3				
4-F	10	108.4	10.8	3.15	1.08	4.7	13.3	3.6	14.3	TOTAL	49	817.54	
5-F	10	88.9	8.9	3.48	0.06	4.7	13.3	3.6	14.3				

F Ratio = 2.70 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 35.721 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Red Blood Count

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	65.06	6.51	0.461						TREATMENTS	4	0.45	0.11
2-F	10	62.15	6.22	0.423	1.29	5.94	7.07	5.80	7.21	ERROR	45	11.44	0.25
3-F	10	63.96	6.40	0.554	0.49	5.94	7.07	5.80	7.21				
4-F	10	63.87	6.39	0.532	0.53	5.94	7.07	5.80	7.21	TOTAL	49	11.89	
5-F	10	64.23	6.42	0.538	0.37	5.94	7.07	5.80	7.21				

F Ratio = 0.44 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 7.896 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Hemoglobin

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	155.4	15.5	0.95						TREATMENTS	4	1.36	0.34
2-F	10	150.4	15.0	0.77	1.29	14.6	16.5	14.3	16.7	ERROR	45	33.62	0.75
3-F	10	152.4	15.2	0.91	0.78	14.6	16.5	14.3	16.7				
4-F	10	151.6	15.2	0.90	0.98	14.6	16.5	14.3	16.7	TOTAL	49	34.98	
5-F	10	152.6	15.3	0.77	0.72	14.6	16.5	14.3	16.7				

F Ratio = 0.46 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 5.669 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

*-Significant Difference from Control P < .05
Error-within groups

Source-Source of Variation
Treatments-between groups

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069
SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Hematocrit

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	404.9	40.5	2.93						TREATMENTS	4	11.01	2.75
2-F	10	393.4	39.3	2.72	0.85	37.1	43.9	36.3	44.7	ERROR	45	409.80	9.11
3-F	10	395.1	39.5	3.24	0.73	37.1	43.9	36.3	44.7				
4-F	10	401.4	40.1	3.02	0.26	37.1	43.9	36.3	44.7	TOTAL	49	420.81	
5-F	10	404.1	40.4	3.15	0.06	37.1	43.9	36.3	44.7				

F Ratio = 0.30 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 7.548 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Mean Corpuscular Volume

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	622.3	62.2	1.19						TREATMENTS	4	14.98	3.74
2-F	10	633.3	63.3	2.01	1.45	60.3	64.1	59.9	64.6	ERROR	45	129.67	2.88
3-F	10	618.2	61.8	1.50	0.54	60.3	64.1	59.9	64.6				
4-F	10	629.1	62.9	2.04	0.90	60.3	64.1	59.9	64.6	TOTAL	49	144.64	
5-F	10	629.7	63.0	1.60	0.97	60.3	64.1	59.9	64.6				

F Ratio = 1.30 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 2.709 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Mean Corpuscular Hemoglobin

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	239.0	23.9	0.55						TREATMENTS	4	1.28	0.32
2-F	10	242.4	24.2	0.76	0.82	22.9	24.9	22.6	25.2	ERROR	45	38.92	0.86
3-F	10	238.9	23.9	0.88	0.02	22.9	24.9	22.6	25.2				
4-F	10	237.9	23.8	1.25	0.26	22.9	24.9	22.6	25.2	TOTAL	49	40.21	
5-F	10	238.3	23.8	1.05	0.17	22.9	24.9	22.6	25.2				

F Ratio = 0.37 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 3.886 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Error-within groups
Source-Source of Variation
Treatments-between groups

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069
SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Mean Corpuscular Hem. Conc.

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	384.2	38.4	0.76						TREATMENTS	4	5.34	1.34
2-F	10	382.9	38.3	0.94	0.26	37.1	39.7	36.8	40.0	ERROR	45	58.25	1.29
3-F	10	386.6	38.7	1.29	0.47	37.1	39.7	36.8	40.0				
4-F	10	378.3	37.8	1.22	1.16	37.1	39.7	36.8	40.0	TOTAL	49	63.60	
5-F	10	378.4	37.8	1.37	1.14	37.1	39.7	36.8	40.0				

F Ratio = 1.03 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 2.978 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Platelets

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	14189	1419	153.0						TREATMENTS	4	198797	49699
2-F	10	12396	1240	208.1	2.05	1199	1639	1145	1692	ERROR	45	1729216	38427
3-F	10	12735	1274	226.3	1.66	1199	1639	1145	1692				
4-F	10	13048	1305	207.2	1.30	1199	1639	1145	1692	TOTAL	49	1928012	
5-F	10	13554	1355	176.8	0.72	1199	1639	1145	1692				

F Ratio = 1.29 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 14.868 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

MEAN PLATELET VOLUME

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	83.4	8.3	0.49						TREATMENTS	4	2.95	0.74
2-F	10	80.0	8.0	0.84	1.06	7.5	9.1	7.3	9.3	ERROR	45	23.11	0.51
3-F	10	82.7	8.3	0.82	0.22	7.5	9.1	7.3	9.3				
4-F	10	80.3	8.0	0.63	0.97	7.5	9.1	7.3	9.3	TOTAL	49	26.06	
5-F	10	76.5	7.7	0.74	2.15	7.5	9.1	7.3	9.3				

F Ratio = 1.44 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 8.894 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Error-within groups
Source-Source of Variation
Treatments-between groups

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069
SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Prothrombin

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	131.8	13.2	0.41						TREATMENTS	4	2.32	0.58
2-F	10	133.5	13.4	0.29	0.63	12.5	13.9	12.3	14.0	ERROR	45	16.48	0.37
3-F	10	131.7	13.2	0.37	0.04	12.5	13.9	12.3	14.0				
4-F	10	134.8	13.5	0.42	1.11	12.5	13.9	12.3	14.0	TOTAL	49	18.80	
5-F	10	137.5	13.8	1.12	2.11	12.5	13.9	12.3	14.0				

F Ratio = 1.58 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 4.521 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Act. Part. Thromboplastin Time

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	217.3	21.7	2.36						TREATMENTS	4	84.50	21.13
2-F	10	239.4	23.9	3.19	1.71	18.5	25.0	17.7	25.8	ERROR	45	375.66	8.35
3-F	10	234.5	23.5	2.35	1.33	18.5	25.0	17.7	25.8				
4-F	10	252.5	25.3	2.45	2.72	18.5	25.0*	17.7	25.8	TOTAL	49	460.17	
5-F	10	252.1	25.2	3.81	2.69	18.5	25.0*	17.7	25.8				

F Ratio = 2.53 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 12.081 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Nucleated Red Cells

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	0	0	0.0						TREATMENTS	4	0.32	0.08
2-F	10	0	0	0.0	0.00	0	0	0	0	ERROR	45	3.60	0.08
3-F	10	0	0	0.0	0.00	0	0	0	0				
4-F	10	0	0	0.0	0.00	0	0	0	0	TOTAL	49	3.92	
5-F	10	2	0	0.6	1.58	0	0	0	0				

F Ratio = 1.00 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 707.107 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

*-Significant Difference from Control P < .05
Error-within groups
Source-Source of Variation
Treatments-between groups

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Lymphocytes

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-F	10	65.6	6.6	2.44					
2-F	10	98.0	9.8	3.44	2.61	3.4	9.7*	2.7	10.4
3-F	10	83.8	8.4	2.60	1.46	3.4	9.7	2.7	10.4
4-F	10	81.8	8.2	2.52	1.30	3.4	9.7	2.7	10.4
5-F	10	60.3	6.0	2.77	0.43	3.4	9.7	2.7	10.4

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	4	91.51	22.88
ERROR	45	347.60	7.72
TOTAL	49	439.11	

F Ratio = 2.96 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 35.677 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Segmented Neutrophils

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-F	10	21.9	2.2	0.90					
2-F	10	36.0	3.6	3.69	1.72	0.1	4.3	-.4	4.8
3-F	10	23.8	2.4	0.93	0.23	0.1	4.3	-.4	4.8
4-F	10	23.5	2.4	0.96	0.19	0.1	4.3	-.4	4.8
5-F	10	25.9	2.6	0.82	0.49	0.1	4.3	-.4	4.8

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	4	12.77	3.19
ERROR	45	151.70	3.37
TOTAL	49	164.47	

F Ratio = 0.95 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 70.025 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Bands

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-F	10	0.0	0.0	0.00					
2-F	10	0.0	0.0	0.00	0.00	0.0	0.0	-.1	0.1
3-F	10	0.0	0.0	0.00	0.00	0.0	0.0	-.1	0.1
4-F	10	0.3	0.0	0.09	1.58	0.0	0.0	-.1	0.1
5-F	10	0.0	0.0	0.00	0.00	0.0	0.0	-.1	0.1

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	4	0.0072	0.0018
ERROR	45	0.0810	0.0018
TOTAL	49	0.0882	

F Ratio = 1.00 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 707.107 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

*-Significant Difference from Control P < .05
Source-Source of Variation
Error-within groups
Treatments-between groups

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: FEMALE
STUDY NO: 060-069

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Monocytes

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	1.3	0.1	0.15						TREATMENTS	4	0.11	0.03
2-F	10	2.7	0.3	0.49	1.26	-.1	0.4	-.2	0.5	ERROR	45	2.79	0.06
3-F	10	1.7	0.2	0.13	0.36	-.1	0.4	-.2	0.5				
4-F	10	1.9	0.2	0.11	0.54	-.1	0.4	-.2	0.5	TOTAL	49	2.90	
5-F	10	1.7	0.2	0.14	0.36	-.1	0.4	-.2	0.5				

F Ratio = 0.43 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 133.942 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Eosinophils

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	0.9	0.1	0.10						TREATMENTS	4	0.014	0.004
2-F	10	1.2	0.1	0.13	0.54	0.0	0.2	-.1	0.3	ERROR	45	0.691	0.015
3-F	10	0.9	0.1	0.13	0.00	0.0	0.2	-.1	0.3				
4-F	10	0.7	0.1	0.11	0.36	0.0	0.2	-.1	0.3	TOTAL	49	0.705	
5-F	10	0.8	0.1	0.15	0.18	0.0	0.2	-.1	0.3				

F Ratio = 0.23 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 137.686 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Basophils

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	0.0	0.0	0.00						TREATMENTS	4	0.00000	0.00000
2-F	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0	ERROR	45	0.00000	0.00000
3-F	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0				
4-F	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0	TOTAL	49	0.00000	
5-F	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0				

F Ratio = 0.00 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Error-within groups
Source-Source of Variation
Treatments-between groups

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069
SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Abnormal Lymphocytes

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	0.3	0.0	0.05						TREATMENTS	4	0.021	0.005
2-F	10	0.0	0.0	0.00	1.09	0.0	0.1	-.1	0.1	ERROR	45	0.171	0.004
3-F	10	0.6	0.1	0.07	1.09	0.0	0.1	-.1	0.1				
4-F	10	0.5	0.1	0.10	0.73	0.0	0.1	-.1	0.1	TOTAL	49	0.192	
5-F	10	0.3	0.0	0.05	0.00	0.0	0.1	-.1	0.1				

F Ratio = 1.39 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 181.306 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Other

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	0.0	0.0	0.00						TREATMENTS	4	0.00000	0.00000
2-F	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0	ERROR	45	0.00000	0.00000
3-F	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0				
4-F	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0	TOTAL	49	0.00000	
5-F	10	0.0	0.0	0.00	0.00	0.0	0.0	0.0	0.0				

F Ratio = 0.00 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 0.000 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Error-within groups
Source-Source of Variation
Treatments-between groups

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 1-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19109	Nucleated Red Cells	0	
	Lymphocytes	72	9.7
	Segmented Neutrophils	15	2.0
	Bands	0	0.0
	Monocytes	8	1.1
	Eosinophils	5	0.7
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		13.5
19115	Nucleated Red Cells	0	
	Lymphocytes	72	11.4
	Segmented Neutrophils	17	2.7
	Bands	0	0.0
	Monocytes	10	1.6
	Eosinophils	1	0.2
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		15.9
19116	Nucleated Red Cells	0	
	Lymphocytes	77	11.6
	Segmented Neutrophils	20	3.0
	Bands	0	0.0
	Monocytes	2	0.3
	Eosinophils	1	0.2
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		15.1

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 1-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19119	Nucleated Red Cells	0	
	Lymphocytes	72	9.1
	Segmented Neutrophils	17	2.2
	Bands	0	0.0
	Monocytes	10	1.3
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		12.7
19122	Nucleated Red Cells	0	
	Lymphocytes	86	14.1
	Segmented Neutrophils	9	1.5
	Bands	0	0.0
	Monocytes	1	0.2
	Eosinophils	1	0.2
	Basophils	0	0.0
	Abnormal Lymphocytes	3	0.5
	Other	0	0.0
	WBC		16.4
19125	Nucleated Red Cells	0	
	Lymphocytes	81	14.3
	Segmented Neutrophils	8	1.4
	Bands	0	0.0
	Monocytes	6	1.1
	Eosinophils	3	0.5
	Basophils	0	0.0
	Abnormal Lymphocytes	2	0.4
	Other	0	0.0
	WBC		17.6

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 1-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19131	Nucleated Red Cells	0	
	Lymphocytes	74	13.1
	Segmented Neutrophils	15	2.7
	Bands	0	0.0
	Monocytes	9	1.6
	Eosinophils	1	0.2
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.2
	Other	0	0.0
	WBC		17.7
19132	Nucleated Red Cells	0	
	Lymphocytes	85	12.7
	Segmented Neutrophils	10	1.5
	Bands	0	0.0
	Monocytes	3	0.4
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	2	0.3
	Other	0	0.0
	WBC		14.9
19134	Nucleated Red Cells	0	
	Lymphocytes	73	11.0
	Segmented Neutrophils	23	3.5
	Bands	0	0.0
	Monocytes	3	0.5
	Eosinophils	1	0.2
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		15.0

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 1-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19135	Nucleated Red Cells	0	
	Lymphocytes	85	12.2
	Segmented Neutrophils	11	1.6
	Bands	0	0.0
	Monocytes	2	0.3
	Eosinophils	2	0.3
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		14.3
19143	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19151	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--

(--) - Data Unavailable

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 1-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19157	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—
19161	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—
19167	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—

(—) - Data Unavailable

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 2-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19102	Nucleated Red Cells	0	
	Lymphocytes	60	6.5
	Segmented Neutrophils	25	2.7
	Bands	0	0.0
	Monocytes	9	1.0
	Eosinophils	3	0.3
	Basophils	0	0.0
	Abnormal Lymphocytes	3	0.3
	Other	0	0.0
	WBC		10.9
19106	Nucleated Red Cells	0	
	Lymphocytes	71	12.1
	Segmented Neutrophils	17	2.9
	Bands	0	0.0
	Monocytes	8	1.4
	Eosinophils	3	0.5
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.2
	Other	0	0.0
	WBC		17.0
19108	Nucleated Red Cells	0	
	Lymphocytes	86	10.9
	Segmented Neutrophils	11	1.4
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	2	0.3
	Other	0	0.0
	WBC		12.7

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 2-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19110	Nucleated Red Cells	0	
	Lymphocytes	76	10.0
	Segmented Neutrophils	15	2.0
	Bands	0	0.0
	Monocytes	5	0.7
	Eosinophils	2	0.3
	Basophils	0	0.0
	Abnormal Lymphocytes	2	0.3
	Other	0	0.0
	WBC		13.1
19113	Nucleated Red Cells	0	
	Lymphocytes	71	11.1
	Segmented Neutrophils	23	3.6
	Bands	0	0.0
	Monocytes	5	0.8
	Eosinophils	1	0.2
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		15.7
19120	Nucleated Red Cells	0	
	Lymphocytes	73	13.4
	Segmented Neutrophils	17	3.1
	Bands	0	0.0
	Monocytes	8	1.5
	Eosinophils	2	0.4
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		18.4

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 2-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19129	Nucleated Red Cells	0	
	Lymphocytes	64	9.4
	Segmented Neutrophils	27	4.0
	Bands	0	0.0
	Monocytes	5	0.7
	Eosinophils	4	0.6
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		14.7
19136	Nucleated Red Cells	0	
	Lymphocytes	82	8.6
	Segmented Neutrophils	13	1.4
	Bands	0	0.0
	Monocytes	3	0.3
	Eosinophils	2	0.2
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		10.5
19138	Nucleated Red Cells	0	
	Lymphocytes	66	11.4
	Segmented Neutrophils	30	5.2
	Bands	0	0.0
	Monocytes	1	0.2
	Eosinophils	3	0.5
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		17.2

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 2-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19139	Nucleated Red Cells	0	
	Lymphocytes	86	16.3
	Segmented Neutrophils	13	2.5
	Bands	0	0.0
	Monocytes	1	0.2
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		19.0
19147	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—
19153	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—

(—) - Data Unavailable

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 2-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19164	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19165	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19171	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 3-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19101	Nucleated Red Cells	0	
	Lymphocytes	77	10.1
	Segmented Neutrophils	16	2.1
	Bands	0	0.0
	Monocytes	4	0.5
	Eosinophils	2	0.3
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		13.1
19105	Nucleated Red Cells	0	
	Lymphocytes	80	8.8
	Segmented Neutrophils	17	1.9
	Bands	0	0.0
	Monocytes	2	0.2
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		11.0
19107	Nucleated Red Cells	0	
	Lymphocytes	78	9.8
	Segmented Neutrophils	5	0.6
	Bands	1	0.1
	Monocytes	12	1.5
	Eosinophils	4	0.5
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		12.5

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 3-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19112	Nucleated Red Cells	0	
	Lymphocytes	83	11.0
	Segmented Neutrophils	10	1.3
	Bands	0	0.0
	Monocytes	4	0.5
	Eosinophils	2	0.3
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		13.3
19114	Nucleated Red Cells	0	
	Lymphocytes	70	7.8
	Segmented Neutrophils	24	2.7
	Bands	0	0.0
	Monocytes	5	0.6
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		11.2
19121	Nucleated Red Cells	0	
	Lymphocytes	71	14.8
	Segmented Neutrophils	19	4.0
	Bands	0	0.0
	Monocytes	7	1.5
	Eosinophils	2	0.4
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.2
	Other	0	0.0
	WBC		20.9

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 3-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19123	Nucleated Red Cells	0	
	Lymphocytes	74	10.4
	Segmented Neutrophils	24	3.4
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		14.1
19130	Nucleated Red Cells	0	
	Lymphocytes	84	11.7
	Segmented Neutrophils	12	1.7
	Bands	0	0.0
	Monocytes	3	0.4
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		13.9
19137	Nucleated Red Cells	0	
	Lymphocytes	87	10.6
	Segmented Neutrophils	9	1.1
	Bands	0	0.0
	Monocytes	2	0.2
	Eosinophils	2	0.2
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		12.2

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 3-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19146	Nucleated Red Cells	0	
	Lymphocytes	85	13.1
	Segmented Neutrophils	9	1.4
	Bands	0	0.0
	Monocytes	2	0.3
	Eosinophils	4	0.6
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		15.4
19155	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—
19159	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 3-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19172	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—
19173	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—
19174	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 4-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19100	Nucleated Red Cells	0	
	Lymphocytes	61	7.7
	Segmented Neutrophils	32	4.0
	Bands	0	0.0
	Monocytes	5	0.6
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		12.6
19103	Nucleated Red Cells	0	
	Lymphocytes	78	16.4
	Segmented Neutrophils	11	2.3
	Bands	0	0.0
	Monocytes	8	1.7
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	3	0.6
	Other	0	0.0
	WBC		21.0
19104	Nucleated Red Cells	0	
	Lymphocytes	67	12.1
	Segmented Neutrophils	17	3.1
	Bands	0	0.0
	Monocytes	12	2.2
	Eosinophils	2	0.4
	Basophils	0	0.0
	Abnormal Lymphocytes	2	0.4
	Other	0	0.0
	WBC		18.1

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 4-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19118	Nucleated Red Cells	0	
	Lymphocytes	78	9.4
	Segmented Neutrophils	12	1.4
	Bands	0	0.0
	Monocytes	4	0.5
	Eosinophils	2	0.2
	Basophils	0	0.0
	Abnormal Lymphocytes	4	0.5
	Other	0	0.0
	WBC		12.0
19133	Nucleated Red Cells	0	
	Lymphocytes	79	17.4
	Segmented Neutrophils	13	2.9
	Bands	0	0.0
	Monocytes	3	0.7
	Eosinophils	4	0.9
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.2
	Other	0	0.0
	WBC		22.0
19141	Nucleated Red Cells	0	
	Lymphocytes	73	12.7
	Segmented Neutrophils	21	3.7
	Bands	0	0.0
	Monocytes	3	0.5
	Eosinophils	2	0.3
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.2
	Other	0	0.0
	WBC		17.4

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 4-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19142	Nucleated Red Cells	0	
	Lymphocytes	67	8.6
	Segmented Neutrophils	22	2.8
	Bands	1	0.1
	Monocytes	8	1.0
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		12.8
19144	Nucleated Red Cells	0	
	Lymphocytes	81	15.9
	Segmented Neutrophils	14	2.7
	Bands	0	0.0
	Monocytes	3	0.6
	Eosinophils	2	0.4
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		19.6
19148	Nucleated Red Cells	0	
	Lymphocytes	79	12.3
	Segmented Neutrophils	20	3.1
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	1	0.2
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		15.6

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 4-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19150	Nucleated Red Cells	0	
	Lymphocytes	75	8.3
	Segmented Neutrophils	22	2.4
	Bands	0	0.0
	Monocytes	2	0.2
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		11.1
19156	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19160	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 4-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19162	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19163	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19166	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 5-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19111	Nucleated Red Cells	0	
	Lymphocytes	83	13.0
	Segmented Neutrophils	9	1.4
	Bands	0	0.0
	Monocytes	4	0.6
	Eosinophils	1	0.2
	Basophils	0	0.0
	Abnormal Lymphocytes	3	0.5
	Other	0	0.0
	WBC		15.7
19117	Nucleated Red Cells	0	
	Lymphocytes	79	11.3
	Segmented Neutrophils	12	1.7
	Bands	0	0.0
	Monocytes	6	0.9
	Eosinophils	3	0.4
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		14.3
19124	Nucleated Red Cells	0	
	Lymphocytes	94	10.2
	Segmented Neutrophils	3	0.3
	Bands	0	0.0
	Monocytes	2	0.2
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		10.8

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 5-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19126	Nucleated Red Cells	0	
	Lymphocytes	81	10.1
	Segmented Neutrophils	9	1.1
	Bands	0	0.0
	Monocytes	7	0.9
	Eosinophils	3	0.4
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		12.5
19127	Nucleated Red Cells	0	
	Lymphocytes	73	8.0
	Segmented Neutrophils	22	2.4
	Bands	0	0.0
	Monocytes	2	0.2
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	2	0.2
	Other	0	0.0
	WBC		11.0
19128	Nucleated Red Cells	0	
	Lymphocytes	87	12.4
	Segmented Neutrophils	10	1.4
	Bands	0	0.0
	Monocytes	2	0.3
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		14.2

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 5-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19140	Nucleated Red Cells	0	
	Lymphocytes	80	12.2
	Segmented Neutrophils	14	2.1
	Bands	0	0.0
	Monocytes	1	0.2
	Eosinophils	2	0.3
	Basophils	0	0.0
	Abnormal Lymphocytes	3	0.5
	Other	0	0.0
	WBC		15.2
19145	Nucleated Red Cells	0	
	Lymphocytes	83	17.2
	Segmented Neutrophils	12	2.5
	Bands	0	0.0
	Monocytes	4	0.8
	Eosinophils	1	0.2
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		20.7
19149	Nucleated Red Cells	0	
	Lymphocytes	88	16.1
	Segmented Neutrophils	12	2.2
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		18.3

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 5-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19152	Nucleated Red Cells	0	
	Lymphocytes	94	13.1
	Segmented Neutrophils	3	0.4
	Bands	0	0.0
	Monocytes	3	0.4
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		13.9
19154	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19158	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 5-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19168	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—
19169	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—
19170	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 1-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19010	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19012	Nucleated Red Cells	0	
	Lymphocytes	79	12.6
	Segmented Neutrophils	17	2.7
	Bands	0	0.0
	Monocytes	3	0.5
	Eosinophils	1	0.2
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		15.9
19019	Nucleated Red Cells	0	
	Lymphocytes	66	4.4
	Segmented Neutrophils	31	2.0
	Bands	0	0.0
	Monocytes	3	0.2
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		6.6

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 1-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19021	Nucleated Red Cells	0	
	Lymphocytes	77	5.7
	Segmented Neutrophils	19	1.4
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	4	0.3
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		7.4
19023	Nucleated Red Cells	0	
	Lymphocytes	83	6.1
	Segmented Neutrophils	12	0.9
	Bands	0	0.0
	Monocytes	2	0.1
	Eosinophils	2	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		7.3
19041	Nucleated Red Cells	0	
	Lymphocytes	63	5.0
	Segmented Neutrophils	36	2.9
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		8.0

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 1-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19042	Nucleated Red Cells	0	
	Lymphocytes	78	5.3
	Segmented Neutrophils	22	1.5
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		6.8
19044	Nucleated Red Cells	0	
	Lymphocytes	69	7.3
	Segmented Neutrophils	29	3.1
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		10.6
19050	Nucleated Red Cells	0	
	Lymphocytes	74	6.1
	Segmented Neutrophils	22	1.8
	Bands	0	0.0
	Monocytes	3	0.2
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		8.2

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 1-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19053	Nucleated Red Cells	0	
	Lymphocytes	71	4.7
	Segmented Neutrophils	28	1.8
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		6.6
19065	Nucleated Red Cells	0	
	Lymphocytes	67	8.4
	Segmented Neutrophils	30	3.8
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		12.5
19068	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 1-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19072	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19074	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19075	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 2-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19004	Nucleated Red Cells	0	
	Lymphocytes	74	5.8
	Segmented Neutrophils	25	2.0
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		7.8
19009	Nucleated Red Cells	0	
	Lymphocytes	87	12.7
	Segmented Neutrophils	11	1.6
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		14.6
19016	Nucleated Red Cells	0	
	Lymphocytes	80	13.6
	Segmented Neutrophils	18	3.1
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	2	0.3
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		17.0

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 2-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19018	Nucleated Red Cells	0	
	Lymphocytes	82	10.9
	Segmented Neutrophils	17	2.3
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		13.3
19026	Nucleated Red Cells	0	
	Lymphocytes	85	7.7
	Segmented Neutrophils	15	1.4
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		9.1
19036	Nucleated Red Cells	0	
	Lymphocytes	84	15.1
	Segmented Neutrophils	12	2.2
	Bands	0	0.0
	Monocytes	2	0.4
	Eosinophils	2	0.4
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		18.0

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 2-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19037	Nucleated Red Cells	0	
	Lymphocytes	42	11.0
	Segmented Neutrophils	52	13.7
	Bands	0	0.0
	Monocytes	6	1.6
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		26.3
19043	Nucleated Red Cells	0	
	Lymphocytes	71	9.6
	Segmented Neutrophils	26	3.5
	Bands	0	0.0
	Monocytes	2	0.3
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		13.5
19047	Nucleated Red Cells	0	
	Lymphocytes	56	6.2
	Segmented Neutrophils	41	4.6
	Bands	0	0.0
	Monocytes	2	0.2
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		11.1

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 2-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19048	Nucleated Red Cells	0	
	Lymphocytes	76	5.4
	Segmented Neutrophils	23	1.6
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		7.1
19052	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—
19055	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 2-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19061	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19067	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19071	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 3-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19003	Nucleated Red Cells	0	
	Lymphocytes	59	6.5
	Segmented Neutrophils	36	4.0
	Bands	0	0.0
	Monocytes	3	0.3
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		11.1
19007	Nucleated Red Cells	0	
	Lymphocytes	72	5.7
	Segmented Neutrophils	25	2.0
	Bands	0	0.0
	Monocytes	2	0.2
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		7.9
19008	Nucleated Red Cells	0	
	Lymphocytes	72	5.0
	Segmented Neutrophils	27	1.9
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		7.0

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 3-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19013	Nucleated Red Cells	0	
	Lymphocytes	74	12.3
	Segmented Neutrophils	23	3.8
	Bands	0	0.0
	Monocytes	2	0.3
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.2
	Other	0	0.0
	WBC		16.6
19014	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19015	Nucleated Red Cells	0	
	Lymphocytes	77	5.7
	Segmented Neutrophils	22	1.6
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		7.4

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 3-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19017	Nucleated Red Cells	0	
	Lymphocytes	76	9.8
	Segmented Neutrophils	20	2.6
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	3	0.4
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		12.9
19024	Nucleated Red Cells	0	
	Lymphocytes	70	7.4
	Segmented Neutrophils	25	2.6
	Bands	0	0.0
	Monocytes	2	0.2
	Eosinophils	2	0.2
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		10.5
19029	Nucleated Red Cells	0	
	Lymphocytes	82	10.3
	Segmented Neutrophils	17	2.1
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		12.5

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 3-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19034	Nucleated Red Cells	0	
	Lymphocytes	90	10.9
	Segmented Neutrophils	8	1.0
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		12.1
19038	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—
19056	Nucleated Red Cells	0	
	Lymphocytes	80	10.2
	Segmented Neutrophils	17	2.2
	Bands	0	0.0
	Monocytes	3	0.4
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		12.7

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 3-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19057	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19060	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19064	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 4-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19002	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19005	Nucleated Red Cells	0	
	Lymphocytes	81	7.7
	Segmented Neutrophils	17	1.6
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		9.5
19035	Nucleated Red Cells	0	
	Lymphocytes	74	7.1
	Segmented Neutrophils	24	2.3
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		9.6

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 4-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19039	Nucleated Red Cells	0	
	Lymphocytes	75	9.6
	Segmented Neutrophils	22	2.8
	Bands	0	0.0
	Monocytes	2	0.3
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		12.8
19040	Nucleated Red Cells	0	
	Lymphocytes	77	7.7
	Segmented Neutrophils	22	2.2
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		10.0
19045	Nucleated Red Cells	0	
	Lymphocytes	56	5.4
	Segmented Neutrophils	39	3.8
	Bands	3	0.3
	Monocytes	2	0.2
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		9.7

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 4-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19046	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—
19051	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—
19054	Nucleated Red Cells	0	
	Lymphocytes	82	12.2
	Segmented Neutrophils	13	1.9
	Bands	0	0.0
	Monocytes	3	0.4
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	2	0.3
	Other	0	0.0
	WBC		14.9

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 4-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19058	Nucleated Red Cells	0	
	Lymphocytes	73	11.5
	Segmented Neutrophils	25	3.9
	Bands	0	0.0
	Monocytes	1	0.2
	Eosinophils	1	0.2
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		15.7
19062	Nucleated Red Cells	0	
	Lymphocytes	77	4.8
	Segmented Neutrophils	22	1.4
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		6.2
19063	Nucleated Red Cells	0	
	Lymphocytes	76	9.8
	Segmented Neutrophils	20	2.6
	Bands	0	0.0
	Monocytes	2	0.3
	Eosinophils	2	0.3
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		12.9

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 4-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19066	Nucleated Red Cells	0	
	Lymphocytes	84	6.0
	Segmented Neutrophils	14	1.0
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		7.1
19069	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—
19073	Nucleated Red Cells	0	
	Lymphocytes	0	—
	Segmented Neutrophils	0	—
	Bands	0	—
	Monocytes	0	—
	Eosinophils	0	—
	Basophils	0	—
	Abnormal Lymphocytes	0	—
	Other	0	—
	WBC		—

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 5-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19001	Nucleated Red Cells	0	
	Lymphocytes	67	10.1
	Segmented Neutrophils	28	4.2
	Bands	0	0.0
	Monocytes	3	0.5
	Eosinophils	2	0.3
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		15.1
19006	Nucleated Red Cells	0	
	Lymphocytes	61	4.6
	Segmented Neutrophils	36	2.7
	Bands	0	0.0
	Monocytes	3	0.2
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		7.6
19011	Nucleated Red Cells	0	
	Lymphocytes	69	4.4
	Segmented Neutrophils	28	1.8
	Bands	0	0.0
	Monocytes	2	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		6.4

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 5-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19020	Nucleated Red Cells	2	
	Lymphocytes	52	2.2
	Segmented Neutrophils	46	1.9
	Bands	0	0.0
	Monocytes	2	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		4.2
19022	Nucleated Red Cells	0	
	Lymphocytes	58	3.1
	Segmented Neutrophils	37	2.0
	Bands	0	0.0
	Monocytes	3	0.2
	Eosinophils	2	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		5.4
19025	Nucleated Red Cells	0	
	Lymphocytes	71	5.2
	Segmented Neutrophils	27	2.0
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		7.3

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 5-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19027	Nucleated Red Cells	0	
	Lymphocytes	83	10.2
	Segmented Neutrophils	16	2.0
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		12.3
19028	Nucleated Red Cells	0	
	Lymphocytes	70	7.1
	Segmented Neutrophils	27	2.8
	Bands	0	0.0
	Monocytes	3	0.3
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		10.2
19030	Nucleated Red Cells	0	
	Lymphocytes	64	5.2
	Segmented Neutrophils	34	2.8
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		8.1

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 5-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19031	Nucleated Red Cells	0	
	Lymphocytes	67	8.2
	Segmented Neutrophils	30	3.7
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	3	0.4
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		12.3
19032	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19033	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--

(--) - Data Unavailable

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: ARGUS 418-028
STUDY NO: 060-069 GROUP: 5-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
19049	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19059	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--
19070	Nucleated Red Cells	0	
	Lymphocytes	0	--
	Segmented Neutrophils	0	--
	Bands	0	--
	Monocytes	0	--
	Eosinophils	0	--
	Basophils	0	--
	Abnormal Lymphocytes	0	--
	Other	0	--
	WBC		--

(--) - Data Unavailable

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	TP g/dL	ALB g/dL	GLU mg/dL	CHOL mg/dL	T-BIL mg/dL	BUN mg/dL	CREAT mg/dL	CK U/L
GROUP: 1-M								
19109	5.9	3.9	164	46	0.1	16	0.3	263
19115	6.5	4.4	165	62	0.2	19	0.4	164
19116	5.8	4.0	119	61	0.2	16	0.3	330
19119	6.0	4.1	134	44	0.1	14	0.3	105
19122	6.2	4.3	140	62	0.1	15	0.3	177
19125	6.5	4.3	169	56	0.3	15	0.4	260
19131	6.5	4.2	128	59	0.1	18	0.3	385
19132	6.1	4.3	141	51	0.1	15	0.3	250
19134	6.3	4.3	140	56	0.2	15	0.3	722
19135	7.0	4.7	153	72	0.2	15	0.3	221
19143	--	--	--	--	--	--	--	--
19151	--	--	--	--	--	--	--	--
19157	--	--	--	--	--	--	--	--
19161	--	--	--	--	--	--	--	--
19167	--	--	--	--	--	--	--	--
MEAN	6.3	4.3	145	57	0.2	16	0.3	288
SD	0.36	0.22	16.8	8.3	0.07	1.5	0.04	172.6
N	10	10	10	10	10	10	10	10

(--) - Data Unavailable

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	TP g/dL	ALB g/dL	GLU mg/dL	CHOL mg/dL	T-BIL mg/dL	BUN mg/dL	CREAT mg/dL	CK U/L
GROUP: 2-M								
19102	6.1	4.1	172	40	0.2	16	0.3	169
19106	6.2	4.0	166	44	0.1	17	0.3	151
19108	5.8	3.9	152	38	0.1	15	0.3	235
19110	6.1	4.1	104	33	0.1	16	0.3	307
19113	5.6	3.9	157	30	0.1	16	0.3	133
19120	6.5	4.3	115	28	0.2	17	0.4	350
19129	5.7	3.9	149	33	0.1	17	0.3	292
19136	6.2	4.3	123	52	0.1	17	0.3	134
19138	6.3	4.4	108	60	0.2	15	0.4	478
19139	6.1	4.2	165	55	0.2	16	0.4	213
19147	—	—	—	—	—	—	—	—
19153	—	—	—	—	—	—	—	—
19164	—	—	—	—	—	—	—	—
19165	—	—	—	—	—	—	—	—
19171	—	—	—	—	—	—	—	—
MEAN	6.1	4.1	141	41	0.1	16	0.3	246
SD	0.28	0.19	26.0	11.1	0.05	0.8	0.05	111.5
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

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27-JUN-2002

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	TP g/dL	ALB g/dL	GLU mg/dL	CHOL mg/dL	T-BIL mg/dL	BUN mg/dL	CREAT mg/dL	CK U/L
GROUP: 3-M								
19101	6.2 H	4.0 H	304 H	27 H	0.3 H	18 H	0.4 H	129 H
19105	6.1	4.3	254	52	0.1	16	0.3	118
19107	5.8	4.1	198	50	0.1	15	0.3	132
19112	6.3	4.3	137	46	0.1	12	0.3	286
19114	6.3	4.3	142	65	0.1	16	0.3	250
19121	6.6	4.4	121	45	0.1	18	0.4	289
19123	6.2	4.4	156	46	0.1	17	0.2	329
19130	5.7	4.1	149	34	0.1	17	0.3	480
19137	6.7	4.4	158	59	0.1	17	0.3	200
19146	6.6	4.4	204	35	0.1	16	0.3	175
19155	—	—	—	—	—	—	—	—
19159	—	—	—	—	—	—	—	—
19172	—	—	—	—	—	—	—	—
19173	—	—	—	—	—	—	—	—
19174	—	—	—	—	—	—	—	—
MEAN	6.3	4.3	182	46	0.1	16	0.3	239
SD	0.33	0.15	58.2	11.6	0.06	1.8	0.06	112.9
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

H - Hemolyzed

LABCAT CC4.43

27-JUN-2002

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	TP g/dL	ALB g/dL	GLU mg/dL	CHOL mg/dL	T-BIL mg/dL	BUN mg/dL	CREAT mg/dL	CK U/L
GROUP: 4-M								
19100	6.0	4.0	175	42	0.1	16	0.3	111
19103	5.7	4.0	202	28	0.1	20	0.3	145
19104	5.9	4.1	167	42	0.1	16	0.3	196
19118	6.0	4.2	131	39	0.1	20	0.4	187
19133	6.3	4.4	179	49	0.1	17	0.3	146
19141	6.2	4.3	147	70	0.2	16	0.3	182
19142	6.6	4.4	132	56	0.2	17	0.3	270
19144	6.2	4.1	130	29	0.1	18	0.3	242
19148	6.5	4.4	175	42	0.1	16	0.3	267
19150	6.4	4.4	181	30	0.2	18	0.3	218
19156	—	—	—	—	—	—	—	—
19160	—	—	—	—	—	—	—	—
19162	—	—	—	—	—	—	—	—
19163	—	—	—	—	—	—	—	—
19166	—	—	—	—	—	—	—	—
MEAN	6.2	4.2	162	43	0.1	17	0.3	196
SD	0.28	0.17	25.2	13.1	0.05	1.6	0.03	53.5
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

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27-JUN-2002

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	TP g/dL	ALB g/dL	GLU mg/dL	CHOL mg/dL	T-BIL mg/dL	BUN mg/dL	CREAT mg/dL	CK U/L
GROUP: 5-M								
19111	6.6 H	4.6 H	173 H	38 H	0.2 H	26 H	0.4 H	211 H
19117	6.1 H	4.3 H	177 H	37 H	0.3 H	23 H	0.3 H	269 H
19124	6.6	4.8	226	25	0.1	20	0.4	94
19126	6.4	4.6	165	29	0.1	20	0.3	156
19127	6.6	4.6	156	47	0.2	22	0.3	379
19128	6.5	4.8	181	35	0.2	21	0.4	472
19140	6.0	4.3	110	24	0.2	18	0.3	304
19145	6.4	4.5	134	27	0.2	19	0.3	239
19149	6.3	4.5	195	38	0.2	19	0.3	175
19152	5.8	4.2	132	31	0.2	19	0.3	128
19154	—	—	—	—	—	—	—	—
19158	—	—	—	—	—	—	—	—
19168	—	—	—	—	—	—	—	—
19169	—	—	—	—	—	—	—	—
19170	—	—	—	—	—	—	—	—
MEAN	6.3	4.5	165	33	0.2	21	0.3	243
SD	0.28	0.20	33.7	7.2	0.06	2.4	0.05	117.4
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

H - Hemolyzed

LABCAT CC4.43

27-JUN-2002

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	TP g/dL	ALB g/dL	GLU mg/dL	CHOL mg/dL	T-BIL mg/dL	BUN mg/dL	CREAT mg/dL	CK U/L
GROUP: 1-F								
19010	--	--	--	--	--	--	--	--
19012	5.4	3.7	149	63	0.2	32	0.4	166
19019	6.3	4.3	139	92	0.1	29	0.3	212
19021	7.1	4.9	157	136	0.1	33	0.4	210
19023	6.1	4.3	156	85	0.2	26	0.4	222
19041	5.9	4.3	165	62	0.2	28	0.3	201
19042	6.3	4.3	155	77	0.1	25	0.4	178
19044	6.6	4.4	144	93	0.3	27	0.4	332
19050	5.8	3.9	184	78	0.2	34	0.3	198
19053	5.5	3.7	108	43	0.1	28	0.3	123
19065	5.7	3.5	163	40	0.1	19	0.3	175
19068	--	--	--	--	--	--	--	--
19072	--	--	--	--	--	--	--	--
19074	--	--	--	--	--	--	--	--
19075	--	--	--	--	--	--	--	--
MEAN	6.1	4.1	152	77	0.2	28	0.4	202
SD	0.52	0.42	19.8	27.8	0.07	4.4	0.05	54.1
N	10	10	10	10	10	10	10	10

(--) - Data Unavailable

LABCAT CC4.43

27-JUN-2002

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	TP g/dL	ALB g/dL	GLU mg/dL	CHOL mg/dL	T-BIL mg/dL	BUN mg/dL	CREAT mg/dL	CK U/L
GROUP: 2-F								
19004	5.9	4.3	178	56	0.2	20	0.3	144
19009	5.7	3.9	166	62	0.2	26	0.4	311
19016	5.5	4.2	173	83	0.2	26	0.3	237
19018	5.6	4.2	152	77	0.2	27	0.4	151
19026	5.5	3.9	170	85	0.1	32	0.3	208
19036	5.9	4.2	203	84	0.2	22	0.4	228
19037	5.0	3.5	153	54	0.2	22	0.3	369
19043	5.7	3.8	149	92	0.2	21	0.4	269
19047	4.3	3.3	135	57	0.2	16	0.3	392
19048	5.9	4.2	142	73	0.2	29	0.4	186
19052	—	—	—	—	—	—	—	—
19055	—	—	—	—	—	—	—	—
19061	—	—	—	—	—	—	—	—
19067	—	—	—	—	—	—	—	—
19071	—	—	—	—	—	—	—	—
MEAN	5.5	4.0	162	72	0.2	24	0.4	250
SD	0.50	0.34	20.0	14.0	0.03	4.7	0.05	85.6
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

LABCAT CC4.43.

27-JUN-2002

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	TP g/dL	ALB g/dL	GLU mg/dL	CHOL mg/dL	T-BIL mg/dL	BUN mg/dL	CREAT mg/dL	CK U/L
GROUP: 3-F								
19003	5.6	3.9	179	54	0.1	36	0.3	199
19007	5.3	3.8	121	45	0.1	41	0.3	159
19008	5.7	4.0	171	56	0.1	20	0.3	206
19013	5.8	4.1	146	59	0.2	24	0.4	160
19014	—	—	—	—	—	—	—	—
19015	5.6	3.7	155	61	0.2	28	0.3	212
19017	5.8	4.1	164	87	0.2	22	0.4	190
19024	6.7	4.5	140	96	0.2	33	0.4	215
19029	5.8	4.0	142	79	0.2	26	0.3	212
19034	6.4	4.3	151	105	0.1	23	0.4	169
19038	—	—	—	—	—	—	—	—
19056	6.1	4.2	179	63	0.1	28	0.3	197
19057	—	—	—	—	—	—	—	—
19060	—	—	—	—	—	—	—	—
19064	—	—	—	—	—	—	—	—
MEAN	5.9	4.1	155	71	0.2	28	0.3	192
SD	0.41	0.24	18.7	20.0	0.05	6.7	0.05	21.7
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

LABCAT CC4.43

27-JUN-2002

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	TP g/dL	ALB g/dL	GLU mg/dL	CHOL mg/dL	T-BIL mg/dL	BUN mg/dL	CREAT mg/dL	CK U/L
GROUP: 4-F								
19002	—	—	—	—	—	—	—	—
19005	6.1	4.3	167	70	0.2	30	0.4	259
19035	5.7	4.0	161	47	0.1	27	0.4	193
19039	5.5	4.0	163	71	0.2	26	0.4	160
19040	5.8	3.9	127	63	0.1	20	0.3	233
19045	5.6	3.7	160	91	0.2	25	0.5	398
19046	—	—	—	—	—	—	—	—
19051	—	—	—	—	—	—	—	—
19054	6.3	4.5	129	41	0.1	25	0.4	124
19058	5.6	3.9	150	64	0.1	20	0.3	267
19062	6.0	4.4	127	49	0.1	34	0.3	176
19063	5.2	3.6	145	62	0.1	23	0.4	172
19066	5.9	4.1	132	63	0.1	22	0.2	147
19069	—	—	—	—	—	—	—	—
19073	—	—	—	—	—	—	—	—
MEAN	5.8	4.0	146	62	0.1	25	0.4	213
SD	0.32	0.29	16.2	14.2	0.05	4.4	0.08	80.4
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069
SEX: FEMALE

Animal ID	TP g/dL	ALB g/dL	GLU mg/dL	CHOL mg/dL	T-BIL mg/dL	BUN mg/dL	CREAT mg/dL	CK U/L
GROUP: 5-F								
19001	5.5	4.0	165	55	0.1	23	0.3	341
19006	5.7	4.0	119	58	0.1	19	0.3	373
19011	5.8	4.3	154	48	0.1	29	0.4	149
19020	5.6	3.5	53	33	0.2	73	0.2	438
19022	5.8	4.1	132	60	0.1	25	0.3	186
19025	5.8	3.7	133	49	0.1	28	0.4	143
19027	5.5	3.8	152	71	0.1	27	0.3	252
19028	5.9	4.0	159	70	0.2	23	0.3	261
19030	6.3	4.5	180	58	0.1	26	0.3	168
19031	6.3	4.4	157	108	0.2	25	0.3	210
19032	—	—	—	—	—	—	—	—
19033	—	—	—	—	—	—	—	—
19049	—	—	—	—	—	—	—	—
19059	—	—	—	—	—	—	—	—
19070	—	—	—	—	—	—	—	—
MEAN	5.8	4.0	140	61	0.1	30	0.3	252
SD	0.29	0.31	35.5	19.8	0.05	15.4	0.06	101.6
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	ALT U/L	AST U/L	ALP U/L	CA mg/dL	PHOS mg/dL	TRIG mg/dL	NA mmol/L	K mmol/L
GROUP: 1-M								
19109	36	78	91	10.6	12.0	23	143	10.3
19115	38	77	77	11.8	11.6	48	146	10.5
19116	40	93	102	10.3	9.7	59	145	6.6
19119	33	83	112	10.8	7.9	43	147	4.6
19122	51	86	103	11.3	9.4	28	146	5.9
19125	49	113	115	10.6	8.7	65	145	5.5
19131	39	116	107	11.1	7.9	93	146	4.9
19132	42	80	98	11.1	9.8	45	146	6.2
19134	49	146	126	10.4	8.5	36	147	5.7
19135	43	85	119	11.4	9.2	76	148	5.5
19143	--	--	--	--	--	--	--	--
19151	--	--	--	--	--	--	--	--
19157	--	--	--	--	--	--	--	--
19161	--	--	--	--	--	--	--	--
19167	--	--	--	--	--	--	--	--
MEAN	42	96	105	10.9	9.5	52	146	6.6
SD	6.0	22.4	14.3	0.48	1.40	21.8	1.4	2.10
N	10	10	10	10	10	10	10	10

(--) - Data Unavailable

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	ALT U/L	AST U/L	ALP U/L	CA mg/dL	PHOS mg/dL	TRIG mg/dL	NA mmol/L	K mmol/L
GROUP: 2-M								
19102	37	84	101	10.5	10.3	26	145	6.8
19106	38	77	70	11.6	12.0	60	144	8.0
19108	37	81	99	10.3	9.1	62	145	6.0
19110	57	116	141	10.3	8.9	44	146	5.4
19113	40	91	130	11.2	8.9	43	147	5.2
19120	46	111	91	10.7	9.3	29	146	5.5
19129	48	104	99	10.6	9.3	27	145	6.2
19136	34	80	88	10.7	8.8	78	144	6.9
19138	261	382	199	10.3	7.8	57	147	5.5
19139	33	87	95	11.1	9.3	43	148	5.5
19147	—	—	—	—	—	—	—	—
19153	—	—	—	—	—	—	—	—
19164	—	—	—	—	—	—	—	—
19165	—	—	—	—	—	—	—	—
19171	—	—	—	—	—	—	—	—
MEAN	63	121	111	10.7	9.4	47	146	6.1
SD	69.9	92.6	36.9	0.44	1.11	17.2	1.3	0.89
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	ALT U/L	AST U/L	ALP U/L	CA mg/dL	PHOS mg/dL	TRIG mg/dL	NA mmol/L	K mmol/L
GROUP: 3-M								
19101	60 H	124 H	101 H	11.5 H	10.4 H	20 H	143 H	8.9 H
19105	35	70	107	11.5	9.5	56	147	5.6
19107	35	82	97	11.5	15.6	34	148	8.4
19112	45	99	92	10.2	8.8	51	147	6.5
19114	141	197	108	10.8	9.9	35	145	7.0
19121	42	92	88	10.7	9.0	56	147	5.5
19123	101	171	80	11.2	9.4	21	146	6.1
19130	55	140	124	10.7	9.4	34	148	5.4
19137	44	102	108	11.3	8.3	22	146	5.7
19146	42	94	96	11.3	8.8	35	148	5.4
19155	—	—	—	—	—	—	—	—
19159	—	—	—	—	—	—	—	—
19172	—	—	—	—	—	—	—	—
19173	—	—	—	—	—	—	—	—
19174	—	—	—	—	—	—	—	—
MEAN	60	117	100	11.1	9.9	36	147	6.5
SD	34.4	40.9	12.4	0.44	2.09	13.8	1.6	1.27
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

H - Hemolyzed

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	ALT U/L	AST U/L	ALP U/L	CA mg/dL	PHOS mg/dL	TRIG mg/dL	NA mmol/L	K mmol/L
GROUP: 4-M								
19100	51	91	122	10.9	8.3	14	146	5.5
19103	37	83	76	11.0	13.3	19	147	6.6
19104	50	107	98	11.5	8.6	35	148	5.6
19118	439	887	154	10.8	9.8	23	148	6.9
19133	54	106	152	11.7	9.3	32	147	5.3
19141	46	91	93	10.7	10.7	113	145	6.4
19142	45	108	98	10.7	8.8	35	148	5.3
19144	48	119	124	11.2	9.8	30	147	5.5
19148	138	277	112	11.2	9.2	28	147	6.1
19150	46	107	123	11.3	9.3	32	146	6.5
19156	—	—	—	—	—	—	—	—
19160	—	—	—	—	—	—	—	—
19162	—	—	—	—	—	—	—	—
19163	—	—	—	—	—	—	—	—
19166	—	—	—	—	—	—	—	—
MEAN	95	198	115	11.1	9.7	36	147	6.0
SD	124.1	248.7	25.1	0.34	1.43	27.9	1.0	0.60
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

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27-JUN-2002

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	ALT U/L	AST U/L	ALP U/L	CA mg/dL	PHOS mg/dL	TRIG mg/dL	NA mmol/L	K mmol/L
GROUP: 5-M								
19111	38 H	86 H	115 H	11.7 H	12.9 H	7 H	142 H	10.7 H
19117	49 H	114 H	153 H	11.0 H	9.2 H	18 H	144 H	6.6 H
19124	33	76	204	11.9	9.8	2	147	5.5
19126	52	88	159	11.3	9.6	17	146	6.8
19127	49	104	182	11.8	11.1	21	147	7.1
19128	50	112	83	11.6	8.4	17	148	6.0
19140	40	95	169	10.9	9.0	23	148	5.5
19145	54	125	137	11.3	10.8	16	143	7.9
19149	40	87	140	12.0	10.2	16	147	7.1
19152	42	87	99	11.8	11.3	31	148	5.8
19154	—	—	—	—	—	—	—	—
19158	—	—	—	—	—	—	—	—
19168	—	—	—	—	—	—	—	—
19169	—	—	—	—	—	—	—	—
19170	—	—	—	—	—	—	—	—
MEAN	45	97	144	11.5	10.2	17	146	6.9
SD	7.0	15.6	37.5	0.38	1.33	8.0	2.2	1.55
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

H - Hemolyzed

LABCAT CC4.43

27-JUN-2002

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	ALT U/L	AST U/L	ALP U/L	CA mg/dL	PHOS mg/dL	TRIG mg/dL	NA mmol/L	K mmol/L
GROUP: 1-F								
19010	—	—	—	—	—	—	—	—
19012	144	123	217	10.5	6.8	70	143	6.0
19019	136	182	77	10.9	11.4	65	142	5.8
19021	177	167	345	11.8	8.3	47	159	5.4
19023	115	114	89	10.3	8.6	91	140	5.5
19041	142	154	171	9.9	9.2	46	140	6.2
19042	104	121	82	10.2	8.7	44	138	5.7
19044	153	149	100	11.7	8.3	70	149	4.8
19050	156	157	202	10.5	10.4	51	140	7.4
19053	87	123	92	9.6	7.6	40	140	5.7
19065	80	133	73	10.1	8.2	20	143	5.6
19068	—	—	—	—	—	—	—	—
19072	—	—	—	—	—	—	—	—
19074	—	—	—	—	—	—	—	—
19075	—	—	—	—	—	—	—	—
MEAN	129	142	145	10.6	8.8	54	143	5.8
SD	31.7	22.8	88.7	0.72	1.33	19.9	6.3	0.67
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	ALT U/L	AST U/L	ALP U/L	CA mg/dL	PHOS mg/dL	TRIG mg/dL	NA mmol/L	K mmol/L
GROUP: 2-F								
19004	97	133	80	11.3	8.4	45	139	5.3
19009	116	110	193	11.7	7.6	60	144	5.9
19016	150	141	242	11.6	7.8	68	147	5.4
19018	136	102	240	11.6	6.7	45	144	5.0
19026	145	142	183	10.7	9.6	45	141	5.0
19036	176	125	200	11.9	8.5	47	145	5.4
19037	115	181	48	10.9	5.3	43	143	5.2
19043	150	139	252	11.5	8.3	55	142	6.1
19047	117	131	46	10.0	5.3	55	142	5.6
19048	132	147	102	10.4	11.8	32	140	6.9
19052	—	—	—	—	—	—	—	—
19055	—	—	—	—	—	—	—	—
19061	—	—	—	—	—	—	—	—
19067	—	—	—	—	—	—	—	—
19071	—	—	—	—	—	—	—	—
MEAN	133	135	159	11.2	7.9	50	143	5.6
SD	23.0	21.6	81.7	0.63	1.94	10.2	2.4	0.58
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: FEMALE
STUDY NO: 060-069

Animal ID	ALT U/L	AST U/L	ALP U/L	CA mg/dL	PHOS mg/dL	TRIG mg/dL	NA mmol/L	K mmol/L
GROUP: 3-F								
19003	182	134	101	9.6	9.7	26	142	5.5
19007	90	113	60	9.3	9.2	17	139	5.8
19008	107	143	64	9.7	7.3	28	139	5.7
19013	137	125	154	10.6	5.6	65	144	5.4
19014	--	--	--	--	--	--	--	--
19015	178	137	97	9.3	14.3	116	141	4.9
19017	166	153	418	11.3	5.9	33	145	5.4
19024	121	139	60	11.3	11.5	46	142	6.0
19029	189	151	190	11.5	6.1	53	147	5.4
19034	124	140	108	11.0	10.5	72	141	5.5
19038	--	--	--	--	--	--	--	--
19056	130	133	111	10.7	9.9	34	142	5.9
19057	--	--	--	--	--	--	--	--
19060	--	--	--	--	--	--	--	--
19064	--	--	--	--	--	--	--	--
MEAN	142	137	136	10.4	9.0	49	142	5.6
SD	34.2	11.8	107.3	0.87	2.80	29.4	2.5	0.32
N	10	10	10	10	10	10	10	10

(--) - Data Unavailable

LABCAT CC4.43 27-JUN-2002

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	ALT U/L	AST U/L	ALP U/L	CA mg/dL	PHOS mg/dL	TRIG mg/dL	NA mmol/L	K mmol/L
GROUP: 4-F								
19002	—	—	—	—	—	—	—	—
19005	134	127	108	10.6	9.6	49	142	6.2
19035	115	128	107	10.0	9.2	67	142	5.5
19039	174	125	228	11.0	4.4	62	147	5.8
19040	134	132	90	9.7	10.8	77	138	7.0
19045	157	149	432	11.1	8.6	55	145	5.9
19046	—	—	—	—	—	—	—	—
19051	—	—	—	—	—	—	—	—
19054	94	107	70	10.0	10.1	28	139	6.5
19058	124	117	171	10.7	5.4	30	142	5.3
19062	98	129	102	10.3	10.7	18	144	7.1
19063	119	114	388	10.7	5.0	34	143	5.1
19066	116	112	88	10.3	13.2	33	142	6.6
19069	—	—	—	—	—	—	—	—
19073	—	—	—	—	—	—	—	—
MEAN	127	124	178	10.4	8.7	45	142	6.1
SD	24.7	12.1	131.0	0.46	2.88	19.5	2.6	0.70
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	ALT U/L	AST U/L	ALP U/L	CA mg/dL	PHOS mg/dL	TRIG mg/dL	NA mmol/L	K mmol/L
GROUP: 5-F								
19001	116	133	135	10.1	10.7	37	141	6.8
19006	160	149	71	10.1	9.0	49	138	6.8
19011	132	131	131	10.3	8.2	53	142	5.2
19020	151	263	138	9.8	13.7	7	143	6.9
19022	143	167	101	10.3	10.0	38	145	6.4
19025	113	141	142	9.6	9.4	30	142	5.4
19027	149	138	58	9.6	10.6	44	141	7.6
19028	179	127	122	12.0	9.2	45	147	5.1
19030	156	177	171	10.9	11.6	77	139	6.3
19031	148	138	211	11.6	8.6	57	143	5.1
19032	--	--	--	--	--	--	--	--
19033	--	--	--	--	--	--	--	--
19049	--	--	--	--	--	--	--	--
19059	--	--	--	--	--	--	--	--
19070	--	--	--	--	--	--	--	--
MEAN	145	156	128	10.4	10.1	44	142	6.2
SD	20.0	40.7	44.7	0.82	1.64	18.3	2.6	0.90
N	10	10	10	10	10	10	10	10

(—) - Data Unavailable

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	CL mmol/L	GLOB g/dL	A/G none
GROUP: 1-M			
19109	103	2.0	2.0
19115	100	2.1	2.1
19116	98	1.8	2.2
19119	100	1.9	2.2
19122	97	1.9	2.3
19125	96	2.2	2.0
19131	98	2.3	1.8
19132	99	1.8	2.4
19134	98	2.0	2.2
19135	93	2.3	2.0
19143	—	—	—
19151	—	—	—
19157	—	—	—
19161	—	—	—
19167	—	—	—
MEAN	98	2.0	2.1
SD	2.7	0.19	0.18
N	10	10	10

(—) - Data Unavailable

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	CL mmol/L	GLOB g/dL	A/G none
GROUP: 2-M			
19102	98	2.0	2.1
19106	99	2.2	1.8
19108	101	1.9	2.1
19110	101	2.0	2.1
19113	98	1.7	2.3
19120	96	2.2	2.0
19129	99	1.8	2.2
19136	99	1.9	2.3
19138	99	1.9	2.3
19139	98	1.9	2.2
19147	—	—	—
19153	—	—	—
19164	—	—	—
19165	—	—	—
19171	—	—	—
MEAN	99	2.0	2.1
SD	1.5	0.16	0.16
N	10	10	10

(—) - Data Unavailable

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	CL mmol/L	GLOB g/dL	A/G none
GROUP: 3-M			
19101	101 H	2.2 H	1.8 H
19105	96	1.8	2.4
19107	105	1.7	2.4
19112	100	2.0	2.2
19114	99	2.0	2.2
19121	99	2.2	2.0
19123	100	1.8	2.4
19130	100	1.6	2.6
19137	98	2.3	1.9
19146	99	2.2	2.0
19155	—	—	—
19159	—	—	—
19172	—	—	—
19173	—	—	—
19174	—	—	—
MEAN	100	2.0	2.2
SD	2.3	0.24	0.26
N	10	10	10

(—) - Data Unavailable

H - Hemolyzed

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	CL mmol/L	GLOB g/dL	A/G none
GROUP: 4-M			
19100	104	2.0	2.0
19103	104	1.7	2.4
19104	100	1.8	2.3
19118	103	1.8	2.3
19133	98	1.9	2.3
19141	99	1.9	2.3
19142	96	2.2	2.0
19144	99	2.1	2.0
19148	98	2.1	2.1
19150	99	2.0	2.2
19156	—	—	—
19160	—	—	—
19162	—	—	—
19163	—	—	—
19166	—	—	—
MEAN	100	2.0	2.2
SD	2.7	0.16	0.15
N	10	10	10

(—) - Data Unavailable

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

Animal ID	CL mmol/L	GLOB g/dL	A/G none
GROUP: 5-M			
19111	101 H	2.0 H	2.3 H
19117	101 H	1.8 H	2.4 H
19124	99	1.8	2.7
19126	100	1.8	2.6
19127	101	2.0	2.3
19128	98	1.7	2.8
19140	101	1.7	2.5
19145	98	1.9	2.4
19149	100	1.8	2.5
19152	99	1.6	2.6
19154	—	—	—
19158	—	—	—
19168	—	—	—
19169	—	—	—
19170	—	—	—
MEAN	100	1.8	2.5
SD	1.2	0.13	0.17
N	10	10	10

(—) - Data Unavailable

H - Hemolyzed

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	CL mmol/L	GLOB g/dL	A/G none
GROUP: 1-F			
19010	—	—	—
19012	96	1.7	2.2
19019	92	2.0	2.2
19021	100	2.2	2.2
19023	91	1.8	2.4
19041	93	1.6	2.7
19042	92	2.0	2.2
19044	96	2.2	2.0
19050	99	1.9	2.1
19053	99	1.8	2.1
19065	98	2.2	1.6
19068	—	—	—
19072	—	—	—
19074	—	—	—
19075	—	—	—
MEAN	96	1.9	2.2
SD	3.4	0.22	0.28
N	10	10	10

(—) - Data Unavailable

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27-JUN-2002

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	CL mmol/L	GLOB g/dL	A/G none
GROUP: 2-F			
19004	89	1.6	2.7
19009	93	1.8	2.2
19016	98	1.3	3.2
19018	97	1.4	3.0
19026	94	1.6	2.4
19036	95	1.7	2.5
19037	96	1.5	2.3
19043	91	1.9	2.0
19047	93	1.0	3.3
19048	95	1.7	2.5
19052	—	—	—
19055	—	—	—
19061	—	—	—
19067	—	—	—
19071	—	—	—
MEAN	94	1.6	2.6
SD	2.7	0.26	0.43
N	10	10	10

(—) - Data Unavailable

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	CL mmol/L	GLOB g/dL	A/G none
GROUP: 3-F			
19003	92	1.7	2.3
19007	97	1.5	2.5
19008	96	1.7	2.4
19013	97	1.7	2.4
19014	—	—	—
19015	92	1.9	1.9
19017	99	1.7	2.4
19024	94	2.2	2.0
19029	101	1.8	2.2
19034	88	2.1	2.0
19038	—	—	—
19056	93	1.9	2.2
19057	—	—	—
19060	—	—	—
19064	—	—	—
MEAN	95	1.8	2.2
SD	3.8	0.21	0.21
N	10	10	10

(—) - Data Unavailable

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	CL mmol/L	GLOB g/dL	A/G none
GROUP: 4-F			
19002	—	—	—
19005	90	1.8	2.4
19035	96	1.7	2.4
19039	101	1.5	2.7
19040	91	1.9	2.1
19045	97	1.9	1.9
19046	—	—	—
19051	—	—	—
19054	94	1.8	2.5
19058	97	1.7	2.3
19062	98	1.6	2.8
19063	97	1.6	2.3
19066	93	1.8	2.3
19069	—	—	—
19073	—	—	—
MEAN	95	1.7	2.4
SD	3.4	0.13	0.26
N	10	10	10

(—) - Data Unavailable

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

Animal ID	CL mmol/L	GLOB g/dL	A/G none
GROUP: 5-F			
19001	91	1.5	2.7
19006	93	1.7	2.4
19011	92	1.5	2.9
19020	91	2.1	1.7
19022	100	1.7	2.4
19025	94	2.1	1.8
19027	96	1.7	2.2
19028	95	1.9	2.1
19030	95	1.8	2.5
19031	89	1.9	2.3
19032	--	--	--
19033	--	--	--
19049	--	--	--
19059	--	--	--
19070	--	--	--
MEAN	94	1.8	2.3
SD	3.1	0.21	0.37
N	10	10	10

(--) - Data Unavailable

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: MALE
STUDY NO: 060-069

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	TP	ALB	GLU	CHOL	T-BIL	BUN	CREAT	CK	ALT
UNITS:	g/dL	g/dL	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	U/L	U/L
Group: 1-M									
MEAN	6.3	4.3	145	57	0.2	16	0.3	288	42
SD	0.36	0.22	16.8	8.3	0.07	1.5	0.04	172.6	6.0
N	10	10	10	10	10	10	10	10	10
Group: 2-M									
MEAN	6.1	4.1	141	41**	0.1	16	0.3	246	63
SD	0.28	0.19	26.0	11.1	0.05	0.8	0.05	111.5	69.9
N	10	10	10	10	10	10	10	10	10
Group: 3-M									
MEAN	6.3	4.3	182	46	0.1	16	0.3	239	60
SD	0.33	0.15	58.2	11.6	0.06	1.8	0.06	112.9	34.4
N	10	10	10	10	10	10	10	10	10
Group: 4-M									
MEAN	6.2	4.2	162	43*	0.1	17	0.3	196	95
SD	0.28	0.17	25.2	13.1	0.05	1.6	0.03	53.5	124.1
N	10	10	10	10	10	10	10	10	10
Group: 5-M									
MEAN	6.3	4.5**	165	33**	0.2	21**	0.3	243	45
SD	0.28	0.20	33.7	7.2	0.06	2.4	0.05	117.4	7.0
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05 **-Significant Difference from Control P < .01

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: MALE
STUDY NO: 060-069

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	AST	ALP	CA	PHOS	TRIG	NA	K	CL	GLOB
UNITS:	U/L	U/L	mg/dL	mg/dL	mg/dL	mmol/L	mmol/L	mmol/L	g/dL
Group: 1-M									
MEAN	96	105	10.9	9.5	52	146	6.6	98	2.0
SD	22.4	14.3	0.48	1.40	21.8	1.4	2.10	2.7	0.19
N	10	10	10	10	10	10	10	10	10
Group: 2-M									
MEAN	121	111	10.7	9.4	47	146	6.1	99	2.0
SD	92.6	36.9	0.44	1.11	17.2	1.3	0.89	1.5	0.16
N	10	10	10	10	10	10	10	10	10
Group: 3-M									
MEAN	117	100	11.1	9.9	36	147	6.5	100	2.0
SD	40.9	12.4	0.44	2.09	13.8	1.6	1.27	2.3	0.24
N	10	10	10	10	10	10	10	10	10
Group: 4-M									
MEAN	198	115	11.1	9.7	36	147	6.0	100	2.0
SD	248.7	25.1	0.34	1.43	27.9	1.0	0.60	2.7	0.16
N	10	10	10	10	10	10	10	10	10
Group: 5-M									
MEAN	97	144**	11.5**	10.2	17**	146	6.9	100	1.8
SD	15.6	37.5	0.38	1.33	8.0	2.2	1.55	1.2	0.13
N	10	10	10	10	10	10	10	10	10

**-Significant Difference from Control P < .01

LABCAT CC4.43 27-JUN-2002

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	A/G
UNITS:	none
Group: 1-M	
MEAN	2.1
SD	0.18
N	10
Group: 2-M	
MEAN	2.1
SD	0.16
N	10
Group: 3-M	
MEAN	2.2
SD	0.26
N	10
Group: 4-M	
MEAN	2.2
SD	0.15
N	10
Group: 5-M	
MEAN	2.5**
SD	0.17
N	10

**-Significant Difference from Control P < .01

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Total Protein

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	62.8	6.3	0.36						TREATMENTS	4	0.44	0.11
2-M	10	60.6	6.1	0.28	1.60	5.9	6.6	5.9	6.7	ERROR	45	4.26	0.09
3-M	10	62.5	6.3	0.33	0.22	5.9	6.6	5.9	6.7				
4-M	10	61.8	6.2	0.28	0.73	5.9	6.6	5.9	6.7	TOTAL	49	4.70	
5-M	10	63.3	6.3	0.28	0.36	5.9	6.6	5.9	6.7				

F Ratio = 1.16 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 4.948 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Albumin

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	42.5	4.3	0.22						TREATMENTS	4	0.90	0.22
2-M	10	41.1	4.1	0.19	1.66	4.0	4.5	4.0	4.5	ERROR	45	1.59	0.04
3-M	10	42.7	4.3	0.15	0.24	4.0	4.5	4.0	4.5				
4-M	10	42.3	4.2	0.17	0.24	4.0	4.5	4.0	4.5	TOTAL	49	2.49	
5-M	10	45.2	4.5	0.20	3.21	4.0	4.5*	4.0	4.5**				

F Ratio = 6.35 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 4.399 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Glucose

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	1453	145	16.8						TREATMENTS	4	10942	2735
2-M	10	1411	141	26.0	0.27	106	185	96	194	ERROR	45	55071	1224
3-M	10	1823	182	58.2	2.37	106	185	96	194				
4-M	10	1619	162	25.2	1.06	106	185	96	194	TOTAL	49	66013	
5-M	10	1649	165	33.7	1.25	106	185	96	194				

F Ratio = 2.24 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 21.988 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Cholesterol

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-M	10	569	57	8.3					
2-M	10	413	41	11.1	3.32	45	69*	42	72**
3-M	10	459	46	11.6	2.34	45	69	42	72
4-M	10	427	43	13.1	3.03	45	69*	42	72
5-M	10	331	33	7.2	5.07	45	69*	42	72**

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	4	2978.08	744.52
ERROR	45	4954.90	110.11
TOTAL	49	7932.98	

F Ratio = 6.76 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 23.859 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Total Bilirubin

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-M	10	1.6	0.2	0.07					
2-M	10	1.4	0.1	0.05	0.76	0.1	0.2	0.1	0.2
3-M	10	1.2	0.1	0.06	1.53	0.1	0.2	0.1	0.2
4-M	10	1.3	0.1	0.05	1.15	0.1	0.2	0.1	0.2
5-M	10	1.9	0.2	0.06	1.15	0.1	0.2	0.1	0.2

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	4	0.031	0.008
ERROR	45	0.154	0.003
TOTAL	49	0.185	

F Ratio = 2.25 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 39.527 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Blood Urea Nitrogen

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-M	10	158	16	1.5					
2-M	10	162	16	0.8	0.53	14	18	13	18
3-M	10	162	16	1.8	0.53	14	18	13	18
4-M	10	174	17	1.6	2.11	14	18	13	18
5-M	10	207	21	2.4	6.46	14	18*	13	18**

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	4	162.32	40.58
ERROR	45	129.30	2.87
TOTAL	49	291.62	

F Ratio = 14.12 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 9.821 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069
SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Creatinine

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	3.2	0.3	0.04						TREATMENTS	4	0.0040	0.0010
2-M	10	3.3	0.3	0.05	0.48	0.3	0.4	0.3	0.4	ERROR	45	0.0960	0.0021
3-M	10	3.1	0.3	0.06	0.48	0.3	0.4	0.3	0.4				
4-M	10	3.1	0.3	0.03	0.48	0.3	0.4	0.3	0.4	TOTAL	49	0.1000	
5-M	10	3.3	0.3	0.05	0.48	0.3	0.4	0.3	0.4				

F Ratio = 0.47 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 14.434 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Creatine Kinase

1-M	10	2877	288	172.6						TREATMENTS	4	41956	10489
2-M	10	2462	246	111.5	0.78	153	422	121	455	ERROR	45	644538	14323
3-M	10	2388	239	112.9	0.91	153	422	121	455				
4-M	10	1964	196	53.5	1.71	153	422	121	455	TOTAL	49	686494	
5-M	10	2427	243	117.4	0.84	153	422	121	455				

F Ratio = 0.73 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 49.381 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Alanine Aminotransferase

1-M	10	420	42	6.0						TREATMENTS	4	18155	4539
2-M	10	631	63	69.9	0.72	-32	116	-50	134	ERROR	45	194111	4314
3-M	10	600	60	34.4	0.61	-32	116	-50	134				
4-M	10	954	95	124.1	1.82	-32	116	-50	134	TOTAL	49	212266	
5-M	10	447	45	7.0	0.09	-32	116	-50	134				

F Ratio = 1.05 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 107.598 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Error-within groups
Source-Source of Variation
Treatments-between groups

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: MALE
STUDY NO: 060-069

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Aspartate Aminotransferase

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	957	96	22.4						TREATMENTS	4	69637	17409
2-M	10	1213	121	92.6	0.47	-40	231	-73	264	ERROR	45	655378	14564
3-M	10	1171	117	40.9	0.40	-40	231	-73	264				
4-M	10	1976	198	248.7	1.89	-40	231	-73	264	TOTAL	49	725015	
5-M	10	974	97	15.6	0.03	-40	231	-73	264				

F Ratio = 1.20 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 95.916 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Alkaline Phosphatase

1-M	10	1050	105	14.3						TREATMENTS	4	11825	2956
2-M	10	1113	111	36.9	0.51	74	136	67	143	ERROR	45	33780	751
3-M	10	1001	100	12.4	0.40	74	136	67	143				
4-M	10	1152	115	25.1	0.83	74	136	67	143	TOTAL	49	45604	
5-M	10	1441	144	37.5	3.19	74	136*	67	143**				

F Ratio = 3.94 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 23.795 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Calcium

1-M	10	109.4	10.9	0.48						TREATMENTS	4	3.45	0.86
2-M	10	107.3	10.7	0.44	1.12	10.5	11.4	10.4	11.5	ERROR	45	7.97	0.18
3-M	10	110.7	11.1	0.44	0.69	10.5	11.4	10.4	11.5				
4-M	10	111.0	11.1	0.34	0.85	10.5	11.4	10.4	11.5	TOTAL	49	11.42	
5-M	10	115.3	11.5	0.38	3.14	10.5	11.4*	10.4	11.5**				

F Ratio = 4.87 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 3.800 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Phosphorus

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	94.7	9.5	1.40						TREATMENTS	4	4.80	1.20
2-M	10	93.7	9.4	1.11	0.15	7.8	11.2	7.4	11.6	ERROR	45	102.32	2.27
3-M	10	99.1	9.9	2.09	0.65	7.8	11.2	7.4	11.6				
4-M	10	97.1	9.7	1.43	0.36	7.8	11.2	7.4	11.6	TOTAL	49	107.12	
5-M	10	102.3	10.2	1.33	1.13	7.8	11.2	7.4	11.6				

F Ratio = 0.53 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 15.485 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Triglycerides

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	516	52	21.8						TREATMENTS	4	7188	1797
2-M	10	469	47	17.2	0.55	30	73	25	78	ERROR	45	16244	361
3-M	10	364	36	13.8	1.79	30	73	25	78				
4-M	10	361	36	27.9	1.82	30	73	25	78	TOTAL	49	23432	
5-M	10	168	17	8.0	4.10	30	73*	25	78**				

F Ratio = 4.98 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 50.584 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Sodium

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	1459	146	1.4						TREATMENTS	4	9.60	2.40
2-M	10	1457	146	1.3	0.29	144	148	144	148	ERROR	45	108.40	2.41
3-M	10	1465	147	1.6	0.86	144	148	144	148				
4-M	10	1469	147	1.0	1.44	144	148	144	148	TOTAL	49	118.00	
5-M	10	1460	146	2.2	0.14	144	148	144	148				

F Ratio = 1.00 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 1.062 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Potassium

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	65.7	6.6	2.10						TREATMENTS	4	5.56	1.39
2-M	10	61.0	6.1	0.89	0.76	5.0	8.1	4.6	8.5	ERROR	45	86.21	1.92
3-M	10	64.5	6.5	1.27	0.19	5.0	8.1	4.6	8.5				
4-M	10	59.7	6.0	0.60	0.97	5.0	8.1	4.6	8.5	TOTAL	49	91.77	
5-M	10	69.0	6.9	1.55	0.53	5.0	8.1	4.6	8.5				

F Ratio = 0.73 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 21.633 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Chloride

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	982	98	2.7						TREATMENTS	4	23.60	5.90
2-M	10	988	99	1.5	0.62	96	101	95	101	ERROR	45	212.90	4.73
3-M	10	997	100	2.3	1.54	96	101	95	101				
4-M	10	1000	100	2.7	1.85	96	101	95	101	TOTAL	49	236.50	
5-M	10	998	100	1.2	1.64	96	101	95	101				

F Ratio = 1.25 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 2.190 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Globulin

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-M	10	20.3	2.0	0.19						TREATMENTS	4	0.27	0.07
2-M	10	19.5	2.0	0.16	0.99	1.8	2.2	1.8	2.3	ERROR	45	1.46	0.03
3-M	10	19.8	2.0	0.24	0.62	1.8	2.2	1.8	2.3				
4-M	10	19.5	2.0	0.16	0.99	1.8	2.2	1.8	2.3	TOTAL	49	1.72	
5-M	10	18.1	1.8	0.13	2.73	1.8	2.2*	1.8	2.3				

F Ratio = 2.06 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 9.253 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

*-Significant Difference from Control P < .05
Error-within groups

Source-Source of Variation
Treatments-between groups

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Albumin/Globulin Ratio

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI	
1-M	10	21.2	2.1	0.18					
2-M	10	21.4	2.1	0.16	0.24	1.9	2.3	1.9	2.4
3-M	10	21.9	2.2	0.26	0.84	1.9	2.3	1.9	2.4
4-M	10	21.9	2.2	0.15	0.84	1.9	2.3	1.9	2.4
5-M	10	25.1	2.5	0.17	4.67	1.9	2.3*	1.9	2.4**

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	4	1.02	0.25
ERROR	45	1.57	0.03
TOTAL	49	2.59	

F Ratio = 7.31 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 8.368 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups

Source-Source of Variation
Treatments-between groups

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028 SEX: FEMALE
STUDY NO: 060-069

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	TP	ALB	GLU	CHOL	T-BIL	BUN	CREAT	CK	ALT
UNITS:	g/dL	g/dL	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	U/L	U/L
Group: 1-F									
MEAN	6.1	4.1	152	77	0.2	28	0.4	202	129
SD	0.52	0.42	19.8	27.8	0.07	4.4	0.05	54.1	31.7
N	10	10	10	10	10	10	10	10	10
Group: 2-F									
MEAN	5.5	4.0	162	72	0.2	24	0.4	250	133
SD	0.50	0.34	20.0	14.0	0.03	4.7	0.05	85.6	23.0
N	10	10	10	10	10	10	10	10	10
Group: 3-F									
MEAN	5.9	4.1	155	71	0.2	28	0.3	192	142
SD	0.41	0.24	18.7	20.0	0.05	6.7	0.05	21.7	34.2
N	10	10	10	10	10	10	10	10	10
Group: 4-F									
MEAN	5.8	4.0	146	62	0.1	25	0.4	213	127
SD	0.32	0.29	16.2	14.2	0.05	4.4	0.08	80.4	24.7
N	10	10	10	10	10	10	10	10	10
Group: 5-F									
MEAN	5.8	4.0	140	61	0.1	30	0.3	252	145
SD	0.29	0.31	35.5	19.8	0.05	15.4	0.06	101.6	20.0
N	10	10	10	10	10	10	10	10	10

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	AST	ALP	CA	PHOS	TRIG	NA	K	CL	GLOB
UNITS:	U/L	U/L	mg/dL	mg/dL	mg/dL	mmol/L	mmol/L	mmol/L	g/dL
Group: 1-F									
MEAN	142	145	10.6	8.8	54	143	5.8	96	1.9
SD	22.8	88.7	0.72	1.33	19.9	6.3	0.67	3.4	0.22
N	10	10	10	10	10	10	10	10	10
Group: 2-F									
MEAN	135	159	11.2	7.9	50	143	5.6	94	1.6**
SD	21.6	81.7	0.63	1.94	10.2	2.4	0.58	2.7	0.26
N	10	10	10	10	10	10	10	10	10
Group: 3-F									
MEAN	137	136	10.4	9.0	49	142	5.6	95	1.8
SD	11.8	107.3	0.87	2.80	29.4	2.5	0.32	3.8	0.21
N	10	10	10	10	10	10	10	10	10
Group: 4-F									
MEAN	124	178	10.4	8.7	45	142	6.1	95	1.7
SD	12.1	131.0	0.46	2.88	19.5	2.6	0.70	3.4	0.13
N	10	10	10	10	10	10	10	10	10
Group: 5-F									
MEAN	156	128	10.4	10.1	44	142	6.2	94	1.8
SD	40.7	44.7	0.82	1.64	18.3	2.6	0.90	3.1	0.21
N	10	10	10	10	10	10	10	10	10

**-Significant Difference from Control P < .01

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	A/G
UNITS:	none
Group: 1-F	
MEAN	2.2
SD	0.28
N	10
Group: 2-F	
MEAN	2.6*
SD	0.43
N	10
Group: 3-F	
MEAN	2.2
SD	0.21
N	10
Group: 4-F	
MEAN	2.4
SD	0.26
N	10
Group: 5-F	
MEAN	2.3
SD	0.37
N	10

*-Significant Difference from Control P < .05

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069
SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Total Protein

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	60.7	6.1	0.52						TREATMENTS	4	1.70	0.43
2-F	10	55.0	5.5	0.50	3.04	5.6	6.5*	5.5	6.7	ERROR	45	7.91	0.18
3-F	10	58.8	5.9	0.41	1.01	5.6	6.5	5.5	6.7				
4-F	10	57.7	5.8	0.32	1.60	5.6	6.5	5.5	6.7	TOTAL	49	9.62	
5-F	10	58.2	5.8	0.29	1.33	5.6	6.5	5.5	6.7				

F Ratio = 2.42 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 7.220 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Albumin

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	41.3	4.1	0.42						TREATMENTS	4	0.17	0.04
2-F	10	39.5	4.0	0.34	1.24	3.8	4.5	3.7	4.6	ERROR	45	4.78	0.11
3-F	10	40.6	4.1	0.24	0.48	3.8	4.5	3.7	4.6				
4-F	10	40.4	4.0	0.29	0.62	3.8	4.5	3.7	4.6	TOTAL	49	4.94	
5-F	10	40.3	4.0	0.31	0.69	3.8	4.5	3.7	4.6				

F Ratio = 0.39 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 8.059 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Glucose

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	1520	152	19.8						TREATMENTS	4	2750	687
2-F	10	1621	162	20.0	0.98	126	178	120	184	ERROR	45	24006	533
3-F	10	1548	155	18.7	0.27	126	178	120	184				
4-F	10	1461	146	16.2	0.57	126	178	120	184	TOTAL	49	26756	
5-F	10	1404	140	35.5	1.12	126	178	120	184				

F Ratio = 1.29 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 15.288 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

*-Significant Difference from Control P < .05
Error-within groups
Source-Source of Variation
Treatments-between groups

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Cholesterol

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	769	77	27.8						TREATMENTS	4	1862	465
2-F	10	723	72	14.0	0.52	55	99	49	105	ERROR	45	17702	393
3-F	10	705	71	20.0	0.72	55	99	49	105				
4-F	10	621	62	14.2	1.67	55	99	49	105	TOTAL	49	19564	
5-F	10	610	61	19.8	1.79	55	99	49	105				

F Ratio = 1.18 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 28.929 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Total Bilirubin

1-F	10	1.6	0.2	0.07						TREATMENTS	4	0.025	0.006
2-F	10	1.9	0.2	0.03	1.30	0.1	0.2	0.1	0.2	ERROR	45	0.120	0.003
3-F	10	1.5	0.2	0.05	0.43	0.1	0.2	0.1	0.2				
4-F	10	1.3	0.1	0.05	1.30	0.1	0.2	0.1	0.2	TOTAL	49	0.145	
5-F	10	1.3	0.1	0.05	1.30	0.1	0.2	0.1	0.2				

F Ratio = 2.33 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 33.974 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Blood Urea Nitrogen

1-F	10	281	28	4.4						TREATMENTS	4	218.92	54.73
2-F	10	241	24	4.7	1.08	19	37	17	40	ERROR	45	3099.90	68.89
3-F	10	281	28	6.7	0.00	19	37	17	40				
4-F	10	252	25	4.4	0.78	19	37	17	40	TOTAL	49	3318.82	
5-F	10	298	30	15.4	0.46	19	37	17	40				

F Ratio = 0.79 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 30.672 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Error-within groups
Source-Source of Variation

Treatments-between groups

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Creatinine

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-F	10	3.5	0.4	0.05					
2-F	10	3.5	0.4	0.05	0.00	0.3	0.4	0.3	0.4
3-F	10	3.4	0.3	0.05	0.37	0.3	0.4	0.3	0.4
4-F	10	3.6	0.4	0.08	0.37	0.3	0.4	0.3	0.4
5-F	10	3.1	0.3	0.06	1.47	0.3	0.4	0.3	0.4

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	4	0.015	0.004
ERROR	45	0.167	0.004
TOTAL	49	0.182	

F Ratio = 1.00 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 17.813 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Creatine Kinase

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-F	10	2017	202	54.1					
2-F	10	2495	250	85.6	1.44	118	285	98	305
3-F	10	1919	192	21.7	0.30	118	285	98	305
4-F	10	2129	213	80.4	0.34	118	285	98	305
5-F	10	2521	252	101.6	1.52	118	285	98	305

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	4	30624	7656
ERROR	45	247619	5503
TOTAL	49	278244	

F Ratio = 1.39 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 33.472 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Alanine Aminotransferase

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-F	10	1294	129	31.7					
2-F	10	1334	133	23.0	0.33	99	160	91	167
3-F	10	1424	142	34.2	1.07	99	160	91	167
4-F	10	1265	127	24.7	0.24	99	160	91	167
5-F	10	1447	145	20.0	1.26	99	160	91	167

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	4	2546	637
ERROR	45	33396	742
TOTAL	49	35942	

F Ratio = 0.86 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 20.138 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Error-within groups
Source-Source of Variation

Treatments-between groups

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Aspartate Aminotransferase

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	1423	142	22.8						TREATMENTS	4	5587	1397
2-F	10	1351	135	21.6	0.67	115	169	109	176	ERROR	45	26359	586
3-F	10	1368	137	11.8	0.51	115	169	109	176				
4-F	10	1240	124	12.1	1.69	115	169	109	176	TOTAL	49	31946	
5-F	10	1564	156	40.7	1.30	115	169	109	176				

F Ratio = 2.38 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 17.422 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Alkaline Phosphatase

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	1448	145	88.7						TREATMENTS	4	15762	3941
2-F	10	1586	159	81.7	0.32	38	252	12	277	ERROR	45	406995	9044
3-F	10	1363	136	107.3	0.20	38	252	12	277				
4-F	10	1784	178	131.0	0.79	38	252	12	277	TOTAL	49	422757	
5-F	10	1280	128	44.7	0.40	38	252	12	277				

F Ratio = 0.44 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 63.733 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Calcium

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI	Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	105.5	10.6	0.72						TREATMENTS	4	3.99	1.00
2-F	10	111.6	11.2	0.63	1.90	9.7	11.4	9.5	11.6	ERROR	45	23.11	0.51
3-F	10	104.3	10.4	0.87	0.37	9.7	11.4	9.5	11.6				
4-F	10	104.4	10.4	0.46	0.34	9.7	11.4	9.5	11.6	TOTAL	49	27.11	
5-F	10	104.3	10.4	0.82	0.37	9.7	11.4	9.5	11.6				

F Ratio = 1.94 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 6.760 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Error-within groups
Source-Source of Variation

Treatments-between groups

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Phosphorus

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-F	10	87.5	8.8	1.33					
2-F	10	79.3	7.9	1.94	0.83	6.3	11.2	5.7	11.8
3-F	10	90.0	9.0	2.80	0.25	6.3	11.2	5.7	11.8
4-F	10	87.0	8.7	2.88	0.05	6.3	11.2	5.7	11.8
5-F	10	101.0	10.1	1.64	1.37	6.3	11.2	5.7	11.8

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	4	24.53	6.13
ERROR	45	219.09	4.87
TOTAL	49	243.62	

F Ratio = 1.26 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 24.803 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Triglycerides

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-F	10	544	54	19.9					
2-F	10	495	50	10.2	0.54	32	77	26	83
3-F	10	490	49	29.4	0.59	32	77	26	83
4-F	10	453	45	19.5	1.00	32	77	26	83
5-F	10	437	44	18.3	1.17	32	77	26	83

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	4	693	173
ERROR	45	18711	416
TOTAL	49	19404	

F Ratio = 0.42 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 42.148 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Sodium

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-F	10	1434	143	6.3					
2-F	10	1427	143	2.4	0.43	139	147	138	148
3-F	10	1422	142	2.5	0.74	139	147	138	148
4-F	10	1424	142	2.6	0.62	139	147	138	148
5-F	10	1421	142	2.6	0.80	139	147	138	148

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	4	10.92	2.73
ERROR	45	587.40	13.05
TOTAL	49	598.32	

F Ratio = 0.21 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 2.534 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Error-within groups
Source-Source of Variation

Treatments-between groups

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069
SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Potassium

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%- HI		LO -99%- HI		Source	Degree Fdm	Sum of Squares	Mean Square
1-F	10	58.1	5.8	0.67						TREATMENTS	4	3.23	0.81
2-F	10	55.8	5.6	0.58	0.78	5.1	6.6	4.9	6.7	ERROR	45	19.67	0.44
3-F	10	55.5	5.6	0.32	0.88	5.1	6.6	4.9	6.7				
4-F	10	61.0	6.1	0.70	0.98	5.1	6.6	4.9	6.7	TOTAL	49	22.90	
5-F	10	61.6	6.2	0.90	1.18	5.1	6.6	4.9	6.7				

F Ratio = 1.84 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 11.322 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Chloride

1-F	10	956	96	3.4						TREATMENTS	4	29.08	7.27
2-F	10	941	94	2.7	1.01	92	99	91	100	ERROR	45	493.00	10.96
3-F	10	949	95	3.8	0.47	92	99	91	100				
4-F	10	954	95	3.4	0.14	92	99	91	100	TOTAL	49	522.08	
5-F	10	936	94	3.1	1.35	92	99	91	100				

F Ratio = 0.66 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 3.494 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

Globulin

1-F	10	19.4	1.9	0.22						TREATMENTS	4	0.82	0.20
2-F	10	15.5	1.6	0.26	4.12	1.7	2.2*	1.6	2.2**	ERROR	45	2.02	0.04
3-F	10	18.2	1.8	0.21	1.27	1.7	2.2	1.6	2.2				
4-F	10	17.3	1.7	0.13	2.22	1.7	2.2	1.6	2.2	TOTAL	49	2.83	
5-F	10	17.9	1.8	0.21	1.59	1.7	2.2	1.6	2.2				

F Ratio = 4.56 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 11.982 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

*-Significant Difference from Control P < .05
**-Significant Difference from Control P < .01
Error-within groups
Source-Source of Variation
Treatments-between groups

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: ARGUS 418-028
STUDY NO: 060-069

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Albumin/Globulin Ratio

Group	N	Total	Mean	Std. Dev.	DUNNETT'S 't'	DUNNETT'S RANGES LO -95%-	HI	LO -99%-	HI
1-F	10	21.7	2.2	0.28					
2-F	10	26.1	2.6	0.43	3.07	1.8	2.5*	1.7	2.6
3-F	10	22.3	2.2	0.21	0.42	1.8	2.5	1.7	2.6
4-F	10	23.7	2.4	0.26	1.39	1.8	2.5	1.7	2.6
5-F	10	23.0	2.3	0.37	0.91	1.8	2.5	1.7	2.6

Source	Degree Fdm	Sum of Squares	Mean Square
TREATMENTS	4	1.16	0.29
ERROR	45	4.63	0.10
TOTAL	49	5.80	

F Ratio = 2.83 'F' table values F.01 = 3.78 F.05 = 2.58
Coeff. Var. % = 13.734 Dunnett's 'T' table values P.01 = 3.12 P.05 = 2.51

*-Significant Difference from Control P < .05
Error-within groups

Source-Source of Variation
Treatments-between groups

APPENDIX L

STATEMENT OF THE STUDY DIRECTOR

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ARGUS RESEARCH
Charles River Laboratories
Discovery and Development Services

PROTOCOL 418-028: ORAL (GAVAGE) COMBINED REPEATED DOSE TOXICITY STUDY OF T-7706 WITH THE REPRODUCTION/ DEVELOPMENTAL TOXICITY SCREENING TEST

SPONSOR'S STUDY NUMBER: T-7706.1

STATEMENT OF THE STUDY DIRECTOR

This final report accurately reflects the raw data obtained during the performance of the study. No deviations from the U.S. Food and Drug Administration (FDA) Good Laboratory Practice Regulations; Final Rule[a], the Japanese Ministry of Health and Welfare (MHW) *Good Laboratory Practice Standard for Safety Studies on Drugs*[b], the Organisation for Economic Co-operation and Development (OECD). The Revised OECD Principles of Good Laboratory Practices[c] and the Organisation for Economic Co-operation and Development (OECD), The OECD Guideline for Testing of Chemicals[d] occurred that affected the quality or integrity of the study.

31 JUL 2003

Raymond G. York, Ph.D, DABT Date
Associate Director of Research
Study Director
Argus Research

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a. U.S. Food and Drug Administration. *Good Laboratory Practice Regulations; Final Rule.* 21 CFR Part 58.

b. Japanese Ministry of Health and Welfare (1997). *Good Laboratory Practice Standard for Safety Studies on Drugs,* MHW Ordinance No. 21, March 26, 1997.

c. Organisation for Economic Co-operation and Development (1998). *The Revised OECD Principles of Good Laboratory Practices* [C(97)186/Final].

d. Organisation for Economic Co-operation and Development (1996). *OECD Guideline for Testing of Chemicals.* Section 4, No. 422: Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test, adopted 22 March 1996.

APPENDIX M

QUALITY ASSURANCE STATEMENT

905 Sheehy Drive, Bldg. A
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Telefax: (215) 443-8587



ARGUS RESEARCH
Charles River Laboratories
Discovery and Development Services

QUALITY ASSURANCE STATEMENT

Argus Protocol: 418-028

Sponsor's Study Number: T-7706.1

Study Director: Raymond G. York, Ph.D., DABT

The protocol, critical phases, raw data and draft final report were inspected by the Quality Assurance Unit (QAU), to assure conformance with:

Organisation for Economic Co-operation and Development (1998). The Revised OECD Principles of Good Laboratory Practices [C(97)186/Final].

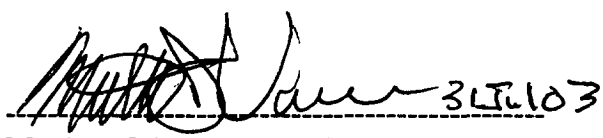
U.S. Food and Drug Administration. Good Laboratory Practice Regulations; Final Rule. 21 CFR Part 58.

Japanese Ministry of Health and Welfare (1997). *Good Laboratory Practice Standard for Safety Studies on Drugs*, MHW Ordinance Number 21, March 26, 1997.

The undersigned indicate that the report is an accurate representation of the raw data. Data provided by the Sponsor or a subcontractor were not audited by the Argus Research Quality Assurance Unit.

The QAU inspection and report audit dates are listed below:

Inspection Phase	Inspection Date(s)	Date(s) Findings Submitted to Study Director	Date(s) Findings Submitted to Management
Protocol	22 MAR 02	22 MAR 02	22 MAR 02
Test Substance Administration	04 APR 02	05 APR 02	05 APR 02
Test Substance Preparation	05 APR 02	06 APR 02	06 APR 02
Motor Activity	08 MAY 02	16 MAY 02	16 MAY 02
Blood Collection	09 MAY 02	10 MAY 02	10 MAY 02
Fetal Blood Collection	09 MAY 02	13 MAY 02	13 MAY 02
Fetal Liver Collection	09 MAY 02	13 MAY 02	13 MAY 02
Satellite Caesarean-Sectioning	09 MAY 02	13 MAY 02	13 MAY 02
Male Sacrifice	14 MAY 02	14 MAY 02	14 MAY 02
Male Blood Collection	14 MAY 02	14 MAY 02	14 MAY 02
Sperm Evaluation	14 MAY 02	14 MAY 02	14 MAY 02
Litter Observations	17 MAY 02	17 MAY 02	17 MAY 02
Functional Observational Battery	24 MAY 02	24 MAY 02	24 MAY 02
Blood Collection	30 MAY 02	04 JUN 02	04 JUN 02
Dam/Litter Sacrifice	30 MAY 02	04 JUN 02	04 JUN 02
In-Life Data	11-20 SEP 02	23 SEP 02	23 SEP 02
Necropsy Data	13-20 SEP 02	20 SEP 02	20 SEP 02
Formulation Data	17 SEP 02	17 SEP 02	17 SEP 02
Report Tables	16-23 SEP 02	23 SEP 02	23 SEP 02
	24 SEP 02	24 SEP 02	24 SEP 02
Report Text	19,22-23 SEP 02	23 SEP 02	23 SEP 02
	25 SEP 02	25 SEP 02	25 SEP 02
Revised Report	06 NOV 02	06 NOV 02	06 NOV 02



Matthew J. Vaneman, B.S. Date
Manager of Regulatory Compliance